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Dose-response relationship between mandibular advancement and OSA burden: Dissociated effects on supine and non-supine AHI

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ABSTRACT

Background and objective: A key unresolved mechanistic question in obstructive sleep apnea (OSA) therapy with mandibular advancement devices (MAD) is how incremental advancement affects position-specific disease burden.
This study aimed to evaluate the dynamic changes in apnea-hypopnea index (AHI) in different body positions in response to stepwise mandibular advancements, using the mandibular jaw movement (MJM)-based monitoring technology.
Methods: A prospective cohort study was conducted in OSA patients eligible for MAD therapy with a standardized titration protocol. Home sleep tests with MJM analysis were performed at baseline, and three successive advancement levels (initial, intermediate, and maximal). Regression analysis with adjustments for time-varying confounding factors was applied to estimate the adjusted changes in residual AHI in supine and non-supine positions.
Results: Ninety-six patients completed titration and follow-up. MAD titration did not significantly modify supine sleep time. Relative to baseline, early and significant improvements were observed for both supine and non-supine AHI at the initial advancement level (relative reduction of −60.1% [95% CI: −67.9; −52.2] and −55.0% [95% CI: −61.1; −48.9], respectively). Thereafter, AHI responses diverged: supine AHI continued a progressive reduction through to end of titration (mean cumulative change: −78.4% [95% CI: −82.7; −74.2]), whereas non-supine AHI showed little additional change beyond the initial improvement (mean cumulative change: −63.3% [95% CI: −68.2; −58.3]). Positional OSA prevalence was reduced from 38.5% at baseline to 18.3% at endpoint.
Conclusions: These findings underscore the value of continuous, home-based monitoring of position-specific residual AHI during MAD titration, and support integrating MJM analysis into MAD therapy workflows.

1. Introduction

Mandibular advancement devices (MADs) are currently recommended as an alternative treatment for patients with obstructive sleep apnea (OSA), with clinical effectiveness comparable to positive airway pressure (PAP) therapy [1,2]. However, unlike PAP, which provides a position-independent pneumatic splint of the upper airway (UA), the stabilizing effect of MADs may be inherently posture-dependent. During

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supine sleep, gravitational forces promote posterior displacement of UA structures, increasing the collapsing load on the pharynx [3]. Accordingly, maintaining UA patency in the supine posture may require a greater mandibular advancement, underscoring the importance of precisely characterizing position-specific residual AHI.

Indeed, studies focusing on positional obstructive sleep apnea (POSA) report an attenuated response in patients with baseline POSA [4], with residual apnea–hypopnea events predominantly occurring during supine sleep [5]. Persistent residual POSA has been observed in a substantial proportion of treated patients [6,7], and in some cases MAD therapy may even induce a shift toward a supine-dependent phenotype [5,6].

A central unresolved mechanistic question is how incremental mandibular advancement progressively modulates position-dependent OSA burden over time, and whether this dose-response trajectory differs between supine and non-supine AHI. Because most POSA-focused studies reduce this dynamic process to a simple pre-post comparison, dose-response dynamics and posture-specific AHI response patterns remain poorly characterized. A multi-level, repeated-measures titration framework is therefore needed to address this gap.

In addition, in-laboratory testing may significantly alter patients' habitual sleep posture, increasing supine exposure due to unfamiliar environment and extensive wiring [8,9]. By contrast, unobtrusive and simplified home sleep tests (HSTs) better preserve habitual sleeping conditions, thereby providing a more accurate representation of real-life positional vulnerability [10].

Recently, a novel mandibular jaw movement (MJM)-based monitoring approach has been clinically validated as a reliable and effective solution for home-based monitoring during MAD titration [11]. In a subsequent study, repeated at-home MJM assessments further enabled characterization of a dose-response relationship, with AHI improving as mandibular advancement levels increased [12]. Beyond its core function of capturing MJM for sleep staging and respiratory event detection [13], the MJM sensor's built-in accelerometer allows continuous real-time monitoring of sleep posture [14]. This enables posture-stratified quantification of sleep time and apnea-hypopnea burden (supine versus non-supine), making MJM-based analysis well suited for home-based monitoring of position-specific AHI reduction during MAD titration.

This study aims to determine the dynamic changes in position-specific residual AHI across stepwise mandibular advancements at home, using MJM-based monitoring.

2. Methods

2.1. Study design and participants

This prospective cohort study enrolled consecutive adults with a confirmed OSA diagnosis who were eligible for MAD therapy and consented to a longitudinal follow-up program with repeated home-based measurements at successive mandibular advancement levels. Participants were recruited at the sleep laboratory of CHU-UCL Hospital (Namur, Belgium) between January 2021 and December 2022. Detailed eligibility criteria are provided in the Supplementary Methods (Section 1), and the study workflow is summarized in Fig. 1.

2.2. OSA diagnosis

OSA diagnosis was confirmed using in-laboratory polysomnography (PSG) (Somnoscreen Plus, Somnomedics, Randersacker, Germany), scored by two trained technicians according to American Academy of Sleep Medicine (AASM) criteria, applying the recommended apnea and hypopnea definitions [15,16]. Final diagnosis and severity grading were determined following the International Classification of Sleep Disorders, 3rd edition (ICSD-3) [17].

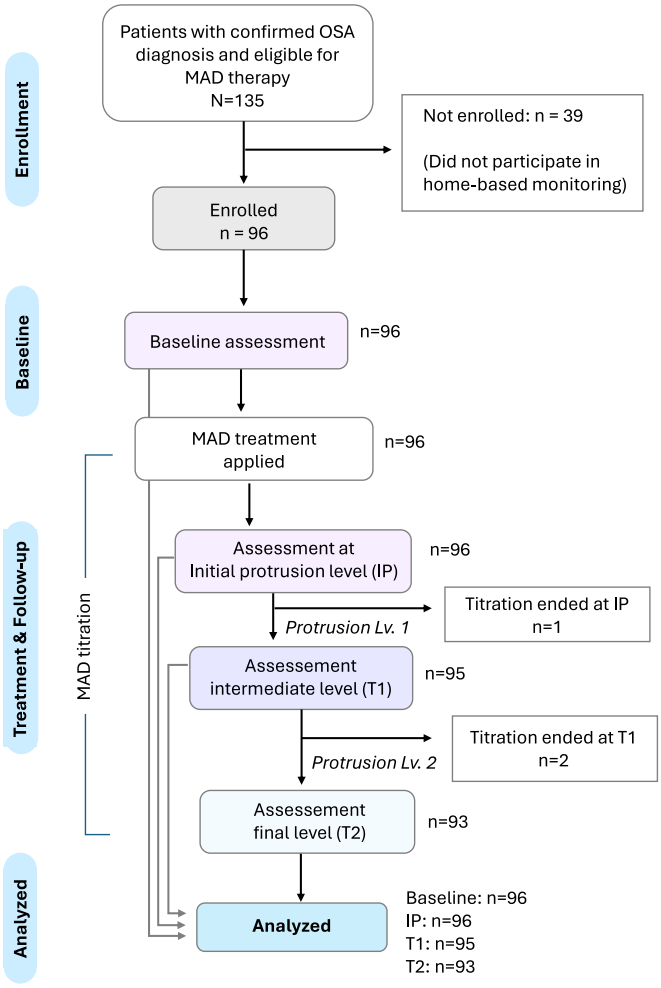

Fig. 1. Study flowchart.
Legend: MAD = mandibular advancement device; IP = initial protrusion level; T1 = intermediate level; T2 = final level; OSA = obstructive sleep apnea.

2.3. MAD titration protocol

MAD therapy was offered to patients with PSG-confirmed OSA, in accordance with the AASM joint guideline on MAD therapy [1]. Patients were excluded if they had significant cardiovascular or metabolic comorbidities, severe daytime sleepiness, safety-critical driving occupations, or compromised stomatognathic conditions (fewer than eight teeth per arch, temporomandibular disorder, or periodontitis).

Treatment was performed using a two-piece, custom-made, adjustable MAD (NOA; OrthoApnea, Málaga, Spain) (further details are provided in Section 2 of the Supplemental Methodology).

For each patient, the maximal protrusion range (MPR) was determined, as the distance (in millimeters) between the mandibular positions of maximal retrusion and voluntary maximal protrusion. At initiation, the device was uniformly set at 60% of the MPR for all patients. At each titration step, patients self-assessed their clinical status through telephone interviews and digital surveys, collecting information on sleep satisfaction, residual sleepiness, snoring (as reported by the bed partner), and adverse events. Under the supervision of a sleep-specialized dentist, the MAD was advanced in 1-mm or 2-mm increments at successive steps, based on persistence or worsening of OSA symptoms and patient tolerability.

During the titration and follow-up period, MAD therapy was the only OSA-directed intervention, with no additional medications or adjunctive treatments intended to modify OSA severity.

2.4. Multiple at-home assessments of treatment response

Over the 6-month study period, each patient underwent single-night, home-based sleep testing at four time points corresponding to incremental mandibular advancement levels (Fig. 1): 1) baseline, 2) initial advancement (60% of MPR), 3) intermediate advancement (+1 or +2 mm beyond the starting point), and 4) final advancement (an additional 1 mm beyond the intermediate level). This design enabled the evaluation of residual, position-dependent OSA burden at each therapeutic level. Assessments were performed only after patients had reached a stable condition, defined as maintaining the target advancement level for at least 10–15 days without discomfort. Importantly, test results were not disclosed to the treating physician and were not used to guide titration. Each evaluation was conducted at home under naturalistic sleep conditions using MJM-based monitoring (Sunrise, Namur, Belgium) to quantify position-specific clinical indices, including total sleep time (TST) proportions and residual AHI in supine and non-supine postures.

The operating mechanisms of MJM analysis are described in the Supplementary Methodology (Section 3). Briefly, MJM signals are captured using a lightweight, single-point sensor affixed to the patient's chin. The sensor's inertial measurement unit includes a gyroscope and an accelerometer, which respectively record the movement and position of the mandible across three axes. Using artificial intelligence, the system identifies specific MJM signal patterns associated with physiological or pathological events, such as sleep stages, arousals, and respiratory disturbances. Supine versus non-supine position is determined from the accelerometer signal (e-Fig. 1). Combining these outputs enables position-specific estimation of TST proportions and AHI.

2.5. Data analysis

The R programming language [18] was used to perform data analysis and visualization.

Sample size: The dataset was derived from a previously published prospective study [11]. An *ad-hoc* analysis was conducted to assess whether the sample size was adequate to detect a significant dose-response relationship between incremental mandibular advancement and supine AHI, in line with the primary objective. This procedure is detailed in Section 4.2 of the Supplemental Methodology.

Main analysis: Baseline characteristics and titration data, including incremental protrusion levels, self-reported symptoms and tolerability outcomes were summarized by using descriptive statistics. Categorial variables were presented as proportions and quantitative variables as medians with interquartile range (IQR). Primary outcomes were supine and non-supine sleep time proportions, as well as supine and non-supine AHI. Positional (supine-dependent) OSA was defined as supine AHI at least twice the non-supine AHI, per the commonly used Cartwright criterion (1984) [19]. A full list of position-dependent outcomes and their definitions is provided in Section 4.1 of the Supplemental Methodology.

Average treatment effects across the four advancement levels on position-dependent outcomes were estimated using generalized linear mixed model (GLMM) regression analysis with appropriate probability distributions according to the outcome variables (zero-adjusted Gamma for hourly indices, zero-inflated negative binomial for event counts, and beta distribution for sleep time proportions). The regression analysis also implemented a generalized inverse probability treatment weighting (IPTW) process [20–24] to adjust for the time-varying confounding (detailed in Section 4.3 of the Supplemental Methodology). As an exploratory post-hoc analysis, sex-specific conditional average marginal effects for the principal outcomes were estimated from regression models. These analyses were implemented using the gamlss [25] and marginaleffects [26] packages. Statistical inference was based on 95% confidence intervals (CIs) and two-sided Wald tests, with Benjamini-Hochberg adjustment for multiple comparisons and a significance threshold of $p < 0.005$.

3. Results

3.1. Study population characteristics

A total of 96 OSA patients were included in the final analysis (Fig. 1). Baseline demographic and clinical characteristics are detailed in Table 1. Participants were predominantly middle-aged adults with excess body weight and a male predominance. At diagnosis, OSA severity was heterogeneous, with most patients exhibiting moderate to severe disease. Subjective daytime sleepiness was frequently reported. Polysomnographic evaluation revealed a moderate to severe AHI (10th-90th percentile range: 18.6 to 34.6 events/h), accompanied by impaired sleep continuity and intermittent oxygen desaturation.

3.2. Baseline position-dependent OSA profile

Baseline assessments conducted under natural home-sleeping conditions showed relatively limited supine position exposure, accounting for a modest proportion of TST (5th–95th percentile: 6.8-37.9% of TST).

Despite a lower event density (median: 17.4 events/h), the non-supine position contributed more substantially to the overall apnea-hypopnea event burden (84 vs 35.5 events). Conversely, the supine position was associated with a higher event density (median: 20.3 events/h), resulting in a disproportionate contribution to the total event burden despite shorter exposure time.

A substantial subset of patients (38.5%) met Cartwright's criteria [19] for positional OSA, consistent with a mixed phenotype characterized by a clinically relevant positional component.

Table 1
Study population characteristics at baseline.

Parameters (unit/scale)	Median [IQR] or Frequency (%) (n = 96)
Age (year)	46.81 [39.75 – 52.65]
Male sex (n)	72 (75.0 %)
BMI (kg/m^2)	27.17 [25.37 – 29.05]
Neck circumference (cm)	40.00 [37.75 – 42.00]
Maximal protrusion range (mm)	13.0 [11.0 – 14.0]
ESS score (0–24)	10.0 [8.0 – 14.0]
Diagnostic PSG indices	
TST (hours)	7.07 [6.09 – 7.64]
SEff (% recording time)	68.41 [57.27 – 77.40]
AHI (n/h)	24.16 [18.61 – 34.62]
ArI (n/h)	27.62 [21.55 – 37.06]
ODI (n/h)	15.85 [6.79 – 27.48]
OSA severity	
Mild (AHI 5 to <15/h)	13 (13.54 %)
Moderate (AHI 15 to <30/h)	49 (51.04 %)
Severe (AHI ≥30/h)	34 (35.42%)
Position-specific indices *	
Supine sleep time proportion (%)	19.09 [6.81 – 37.90]
nAH supine (n)	33.5 [0.0 – 69.5]
nAH non-supine (n)	84.0 [44.0 – 125.75]
Supine AHI (n/h)	20.29 [0.00 – 36.66]
Non-supine AHI (n/h)	17.43 [9.81 – 23.94]
Supine AH proportion (%)	30.29 [0.00 – 58.62]
Supine/non-supine AHI ratio	1.47 [0.00 – 2.58]
POSA prevalence	37 (38.54 %)

Note: Numeric variables are presented as median [interquartile range]; categorical variables are presented as frequency (%). Abbreviations: AHI = apnea–hypopnea index; ArI = arousal index; BMI = body mass index; ESS = Epworth Sleepiness Scale; nAH = apnea/hypopnea event count; ODI = oxygen desaturation index; POSA = positional obstructive sleep apnea, defined as supine/non-supine AHI ratio ≥2; PSG = polysomnography; SEff = sleep efficiency; TST = total sleep time. *Position-specific indices were measured using mandibular jaw movement (MJM)-based analysis performed at home prior to MAD treatment. Supine and non-supine positions were determined by continuous tri-axial accelerometer monitoring.

3.3. Progression of mandibular advancement during titration

As summarized in e-Table 2, MAD titration followed a standardized stepwise protocol and demonstrated consistent tolerability. The MAD was applied to all patients at a uniform, conventional initial protrusion of 60% of MPR. At the intermediate step, mandibular advancement was increased to approximately 68% of MPR, with only one patient requiring treatment discontinuation. Thereafter, advancement was gradually and individually adjusted until subjective symptom resolution or attainment of a maximally comfortable position. At the final step, 93 patients achieved a median advancement of approximately 76% of MPR, corresponding to an absolute position of 9.8 mm. Across all titration levels, no clinically meaningful increase in adverse effects was observed. Patient-reported functional discomfort and oro-facial side effects remained low and stable throughout titration.

3.4. Supine sleep exposure across titration steps

Overall, MAD titration did not produce a clinically meaningful change in supine sleep exposure, defined as the proportion of TST spent in the supine position (e-Table 3, Table 2, e-Fig. 4). Relative to baseline, the initial protrusion was associated with a small reduction in supine sleep proportion (−4.3 %TST; 95% CI: −7.5 to −1.2). The proportion of supine sleep then returned toward baseline at the intermediate level (median: 18.1 %TST) and remained stable at the final level (median: 17.0 %TST), corresponding to a modest cumulative change from baseline (−3.3 %TST, 95% CI: −6.5 to −0.1). After adjustment for multiple comparisons, none of these pairwise contrasts for supine sleep proportion was statistically significant.

3.5. Dose-response pattern of residual position-specific AHI

Data visualization (Fig. 2) and model-based estimates (Table 2) revealed distinct trajectories of supine versus non-supine residual AHI across incremental mandibular advancement levels.

Relative to baseline, both supine and non-supine AHI improved early, substantially and to a similar extent at the initial protrusion (−60.1% [95% CI: −67.9 to −52.2] and −55.0% [95% CI: −61.1 to −48.9], respectively). Thereafter, responses diverged. Supine AHI showed additional reduction beyond the initial protrusion, with mean cumulative reductions of −72.5% at the intermediate level and −78.4% at the final level. In contrast, non-supine AHI showed attenuated additional improvement despite further advancement (−16.0% from initial to intermediate, and −2.9% from intermediate to final protrusion). Correspondingly, residual apnea-hypopnea event counts decreased in both postural conditions but remained predominantly non-supine throughout titration (e-Table 4, e-Fig. 5), indicating early and sustained suppression of supine-dependent events alongside a persisting non-supine residual burden.

Beyond the initial protrusion, the reduction in supine AHI exceeded the reduction observed in non-supine AHI. Accordingly, the supine-to-non-supine AHI ratio showed minimal change at the initial level (−0.1, corresponding to −3.6%) but decreased significantly from baseline at the intermediate and final titration levels (median ratios: 0.5 and

Table 2
Average treatment effects of MAD on position-specific apnea-hypopnea indices.

Outcomes	Contrast	Absolute change			Relative change (% of prior level)		
		Estimated	95% CI	p-value#	Estimated	95% CI	p-value#
Supine AHI *(n/h)*	IP – Base	−22.78	−28.46; −17.11	<0.0001	−60.06 %	−67.92; −52.21	<0.0001
	Intermediate – Base	−27.49	−32.86; −22.11	<0.0001	−72.47 %	−77.76; −67.17	<0.0001
	Final – Base	−29.75	−35.19; −24.31	<0.0001	−78.44 %	−82.68; −74.19	<0.0001
	Intermediate – IP	−4.70	−7.34; −2.07	0.0006	−31.06 %	−45.10; −17.01	<0.0001
	Final – IP	−6.97	−9.47; −4.47	<0.0001	−46.00 %	−57.04; −34.96	<0.0001
	Final – Intermediate	−2.26	−4.19; −0.34	0.0211 (NS)	−21.68 %	−37.61; −5.74	0.0077 (NS)
Non-supine AHI *(n/h)*	IP – Base	−10.99	−13.07; −8.91	<0.0001	−55.01 %	−61.11; −48.91	<0.0001
	Intermediate – Base	−12.43	−14.43; −10.42	<0.0001	−62.19 %	−67.22; −57.16	<0.0001
	Final – Base	−12.65	−14.66; −10.63	<0.0001	−63.29 %	−68.24; −58.34	<0.0001
	Intermediate – IP	−1.43	−2.57; −0.30	0.0162 (NS)	−15.96 %	−27.47; −4.45	0.0079 (NS)
	Final – IP	−1.65	−2.78; −0.53	0.006 (NS)	−18.40 %	−29.60; −7.20	0.0019
	Final – Intermediate	−0.22	−1.23; 0.80	0.6722 (NS)	−2.90 %	−16.14; 10.34	0.6675 (NS)
Supine AH proportion *(% of total AH events)*	IP – Base	−10.71	−16.60; −4.81	0.0007	−23.92 %	−35.63; −12.21	0.0001
	Intermediate – Base	−11.77	−17.48; −6.06	0.0002	−26.27 %	−37.37; −15.18	<0.0001
	Final – Base	−15.48	−21.27; −9.70	<0.0001	−34.43 %	−45.23; −23.64	<0.0001
	Intermediate – IP	−1.07	−6.92; 4.79	0.7209 (NS)	−3.12 %	−19.96; 13.71	0.716
	Final – IP	−4.78	−10.70; 1.14	0.114	−13.92 %	−29.93; 2.10	0.088
	Final – Intermediate	−3.71	−9.44; 2.02	0.204	−11.15 %	−27.44; 5.14	0.180
Supine/non-supine AHI ratio	IP – Base	−0.09	−0.66; 0.47	0.7466 (NS)	−3.55 %	−24.72; 17.63	0.7426 (NS)
	Intermediate – Base	−0.89	−1.36; −0.42	0.0005	−34.06 %	−48.12; −20.00	<0.0001
	Final – Base	−0.99	−1.45; −0.52	0.0002	−37.63 %	−51.15; −24.11	<0.0001
	Intermediate – IP	−0.80	−1.29; −0.30	0.0016	−31.64 %	−47.13; −16.15	<0.0001
	Final – IP	−0.89	−1.38; −0.40	0.0004	−35.33 %	−50.15; −20.51	<0.0001
	Final – Intermediate	−0.09	−0.47; 0.28	0.6256 (NS)	−5.40 %	−26.52; 15.71	0.7391 (NS)
Supine sleep time proportion (%TST)	IP – Base	−4.34	−7.54; −1.15	0.0466 (NS)	−19.87 %	−33.04; −6.70	0.0187 (NS)
	Intermediate – Base	−1.30	−4.53; 1.93	0.5164 (NS)	−6.02 %	−20.52; 8.48	0.4992 (NS)
	Final – Base	−3.32	−6.52; −0.13	0.1249 (NS)	−15.26 %	−28.80; −1.71	0.0818 (NS)
	Intermediate – IP	3.04	−0.17; 6.26	0.1267 (NS)	17.39 %	−2.61; 37.40	0.1767 (NS)
	Final – IP	1.02	−2.16; 4.20	0.5283 (NS)	5.79 %	−12.75; 24.33	0.5404 (NS)
	Final – Intermediate	−2.02	−5.23; 1.19	0.3259 (NS)	−9.85 %	−24.69; 5.00	0.2905 (NS)

Note: The table reports the average absolute and relative changes in five targeted outcomes at a given MAD protrusion level compared with a preceding level during titration (IP = initial protrusion level). Estimates were obtained from regression models using the appropriate probability distributions law for each outcome (zero-adjusted gamma for supine/non-supine AHI and the positional AHI ratio; beta distribution for the proportion of supine AHI and supine sleep time proportion). For each pair of comparison, results are presented as average marginal effects with 95% confidence intervals. All models incorporated inverse probability weighting (IPW) to adjust for the effects of age, sex, BMI, MPR, and the time-varying confounding attributable to residual ESS, snoring, and adverse effects at each MAD protrusion level.
#: p values were derived from two-sided Wald tests assessing the null hypothesis of no change, with Benjamini–Hochberg adjustment for multiple comparisons and a significance threshold of 0.005.
Abbreviations: AH = apneas and hypopneas; AHI = apnea–hypopnea index; TST = total sleep time; NS = not significant.

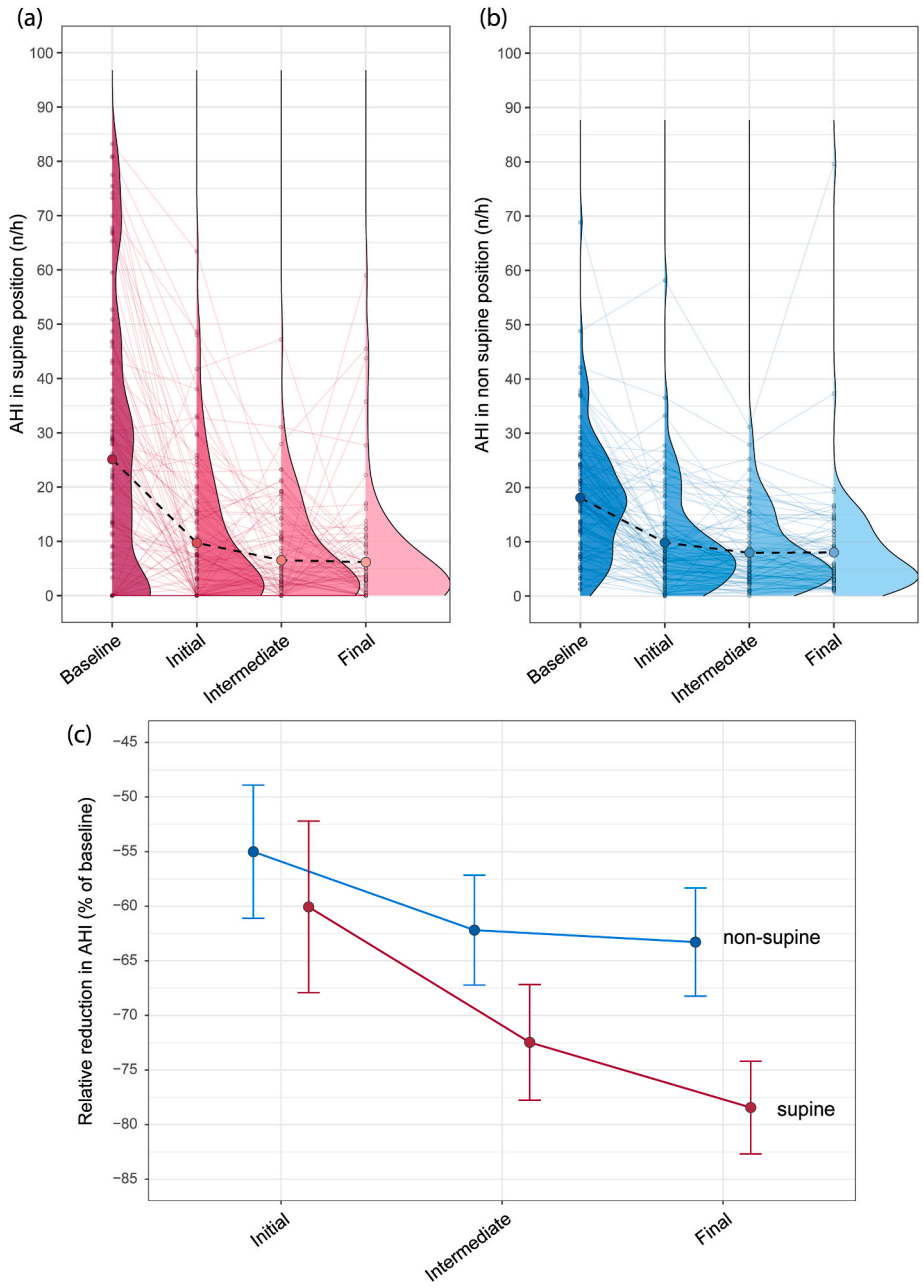

Fig. 2. Changes in position-specific apnea-hypopnea indices during MAD titration.
Legend: Upper panel: Two plots illustrate the changes in the distribution of supine AHI (a) and non-supine AHI (b) on the y-axis across four incremental levels of MAD protrusion on the x-axis. Each plot includes two layers: a background layer showing kernel density curves for the distribution of the outcome at each time point, and a foreground layer showing individual trajectories as connected points, with each dot representing an individual value. Larger dots indicate the median value at each time point, and the dashed line connecting them represents the population-level trend. Lower panel: Divergence between the supine and non-supine trajectories of dose-dependent AHI reduction relative to baseline. Supine is shown in red (lower curve) and non-supine in blue (upper curve). The x-axis indicates the three mandibular advancement levels; the y-axis shows the cumulative reduction for each outcome (as % of baseline). Circles and error bars indicate the mean effect and its 95% confidence interval, respectively.

0.6; mean changes: −34.1% and −37.6%, respectively), with median values remaining below 1 (Fig. 3). This divergence in response patterns was reflected in the response-rate curves across prespecified relative-change thresholds (Fig. 4).

In an exploratory post-hoc analysis, we examined whether MAD titration effects on principal outcomes differed between female and male patients. Sex-specific conditioned average marginal effects were estimated from regression models incorporating a sex-by-MAD level interaction. Overall, the direction and magnitude of absolute changes in supine and non-supine AHI were similar in male and female patients, indicating no meaningful heterogeneity by sex (e-Table 5).

4. Discussion

In this real-life OSA cohort studied under naturalistic home-sleep conditions, the main findings indicate that MAD therapy produced early and substantial improvements in AHI in both supine and non-supine positions. However, as titration progressed, a posture-specific, dose-dependent divergence emerged: supine AHI showed additional reduction beyond the initial protrusion, whereas the non-supine

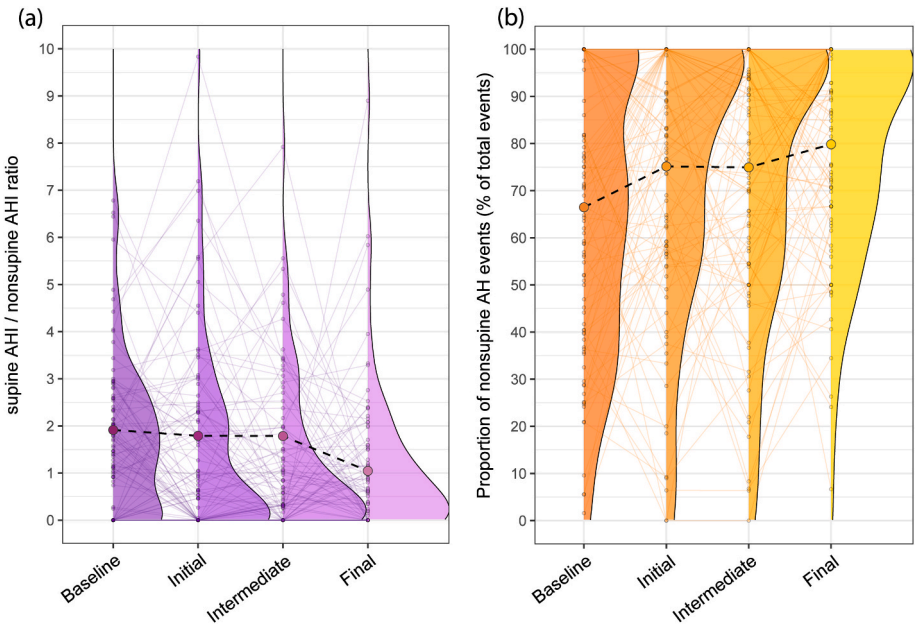

Fig. 3. Changes in supine versus non-supine AHI ratio and proportion of non-supine residual apnea-hypopnea events.
Legend: The figure illustrates changes in the distribution of: (a) the ratio of supine AHI/non supine AHI, and (b): the proportion of residual apnea and hypopnea events in non-supine position, across four time points during the MAD titration process (x-axis), with the same graphical structure as in Fig. 2.

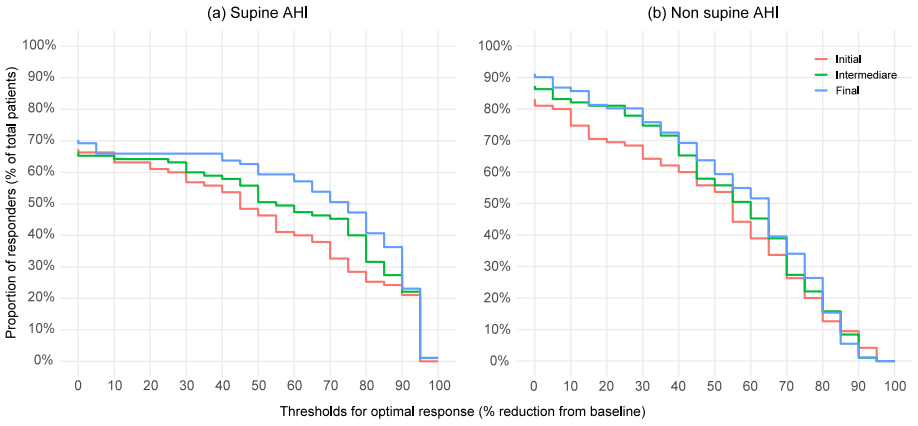

Fig. 4. Response rate across different relative change thresholds.
Legend: The curves show the proportion of patients (y-axis) meeting the response criterion at each prespecified relative-change threshold (x-axis) at 3 protrusion levels, for supine AHI (left) and non-supine AHI (right). For each threshold, responders were defined as patients with a relative change from baseline greater than the threshold.

response attenuated after the initial protrusion and showed little additional change thereafter. Notably, these effects were independent of changes in supine sleep time.

Prior experimental data have suggested a dose-dependent effect of mandibular advancement on UA collapsibility in OSA [27,28], and a clinical dose-response relationship has recently been reported for overall AHI [12]. However, to our knowledge, this study is the first to clinically characterize the dose-dependent patterns of MAD therapy on position-specific OSA, while clearly separating the observed improvements in residual respiratory event rate from random fluctuations in supine sleep time driven by postural behavior.

A key strength of this study is the implementation of a standardized MAD titration protocol with a uniform initial protrusion (60%), predefined, and clinically driven adjustment criteria, and multiple assessment points scheduled at relatively consistent intervals across participants. Clinical relevance is further enhanced by home-based measurements under natural sleep conditions, enabled by a compact sensor with AI-supported analysis, thereby minimizing measurement bias related to laboratory testing and observer-dependent scoring variability.

Beyond capturing detailed response trajectories across incremental MAD levels, our multiple-measurement approach mitigates major limitations of simple pre–post designs in prior MAD studies, including susceptibility to regression to the mean, night-to-night postural variability, and titration-related time-varying confounding. Our longitudinal framework also supports a more refined mechanistic interpretation of MAD-position interactions and posture-dependent UA collapsibility, yielding clinically actionable patterns rather than simple pre-post contrast.

This study has several limitations that should be acknowledged when interpreting the causal inference and clinical generalizability of the findings. First, the lack of a control or sham comparator may limit definitive causal attribution of the observed improvements to MAD alone, as regression to the mean, natural history, expectancy effects, and

other contextual influences cannot be fully excluded despite the repeated-measures design and IPTW adjustment. Second, body weight and neck circumference were not reassessed during follow-up. Although major anthropometric changes were considered unlikely over the relatively short titration period in the absence of adjunctive weight-loss interventions, the lack of repeated measurements may have limited our ability to account for these factors as potential time-varying confounders.

Additionally, because our findings were derived using a specific MAD design, they may not fully generalize to other appliances with different mechanical characteristics. Second, each MAD level was assessed only once, which may reduce the ability to separate true treatment effects from inter-night variability and to assess response stability at a given protrusion level.

Our cohort is comparable to previous oral appliance studies [5,6,29,30] in terms of demographic profile: a typical middle-aged, male-predominant population with moderate OSA. By intentionally including a mixed sample with both POSA and non-POSA phenotypes, the POSA prevalence in our study (38.5%) is lower than in POSA-enriched cohorts [5,6] (between 27 and 67.5%, depending on the definition applied). However, this approach is essential to achieve a balanced estimate of MAD effects across both supine and non-supine conditions, reducing the risk of overestimating supine-driven benefit in enriched POSA samples, and enhancing the external validity and clinical relevance of our findings for routine oral appliance prescribing in general OSA populations. We adopted the Cartwright definition [19] as it is the most widely used definition of POSA in clinical research and aligns best with our longitudinal design, which focuses primarily on respiratory event rates.

Our initial protrusion of 60% of MPR is consistent with prior POSA-specific protocols [30,31], and the intermediate advancement closely matches the 68% effective target reported using a remotely controlled mandibular titration approach, supporting its clinical relevance [32]. The therapeutic position achieved in our protocol is also comparable to the 75% maximal protrusion level reported in long-term comparative trials [30,33], which preserves efficacy while reducing adverse effects.

Our findings show early and significant responses in both supine and non-supine AHI at the starting point, which is consistent with prior observations of overall AHI [34]. However, early treatment response is not routinely reported in most previous studies [6,29,31], precluding direct cross-study comparison.

At the endpoint, the absolute reduction in supine AHI observed in our cohort falls within the range across four similar studies [5,6,29,31] (−20 to −36 events/h); however, cumulative outcomes may be influenced by heterogeneities in baseline severity and titration protocols. Our observed relative effect on supine AHI (−78%) closely matches the post-treatment outcomes reported by Lee et al. (2012) [29] and Fransson et al. (2022) [5], but appears more favorable than the relative effects described by Dieltjens et al. (2014) [6] and Chung et al. (2010) [31]. Notably, because our cohort included a mixture of positional and non-positional phenotypes, we observed substantial improvements in both supine and non-supine AHI, differing from POSA-enriched cohorts where non-supine AHI often shows only modest relative reductions (32-49%), likely constrained by a floor-effect due to already low baseline non-supine AHI. The residual prevalence of POSA in our cohort declined to 18.3%, closely matching the residual POSA rates reported by Dieltjens et al. (2014) [6]. Taken together, these data suggest that MAD is effective for both supine and non-supine AHI; however, each appears to require a different degree of protrusion and has its own response limit.

Preferential and dose-responsive reductions in supine AHI with incremental mandibular advancement may be explained by posture-dependent UA mechanics. In the supine position, gravitational posterior tissue loading and reduced lung volume shift the pharynx toward a more collapsible operating point, increasing obstruction risk [3]. MAD counteracts this vulnerability by anteriorly displacing the mandible and tongue-hyoid complex, enlarging and stiffening the pharyngeal lumen, and lowering collapsibility [27,35]. Beyond structural effects, protrusion likely modifies the interaction between ventilatory control and airway mechanics, with dose-dependent reductions in collapsibility threshold and UA cross-sectional area [27,36]. By improving mechanical stability, MAD also reduces the need for compensatory dilator recruitment [37]. Within this framework, respiratory-phasic MJM can be interpreted as a respiratory drive-dependent marker of neuromuscular compensation, reflecting reflex UA dilator activation in response to increased airway load [38]. As effective titration reduces collapsing pressure, particularly in the supine posture where gravitational load is greatest, the compensatory drive and associated MJMs decline accordingly.

In contrast, the baseline collapsing load is lower in non-supine posture; once the anatomical component is mitigated, residual events are more influenced by non-anatomical traits (loop gain, arousal threshold, and limited dilator responsiveness) that MAD does not robustly modify [35,39–41], explaining the limited additional benefit on non-supine AHI.

From a clinical perspective, these findings suggest that the effectiveness of MAD therapy should be assessed under naturalistic sleep conditions at home, with explicit attention to position-dependent OSA burden. In this context, integrating MJM-based home monitoring into the therapy workflow offers a practical way to achieve repeatable, posture-stratified evaluation of residual AHI across multiple nights. This continuous feedback may support earlier phenotype confirmation, improved characterization of individual response patterns, and more adaptive clinical decision-making aligned with the dose-response trajectories observed during titration. In the absence of validated minimal clinically important difference (MCID) thresholds for positional AHI outcomes, a response pattern-centered approach may provide a more flexible framework for interpreting individual responses during MAD titration. For example, progressive improvement in AHI may support continued advancement until a comfort-limited position or a treatment target is reached. Conversely, little additional improvement may suggest that the therapeutic position has been reached; if the overall response remains suboptimal, it points toward the need for adjunctive strategies such as positional therapy, weight management, or nasal optimization. The distinct response patterns observed for supine and non-supine AHI also suggest that combining MAD with positional therapy could reduce the degree of protrusion required to achieve AHI normalization, supporting a more individualized treatment approach. An unstable response trajectory may suggest the influence of inter-night variability, adherence issues or behavioral factors. Finally, the absence of response or a declining efficacy trajectory may warrant deeper investigation into mechanisms of treatment failure or consideration of alternative treatments. Beyond respiratory indices, optimization of MAD therapy may also benefit coexisting sleep bruxism, as MAD treatment has been reported to reduce the frequency of sleep bruxism episodes in such patients [42].

This study also provides a foundation for future research to develop and refine MJM-guided titration strategies by determining key implementation parameters, including the monitoring window, the required number of nights, actionable thresholds, and response pattern-driven decision rules.

5. Conclusion

In conclusion, this study provides clinical evidence for a dose-response relationship between mandibular advancement and positional OSA, further clarifying the dynamic interplay between incremental mandibular advancement and posture-dependent UA collapsibility. This interaction is reflected by divergent response trajectories between supine and non-supine AHI across advancement levels. These findings underscore the value of continuous home-based monitoring of position-specific AHI under naturalistic sleep conditions during MAD titration and support the integration of MJM-based

monitoring into the conventional MAD therapy workflow. Such an approach is expected to shorten the time to optimal therapeutic mandibular position, enable earlier identification of treatment success or failure, and optimize MAD titration efficiency, ultimately contributing to better patient clinical outcomes.

CRediT authorship contribution statement

Jean-Benoît Martinot: Writing – review & editing, Writing – original draft, Validation, Investigation, Data curation, Conceptualization. **Nhat-Nam Le-Dong:** Writing – original draft, Validation, Methodology, Formal analysis, Conceptualization. **Chloé Cantero:** Writing – original draft, Validation. **Didier Clause:** Writing – review & editing, Investigation, Data curation. **Fernanda R. de Almeida:** Writing – original draft, Validation, Methodology, Formal analysis. **Peter A. Cistulli:** Writing – review & editing, Validation, Methodology, Conceptualization. **Jean-Louis Pépin:** Writing – review & editing, Validation, Methodology, Conceptualization.

Ethics

The study was approved by the Comité d'Ethique Hospitalo-Facultaire-Universitaire de Liège (IRB #00004890), and all participants provided written informed consent.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: JBM is a scientific advisor to Sunrise and has been an investigator in pharmaceutical trials for Jazz Pharmaceuticals and Takeda.

NNLD is an employee of Sunrise.

CC has no financial disclosure.

DC has no financial disclosure.

FRA has no financial disclosure.

PAC 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, Nox Medical, and MyCardio. He is a consultant/adviser to ResMed, SomnoMed, Sunrise, and Eli Lilly.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2026.108996.

Data availability

Data is not publicly available. However, de-identified data may be obtained from the corresponding author upon reasonable request, subject to a data-sharing agreement and approval by the relevant ethics committee.

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