Treatment choice in mild to moderate sleep apnoea in the European Sleep Apnea Database

Benedikt Fridriksson[1,2], Jan Hedner[1,2], Ding Zou[2], Johan Verbraecken[3], Sophia Schiza[4], Ozen K. Basoglu[5], Dries Testelmans[6], Pavol Joppa[7], Zoran Dogas[8], Stefan Mihaicuta[9], Tarja Saaresranta[10], Ondrej Ludka[11], Marta Drummond[12], Sebastien Bailly[10], Ludger Grote[1,2] and the ESADA study group[1]

[1]Sleep Disorders Centre, Respiratory Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden. [2]Centre for Sleep and Wake Disorders, Institute of Medicine, Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden. [3]Department of Pulmonary Medicine and Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium. [4]Sleep Disorders Unit, Department of Respiratory Medicine, School of Medicine, University of Crete, Heraklion, Greece. [5]Department of Respiratory Medicine, Ege University Faculty of Medicine, Izmir, Türkiye. [6]Department of Respiratory Diseases, University Hospitals Leuven, Leuven, Belgium. [7]Department of Respiratory Medicine and Tuberculosis, Faculty of Medicine, P.J. Safarik University and L. Pasteur University Hospital, Kosice, Slovakia. [8]Department of Neuroscience and Sleep Medicine Center, University of Split School of Medicine, Split Croatia. [9]Center for Research and Innovation in Precision Medicine of Respiratory Diseases, Department of Pulmonology, Timisoara, Romania. [10]Division of Medicine, Department of Pulmonary Diseases, Turku University Hospital, University of Turku, Turku, Finland. [11]Department of Internal Medicine, Geriatrics and Practical Medicine, University Hospital Brno, Faculty of Medicine, Masaryk University, Brno, Czech Republic. [12]Sleep and Non-Invasive Ventilation Unit, Hospital São João, Medicine Faculty of Porto University, Porto, Portugal. [13]Grenoble Alpes University, Inserm, U1300, Grenoble Alpes Hospital, Grenoble, France.

Corresponding author: Benedikt Fridriksson (benedikt.fridriksson@gu.se)

Shareable abstract (@ERSpublications)
There are large differences in mandibular advancement device (MAD) use for mild to moderate sleep apnoea within Europe, in part due to discrepancies in accessibility and reimbursement. MADs seem to be an underused treatment option compared to PAP. https://bit.ly/3TcFCfW

Cite this article as: Fridriksson B, Hedner J, Zou D, *et al*. Treatment choice in mild to moderate sleep apnoea in the European Sleep Apnea Database. *ERJ Open Res* 2025; 11: 00360-2025 [DOI: 10.1183/23120541.00360-2025].

Received: 17 March 2025
Accepted: 28 May 2025

Abstract

Introduction In mild to moderate obstructive sleep apnoea (OSA), positive airway pressure (PAP) and mandibular advancement devices (MADs) are recommended treatments according to guidelines. This cross-sectional study aimed to determine the clinical and organisational predictors for treatment recommendations in mild to moderate OSA.

Methods In the European Sleep Apnea Database, factors predicting the choice of MAD or PAP treatment were determined in patients with newly diagnosed mild to moderate OSA. Accessibility and reimbursement of MADs study sites was obtained *via* questionnaire. The regression model included anthropometrics, Epworth Sleepiness Scale score, OSA severity, MAD accessibility and reimbursement, and a comorbidity index variable.

Results 6618 (65.5%) patients received PAP and 3491 (34.5%) were recommended MADs. MAD recommendations varied between centres (0% to 76%). Significant factors favouring MADs include mild *versus* moderate OSA (odds ratio 6.0, 95% CI 5.3–6.8), negligible *versus* moderate intermittent hypoxia (OR 2.0, 95% CI 1.7–2.4), no *versus* excess daytime sleepiness (OR 2.6, 95% CI 2.1–3.1), a comorbidity index score of 0 compared to 3 or more (OR 3.8, 95% CI 3.1–4.6) and no insomnia diagnosis *versus* diagnosed insomnia (OR 2.0, 95% CI 1.7–2.4). MAD accessibility and reimbursement predicted MAD treatment recommendations (OR 2.3, 95% CI 1.8–2.9 and OR 1.5, 95% CI 1.4–1.7, respectively).

Conclusion In mild to moderate OSA, MADs are less frequently recommended than PAP, particularly amongst patients with a higher disease burden. MADs were more frequently used when they were more accessible and reimbursed. Thus, MADs are likely an underused treatment in mild to moderate OSA.

Introduction

Obstructive sleep apnoea (OSA) is a disorder characterised by episodes of upper airway collapse and intermittent hypoxia during sleep, resulting in excessive daytime sleepiness (EDS), fatigue, cognitive

impairment and increased risk for cardiovascular and metabolic disease [1–4]. The main treatment option for OSA is positive airway pressure (PAP), which can eliminate apnoeas and hypopnoeas completely [5, 6], reduce EDS [7], the risk for traffic- and work-related accidents, and mitigate hypertension [8]. However, adherence to PAP can be challenging [9, 10]. PAP adherence has been found to be lower in mild compared to severe OSA [11].

Compared to severe OSA, where PAP is standard, management can be less straightforward in milder cases. Since OSA is a heterogenous condition, there is a need for personalised treatment options [12–16]. One such alternative is a mandibular advancement device (MAD) [17]. MADs are less potent than PAP in reducing respiratory events, but adherence is better with MADs compared to PAP in nonsevere OSA [18]. The effect of these treatments is regarded as comparable [19] in that context and MADs are considered a valid treatment option in mild to moderate sleep apnoea [15, 20].

Some European data is available on the prevalence of each treatment option. In a French cohort of OSA patients recruited between 2007 and 2014, 351 (12.4%) were treated with MADs and 2471 (87.6%) with PAP. It was concluded that MADs could be prescribed more often than they were [21]. Another French study based on reimbursement data reported an incidence of 4.2 per 1000 for PAP and 0.3 per 1000 for MADs in 2017. The same study reported that rates for PAP and MAD prescriptions increased 1.9-fold and 7.6-fold, respectively, between 2008 and 2018 [22]. The Swedish Sleep Apnea Registry reported that that 65% of treatment-naïve OSA patients were treated with PAP while 25% of patients were treated with MADs [23].

Due to the difficulties with PAP adherence among OSA patients, it is essential for the sleep medicine field to gain further insights into the current implementation and potential barriers to the utilisation of more recent alternative treatments such as MADs. Treatment traditions, clinical infrastructure and reimbursement policies for non-PAP treatments such as MADs vary within Europe. How these factors interplay with MAD prescription has not been studied. Outlining the situation up until now is a necessary first step towards shaping policies that facilitate optimal OSA management. We conducted our study to determine the combined impact of clinical and system factors on first-line treatment recommendations for MADs *versus* PAP in mild to moderate OSA. Our hypothesis was that patient characteristics as well as healthcare system factors influence treatment recommendation for nonsevere OSA.

Methods

Study design and patients

Determinants for treatment recommendations (PAP or MAD) in treatment-naïve patients with mild to moderate OSA were analysed within the European Sleep Apnea Database (ESADA) [24]. ESADA is a prospective registry cohort of OSA patients referred for suspected OSA within a network of European sleep clinics. The detailed study methodology has been described elsewhere [24]. For the scoring of hypopneas and oxygen desaturations, a 4% desaturation cut-off was applied.

In short, adults referred for primary diagnosis of suspected OSA are eligible for participation. Data on anthropometrics, comorbidities, sleep-study findings, first-line treatment recommendations and comedication are captured in the registry. Standardised data input is defined in a study protocol and supervised by data management and joint scientific committees [24]. The analysis focused on data from the first diagnostic visit for treatment-naïve patients to participating sleep clinics (n=30 centres in 18 countries). These include pulmonary medicine, neurology or standalone units. The vast majority are university affiliated and all receive referrals ranging from primary to tertiary care. Furthermore, only patients with mild to moderate OSA and a first-line treatment recommendation including either PAP or MAD were included (figure 1). The analysis included data from 2007 to January 2022.

ESADA collaborator questionnaire data

The following questions were posed in the questionnaire for ESADA collaborators in 2022 to give one of the following answers best fitting to the situation at their clinic (response alternatives within quotation marks):

1) Question: Mandibular advancement devices are available in our healthcare area.
   Answers: “Yes, fully or partially available access to MAD treatment” or “No, not available at all or very difficult to find a competent dentist”.
2) Question: How are MADs reimbursed in your health care environment?
   Answers: “Yes, fully or partially reimbursed by insurance/tax system” or “No reimbursement, the patient has to pay”.

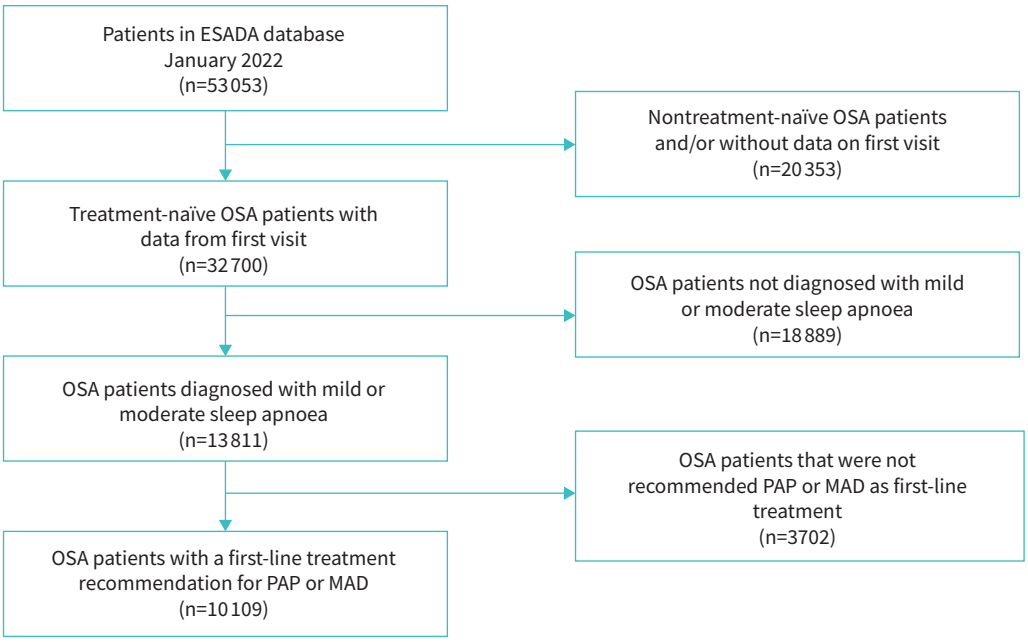

FIGURE 1 Patient inclusion flowchart. ESADA: European Sleep Apnea Database; MAD: mandibular advancement device; OSA: obstructive sleep apnoea; PAP: positive airway pressure.

3) Question: MAD is a frequent primary treatment recommendation in patients with mild OSA (apnoea hypopnea index (AHI) 5–15).
   Answers: "Yes" or "No".
4) Question: MAD is a frequent primary treatment recommendation in patients with moderate OSA (AHI 15–30).
   Answers: "Yes" or "No".
5) Question: It is the patient's preference which decides if CPAP or MAD will be prescribed in mild to moderate OSA if outcomes for both treatment modalities are considered comparable.
   Answers: "Yes" or "No".

Answers were obtained from 26 centres.

Ethical considerations

Local ethics committees at each study site approved the foundational protocol for the registry. Informed consent was obtained from all patients [24]. Approval from the Regional Ethical Committee was obtained before our study was conducted (DNR 386-09).

Statistics

Primary analysis

All statistical analyses were performed using IBM SPSS Statistics, USA, version 29.0. Descriptive statistics (mean±SD for continuous data, percentages for categorical data) were used to compare clinical data in patients recommended PAP or MADs (independent sample t-test and Chi-square test, respectively). In the primary analysis, a generalised linear regression model (GLM) was used to assess the various factors' impact on the likelihood of first-line treatment choice of PAP or MAD. Factors in the GLM included:

- age
- sex
- AHI at diagnosis classed as mild or moderate (defined by AHI of at least 5 events·h^{-1} but below 15 events·h^{-1} and AHI of at least 15 events·h^{-1} but below 30 events·h^{-1}, respectively)
- oxygen desaturation index (ODI) (4% cutoff) at diagnosis classed as negligible (<5 events·h^{-1}), mild (⩾5 events·h^{-1} and <15 events·h^{-1}) and moderate to severe (⩾15 events·h^{-1})
- body mass index (BMI) classed as nonoverweight (<25 kg·m^{-2}), overweight (25–<30 kg·m^{-2}), class I obesity (30–<35 kg·m^{-2}) and class II obesity or higher (⩾35 kg·m^{-2}),

- Epworth Sleepiness Scale (ESS) score classed as 0–6, 7–10, 11–15 and 16–24
- a comorbidity index including the following conditions: systemic hypertension, atrial fibrillation, ischaemic heart disease, congestive heart failure, cerebrovascular disease, hyperlipidaemia, diabetes mellitus type 1 or 2 and obstructive lung disease (classed as 0, 1, 2 or 3⩽ diagnoses)
- diagnosed insomnia (yes/no)
- MAD reimbursement at the study site (yes/no) and
- MAD accessibility at the study site (yes/no).

Before the model was constructed, it was confirmed that age did not significantly deviate from normal distribution in the dataset. Due to missing data on at least one of the abovementioned variables, 1469 cases were excluded from the primary analysis. Imputation was not used due to high numbers of participants with valid data, providing sufficient statistical power.

Secondary analyses

As sensitivity analysis, the GLM was run in the following subgroups: males, females, patients with mild OSA and patients with moderate OSA. In the subgroup analyses for mild and moderate OSA, AHI was used as a continuous variable to reflect OSA severity within a specific AHI range. In a second sensitivity analysis, our GLM was run separately for patient cases registered in the database before 2017 and for those registered in 2017 or later. That year was chosen as a cutoff as it most evenly splits the patient population in two.

Crosstabulations and Chi-square tests were used to compare the frequencies of MAD prescriptions, based on 1) MAD accessibility and/or reimbursement at each study site and 2) inclusion of patient preference in the choice between PAP and MAD treatment.

Finally, the frequency of combination therapy recommendation with active weight reduction interventions (referral for dietitian, obesity clinic, weight reduction surgery and/or medical treatment) was analysed in obese patients (BMI ⩾30 $kg \cdot m^{-2}$) prescribed PAP or MAD treatment.

Results

Clinical data in patients treated with PAP and MADs

Data from 10 109 patients with mild to moderate OSA recruited from 30 ESADA centres were analysed. The proportion of patients that received an MAD as first-line treatment at each ESADA site varied, ranging from 0 to 76% (figure 2). In total, 6618 (65.5%) patients were recommended PAP and 3491 (34.5%) MADs as first-line treatment. Corresponding numbers for mild OSA were 1838 (41.6%) for PAP *versus* 2579 (58.4%) for MADs and for moderate OSA 4780 (84%) for PAP *versus* 912 (16%) for MADs, both p<0.001. Patients prescribed PAP were marginally older (54.4±12.2 years *versus* 52.4±13.5 years), more obese (BMI 31.1±5.9 $kg \cdot m^{-2}$ *versus* 29.5 ±5.6 $kg \cdot m^{-2}$) and had slightly greater neck circumferences (40.8±3.9 cm *versus* 39.8±3.8 cm) compared with patients recommended MAD treatment (all p<0.001) (table 1). There were no significant differences in sex between patients recommended PAP and those receiving MADs (33.2% *versus* 34.0% females) whereas patients prescribed PAP had a higher baseline AHI and ODI (19.1±6.5 events·h^{-1} *versus* 11.9±5.7 events·h^{-1} and 16.9±11.5 events·h^{-1} *versus* 10.5±9.9 events·h^{-1}, respectively; all p<0.001) (table 1). Patients receiving PAP had higher comorbidity index scores compared to those prescribed an MAD. The group with moderate OSA was older, more overweight and had higher comorbidity index scores compared to the group with mild OSA but had slightly lower ESS scores (table 1).

Combination therapy with active weight reduction

In obese patients, combination therapy with active weight reduction was more common in patients prescribed an MAD *versus* PAP treatment (48.8% *versus* 33.1%, respectively; p<0.001), in patients with mild compared to moderate OSA (42.9% *versus* 34.2%; p<0.001) and in females compared to males (39.8% *versus* 36.1%; p=0.01), figure 3.

Accessibility and reimbursement for MAD treatment at European sites

Responses from 26 ESADA centres showed that MAD accessibility was fair to high at 22 sites (85%) and reimbursement was full or partial at 14 sites (54%). Prior PAP treatment failure was a condition for MAD reimbursement at two centres. Respondents reported that MADs were frequently prescribed for mild OSA at 11 sites (42%) and for moderate OSA at seven sites (27%). Patient preferences were considered when deciding between an MAD or PAP as first-line treatment at 13 out of 26 sites (50%).

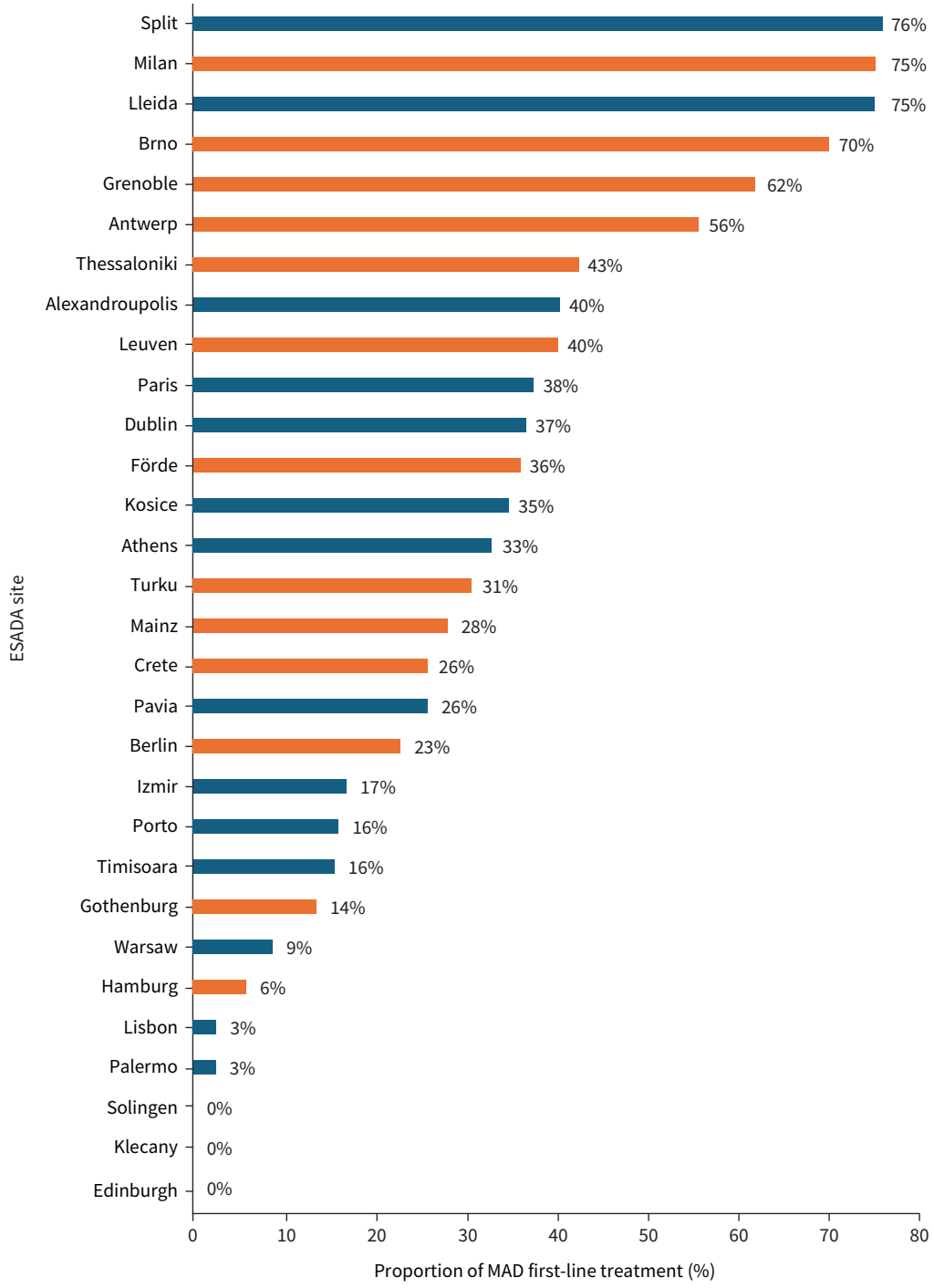

FIGURE 2 Proportion of patients recommended mandibular advancement devices (MADs) as first-line treatment for mild to moderate obstructive sleep apnoea by study site. n=10 109. Blue bars: MADs not reimbursed. Orange bars: MADs reimbursed. ESADA: European Sleep Apnea Database.

Independent predictors of primary treatment recommendations in mild to moderate OSA

The main analysis comprised 8640 patients (table 2). Mild compared to moderate OSA predicted the choice of MAD over PAP treatment most strongly (OR 6.0, 95% CI 5.3–6.8). Other significant predictors for MAD treatment included a low (index score 0) compared to high (index score ⩽3) comorbidity burden (OR 3.8, 95% CI 3.1–4.6), low ESS score (0–6) compared to a high ESS score (16–24) (OR 2.6, 95% CI 2.1–3.1), negligible intermittent hypoxia during sleep (ODI <5) compared to moderate to severe hypoxia (ODI ⩾15) (OR 2.0, 95% CI 1.7–2.4) and absence of diagnosed insomnia compared to diagnosed

TABLE 1 Clinical characteristics of patients with mild or moderate obstructive sleep apnoea (OSA) receiving positive airway pressure (PAP) or a mandibular advancement device (MAD) as primary treatment in the European Sleep Apnea Database cohort as a whole and split by OSA severity

Characteristic	Entire cohort		Mild OSA		Moderate OSA	
	PAP n=6618, 65.5%	MAD n=3491 34.5%	PAP n=1838 41.6%	MAD n=2579 58.4%	PAP n=4780 84.0%	MAD n=912 16.0%
Age (years)	54.4±12.2	52.4±13.5	52.2±12.4	51.4±13.3	55.2±12.0	55.1±13.6
BMI (kg·m^{-2})	31.1±5.9	29.5±5.6	30.4±5.9	29.3±5.7	31.4±5.9	29.9±5.5
Females (%)	33.2	34.0	36.1	35.8	32.1	29.2
Systemic hypertension (%)	44.1	35.2	38.1	33.4	46.4	40.3
ESS total score	9.2±5.0	8.0±4.7	9.5±5.1	8.2±4.8	9.2±5.0	7.5±4.6
AHI (events·h^{-1})	19.1±6.5	11.9±5.7	10.5±2.8	9.1±2.8	22.3±4.1	20.0±4.0
ODI (events·h^{-1})	16.9±11.5	10.5±9.9	9.8±7.5	8.2±8.0	19.8±11.6	16.9±11.6
Comorbidity index score[#] (%[¶])						
0	29.9	45.4	25.8	47.3	31.4	40.1
1	32.7	32.2	36.0	31.0	31.4	35.6
2	21.9	14.8	22.5	13.9	21.6	17.5
⩽3	15.6	7.6	15.7	7.8	15.5	6.8
Insomnia (%)	3.5	2.4	4.3	2.6	3.2	1.8
Mean S_{pO_2} (%)	93.4±0.3	94.2±0.4	93.9±2.7	94.3±2.2	93.1±2.5	93.8±2.3
Lowest S_{pO_2} (%)	81.8±0.1	85.0±0.1	83.7±6.6	85.5±5.7	81.1±7.2	83.3±6.4
T90 (%)	6.9±0.2	2.7±0.2	3.3±10.8	2.3±9.3	7.1±15.1	3.8±10.3
MAD accessibility (%)	87.3	96.9	89.9	96.8	86.3	97.1
MAD reimbursement (%)	47.8	59.2	46.8	58.4	48.2	61.5

Data are presented as mean±SD or %. AHI: apnoea hypopnea index; BMI: body mass index; ESS: Epworth Sleepiness Scale; ODI: oxygen desaturation index; S_{pO_2}: peripheral oxygen saturation; T90: percent of total sleep time under 90% oxygen saturation. [#]: Index with one point for one of the following diagnoses: hypertension, atrial fibrillation, ischemic heart disease, heart failure, coronary vascular disease, hyperlipidaemia, diabetes (including type I and II) or obstructive lung disease (including asthma and COPD). [¶]: Percentage of cases with valid data.

insomnia (OR 2.0, 95% CI 1.7–2.4). Conversely, sex (OR 1.0, 95% CI 9.0–1.1), age (OR 1.0, 95% CI 1.0–1.0) and normal weight *versus* morbid obesity (OR 1.1, 95% CI 0.0–1.4) did not influence treatment preference.

MADs were prescribed in 11.6% of patients at sites with low MAD accessibility and in 37.2% of patients at sites with high MAD accessibility. MADs were prescribed in 39.8% of patients at sites with MAD reimbursement and in 29.5% of those at sites without MAD reimbursement ($p<0.05$, n=9713) (table 3). In the GLM analysis, having accessible and reimbursed MADs predicted the choice of an MAD instead of PAP (OR 3.2, 95% CI 2.5–4.1 and OR 1.3, 95% CI 1.2–1.5, respectively) (table 2).

Sensitivity analyses

Treatment choice prediction analyses were performed in the following subgroups: males, females, patients with mild OSA and patients with moderate OSA (table 2). Factors favouring MAD prescription were similar across subgroups. The AHI, even within each OSA severity group, influenced the treatment choice slightly.

MADs were more frequently prescribed at sites where patient participated in the treatment decision process. (46.1% *versus* 30.2%, $p<0.001$, n=8434) (table 4).

Differences in the odds ratios for factors predicting MAD prescription were observed for both clinical and system factors when comparing patient cases registered to the database prior to 2017 to those registered in 2017 or later (see e-table 1 in the supplementary material). Most notably, high MAD availability more strongly predicted MAD use in cases registered prior to 2017 compared to cases registered during or after 2017 (OR 4.8, 95% CI 3.2–7.3 *versus* OR 2.5, 95% CI 1.8–3.5).

Finally, for comparison, we present descriptive data on treatment naïve patients with severe OSA in the ESADA database (n=11 372) in e-table 2. The group receiving PAP had more comorbidities compared to the MAD group.

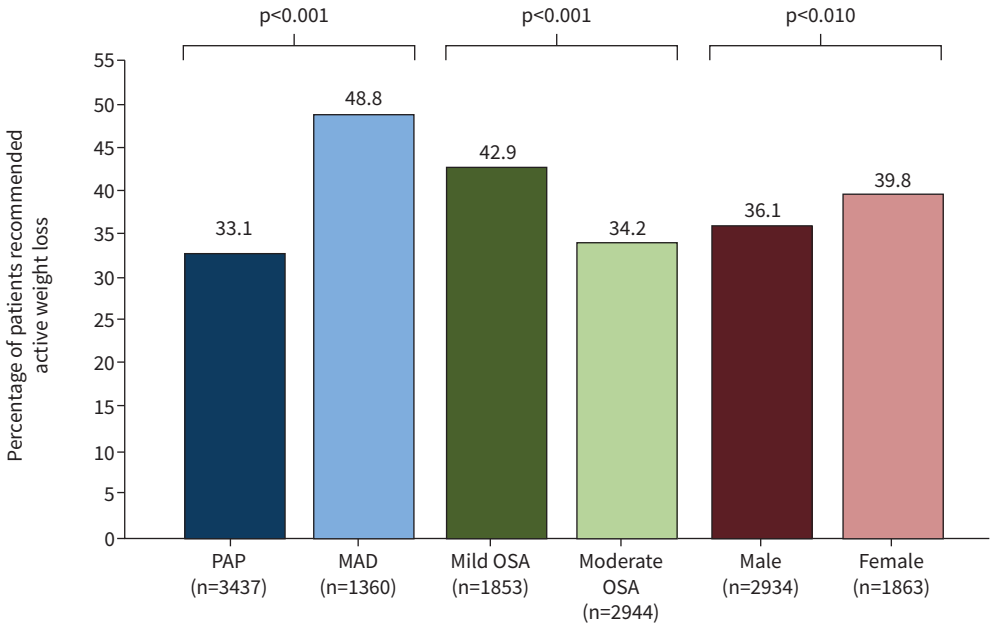

FIGURE 3 Proportion of obese patients with mild and moderate obstructive sleep apnoea (OSA) recommended a combination therapy including "active weight reduction". Obesity was defined as a BMI of 30 $kg \cdot m^{-2}$ and upwards. p: significance as per results of the t-test of difference between groups. MAD: patient group recommended mandibular advancement device as first-line treatment. Mild OSA: patient group diagnosed with mild OSA. Moderate OSA: patient group diagnosed with moderate OSA. PAP: patient group recommended positive airway pressure as first-line treatment.

Discussion

This study in a pan-European cohort provided real-world evidence on how clinical and organisational factors determine first-line management of mild to moderate OSA. First, PAP is prescribed twice as frequently as MADs and prescription rates for MADs vary extensively. Second, clinical factors that predicted the use of MADs over PAP followed current guidelines. Third, organisational factors such as accessibility and reimbursement of MADs significantly impacted the choice between MADs and PAP, as did the inclusion of patient preferences into the treatment decision process. Finally, decisive interventions for comorbid obesity were more frequently combined with MAD treatment, despite a lower BMI in those patients compared to patients prescribed PAP.

Our findings regarding patient factors indicate a prescription pattern largely supported by existing literature. Patients with more respiratory events and hypoxaemia were prescribed PAP more frequently, since PAP more potently normalises respiratory events and hypoxaemia [15, 25]. Importantly, hypoxic burden has been associated with increased cardiovascular mortality [26].

Previous studies in smaller samples have found that younger age and lower BMI predicts successful MAD treatment [27]. In our analysis, age did not influence treatment choice between MADs and PAP. Similarly, the BMI had no substantial effect on treatment choice between PAP and MADs in our model. This is likely due to correlation with diagnoses associated with obesity that are accounted for by our comorbidity index variable.

Patients receiving PAP have higher average BMI, OSA severity and comorbidity burden than patients receiving MAD treatment. Patients also tend to gain weight after PAP initiation [28]. From a holistic perspective, active weight reduction interventions would often be appropriate alongside PAP prescriptions. Despite this, we found that MAD prescriptions were more often combined with such interventions. When using MADs, physicians may more often anticipate residual apnoeas and add active weight reduction to augment the treatment. However, a high BMI is associated with poorer outcomes in cardiometabolic diseases [29], highly prevalent among OSA patients. Therefore, a higher emphasis on holistic approaches to OSA patient care including overweight management might be desirable [30].

TABLE 2 Analysis of independent predictive factors favouring a mandibular advancement device (MAD) over positive airway pressure (PAP) as primary treatment in mild to moderate obstructive sleep apnoea (OSA) in the European Sleep Apnea Database cohort – main and sensitivity analyses

Main analysis and sensitivity analyses	Entire cohort n=8640		Female sex n=2878		Male sex n=5762		Mild OSA n=3830		Moderate OSA n=4810	
Factors predicting prescription of MAD over PAP	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
AHI classes										
Mild (AHI 5–<15) compared to moderate (AHI 15–<30) OSA	6.0 (5.3–6.8)	<0.001	6.6 (5.3–8.3)	<0.001	5.8 (5.0–6.8)	<0.001	0.8 (0.8–0.9)[#]	<0.001	0.9 (0.8–0.9)[#]	<.001
ODI classes										
Negligible hypoxia (ODI <5)	2.0 (1.7–2.4)	<0.001	2.2 (1.6–3.0)	<0.001	2.0 (1.6–2.5)	<0.001	1.3 (1.0–1.8)	0.068	1.3 (1.0–1.8)	0.055
Mild hypoxia (ODI 5–<15)	1.4 (1.2–1.6)	<0.001	1.4 (1.1–1.8)	0.008	1.4 (1.2–1.7)	<0.001	1.1 (0.8–1.4)	0.503	0.9 (0.8–1.1)	0.586
Moderate/severe hypoxia (ODI ⩾15)	1	–	1	–	1	–	1	–	1	–
EDS (ESS score)										
No EDS (ESS 0–6)	2.6 (2.1–3.1)	<0.001	2.4 (1.7–3.4)	<0.001	2.7 (2.1–3.4)	<0.001	2.5 (1.9–3.2)	<0.001	3.1 (2.2–4.4)	<.001
Mild EDS (ESS 7–10)	1.9 (1.6–2.4)	<0.001	2.1 (1.5–2.9)	<0.001	1.9 (1.5–2.9)	<0.001	2.0 (1.6–2.6)	<0.001	2.0 (1.4–2.9)	<.001
Moderate EDS (ESS 11–15)	1.3 (1.0–1.6)	0.016	1.3 (0.9–1.9)	0.105	1.3 (1.0–1.6)	0.068	1.2 (0.9–1.5)	0.271	1.6 (1.1–2.3)	0.017
Severe EDS (ESS 16–24)	1	–	1	–	1	–	1	–	1	–
Weight classes (BMI, kg·m^{-2})										
Normal weight (<25)	1.1 (0.0–1.4)	0.260	1.0 (0.7–1.3)	0.809	1.3 (1.0–1.7)	0.063	0.9 (0.7–1.2)	0.369	1.6 (1.1–2.1)	0.005
Overweight (25–<30)	1.2 (1.0–1.4)	0.046	0.9 (0.7–1.2)	0.442	1.4 (1.1–1.7)	0.003	1.0 (0.8–1.3)	0.943	1.5 (1.2–1.9)	0.002
Obesity (30⩽35)	1.1 (0.9–1.3)	0.275	1.1 (0.9–1.4)	0.415	1.2 (0.9–1.5)	0.179	1.0 (0.8–1.2)	0.820	1.3 (1.0–1.7)	0.055
Morbid obesity (⩾35)	1	–	1	–	1	–	1	–	1	–
Comorbidity index score[¶]										
0	3.8 (3.1–4.6)	<0.001	3.8 (2.7–5.3)	<0.001	3.9 (3.0–5.0)	<.001	4.8 (3.7–6.3)	<0.001	3.5 (2.5–4.8)	<.001
1	2.0 (1.7–2.4)	<0.001	1.9 (1.4–2.6)	<0.001	2.1 (1.6–2.7)	<.001	1.8 (1.4–2.3)	<0.001	2.6 (1.9–3.6)	<.001
2	1.4 (1.1–1.7)	0.002	1.4 (1.0–2.0)	0.036	1.4 (1.1–1.8)	0.013	1.3 (1.0–1.6)	0.091	1.7 (1.2–2.4)	0.002
⩽3	1	–	1	–	1	–	1	–	1	–
Insomnia										
No insomnia compared to diagnosed insomnia	2.0 (1.7–2.4)	<0.001	2.1 (1.4–3.3)	<0.001	2.0 (1.3–3.2)	0.003	1.8 (1.2–2.7)	0.002	2.6 (1.4–5.0)	0.004
Accessibility of MAD										
High compared to limited	3.2 (2.5–4.1)	<0.001	2.9 (1.9–4.4)	<0.001	3.4 (2.5–4.6)	<0.001	2.6 (1.9–3.6)	<0.001	5.0 (3.2–7.7)	<0.001
Reimbursement for MAD										
High compared to limited or none	1.3 (1.2–1.5)	<0.001	1.3 (1.1–1.6)	0.011	1.4 (1.2–1.6)	<0.001	1.4 (1.2–1.6)	<0.001	1.2 (1.0–1.4)	0.086
Sex										
Female compared to male	1.0 (0.9–1.1)	0.972	–	–	–	–	1.0 (0.9–1.2)	0.772	0.9 (0.8–1.1)	0.356
Age	1.0 (1.0–1.0)	<0.001	1.0 (1.0–1.0)	0.008	1.0 (1.0–1.0)	<0.001	1.0 (1.0–1.0)	<0.001	1.0 (1.0–1.0)	0.006

AHI: apnoea hypopnoea index; BMI: body mass index; ODI: oxygen desaturation index, EDS: excessive daytime sleepiness; ESS: Epworth Sleepiness Scale; OR: odds ratio. p-value: significance of between-group differences based on the Wald Chi-square test. [#]: AHI included as a continuous variable within each group of OSA severity. [¶]: Index with one point for one of the following diagnoses: hypertension, atrial fibrillation, ischemic heart disease, heart failure, coronary vascular disease, hyperlipidaemia, diabetes (including type I and II) or obstructive lung disease (including asthma and COPD).

TABLE 3 Primary recommended treatment by mandibular advancement device (MAD) accessibility and reimbursement policy at the corresponding site for each case

	Primary recommended treatment		
	MAD % (n)	PAP % (n)	Total n
High MAD accessibility	37.2 (3276)	62.8 (5526)	8802
Low MAD accessibility	11.6 (106)	88.4 (805)	991
Total (n)	3382	6331	9713[#]
	p-value for group differences based on accessibility: <0.001[¶]		
MAD generally reimbursed	39.8 (2001)	60.2 (3029)	5030
MAD generally not reimbursed	29.5 (1381)	70.5 (3392)	4683
Total (n)	3382	6631	9713[#]
	p-value for group differences based on reimbursement: <0.001[¶]		

Analysis limited to patients that received either positive airway pressure (PAP) or an MAD. [#]: 396 cases excluded due to missing data. [¶]: Significance for between-group differences based on the Pearson Chi-square test.

Previous studies comparing the effects of PAP and MADs on EDS have either found a similar or a greater beneficial effect with PAP treatment [31–33]. In this study, lower ESS scores favoured the choice of MAD treatment. Importantly, PAP has been found to reduce respiratory parameters more potently than MADs [34, 35] and EDS has in turn been linked to nighttime hypoxia [36]. This might explain why physicians prescribe PAP to patients with a higher AHI, hypoxic burden and ESS scores.

There are few studies comparing the effects of PAP and MADs on comorbid insomnia and OSA (COMISA). Some trials have shown similar effects from PAP and MADs on reducing insomnia symptoms [37]. COMISA is associated with worse health consequences and cardiovascular mortality compared to insomnia-free OSA, as well as worse PAP acceptance and adherence [38]. Combination strategies using PAP and cognitive behavioural therapy have shown better outcome compared to monotherapies [39]. There is less data available on MAD use in COMISA patients.

Our findings highlight the heterogenous accessibility and reimbursement for MADs in Europe, and the influence of MAD prescription. Additionally, socioeconomic factors may affect MAD prescriptions. A French study, where initial reimbursement for PAP and MADs is comparable, demonstrated that OSA patients with lower education were prescribed MAD less frequently than patients with higher education [21]. The authors attributed this discrepancy to the costs of subsequent MAD-related dental care and to this group's impaired dental health, which can constitute a contraindication for MADs. In our study, patients preferred MADs more frequently at centres with MAD reimbursement, confirming that financial concerns influence MAD prescriptions. Treatment cost is also a concern for physicians; in a German survey, sleep physicians identified "reimbursement issues" as the main barrier to MAD prescription [40].

The predicted need for subsequent care, such as the optimisation and troubleshooting of MAD therapy by a qualified dentist, should be considered when prescribing MADs. Mandibular protrusion titration and risk assessment for complications [41] require expertise which may not be available at some sites. Indeed, a

TABLE 4 Primary recommended treatment according to the impact of patient preference on selection of a mandibular advancement device (MAD) or positive airway pressure (PAP) as first-line treatment at the corresponding site for each case

	Primary recommended treatment		
	MAD % (n)	PAP % (n)	Total n
Patient preference decides choice of MAD *versus* PAP	46.1 (1790)	53.9 (2095)	3885
Patient preference does not decide choice of MAD *versus* PAP	30.2 (1376)	69.8 (3173)	4549
Total (n)	3166	5268	8434[#]
	p-value for group difference: <0.001[¶]		

Analysis limited to patients that received either PAP or MAD. [#]: 1675 cases excluded due to missing data. [¶]: Significance for between-group differences based on the Pearson Chi-Square test.

recent review found that superior professional guidance during MAD treatment regarding side-effects and titration yielded higher adherence [42]. Furthermore, not all regions have an established frame of collaboration, transparency and continuity of care between sleep centres diagnosing OSA and dental care providers initiating MAD treatment [43]. Accordingly, a prudent physician might avoid recommending an MAD for a clinically fitting patient, depending on local circumstances. The authors estimate that this causes MADs to be underused at several European sleep clinics.

In general, the trends regarding which factors predicted MAD prescription were the same for cases recruited to the database in both the earlier and later years, reflecting a relative continuity of prescription patterns. However, some differences in the odd ratios were observed for both clinical and system factors. Most notably, high MAD availability had a considerably greater impact in earlier years. Presumably, MAD treatment was less established at that time, where MADs may not have been available at all in some regions.

Strengths and limitations

The ESADA encompasses unselected OSA patients from sleep clinics across many European countries. The patient populations, healthcare system frameworks, established routines and treatment options vary considerably. Thus, our findings are expected to have a high generalisability to European and other comparable healthcare systems. The large patient population provides a considerable statistical power. Additionally, the multitude of registered variables allows for a comprehensive analysis of the relevant relationships. By including the comorbidity index variable, the effects of relevant comorbidities on treatment choice were accounted for to a greater extent than in most other analyses.

This study has limitations. Severe OSA patients were not included in the analysis. Other treatment options that were perhaps used alongside an MAD or PAP were not accounted for, such as surgery, positional devices or medications. However, first-line use of these is rare in reported ESADA data. The alternative of offering both PAP and MAD treatment for OSA patients was not considered [44]. Information about the accessibility and reimbursement of MADs is limited to 26 out of 30 sites and only these were included in the prediction analysis. Furthermore, the information on MAD accessibility and reimbursement was obtained in 2022 and the analysis did not account for changes in MAD accessibility and reimbursement policies that may have occurred at participating sites over the entire study period.

Additionally, anatomical traits or polysomnographic variables such as loop gain, arousal threshold and positionality of OSA, that might affect the physician's propensity to use an MAD, were not included in our analysis due to lack of data. However, position dependency is likely present in most patients with mild to moderate OSA and hardly explains the observed variability of MAD prescription. Lastly, our study is limited to treatment-naïve patients and does not address factors affecting choices for second-line therapies.

Future directions

Our results highlight regional disparities in access to MADs, a key treatment for OSA. MAD prescription would likely be more frequent across Europe if treatment choices were solely based on clinical factors and patient preferences. Considering our results, the relevant literature and the current clinical landscape, the authors surmise that to address this issue the following efforts are required from the sleep medicine field:

1) Expand clinical infrastructure and competence for MAD treatment across Europe.
2) Implement holistic reimbursement policies for MADs to ensure adequate OSA treatment attainable for disadvantaged groups.
3) Synergise OSA work-up and follow-up between sleep clinics and dental care.
4) Further investigate long-term outcomes and associated healthcare costs in patients receiving MAD treatment.
5) Evaluate novel implementations of MAD treatment, including telemonitoring and combination treatment strategies [45].

Conclusion

In a large pan-European cohort of patients with mild to moderate OSA, PAP was prescribed twice as often as MADs and the clinical factors predicting the sleep physician's choice for first-line prescription were congruent with current evidence. However, accessibility, reimbursement policy for MADs and patient participation significantly impacted MAD prescription rates. High variations of MAD prescription rates were found between European sites, suggesting that MADs were underutilised in some regions of Europe. This is suboptimal from a clinical perspective since many patients with mild or moderate OSA struggle with low PAP adherence, resulting in insufficient treatment and prolonged symptom burden. These

findings underscore the need for sleep clinics, dental care providers and policy makers to collaborate towards making MADs a feasible treatment option across the continent.

Acknowledgements: The European Sleep Research Society and the European Respiratory Society (ERS) have provided nonfinancial support in terms of logistics for communication, meetings and data presentations of the European Sleep Apnea Database (ESADA). We would like to thank all ESADA collaborators that responded to our questionnaire.

Provenance: Submitted article, peer reviewed.

ESADA study group: Alexandroupolis, Greece: P. Steiropoulos, Sleep Unit, Department of Pneumonology, Democritus University of Thrace, Alexandroupolis, Greece. Antwerp, Belgium: J. Verbraecken, Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium; E. Petiet, Multidisciplinary Sleep Disorders Centre, Antwerp University Hospital and University of Antwerp, Antwerp, Belgium. Athens, Greece: G. Trakada, Pulmonary Medicine, National and Kapodistrian University of Athens, Athens, Greece. Berlin, Germany: I. Fietze, Schlafmedizinisches Zentrum, Charité – Universitätsmedizin Berlin, Germany; T. Penzel, Schlafmedizinisches Zentrum, Charité – Universitätsmedizin Berlin, Germany. Brno, Czech Republic: O. Ludka, Department of Cardiology, University Hospital Brno and International Clinical Research Center, St Ann's University Hospital, Brno, Czech Republic. Crete, Greece: I. Bouloukaki, Sleep Disorders Unit, Department of Respiratory Medicine, Medical School, University of Crete, Greece; S. Schiza, Sleep Disorders Unit, Department of Respiratory Medicine, Medical School, University of Crete, Greece. Dublin, Ireland: W.T. McNicholas, Department of Respiratory Medicine, St Vincent's University Hospital, Dublin, Ireland; S. Ryan, Pulmonary and Sleep Disorders Unit, St Vincent's University Hospital, Dublin, Ireland. Edinburgh, UK: R.L. Riha, Department of Sleep Medicine, Royal Infirmary Edinburgh. Førde, Norway: J.A. Kvamme, Sleep Laboratory, ENT Department, Førde Central Hospital, Førde, Norway. Gothenburg, Sweden: L. Grote, Sleep Disorders Center, Pulmonary Department, Sahlgrenska University Hospital, and Center of Sleep and Wake Disorders, Sahlgrenska Academy, Gothenburg University, Göteborg, Sweden; J. Hedner, Sleep Disorders Center, Pulmonary Department, Sahlgrenska University Hospital, and Center of Sleep and Wake Disorders, Sahlgrenska Academy, Gothenburg University, Göteborg, Sweden; D. Zou, Sleep Disorders Center, Pulmonary Department, Sahlgrenska University Hospital, and Center of Sleep and Wake Disorders, Sahlgrenska Academy, Gothenburg University, Göteborg, Sweden. Ghent, Belgium: K. Hertegonne, Department of Respiratory Medicine, Ghent University Hospital, and Department of Internal Medicine and Pediatrics, Faculty of Medicine and Health Sciences, Ghent University, Gent, Belgium; D. Pevernagie, Department of Respiratory Medicine, Ghent University Hospital, and Department of Internal Medicine and Pediatrics, Faculty of Medicine and Health Sciences, Ghent University, Gent, Belgium. Grenoble, France: S. Bailly, Université Grenoble Alpes, INSERM HP2 (U1042) and Grenoble University Hospital, Grenoble, France; J.L. Pépin, Université Grenoble Alpes, INSERM HP2 (U1042) and Grenoble University Hospital, Grenoble, France; R. Tamisier, Université Grenoble Alpes, INSERM HP2 (U1042) and Grenoble University Hospital, Grenoble, France. Hamburg, Germany: H. Hein, Sleep Disorders Center, St. Adolf Stift, Reinbeck, Germany. Izmir, Türkiye: O.K. Basoglu, Department of Respiratory Medicine, Ege University, Izmir, Türkiye; M.S. Tasbakan, Department of Respiratory Medicine, Ege University, Izmir, Türkiye. Klecany, Czech Republic: J. Buskova, Department of Sleep Medicine, National Institute of Mental Health, Klecany, Czech Republic. Kosice, Slovakia: P. Joppa, Department of Respiratory Medicine and Tuberculosis, Faculty of Medicine, P.J. Safarik University and L. Pasteur University Hospital, Kosice, Slovakia. Lisbon, Portugal: R. Staats, Department of Respiratory Medicine, Hospital de Santa Maria, Lisbon, Portugal. Leuven, Belgium: D. Testelmans, Sleep Disorders Centre, University Hospitals Leuven, Leuven, Belgium; A. Kalkanis, Department of Respiratory Diseases, Louvain University Center for Sleep and Wake Disorders (LUCS), University Hospitals Leuven, KU Leuven, Leuven, Belgium. Mainz, Germany: H. Gouveris, ENT department at Mainz University Hospital, Mainz, Germany; K. Ludwig, ENT department at Mainz University Hospital, Mainz, Germany. Milan, Italy: C. Lombardi, Istituto Auxologico Italiano, IRCCS, Department of Cardiovascular, Neural and Metabolic Sciences, St Luke Hospital, and Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy; G. Parati, Istituto Auxologico Italiano, IRCCS, Department of Cardiovascular, Neural and Metabolic Sciences, St Luke Hospital, and Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy. Palermo, Italy: M.R. Bonsignore, PROMISE Dept, University of Palermo, Palermo, Italy. Pavia, Italy: F. Fanfulla, Unità Operativa di Medicina del Sonno, Istituto Scientifico di Pavia IRCCS, Pavia, Italy. Paris, France: M. Petitjean M, Unité de Médecine du Sommeil, Hopital Antoine-Beclere, Clamart, France; G. Roisman, Unité de Médecine du Sommeil, Hopital Antoine-Beclere, Clamart, France. Porto, Portugal: M. Drummond, Pulmonology Department Hospital São João, Medicine Faculty of Porto University, Porto, Portugal; M. van Zeller, Pulmonology Department Hospital São João, Medicine Faculty of Porto University, Porto, Portugal. Solingen, Germany: W. Randerath W, Sleep Disorders Centre, Pulmonary Clinic, Solingen, Germany; S. Mathes, Sleep Disorders Centre, Pulmonary Clinic, Solingen, Germany. Split, Croatia: Z. Dogas, Sleep Medicine Center, Department of Neuroscience, University of Split School of Medicine, Split, Croatia; T. Galic, Sleep Medicine Center, Department of Neuroscience, University of Split School

of Medicine, Split, Croatia; R. Pecotic, Sleep Medicine Center, Department of Neuroscience, University of Split School of Medicine, Split, Croatia. Thessaloniki, Greece: A. Pataka, Respiratory Failure Unit, G. Papanikolaou Hospital, Thessaloniki, Greece. Timisoara, Rumania: S. Mihaicuta S, Pulmonary Department, Victor Babes University of Medicine and Pharmacy, Victor Babes Hospital, Timisoara, Rumania. Turku, Finland: U. Anttalainen, Division of Medicine, Department of Pulmonary Diseases, Turku University Hospital and Sleep Research Centre, Department of Pulmonary Diseases and Clinical Allergology, University of Turku, Finland; T. Saaresranta, Division of Medicine, Department of Pulmonary Diseases, Turku University Hospital and Sleep Research Centre, Department of Pulmonary Diseases and Clinical Allergology, University of Turku, Finland. Warsaw, Poland: P. Sliwinski, 2nd Department of Respiratory Medicine, Institute of Tuberculosis and Lung Diseases, Warsaw, Poland.

Ethics statement: Local ethics committees at each study site approved the foundational protocol for the registry. Informed consent was obtained from all patients. Approval from the Regional Ethical Committee was obtained before our study was conducted (DNR 386-09).

Author contributions: L. Grote wrote the draft of the study protocol, which was amended by all authors. Analysis was performed by B. Fridriksson, L. Grote and D. Zou. B. Fridriksson wrote the first draft of the manuscript. L. Grote, D. Zou and J. Hedner contributed with interpretation of data, and critical revision and adjustments of the first version of the manuscript. All authors participated in critical review of the analysis and the draft. After review of the draft, all authors approved the final version of the manuscript.

Conflict of interest: B. Fridriksson has received one-time lecturing fees from ResMed and AstraZeneca, and a one-time fee for advisory board participation for GSK. L. Grote has received institutional grants from the Swedish Heart and Lung Foundation, from the Regional Research Support (ALF), and funding from the European Union Horizon 2020 grant “Sleep Revolution” as Work Package Leader; received unrestricted funding for the ESADA study from Resmed and Philips Foundations in 2007 and 2011 as well as from Bayer AG (2018–2021) for a scientific collaboration; owns shares in company with a licensed patent to Desistin GmbH, Germany, for pharmacological treatment in obstructive sleep apnoea; received fees participating in education activities for Astra, Lundbeck, Resmed, Philips and Itamar; has chaired the National guideline committee for OSA in adults, the National Quality Registry for OSA in Adults (SESAR), and the Clinical Research Collaboration ESADA of the ERS; has received support as ERS Representative for Assembly 4 2020–2023 and as an European Sleep Research Society examination committee member; and outside the current manuscript, is a medical advisor for Onera BV, Netherlands. J. Hedner has received a Desitin GmbH research grant related to carbonic anhydrase inhibition in sleep apnoea (CAISA study, 2021–2023) as payment to his institution; has received payment from Desitin GmbH *via* a institutional clinical trial agreement with independent monitor (and University of Gothenburg) proof of concept trial (STM026) for sulthiame in obstructive sleep apnoea (2018–2020); received unrestricted funding for the ESADA study from Resmed and Philips Foundations in 2007 and 2011 as well as from Bayer AG (2018–2021) for a scientific collaboration; has received university grants from Swedish Heart and Lung Foundation and the Västra Götaland Regionen (ALF Agreement); owns shares in a company with a licensed patent relating to drug treatment in sleep apnea (Apnimed); and has received consulting fees as member of a medical advisory board for SomnoMed (discontinued 2024). D. Zou has received an institutional grant from the Swedish Heart Lung Foundation. J. Verbraecken reports grants and fees from AirLiquide AstraZen, Atos Medical, Azelis, Bioprojet, Desitin, Epilog, Idorsia, Inspire Medical Systems, Löwenstein Medical, Mediq, Micromed OSG, Philips, ProSomnus, ResMed, Sefam, SD Worx, SomnoMed, SOS Oxygène, Tilman, Total Care, Vivisol, Vlaamse Gemeenschap, Vlerick, Westfalen Medical and Zoll Itamar outside the submitted work; and consultancy for Bioprojet and Epilog; and is an associate editor of this journal. S. Bailly is supported by funding through the French National Research Agency in the framework of the “Investissements d’avenir” programme (ANR-15-IDEX-02) and the “e-health and integrated care and trajectories medicine and MIAI artificial intelligence” Chairs of excellence from the Grenoble Alpes University Foundation (ANR-19-P3IA-0003). D. Testelmans has received fees for lecturing from ResMed and for advisory board membership from Bioproject. T. Saaresranta has received institutional support from Finnish Governmental VTR Grant #13542, Finnish Anti-Tuberculosis Association Foundation, Tampere Tuberculosis Foundation, Foundation for Respiratory Diseases, Jalmari and Rauha Ahokas Foundation; and reports the task force roles as Chair of the Finnish Task Force of Current Care Guidelines for Adult Sleep Apnea, and Member of the ESRS Task Force BPAP in Obstructive Sleep Apnea. S. Schiza, P. Joppa, S. Mihaicuta, O.K. Basoglu, O. Ludka, Z. Dogas and M. Drummond report no conflict of interest.

Support statement: The ESADA network was supported by the European Union COST action B26 (2005–2009). In addition, the ERS has funded ESADA as a Clinical Research Collaboration (2015–ongoing). The ResMed Foundation and the Philips Respironics Foundation have provided unrestricted seeding grants for establishment of the database in 2007 and 2011. The ESADA has a scientific collaboration with Bayer AG (2018–2022). The ESADA is part of the European Union Horizon 2020-funded “Sleep Revolution project” (grant agreement number 965417). In this context, the current study explored contemporary patient management in obstructive sleep apnoea and the

current level of patient participation on the European level. L. Grote and J. Hedner received institutional grants from the Swedish Heart and Lung Foundation, which included the analysis of data from the ESADA.

References

1 Moyer CA, Sonnad SS, Garetz SL, *et al.* Quality of life in obstructive sleep apnea: a systematic review of the literature. *Sleep Med* 2001; 2: 477–491.
2 Coughlin SR, Mawdsley L, Mugarza JA, *et al.* Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. *Eur Heart J* 2004; 25: 735–741.
3 Parish JM, Somers VK. Obstructive sleep apnea and cardiovascular disease. *Mayo Clin Proc* 2004; 79: 1036–1046.
4 Terán-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. *N Engl J Med* 1999; 340: 847–851.
5 Grote LMB, Friberg D, Tegelberg Å, *et al.* Nationellt vårdprogram för behandling av obstruktiv sömnapné hos vuxna Sweden: Nationell arbetsgrupp för behandling av obstruktiv sömnapné hos vuxna. Date last updated: 6 September 2021. Date last accessed: 12 September 2025. https://vardpersonal.1177.se/globalassets/nkk/nationell/media/dokument/kunskapsstod/vardprogram/nationellt-vardprogram-for-behandling-av-obstruktiv-somnapne-hos-vuxna-slutversion.pdf
6 Sullivan CE, Issa FG, Berthon-Jones M, *et al.* Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981; 1: 862–865.
7 Weaver TE, Maislin G, Dinges DF, *et al.* Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 2007; 30: 711–719.
8 Hu X, Fan J, Chen S, *et al.* The role of continuous positive airway pressure in blood pressure control for patients with obstructive sleep apnea and hypertension: a meta-analysis of randomized controlled trials. *J Clin Hypertens (Greenwich)* 2015; 17: 215–222.
9 Patil SP, Ayappa IA, Caples SM, *et al.* Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med* 2019; 15: 301–334.
10 Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. *J Otolaryngol Head Neck Surg* 2016; 45: 43.
11 Jacobsen AR, Eriksen F, Hansen RW, *et al.* Determinants for adherence to continuous positive airway pressure therapy in obstructive sleep apnea. *PLoS One* 2017; 12: e0189614.
12 Finnsson E, Arnardóttir E, Cheng W-J, *et al.* Sleep apnea endotypes: from the physiological laboratory to scalable polysomnographic measures. *Frontiers in Sleep* 2023; 2: 1188052.
13 Turnbull CD, Stradling JR. Endotyping, phenotyping and personalised therapy in obstructive sleep apnoea: are we there yet? *Thorax* 2023; 78: 726–732.
14 Matthes S, Treml M, Grote L, *et al.* The modified Baveno classification for obstructive sleep apnoea: development and evaluation based on the ESADA database. *Eur Respir J* 2024; 64: 2401371.
15 Randerath W, Verbraecken J, de Raaff CAL, *et al.* European Respiratory Society guideline on non-CPAP therapies for obstructive sleep apnoea. *Eur Respir Rev* 2021; 30: 210200.
16 Lisik D, Zou D. Breaking ground: from CPAP treatment to the first medicine for OSA patients with obesity. *Curr Pulmonol Rep* 2025; 14: 3.
17 Marklund M, Braem MJA, Verbraecken J. Update on oral appliance therapy. *Eur Respir Rev* 2019; 28: 190083.
18 Dieltjens M, Braem MJ, Vroegop A, *et al.* Objectively measured *vs* self-reported compliance during oral appliance therapy for sleep-disordered breathing. *Chest* 2013; 144: 1495–1502.
19 Phillips CL, Grunstein RR, Darendeliler MA, *et al.* Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. *Am J Respir Crit Care Med* 2013; 187: 879–887.
20 Grote L, Anderberg C-P, Friberg D, *et al.* National knowledge-driven management of obstructive sleep apnea–the Swedish approach. *Diagnostics (Basel)* 2023; 13: 1179.
21 Fleury M, Le Vaillant M, Pelletier-Fleury N. Socio-economic status: a barrier to access to mandibular advancement device therapy for patients with obstructive sleep apnea syndrome in France. *PLoS One* 2015; 10: e0138689.
22 Mandereau-Bruno L, Léger D, Delmas MC. Obstructive sleep apnea: a sharp increase in the prevalence of patients treated with nasal CPAP over the last decade in France. *PLoS One* 2021; 16: e0245392.
23 Grote L. 2023. SESAR Årsrapport 2023. Date last updated: 2023. Date last accessed: 12 September 2025. https://registercentrum.blob.core.windows.net/sesar/r/SESAR-rsrapport2023-Bgh-gzvrB.pdf.
24 Hedner J, Grote L, Bonsignore M, *et al.* The European Sleep Apnoea Database (ESADA): report from 22 European sleep laboratories. *Eur Respir J* 2011; 38: 635–642.
25 Cammaroto G, Galletti C, Galletti F, *et al.* Mandibular advancement devices *vs* nasal-continuous positive airway pressure in the treatment of obstructive sleep apnoea. Systematic review and meta-analysis. *Med Oral Patol Oral Cir Bucal* 2017; 22: e417–e424.

26 Azarbarzin A, Sands SA, Stone KL, *et al.* The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study. *Eur Heart J* 2019; 40: 1149–1157.

27 Lettieri CJ, Paolino N, Eliasson AH, *et al.* Comparison of adjustable and fixed oral appliances for the treatment of obstructive sleep apnea. *J Clin Sleep Med* 2011; 7: 439–445.

28 Chen B, Drager LF, Peker Y, *et al.* Effect of continuous positive airway pressure on weight and local adiposity in adults with obstructive sleep apnea: a meta-analysis. *Ann Am Thorac Soc* 2021; 18: 1717–1727.

29 Bastien M, Poirier P, Lemieux I, *et al.* Overview of epidemiology and contribution of obesity to cardiovascular disease. *Prog Cardiovasc Dis* 2014; 56: 369–381.

30 Lisik D, Zou D. Treatable traits-based pharmacologic treatment of sleep apnea. *Sleep Med Clin* 2025; 20: 103–114.

31 Grote L, Jonzon YA, Barta P, *et al.* The Swedish Sleep Apnea Registry (SESAR) cohort – “real world data” on a national level. *Sleep Med* 2024; 124: 362–370.

32 Schwartz M, Acosta L, Hung Y-L, *et al.* Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis. *Sleep Breath* 2018; 22: 555–568.

33 Li P, Ning X-H, Lin H, *et al.* Continuous positive airway pressure *versus* mandibular advancement device in the treatment of obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Med* 2020; 72: 5–11.

34 Li W, Xiao L, Hu J. The comparison of CPAP and oral appliances in treatment of patients with OSA: a systematic review and meta-analysis. *Respir Care* 2013; 58: 1184–1195.

35 Lim J, Lasserson TJ, Fleetham J, *et al.* Oral appliances for obstructive sleep apnoea. *Cochrane Database Syst Rev* 2006; 2006: Cd004435.

36 Lal C, Weaver TE, Bae CJ, *et al.* Excessive daytime sleepiness in obstructive sleep apnea. Mechanisms and clinical management. *Ann Am Thorac Soc* 2021; 18: 757–768.

37 Nikolopoulou M, Byraki A, Ahlberg J, *et al.* Oral appliance therapy *versus* nasal continuous positive airway pressure in obstructive sleep apnoea syndrome: a randomised, placebo-controlled trial on self-reported symptoms of common sleep disorders and sleep-related problems. *J Oral Rehabil* 2017; 44: 452–460.

38 Sweetman A. Co-morbid insomnia and sleep apnoea (COMISA): latest research from an emerging field. *Curr Sleep Med Rep* 2023; 9: 180–189.

39 Ragnoli B, Pochetti P, Raie A, *et al.* Comorbid insomnia and obstructive sleep apnea (COMISA): current concepts of patient management. *Int J Environ Res Public Health* 2021; 18: 9248.

40 Braun M, Stuck BA. Physician self-reported knowledge of and barriers to indication of alternative therapies for treatment of obstructive sleep apnea. *Somnologie* 2024; 28: 245–252.

41 Tsolakis IA, Palomo JM, Matthaios S, *et al.* Dental and skeletal side effects of oral appliances used for the treatment of obstructive sleep apnea and snoring in adult patients–a systematic review and meta-analysis. *J Pers Med* 2022; 12: 483.

42 van der Hoek LH, Rosenmöller BRAM, van de Rijt LJM, *et al.* Factors associated with treatment adherence to mandibular advancement devices: a scoping review. *Sleep Breath* 2023; 27: 2527–2544.

43 Fleury B, Lowe A. Current barriers and study needs for oral appliance therapy: the personal perspective of a physician and dentist. *J Dental Sleep Med* 2014; 1: 5.

44 Hamoda MM, Huynh N, Ayas NT, *et al.* Continuous positive airway pressure and mandibular advancement splints: the CHOICE multicentre, open-label randomised clinical trial. *Eur Respir J* 2025; 65: 2401100.

45 Mohammadieh A, Tong B, De Chazal P, *et al.* Innovations in mandibular advancement splint therapy for obstructive sleep apnoea. *Front Sleep* 2023; 2: 1144327.