Oral Appliance Therapy in Patients With Daytime Sleepiness and Snoring or Mild to Moderate Sleep Apnea
A Randomized Clinical Trial

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**IMPORTANCE**
Oral appliances that move the mandible forward during sleep are suggested as treatment for mild to moderate obstructive sleep apnea.

**OBJECTIVE**
To test whether an adjustable, custom-made oral appliance improves daytime sleepiness and quality of life in patients with daytime sleepiness and snoring or mild to moderate obstructive sleep apnea.

**DESIGN, SETTING, AND PARTICIPANTS**
Ninety-six patients with daytime sleepiness and an apnea-hypopnea index (AHI) lower than 30 were included in a randomized, placebo-controlled, parallel trial in Umeå, Sweden, from May 2007 through August 2011.

**INTERVENTIONS**
Four months’ intervention with an oral appliance or a placebo device.

**MAIN OUTCOMES AND MEASURES**
Daytime sleepiness was measured with the Epworth Sleepiness Scale, the Karolinska Sleepiness Scale, and the Oxford Sleep Resistance (OSLER) test. Quality of life was assessed with the Short-Form 36-Item Health Survey (SF-36) and the Functional Outcomes of Sleep Questionnaire (FOSQ). Secondary outcomes included the apnea-hypopnea index, headaches, symptoms of restless legs, and insomnia.

**RESULTS**
Oral appliance therapy was not associated with improvements in daytime sleepiness from baseline to 4-month follow-up when compared with the placebo device; Epworth score >10: 53% at baseline to 24% at follow-up for the oral appliance group vs 54% at baseline to 40% at follow-up for the placebo device group, \( P = .11 \); median (IQR) for Karolinska score /wk: 10 (8 to 14) at baseline to 7 (4 to 9) at follow-up for the oral appliance group vs 12 (6 to 15) at baseline to 8 (5 to 12) at follow-up for the placebo device group, \( P = .11 \); mean between-group difference in OSLER test, −2.4 min (95% CI, −6.3 to 1.4). The mean between-group difference for the total FOSQ score was insignificant (−1.2 [95% CI, −2.5 to 0.1]). No domain of the SF-36 differed significantly between the groups. The AHI was below 5 in 49% of patients using the active appliance and in 11% using placebo, with an odds ratio of 7.8 (95% CI, 2.6-23.5) and a number needed to treat of 3. Snoring (\( P < .001 \)) and symptoms of restless legs (\( P = .02 \)) were less frequent when using the oral appliance vs placebo, but this did not apply to headache or insomnia.

**CONCLUSIONS AND RELEVANCE**
A custom-made, adjustable oral appliance reduces obstructive sleep apnea, snoring, and possibly restless legs without effects on daytime sleepiness and quality of life among patients with daytime sleepiness and snoring or mild to moderate sleep apnea.

**TRIAL REGISTRATION**
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Many patients seek medical attention for obstructive sleep apnea because of snoring and daytime sleepiness. Young and colleagues estimated that 24% of middle-aged men and 9% of women have sleep apnea, with 5 or more apneas and hypopneas per hour of sleep, but only 4% of men and 2% of women had the combination of sleep apnea and daytime sleepiness. Obstructive sleep apnea is associated with serious long-term consequences, such as hypertension, stroke, traffic accidents, and early death. Symptoms include daytime sleepiness, poor sleep quality, headache, and restless legs. Continuous positive airway pressure is a highly effective treatment for patients with daytime sleepiness and sleep apnea, but adherence problems as a result of nasal stuffiness, claustrophobia, and the risk of disturbing bed partners limit the overall usefulness of this therapy.

An oral appliance that holds the lower jaw forward to improve breathing during sleep is suggested as a treatment option for mild and moderate sleep apnea. However, previous placebo-controlled studies of oral appliances have included patients predominantly with moderate to severe sleep apnea, but adherence problems as a result of nasal stuffiness, claustrophobia, and the risk of disturbing bed partners limit the overall usefulness of this therapy.

The primary aims were to study the effects on daytime sleepiness and quality of life of a custom-made, adjustable oral appliance in patients with daytime sleepiness and snoring or mild to moderate sleep apnea. The secondary aims included the effects on sleep apneas, sleep stage patterns, snoring, and symptoms including headaches, restless legs, insomnia, and nasal congestion at bedtime.

Methods

Study Design
A randomized, single-blinded, parallel study of the efficacy of an oral appliance vs an intraoral placebo device after a 4-month intervention was designed according to the CONSORT statement. The study protocol was approved by the ethics review board at Umeå University and all the patients gave their written informed consent (see the trial protocol in Supplement 1).

The sample size was estimated at 60 patients plus 15 patients for potential loss, thus, in total, 75 patients in each group to detect changes of 25% in the occurrence of categorical data with reports of daytime sleepiness according to the Epworth Sleepiness Scale (ESS) and symptoms such as headaches, insomnia, and an urgent need to move the legs. The statistical tests had a power of 0.8 and a P value less than .05 was considered significant.

A computer-generated table was used for randomization and was kept by a person outside the study staff. The patients were blinded to the type of device and the device’s mechanisms of action. All recordings were blinded with respect to the type of device.

Setting and Patients
Patients with snoring who were referred from the Department of Pulmonary Medicine at Umeå University Hospital to the Department of Orthodontics at Umeå University for treatment with oral appliances were asked to participate in the study. Patients who snored and patients with mild to moderate sleep apnea with an apnea-hypopnea index (AHI) lower than 30 were included. The patients also had daytime sleepiness according to 1 or more of the following criteria: (1) an ESS score of 10 or higher; (2) daytime sleepiness assessed as “often” or “always,” or (3) unwillingly falling asleep during the daytime assessed as “sometimes,” “often,” or “always” (on a scale ranging of “never,” “seldom,” “sometimes,” “often,” and “always”), or (4) an irresistible tendency to fall asleep during the daytime 1 or more times per week. The patients were aged 20 to 70 years and had a body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) lower than 35.

Patients with tonsil hypertrophy criteria grade 3 or 4 on the Friedman scale, severe psychiatric diseases or dementia, untreated caries or periodontal disease, few teeth for anchoring a device, occupational drivers, participation in other studies, or patients with a bias with regard to the study (ie, physicians or nurses at the clinic) were excluded.

Interventions
The oral appliance was made individually from plaster casts produced by a dental technician. It consisted of an upper and lower part of elastomer (SR Ivocap Elastomer; Ivoclar Vivadent) and was interconnected with a screw that allowed continuous advancement of the lower jaw (Herbst telescope mechanism, 3.5 mm in diameter, Scheu Dental Technology) (eFigure 1 in Supplement 2). We aimed to advance the mandible by at least 6 mm to 7 mm in all patients. The mandible was advanced 4 mm to 5 mm at the start, sometimes more, and then titrated forward until symptom relief or until adverse effects prevented more advancement. The final mandibular advancement after titration was a mean of 6.8 mm (SD, 1.1).

The placebo upper-jaw device consisted of a bilaminate splint with a hole in the anterior part to reduce size and improve retention to the palate by suction (eFigure 1 in Supplement 2).

Primary Outcomes
Daytime sleepiness and quality of life were the primary outcomes. Subjective sleepiness was measured using the ESS and the Karolinska Sleepiness Scale (KSS). Objective sleepiness was assessed with the Oxford Sleep Resistance (OSLER) test. The ESS questionnaire consists of 8 questions about daytime sleepiness in various situations. Each question could be rated from 0 to 3 with increasing likelihood of falling asleep. Thus, the summarized score ranges in between 0 and 24. A score higher than 10 defines daytime sleepiness. The KSS questions were answered 4 times a day for 1 week. It assesses sleepiness on a scale from 1 to 9 and a score of 7 or higher is regarded as daytime sleepiness corresponding to sleepy or very sleepy. The number of times a patient reported a score of 7 or higher was counted. The OSLER test (Stowood Scientific Instruments) measures sleep latency during the daytime and is regarded as an objective measurement of sleepiness. The Short-Form 36-Item Health Survey (SF-36) was used to measure quality of life. Results are expressed in summary scores.
of mental and physical health. The Functional Outcomes of Sleep Questionnaire (FOSQ) was used as a specific measure of functional outcomes of sleep.34

Secondary Outcomes
The AHI and sleep quality were derived from overnight polysomnography. The reaction time was assessed with the Multiple Unprepared Reaction Time test (Stowood Scientific Instruments). Snoring, fatigue, insomnia, symptoms of restless legs syndrome including an urgent need to move the legs,35 nasal congestion at bedtime, nightly awakenings, and nightmares were assessed in questions designed as in the Basic Nordic Sleep Questionnaire.26

Headaches were assessed in terms of length, intensity, time of day, and character (such as pulsating or pressing).36

Adverse effects were measured on a visual analogue scale from 1 to 10 for 1 or more of the various reported complications: tender teeth, tender jaws, increased salivation, dry mouth, or changed bite.

Polysomnography
Polysomnographic sleep recordings (Embla, Natus Neurology) included continuous recordings of electroencephalogram (channels C3/M2 and C4/M1), electro-oculagrams, submental electromyography, nasal flow pressure sensor, piezoelectric belts (Resp-EZ, EPM Systems), pulse oximetry (Nonin XPOD + 8000J Sensor Adult Flex System, Nonin Medical), piezo respiratory effort sensor (Pro-Tech, Philips), electrocardiograms (V1), and a body position sensor. Sensors were attached in the evening and the recordings were made at home. All recordings were scored manually. An obstructive apnea was defined as the cessation of airflow in nasal pressure for at least 10 seconds with continuing abdominal and thoracic movements.37 An obstructive hypopnea was defined as a 50% reduction in nasal pressure for at least 10 seconds, accompanied by abdominal and thoracic movements in combination with an arousal or an oxygen desaturation of 3% or more. Sleep was scored in 30-second epochs according to Rechtschaffen and Kales.38 The obstructive AHI was defined as the mean number of obstructive apneas and hypopneas per hour of sleep.

Statistical Methods
Continuous data were described as the mean, standard deviation, and 95% CIs. Non-normally distributed data and ordinal data were described in median and interquartile ranges (IQRs). Normally distributed data were analyzed with a paired-samples t test and a t test for independent samples. Non-normally distributed data and ordinal data were analyzed with the Mann-Whitney U test for independent samples and Wilcoxon test for paired samples. Linear regression analysis was used to adjust for baseline values and the AHI, BMI, age, and sex. The χ2 and McNemar tests were used to analyze categorical data. Comparisons between placebo device and the active oral appliance were made on outcome values at follow-up after 4 months of treatment. The SPSS 21 statistical software package (IBM) was used in all calculations and a P value less than .05 was considered significant.

Results

Patients
Ninety-six patients were randomized and 91 patients completed the study from May 2007 through August 2011 (eFigure 2 and eTable 1 in Supplement 2). The mean time between baseline and follow-up was 175 days (SD, 76; IQR, 133-195). The baseline characteristics are summarized in Table 1. The BMI did not change for either group during the study period.

All 45 patients in the active oral appliance group used their devices and they wore them for a mean of 96% of the nights (SD, 16%). In this group, 76% of the patients used the device for the whole night and the remaining 24% used their devices parts of the nights. All 46 patients in the placebo device group also used their devices. They used them on 83% of the nights (SD, 21%). In this group, 89% of the patients used them for the whole night. There were no differences in compliance with therapy (P = .49) or nightly use (P = .11).

Daytime Sleepiness and Quality of Life
Oral appliance therapy was not associated with improvements from baseline at 4 months when compared with placebo device therapy in daytime sleepiness, according to the ESS or the KSS, or in sleep latency (according to the OSLER test). From baseline to 4-month follow-up, an ESS score higher than 10 was reported by 53% at baseline and 24% at follow-up for the oral appliance group vs 54% at baseline and 40% at follow-up for the placebo device group (P = .11) (Figure 1A and Table 2). The median KSS score of 7 or higher measured 4 times daily for 1 week was 10 times (IQR, 8-14) at baseline and 7 times (IQR, 4-9) at follow-up for the oral appliance group vs 12 times at follow-up.

| Table 1. Baseline Characteristics for Patients With Daytime Sleepiness and Mild to Moderate Sleep Apnea Treated With an Oral Appliance or a Placebo Device |
|-------------------------------------------------|-----------------|----------------|-----------------|
| Oral Appliance Group (n = 45) | Placebo Device Group (n = 46) | P Value |
| Age, mean (SD) | 49.8 (10.6) | 54.1 (9.4) | .05 |
| BMI, mean (SD) | 27.6 (3.5) | 27.9 (3.5) | .77 |
| Neck size, mean (SD), cm | 42.6 (3.6) | 42.0 (3.7) | .37 |
| Women, No./total patients (%) | 12/45 (27) | 17/46 (37) | .29 |
| Women in or after menopause, No./total women (%) | 11/11 (55%) | 12/16 (75%) | .27 |
| Current smoker, No./total patients (%) | 6/45 (13) | 9/46 (20) | .42 |
| Alcohol intake every week, No./total patients (%) | 13/45 (29) | 12/45 (27) | .81 |

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

*Some patients responded with “did not know.”
(IQR, 6-15) at baseline and 8 times (IQR, 5-12) at follow-up for the placebo device group (P = .11) (Table 2). The mean sleep latency was 33 minutes (SD, 10) at baseline and 35 minutes (SD, 9) at follow-up for the oral appliance group vs 31 minutes (SD, 11) at baseline and 31 minutes (SD, 12) at follow-up for the placebo device group (P = .10) (Table 3).

There was no difference in any domain of the SF-36 health survey (eTable 2 in Supplement 2). The mean physical health score from baseline to 4-month follow-up was 45.9 (SD, 8.9) at baseline and 48.2 (SD, 8.4) at follow-up for the oral appliance group compared with 45.3 (SD, 8.5) at baseline and 46.0 (SD, 10.3) at follow-up for the placebo device group (P = .33). The mean difference between the placebo device group and the oral appliance group in the mental health score from the SF-36 questionnaire was −0.9 (95% CI, −5.6 to 3.8). The mean mental health score from baseline to 4-month follow-up was 44.3 (SD, 10.8) at baseline and 48.1 (SD, 9.7) at follow-up for the oral appliance group compared with 46.1 (SD, 10.5) at baseline and 47.2 (SD, 12.1) at follow-up for the placebo device group (P = .97).

There was no difference in any domain of the FOSQ, including general productivity, social outcome, activity level,
vigilance, or intimate relationships, between patients treated with the active oral appliance vs the placebo device at 4-month follow-up (eTable 3 in Supplement 2). The mean difference between the placebo device group and the active oral appliance group for the total FOSQ score was insignificant (−1.2 [95% CI, −2.5 to 0.1]). The FOSQ total score from baseline to follow-up was a mean of 16.1 (SD, 2.3) at baseline and 17.6 (SD, 2.3) at follow-up for the oral appliance group compared with 16.3 (SD, 2.6) at baseline and 16.4 (SD, 3.4) at follow-up for the placebo device group (P = .11).

Secondary Outcomes
The mean AHI at baseline was 15.6 (SD, 9.8) for the oral appliance group and 15.3 (SD, 10.5) for the placebo device group, without any difference between groups. The AHI was 6.7 (SD, 4.9) for the oral appliance group, which was significantly lower than in patients using the placebo device (16.7 [SD, 10.0]; P < .001) (Table 3, Figure 1B). An AHI lower than 5 was recorded in 49% of the patients using the oral appliance and in 11% of the patients using the placebo device (P = .001), with an odds ratio of 7.8 (95% CI, 2.6–23.5) and a number needed to treat of 3.

Total sleep time, sleep efficiency, and sleep stages did not differ between the oral appliance group compared with the placebo device group (Table 3). Patients spent more time sleeping supine with the oral appliance compared with the placebo device (P < .001) (Table 3).

Snoring appeared less than once a week during treatment with the oral appliance, which was less than with the placebo device (P < .001) (Table 2).

Weekly complaints of an urgent need to move the legs were less frequent with the oral appliance than with the placebo device (P = .02) (Table 2, Figure 2). Weekly symptoms of restless legs were reported in 13% of the oral appliance group and 32% of the placebo device group, with an odds ratio of 0.3 (95% CI, 0.1–0.9) and number needed to treat of 5.

The number of days with headaches and the intensity and character of headaches, nasal congestion, difficulty falling asleep at bedtime, nighttime awakenings, nightmares, and objective reaction time did not differ between the 2 groups (Table 2 and Table 3; eFigure 3 in Supplement 2).

Patients’ Expectations and Adverse Effects
Totally or sufficiently fulfilled expectations of treatment were reported in 73% of patients in the oral appliance group and 11% of patients in the placebo device group (P < .001). Eighty-nine percent of the patients in the oral appliance

### Table 3. Effect on Respiratory Variables and Sleep and Alertness From the Oral Appliance and the Placebo Device in 91 Patients With Mild to Moderate Sleep Apnea

<table>
<thead>
<tr>
<th></th>
<th>Oral Appliance (n = 45)</th>
<th>Placebo Device (n = 46)</th>
<th>Oral Appliance vs Placebo Device</th>
<th>Adjusted Oral Appliance vs Placebo Device*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td></td>
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<tr>
<td>Total sleep time, min</td>
<td>413 (44)</td>
<td>401 (57)</td>
<td>433 (63)</td>
<td>427 (59)</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>90.7 (8.1)</td>
<td>90.8 (9.3)</td>
<td>91.7 (5.7)</td>
<td>91.5 (6.5)</td>
</tr>
<tr>
<td>Supine sleep, %</td>
<td>35.0 (24.2)</td>
<td>42.0 (24.2)</td>
<td>37.7 (22.1)</td>
<td>30.8 (22.5)</td>
</tr>
<tr>
<td>AHI</td>
<td>15.6 (9.8)</td>
<td>6.7 (4.9)</td>
<td>15.3 (10.5)</td>
<td>16.7 (10.0)</td>
</tr>
<tr>
<td>AHI supine</td>
<td>26.7 (19.8)</td>
<td>10.8 (9.7)</td>
<td>28.0 (22.5)</td>
<td>28.6 (21.1)</td>
</tr>
<tr>
<td>AHI nonsupine, median (range)</td>
<td>9.7 (2.9 to 14.4)</td>
<td>4.9 (0.9 to 5.4)</td>
<td>9.8 (2.1 to 12.9)</td>
<td>11.5 (2.7 to 18.6)</td>
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<tr>
<td>Sleep stages, %</td>
<td></td>
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<tr>
<td>1</td>
<td>11.4 (6.4)</td>
<td>10.5 (5.3)</td>
<td>12.1 (6.8)</td>
<td>13.8 (11.0)</td>
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<tr>
<td>2</td>
<td>53.8 (8.6)</td>
<td>50.7 (7.1)</td>
<td>52.5 (10.4)</td>
<td>48.9 (10.4)</td>
</tr>
<tr>
<td>3 and 4</td>
<td>15.0 (6.9)</td>
<td>16.7 (6.9)</td>
<td>14.8 (8.0)</td>
<td>16.3 (7.7)</td>
</tr>
<tr>
<td>REM, %</td>
<td>20.2 (5.7)</td>
<td>21.9 (5.8)</td>
<td>20.8 (6.0)</td>
<td>21.1 (7.4)</td>
</tr>
<tr>
<td>OSLER test, min</td>
<td>33.1 (10.1)</td>
<td>34.6 (8.5)</td>
<td>31.3 (11.3)</td>
<td>30.9 (12.4)</td>
</tr>
<tr>
<td>MURT test, min</td>
<td>273 (62)</td>
<td>264 (54)</td>
<td>273 (55)</td>
<td>273 (68)</td>
</tr>
<tr>
<td><strong>Mean (95% CI)</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Total sleep time, min</td>
<td>12.1 (−8.3 to 32.4)</td>
<td>6.8 (−8.7 to 21.8)</td>
<td>25.7 (1.5 to 49.9)^</td>
<td>18.3 (−5.0 to 41.6)</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>−0.1 (−2.9 to 2.8)</td>
<td>0.2 (−1.4 to 1.9)</td>
<td>0.7 (−2.6 to 4.0)</td>
<td>1.2 (−1.6 to 4.0)</td>
</tr>
<tr>
<td>Supine sleep, %</td>
<td>−7.0 (−12.7 to −1.2)</td>
<td>6.9 (2.2 to 11.5)</td>
<td>−11.2 (−20.9 to −1.5)^</td>
<td>−13.4 (−20.3 to −6.0)^</td>
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<tr>
<td>AHI</td>
<td>8.9 (6.4 to 11.4)</td>
<td>−1.4 (−3.8 to 1.1)</td>
<td>10.0 (6.7 to 13.3)^</td>
<td>9.3 (6.6 to 12.0)^</td>
</tr>
<tr>
<td>AHI supine</td>
<td>15.7 (9.7 to 21.7)</td>
<td>−0.6 (−6.1 to 4.9)</td>
<td>17.8 (10.9 to 24.7)^</td>
<td>17.2 (10.9 to 23.5)^</td>
</tr>
<tr>
<td>AHI nonsupine, median (range)</td>
<td>P &lt; .001</td>
<td>P = .31</td>
<td>P &lt; .001</td>
<td></td>
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<tr>
<td>REM, %</td>
<td>9.1 (0.1 to 2.1)</td>
<td>1.1 (0.1 to 2.1)</td>
<td>−2.7 (−4.5 to −0.9)^</td>
<td>−1.9 (−3.3 to −0.5)^</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>88.0 (4.4)</td>
<td>88.6 (4.2)</td>
<td>87.0 (4.0)</td>
<td>85.9 (4.5)</td>
</tr>
<tr>
<td><strong>Abbreviations:</strong></td>
<td></td>
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<tr>
<td>AHI</td>
<td>apnea-hypopnea index</td>
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<tr>
<td>MURT</td>
<td>Multiple Unprepared Reaction Time</td>
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<tr>
<td>OSLER</td>
<td>Oxford Sleep Resistance</td>
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<tr>
<td>REM</td>
<td>rapid eye movement</td>
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<tr>
<td>SaO2</td>
<td>arterial oxygen saturation</td>
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group and 52% of the patients in the placebo device group were interested in continuing the treatment they had received (P < .001).

Adverse effects were more common with the oral appliance than with the placebo device, with more complaints of jaw pain (P = .004), tooth pain (P = .02), hypersalivation (P = .03), and bite changes (P < .001) (eFigure 4 in Supplement 2).

**Discussion**

Daytime sleepiness measured subjectively using the ESS and the KSS and measured objectively using the OSLER test did not differ using active or placebo devices among patients with daytime sleepiness and snoring or mild to moderate sleep apnea. Moreover, quality of life and functional outcomes of sleep did not differ between the oral appliance group and placebo device group. The oral appliance was significantly more effective than the placebo device in reducing sleep apneas, snoring, and symptoms of restless legs.

Previous studies had conflicting results; 3 smaller studies found no significant effect on the ESS score for an oral appliance vs a placebo device, whereas Gotsopoulos and colleagues, in the largest study to our knowledge, reported a small, significant reduction in a randomized, crossover study of patients with moderate sleep apnea. In the future, we suggest randomized clinical trials comparing oral appliances with continuous positive airway pressure on daytime sleepiness.

Aarab and colleagues compared the effect of an oral appliance with both a placebo device and continuous positive airway pressure, which is another alternative.

Quality of life and functional outcomes of sleep did not differ between using the oral appliance and placebo device among our patients. Few studies have evaluated the quality-of-life benefits of oral appliances vs placebo devices, but some positive effects on vigor, fatigue, and vitality domains are found in patients with moderate and severe sleep apnea.

In our trial, complaints of an urgent need to move the legs were significantly reduced from 41% at baseline to 13% at 4-month follow-up for the oral appliance group. Restless legs syndrome affects 5% to 10% of the general population and is more common in individuals with obstructive sleep apnea. The severity of the symptoms varies substantially, but it may have a strong effect on quality of life. In line with our data, an earlier study found improvements using continuous positive airway pressure on restless legs syndrome in patients with more severe sleep apnea.

The number of days with headaches, headache intensity, combinations of headaches, and morning headaches did not differ between the oral appliance and placebo device group in our study. More than 75% of our study sample had headaches. Headaches are common in patients with sleep apnea, are of the tension type, and usually appear at awakening. Continuous positive airway pressure reduces headaches to some degree. Uncontrolled studies report a reduction in headaches as a result of treatment with an oral appliance.

Future research on the effects of an oral appliance on headaches requires samples of patients with more specific headache diagnoses such as migraine, with or without aura, tension-type headache, or multiple types of headache.

The compliance rate was very high with both the oral appliance and the placebo device and 89% of the oral appliance group and 52% of the placebo device group reported an interest in continuing treatment with the same device. This indicates that the patients are often unable to define effective treatment in terms of apnea reduction. An objective estimation of treatment effects from oral appliances is therefore crucial to avoid suboptimal treatment effects.

A total of 1247 patients were investigated for a suspicion of sleep apnea at the Department of Respiratory Medicine during the study period (eFigure 2 in Supplement 2). Fifty-seven percent of patients were not considered eligible for an oral appliance by the respiratory physicians and were therefore not referred to the Department of Orthodontics. Thirty-five percent of referred patients were excluded by the dentist, as they did not fulfill the inclusion criteria for the study (eTable 1 in Supplement 2). The main reasons for exclusion were that they refused participation, were not sleepless, had severe sleep apnea, severe obesity, dental problems, or another treatment, or were not interested in treatment. Thus, many of the excluded patients were outside the generally accepted recommendation for treatment using an oral appliance and we found it unlikely that exclusion would bias the results.

The strengths of our study include the randomized design with few dropouts. An adjustable oral appliance, which permitted the titration of the lower jaw forward, was used. The intraoral placebo device did not restrict the lower jaw position during sleep. Another strength was that patients with snoring and mild to moderate sleep apnea were included (ie, the primary target group for oral appliances). Patients were investigated with polysomnography including a body position sensor. Sleep apneas are most prominent in the supine sleep position compared with other sleep positions. It was observed that patients using an active oral appliance slept more in the supine position than in nonsupine positions, indicating that the effect of an oral appliance in reducing sleep apneas was even more effective than the results of the AHI revealed (Table 3).

The limitations of our study include the study sample being smaller than intended because of difficulty finding patients fulfilling the inclusion criteria with daytime sleepiness among pa-
tients who snored and those with mild to moderate sleep apnea. We found no effect on subjective or objective measurements of daytime sleepiness when comparing an oral appliance with a placebo device in a selected group of patients with daytime sleepiness. On the other hand, we found a clear, significant treatment effect with a reduction in the AHI, indicating that the present results with no effect on daytime sleepiness are valid and not due to lack of power. We also included patients with an ESS score lower than 10 who reported daytime sleepiness from other questionnaires (n = 26) to include any patient with daytime sleepiness. On the other hand, this reduced the number of patients with severe sleepiness according to the ESS.

We found no difference in subjective compliance between active oral therapy and placebo treatment. Objective assessments of compliance with oral appliances were not available at the beginning of the study and the scientific relevance of subjective data are questionable. There is an inherent limitation to using subjective outcomes, including subjective compliance and symptoms of daytime sleepiness, snoring, and headache, as patients who are convinced of a therapeutic approach tend to describe the effects positively. Therefore, we have only reported effects vs placebo and not within-group effects.

We found that an oral appliance was effective in reducing snoring and sleep apneas but not daytime sleepiness. Daytime sleepiness occurs in a fraction of patients with sleep apnea. Therefore, we suggest an oral appliance when treating patients with mild to moderate sleep apnea without daytime sleepiness. However, for sleep apnea patients with daytime sleepiness, positive airway pressure therapy should be recommended as the first treatment of choice.

Conclusions
A custom-made, adjustable oral appliance reduces obstructive sleep apnea, snoring, and possibly restless legs without effects on daytime sleepiness and quality of life among patients with daytime sleepiness and snoring or mild to moderate sleep apnea.

ARTICLE INFORMATION
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Obstructive sleep apnea (OSA) is a major medical challenge: it affects 4% to 13% of the general population, impairs quality of life, and substantially increases the risk of motor vehicle accidents. Obstructive sleep apnea is associated with cardiovascular and metabolic consequences and increased mortality, particularly among the most severely affected patients. In severe OSA, the most effective treatment for respiratory dysfunction is continuous positive airway pressure (CPAP). However, many patients suffer from mild to moderate OSA, as indicated by the numbers of apneas and hypopneas per hour (mild, 5-15/hour; moderate, 15-30/hour; severe, >30/hour), often presenting to the primary care physician with disturbed sleep, daytime sleepiness, or impaired cognitive functions. The long-term effect of mild to moderate OSA is less clear. What is the most effective and most feasible treatment option for these patients? Because of the discomfort of CPAP, patients seek less burdensome and feasible treatment options. One intervention for which promising data are beginning to emerge are relatively simple devices that move the mandible into a more anterior position to treat OSA, known as mandibular advancement devices (MADs). These oral appliances reposition the lower jaw forward and down and widen the upper airways, thus improving upper airway resistance and reducing the likelihood of apneas and hypopneas.