REVIEW ARTICLES

http://dx.doi.org/10.15331/jdsm.4138

Current Barriers and Study Needs for Oral Appliance Therapy: The Personal Perspective of a Physician and Dentist

Bernard Fleury, MD[1]; Alan A. Lowe, DMD, PhD[2]; ORal Appliance Network for Global Effectiveness Group

[1]Centre d'Evaluations et de Traitements des Troubles du Sommeil, Hôpital Saint Antoine-Hôpitaux Universitaires Est Parisien-Université, Paris, France; [2]Professeur invité, UFR d'Odontologie University Paris Diderot, Division of Orthodontics, Faculty of Dentistry, University of British Columbia

From the perspectives of a physician and a dentist, this review article summarizes the major barriers which appear to restrict the increased use of oral appliances in comparison to CPAP for the treatment of sleep disordered breathing. Barriers related to organizational issues, industrial development, differing effectiveness, contraindications, and side effects are discussed in detail. In addition, the perceived barriers between the dental and medical professions at large are outlined. Patients should actively participate in the choice of treatment after they have been informed of the benefits and limitations of both therapies.

Keywords: oral appliance, obstructive sleep apnea, CPAP

Citation: Fleury B, Lowe AA, ORal Appliance Network for Global Effectiveness Group. Current barriers and study needs for oral appliance therapy: the personal perspective of a physician and dentist. *Journal of Dental Sleep Medicine* 2014;1(3):123–127.

Due to its high prevalence and multiple consequences, the obstructive sleep apnea syndrome (OSAS) is a major public health problem. In a recently published study, this problem in France was addressed among 12,203 adults representative of the general population.[1] The prevalence of symptoms highly suggestive of OSAS such as snoring most nights plus witnessed apneas and/or excessive daytime sleepiness (Epworth Sleepiness Scale score > 10) was estimated at 4.9%, which is close to the prevalence reported in the epidemiological literature.[2] This prevalence reached 8% in hypertensive patients and 11% in obese subjects; only 15% of these subjects with a high probability of having OSAS who require treatment in our sample had undergone a sleep study. This underdiagnosis and undertreatment of OSAS is currently reported across the international medical literature.[3]

However, in 1981 effective treatment for sleep apnea was first identified when Collin Sullivan proposed a simple device called continuous positive airway pressure (CPAP) to alleviate the pharyngeal occlusion which occurred during sleep.[4] Room air applied through the nares with a continuous positive pressure provided a pneumatic splint for the nasopharyngeal airway and was a safe and incredibly clever treatment for the OSAS syndrome. But, concurrently with the Sullivan publication, two studies reported the use of oral appliances (OA) to maintain the stability of the upper airway in OSAS patients. Cartwright and Samelson published the first description of the beneficial action of a tongue retaining device in 1982,[5] and three years later, Soll and George published a brief note on the effectiveness of a modified one piece mandibular advancement appliance in a series of five patients.[6] Since then, hundreds of reports have been published in the literature about similar OAs. Nevertheless, some thirty years later, CPAP is accepted as the standard treatment for OSAS and OAs are often used primarily as an alternate therapy when CPAP fails or is not tolerated by the patient. For instance, some 400,000 OSAS patients in France are chronically treated with CPAP and 75,000 new CPAP patients are fitted every year. However, only 15,000 patients are treated long term with OAs, with approximately 3,500 new OA patients added every year.

Why does such a huge difference exist between CPAP and OA use after all these years and the incredible amount of published data that support OA efficacy? What are the possible barriers to the prescription of an OA compared to the prescription of a CPAP machine?

We have identified six major barriers to the development of OA therapy:

1. Barriers related to organizational issues
2. Barriers linked to industrial development
3. Barriers linked to different effectiveness
4. Barriers related to contraindications
5. Barriers related to side effects
6. Barriers between dental and medical professionals

1. Barriers related to organizational issues

For more than two decades, the effects of CPAP on sleep disordered breathing in all stages of sleep, including REM sleep, and in the supine body position was determined by a sleep technician during full-night polysomnography in a sleep laboratory. Today, it is very easy to prescribe a CPAP machine. The use of auto-titrating positive pressure (APAP), with comparable efficiency to that of fixed pressure machines, allows one to simplify the care and avoid a night in the sleep lab.[7] If the practitioner wishes, one can choose a fixed pressure from APAP records obtained over a few weeks of treatment. According to the local insurance reimbursement guidelines, the patient either buys the device and mask directly or they are provided by the social security system via a health homecare provider, as in France for instance. Finally, for the sleep physician, a prescription or a phone call is sufficient to start the treatment. An ambulatory follow-up, after 1 or 2 months of treatment and every year thereafter, is often sufficient to provide adequate care.

To prescribe an OA is much more complicated. After the sleep recording, the sleep physician must refer the patient to a dentist with training in dental sleep medicine who will verify the absence of any intraoral contraindications, select one appliance suitable for the specific patient, and obtain impressions

of the dentition and a bite registration to be sent to a laboratory. After one to three weeks, the definitive OA is obtained and the dentist will adjust the appliance in the patient's mouth to make it comfortable to wear. The titration procedure of slowly advancing the mandible will then begin, the efficacy of which is usually monitored by a sleep recording. It can take several weeks or months and a number of appointments with the dentist.[8] Finally, follow-up should take place once a year by the attending physician and twice a year by the dentist. It is easier and faster and less labor-intensive to prescribe a CPAP device than an OA.

2. Barriers linked to industrial development

From the outset, industry has been interested in the manufacture of CPAP. From 1985, the companies SEFAM and Pierre Medical were created in France; Respironics and DeVilbiss appeared in the USA; ResMed in Australia; and since then many others have started manufacturing around the world. Over the years, the engineers of Pierre Medical,[9] ResMed,[10] and other companies have developed algorithms allowing for auto-titration of effective pressure. Industrial grouping has created marketing giants on the five continents. For any CPAP device, the therapeutic principle to establish a positive pressure in the upper airways is the same. The equivalence of the different CPAP devices is complete for a fixed pressure. The algorithms piloting the APAP vary model by model, but globally their efficiency is satisfactory and a simple modification of the range of pressures chosen initially allows one to correct the SDB. Masks that were initially customized for each patient are today industrially designed and offer a large choice to facilitate implementation of the treatment.

In contrast, OA manufacturing is a more recent phenomenon, which has no scale comparable to the industrial process with CPAP. During many years, more than 100 OAs have been described by a number of inventors. Many were derived from traditional orthodontic appliances, and their design, volume, and structural components differ. Even the principle of action on the mandible, tongue, or both differ. For many appliances, the manufacturing process has not been standardized.[11] More recently, validated OA manufacturing has emerged according to laboratory controlled processes both in North America and internationally.

3. Barriers linked to different effectiveness

Today the effectiveness of a treatment is judged according to the principles of evidence-based medicine. This requires evaluation protocols that are rigorous, prospective, and randomized. To discuss the individual effectiveness of CPAP and OA and to compare their effectiveness, we rely on the systematic analysis of the literature carried out by the Cochrane group. A systematic review has been devoted to each treatment. In 2006, 36 trials were selected to evaluate CPAP, including 1,718 subjects.[12] In 2006, only 17 trials were included to evaluate OAs (including 846 subjects), that were considered methodologically satisfactory by the very demanding group of experts of the Cochrane group.[13] What were the results of their analyses as to the effectiveness of CPAP or OA on the objective parameters of a polysomnographic recording? When the efficacy of CPAP and OA is evaluated on the same patients, the reduction in AHI is systematically greater with CPAP. Whether from crossover or parallel arm studies, the apnea-hypopnea index (AHI) appears to be lower in the group treated with effective CPAP. However, the Cochrane data did not differentiate between single jaw position and titratable OAs, which has a major impact on efficacy. When a titrated OA is compared to a simple splint, the AHI is always lower in the titrated group. For AHI, when mandibular advancement devices were compared with devices that did not advance the mandible, there was a significant effect in favor of active advancement when compared to controls.

This overall superiority in effectiveness of CPAP over OA encompasses a more complex reality. Although CPAP is mechanically effective, three groups of responders to OA can be distinguished as reported in *Chest* in 2004.[14] After careful OA titration, more than half of patients will have their AHI brought to a level comparable to that obtained with CPAP, while about one-quarter will be treatment failures. Between these two groups, one-quarter of patients decreased their AHI by over 50%. This difference in effectiveness is easy to understand if we analyze the mode of action of the two treatments. CPAP increases the overall volume of the upper airway. The level of pressure required to open the airway depends on the subject, but is usually within a reasonable range of pressures that are tolerable to the patient. There is limited mechanical failure with CPAP.

The mode of action of an OA is more complex. Chan et al. reported that mandibular advancement increases the total airway volume predominantly by increasing the volume of the velopharynx.[15] More recently, Brown and al. described a complex movement of the airway associated with a lateral movement of the lateral wall of the nasopharynx via its connections to the mandible.[16] This was associated with an anteroposterior elongation of the tongue overall and a rostrocaudal compression of the posterior tongue. On sequential MRI sections performed during progressive mandibular advancements, one can see the hyoid bone moves upward, resulting in a flattening of the floor of the mouth and a widening of all segments of the pharynx. This upward movement of the hyoid bone was described by Battagel et al., who emphasized its wide variation both in the amount and direction of movement between subjects.[17] Depending on the subject's anatomy, the level of advancement leading to widening of the pharynx may be different. Movement of tissues with OAs is influenced by both anatomical and physiological differences between patients.

OSAS is a chronic disease whose effects on alertness or mood decrease the quality of life of patients.[18] The suppression of abnormal respiratory events by OA or CPAP and their consequences on sleep architecture improves the quality of life of patients.[12,13] Both therapies are only palliative. Which procedure finally brings the greatest improvement in the quality of life? Recently, the Cistulli group compared health effects after one month of optimal CPAP and OA therapy in OSA subjects with a randomized crossover design.[19] Cardiovascular (24-h blood pressure, arterial stiffness), neurobehavioral (subjective sleepiness, driving simulator performance), and quality of life (FOSQ, SF-36) indices were compared between treatments in 126 patients with moderate-to-severe OSAS. Important health outcomes were similar after one month of optimal OA and CPAP treatment. Less discomfort associated with an OA and the close effectiveness on alertness probably explain the results of several studies, which most often conclude a similar improvement in quality of life with OA and CPAP. It could explain why, with equivalent effectiveness, the vast majority of patients prefer an OA.[20]

Adherence with treatment is a key factor, because a less effective OA worn for longer time periods could ultimately have an identical efficacy on the consequences of OSAS. Adherence with OA is likely to be better than adherence with CPAP. Vanderveken et al. recorded an overall objective mean adherence of OA use to be 6.6 hours per night at the 3-month follow-up, and they calculate the mean disease alleviation (MDA) as the product of objective compliance and therapeutic efficacy.[21] MDA serves as a measure of the overall therapeutic effectiveness and turned out to be 51.1% with OA, a value comparable to the MDA reported with CPAP.[22] In the near future, RCT studies will integrate OA adherence monitors to answer these crucial issues over longer time periods.

4. Barriers related to contraindications

Contraindications for OAs are determined in part by the specific appliance used and the patient's overall dentition and dental health. OAs can only be used in patients able and willing to use an OA and are occasionally not tolerated because of claustrophobia issues, although clinicians who have experience with both therapies report much less so than with CPAP. Current practice parameters suggest that OAs are indicated in patients with primary snoring and mild to moderate OSA.[23] They are not generally used in patients with central apnea. OAs have been contraindicated in severe OSA patients unless an unsuccessful trial of CPAP has been completed, but more recent data challenge this specific guideline.[19] OAs should be selected, fitted, and adjusted by qualified dentists who are adequately trained in the field and not by individuals who are not licensed by their local regulatory authority to do so. Mild to moderate TMJ dysfunction is not currently recognized as a contraindication to OA therapy. OAs are commonly used in patients with at least eight teeth in each arch and no limitation in vertical and/or AP jaw position. The ability to comfortably reposition the jaw forward is absolutely mandatory, as is the requirement to adequately open the mouth vertically to allow for placement of the OA.[24,25]

In subjects who are edentulous, do not have at least eight teeth in both arches, have severe limitations in the anteroposterior position of the mandible, or who have significant periodontal disease, traditional OAs may be contraindicated. Instead an appliance such as a tongue repositioner/stabilizer[26] could be used, which delivers less force directly to the teeth and distributes the pressure over other intraoral sites. However, tongue retaining devices are generally contraindicated in obligate mouth breathers, since it may be difficult to breathe through the mouth with these appliances.

5. Barriers related to side effects

Short-term side effects, similar to the insertion of any new dental appliance/prosthesis placed in the mouth, may include excessive salivation, dry mouth (especially in obligate pretreatment nasal breathers), and tooth discomfort. Minor soft tissue discomfort can also occur during the first few weeks of OA wear. Lack of adequate retention is primarily an appliance design issue, dependent in part on which of the OAs currently available on the market is being used and how it has been manufactured. Either too little or too much retention may be a contraindication for a specific appliance. Initial transient side effects usually resolve within several days to several weeks with minor adjustments by the dentist and continued adaptation to the OA by the patient.

More significant side effects may occur during the OA titration stage, which may in some patients continue over several months as the mandible is gradually moved forward. These may include minor tooth movement, occlusal contact changes, soft tissue issues, and TMJ/myofascial discomfort. A sense of the teeth not touching in the morning is reported in some patients. Initial jaw discomfort is often an indication of repositioning the mandible too far forward. Initial titration side effects, if not readily recognized and managed by the dentist, can be a significant deterrent for continued use of an OA in some patients and is one of the main reasons for the need for frequent appointments during this stage of therapy.

Long-term OA side effects (potential tooth movement and myofascial issues) have been well documented.[26-28] Some 14% of OSA patients who had worn a mandibular repositioning appliance for five years or longer were found to have no change in their occlusion, 42% had a favorable change, and 44% had an unfavorable change.[27] Patients with larger overbites and overjets had the most favorable occlusal changes based on cephalometric and study model analyses. Mandibular arch width increased more than maxillary arch width, crowding decreased in both arches, the curve of Spee became flat in the premolar area, the mandibular canine to second molar segment moved forward in relation to the maxillary arch, the bite opened and the overjet decreased. Both jaw exercises and morning repositioning splints have been suggested as potential therapies to reduce occlusal changes when they occur. The most common tongue appliance-induced dental changes included anterior and/or unilateral posterior open bites and reduced anterior overjets.[26] Two possible mechanisms for the TRD side effects have been suggested—one is the forward pressure of the tongue on the anterior dentition and the other is the lateral pressure of the tongue directly on the posterior arch.

Even unfavorable dental side effects should not be considered a contraindication to OA therapy, since occlusal changes are usually readily adapted to by patients when compared to the consequences of life-threatening OSA. It is also important to recognize that two years of nasal CPAP wear may also cause dental and skeletal changes due to the pressures exerted by the mask and straps on the anterior maxilla.[29] After nCPAP use, cephalometric variables demonstrated a significant retrusion of the anterior maxilla, a decrease in maxillary-mandibular discrepancy, a setback of the supramentale and chin positions, a retroclination of maxillary incisors, and a decrease in facial convexity. In summary, both OAs and CPAP have definable long-term effects on dentition.

There appears to be no evidence of consistent undesirable long-term effects of OAs on the TMJ. Indeed, it appears that the intensity of TMJ symptoms decreases significantly throughout treatment in patients who use their OA regularly due possibly to the unloading of the joint when the condyle is held down and out of the fossa by the OA and/or the resolution of tooth grinding observed subsequent to improved sleep parameters. A crossover study of an adjustable OA and a mandibular occlusal splint in sleep bruxism patients found that an OA reduced sleep bruxism episodes to a greater extent than a splint alone.[30] If myofascial problems due to the jaw not settling back to its regular position

throughout the day are not resolved during the first few weeks, specific jaw exercises (jig exercise and stretching movements) may reduce the occlusal functional impairment.[31] Both exercises produced significant increases in occlusal contact area and bite force in the morning compared with periods of no exercise. There was no significant difference between the two exercises, although the jig exercise tended to be more effective in the anterior region while the stretching movements tended to more effective in the molar region. Using MRI, OAs did not result in any observable remodeling of the TMJ. Remodeling was not observed after 11.5 months, which suggests that the appliance does not significantly alter the TMJ, but long-term studies with a greater sample size are required to determine whether there is a remodeling of the TMJ or neighboring structures after two or more years.[32]

Different side effects have been documented for thermoplastic boil and bite type OAs (especially those only available in one preformed size) when compared to custom-made titratable appliances. Difficulty in optimum fit has been documented, and "uncomfortable" appears to be the most common reason to stop wearing a boil and bite appliance.[33] A clinical trial where both types of appliances were used in the same patients for a period of four months identified that the AHI was only reduced with the custom-made device and that it also reduced snoring to a greater extent than the thermoplastic device.[34] The success rate was higher with the custom-made device (60% vs. 31%). One-third of the patients demonstrated adherence failure with the thermoplastic device mainly because of insufficient overnight retention. Total failure rate with the thermoplastic device was 69%; the majority (63%) of these were successfully treated with the custom-made device. At the end of the study, a large majority of the patients chose the custom-made device.

6. Barriers between dental and medical professionals

Based on our joint clinical experiences as a sleep physician and an orthodontist over the past three decades, it appears that a number of barriers between the dental and medical professions have slowed down the wide acceptance of OAs for the treatment of OSAS. Although both groups are credentialed by their respective professional organizations, dentists often receive their education in sleep from continuing dental education courses and oral appliance manufacturers whereas physicians can obtain formal training as sleep specialist and from those CPAP companies who also market oral appliances. Dentists often see patients of various ages in a clinical setting where they may suspect sleep disordered breathing. Sleep physicians traditionally operate referral practices. Dentists depend on a medical diagnosis from a physician and, on occasion, use ambulatory monitoring as an aid to titration. In contrast, physicians routinely utilize both polysomnographic studies and ambulatory monitors. Dentists often refer patients to physicians for sleep issues and physicians on occasion refer patients to dentists. Appliance choices are made by dentists based on continuing education courses and oral appliance manufacturers. Physicians are more likely to learn of oral appliance types from the literature or CPAP suppliers. As to titration tools, it may take several months for a dentist to titrate an oral appliance based on symptomatic improvement or ambulatory monitoring. Physicians often utilize polysomnography or autoPAP for CPAP titration. Payment for oral appliance follow up may be an insurance issue in many jurisdictions. Dentists readily observe and manage oral appliance side effects, but physicians may not understand the significance of occlusal changes and generally are unaware of the long-term effects of oral appliances on dentition. Outcome measurements differ between dentists, who use snoring and symptomatic improvement to reduce the AHI to less than 10/h, and physicians who utilize both polysomnographic and ambulatory monitoring and often look for a reduction in AHI to less than 5/h, similar to what they use with CPAP. Physicians also emphasize improved oxygenation and decreased arousals when they evaluate outcomes and generally have lower expectations of oral appliance effectiveness. Dentists generally follow their patients annually and replace the oral appliances every three to five years, whereas physicians traditionally respond to patient requests for recall appointments, and the CPAP provider is more actively involved in the long-term maintenance of the patient. From a patient management perspective, some or all of these factors have been shown to be barriers between the medical and dental professions when oral appliances are used.

Future Considerations

Based on this analysis of the barriers to the continued development of OA use, we would like to make several proposals for the future. OA therapy has a definite place in the treatment decision-making process for OSAS. A better knowledge by sleep physicians of the current data on the efficiency of OA therapy according to principles of evidence-based medicine is required. Tests of OA titration efficacy with a cost-effective portable monitoring system as used by some dentists could be an elegant way to convince the sleep physician to prescribe future OAs after being reassured of their efficacy. In addition, the sleep community has to admit that if CPAP remains the reference treatment of OSAS, it is only effective if it is worn during adequate time periods every night. Clinicians who routinely utilize both therapies report that long term adherence with CPAP is a major issue and that the adherence with OA appears to be superior. However, randomized controlled trials to compare objective adherence for both OA and CPAP patients are required to accurately quantify these differences. It could be debated whether greater adherence with a less effective treatment might lead to a similar result in term of vigilance or cardiovascular outcomes. The place of CPAP as reference treatment could be challenged. The patient, informed about the benefits and limitations of the two treatments, should participate in the choice of treatment, even in the case of severe OSA. Apart from those patients with a major impairment in alertness that puts them or the community at risk or patients with unstable cardiovascular disease, for the majority of cases we have the opportunity to choose the most appropriate treatment.[35]

In all cases, it is necessary to improve the options offered to the patient as to the possibility of being treated with an OA. In the future, it is therefore obligatory to include sleep medicine in the undergraduate education of both dentists and physicians, preferably in a collaborative way. Hand in hand with that development, the creation and enhancement of specific academic and nonacademic training programs in dental sleep medicine are highly desired in order to significantly increase the number of trained dentists able to adequately respond to the requests of sleep physicians. This will promote the communication between sleep physicians and dental sleep practitioners.

Finally, these barriers for the prescription of OAs are likely to have different impacts according to specific countries or continents. If we wish to better establish OA therapy in the therapeutic strategy of OSAS, it is imperative that we understand the place of OA in the therapeutic strategies around the world. It is in this spirit that an international group of trained practitioners from the USA, Canada, Japan, and Europe met under the auspices of the AADSM to construct ORANGE36, a large cohort of OA patient data that will allow us to gradually answer the questions that we ask ourselves today.

REFERENCES

1. Furhman C, Fleury B, Nguyen XL, Delmas MC. Symptoms of sleep apnea syndrome: high prevalence and underdiagnosis in the French population. *Sleep Med* 2012;13:852-8.
2. Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, Hla KM. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort study. *WMJ* 2009;108:246-9.
3. Mold JW, Quattlebaum C, Schinnerer E, Boeckman L, Orr W, Hollabaugh K. Identification by primary care clinicians of patients with obstructive sleep apnea: a practice-based research network (PBRN) study. *J Am Board Fam Med* 2011;24:138-45.
4. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981;18:862-5.
5. Cartwright RD, Samelson CF. The effects of a nonsurgical treatment for obstructive sleep apnea. The tongue-retaining device. *JAMA* 1982;248:705-9.
6. Soll BA, George PT. Treatment of obstructive sleep apnea with a nocturnal airway-patency appliance. *N Engl J Med* 1985;313:386-7.
7. Nolan GM, Doherty LS, Mc Nicholas WT. Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. *Sleep* 2007;30:189-94.
8. Almeida FR, Lowe AA. Principles of oral appliance therapy for the management of snoring and sleep disordered breathing. *Oral Maxillofac Surg Clin North Am* 2009;21:413-20.
9. Meurice JC, Marc I, Sériès F. Efficacy of auto-CPAP in the treatment of obstructive sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med* 1996;153:794-8.
10. Gagnadoux F, Rakotonanahary D, Martins de Araujo MT, Barros-Vieira S, Fleury B. Long-term efficacy of fixed CPAP recommended by Autoset for OSAS. *Sleep* 1999;15:1095-9.
11. Ahrens A, McGrath C, Hägg U. A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnoea. *Eur J Orthod* 2011;33:318-24.
12. Giles TL, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2006 Jul 19:CD001106.
13. Lim J, Lasserson TJ, Fleetham J, Wright J. Oral appliances for obstructive sleep apnoea. *Cochrane Database Syst Rev* 2006 Jan 25:CD004435.
14. Fleury B, Rakotonanahary D, Petelle B, et al. Mandibular advancement titration for obstructive sleep apnea: optimization of the procedure by combining clinical and oximetric parameters. *Chest* 2004;125:1761-7.
15. Chan AS, Lee RW, Srinivasan VK, Darendeliler MA, Grunstein RR, Cistulli PA. Nasopharyngoscopic evaluation of oral appliance therapy for obstructive sleep apnoea. *Eur Respir J* 2010;35:836-42.
16. Brown EC, Cheng S, McKenzie DK, Butler JE, Gandevia SC, Bilston LE. Tongue and lateral upper airway movement with mandibular advancement. *Sleep* 2013;36:397-404.
17. Battagel JM, Johal A, L'Estrange PR, Croft CB, Kotecha B. Changes in airway and hyoid position in response to mandibular protrusion in subjects with obstructive sleep apnoea (OSA). *Eur J Orthod* 1999;21:363-76.
18. Karkoulias K, Lykouras D, Sampsonas F, et al. The impact of obstructive sleep apnea syndrome severity on physical performance and mental health. The use of SF-36 questionnaire in sleep apnea. *Eur Rev Med Pharmacol Sci* 2013;17:531-6.
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;187:879-87.
20. Gagnadoux F, Fleury B, Vielle B, et al. Titrated mandibular advancement versus positive airway pressure for sleep apnoea. *Eur Respir J* 2009;34:914-20.
21. Vanderveken OM, Dieltjens M, Wouters K, De Backer WA, Van de Heyning PH, Braem MJ. Objective measurement of compliance during oral appliance therapy for sleep-disordered breathing. *Thorax* 2013;68:91-6.
22. Ravesloot MJ, de Vries N. Reliable calculation of the efficacy of non-surgical and surgical treatment of obstructive sleep apnea revisited. *Sleep* 2011;34:105-10.
23. Kushida C, Morgenthaler T, Littner M, et al. Practice parameters for the treatment of snoring and OSA with oral appliances: an update for 2005. *Sleep* 2006;29:240-3.
24. Chen H, Lowe A. Updates in oral appliance therapy for snoring and OSA. *Sleep Breath* 2013;17:473-86.
25. Cistulli P, Ferguson K, Lowe A. Oral appliances for sleep disordered breathing. In: Kryger M, Roth T, Dement W, eds., *Principles and practice of sleep medicine.* Elsevier Saunders, Quintessence, 2011:1266-77.
26. Chen H, Lowe AA, Strauss AM, de Almeida FR, et al. Dental changes evaluated with a 3D computer-assisted model analysis after long-term tongue retaining device wear in OSA patients. *Sleep Breath* 2008;12:169-78.
27. Almedia F, Lowe A, Otsuka R, et al. Long-term sequelae of oral appliance therapy in OSA patients. Part 2. Study model analysis. *Am J Orthod Dentofacial Orthop* 2006;129:205-13.
28. Marklund M, Franklin K, Persson M. Orthodontic side effects of mandibular advancement devices during treatment of snoring and sleep apnoea. *Eur J Orthod* 2001;23:135-44.
29. Tsuda H, Almeida F, Tsuda T, Moritsuchi Y, Lowe A. Craniofacial changes after two years of nCPAP use in OSA patients. *Chest* 2010;138:870-4.
30. Landry-Schonbeck A, de Grandmont P, Rompre P, Lavigne G. Effect of an adjustable mandibular advancement appliance on sleep bruxism: a crossover sleep laboratory study. *Int J Prosthodont* 2009;22:251-9.
31. Ueda H, Almeida F, Chen H, Lowe A. The effect of two jaw exercises on occlusal function in OSA patients during oral appliance therapy–a randomized controlled trial. *Am J Orthod Dentofacial Orthop* 2009;135:430-1.
32. de Almeida FR, Bittencourrt LR, de Almeida CI, Tsuiki S, Lowe AA, Tufik S. Effects of mandibular posture on OSA severity and the temporomandibular joint in patients fitted with an oral appliance. *Sleep* 2002;25:507-13.
33. Tsuda H, Almeida F, Masumi S, Lowe A. Side effects of boil and bite type oral appliance therapy in sleep apnea patients. *Sleep Breath* 2010;14:227-32.
34. Vanderveken O, Devolder A, Marklund M, et al. Comparison of a custom-made and a thermoplastic oral appliance for the treatment of mild sleep apnea. *Am J Respir Crit Care Med* 2008:178:197-202.
35. Krucien N, Gafni A, Fleury B, Pelletier-Fleury N. Patients' with obstructive sleep apnoea syndrome (OSAS) preferences and demand for treatment: a discrete choice experiment. *Thorax* 2013:68:487-8.
36. Almeida F, Vanderveken O, Cistulli P, et al. ORal Appliance Network on Global Effectiveness (ORANGE): start-up and design description. *Journal of Dental Sleep Medicine* 2014;1;17-20.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication January, 2014
Submitted in final revised form May, 2014
Accepted for publication May, 2014

Address correspondence to: Bernard Fleury, MD, Centre d'Evaluations et de Traitements des Troubles du Sommeil, Hôpital Saint Antoine, 184 rue du Faubourg Saint Antoine-75012 Paris, France; E-mail: Bernard.fleury@sat.aphp.fr

DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Fleury holds an oral appliance patent. Dr. Lowe holds an adjustable oral appliance patent.