Alternatives to CPAP in the treatment of the obstructive sleep apnoea syndrome

Konrad E. Bloch

Pulmonary Division, Department of Internal Medicine, University Hospital of Zürich, Switzerland

Summary

The obstructive sleep apnoea syndrome (OSAS) results in excessive daytime sleepiness, impaired quality of life, and is associated with an increased risk of traffic accidents and cardiovascular disease. Nasal continuous positive airway pressure (CPAP), the standard treatment for OSAS provides immediate relief of symptoms and has only minor side effects. Nevertheless, an alternative treatment is needed if CPAP is not feasible for medical or psychological reasons. Removable oral appliances that advance the mandible when fitted to the teeth during sleep also improve nocturnal breathing disturbances, symptoms, quality of life, vigilance and blood pressure in OSAS patients. Their long-term effectiveness and side effects require further study. In morbidly obese patients suffering from OSAS bariatric surgery should be considered as a treatment that reduces obesity and at the same time improves OSAS. In selected patients including those with adeno-tonsillar hypertrophy, and cranio-facial malformations various surgical techniques that enlarge the upper airway may be a treatment option for OSAS.

Key words: sleep apnoea hypopnea; treatment; continuous positive airway pressure; mandibular advancement device; oral appliance; uvulopalatopharyngoplasty; nasal surgery; obesity; bariatric surgery

Introduction

The obstructive sleep apnoea syndrome (OSAS) is characterised by intermittent collapse of the upper airway during sleep resulting in hypopnoea, apnoea, repetitive oxygen desaturation and sleep disruption [1]. Daytime consequences include excessive sleepiness, impaired cognitive performance, disturbed mood, and reduced quality of life [2, 3]. The increased risk of traffic accidents due to sleepiness is an obvious individual and public health concern [4]. Furthermore, OSAS is an independent risk factor for hypertension [5], myocardial infarction [6] and stroke [7]. Epidemiological studies have suggested that 2 to 4% of the adult population suffer from OSAS [8] but the prevalence may have increased with the epidemic of obesity [9]. The diagnosis of OSAS relies on typical symptoms including excessive daytime sleepiness and lack of concentration, habitual snoring, nocturnal choking, and witnessed apnoea [10]. Male gender, obesity, a large neck size [11] and certain cranio-facial characteristics further enhance the suspicion of OSAS [12]. The diagnosis is confirmed by a sleep study.

General treatment recommendations for patients with OSAS include sufficient and regular sleep hours (sleep hygiene), avoidance of smoking and alcohol consumption, and diet to reduce weight in obese patients. However, a persistent weight reduction is difficult to achieve and maintain, and behavioural modification is only minimally effective [13]. The current standard treatment for OSAS consists in nocturnal application of continuous positive airway pressure (CPAP) via a nasal mask [14]. Several randomised trials have established the effectiveness of CPAP in patients with various degrees of OSAS severity [15, 16]. Excessive sleepiness and other symptoms, quality of life, objective vigilance, driving simulator performance and other cognitive tasks are significantly improved by CPAP over baseline when compared to treatment with sham (placebo) CPAP or placebo medication [17, 18]. The effect size achieved with CPAP for several clinical outcomes is large or moderate, and is largest in the most severe cases of OSAS [17, 19, 20]. In addition to providing symptomatic improvement, there is evidence that CPAP reduces fatal and nonfatal cardiovascular events in moderate to severe OSAS [6], and modifies cardiovascular risk since it reduces blood pressure [21] and circulating markers of cardiovascular risk such as cholesterol [22], C-reactive protein and interleukin-6 [23]. Side effects of CPAP therapy are generally mild and reversible [16].

Current guidelines suggest treatment of *symptomatic* OSAS patients with more than 5 to 30 apnoea/hypopnoea per hour of sleep [24] depending

Supported by Grants from the Swiss National Science Foundation and the Lung League of Zurich.

on severity of symptoms and comorbidity. Generally, severely symptomatic patients with frequent apnoea/hypopnoea (>30 events/hour) readily improve with CPAP therapy. Conversely, in asymptomatic patients even with a markedly elevated apnoea/hypopnoea index (>30 events/h), there was no measurable benefit of CPAP therapy [25]. In practice, a trial of CPAP therapy over a limited time period may help to identify patients who might benefit from long-term therapy [26]. In a recent study we even found that a favourable response to a 2-week CPAP trial was more accurate in predicting OSAS patients successfully treated over >4 months than polysomnography, the conventional diagnostic "gold-standard" for OSAS [27]. In summary, OSAS therapy is performed to improve symptoms and quality of life, and to prevent sleepiness-related accidents. Treatment of asymptomatic patients solely for correction of a laboratory abnormality, ie, for reducing an increased apnoea/hypopnoea index, or for reduction of the cardiovascular risk or prevention of potential disease progression is not established.

Despite its effectiveness CPAP therapy is used less then prescribed [28, 29]. This may relate to the inconvenience of the therapy, psychological factors, discomfort due to the pressure, skin irritation and other factors. In patients not able or not willing to perform CPAP therapy other treatment options have to be considered. The purpose of this article is to review the current alternatives to CPAP in the treatment of OSAS.

Mandibular advancement devices

Removable oral appliances are attractive treatment options for patients with OSAS not able or not willing to tolerate the standard CPAP therapy [30–33]. This is because oral appliances are easy to apply, handy, not dependent on electricity and thus particularly suitable for the use during travel. Furthermore, sleeping with an oral appliance is perceived as less socially disturbing than wearing a CPAP mask. The most effective oral appliances used today are designed to hold the mandible in an anterior position (protrusion). The so-called mandibular advancement devices (MAD) are fitted onto the lower and upper dental arches before going to sleep and removed in the morning (figure 1). They increase the upper airway lumen during sleep by protrusion of the mandible and tongue [34], increase the upper airway muscle tone [35], and reduce the passive pharyngeal wall compliance [36].

Several randomised studies, some of them using a sham appliance without mandibular advancement or medication as a placebo control, have demonstrated that MAD are effective in controlling symptoms of OSAS, nocturnal breathing disturbances, oxygenation and sleep disturbances, and even blood pressure [37–39]. In one study, patients with mild sleep apnoea (less than 30 apnoea/hypopnoea per hour of sleep) were randomised to a sequence of 3 periods of 3 months with either a MAD, nasal CPAP or a placebo tablet [40]. At the end of each 3-month period, the outcomes were compared. CPAP and MAD significantly improved symptoms to a similar degree. CPAP was more effective in reducing sleep disordered breathing, while a reduction in blood pressure was achieved with MAD only. Patients rated CPAP to be more effective than MAD but the latter to be more convenient. This may have contributed to a higher treatment adherence with MAD [40]. In another study, MAD were shown to be effective in even severe cases of OSAS. The higher the number of apnoea/hypopnoea, the greater was their reduction by MAD [41]. Side effects of MAD are relatively common but only rarely require discontinuation of therapy. They include tooth pain, hypersalivation, mucosal dryness, and occlusal changes [42]. Potential limitations of MAD are the requirement of a minimal number of stable teeth (ie, at least 8 teeth in the upper and lower jaw), absence of gingival disease and temporo-mandibular joint pain. Individual adaptation by an experienced orthodontist in cooperation with a pulmonary physician is crucial for achieving an optimal therapeutic result. It may take several weeks and require repeated consulta-

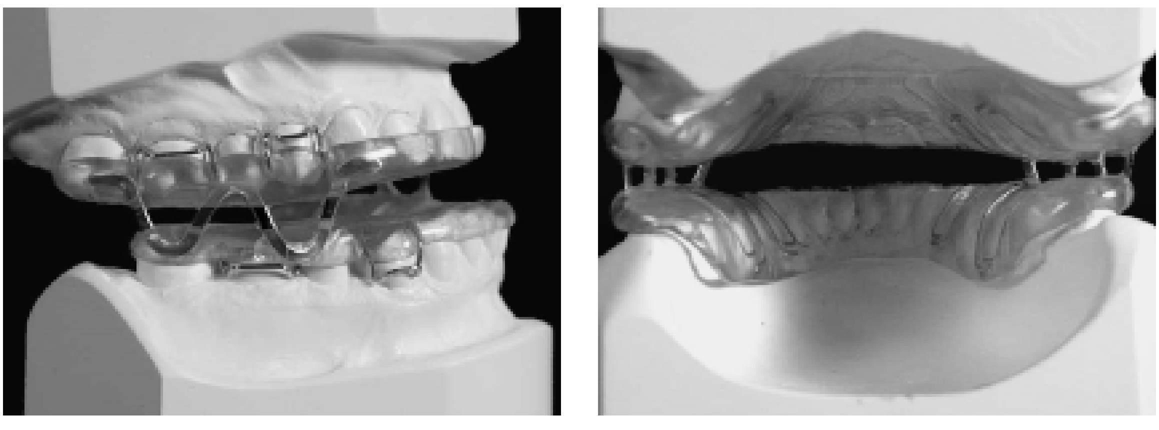


Figure 1

Monobloc mandibular advancement device as used at the University Hospital of Zurich. The custom-fitted appliance is snapped onto the dental arches for overnight treatment and held in place by metallic clasps. The protrusive forces acting onto the mandible are distributed over a large area of the alveolar process (modified from [33]).

tions to complete the conctruction of MAD and one or several follow-up sleep studies to establish the desired effect. Whether MAD remain effective over several years, and whether there are relevant and potentially irreversible side effects such as orthodontic changes and damage to the mandibulo-maxillary joints requires further study. It is important to realise that the favourable results reported in the cited studies [37–39] conducted with specific devices may not be extrapolated to the large number of other commercially available appliances which have not been subjected to a rigorous scientific evaluation. In conclusion, individually fitted and scientifically validated MAD are a valuable alternative for treatment of patients with mild and even severe OSAS if CPAP therapy is not feasible and if initial adaptation and long-term follow-up is performed by experienced professionals.

Reduction of excess weight

Obesity is a major risk factor for OSAS as well as for other diseases including hypertension and cardiovascular disease [9]. Therefore, reduction of excessive weight is an important therapeutic goal independent of its beneficial effects on OSAS. While diet supported by pharmacological treatment has not resulted in major and persistent weight loss, favourable results have been achieved by bariatric surgery including adjustable gastric banding and gastric bypass surgery [43, 44]. A meta-analysis has evaluated the effects of bariatric surgery on OSAS [45]. Among 12 266 obese patients undergoing bariatric surgery and evaluated by sleep studies, OSAS was diagnosed in 2399 (20%). In 1636 of 1921 patients (85%) in whom the information was available, OSAS improved or was resolved. In addition to the favourable effects on sleep related breathing disturbances, bariatric surgery improved diabetes mellitus, hypertension and hyperlipidaemia in a substantial majority of the patients. Therefore, bariatric surgery has an important role in the treatment of obese OSAS patients.

Upper airway surgery

Various techniques of soft tissue surgery for treatment of OSAS have been proposed but their role still remains controversial [46–48]. An exception is adeno-tonsillectomy which is successfully performed in children and in adult OSAS patients with adeno-tonsillar hypertrophy [49]. Uvulo-palato-pharyngoplasty (UPPP) performed by conventional techniques or with the use of laser [50] has provided inconsistent and unpredictable results in regard to improving OSAS and snoring. In one study, temperature-controlled radiofrequency tissue ablation applied in local anaesthesia to the tongue base and palate over the course of several weeks was compared to the effects of a sham procedure in patients with mild OSAS (mean apnoea/hypopnoea index 20/h). The verum surgery improved subjective sleepiness, quality of life and objectively measured reaction time more than the sham procedure but the apnoea/hypopnoea index remained unchanged. Side effects included haematomas, ulceration, pain and difficulty swallowing for several weeks in some patients. The follow-up time was not mentioned [51]. Tongue base procedures including suspension or resection have been performed in small patient groups and the results require further confirmation [52]. Tracheotomy and maxillo-facial surgery are considered too aggressive to be recommended routinely as first-line therapy. The Stanford step-by-step approach for surgery in OSAS is considered in patients not successfully treated with CPAP [46, 53]. The first stage comprises limited mandibular osteotomy (with or without UPPP, genioglossus advancement, hyoid myotomy, and hyothyroidopexy). Maxillo-mandibular advancement osteotomy, stage II surgery, is considered if stage I is not successful, or in the first place if cranio-facial dysmorphia is present [54]. In a single centre report on 51 OSAS patients treated surgically, stage I surgery was performed in 44 patients [54]. In only 10 of them satisfactory improvement was achieved while 34 were treatment failures. In 13 of these patients maxillomandibular advancement osteotomy was subsequently performed and additional 7 patients with cranio-facial dysmorphias underwent maxillo-facial surgery in the first place. Maxillo-mandibular advancement osteotomy was successful in 15 of the 20 operated patients, 5 patients were treatment failures. Over the same time period in which the 51 OSAS patients underwent upper airway surgery, 939 patients were started with CPAP at this center. Thus, the staged surgical concept seems to be successfully applicable in a very minor fraction of OSAS patients, namely those not successfully treated with CPAP or a MAD, and those with significant adeno-tonsillar hypertrophy, or cranio-facial dysmorphias and other anatomical obstacles amenable to surgery.

Treatment of nasal obstruction

It has been a long-standing clinical observation that snoring is particularly common in patients with nasal obstruction, and early reports have shown that experimental nasal occlusion promotes obstructive sleep apnoea [55]. Whether nasal obstruction due to chronic rhinitis, nasal polyposis or nasal septal deviation is a predisposing factor for OSAS is not clear. Epidemiological studies have shown that chronic rhinitis symptoms, and increased nasal resistance measured by rhinomanometry are associated with habitual snoring but a similar association was not demonstrated for OSAS [56, 57]. Nevertheless, treating OSAS patients with chronic rhinitis with fluticasone administered intra-nasally for one month improved sleepiness, and reduced the apnoea/hypopnoea index with statistical significance, though only to a minimal degree compared to placebo [58]. In another non-randomised study, 19 OSAS patients and 7 snorers with impaired nasal breathing underwent nasal surgery [59]. Sleep related breathing disturbances were not significantly changed but patients reported being less sleepy after the intervention. Nasal obstruction appears therefore to have a minor role in the pathophysiology of OSAS. Treating impaired nasal breathing may still be beneficial in selected patients since it improves subjective symptoms and sleep quality [60] and may contribute to successful nasal CPAP therapy in OSAS patients.

Drug therapy, adjunctive and experimental measures

Unfortunately there are currently no drugs that allow effective pharmacological therapy of OSAS. Research in this field however is ongoing. Recently, interesting observations have been made in children with minimal adeno-tonsillar enlargement and very mild sleep disordered breathing [66]. They were treated for 16 weeks with the leukotriene modifier montelukast achieving reductions in adenoid size and in sleep related breathing disturbances. Although these effects were modest, the results are promising. In compliant OSAS patients with residual hypersomonolence despite exclusion of other causes and effective CPAP treatment, modafinil, a drug prescribed to treat hypersomnolence in narcoleptics, has been used as an adjunct to improve alertness. In a randomised placebo controlled cross-over study with a 2 week period on modafinil no improvement in subjective sleepiness assessed by the Epworth score, no change in the multiple sleep latency test (MSLT) and only minor improvement in the ability to stay awake in a sleep-seductive environment (maintenance of wakefulness test) were found [67]. In another placebo-controlled parallel trial extending over 4 weeks with a final daily dose of 400 mg of modafinil, a statistically significant but clinically minor improvement in objective vigilance measured by the MSLT was demonstrated [68]. During extended open label use of modafinil over 4 months, patients continued to perceive an overall benefit in regard to improved sleepiness and quality of life [69]. Side effects of modafinil were generally mild and most commonly consisted of headache (28%), anxiety (16%), nervousness (14%), insomnia (11%), and nausea (11%) [69]. Despite the relatively favourable results regarding residual sleepiness the use of modafinil is still controversial. Arguments in favour of modafinil in this setting are some subjective and objective improvements of alertness and of quality of life. Conversely, the use of a stimulant may reduce compliance with CPAP treatment as shown in the cited studies [67, 69] and the stimulant drug may divert from inappropriate functioning of CPAP therapy and expose the OSAS patients to increased cardiovascular risk.

In mild positional OSAS, sleep in lateral position is often recommended. One randomised trial has evaluated the effect of 2 weeks of positional treatment consisting of a backpack with a soft ball inside. Thirteen patients with positional OSAS defined by more than twice the number of apnoea/hypopnoea in the supine as compared to the lateral position were included [70]. Positional training improved subjective sleepiness, maintenance of wakefulness time measured objectively, and psychometric test performance to a similar degree as CPAP but the latter was more effective in reducing apnoea/hypopnoea and oxygen desaturations. Therefore, positional treatment is a reasonable therapy for selected patients with positional OSAS who are not tolerating CPAP. A nasal dilator [71] and a number of other appliances have also been promoted for treatment of snoring and OSAS but have not revealed consistent effects and can therefore not be recommended.

Nocturnal electrical stimulation of the hypoglossal nerve by an implanted pace-maker has been thought to prevent sleep related upper airway collapse in OSAS patients by activating submandibular muscles [61]. However, this treatment is still experimental and there is insufficient evidence to support its clinical use. In one randomised, placebo-controlled trial, tongue muscle training by electrical neurostimulation applied twice during daytime for 8 weeks has been found to reduce snoring but not sleep apnoea in 33 patients [62]. Whether this treatment modality is acceptable and effective in the long-term treatment of snoring remains open. The initial success achieved with atrial overdrive pacing as a therapy for OSAS patients treated with a cardiac pacemaker for other reasons has not been confirmed in subsequent trials, and this treatment is therefore not recommended [63, 64]. Whether biventricular pacing in heart failure patients with ventricular asynchrony improves co-existing sleep apnoea requires further studies [65].

Conclusions

Figure 2 summarises the current options for treatment of OSAS and the suggested sequence of evaluations. CPAP remains the standard treatment for the vast majority of OSAS patients due to its immediate and persistent effectiveness and the lack of major side effects. For patients in whom CPAP therapy is not feasible because of mask intolerance or other reasons, a custom-fitted MAD may be a valuable and effective alternative treatment but long-term effectiveness and side effects need to be monitored. In morbidly obese OSAS patients, bariatric surgery should be considered as an option to treat both excess weight, and OSAS and to prevent cardiovascular consequences. Upper airway surgery has a role in children and adults with enlarged adenoids and tonsils, or with cranio-facial dysmorphia and other selected patients in whom CPAP is not an option.

I thank Karsten Fritsch, MD, for careful review of the manuscript.

Correspondence:
Konrad E. Bloch, MD
Pulmonary Division,
Dept. of Internal Medicine
University Hospital of Zürich
Rämistrasse 100,
CH-8091 Zürich
Switzerland
E-Mail: pneubloc@usz.unizh.ch

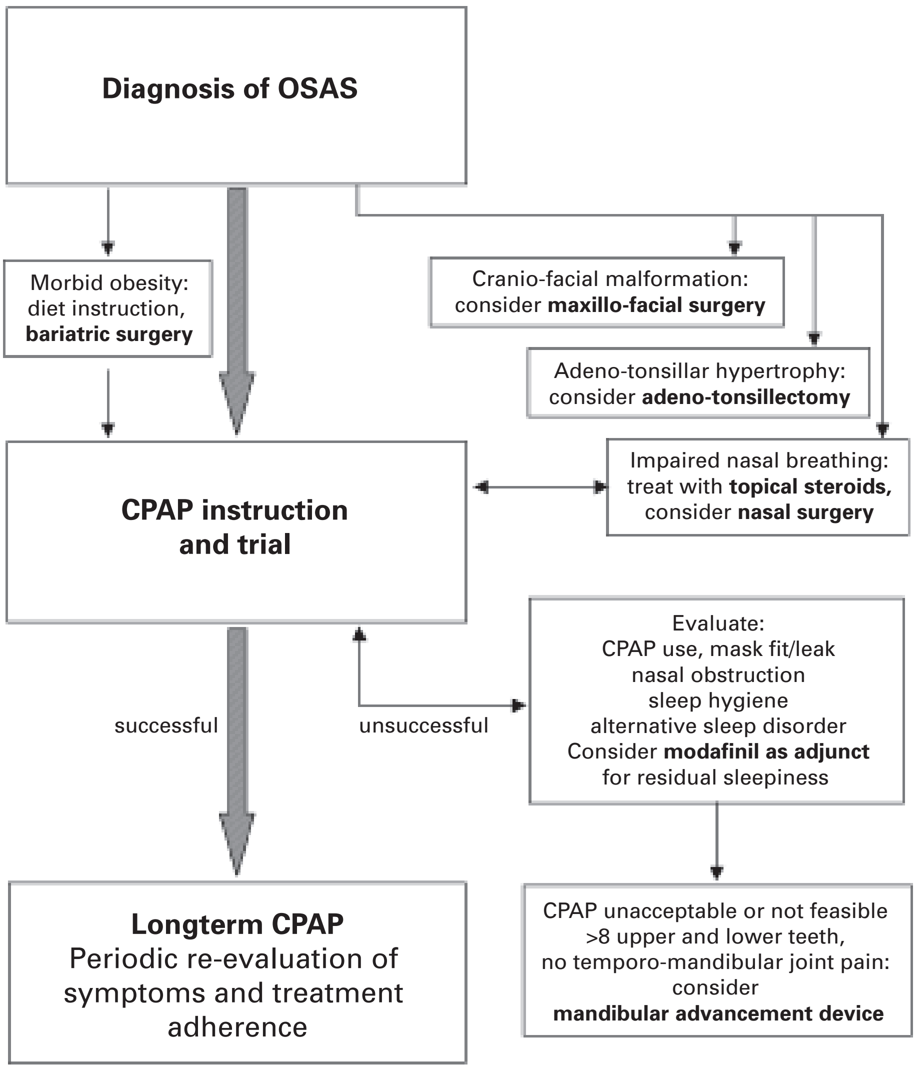


Figure 2

Treatment options for the obstructive sleep apnoea syndrome (OSAS). The standard therapy consisting of nasal continuous positive airway pressure (CPAP) and alternative treatment modalities along with suggested evaluations are outlined.

References

1 Guilleminault C, van den Hoed J, Mitler M. Clinical features and evaluation of obstructive sleep apnea.1994. In Principles and Practice of Sleep Medicine. Kryger M.H., Roth T. Dement W.C. eds. W.B. Saunders Co, Philadelphia;65:667–77.
2 Schlosshan D and Elliott MW. Sleep. 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome. Thorax 2004;59:347–52.
3 Jenkinson C, Stradling J, Petersen S. Comparison of three measures of quality of life outcome in the evaluation of continuous positive airways pressure therapy for sleep apnoea. J Sleep Res 1997;6:199–204.
4 Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J. The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander [see comments]. N Engl J Med 1999;340:847–51.
5 Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378–84.
6 Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005; 365:1046–53.
7 Yakki HK, Concato J, Kernan WN, Lichtman JHBLM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med 2005;353:2034–41.
8 Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–5.
9 Young T, Peppard PE, Taheri S. Excess weight and sleep-disordered breathing. J Appl Physiol 2005;99:1592–9.
10 Douglas NJ. Clinician's guide to sleep medicine. 2002;1, Arnold, London.
11 Davies RJO, Ali NJ, Stradling JR. Neck circumference and other clinical features in the diagnosis of the obstructive sleep apneoa syndrome. Thorax 1992;47:101–5.
12 Tsai WH, Remmers JE, Brant R, Flemons WW, Davies J, Macarthur C. A decision rule for diagnostic testing in obstructive sleep apnea. Am J Respir Crit Care Med 2003;167:1427–32.
13 Ballester E, Badia JR, Hernández L, Carrasco E, de Pablo J, Fornas C, et al. Evidence of the effectiveness of continuous positive airway pressure in the treatment of sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999;159:495–501.
14 Sullivan CE, Berthon-Jones M, Issa FG, Eves L. Reversal of obstructive sleep apnea by continuous positive airway pressure applied trough the nares. Lancet 1981;I:862–5.
15 Engleman HM, Martin SE, Deary IJ, Douglas NJ. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoe/hypopnoe syndrome. Lancet 1994;343: 572–5.
16 Gordon P and Sanders MH. Sleep 7: Positive airway pressure therapy for obstructive sleep apnoea/hypopnoea syndrome. Thorax 2005;60:68–75.
17 Jenkinson C, Davies RJ, Mullins R, Stradling JR. Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet 1999;353:2100–5.
18 Montserrat JM, Ferrer M, Hernandez L, Farre R, Vilagut G, Navajas D, et al. Effectiveness of CPAP treatment in daytime function in sleep apnea syndrome: a randomized controlled study with an optimized placebo. Am J Respir Crit Care Med 2001;164:608–13.
19 Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ. Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep Apnea/Hypopnea syndrome. Am J Respir Crit Care Med 1999;159:461–7.
20 Senn O, Brack T, Matthews F, Russi EW, Bloch KE. Randomized short-term trial of two autoCPAP devices versus fixed continuous positive airway pressure for the treatment of sleep apnea. Am J Respir Crit Care Med 2003;168:1506–11.
21 Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, Mullins R, Jenkinson C, Stradling JR, et al. Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. Lancet 2002;359:204–10.
22 Robinson GV, Pepperell JC, Segal HC, Davies RJ, Stradling JR. Circulating cardiovascular risk factors in obstructive sleep apnoea: data from randomised controlled trials. Thorax 2004;59: 777–82.
23 Yokoe T, Minoguchi K, Matsuo H, Oda N, Minoguchi H, Yoshino G, et al. Elevated levels of C-reactive protein and interleukin-6 in patients with obstructive sleep apnea syndrome are decreased by nasal continuous positive airway pressure. Circulation 2003;107:1129–34.
24 Loube DI, Gay PC, Strohl KP, Pack AI, White DP, Collop NA. Indications for positive airway pressure treatment of adult obstructive sleep apnea patients. Chest 1999;115:863–6.
25 Barbe F, Mayoralas LR, Duran J, Masa JF, Maimo A, Montserrat JM, et al. Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. a randomized, controlled trial. Ann Intern Med 2001;134:1015–23.
26 Popescu G, Latham M, Allgar V, Elliott MW. Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. Thorax 2001;56:727–33.
27 Senn O, Brack T, Russi EW, Bloch KE. A continuous positive airway pressure trial as a novel approach to the diagnosis of the obstructive sleep apnea syndrome. Chest 2006;129:67–75.
28 Kaplan V, Li Y, Hess T, Russi EW, Bloch KE. Compliance mit nasaler Ueberdruckbehandlung (CPAP) bei obstruktiven Schlafapnoe Syndrom. Schweiz Med Wochenschr 1996;130: 15–22.
29 Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, et al. Objective measurement of patterns of CPAP use by patients with obstructiv sleep apnea. Am Rev Respir Dis 1993;147:887–95.
30 American Sleep Disorders Association. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances. Sleep 1995;18:511–3.
31 Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S. Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 1995;18:501–10.
32 Lowe AA. Oral appliances for sleep breathing disorders. In Principles and Practice of Sleep Medicine. Kryger M.H., Roth T. Dement W.C. eds. W.B. Saunders Co, Philadelphia;78: 929–39.
33 Bloch KE, Senn O, Iseli A. Oral appliances for treatment of snoring and obstructive sleep apnea. In surgery for sleep apnea. Fabiani M, Saponara M, eds. Kugler Publications, the Hague 2003;1:559–75.
34 Ferguson KA, Love LL, Ryan CF. Effect of mandibular and tongue protrusion on upper airway size during wakefulness. Am J Respir Crit Care Med 1997;155:1748–54.
35 Yoshida K. Effect of a prosthetic appliance for treatment of sleep apnea syndrome on masticatory and tongue muscle activity. J Prosthet Dent 1998;79:537–44.
36 Kato J, Isono S, Tanaka A, Watanabe T, Araki D, Tanzawa H, et al. Dose-dependent effects of mandibular advancement on pharyngeal mechanics and nocturnal oxygenation in patients with sleep-disordered breathing. Chest 2000;117:1065–72.
37 Bloch KE, Iseli A, Zhang JN, Xie X, Stoeckli PW, Russi EW. Randomized, controlled trial of two oral appliances for sleep apnea treatment. Am J Respir Crit Care Med 2000;162:246–51.
38 Gotsopoulos H, Chen C, Qian J, and Cistulli PA. Oral appliance therapy improves symptoms in obstructive sleep apnea: a randomized, controlled trial. Am J Respir Crit Care Med 2002;166:743–8.
39 Gotsopoulos H, Kelly JJ, Cistulli PA. Oral appliance therapy reduces blood pressure in obstructive sleep apnea: a randomized controlled trial. Sleep 2004;27:934–41.
40 Barnes M, McEvoy RD, Banks S, Tarquinio N, Murray CG, Vowles N, et al. Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. Am J Respir Crit Care Med 2004;170:656–64.
41 Henke KG, Frantz DE, Kuna ST. An oral elastic mandibular advancement device for obstructive sleep apnea. Am J Respir Crit Care Med 2000;161:420–5.
42 Fritsch K, Iseli A, Russi EW, Bloch KE. Side effects of mandibular advancement devices for sleep apnea treatment. Am J Respir Crit Care Med 2001;164:813–8.
43 Steinbrook R. Surgery for severe obesity. N Engl J Med 2004; 350:1075–9.
44 Sjostrom L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351: 2683–93.

45 Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA 2004;292:1724–37.
46 Powell N. Upper airway surgery does have a major role in the treatment of obstrucive sleep apnea. "The tail end of the dog". J Clin Sleep Med 2005;1:236–40.
47 Phillips B. Upper airway surgery does not have a major role in the treatment of sleep apne. J Clin Sleep Med 2005;1:241–5.
48 Sundaram S, Bridgman S, Lim J, Lasserson T, Sundaram S. Surgery for obstructive sleep apnoea. Cochrane. Database Syst Rev 2005;CD001004.
49 Stewart MG, Glaze DG, Friedman EM, Smith EO, Bautista M. Quality of life and sleep study findings after adenotonsillectomy in children with obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 2005;131:308–14.
50 Larrosa F, Hernandez L, Morello A, Ballester E, Quinto L, Montserrat JM. Laser-assisted uvulopalatoplasty for snoring: does it meet the expectations? Eur Respir J 2004;24:66–70.
51 Woodson BT, Steward DL, Weaver EM, Javaheri S. A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 2003;128:848–61.
52 Thomas AJ, Chavoya M, Terris DJ. Preliminary findings from a prospective, randomized trial of two tongue-base surgeries for sleep-disordered breathing. Otolaryngol Head Neck Surg 2003;129:539–46.
53 Riley RW, Powell NB, Guilleminault C. Obstructive sleep apnea syndrome: A review of 306 consecutively treated surgical patients. Otoloaryngol Head Neck Surg 1993;108:117–25.
54 Bettega G, Pepin JL, Veale D, Deschaux C, Raphael B, Levy P. Obstructive sleep apnea syndrome. fifty-one consecutive patients treated by maxillofacial surgery. Am J Respir Crit Care Med 2000;162:641–9.
55 Zwillich CW, Pickett C, Hanson FN, Weil JV. Disturbed sleep and prolonged apnea during nasal obstruction in normal men. Am Rev Respir Dis 1981;124:158–60.
56 Young T, Finn L, Palta M. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. Arch Intern Med 2001;161:1514–9.
57 Young T, Finn L, Kim H. Nasal obstruction as a risk factor for sleep-disordered breathing. The University of Wisconsin Sleep and Respiratory Research Group. J Allergy Clin Immunol 1997;99:S757–S762.
58 Kiely JL, Nolan P, McNicholas WT. Intranasal corticosteroid therapy for obstructive sleep apnoea in patients with co-existing rhinitis. Thorax 2004;59:50–5.
59 Verse T, Maurer JT, Pirsig W. Effect of nasal surgery on sleep-related breathing disorders. Laryngoscope 2002;112:64–8.
60 Craig TJ, Teets S, Lehman EB, Chinchilli VM, Zwillich C. Nasal congestion secondary to allergic rhinitis as a cause of sleep disturbance and daytime fatigue and the response to topical nasal corticosteroids. J Allergy Clin Immunol 1998;101:633–7.
61 Schwartz AR, Bennett ML, Smith PL, De Backer W, Hedner J, Boudewyns A, et al. Therapeutic electrical stimulation of the hypoglossal nerve in obstructive sleep apnea. Arch Otolaryngol Head Neck Surg 2001;127:1216–23.
62 Randerath WJ, Galetke W, Domanski U, Weitkunat R, Ruhle KH. Tongue-muscle training by intraoral electrical neurostimulation in patients with obstructive sleep apnea. Sleep 2004; 27:254–9.
63 Garrigue S, Bordier P, Jais P, Shah DC, Hocini M, Raherison C, et al. Benefit of atrial pacing in sleep apnea syndrome. N Engl J Med 2002;346:404–12.
64 Pepin JL, Defaye P, Garrigue S, Poezevara Y, Levy P. Overdrive atrial pacing does not improve obstructive sleep apnoea syndrome. Eur Respir J 2005;25:343–7.
65 Sinha AM, Skobel EC, Breithardt OA, Norra C, Markus KU, Breuer C, et al. Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure. J Am Coll Cardiol 2004;44:68–71.
66 Goldbart AD, Goldman JL, Veling MC, Gozal D. Leukotriene modifier therapy for mild sleep-disordered breathing in children. Am J Respir Crit Care Med 2005;172:364–70.
67 Kingshott RN, Vennelle M, Coleman EL, Engleman HM, Mackay TW, Douglas NJ. Randomized, double-blind, placebo-controlled crossover trial of modafinil in the treatment of residual excessive daytime sleepiness in the sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 2001;163:918–23.
68 Pack AI, Black JE, Schwartz JR, Matheson JK. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. Am J Respir Crit Care Med 2001;164:1675–81.
69 Schwartz JR, Hirshkowitz M, Erman MK, Schmidt-Nowara W. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea: a 12-week, open-label study. Chest 2003;124: 2192–9.
70 Jokic R, Klimaszewski A, Crossley M, Sridhar G, Fitzpatrick MF. Positional treatment vs continuous positive airway pressure in patients with positional obstructive sleep apnea syndrome. Chest 1999;115:771–81.
71 Schonhofer B, Franklin KA, Brunig H, Wehde H, Kohler D. Effect of nasal-valve dilation on obstructive sleep apnea. Chest 2000;118:587–90.

Swiss Medical Weekly

Official journal of
the Swiss Society of Infectious disease
the Swiss Society of Internal Medicine
the Swiss Respiratory Society

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website http://www.smw.ch (direct link from each SMW record in PubMed)

- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses

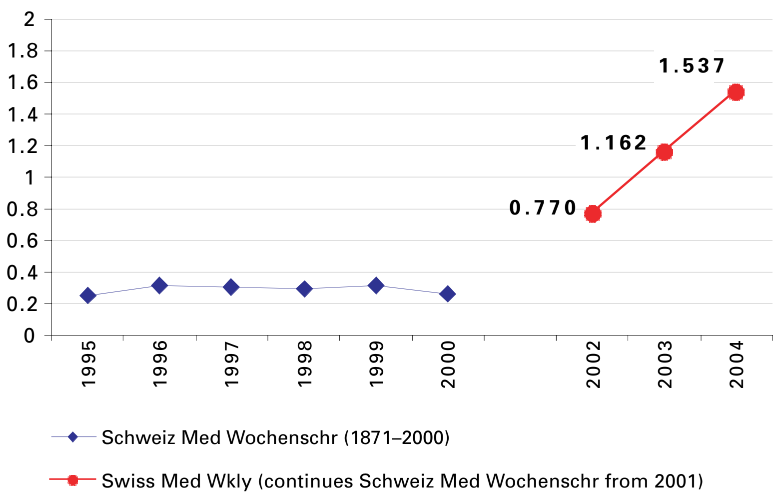
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:
http://www.smw.ch/set_authors.html

Impact factor Swiss Medical Weekly



EMH FMH Schwabe
Editores Medicorum Helveticorum

All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
SMW Editorial Secretariat
Farnsburgerstrasse 8
CH-4132 Muttenz

Manuscripts:	submission@smw.ch
Letters to the editor:	letters@smw.ch
Editorial Board:	red@smw.ch
Internet:	http://www.smw.ch