Obstructive Sleep Apnea: Do Oral Appliances or Hypoglossal Nerve Stimulators Work?

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Abstract: Obstructive sleep apnea (OSA) is a pervasive problem that affects the adult population and it can lead to serious health complications. Continuous positive airway pressure (CPAP) is the gold standard for treating OSA, however, noncompliance and nonadherence to CPAP therapy continues to be a challenge. Oral mandibular devices (OMD) and hypoglossal nerve stimulation (HNS) are alternative therapies used in patients who cannot tolerate CPAP therapy. A comprehensive literature search was performed using reliable search engines using the PICO question and the results were analyzed. The benefits and deficiencies of the OMD and HNS were examined and identified. HNS seems to be a promising therapy for patients with moderate to severe sleep apnea who failed CPAP. However, HNS is an expensive invasive procedure with identified short-term benefits. However, long-term benefits and disadvantages are yet to be known.

Background and Clinical Significance

In the United States, obstructive sleep apnea (OSA) is estimated to affect approximately 2%–9% of the adult population (Suni, 2021). OSA occurs when the throat muscles intermittently relax and block the airway during sleep, lowering oxygen levels in the blood and building up carbon dioxide (Mayo Clinic Staff, n.d.). A sudden drop in blood oxygen levels can lead to cardiovascular complications such as hypertension and increase the strain on the cardiovascular system (Mayo Clinic Staff, n.d.). Although continuous positive airway pressure (CPAP) is the standard prescribed treatment, only a fraction of patients adhere to the long-term treatment (Costantino et al., 2020). An oral appliance and hypoglossal nerve stimulator are some of the other devices used in OSA patients who have difficulty accepting and adhering to their treatments; however, their efficacy is not yet clearly understood.

Problem Statement

Different treatment modalities like surgical and mechanical devices are used in the treatment of OSA; however, nonadherence to the treatment therapy places the OSA patients at an increased cardiovascular risk. The utilization of oral appliance devices and HNS are alternatives considered in the treatment of OSA, and this paper explores the efficiency of these devices.

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Research Question

Does treatment of obstructive sleep apnea (OSA) with oral appliance devices or hypoglossal nerve stimulators in comparison to no intervention reduce adverse long-term cardiovascular outcomes?

Population: OSA patients
Intervention: Oral device and hypoglossal nerve stimulation
Comparison: OSA patients with no treatment or problem adhering to treatment
Outcome: Reduce cardiovascular outcomes

PICO is a format that aids in developing a clinical research question to facilitate the research.

Theoretical Model/Conceptual Framework

The Stetler model is one of the evidence-based practice models used to integrate the current research evidence into nursing clinical practice. The Stetler model utilizes the following five phases: (a) preparation, (b) validation, (c) comparative evaluation, (d) application, and (e) evaluation, which were applied to research findings to facilitate the evidence-based practice determination (McEwen & Willis, 2018). By using this model, it can provide a pathway to show how the research was executed and how it can be disseminated to the healthcare community.

For the preparation phase, a literature search was completed using Google Scholar, PubMed and CINAHL. The search was narrowed to the utilization of oral devices and hypoglossal nerve stimulation for the treatment of OSA and the cardiovascular outcomes post-treatment. The validation phase of the research includes choosing credible literature, reassessing fit for narrowed topic search, clinical significance, and level of evidence using the evidence-based medicine pyramid. The pyramid rates research studies from I-V based on the quality and validity of the evidence, with Level I being the strongest. The Cochrane level of evidence provides a Level 1 or high quality, reliable, and relevant strength of recommendation for healthcare interventions (Cochrane Collaboration, 2021). The Cochrane level of evidence is recognized internationally and used in aiding the best practice guidelines for primary care and patient decision making initiatives. Other articles were systematic reviews and meta-analyses with Level 1 evidence based on the evidence-based medicine pyramid; however, some cardiovascular effects articles were rated at a lower level because of limited research. In the comparative phase, literature analyses were performed and summarized into a literature review table (See Appendix). The strengths and the summary of findings were analyzed and taken into account, and an analysis of literature was done to find the conclusion.

The next phase was the application phase, in which the research results were actively disseminated into different methods of discourse like public seminars and posters, and then the practice change strategies would be applied. Last, an evaluation of the change and a cost-benefit analysis would be done to assess the credibility and outcome of the change.

Review of Literature

Search Strategy and Method

A comprehensive literature search was performed using Google Scholar, TWU library databases like CINAHL, PubMed using the keywords "obstructive sleep apnea and hypoglossal nerve stimulation," "hypoglossal nerve stimulation (HNS) and cardiovascular outcomes," and "oral devices for obstructive sleep apnea, and cardiovascular outcomes"; relevant articles were narrowed to interest. Google Scholar produced the most results with 7,620 results for OSA and HNS, which was narrowed by custom range period, hierarchy of evidence, and relevance to the PICO question. The inclusion criteria also included peer-reviewed and full-text articles. Similarly, OSA and oral devices were searched with custom range period and hierarchy of evidence. Finally, four peer reviewed full text articles were selected for HNS and HNS and cardiovascular outcomes; similarly, two articles were identified for the oral devices.

The first-line therapy for moderate to severe OSA is the use of CPAP, which acts as an upper airway stent to maintain an open airway during sleep; however, its use is limited by poor patient acceptance and challenges with long-term adherence (Woodson et al., 2014). Aslan et al. (2018) established that CPAP improves left ventricular ejection fraction and has beneficial effects on cardiovascular mortality rates. It is therefore imperative to find an alternative therapy for patients who fail the usage of CPAP therapy.
An oral device or mandibular advancement device (MAD) is an exclusive custom-fitted oral appliance used for patients who prefer an alternative treatment. Another therapeutic approach used is the hypoglossal nerve stimulation (HNS), which is a device that generates an electrical impulse through a generator that is then transmitted through a tunneled lead. The device is implanted in the upper right chest and ends with a cuff that delivers the stimulation to the hypoglossal nerve (Mashaqi et al., 2021). The hypoglossal nerve is involved in controlling the motor movement of the tongue, speech and swallowing (Cleveland Clinic, 2021). Once the device is implanted, the patient is given a remote to activate the therapy according to their need (Mashaqi et al., 2021).

Summary of article review

Costantino et al. (2020) evaluated long-term clinical outcomes and found that the HNS has shown to be a safe surgical procedure with a low rate of serious adverse events such as life-threatening illness or permanent impairment. This was a systematic review and meta-analysis of the three different types of HNS: (a) Inspire, (b) ImThera, and (c) Apnex. The results were acquired from the stimulation therapy for apnea reduction trial (STAR), which demonstrated that after 60 months, the adherence rate was 75% with an optimal objective and subjective benefit without long-term complications (Costantino et al., 2020). The study revealed that HNS is an excellent long-term treatment for moderate-severe OSA; however, cardiovascular outcomes were not studied.

Kompelli et al. (2019) assessed the effectiveness and safety of HNS for CPAP refractory OSA and established that HNS is a safe and effective treatment with high compliance, and it significantly improves the subjective and objective outcomes of sleep. The authors found minor complications and device malfunctions, although they were uncommon and benign.

The effects of HNS on heart rate variability as a measure of autonomic function was studied by Dedhia et al. (2019) in a single group cohort study. Dedhia et al. found that 12 months post-implantation of the HNS, a decrease was evident in heart rate variability (HRV) during sleep and less than 50% reduction in the apnea-hypopnea index (AHI) from baseline. These measures were similar to the compliant CPAP users.

Holfinger et al. (2021) reviewed multiple treatment modalities such as positive airway pressure (PAP), oral devices, neuromodulation like HNS, phrenic nerve stimulation (PNS), cardiac resynchronization therapy (CRT), and low flow oxygen therapy as well as using medications like acetazolamide and theophylline for sleep-disordered breathing in heart failure patients. Holfinger et al. found that all were effective in reducing AHI in central sleep apnea.

Sato and Nakajima (2020) studied the use of oral devices for OSA and found that long-term use of oral devices causes posterior open bite, and the nonadherence rate was high. They did not find any evidence of cardiovascular disease improvement. DeVries et al. (2018) did a similar study and found that while oral appliances were beneficial, no cardiovascular effects were apparent; however, the study was inconclusive.

Analysis of Literature

Even though oral devices are used for OSA, there is insufficient information regarding the efficacy of this device. The oral devices are easily obtainable and are not invasive. Sato and Nakajima (2020) found that the non-adherence rate was high among the users, and DeVries et al. (2018) did not find any cardiovascular benefits. Oral devices also have dental and skeletal side effects with long-term use. Consequently, the oral-device might not be a good choice for long-term therapy in OSA patients.

HNS appears to be an excellent long-term treatment for moderate-severe OSA. HNS is found to be safe and effective with minimal surgical complications. The subjective and objective outcomes of sleep study variables improved for HNS users. The reviews regarding cardiovascular outcomes for HNS remain to be studied, but more recent reviews show that the AHI and HRV index had an acute reduction from baseline in patients using HNS. The most indispensable fact about HNS is the high compliance rate seen among the users.

Nonetheless, more prospective studies comparing the various stimulation devices and cardiovascular outcomes with homogenous selection criteria using a longitudinal study will demonstrate that this therapy is reputable one. Also, most of the longitudinal studies are fewer than 10 years; therefore, device malfunction, replacement complications, or long-term nerve or tissue damage was not discussed in the studies.

Conclusion

Obstructive sleep apnea is a prevalent condition that affects all age groups, especially older adults with comorbid cardiovascular diseases. CPAP is the standard treatment for OSA; however, patient tolerance and rates of adherence to the therapy remain low. This paper reviewed studies that investigated the effectiveness of oral mandibular devices and hypoglossal nerve stimulation therapy. The studies found that OMD and HNS help alleviate the symptoms of OSA in comparison to no intervention. The oral appliance might be beneficial, but long-term use of oral devices can cause posterior open bite, and there was no evidence of cardiovascular disease improvement. HNS was found to be safe and effective for moderate to severe OSA for patients who cannot tolerate CPAP and have not evidenced a long-term adherence rate. HNS is an invasive surgical procedure; however, complications from the procedure were benign and unremarkable. HNS was found to improve short term cardiovascular variables, albeit more research is needed. Although promising, prospective research studies need to be done to determine long-term cardiovascular outcomes and replacement complications.

References

Aslan, G., Afsar, B., Siriopol, D., Kanbay, A., Sal, O., Benli, C., Okcuoglu, J., Covic, A., & Kanbay, M. (2018). Cardiovascular effects of continuous positive airway pressure treatment in patients with obstructive sleep apnea: A meta-analysis. *Angiology, 69*(3), 195–204. https://doi.org/10.1177/0003319717709175

Centers for Medicare and Medicaid Services. (2020). Local coverage determination for hypoglossal nerve stimulation for the treatment of obstructive sleep apnea (L38310). https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38310&ver=7&articleId=57948&bc=AAAAAAAAQAAA&

Certal, V. F., Zaghi, S., Riaz, M., Vieira, A. S., Pinheiro, C. T., Kushida, C., Capasso, R., & Camacho, M. (2015). Hypoglossal nerve stimulation in the treatment of obstructive sleep apnea: A systematic review and meta-analysis. *The Laryngoscope, 125*(5), 1254–1264. https://doi.org/10.1002/lary.25032

Cleveland Clinic. (2021, June 4). *Hypoglossal Nerve: Function, Common Conditions & Disorders.* https://my.clevelandclinic.org/health/body/21592-hypoglossal-nerve

The Cochrane Collaboration. (2021). *Cochrane and systematic reviews*. Retrieved November 9, 2021, from https://consumers.cochrane.org/cochrane-and-systematic-reviews

Costantino, A., Rinaldi, V., Moffa, A., Luccarelli, V., Bressi, F., Cassano, M., Casale, M., & Baptista, P. (2020). Hypoglossal nerve stimulation long-term clinical outcomes: A systematic review and meta-analysis. *Sleep and Breathing*, *24*(2), 399–411. https://doi.org/10.1007/s11325-019-01923-2

Dedhia, R. C., Shah, A. J., Bliwise, D. L., Quyyumi, A. A., Strollo, P. J., Li, Q., Da Poian, G., & Clifford, G. D. (2019). Hypoglossal nerve stimulation and heart rate variability: Analysis of STAR trial responders. *Otolaryngology–Head and Neck Surgery, 160*(1), 165–171. https://doi.org/10.1177/0194599818800284

de Vries, G. E., Wijkstra, P. J., Houwerzijl, E. J., Kerstjens, H. A. M., & Hoekema, A. (2018). Cardiovascular effects of oral appliance therapy in obstructive sleep apnea: A systematic review and meta-analysis*. Sleep Medicine Reviews, 40,* 55–68. https://doi.org/10.1016/j.smrv.2017.10.004

Holfinger, S., Chan, L., & Donald, R. (2021). All you need is sleep: The effects of sleep apnea and treatment benefits in the heart failure patient. *Current Heart Failure Reports, 18*(3), 144–152. https://doi.org/10.1007/s11897-021-00506-1

Kompelli, A. R., Ni, J. S., Nguyen, S. A., Lentsch, E. J., Neskey, D. M., & Meyer, T. A. (2019). The outcomes of hypoglossal nerve stimulation in the management of OSA: A systematic review and meta-analysis. *World Journal of Otorhinolaryngology—Headand Neck Surgery, 5*, 41–48. https://doi.org/10.1016/j.wjorl.2018.04.006

Mashaqi, S., Patel, S., Combs, D., Estep, L., Helmick, S., Machamer, J., & Parthasarathy, S. (2021). The hypoglossal nerve stimulation as a novel therapy for treating obstructive sleep apnea—A literature review. *International Journal of Environmental Research and Public Health, 18*(4), 1642. https://doi.org/10.3390/ijerph18041642

Mayo Clinic Staff. (n.d.). *Obstructive sleep apnea*. https://www.mayoclinic.org/diseases-conditions/obstructive-sleep-apnea/symptoms-causes/syc-20352090\

McEwen, M., & Willis, E. M. (2018). *Theoretical basis for nursing* (5th ed.). Wolters Kluwer.

Rodriguez, J. (2018, February 22). *What is hypoglossal nerve stimulation therapy for sleep apnea?* Advanced Sleep Medicine Services, Inc. https://www.sleepdr.com/the-sleep-blog/what-is-hypoglossal-nerve-stimulation-therapy-for-sleep-apnea/

Sato, K., & Nakajima, T. (2020). Review of systematic reviews on mandibular advancement oral appliance for obstructive sleep apnea: The importance of long-term follow-up. *The Japanese Dental Science Review*, *56*, 32–37. https://doi.org/10.1016/j.jdsr.2019.10.002

Suni, E. (2021, July 9). *Sleep apnea.* Sleep Foundation. https://www.sleepfoundation.org/sleep-apnea

Woodson, B. T., Gillespie, M. B., Soose, R. J., Maurer, J. T., de Vries, N., Steward, D. L., Baskin, J. Z., Padhya, T. A., Lin, H.-S., Mickelson, S., Badr, S. M., Strohl, K. P., & Strollo, P. J., Jr. (2014). Randomized controlled withdrawal study of upper airway stimulation on OSA: Short- and long-term effect. *Otolaryngology–Head and Neck Surgery*, *151*(5), 880–887. https://doi.org/10.1177/0194599814544445

Appendix
Review of Literature Table

Summary of Primary Sources of Evidence

Citation of Evidence	Study Question or Hypothesis	Study Design	Sample/ Setting	Independent and Dependent Variables and Tools Used	Data Collection and Analysis	Findings	Recommendations/ Implications	Evidence Level
Costantino, A., Rinaldi, V., Moffa, A., Luccarelli, V., Bressi, F., Cassano, M., Casale, M., & Baptista, P. (2020). Hypoglossal nerve stimulation long-term clinical outcomes: A systematic review and meta- analysis. *Sleep and Breathing*, *24*(2), 399–411. https://doi.org/10.1007/s11325-019-01923-2	What are the long-term clinical outcomes of using HNS in the treatment of OSA?	System- atic review / Meta-analysis	350 patients from 12 studies	IV: pre-implementation, post-implementation, post- implementation of HNS (Inspire, ImThera, Apnex) DV: 6- and 12-month intervals Tools: A. Apnea-hypopnea index (AHI) B. Oxygen desaturation index (ODI) C. Epworth Sleepiness Scale (ESS) D. Pretreatment to post- implantation measures for meta-analysis E. RevMan v. 5.3 to calculate the magnitude of the treatment effect F. Cochran's Q method to assess heterogeneity G. Clinical measure reported as ±SD H. Statistical significance defined at	Adherence to therapy: Inspire = 70% ImThera = 35% Apnex = 60% adherence at 6 mos Inspire = 72% ImThera = 77% Apnex = 55% at 12 mos STAR trial: Overall long-term success. 18 mos = 64% 36 mos = 74% 60 mos = 75% Used 5.8 hrs /night A. Improvement in objective and subjective clinical outcomes. B. Elective surgery for patients who failed other therapies	HNS was shown to be a safe surgical procedure with a low rate of serious adverse events such as life-threatening illness, permanent impairment, or new or prolonged hospitalization with serious health impairment. HNS maintains an optimal objective and subjective improvement without long-term complications related to the device implanted.	Although further prospective studies with longer follow- up and comparing various stimulation systems should be performed, these findings reveal that HNS is an excellent long-term treatment for moderate-severe OSA.	Cochrane I

				$p < 0.05$				

Note. Three HGNS devices were tested in clinical trials. The Apnex Medical Inc. (St. Paul, MN, USA) device was promising in a phase II trial, but failed at phase III because it did not meet efficacy standards and the company no longer exists. The second device is the ImThera Aura 6000 (San Diego, CA, USA). It places six electrodes around the trunk of the hypoglossal nerve. It is still in phase III clinical trial. The third device, which is the only one approved by the FDA, is Inspire Medical Systems (Maple Grove, MN, USA) (Mashaqi et al., 2021).

Citation of Evidence	**Study Question or Hypothesis**	**Study Design**	**Sample/ Setting**	**Independent and Dependent Variables and Tools Used**	**Data Collection and Analysis**	**Findings**	**Recommendations/ Implications**	**Evidence Level**

Kompelli, A. R., Ni, J. S., Nguyen, S. A., Lentsch, E. J., Neskey, D. M., & Meyer, T. A. (2019). The outcomes of hypoglossal nerve stimulation in the management of OSA: A systematic review and meta- analysis. *World Journal of Otorhinolaryngology—Head and Neck Surgery, 5*, 41–48. https://doi.org/10.1016/j.wjorl.2018.04.006	Is HNS a safe and effective treatment for CPAP refractory OSA?	System-atic review and Meta-analysis	16 studies 381 patients	IV: Pre- and post-implantation of HNS DV: AHI, ODI, ESS Tools: PubMed, SCOPUS, Cochrane library.	Systematic review of 16 eligible articles; MedCalc 17.9.7 lists proportions with 95% CI; Fixed effects model and random effects model used; Heterogeneity I^2 = 64%, $p < 0.00001$; meta-analysis using RevMan v.5.3 with fixed and random effects models.	Across all trials, patients that receive HNS have significantly improved AHI, ODI, and FOSQ at 6 and 12 months. Patients experienced pain, tongue abrasion with or without lesions, and some device malfunction. Other adverse effects included abnormal sensations, paresthesia, change in salivary flow, and lip weakness. HNS is safe and effective treatment for CPAP refractory OSA. It is associated	CPAP is still first-line OSA treatment; however, poor compliance and improper use call for the HNS alternative. Difficulties with compliance with CPAP may warrant HNS use as compliance was reported to be 86% at 12 months compared to 40%–60% with CPAP. Long-termfollow-up needed.	I PubMED

						with high		
Citation of Evidence	**Study Question or Hypothesi s**	**Study Desig n**	**Sample/ Setting**	**Independent and Dependent Variables and Tools Used**	**Data Collection and Analysis**	**Findings**	**Recommendation s/ Implications**	**Evidence Level**

						compliance and significantly improves subjective and objective outcomes of sleep. Complications are uncommon and benign.		
Holfinger, S., Chan, L., & Donald, R. (2021). All you need is sleep: The effects of sleep apnea and treatment benefits in the heart failure patient. *Current Heart Failure Reports, 18*(3), 144–152. https://doi.org/10. 1007/s11897-021-00506-1	Does treatment for sleep disordered breathing improve the survival rates of patients with heart failure?	Review of current guide-lines.	Review of multiple treatment modalities for CSA or OSA given in current guidelines.	IV: ESS and AHI. DV: Heart failure patients who have OSA and CSA.	CPAP: first line treatment for CSA. BPAP improved AHI, LVEF, mitral regurgitation. Oral devices may reduce AHI, ODI, and sleep r/t sx- limited studies. Lateral sleep position might be more beneficial.	Neuromodulation: HNS reduced AHI by 50%. Phrenic nerve stimulation: Transvenous unilateral stimulation of diaphragm with implanted pulse generator when activated, leads to contraction of the diaphragm, maintains normal breathing.	High clinical suspicion for sleep apnea should be maintained for heart failure. Adaptive servo ventilation (ASV) shows reduction in AHI in CSA, but with LVEF ≤ 45% is contraindicated. Neurostimulation, CRT improves CSA; targeted loop gain is showed to be	III PubMED

Citation of Evidence	Study Question or Hypothesis	Study Design	Sample/ Setting	Independent and Dependent Variables and Tools Used	Data Collection and Analysis	Findings	Recommendations/ Implications	Evidence Level
						CRT reduced AHI by 16.9 events/hr. O_2: low flow nocturnal O_2 (NOXT) with 4LNC decreased AHI Acetazolamide: useful to treat periodic breathing and mild diuretic for metabolic alkalosis and for pt with CSA and LVEF ≤ 40%. Theophylline: lowers loop gain/stimulates breathing.	effective, but no long-term studies. More studies and reviews of studies needed.	
Dedhia, R. C., Shah, A. J., Bliwise, D. L., Quyyumi, A. A., Strollo, P. J., Li, Q., Da Poian, G., & Clifford, G. D. (2019). Hypoglossal nerve stimulation	What are the effects of HNS on heart rate variability (HRV), a	RCT; Single group cohort; a sub-study of the STAR	Academic and private practice centers in the U.S. and Europe. Subset of participants (*n* = 46) in	IV: HNS implanted patients DV: AHI, HRV and sleep stage.	At 12 mos post-surgery analyzed HRV with SD of R-R interval (SDNN), low-frequency power of R-R interval, high-frequency power of R-R interval.	Significant improvement from baseline to 12 mos in HRV for SDNN and low frequency	Prospective studies needed to examine HRV alterations during wake as well as other clinical sequelae, such as arrhythmia	11 PubMED

Citation of Evidence	Study Question or Hypothesis	Study Design	Sample/ Setting	Independent and Dependent Variables and Tools Used	Data Collection and Analysis	Findings	Recommendations/ Implications	Evidence Level
	measure							
and heart rate variability: Analysis of STAR trial responders. *Otolaryngology–Head and Neck Surgery, 160*(1), 165–171. https://doi.org/10.1177/0194599818800284	of autonomic function?	(Stimulation Therapy for Apnea Reduction) trial.	two groups: Therapy withdrawal or Therapy maintenance	Tools: Assessed effects of HNS at 12 mos using HRV on HF/LF.	Analysis by sleep with 5-min. sliding window epochs during baseline, 12 mos., and maintenance/ withdrawal period.	across all sleep stages. SDNN analysis: no change in wake period (mean ± SD: 0.042 ± 0.01 vs 0.077 ± 0.07, *P* = .19) Reduction in SDNN correlated to improvement in AHI (*r* = 0.39, *P* = .03). No changes in SDNN for therapy withdrawal group.	burden, before and after HNS implantation.	

Citation of Evidence	Study Question or Hypothesis	Study Design	Sample/ Setting	Independent and Dependent Variables and Tools Used	Data Collection and Analysis	Findings	Recommendations/ Implications	Evidence Level
Sato, K., & Nakajima, T. (2020). Review of systematic reviews on mandibular advancement oral appliance for obstructive sleep apnea: The importance of	Does mandibular oral appliance (OA) aid in the treatment of OSA?	Review of system-atic reviews	Sample: Clinic-based dentists; patients with OSA using either OAm or CPAP.	IV: OAm vs CPAP DV: AHI, ESS, quality of life (QOL) Comparison with another tx—mandibular advancement OA (OAm)	Baseline and 3 yrs. Compared OAm and CPAP use in 27 research articles and with 46 patients; however, most patients dropped out before the end of the 3-yr study.	• CPAP is superior to OA in improving OSA symptoms. • Should survey the adherence to	More studies needed on the effectiveness of OAm vs CPAP. Clinic-based dentists can treat with OAm. Dental education should include sleep medicine, and a	I PubMED

long-term follow- up. *The Japanese Dental Science Review*, *56*, 32–37. https://doi.org/10.1016/j.jdsr.2019.10.002			Setting: Ichikawa General Hospital, Tokyo Dental College	Review of SR done using PubMed. 50 articles considered, and 27 articles included. 10 articles on comparison with other txt; 5 articles on the types of OAM; 6 articles on the effect of OAM and associated side effects, 3 articles on predicting the therapeutic effect of OAM; 2 articles on changes in URT caused by OAM therapy, and 1 article on predicting the therapeutic effect of OAM.	CPAP is superior to OA in improving OSA symptoms One of the long-term side effects is posterior open bite Nonadherence of OAm devices	OAm therapy of patients who stopped CPAP therapy. • Little evidence supports the theory that OAm therapy prevents CV disease or improves life prognosis. • OAm therapy has dental and skeletal side effects with long-term use. • Still room for investigating the types of OAm; particularly essential to look at adherence and side effects after starting follow-up	specialty for dentists in OAm use and installation should be considered.	

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Citation of Evidence	**Study Question or Hypothesi s**	**Study Desig n**	**Sample/ Setting**	**Independent and Dependent Variables and Tools Used**	**Data Collection and Analysis**	**Findings**	**Recommendation s/ Implications**	**Evidence Level**

Citation of Evidence	Study Question or Hypothesi	Study Desig n	Sample/ Setting	Independent and Dependent Variables and Tools Used	Data Collection and Analysis	Findings	Recommendation s/ Implications	Evidence Level
						confirmed effect of OAm). • A certain percentage of patients discontinue consultation s.		
de Vries, G. E., Wijkstra, P. J., Houwerzijl, E. J., Kerstjens, H. A. M., & Hoekema, A. (2018). Cardiovascular effects of oral appliance therapy in obstructive sleep apnea: A systematic review and meta- analysis. *Sleep Medicine Reviews, 40,* 55–68. https://doi.org/ 10. 1016/j.smrv.201 7. 10.004	Does the use of oral appliance therapy (OAT) decrease the cardio- vascular effects (BP, HR, endotheli a l function, arterial stiffness, circulatin g cardio- vascular bio- markers, cardiac function, and cardio-	System - atic review and meta- analysi s	Sample: 25 full- text articles; 16 considere d method- logically sufficient, including 11 RCTs. Setting: N/A.	IV: Pretreatment vs OAT. DV: HR, HRV, endothelial function, arterial stiffness, circulating cardiovascular (CV) biomarkers, cardiac function, cardiovascular death. Tools: 2 independent reviewers using quality of study tool that has 53 weighted items on 15 dimensions; studies to be used had to meet 47/100 points for inclusion SD and 95% CI of each study.	Data from the RCTs were pooled to compare IV and DV. No major CV outcomes in severe OSA due to inconclusive data and small studies.	OAT may be beneficial, but minor effects on BP compared to baseline. Inconclusive/n o effects on cardiac function. OAT showed minor + effects on daytime SBP/ DBP; minor effects on mean daytime SBP and DBP compared to inactive therapies.	More methodologicall y high-quality longitudinal studies needed to determine if OAT leads to a reduction in long- term CV morbidity and mortality in OSA patients. Small studies limited range of OSA severity; therefore, larger studies needed. Better technology needed for assessment of effectiveness of	I PubMED

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	vascula r death) ?			ReviewManager (RevMan v. 5.3. Chi-square and i2 tests assessed heterogeneity.		OAT and CPAP equally effective in reducing BP, but only 2 RCTs were used in study. No major CV outcomes in severe OSA due to inconclusive data and small studies. Effect of medication for BP might have influenced results.	OAT and compliance.	