

SASM 6TH ANNUAL MEETING

October 20, 2016

Chicago, IL

**Alternative Treatments to
Positive Airway Pressure
Therapy for OSA**

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Mayo Clinic**

Objectives

- Explore data supporting role of alternative treatments for OSA patients
- Answer the following questions:
 - What can I tell my patients about?
 - Weight loss methods/lifestyle changes
 - Positional therapy
 - Oral Appliances
 - Assorted other therapies
 - Upper Airway Stimulation
 - Surgery

Disclosures

- Acknowledgment: Several Colleagues
- Conflicts- Nothing to Declare



Body Weight and OSA



Effects of Change in Weight on OSA: Longitudinal Studies

- 690 Healthy volunteers underwent repeat sleep studies 4 yrs after their initial PSG
- The changes in AHI were correlated to changes in weight after potential covariates were taken into account.
 - 10% wt loss yields ~ 30% AHI reduction
 - In patients with AHI 5-15/hr, 10% wt gain = 6 fold increase risk of AHI>15

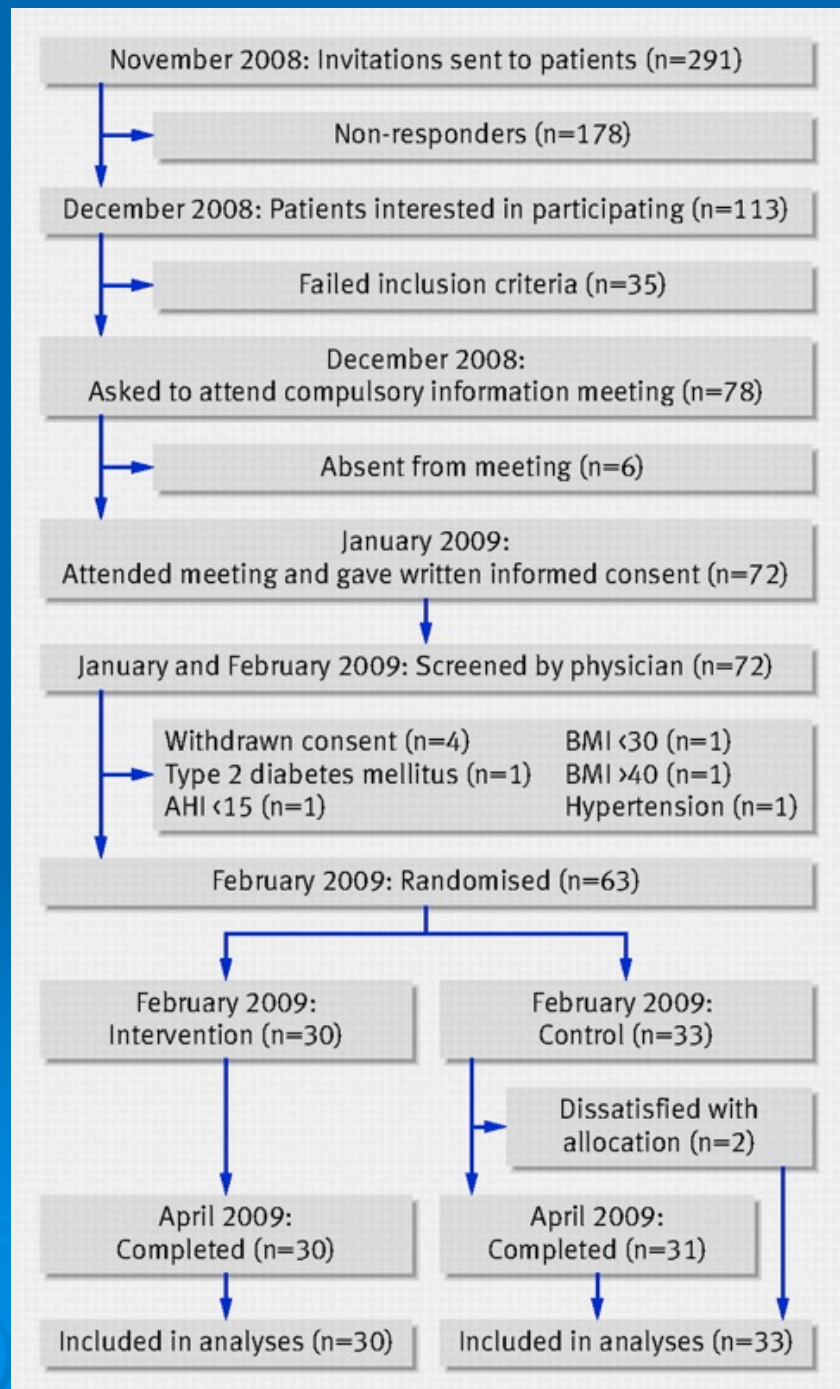
Short Term Crash Diets

Intervention group-

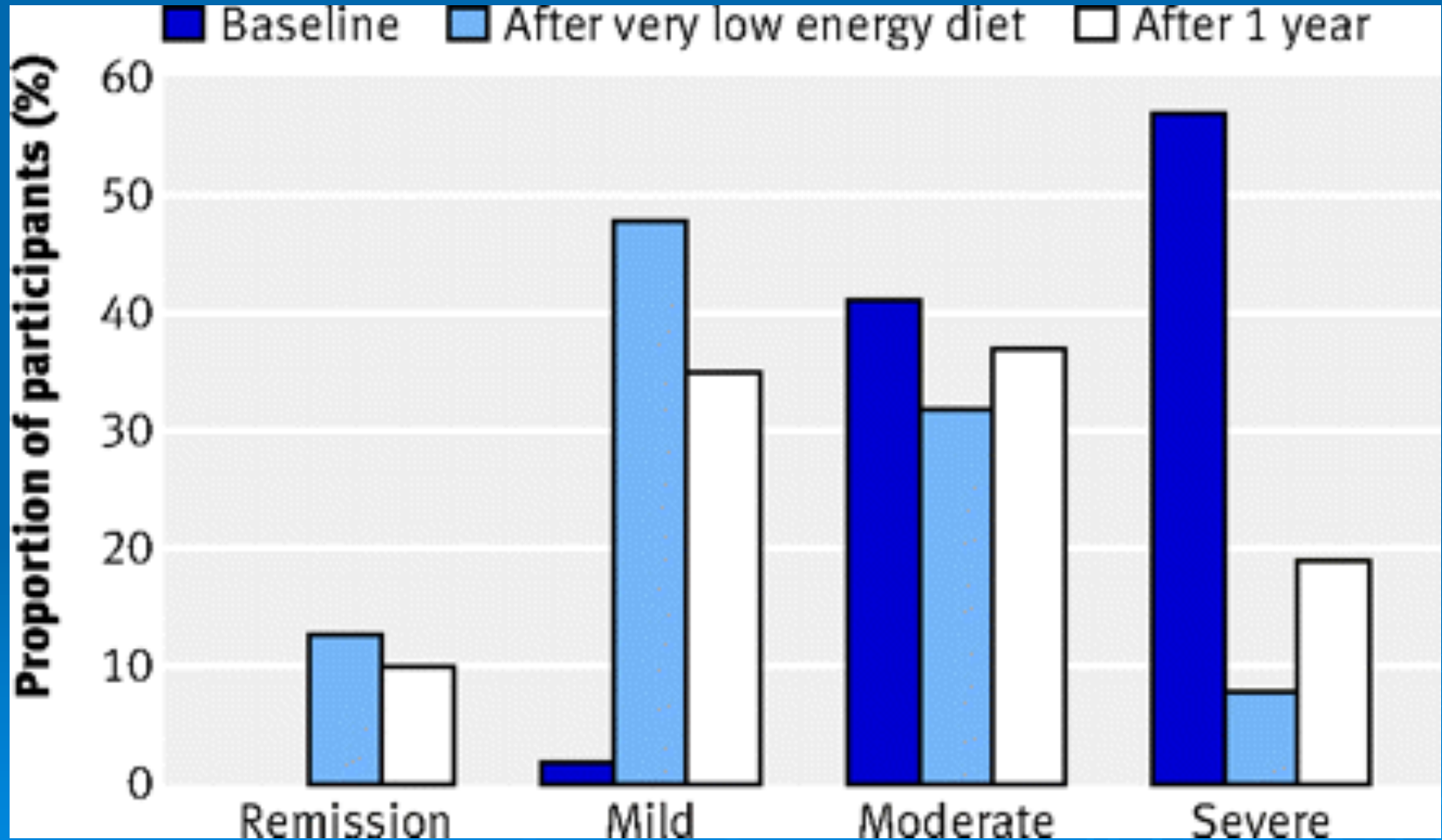
- Liquid low energy diet (2.3 MJ/day) for 7 wks
- 2 wks gradual restart normal food, reaching 6.3 MJ/day at wk 9

Control group-

- Adhere to usual diet during 9 wks follow-up



Short Term Crash Diets



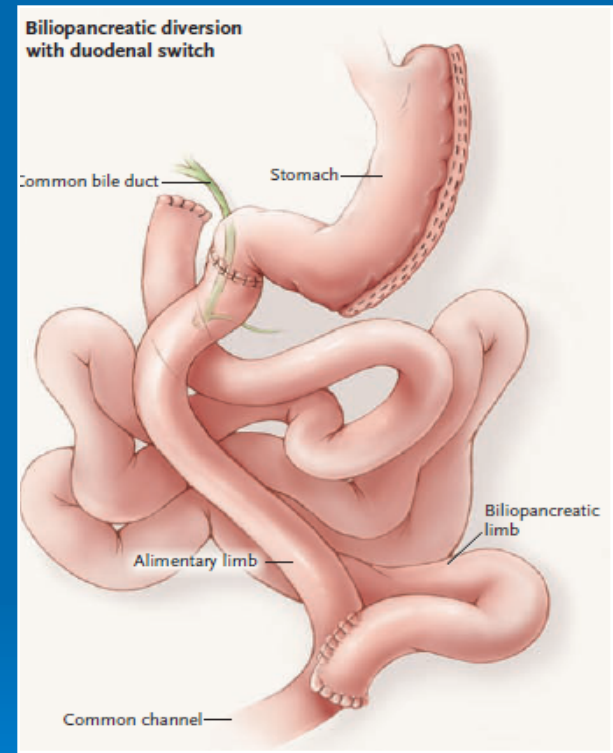
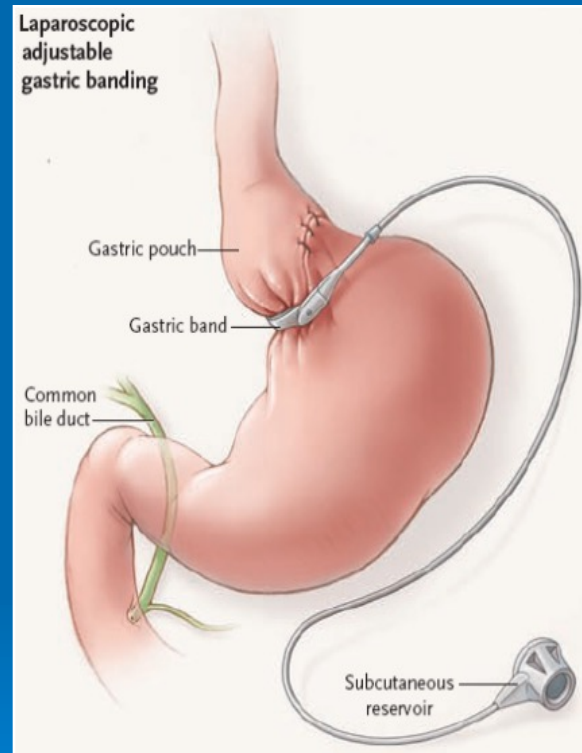
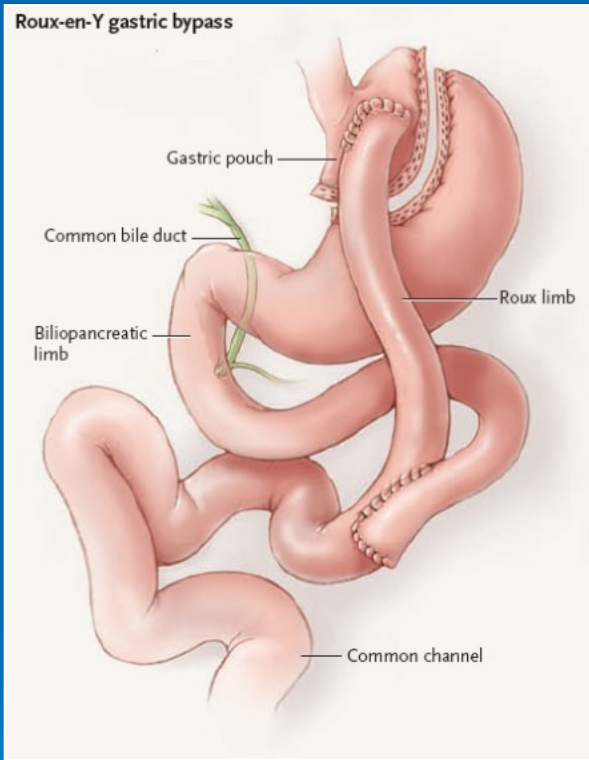
Weight Loss and AHI

Table 1. Dietary weight loss: effect on sleep apnea

| | <i>n</i> | Length of follow-up | Method of weight loss | Weight change kg (%) | AHI pre | AHI post |
|---------------------------------------|----------|---------------------|---|----------------------|---------|----------|
| Smith et al [11] | 15 | 5.3 mo | Dietary advice/follow-up | -9.6 (-9) | 55 | 29.2 |
| Schwartz et al [9] | 13 | 17 mo | Dietary advice/follow-up | -11.8 (-17.4) | 83.3 | 32.5 |
| Rubinstein et al [12] | 12 | 8-18 mo | Diet/gastroplasty | -24 (-20.5) | 57 | 14 |
| Kiselak et al [13] | 19 | 18-20 wk | Diet/exercise/behavioral therapy | -27.2 (-23.9) | 17.6 | ? |
| Suratt et al [14] | 8 | 24 mo | Very low calorie diet | -21.0 (-14) | 90.0 | 62.0 |
| Pasquali et al [18] | 23 | ? | Diet or very low calorie diet/ follow-up | -18.5 (-17.5) | 66.5 | 33 |
| Rajala et al [15] | 8 | ? | Diet | ? (-13) | 39.5 | 31.6 |
| Lojander et al [16] | 24 | 1 y | Very low calorie diet/diet/follow-up | -11.0 (-10.0) | ? | ? |
| Kansanen et al [17] | 15 | 3 mo | Very low calorie diet | -9.0 (-7.9) | 31 | 19 |

In patients with significant OSA, even when there are large changes in weight, cure is not at all certain.

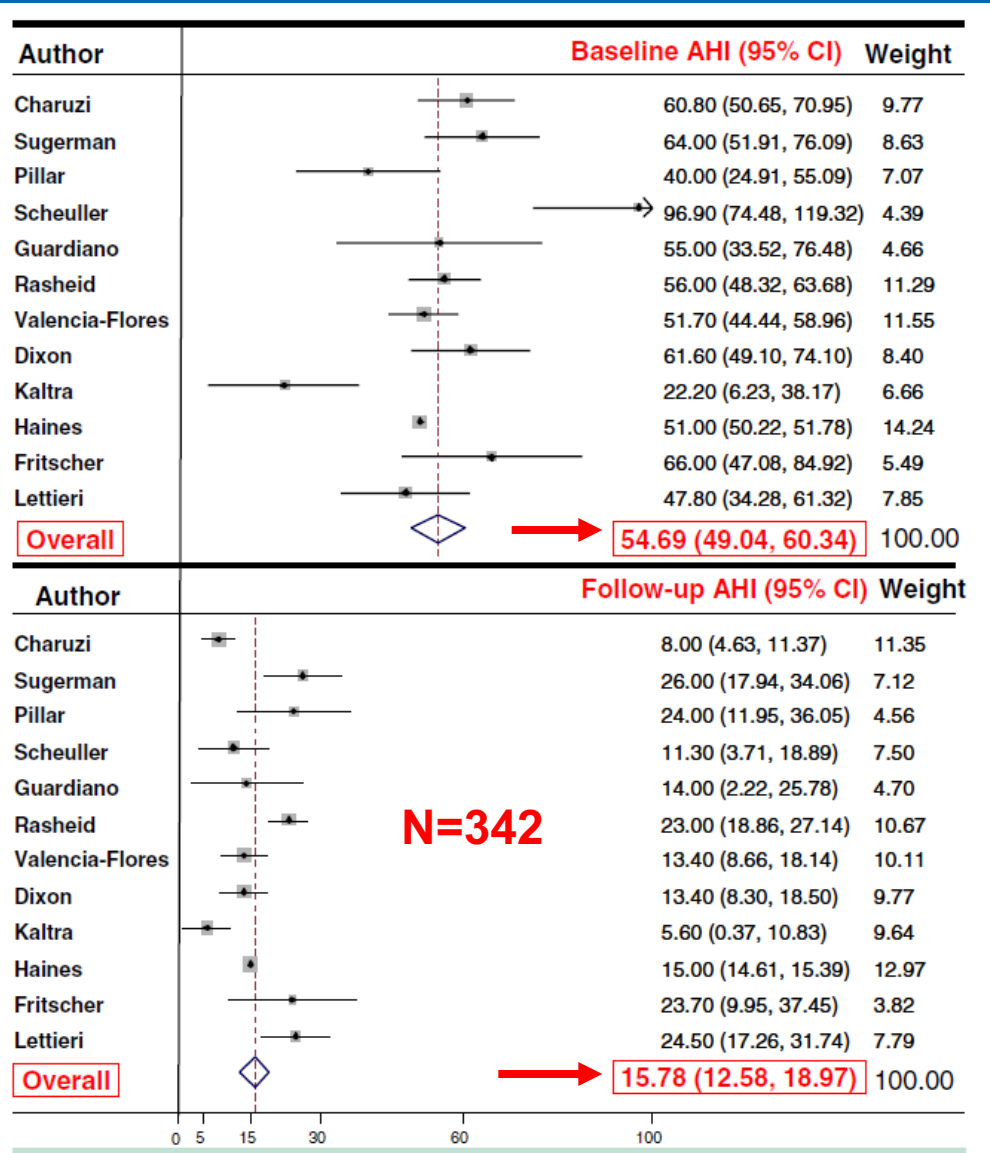
Bariatric Surgery



Indications

BMI \geq 40 OR \geq 35 plus \geq 1 co-morbid condition
Failed an adequate exercise and diet program

Bariatric Surgery: Outcomes



- ## Bariatric Surgery
- **Mean AHI ↓ 38/hr**
 - **Post-op AHI: 15.8/hr**
 - **Post-op BMI: 37.7/hr**
 - **Mean Wt ↓ 40 kg (30%)**
 - **BMI ↓ 14.2 kg/m² (30%)**

Greenburg DL. Am J Med 2009; 122: 535
 Buchwald H. JAMA 2004; 292:1724
 Maggard MA. Ann Int Med 2005; 142:547

Positional Therapy



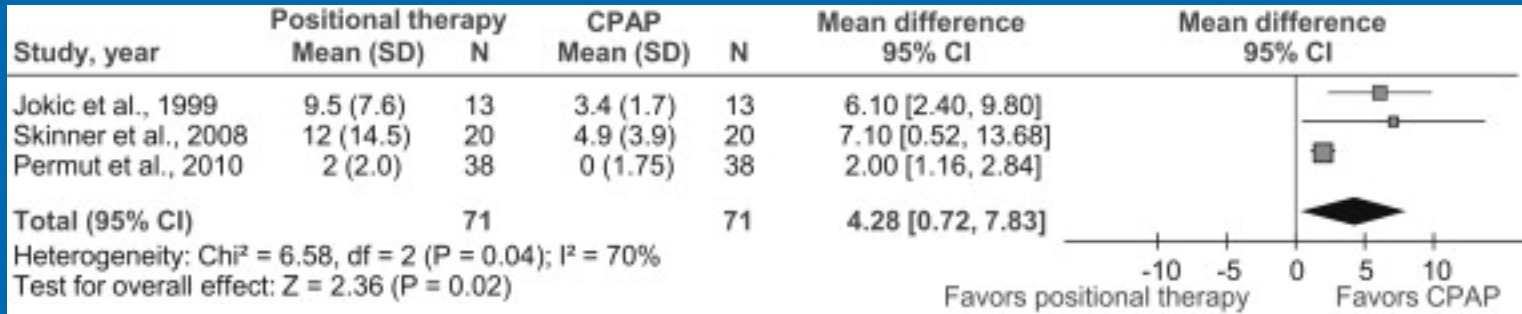
Positional Therapy



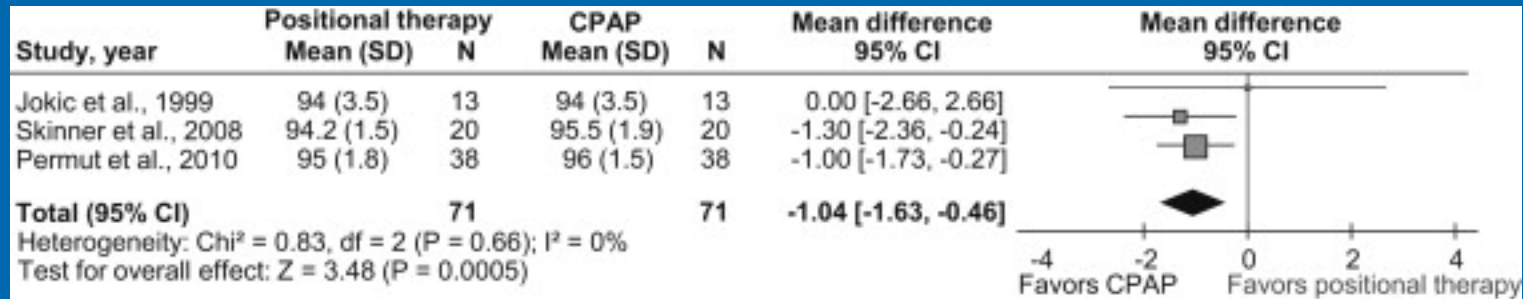
Positional Therapy Indications

- Mild OSA (AHI <15)
- $AHI_{\text{supine}} \geq 2X AHI_{\text{lateral}}$, with $AHI_{\text{total}} < 15$ in lateral position
- No positional pain issues-
hip surgery, shoulder pain

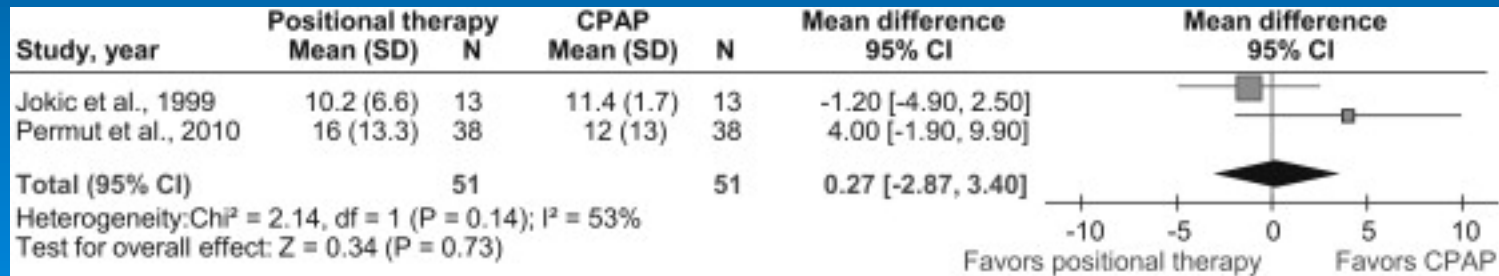
AHI



Mean O2



ArsI



Stanley CN et al. Comparison of positional therapy versus continuous positive airway pressure in patients with positional obstructive sleep apnea: A meta-analysis of randomized trials. Sleep Med Rev 2014; Vol 18(1):19-24

Positional Therapy (AASM)

- Positional therapy, consisting of a method that keeps the patient in a non-supine position, is an effective secondary therapy or can be a supplement to primary therapies for OSA in patients who have a low AHI in the non-supine versus that in the supine position. (Guideline)

Morgenthaler TI; Kapen S; Lee-Chiong T et al. Practice parameters for the medical therapy of obstructive sleep apnea.

SLEEP 2006;29(8):1031-35

Positional Therapy

Bottom Line

- Not for patients with mod-severe OSA
- All studies report a positive effect of PosTx on AHI
- Snoring decreases in nonapneic snorers; BUT LESS reliably in patients with OSA
- Short term compliance is better than with CPAP
- Long term compliance is poor- 28-38% at 1-2 years
- PosTx helps with OralA and UUUP patients
- Less CPAP needed non-supine vs supine posture
- nEPAP therapy better tolerated in non-supine posture

Pharmacologic therapy of OSA:

- Modafinil is recommended for the treatment of residual excessive daytime sleepiness in OSA patients who have sleepiness despite effective PAP treatment and who are lacking any other identifiable cause for their sleepiness. (Standard)
- Oxygen supplementation is not recommended as a primary treatment for OSA. (Option)

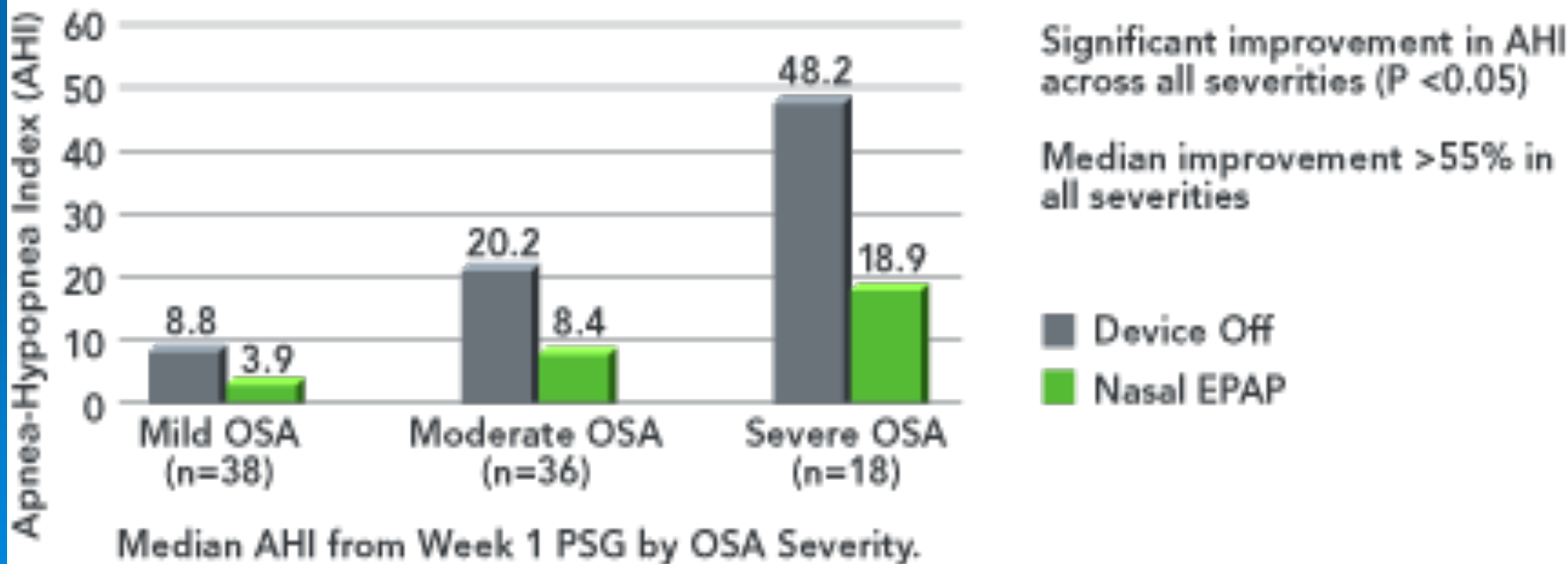
Pharmacologic Therapy of OSA: Nasal Therapies

- Short-acting nasal decongestants are not recommended for treatment of OSA. (Option)
- Topical nasal corticosteroids may improve the AHI in patients with OSA and concurrent rhinitis, and thus may be a useful adjunct to primary therapies for OSA. (Guideline)

Nasal Therapy EPAP Provent™



Provent Therapy Works Across All OSA Severities¹

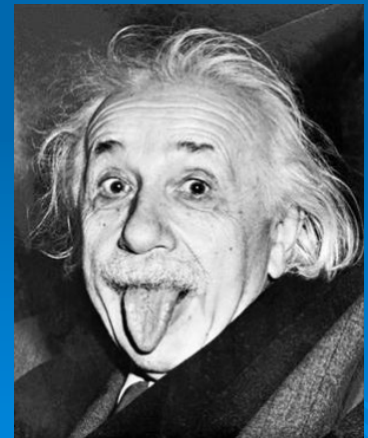


Berry RB; Kryger MH; Massie CA. A novel nasal expiratory positive airway pressure (nEPAP) device for the treatment of obstructive sleep apnea: a randomized controlled trial. SLEEP 2011;34(4):479-85



**CAN I GET SOMETHING
FROM THE DENTIST INSTEAD?**

2011: More than 90 FDA-Approved Devices



<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/PMNSimpleSearch.cfm>

Type "LRK" or "LQZ"

MRA: Mandibular Repositioning Appliance

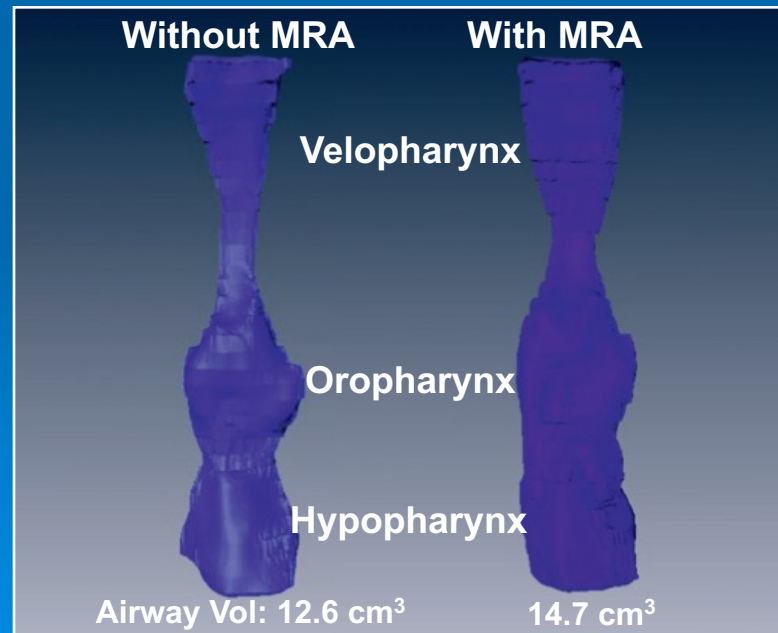
Oro- vs Velopharyngeal Impact

Primary site of action of MRA

Oropharynx¹

Velopharynx²

| | Site of Obstruction | |
|--------------------|---------------------|------------|
| | Velopharynx | Oropharynx |
| Complete responder | 1 | 4 |
| Partial responder | 2 | 0 |
| Failure | 5 | 0 |



Awake MRI:
Velopharyngeal dimensions with MRA
In responders

¹Ng AT. Sleep 2006; 29:666

²Chan ASL. Thorax 2010; 65:726

MRA Clinical Outcomes

➤ : Impact on AHI*- **50/50 Rule**

- AHI ≤ 5 (8 studies): 42%
- AHI ≤ 10 (30 studies): 52%
- 50% AHI reduction (10 studies): 65%

➤ Other PSG Parameters*

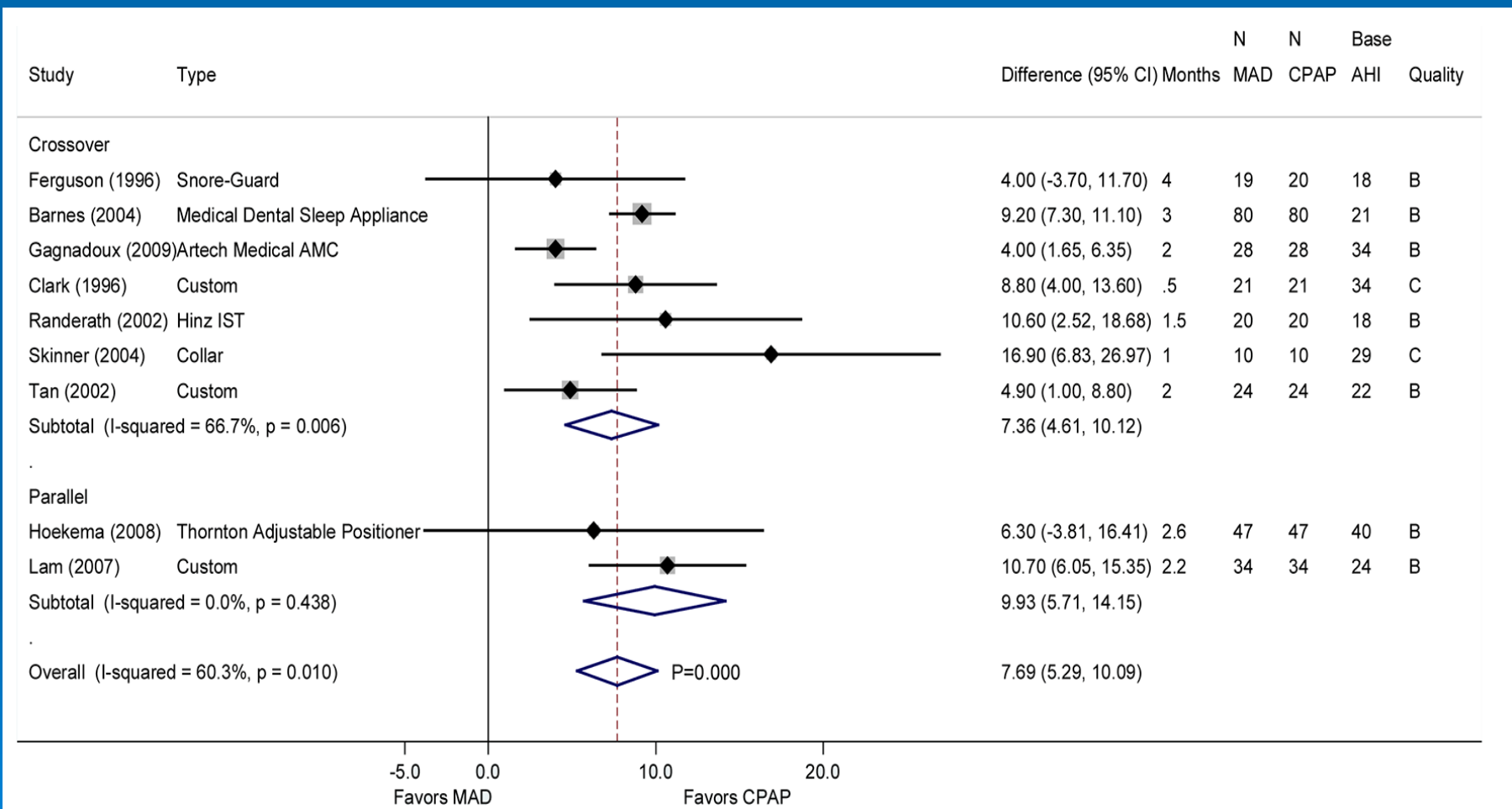
- Minimum SpO₂: Small increase (3%), not normalized
- Arousals: Reduced (-10/hr)
- Snoring: Frequency \downarrow 40-60%; intensity \downarrow 3dB

➤ Sleepiness

- Epworth: \downarrow -2.1 points¹ ; MSLT: \uparrow 1.2 mins² ;MWT: equivocal^{3,4}

*Ferguson KA Sleep 2006; 29:244, ¹Lim J Cochrane Data Base Syst Rev 2006, ²Gotsopoulos H Am J Respir CCM 2002; 166:743, ³Menn SJ. Sleep 1996; 19:794, ⁴Barnes M. Am J Respir CCM 2004; 170:656

CPAP vs MRA: AHI



CPAP: Favored at reducing AHI, arousals, and improving SpO₂

CPAP vs MRA- Other Endpoints

- Health-related quality of life
 - FOSQ, SAQLI, SF-36
- Psychological outcomes
- Cognitive outcomes
- Driving performance
- Compliance

No consistent differences

Practice Parameters for the Treatment of Snoring and Obstructive Sleep Apnea with Oral Appliances: An Update for 2005

An American Academy of Sleep Medicine Report **Sleep 2006; 29:240**

Clete A. Kushida, MD, PhD¹; Timothy I. Morgenthaler, MD²; Michael R. Littner, MD³; Cathy A. Alessi, MD⁴; Dennis Bailey, DDS⁵; Jack Coleman, Jr., MD⁶; Leah Friedman, PhD⁷; Max Hirshkowitz, PhD⁸; Sheldon Kapen, MD⁹; Milton Kramer, MD¹⁰; Teofilo Lee-Chiong, MD¹¹; Judith Owens, MD¹²; Jeffrey P. Pancer, DDS¹³

- Primary snorers who do not respond to or not appropriate for risk factor modifications

- Patients with mild to mod OSA (AHI < 30) who:
 - Prefer OA
 - Fail to respond to CPAP or risk factor modifications

- Severe OSA: CPAP should be tried first

Predictors of Treatment Outcome

- Lower AHI and CPAP pressure need
- Greater protrusion by device
- Positional OSA with Lower BMI
- Younger age
- Smaller neck circumference
- Lateral cephalometrics
 - normal mandibular length and facial height
 - Small, narrow oropharynx
 - Smaller overjet and shorter soft palate length
 - Increased retropalatal airway space

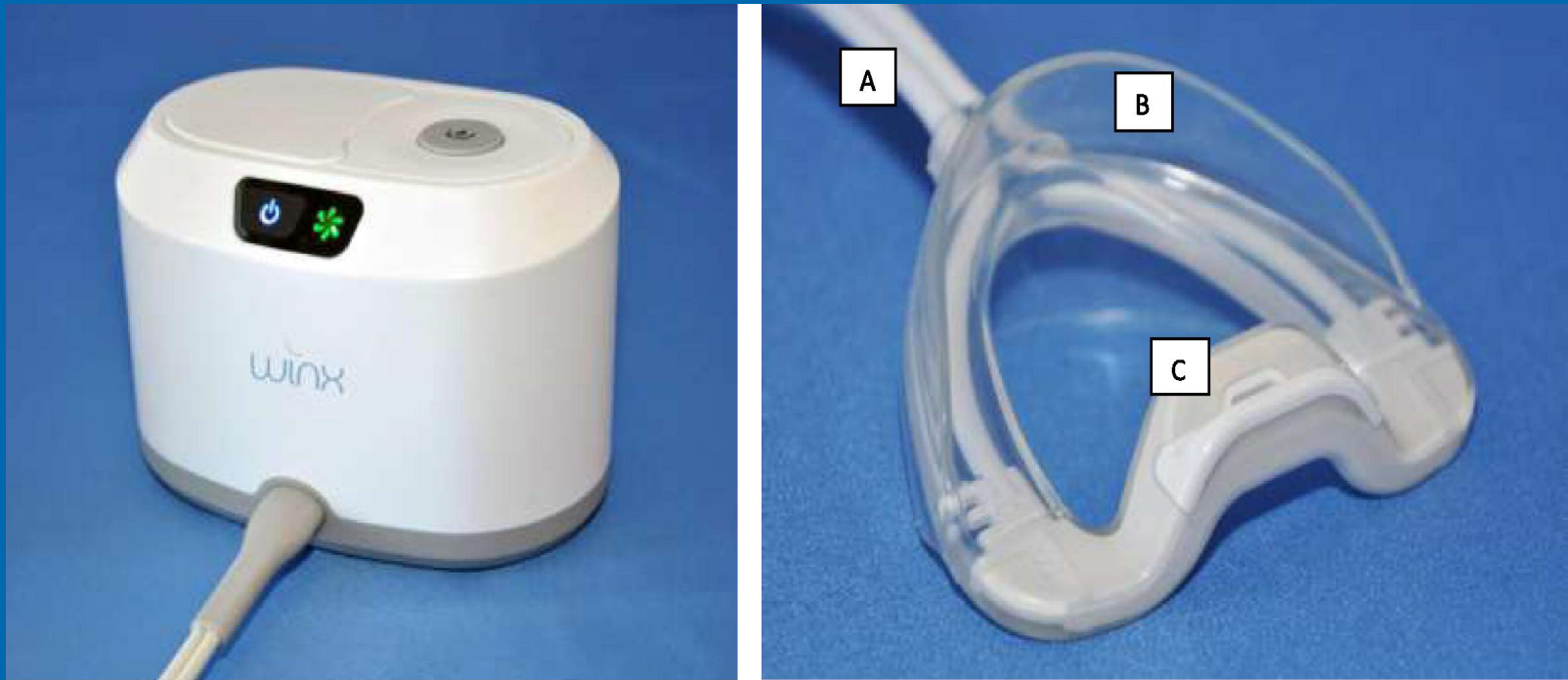
Complications from Oral Appliances

- Occlusive changes
- Tooth movement
- Dry mouth
- TMJ pain or sound
- Myofascial pain
- Tooth/Tongue pain
- Salivation
- Mandible Deviation
- Loosening of teeth
- Gum irritation
- Bruxism
- Skeletal changes
- Gagging

Dental Contraindications to OA

- Adequate number of healthy teeth in each dental arch (usually 8)
- Inability to protrude the mandible forward by ≥ 5 mm without limitation
- Moderate to severe TMJ problems
- Significant bruxism- maybe
- Full dentures generally unable to use MRA but may be treated with a tongue-repositioning device.

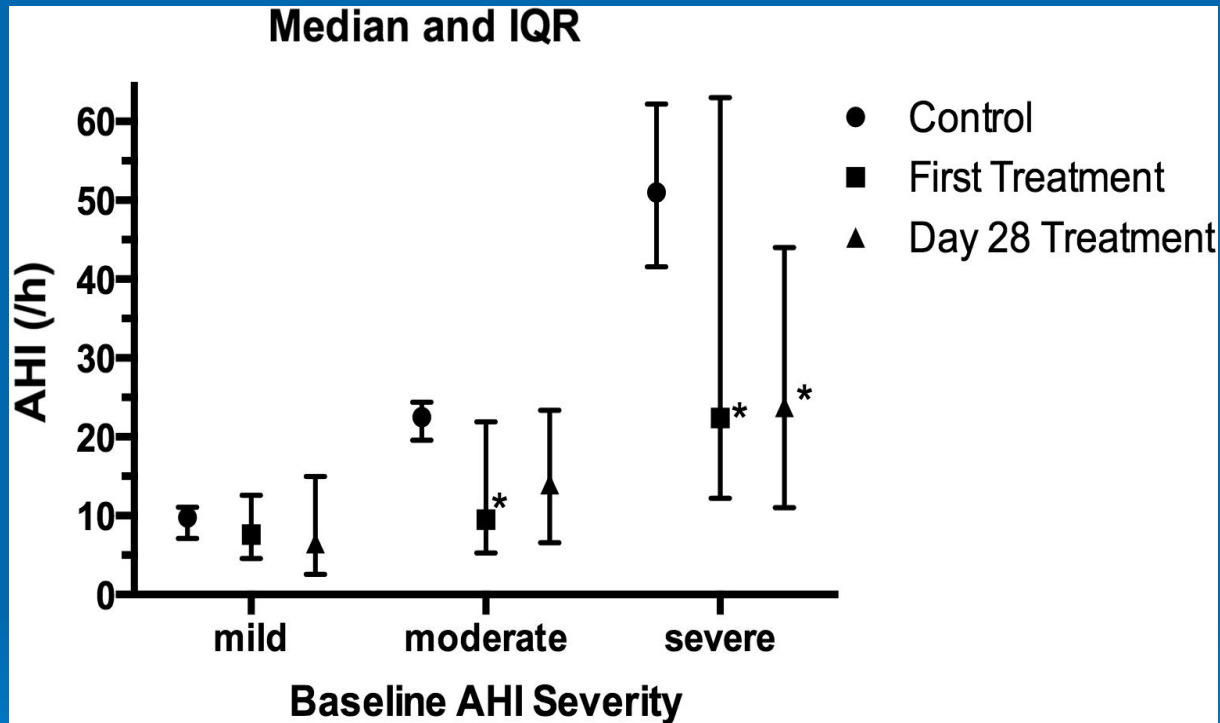
Oral Pressure Therapy



Oral pressure therapy (OPT) system (Winx™). The left panel shows the nightstand console unit containing the vacuum pump and saliva reservoir. The right panel shows the mouthpiece, vacuum pressure and sensor tubing

Colrain IM et al. A multicenter evaluation of oral pressure therapy for the Treatment of obstructive sleep apnea. *Sleep Med* 2013; Vol 14(9): 830-37

Oral Pressure Therapy



- AHI at control, first treatment night, and after 28 days of treatment vs control OSA severity
- Control AHI severity was classified as mild (5–15/h), moderate (15–30/h), or severe (>30/h)

Summary for OA Therapy

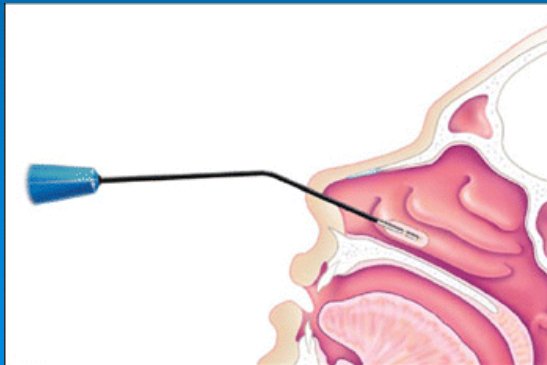
- ~ 50% achieve 50% fall or $AHI \leq 10$
- Works best with lower AHI or BMI, positional pts
- Best not to suggest to those with significant TMJ or dental problems
- Occlusion changes very likely yet usually mild
- Dental professional fits and follows complications
- Follow up for sleep issues is needed
- CPAP > MRA lowering AHI; other outcomes =

OSA Surgical Procedures

- Procedures involving:
 - Nasopharynx
 - Palate and Oropharynx
 - Upper airway stimulation
 - Mandibular other major skeletal areas
- Bypass procedures- Tracheostomy

Nasal Surgeries

- Septoplasty
- Polypectomy
- Turbinectomy
 - Radiofrequency ablation:
 - necrosis → tissue volume reduction

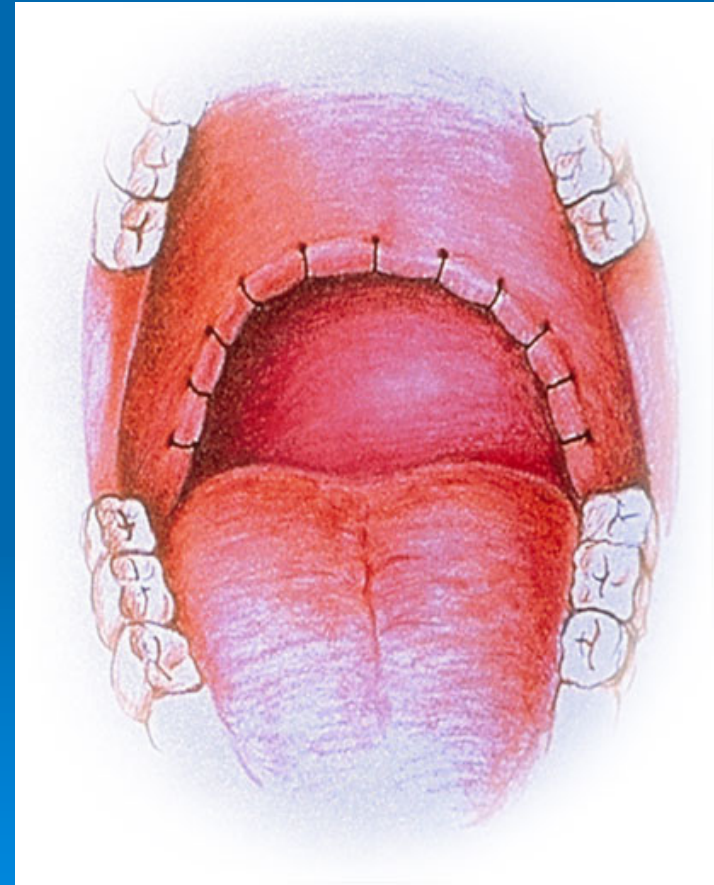
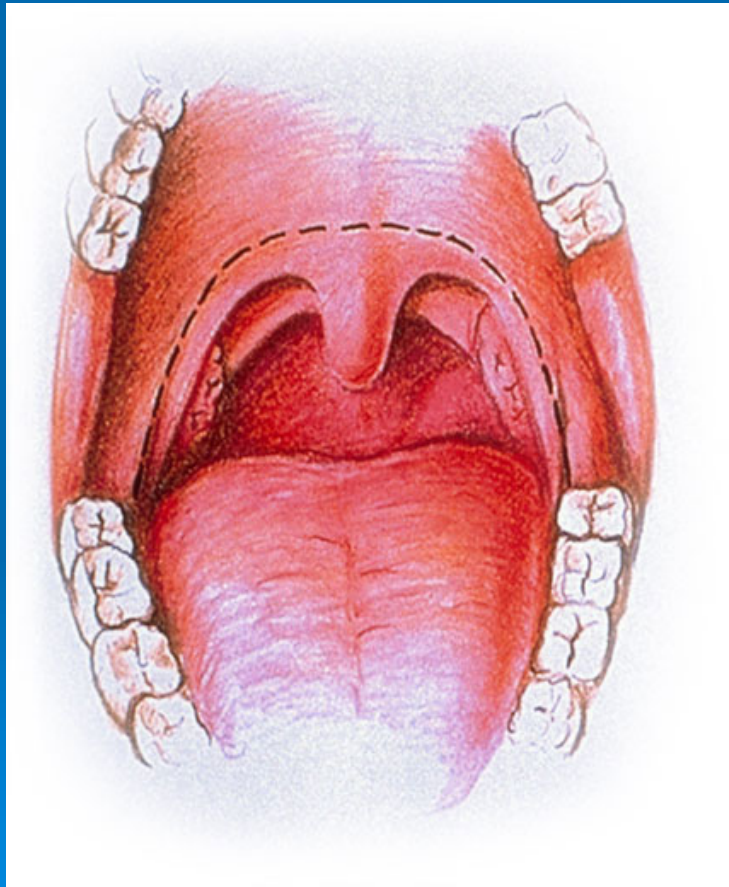


5/302 (1.6%) minor complication rate
(mucosal irritation)

Nasal Surgeries: Outcomes

- Very limited data support as sole therapy
- AASM practice parameter don't address
- Practically:
 - Means to improve PAP adherence
 - Part of multilevel surgical approach to OSA

Uvulopalatopharyngoplasty (UPPP)



UPPP- Indications and Predictors

➤ AASM Indications:

- Patients with severe OSA should be initially offered PAP therapy
- Those with moderate OSA should initially be offered either PAP or oral appliance (option)

➤ Predictors of success:

- DISE retropalatal obstruction associated with better UPPP outcomes
- Awake endoscopy with Muller maneuver not predictive of UPPP outcomes

UPPP: Outcomes

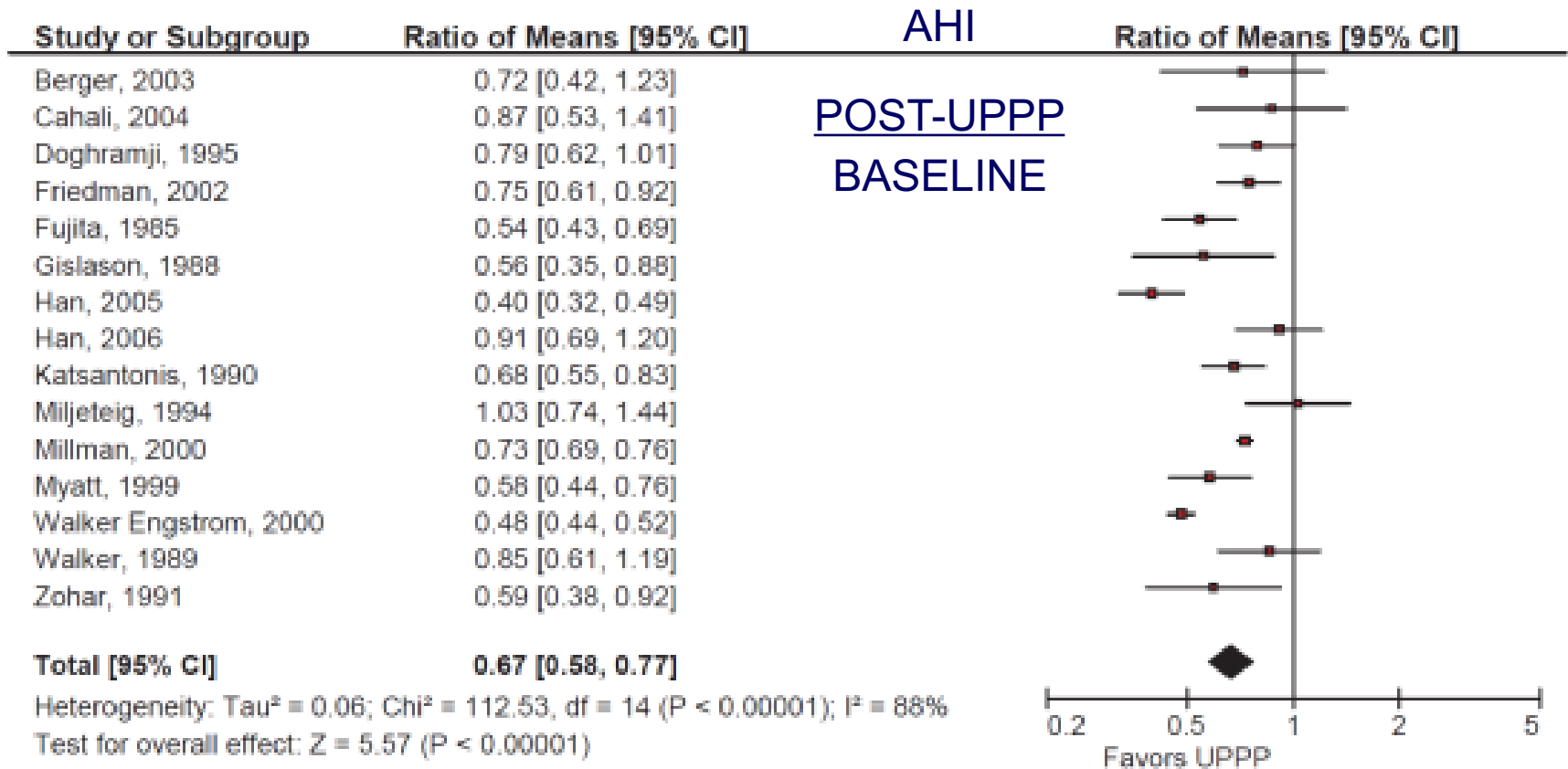


Figure 4—Ratio of means meta-analysis of UPPP. CI refers to confidence interval.

Pooled AHI Reduction: 33% (95% CI 23%-42%)

UPPP: Chronic Complications

- Dysphagia (31%)
- Voice changes (13%)
- Taste disturbances (5%)
- Residual OSA (80%)
 - Close follow-up required!

Laser Assisted Uvulopalatoplasty (LAUP)

- 2 RCTs: no significant changes in AHI, secondary outcomes vs controls
 - AHI may worsen
- Persistent side effects common
 - Dysphagia
 - Globus sensation
- AASM: **Not** routinely recommended as a treatment for OSA (standard)¹

Radiofrequency Ablation (RFA) of Soft Palate and Tongue

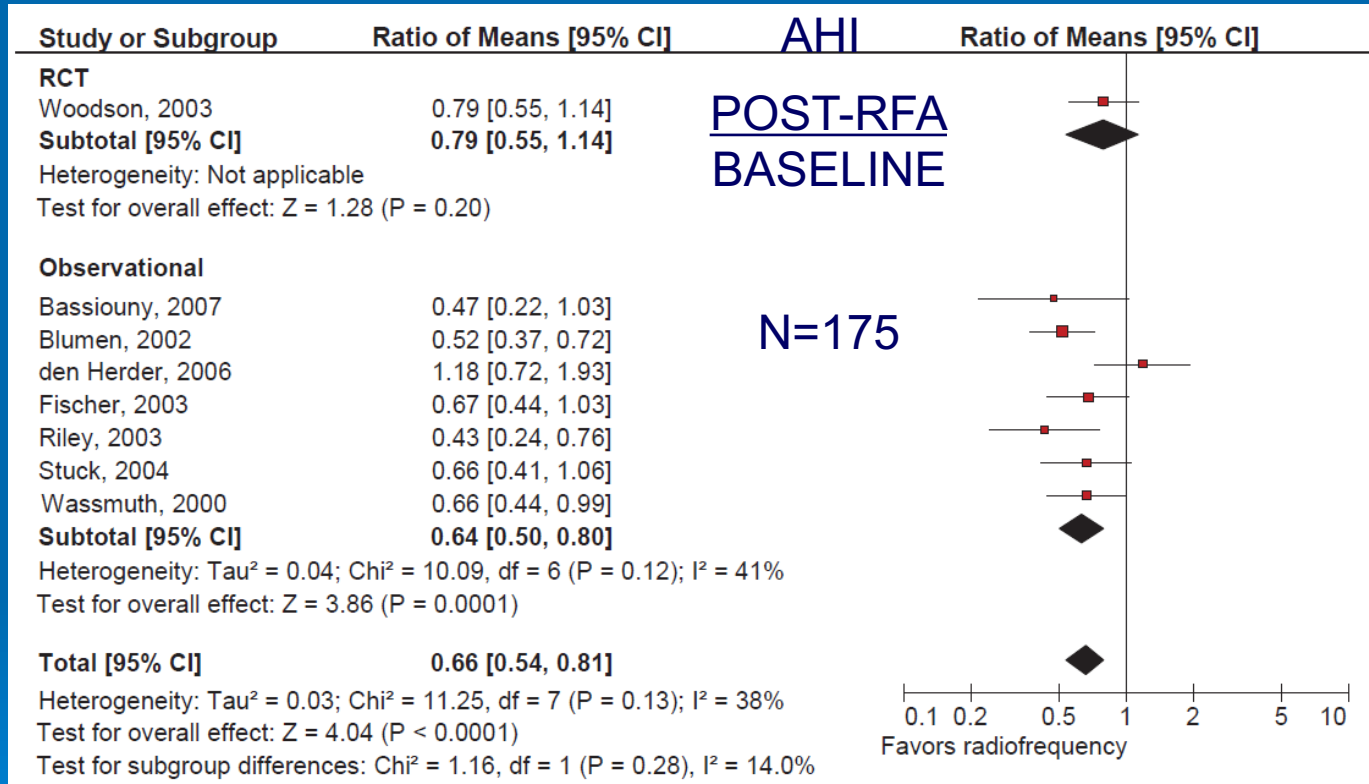
- Outpatient application
- Applicable to multiple upper airway structures
- Repeatable



RFA: Indications

- AASM: Can be considered as a treatment in patients with mild to moderate OSA who cannot tolerate or who are unwilling to adhere to PAP or in whom oral appliances have been considered and found ineffective or undesirable (Option)
- Practically: Adjunctive procedures

RFA: Outcomes



Pooled AHI Reduction: 34%

ESS reduction: 31%²

Residual AHI: 14.9

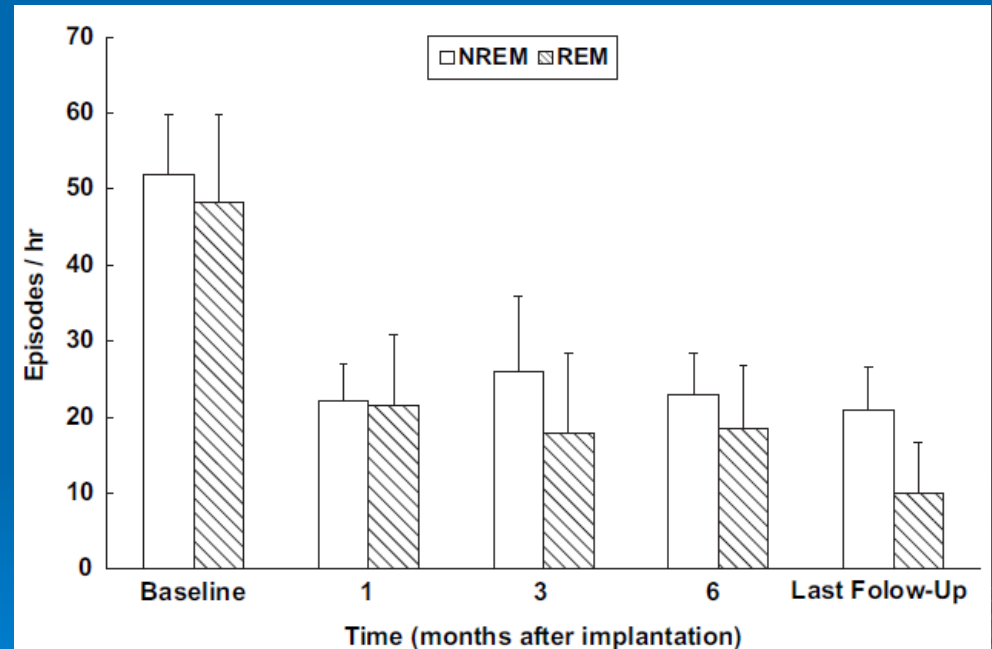
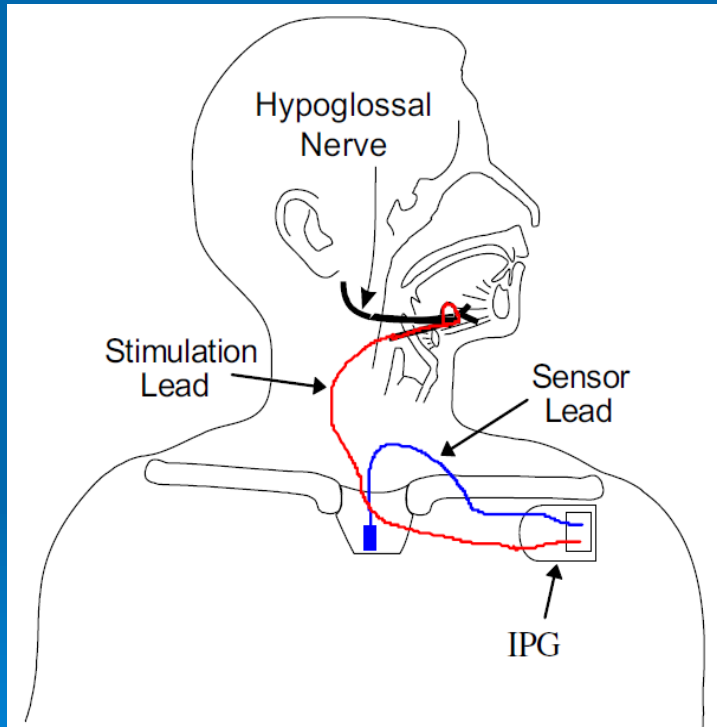
¹Caples SM. Sleep 2010; 33:1408

²Farrar J. Laryngoscope 2008; 118:1878

RFA: Complications

| Soft Palate RFA Complications | Events (Rate Per Total # Treatments) (144 Patients Over 331 Treatment Sessions) |
|---|---|
| Mucosal ulceration | 8 (2.4%) |
| Palate perforation | 4 (1.2%) |
| Peritonsillar abscess | 1 (0.3%) |
| Total | 13 (3.9%) |
| Tongue base RFA complications | (252 patients over 1092 treatment sessions) |
| Floor of mouth hematoma | 8 (0.7%) |
| Tongue cellulitis w/o abscess | 7 (0.6%) |
| Tongue edema requiring hospitalization | 7 (0.6%) |
| Mucosal ulceration | 6 (0.6%) |
| Tongue base abscess | 3 (0.3%) |
| Hypoglossal nerve paresis | 3 (0.3%) |
| Lingual nerve hypesthesia | 2 (0.2%) |
| Prolonged odynophagia | 1 (0.1%) |
| Vasovagal syncope | 1 (0.1%) |
| Total | 38 (3.5%) |

Hypoglossal Nerve Stimulation



Hypoglossal Nerve Stimulation

Stimulation Therapy for Apnea Reduction (STAR Trial) [ClinicalTrials.gov NCT01161420](https://clinicaltrials.gov/ct2/show/study/NCT01161420)

Strollo et al, NEJM 2014 370:139-49

Hypothesis: Unilateral Stimulation of the Hypoglossal Nerve during sleep will safely and effectively treat Obstructive Sleep Apnea

Methods

- Prospective, multicenter trial with a randomized therapy withdrawal arm in participants with moderate to severe OSA who had failed or had not tolerated CPAP.
- All underwent a screening polysomnographic (PSG) study, surgical consultation, and drug-induced sedation endoscopy (DISE).

Inclusion Criteria

- AHI between 20 and 50
- Have failed or have not tolerated CPAP
- Central and mixed sleep apnea accounted for < 25% of all AHI events
- Absence of significant apnea when sleeping in a non-supine position ($AHI_{\text{non-supine}} > 10$)

Exclusion Criteria

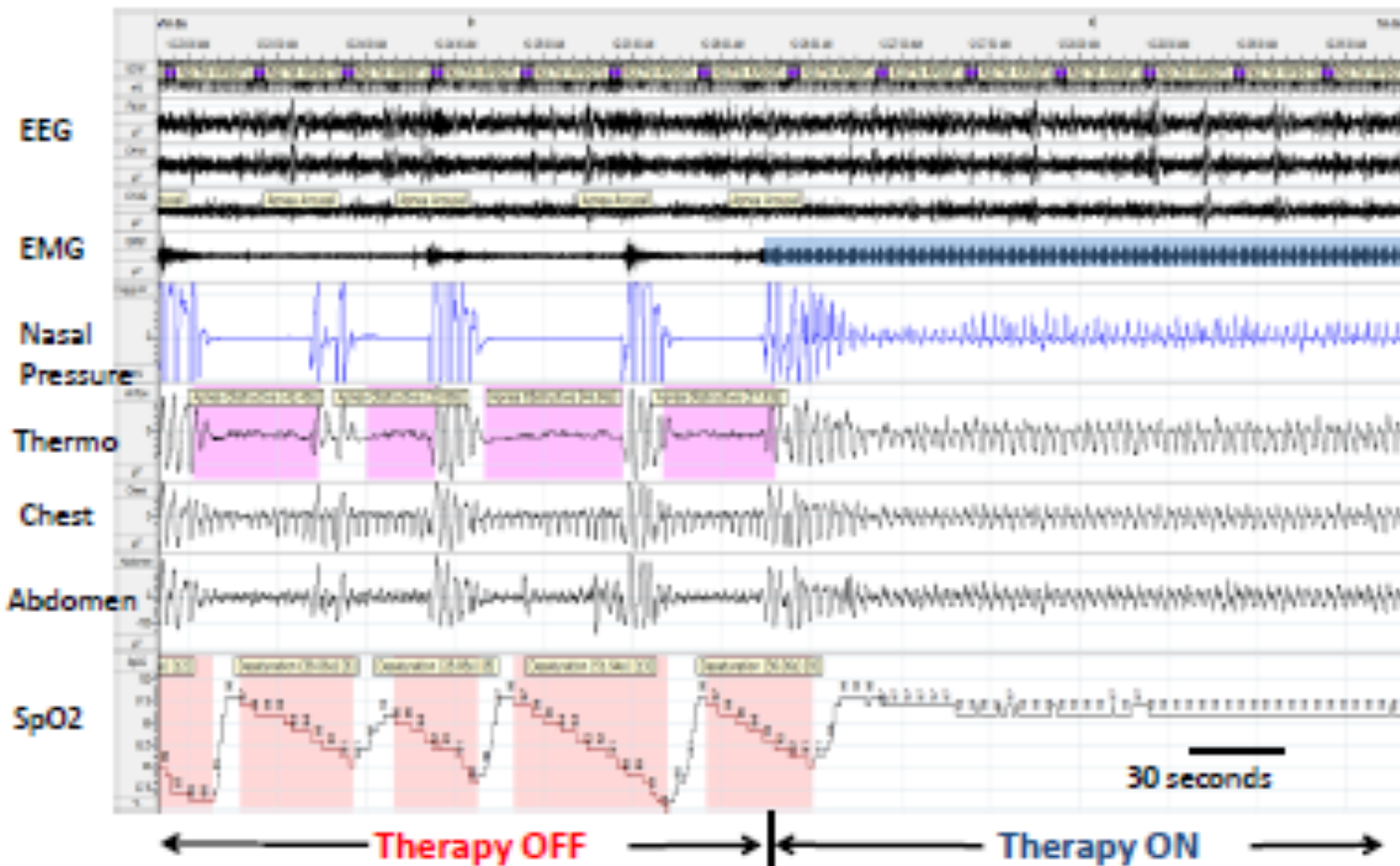
- BMI > 32
- Neuromuscular diseases
- Severe Co-Morbid Cardiopulmonary Disease
- Other chronic sleep disorders
- Complete concentric collapse at the level of soft palate during drug-induced sedation endoscopy (DISE)

Outcome Measures: Baseline vs. 12-Months

- Co-Primary
 - Apnea Hypopnea Index
 - Oxygen desaturation index ($ODI_{4\%}$)

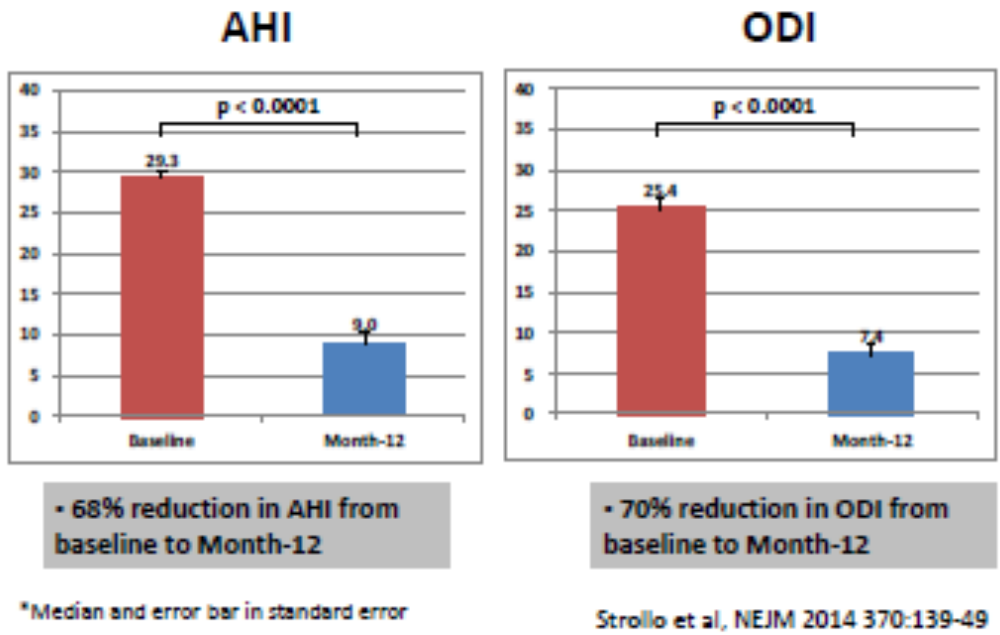
Hypoglossal Nerve Stimulation

PSG: Effect of Stimulation



Hypoglossal Nerve Stimulation

Primary Outcome Measures: AHI and ODI (n = 124)



12 Month F\U

- 37/126 (29%) AHI < 5/hr
- 67/126 (53%) AHI < 10/hr=R
- 80/126 (63%) AHI < 15/hr

Significant but Clinically Questionable Differences

- 10% less total sleep
- 10% less REM

Hypoglossal Nerve Stimulation

Relevant Adverse Events

- **Serious: Device related**
 - *1% Device revision*
- **Non Serious: Procedure related**
 - *~ 25% Pain* (minimal, most did not require narcotics - substantially less than UPPP)
- **Non-Serious: Device related**
 - *~ 33% Tongue discomfort / abrasion* (time limited)
 - *1% Mild or Mod Infection* (cellulitis)

* One Death Unrelated to the Trial

Conclusions

- Upper Airway Stimulation is an additional tool for the management of properly selected “at risk” patients who do not accept or adhere to positive pressure therapy
- The STAR Trial has provided robust evidence that upper airway stimulation is safe and effective in participants with moderate to severe OSA
- The treatment effect is maintained beyond the 12 month endpoint

Review of Hypopharyngeal Surgeries*

| Procedure | Studies, N | Success** |
|--------------------------|------------|-----------|
| Genioglossus advancement | 4, 91 | 39%-69% |
| Hyoid suspension | 4, 101 | 17%-78% |
| Midline glossectomy | 5, 74 | 25%-83% |
| Tongue stabilization | 6, 77 | 20%-57% |

Low baseline AHI, BMI inconsistent predictors of success

*Concurrent palatal operation in all subjects

**AHI ↓ 50% and post-op AHI < 20

MMA: Indications

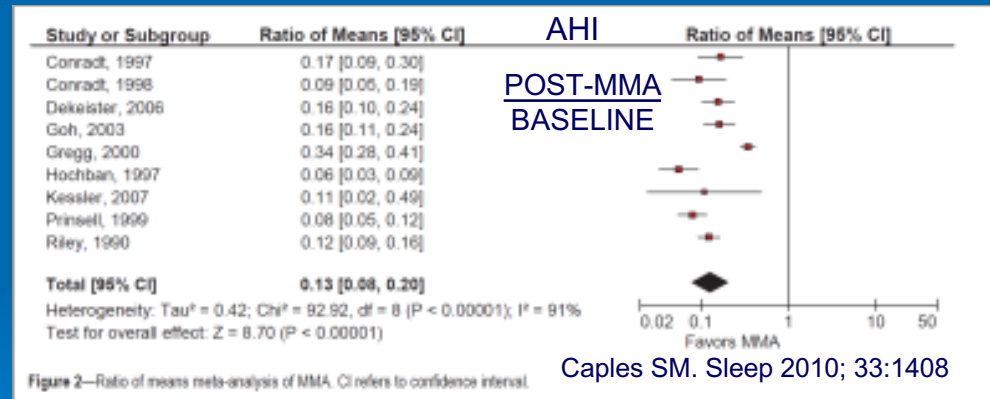
- AASM: Indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to PAP, or in whom oral appliances, which are more often appropriate in mild to moderate OSA, have been considered and found ineffective or undesirable (option)

MMA: Predictors of Response

- Younger age
- Lower pre-op AHI and BMI
- Greater maxillary advancement

MMA: Outcomes

- Residual AHI 9.5 ± 10.7 events/hr
 - AHI < 5: 43%; AHI < 10: 63%
 - Pooled AHI reduction: 87%
- Long-term response
- Improvements in:
 - ESS (13.2 → 5.1)
 - Lowest SpO₂
 - Functional outcomes
- Cosmetic changes generally viewed as favorable



MMA versus CPAP

- N=50
- Randomized Auto-PAP or MMA
- Groups comparable at baseline
- At 1 year:
 - Similar reductions in AHI, ESS
 - Rx satisfaction (per VAS) higher with MMA

MMA: Complications

- Major complications: 1%
- Facial paresthesias inevitable
 - resolved in 86% @ 12 mos
- Malocclusion: mild
- Dysphagia: rare

SURGERY FOR OSA IN ADULTS: REVIEW AND META-ANALYSIS

Surgical Modifications of the Upper Airway for Obstructive Sleep Apnea in Adults: A Systematic Review and Meta-Analysis

Sleep 2010; 33:1396

Sean M. Caples, DO¹; James A. Rowley, MD²; Jeffrey R. Prinsell, DMD, MD³; John F. Pallanch, MD⁴; Mohamed B. Elamin, MBBS⁵; Sheri G. Katz, DDS⁶; John D. Harwick, MD⁷

PRACTICE PARAMETERS FOR SURGERY FOR OSA IN ADULTS

Practice Parameters for the Surgical Modifications of the Upper Airway for Obstructive Sleep Apnea in Adults

R. Nisha Aurora, MD¹; Kenneth R. Casey, MD²; David Kristo, MD³; Sanford Auerbach, MD⁴; Sabin R. Bista, MD⁵; Susmita Chowdhuri, MD⁶; Anoop Karippot, MD⁷; Carin Lamm, MD⁸; Kannan Ramar, MD⁹; Rochelle Zak, MD¹⁰; Timothy I. Morgenthaler, MD⁹

Recommendations

- **Option level recommendations:**
 - **UPPP:** As a sole procedure, with or without tonsillectomy, does not reliably normalize the AHI when treating moderate to severe obstructive sleep apnea syndrome. Therefore, patients with severe OSA should initially be offered positive airway pressure therapy, while those with moderate OSA should initially be offered either PAP therapy or oral appliances.
 - **RFA:** A treatment in patients with mild to moderate obstructive sleep apnea who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable
 - **MMA:** Surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable
 - **Palatal Implants:** May be effective in some patients with mild obstructive sleep apnea who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable

Tracheostomy: Outcomes

- Very effective at eliminating obstructive apneas
 - Apnea Index: 88.4 → 0.5¹
- Improvements in:
 - Daytime sleepiness
 - OSA-related arrhythmias
 - Pulmonary artery pressure
 - Systemic blood pressure
 - Diabetes
 - Mortality^{2,3}



¹Holty JEC. Med Clin N Am 2010; 94:479 ²He J. Chest 1988; 94:9

³Partinen M. Chest 1988; 94:1200

Tracheostomy: Complications

- Low patient acceptance
- Periop problems: Wound infections, bleeding
- Recurrent bronchitis
- Granulation tissue
- Trach tube kinking
- Blockage of tube by redundant neck tissue
- Tracheomalacia
- Residual disordered breathing
 - Hypopneas
 - CSA

Rebuttals from Surgical Proponents

- Ethical, logistical limitations to RCTs
- Post-op AHI < 5 target unreasonable and not always achieved by CPAP
- Remedy is in effect every night
- No consensus on medical risk of persistent low levels of OSA

Summary: OSA Surgery

- Outcome predictors incompletely defined
- MMA consistently results in substantial AHI reductions
- UPPP: ~ 30% AHI reduction
- Post-surgery assessment required!

Summary

- CPAP remains the mainstay and easiest sell to patients
- Weight loss is laudable for good health and OSA
- Positional therapy is plausible but not that simple
- Oral appliance therapy is preferred second line Rx
- Surgery may be effective but incomplete therapy
- Ideal ascension and combined therapy effects unclear

No Time for a Nap



-Viktor-

Photo by Vincent Laforet / The New York Times