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Obstructive Sleep Apnea Non-CPAP Treatments

Nancy A. Collop, M.D.

Conflicts of Interest

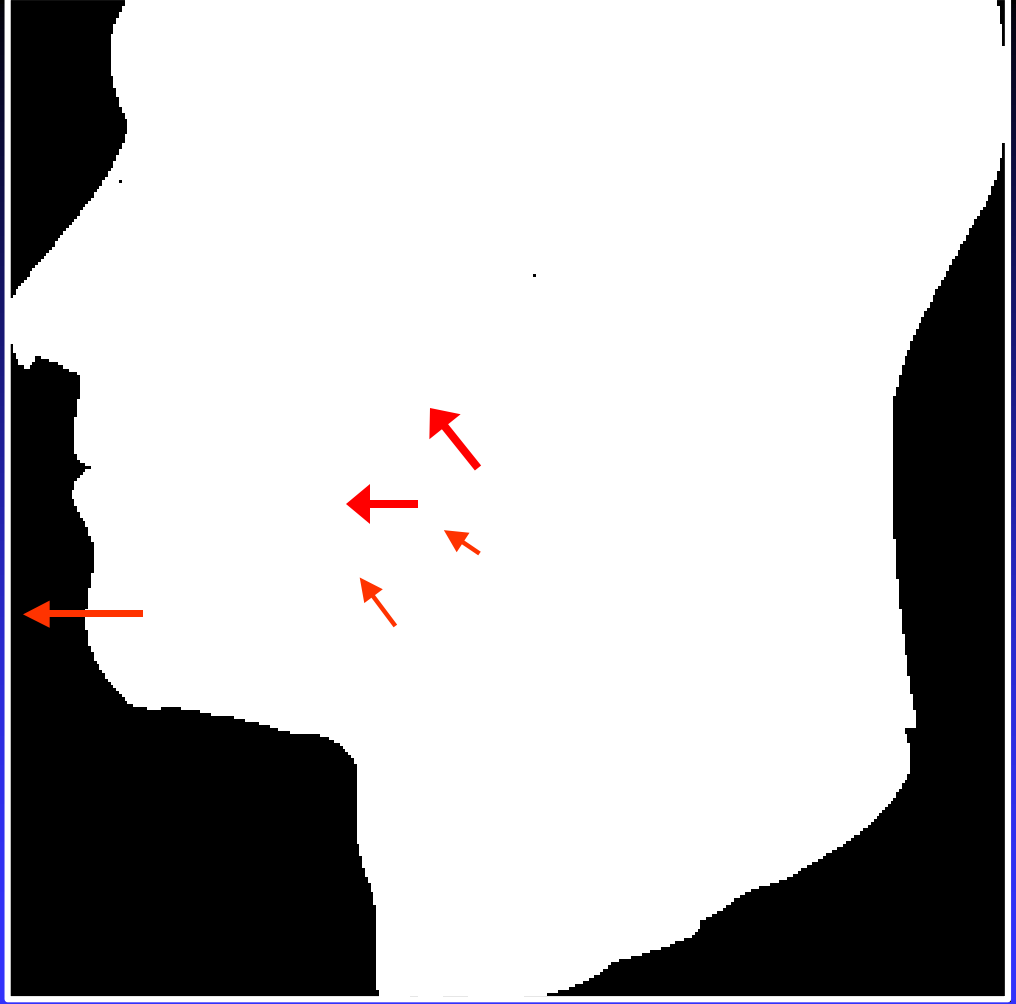
- Royalties from UPTODATE as an author and editor
- Received grant monies and was on advisory council for Jazz Pharmaceuticals (2017-2018)

Learning Objectives

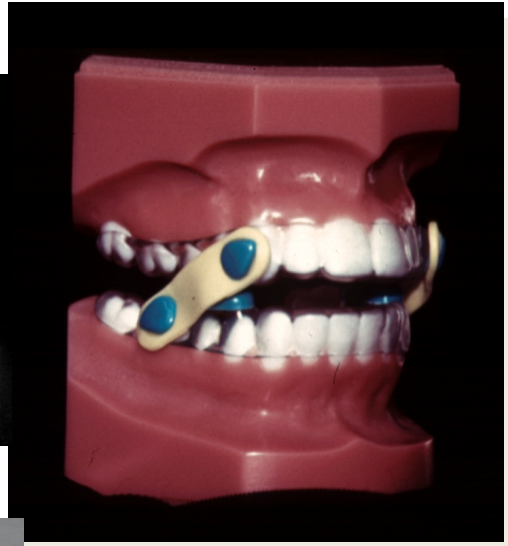
1. Discuss the role of oral appliances for the treatment of OSA including indications, patient selection and outcomes.
2. Review surgical methods including hypoglossal nerve stimulation used for the treatment of OSA and relevant outcome data.
3. Evaluate the effect of weight loss on the treatment of OSA including gastric bypass surgery
4. Outline other treatments used for OSA including position modification, medications and exercise

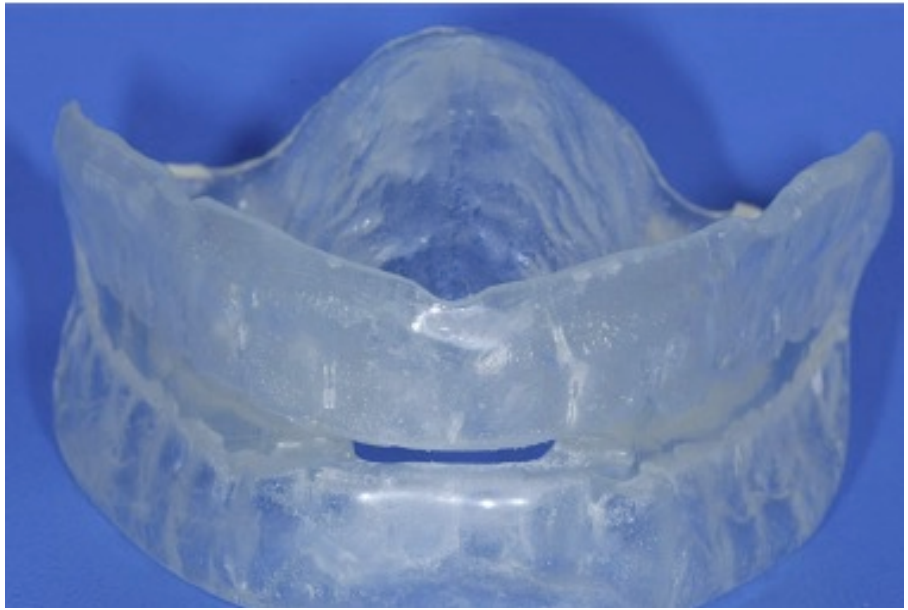
Oral Appliance

- Mechanisms:
  - Increase palatopharyngeal and palatoglossus muscle activity
  - Reduce pharyngeal tissue folds
  - Posture the tongue forward
  - Stabilize the mandible and hyoid bone
- Typically fit by a dentist or oral surgeon



Slide courtesy S. Scherr





Ramar K, Dort LC, Katz SG, et al. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an up-date for 2015.
J Clin Sleep Med 2015;11(7): 773–827.

- We recommend that sleep physicians prescribe OAs, rather than no therapy, for adult patients who request **treatment of primary snoring** (STANDARD)
- When OA is prescribed by a sleep physician for an adult patient with OSA, we suggest that a **qualified dentist use a custom, titratable appliance** over non-custom oral devices. (GUIDELINE)
- We recommend that sleep physicians consider prescription of OAs, rather than no treatment, for adult patients with obstructive sleep apnea **who are intolerant of CPAP therapy or prefer alternate th**erapy. (STANDARD)
- We suggest that **qualified dentists provide oversight**— rather than no follow-up—of OAT in adult patients with OSA, to survey for **dental-related side effe**cts or occlusal changes and reduce their incidence. (GUIDELINE)

Ramar K, Dort LC, Katz SG, et al. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an up-date for 2015.
J Clin Sleep Med 2015;11(7): 773–827.

- We suggest that **sleep physicians conduct follow-up sleep testing** to improve or confirm treatment efficacy, rather than conduct follow-up without sleep testing, for patients fitted with OAs. (GUIDELINE)
- We suggest that sleep physicians and qualified dentists instruct adult patients treated with oral appliances for obstructive sleep apnea to return for **periodic office visits**— as opposed to no follow-up—with a qualified dentist and a sleep physician. (GUIDELINE)

Appliance Differences

- Position/presence of adjustment mechanism
- Minimum upper and lower jaw separation required
- Degree of condylar movement permitted
- Construction materials – durability, hypoallergenic
- Adaptability for future dental changes

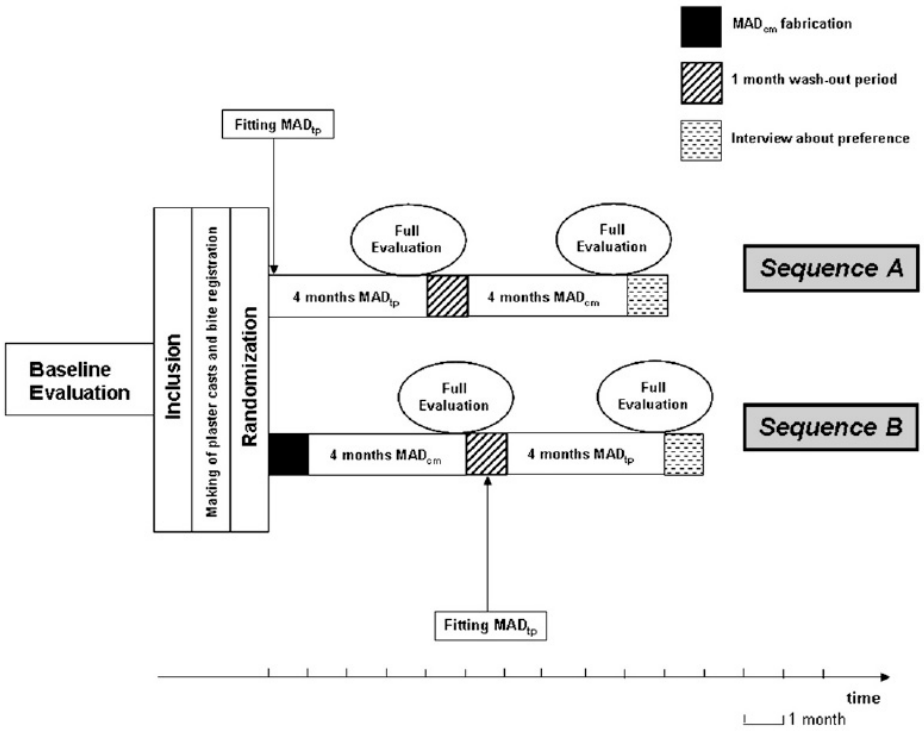
Selection Criteria

- State of dental and TM health
- Mandibular plane angulation
- Anatomy – exostoses, palatal width, tongue size
- Sleep and other habits
- Tooth form, arrangement, and contour
- Patient preference and dexterity

Compliance and Side Effects

- Regular use reported in 76-90% of pts
- Side effects:
  - Excessive salivation
  - Jaw stiffness, TMJ or tooth pain
  - Altered occlusion
  - Loosening of dental work
- Bite change occurs in 75% (50% judged favorable)
  - Must alert patient to this possibility

Custom vs Prefabricated



Vanderveken et al. AJRCCM 2008.

Findings

- Only the custom devices significantly reduced the AHI
- Failure rate with prefabricated (non-custom) devices was 69%
- 63% of patients who failed with the prefabricated device were successfully treated with the custom device.
- 82% of patients preferred the custom device

Vanderveken et al. AJRCCM 2008.

When comparing OAT to CPAP, which of the following is consistently lower with OAT?

A. AHI

B. Nightly adherence

C. Patient preference

D. Changes in bite

E. Nightly SPO2

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D. Changes in bite

E. Nightly SPO2

Predictors for favorable response to MAD

Clinical

- Younger age
- Lower BMI
- Lower neck circumference
- Positional OSA
- Lower AHI (not consistently)
- Increased protrusion

Craniofacial

- Small/narrow oropharynx
- Smaller overjet
- Short soft palate length
- Shorter mandibular plane to hyoid distance
- Larger angle cranial base to mandibular plane

Effectiveness of MAD

- Prospective studies: 54-81% have 50% reduction in AHI; 51-64% had post-tx AHI < 10
- Cross-over trials with CPAP show CPAP reduces AHI (- 8 events/hr), snoring, improves SpO2 (+ 3%) but pts generally prefer MAD over CPAP
- Adherence better than PAP (Avg 0.7 – 1.1 hrs/nt)
- Trials show improvement in:
  - Sleepiness
  - Blood pressure
  - QOL
  - Mortality ? (1 study)

Predicting Efficacy

- Titrate during PSG – patient or tech removes device on command for events to advance
- Use device to automatically advance device during PSG
- DISE
- Imaging – no consistent findings predictable

John E. Remmers, MD[1,2]; Zbigniew Topor, PhD[1,2]; Joshua Grosse, MMath[2]; Nikola Vranjes, DDS[3]; Erin V. Mosca, PhD[2]; Rollin Brant, PhD[4]; Sabina Bruehlmann, PhD[2]; Shouresh Charkhandeh, DDS[2,3]; Seyed Abdolali Zareian Jahromi, PhD[1,2]

MATRx 2.0

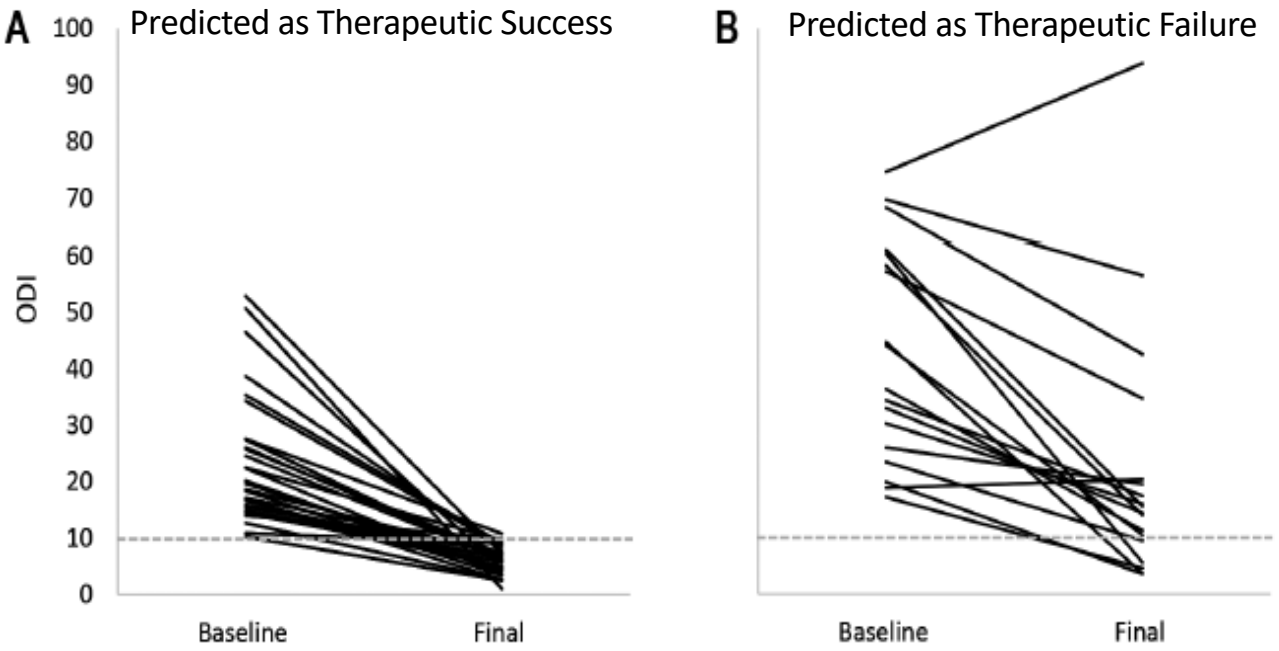
- Developed a feedback controlled mandibular positioning program
- Part 1 of study to develop a predictive model (n = 149, 131 completed); Part 2 of study was to prospectively test the model (n = 53, 48 completed)
- MATRx device used and the FCMP processed signals from nasal pressure and oximetry
- 2 night study: 1st night with dynamic interaction with plates and respiratory events; 2nd night "fine tuning" to evaluate accuracy (only move if ODI > 10 for > 2 hrs)
- If protrusive position > 80%, a third night was done starting at 70% to see if it was effective

J Clin Sleep Med. 2017;13(7):871–880.

A Feedback-Controlled Mandibular Positioner Identifies Individuals With Sleep Apnea Who Will Respond to Oral Appliance Therapy

John E. Remmers, MD[1,2]; Zbigniew Topor, PhD[1,2]; Joshua Grosse, MMath[2]; Nikola Vranjes, DDS[3]; Erin V. Mosca, PhD[2]; Rollin Brant, PhD[4]; Sabina Bruehlmann, PhD[2]; Shouresh Charkhandeh, DDS[2,3]; Seyed Abdolali Zareian Jahromi, PhD[1,2]

MATRx 2.0



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MATRx 2.0

	Predicted Success	Predicted Failure	
Therapeutic Success	29	5	Sensitivity 85%
Therapeutic Failure	1	13	Specificity 93%
	PPV 97%	NPV 72%	

J Clin Sleep Med. 2017;13(7):871–880.

Kate Sutherland, PhD[1,2]; Joachim Ngiam, BDS (Hons), MSD, MPhil[1]; Peter A. Cistulli, MD, PhD[1,2]

Methods

- AHI > 10
- Enough teeth (10/arch); no significant periodontal disease
- Underwent overnight PSG with RCMP after dental trays fitted by a dentist
- Advanced as per algorithm up to 3 x by 0.2 mm increments
- Success = < 1 event detected per 5 min supine REM sleep (lateral was acceptable if that was the primary position for most of the night)
- Patient then had an OA fabricated and started wearing at 70% maximum protrusion, then increased to maximum comfortable limit → repeat PSG
- “treatment response” = AHI < 10 with 50% reduction in AHI from BL

J Clin Sleep Med. 2017;13(3):411–417.

Kate Sutherland, PhD[1,2]; Joachim Ngiam, BDS (Hons), MSD, MPhil[1]; Peter A. Cistulli, MD, PhD[1,2]

Results

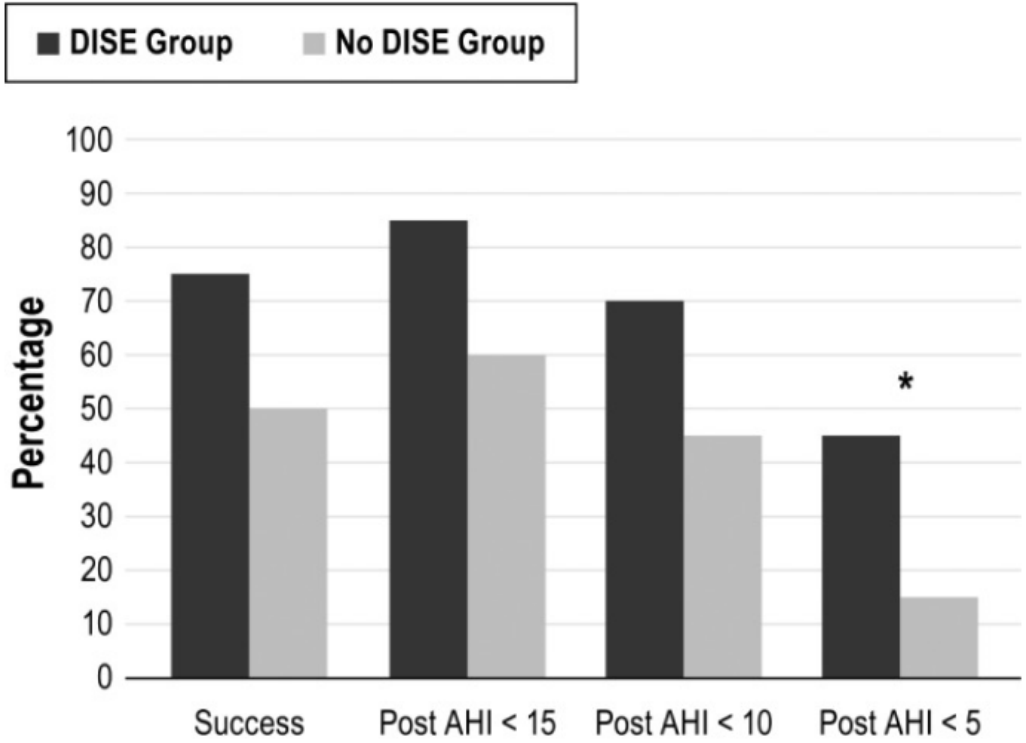
- 40 completed RCMP study; 33 completed OA PSG
- Mean age 57.1 (38-78)
- Mean BMI 29.6 (22.8-43.3)
- Mean AHI 31.5 (10-93)
- 15 were TR's (45%)
- Mandibular advancement mean was 92% of max
- 88% were predicted correctly (25/33); in 8/33 RCMP study was inconclusive

	Responder	Nonresponder	p value
n (%)	15 (45)	18 (55)	
Age (y)	54.6 ± 12.2	61.6 ± 11.0	0.095
Sex (% male)	56	67	0.515
BMI (kg/m²)	27.8 ± 2.3	30.1 ± 4.6	0.097
AHI (events/h)	23.5 ± 11.4	38.1 ± 24.6	0.033*
Oral appliance treatment level (%	94.6 ± 8.4	89.4 ± 12.3	0.202

	Predicted Treatment Outcome	
Actual Treatment Outcome	Success	Failure
Responder	9	2
Nonresponder	1	13

J Clin Sleep Med. 2017;13(3):411–417.

Using DISE to Predict



J Clin Sleep Med. 2018;14(8):1333–1337.

Tongue Retaining Device

- Indications:
  - Edentulous patients
  - TMJ problems
- Problems:
  - Sore tongue
  - Tongue elongation
  - Appliance dislodgement

http://dx.doi.org/10.15331/jdsm.6746

Management of Side Effects of Oral Appliance Therapy for Sleep-Disordered Breathing

Rose D. Sheats, DMD[1]; Thomas G. Schell, DMD[2]; Alan O. Blanton, DDS[3]; Patricia M. Braga, DDS[4]; B. Gail Demko, DMD[5]; Leslie C. Dort, DDS[6]; Donald Farquhar, DDS[7]; Sheri G. Katz, DDS[8]; Jean-Francois Masse, DMD[9]; Robert R. Rogers, DMD[10]; Steven C. Scherr, DDS[11]; David B. Schwartz, DDS[12]; Jamison Spencer, DMD, MS[13]

Table 1—Side effects.

Temporomandibular joint-related side effects
- Transient morning jaw pain
- Persistent temporomandibular joint pain
- Tenderness in muscles of mastication
- Joint sounds

Intraoral tissue-related side effects
- Soft tissue and tongue irritation
- Gingival irritation
- Excessive salivation/drooling
- Dry mouth

Occlusal changes
- Altered occlusal contacts/bite changes
- Incisor changes
- Decreased overjet and overbite
- Alterations in position of mandibular canines and molars
- Interproximal gaps

Damage to teeth or restorations
- Tooth mobility
- Tooth fractures or damage to dental restorations

Appliance issues
- Appliance breakage
- Allergies to appliance material
- Gagging
- Anxiety

Dental Changes Over Time

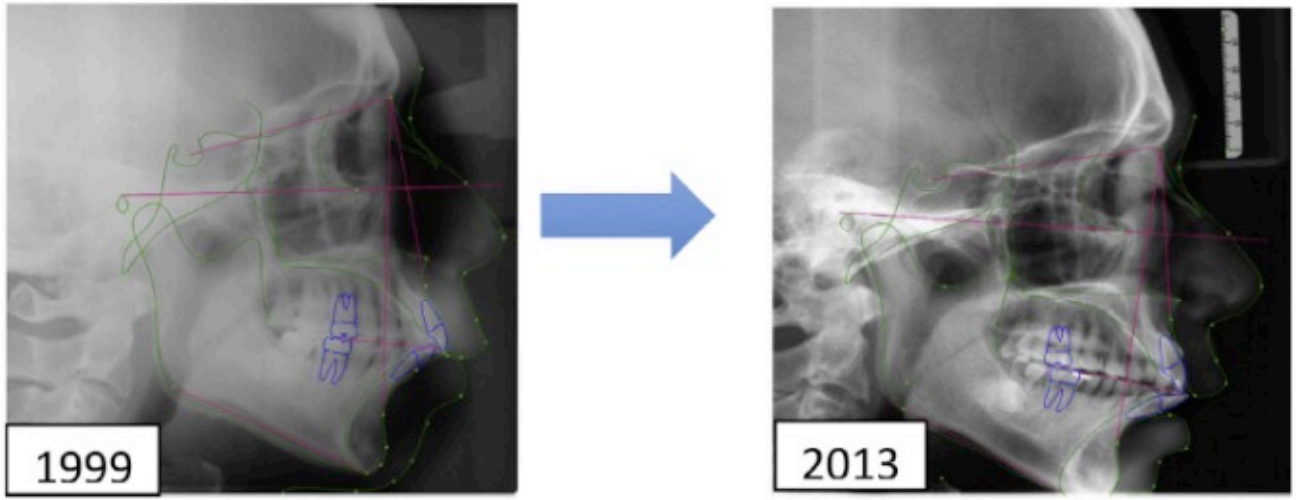


Fig. 3. Tracing of one of the study patient's initial (T_0) and final (T_F) lateral cephalograms showing the lower incisor proclination and upper incisor retroclination.

Dental Changes Over Time

- Wearing minimum of 8 yrs
- maxillary incisor retroclination
  - mean 6°
  - constant rate of retroclination = 0.5° /year
- mandibular incisor proclination
  - mean 8°
  - variable rate

https://doi.org/10.1016/j.sleep.2018.12.012

Long Term Efficacy

Marklund et al:

- cohort using OAT > 5 yrs
  - Of those initially successful with therapy, the improvement in symptoms and PSG outcomes remained robust at 5 - 10 years
- cohort > 15 yrs
  - (controlled for weight gain) pts remained pleased with treatment and control of snoring
  - almost doubled their baseline AHI in 16 years (17 to 32 per hour)
  - with OA: treated AHI increased from 7.2 to 35.1 per hour!
- May require continued titration

Chest 2001;120(1):162–9.

Oral Appliances

- Efficacy not as good as CPAP but patients use more and prefer in most head-to-head trials
- Predicting response:
  - Severity, POSA, age, sex, weight, other features somewhat helpful in predicting response but imperfect
  - Use of remotely controlled mandibular positioner or DISE may improve selection but many “non-responders” may respond
  - Cost and inconvenience of using during PSG have limited its usefulness
- Long term:
  - Efficacy good, lower BP shown
  - Bite changes likely

Surgical techniques for OSA

- Tracheostomy
- Maxillomandibular advancement
- Uvulopalatopharyngoplasty
- Nasal surgery
- Tonsillectomy
- Hypoglossal nerve stimulator

Aside from tracheostomy, which single surgical procedure for adult OSA has the best efficacy?

A. Uvulopalatopharyngoplasty

B. Tonsillectomy

C. Anterior hyoid advancement

D. Palatal implants

E. Maxillomandibular advancement

Q3: Collop

Aside from tracheostomy, which single surgical procedure for adult OSA has the best efficacy?

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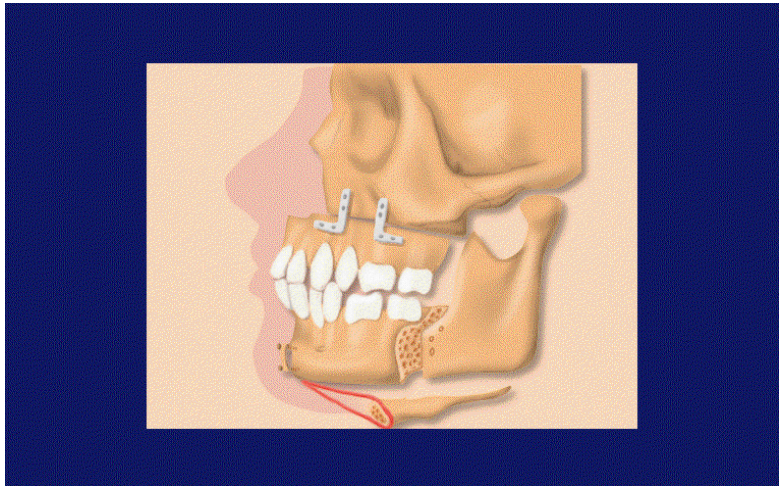
Q3: Collop

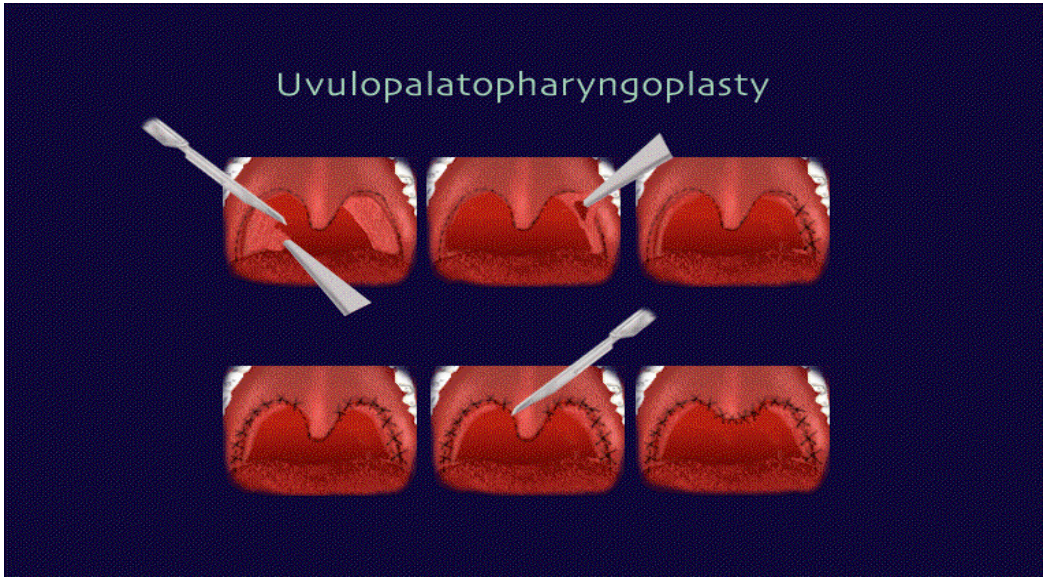
Tracheostomy

- Effective single surgical intervention
- Reserved for severe OSA
  - Other options exhausted
  - Life threatening complications

Maxillomandibular Advancement

- For Level III
- High success: 90%
- Overnight stay + diet modification
- Pt likes “strong jaw”

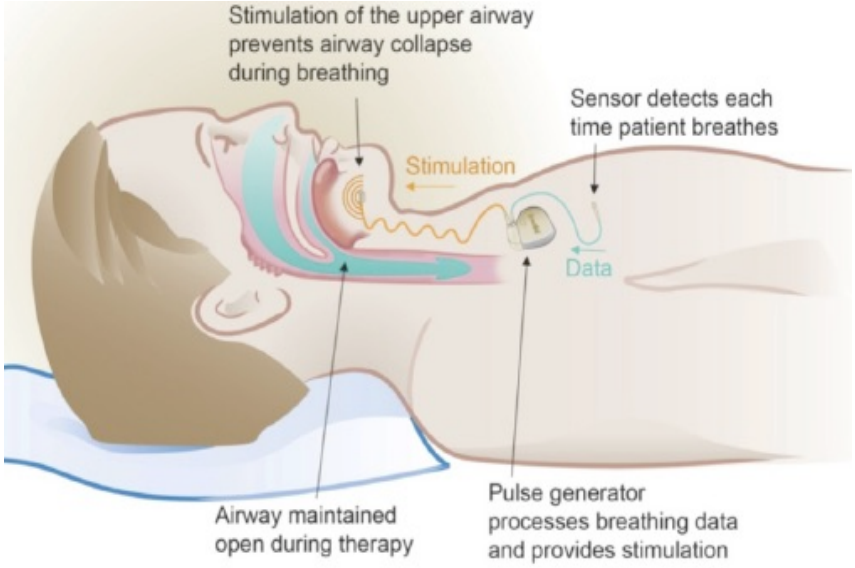




- Does NOT normalize AHI in moderate to severe OSA
- Efficacy may fade with time - ? Weight gain
- Makes CPAP more difficult due to mouth leak
- Fallen out of favor with most sleep surgeons

Hypoglossal nerve stimulation

- Implanted device
- Receives input from sensing lead to time delivery of stimulation to nerve with onset of inspiration
- Outcome (STAR Trial):
  - Reduced AHI by 68%; 29.3 to 9.0
  - Therapy maintenance group showed sustained reduction



N Engl J Med 2014;370:139-49.

Upper Airway Stimulation for Obstructive Sleep Apnea: Patient-Reported Outcomes after 48 Months of Follow-up

M. Boyd Gillespie, MD, MSc[1], Ryan J. Soose, MD[2], B. Tucker Woodson, MD[3], Kingman P. Strohl, MD[4], Joachim T. Maurer, MD[5], Nico de Vries, MD[6], David L. Steward, MD[7], Jonathan Z. Baskin, MD[4], M. Safwan Badr, MD[8], Ho-sheng Lin, MD[8], Tapan A. Padhya, MD[9], Sam Mickelson, MD[10], W. McDowell Anderson, MD[9], Olivier M. Vanderveken, MD[11], and Patrick J. Strollo Jr, MD[2]; on Behalf of the STAR Trial Investigators

Followup study from original STAR Trial

- 91 participants (original cohort 126; 73%)
  - Exclusion: BMI > 32; AHI < 20, > 50; DISE w/o circumferential collapse
- Epworth, FOSQ, snoring vs baseline data

Otolaryngology–
Head and Neck Surgery
2017, Vol. 156(4) 765–771

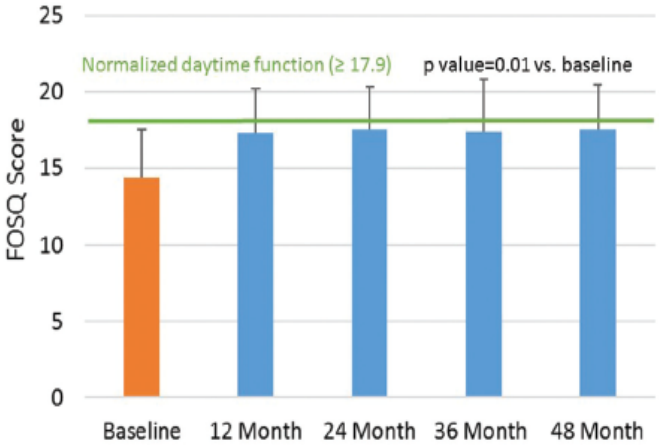
- 95 subjects showed up; 4 had incomplete data
  - Of the original cohort:
    - 3 had died: 2 from CVD, 1 homocide
    - 3 had elective explantation of HGNS
    - 25 lost to followup:
      - 15 missed 48 month visit
      - 5 exited study
      - 5 were from study sites that closed
  - 2 required surgery to replace malfunctioning components

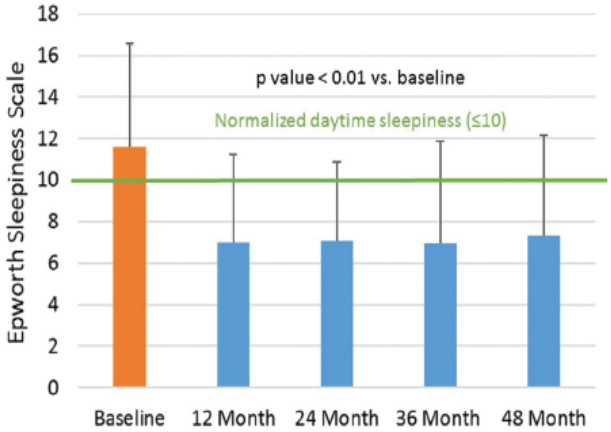
Table 2. Comparison of Baseline Characteristics of Initial STAR Cohort and Those Completing 12- and 48-Month Follow-up.[a]

Baseline Characteristics	Preimplant (N = 126)	12 mo (n = 124)	48 mo (n = 91)
Age, y	54 ± 10.2	54.3 ± 10.2	55.7 ± 10.2
BMI, kg/m^2	28.4 ± 2.6	28.5 ± 2.6	28.6 ± 3.2
AHI, events/h	32.0 ± 11.8	31.7 ± 11.6	30.2 ± 11.0

Otolaryngology–Head and Neck Surgery 2017, Vol. 156(4) 765–771

Epworth and FOSQ Scores





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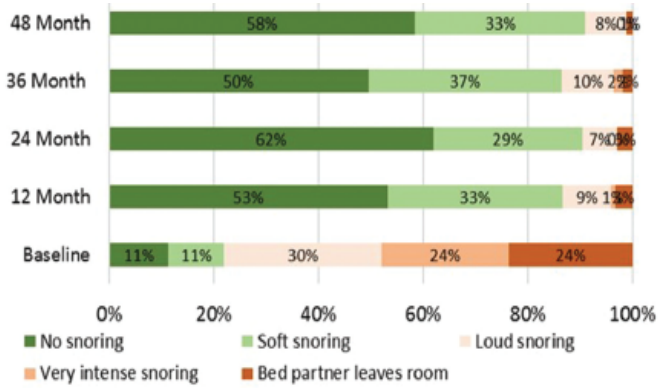
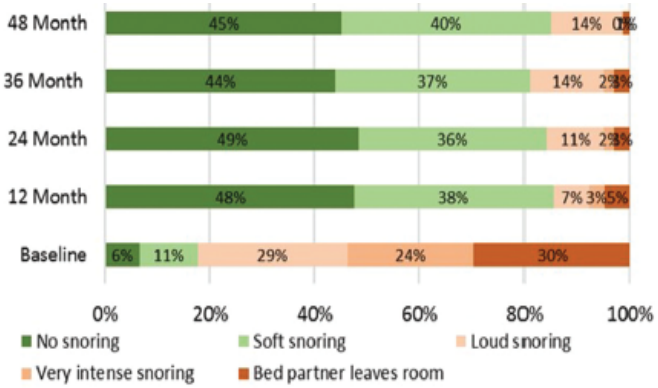
Upper Airway Stimulation for Obstructive Sleep Apnea: Patient-Reported Outcomes after 48 Months of Follow-up

Snoring



Patient Report (A)



Bed Partner Report (B)

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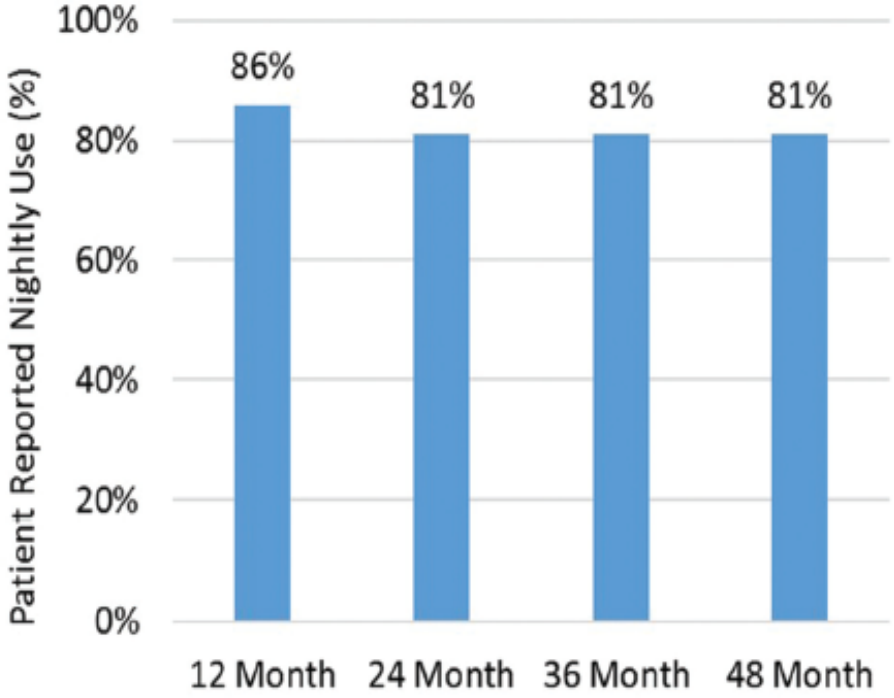
Patient Self Reported "Nightly Usage"



Otolaryngology–Head and Neck Surgery 2017, Vol. 156(4) 765–771

Adverse Events

- Procedure Related:
  - Postop pain from incision or surgery
  - Temporary tongue weakness
  - Intubation effects
  - Headache
  - Infection
- Device Related:
  - Discomfort due to stimulation
  - Tongue abrasion
  - Mechanical pain associated with device presence
  - Problem with device functionality or usability
  - Infection

Otolaryngology–Head and Neck Surgery 2017, Vol. 156(4) 765–771

Upper airway stimulation for treatment of obstructive sleep apnea; an evaluation and comparison of outcomes at two academic centers

C Huntley, T Kaffenberger, K Doghramji, R Soose, M Boon

- HGNS implantation from May-August 2016 comparing Univ Pittsburgh (UP) to Thomas Jefferson (TJ)
- Data collection:
  - Gender
  - BMI
  - ESS
  - PSG (pre and postop)
  - Adherence (objective)
- 63 implantations TJ, 57 implantations UP with 48 and 49 postop PSG available respectively

J Clin Sleep Med 2017;13(9):1075-1079

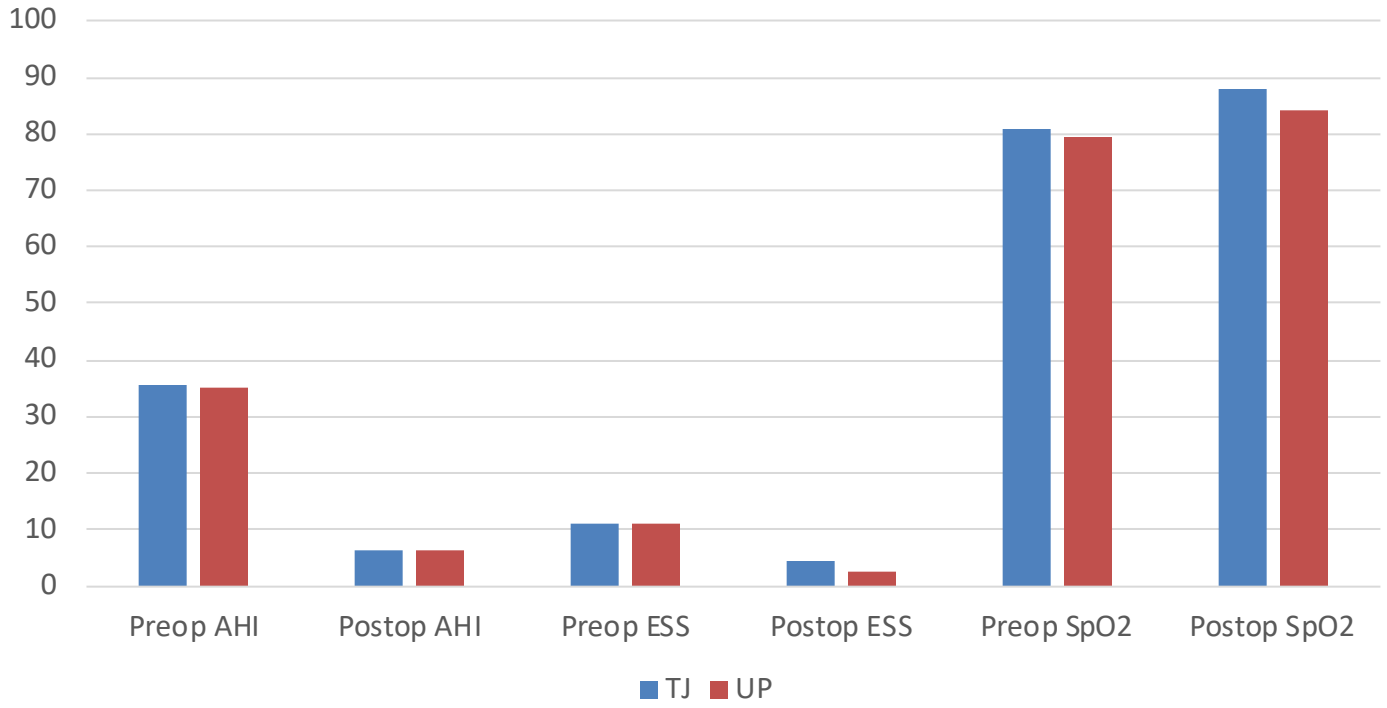
Upper airway stimulation for treatment of obstructive sleep apnea; an evaluation and comparison of outcomes at two academic centers

C Huntley, T Kaffenberger, K Doghramji, R Soose, M Boon

	TJUH	UPMC	p value
N	48	49	
Gender	30 Male 18 Female	30 Male 19 Female	
Age (years)	60.88 ± 11.12	62.84 ± 10.81	0.772
Preoperative BMI	29.29 ± 3.72	27.74 ± 3.66	0.753
Postoperative BMI	29.09 ± 3.71	27.76 ± 3.75	0.826

Table 1. Demographic data. Age and BMI values represent mean ± standard deviation.

J Clin Sleep Med 2017;13(9):1075-1079



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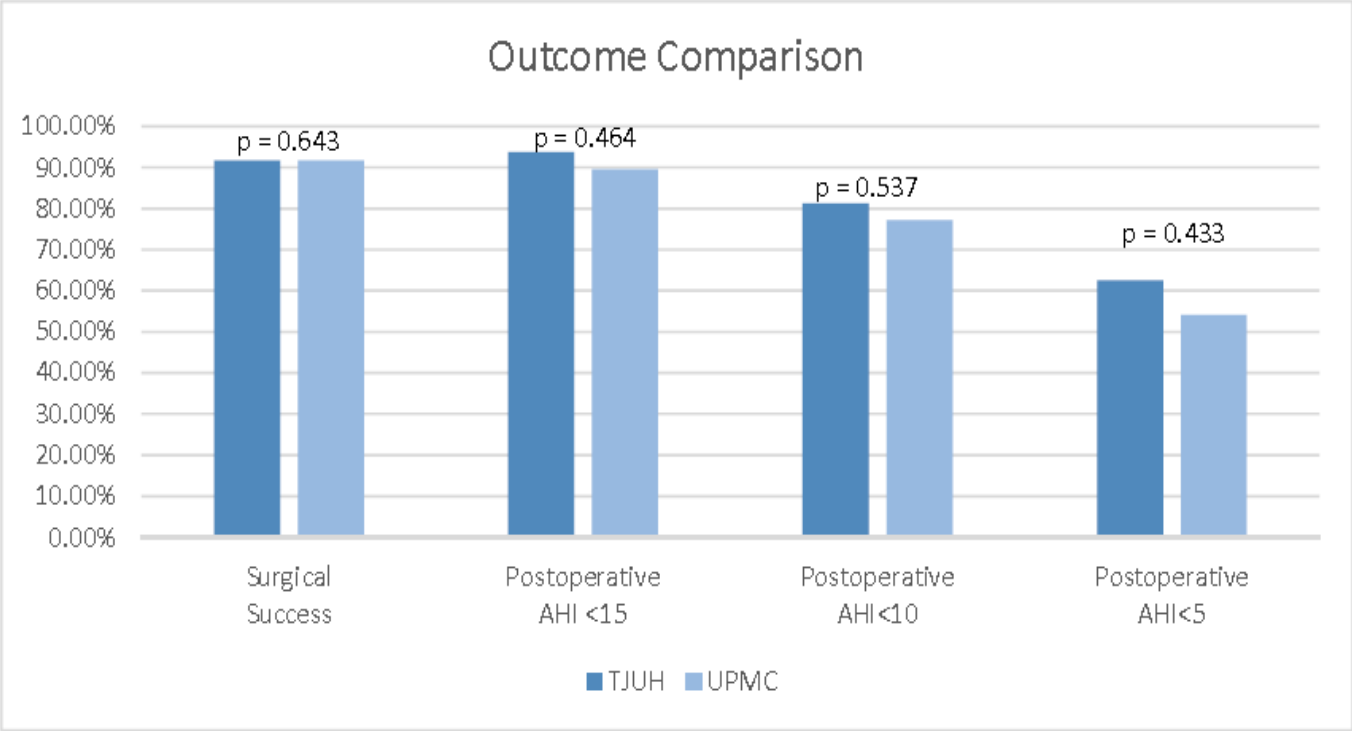


J Clin Sleep Med 2017;13(9):1075-1079

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Hypoglossal Nerve Stimulation in Adolescents With Down Syndrome and Obstructive Sleep Apnea

Gillian R. Dierdis, MD, MPH; Carissa Wentland, DO; Donald Heany, MD, MPH; Thomas Bernard Ignane, MD; Brian Stortio, MD, MPP; Vanessa de Guzman, MS; Ellen Grealish, RPSGT, REEGT; John Dobrowski, MD; Ryan Soose, MD; Christopher J. Hartnick, MD

- OSA is present in ~ 60% of Down Syndrome children and frequently persists after T&A
- DS patients often have trouble with PAP therapy
- Case series of 6 DS adolescents with OSA (AHI > 10), s/p T & A
- Underwent HGNS – evaluated efficacy (AHI) and OSA-18 (QOL measure) at 6 and 12 months

JAMA Otolaryngol Head Neck Surg. 2018;144(1):37-42.

Hypoglossal Nerve Stimulation in Adolescents With Down Syndrome and Obstructive Sleep Apnea

Table 1. Patient Characteristics and Baseline Polysomnogram Findings

Patient No.	Sex	Age, y	BMI	Baseline, Events/h	
				AHI	CAI
1	M	14	24.6	48.5[a]	2.4
2	M	15	26.1	17.1[b]	0.8[b]
3	M	13	19.2	30.7	0.0
4	F	12	20.3	22.7	4.7
5	M	17	28.8	13.9	2.9
6	F	18	25.8	25.6[b]	6.3[b]

Table 3. Polysomnogram Results Before and After Implantation

Patient No.	Preimplantation AHI, Events/h	Follow-up, mo	Stimulator Parameters, V	Postimplantation AHI, Events/h	Device Use, Mean, h/Night
1	48.5[a]	12	1.7-1.9	7.4[b]	9.6
2	17.1	12	1.9	2.7	10.0
3	30.7	12	1.5	4.6	9.3
4	22.7	12	1.5	4.7	5.6
5	13.9	6	1.5-1.7	6.1[c]	9.0
6	25.6	12	1.9-2.3	4.7[d]	9.4

JAMA Otolaryngol Head Neck Surg. 2018;144(1):37-42.

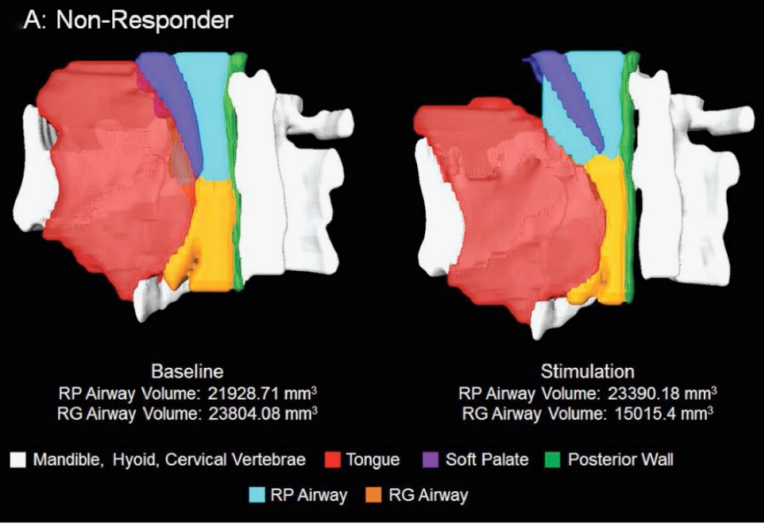
Hypoglossal Nerve Stimulation in Adolescents With Down Syndrome and Obstructive Sleep Apnea

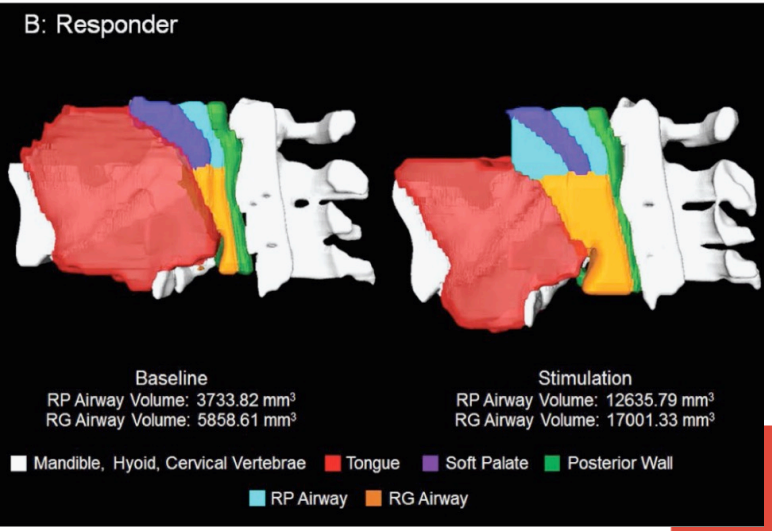
Table 4. Baseline and Follow-up Domain Scores for the Obstructive Sleep Apnea-18 (OSA-18) Survey (n = 5)

OSA-18 Domain	Domain Content Items	Change Score, Mean (SD), Range	Change Degree[a]
Sleep disturbance	Loud snoring; breath holding or pauses in breathing; choking or gasping; fragmented sleep	1.9 (1.4), −0.5 to 3.0	Large
Physical suffering	Mouth breathing; frequent colds or upper respiratory infections; rhinorrhea; dysphagia	0.4 (0.7), −0.8 to 1.0	Trivial
Emotional distress	Mood swings or temper tantrums; aggressive or hyperactive behavior; discipline problems	0.9 (1.3), −0.7 to 2.7	Small
Daytime problems	Excessive drowsiness or sleepiness; poor attention span; difficulty awakening	1.4 (1.0), 0.3 to 1.5	Moderate
Caregiver concerns	Caregiver worried over child health; concerned not getting enough air; missed activities; frustration	2.2 (0.9), 1 to 3.3	Large
Overall survey score	Mean score for all 18 items	1.5 (0.6), 0.9 to 2.3[b]	Large

JAMA Otolaryngol Head Neck Surg. 2018;144(1):37-42.

MRI of HGNS Pts





- 13 pts (6 nonresponders)
- CT awake with and w/o HGNS on
- Responders had:
  - smaller baseline soft palate volume
  - with stimulation - greater increase in retroglossal airway size; increased shortening of the mandible-hyoid distance; greater anterior displacement of the tongue

SLEEPJ, 2018, 1–12

Standardized Reporting for Hypoglossal Nerve Stimulation Outcomes

Raj C. Dedhia, MD, MSCR[1,2]; B. Tucker Woodson, MD[3]

- "Treatment AHI is fraught with issues related to the lack of standardization for minimum duration, position, or sleep stage."
  - Emory HGNS cohort (n = 43)
  - Treatment AHI vs full-night efficacy AHI
    - mean treatment AHI was 7.7 events/h vs 19.2 events/h from full-night efficacy studies

Journal of Clinical Sleep Medicine, Vol. 14, No. 11

Standardized Reporting for Hypoglossal Nerve Stimulation Outcomes

Raj C. Dedhia, MD, MSCR[1,2]; B. Tucker Woodson, MD[3]

1. Full-night efficacy (ie, single device setting) studies from either a HSAT or PSG
2. 4% oxygen desaturation index (ODI) as the primary outcome of therapy effectiveness

Journal of Clinical Sleep Medicine, Vol. 14, No. 11

Conclusions: HGNS

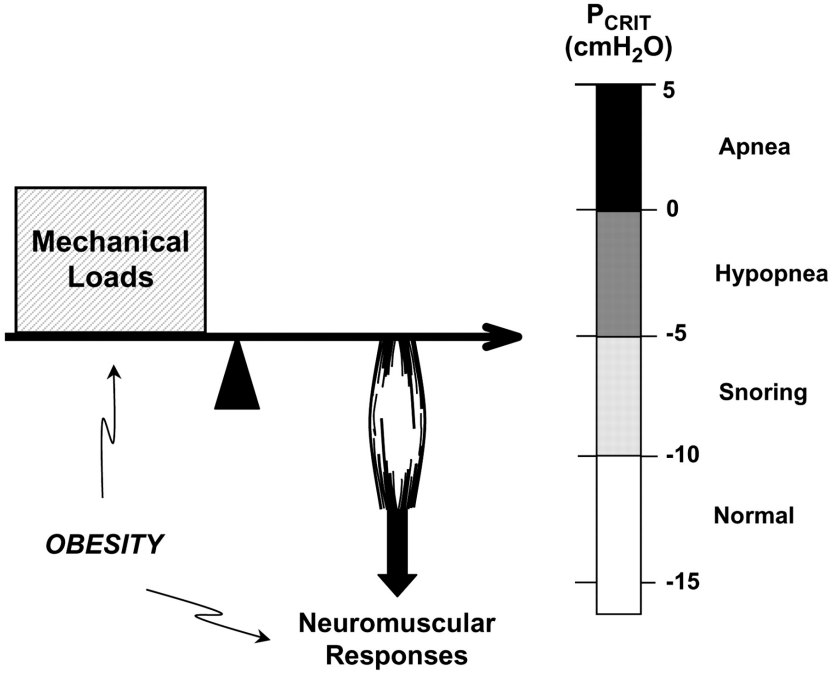
- Hypoglossal nerve stimulation is growing in popularity
- Although it does not reduce AHI as well as CPAP, adherence is better
- Relatively low side effect profile
- Need consistent reporting standards
- No good treatment comparison studies (to other treatments) at this time

Weight Loss

- 1% change in weight results in ~ 3% change in AHI
- Most studies confirm decrease in AHI even with modest amount of weight loss
- Gastric bypass is becoming very popular weight loss method – dramatic results
  - bariatric surgery is indicated for BMI of 35 kg/m ^{2} or more with OSA or other obesity-related complications
  - Asians have higher risks of developing obesity-related complications at lower BMIs when compared with whites; BMI cutoff for Asians is lower: 32.5 kg/m
- Many patients regain weight, therefore long term risk exists

Obesity Effect on the UA

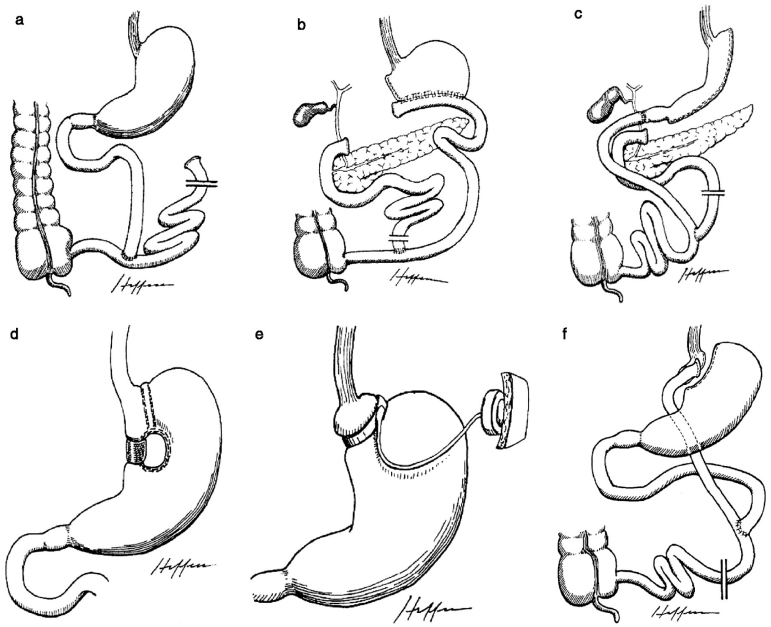
- Increases in neck size leads to reduction in pharyngeal size
- Reduction in lung volumes and loss of caudal traction on UA
- ? Obesity result in modulation of UA neuromuscular control



Proceedings of the American Thoracic Society 5:185-192 (2008)

Gastric Bypass and OSA

- Roux-en-Y is most common GB performed
- Mortality rates < 2%
- Sleep apnea has been independently shown to be an independent risk factor for mortality



Gastric Bypass and OSA

- 1000 surgeries done by same surgeon
- 146 men, 854 women
- Avg age 38.3, mean BMI 51.8
- CAD and OSA were correlated most strongly with mortality

Table 5 Logistic Regression Evaluation of Patient Comorbidity as Predictors of Mortality

	p-Value	Relative Risk	95% Confidence Interval
Age	0.042	1.059	1.002–1.120
BMI	0.130	1.025	0.993–1.058
Female	0.612	0.729	0.215–2.474
DM	0.852	0.889	0.259–3.054
HTN	0.257	2.085	0.585–7.438
CAD	0.001	7.446	2.195–25.258
Dyslipidemia	0.099	0.359	0.106–1.211
Asthma	0.070	3.065	0.913–10.293
SA	0.033	3.342	1.104–10.115
SOB	0.693	0.644	0.073–5.725

J Gastrointest Surg 2007;11:500-7

Gastric Bypass and OSA

- 24 patients before and after GBP (18 female)
- Avg weight reduction 54 kg
- AHI reduced from 47.9 to 24.5; CPAP fell from 11.5 to 8.4 cm H2O
  - 2 pts had increase in AHI !
  - Only 1 patient was “cured”

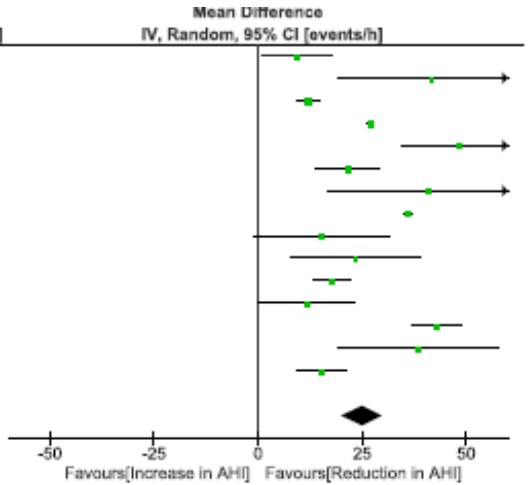
JCSM 2008:4:333-8

Bariatric Surgery and OSA – Meta-analysis

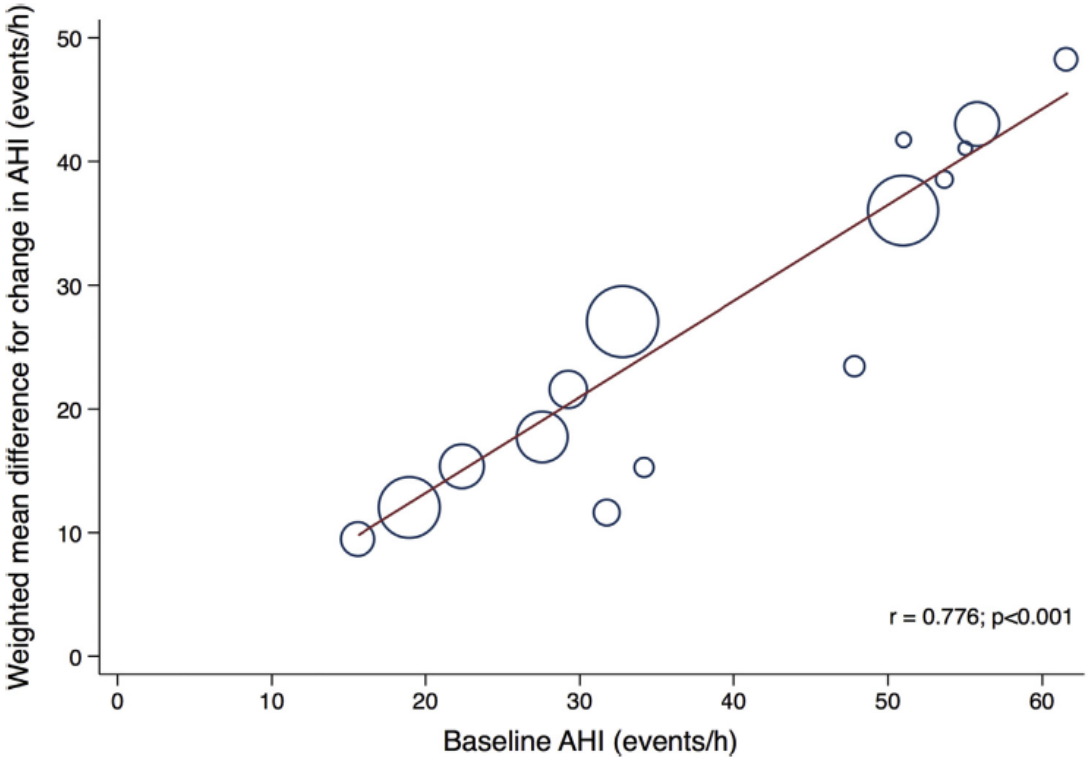
AHI

Study or Subgroup	Pre-surgery Mean [events/h]	Pre-surgery SD [events/h]	Pre-surgery Total	Post-surgery Mean [events/h]	Post-surgery SD [events/h]	Post-surgery Total	Weight	Mean Difference IV, Random, 95% CI [events/h]
Aguair et al. 2014 [39]	15.65	15.51	16	6.26	7.57	16	7.4%	9.39 [0.93, 17.85]
Bae et al. 2014 [73]	51	34.2	10	9.3	12.9	10	3.1%	41.70 [19.05, 64.35]
da Silva et al. 2013 [40]	19	6	17	7	1	17	9.3%	12.00 [9.11, 14.89]
Del Genio 2016 [43]	32.8	1.7	36	5.8	1.2	36	9.6%	27.00 [26.32, 27.68]
Dixon et al. 2005 [26]	61.6	31.9	25	13.4	13	25	5.5%	48.20 [34.70, 61.70]
Fredheim et al. 2013 [30]	29.3	24.1	44	7.8	9.7	44	7.7%	21.50 [13.82, 29.18]
Guardiano et al. 2003 [75]	55	31	8	14	17	8	2.8%	41.00 [16.50, 65.50]
Haines et al. 2006 [46]	51	4	101	15	2	101	9.5%	36.00 [35.13, 36.87]
Krieger et al. 2012 [44]	34.2	34.97	24	19	21.71	24	4.6%	15.20 [-1.27, 31.67]
Lettieri et al. 2008 [36]	47.9	33.8	24	24.5	18.1	24	4.9%	23.40 [8.06, 38.74]
Peromaa-Haavisto et al. 2017 [34]	27.6	24.6	132	9.9	11.2	119	8.8%	17.70 [13.05, 22.35]
Priyadarshini et al. 2017 [45]	31.8	20.4	27	20.2	23.1	27	6.2%	11.60 [-0.02, 23.22]
Shaarawy et al. 2016 [41]	55.8	8.3	22	12.8	11.3	22	8.4%	43.00 [37.14, 48.86]
Valencia-Flores et al. 2004 [42]	53.7	46.9	28	15.2	22.5	28	3.8%	38.50 [19.23, 57.77]
Zou et al. 2015 [37]	22.4	17.8	44	7.1	9.4	44	8.4%	15.30 [9.35, 21.25]
Total (95% CI)			**558**			**545**	**100.0%**	**25.07 [20.20, 29.94]**

Heterogeneity: Tau² = 64.47; Chi² = 521.69, df = 14 (P < 0.00001); I² = 97%
Test for overall effect: Z = 10.09 (P < 0.00001)



Sleep Medicine Reviews 42 (2018) 85e99



Sleep Medicine Reviews 42 (2018) 85e99

Gastric Bypass and OSA

- Bariatric surgery (regardless of type) can lead to substantial weight loss, significant reductions in OSA severity, improvement in daytime sleepiness
- Surgical weight loss is more effective in reducing both AHI and BMI when compared to non-surgical weight loss strategies
- Higher baseline AHI and BMI, as well as a longer duration of follow-up, are associated with greater reductions in weight and AHI
- There is no relationship between the amount of weight lost and the improvement in AHI
- A significant proportion of patients have residual OSA post-surgery despite improvements in clinical symptoms – long term followup needed!!

Other Medications

- Donepezil
  - Shown to reduce AHI in Alzheimer disease
- Mirtazipine
  - Statistically significant reduction in AHI, not clinically significant
- Modafinil/Armodafinil
  - Adjunctive for EDS; should not be used in isolation

Pharmacotherapy of Apnea by Cannabimimetic Enhancement, the *PACE* Clinical Trial: Effects of Dronabinol in Obstructive Sleep Apnea

David W. Carley, PhD[1,2*], Bharati Prasad, MD[2*†], Kathryn J. Reid, PhD[6*], Roneil Malkani, MD[6*], Hryar Attarian, MD[6*], Sabra M. Abbott, MD, PhD[6*], Boris Vern, MD, PhD[1*†], Hui Xie, PhD[7], Chengbo Yuan, MPH[7], Phyllis C. Zee, MD, PhD[6*]

- OSA pharmacotherapy is nonexistent
- A small dose escalation trial showed promise for dronabinol
  - Dampen afferent vagal feedback to the medulla
- Multicenter trial (n = 73) for moderate – severe OSA (AHI ≥ 15)
  - Exclusion criteria included ESS < 7, BMI > 45, severe hypoxemia
- Placebo vs 2.5 mg dose vs 10 mg dose
- Protocol: overnight PSG, MWT, ESS, satisfaction questionnaire at BL; take drug for 6 weeks (60 minutes before bedtime) and return q2 weeks for PSG, MWT, PE and questionnaire completion

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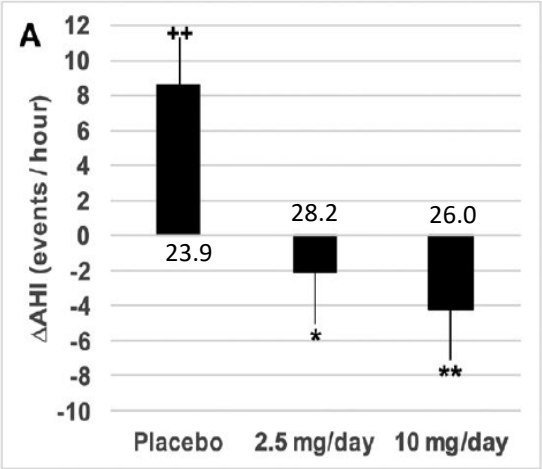

- Increase in AHI in placebo group - NS
- Δ in AHI with drug significant with both doses but not between doses
- Effect driven by reduction in *apneas*
- 6/39 had AHI < 15 + AHI reduced > 50% of BL AHI

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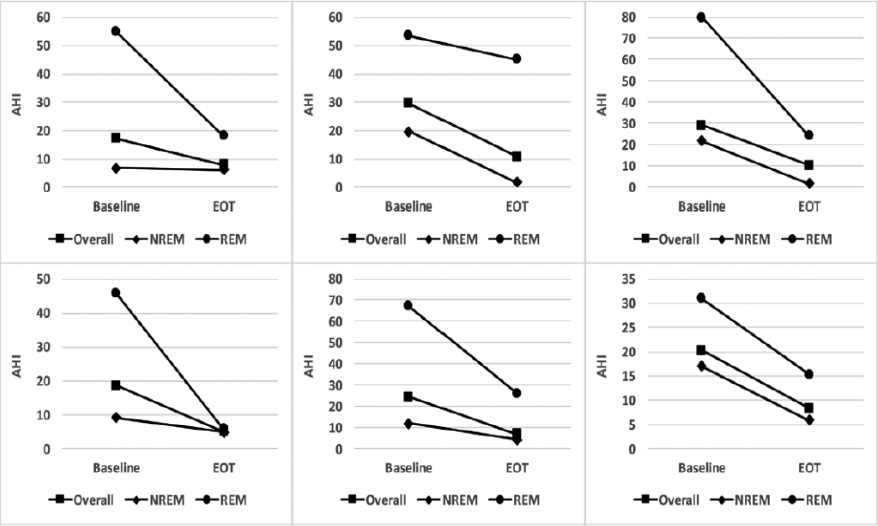

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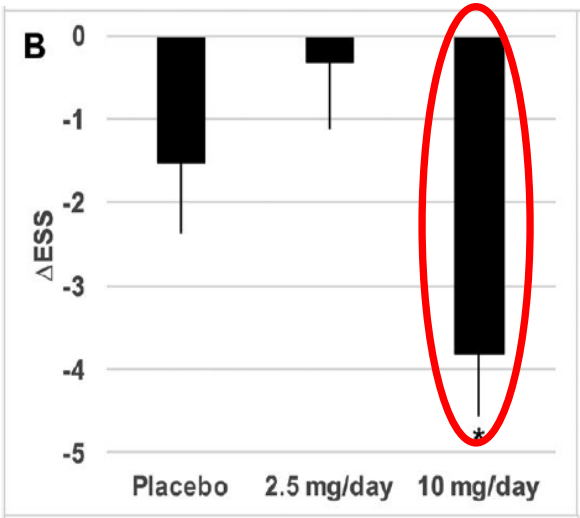

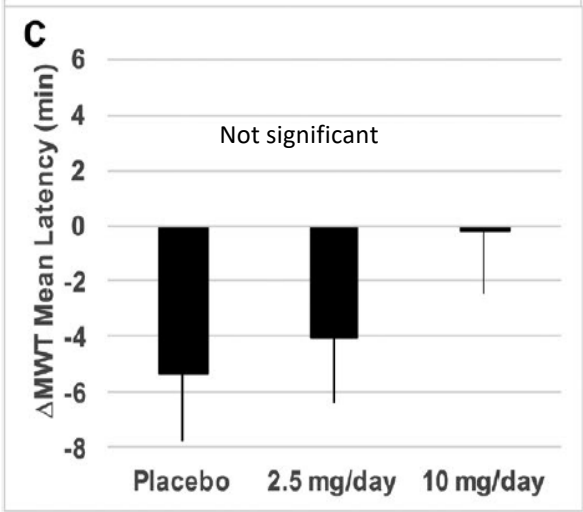

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- "Responders" were younger, longer BL TST, higher BL REM AHI and % REM
- 90% of participants had an AE but NS different between drug and placebo
- 1 serious AE involved transient vomiting and diarrhea – subject completed study
- Greatest satisfaction was in the highest drug dose

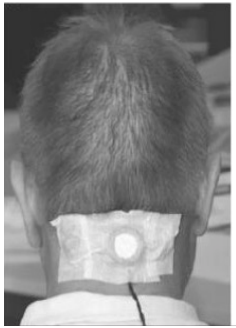
Positional Therapy

- Depending on definition, positional OSA prevalence is > 50%
- Techniques include
  - TBT (tennis ball)
  - Alarm training
  - Position vests
- Compliance with technique not well reported – one study of TBT found only 38% still using after 6 months
- Efficacy is suboptimal in most studies (AHI reduction of < 50%)

Positional therapy

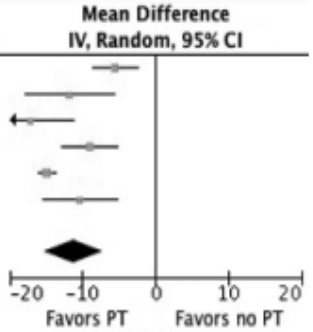
- Up to 75% of patients have a positional component (worsening of OSA)
  - Differing definitions
  - More prevalent in Asians
  - Prevalence decreases as severity increases
- Studies suggest POSA have:
  - backward positioning of the lower jaw
  - lower facial height
  - longer posterior airway space (PAS) measurements
  - smaller volume of lateral pharyngeal wall tissue (greater lateral diameter and elliptoid shape)
  - smaller neck circumference
- Can be effective but most patients abandon over time

Meta-analysis of POSA treatments



Study or Subgroup	mean AHI with PT Mean	SD	Total	mean AHI without PT Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Eijsvogel 2015	5.9	6.6	27	11.4	4.9	29	18.5%	-5.50 [-8.56, -2.44]	2015
Dieltjens 2015	11.6	8.4	20	23.4	11.3	20	13.9%	-11.80 [-17.97, -5.63]	2015
Levendowski 2014	7.5	7.7	30	24.7	14.7	30	14.3%	-17.20 [-23.14, -11.26]	2014
van Maanen 2013	8	8.8	31	17	6.1	31	17.5%	-9.00 [-12.77, -5.23]	2013
van Maanen 2012	12.8	2.2	30	27.7	2.4	30	20.3%	-14.90 [-16.07, -13.73]	2012
Bignold 2011	13.7	1.1	16	24.1	10.5	16	15.4%	-10.40 [-15.57, -5.23]	2011
Total (95% CI)			**154**			**156**	**100.0%**	**-11.33 [-15.37, -7.29]**	

Heterogeneity: Tau² = 20.53; Chi² = 40.26, df = 5 (P < 0.00001); I² = 88%
Test for overall effect: Z = 5.50 (P < 0.00001)

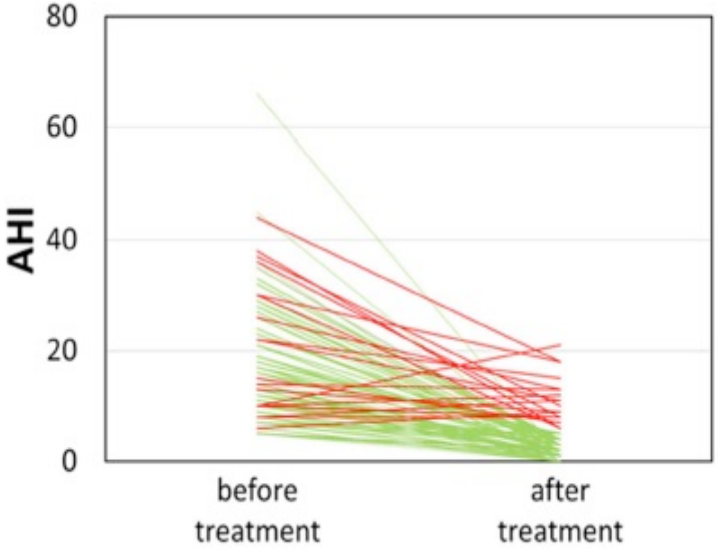


J Clin Sleep Med. 2017;13(6):813–824.

Positional therapy in sleep apnoea - one fits all? What determines success in positional therapy in sleep apnoea syndrome

Natascha Troester[1]*, Michael Palfner[1], Markus Dominco[1], Christoph Wohlkoenig[1], Erich Schmidberger[2], Martin Trinker[1], Alexander Avian[2,3]

- This study examined the followup of patients with pOSA (AHI < 5 in nonsupine positions)
- Instructed to try positional therapy (Backpack with a football or swimming aid, long plastic pipe or commercial model)
- 105 pts with 93 having a repeat PSG on therapy (70% therapy was effective)
- At one year, only 37% of patients were still using therapy
- BMI, female weight, male height were predictors of failure

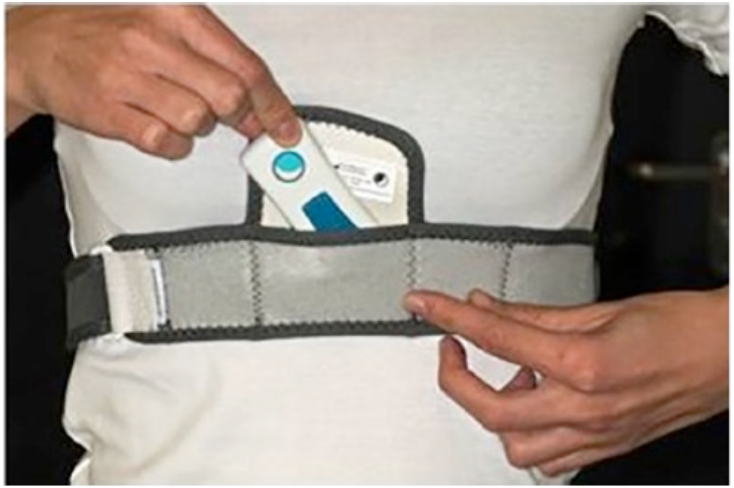


PLoS ONE 2017; 12(4):e0174468

Treatment of sleep-disordered breathing with positional therapy: long-term results

Jolien Beyers[1,2,3] • O. M. Vanderveken[1,2,3] • C. Kastoer[1,2] • A. Boudewyns[1,2] • I. De Volder[3,4] • A. Van Gastel[3,4]
J. A. Verbraecken[2,3,5] • W. A. De Backer[2] • M. J. Braem[2,6] • P. H. Van de Heyning[1,2] • M. Dieltjens[1,2]

- Sleep position trainer – device worn around chest and vibrates when lying supine
- PSG at baseline and 1 year
- 9/58 stopped using by 1 year (16%)
- 34 completed PSG's
  - male/female ratio, 28/6; overall AHI 16
  - significant reduction in overall AHI to 6 ($p < 0.001$)
  - median % of supine sleep decreased to 1% ($p < 0.001$)
  - mean objective SPT use in 28 pts = 7.3 ± 0.9 h/night and 69 ± 26% of the nights
  - 75% of the patients reported a better sleep quality since the start of SPT treatment.



(https://doi.org/10.1007/s11325-019-01792-9)

Treatment of sleep-disordered breathing with positional therapy: long-term results

CHEST Congress 2019 | Thailand
Bangkok | 10-12 April

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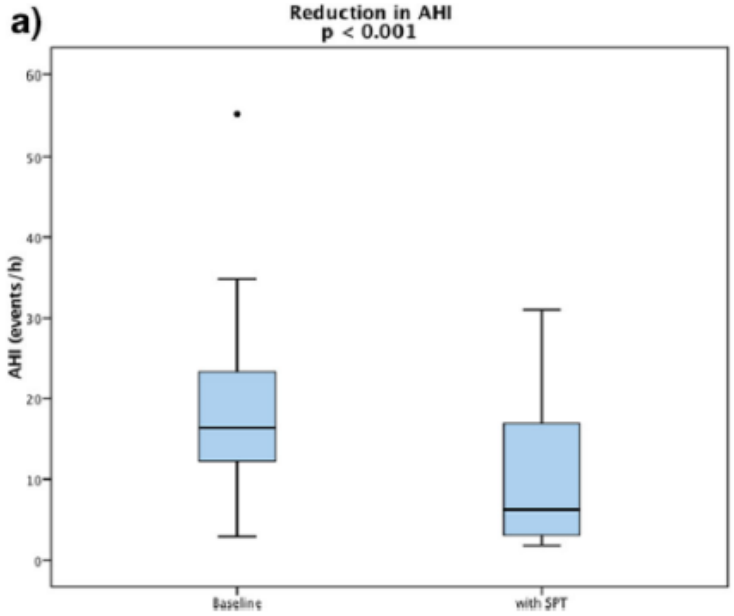
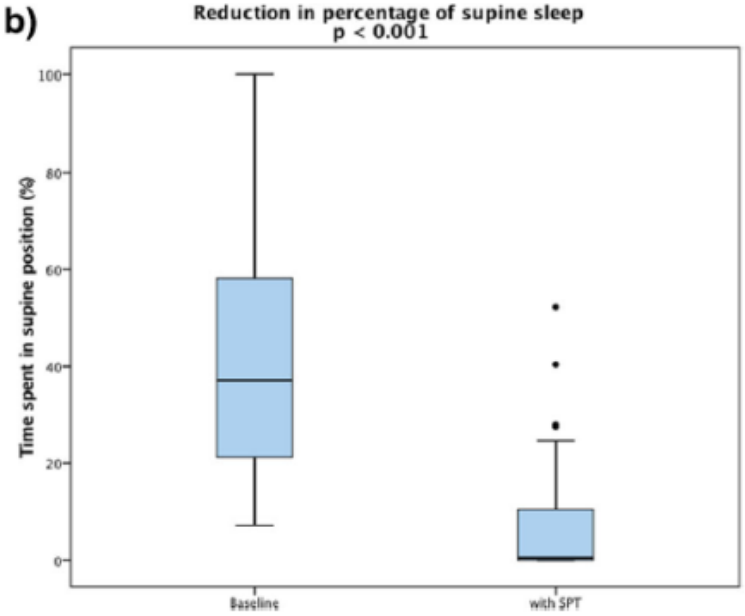
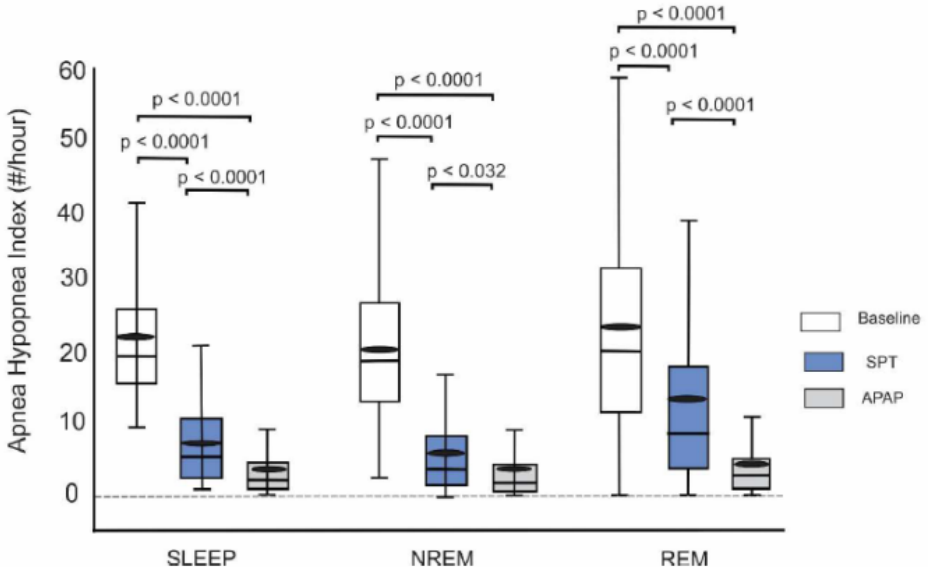
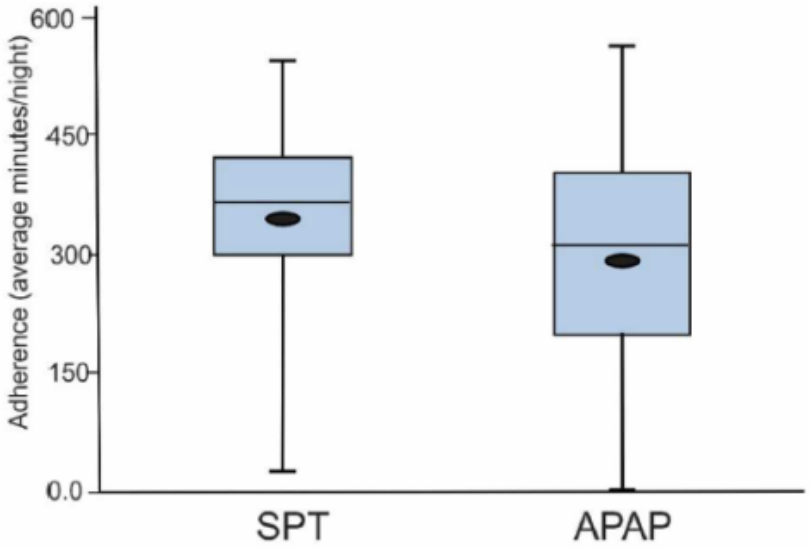




(https://doi.org/10.1007/s11325-019-01792-9)

SPT vs APAP: Randomized, Crossover
N = 110





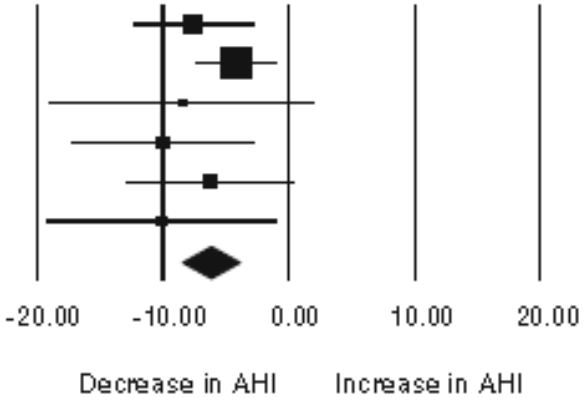
Berry et al, JCSM Accepted Paper (in press)

Positional Therapy

- Can be relatively effective in the right population
  - No real outcome data to date (CV risk, QOL, adherence)
- Patients need long term followup if this is recommended as many abandon over time

Exercise and OSA

Study name	Statistics for each study			
	Difference in means	Standard error	Lower limit	Upper limit
Kline 2011	-7.578	2.499	-12.475	-2.681
Sengul 2011	-4.180	1.694	-7.500	-0.860
Servantes 2011 (Aerobic)	-8.500	5.405	-19.094	2.094
Servantes 2011 (Aerobic+Strength training)	-10.000	3.739	-17.328	-2.672
Barnes 2009	-6.300	3.450	-13.061	0.461
Norman 2000	-10.100	4.687	-19.287	-0.913
	-6.272	1.159	-8.544	-3.999



Lung (2014) 192:175–184

Conclusions

- Best OA are adjustable mandibular advancing devices – work in coordination with a dentist given high likelihood of dental changes; OA have good efficacy and adherence if functional
- MMA has best surgical outcomes
- HGNS becoming more available and popular; needs better reporting standards
- Surgical weight loss has better outcomes that medical; pts may continue to have OSA however
- POSA works well for some patients, newer “training” devices have promise; need long term followup
- Exercise is good for everything!