



OSA : The Dark Side of Sleep



Maurits Boon MD
Chief Medical Officer

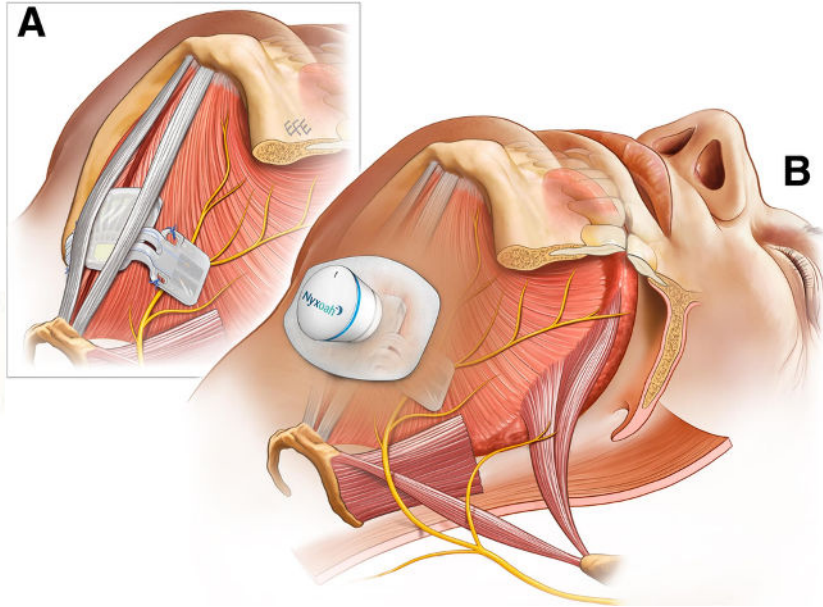
Case Example:

- YO Male with history of OSA diagnosed 15+ years ago
- Significant daytime symptoms
 - ESS 14
- PSG 2018:
 - AHI 29
 - ODI 28
- Attempted CPAP on 3 occasions
 - Claustrophobia
 - Mask fit issues
 - Unable to keep device on
- Initial evaluation 2018 for HNS therapy
 - DISE suggested appropriate candidacy for HNS
 - Insurance denied
 - Repeat evaluation in 2020 when DREAM trial available.



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Case Example:

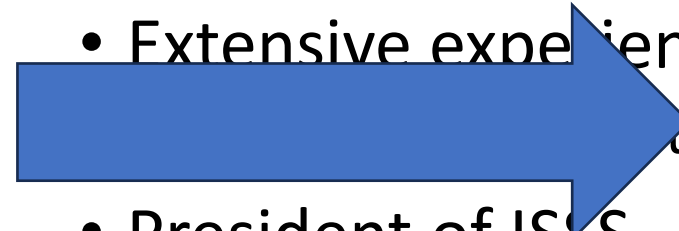


- Candidacy for DREAM confirmed
- Implanted:
- Postoperative course:
 - M12 AHI ESS
 - M24 AHI ESS
 - M36 AHI ESS

My Background



- ENT and Sleep Medicine
- 25 Years of practice
- Extensive experience with U



- President of ISSS
- Took over as Chief Medical Officer of Nyxoah Medical 2024



Introduction:



- What is obstructive sleep apnea
- Why should we care
- Diagnosis
- Treatment
- Hypoglossal Nerve Stimulation
- Genio



How much sleep do we need?

A: 3-4 hours/night

B: 5-6 hours/night

C: 7-9 hours/night

D: >9 hours / night

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What is normal sleep:



- 7-8 hours uninterrupted
 - Concept of short sleeper is extremely rare
 - Impact of less sleep is cumulative
 - <7 and >9 hours of sleep associated with increase in all cause mortality

How do we characterize sleep

- Sleep broken into stages:
 - W – wake
 - N1 – NREM 1 – light sleep 10%
 - N2 – NREM 2 – majority of sleep 50%
 - N3 – NREM 3 – delta or slow wave sleep 20%
 - REM – Rapid eye movement sleep – 20-25%

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NREM:

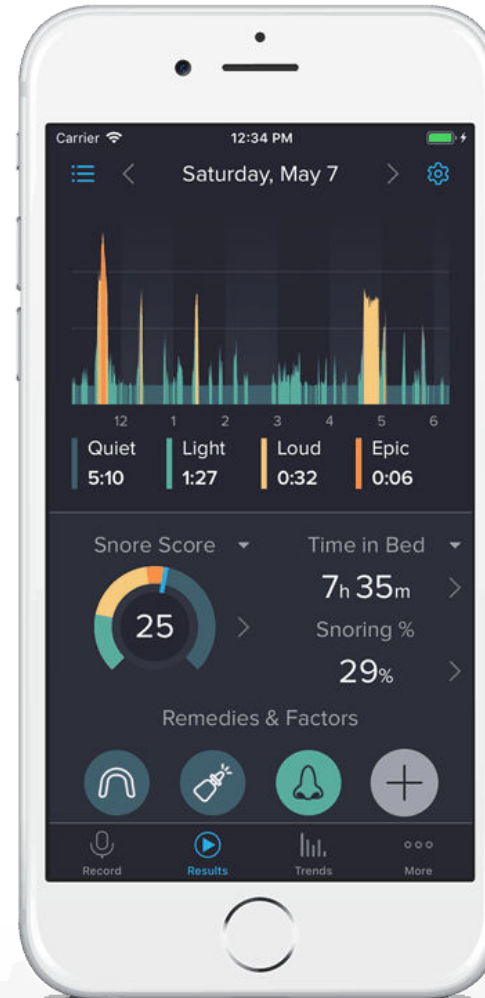
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- Decreased blood pressure
- Decreased heart rate
- Regular breathing
- Decreased upper airway muscle tone relative to wake

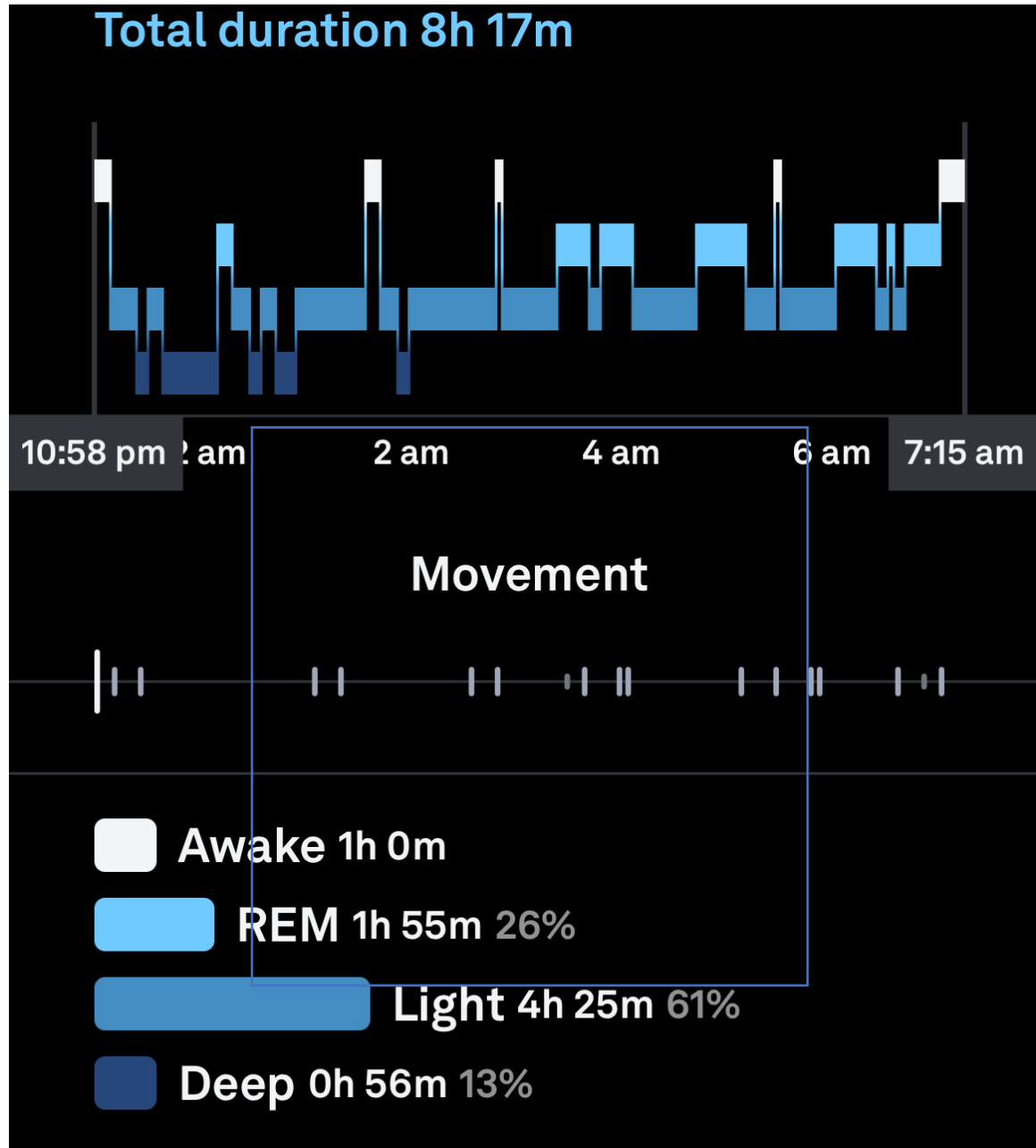
REM sleep



Wearable Technology:



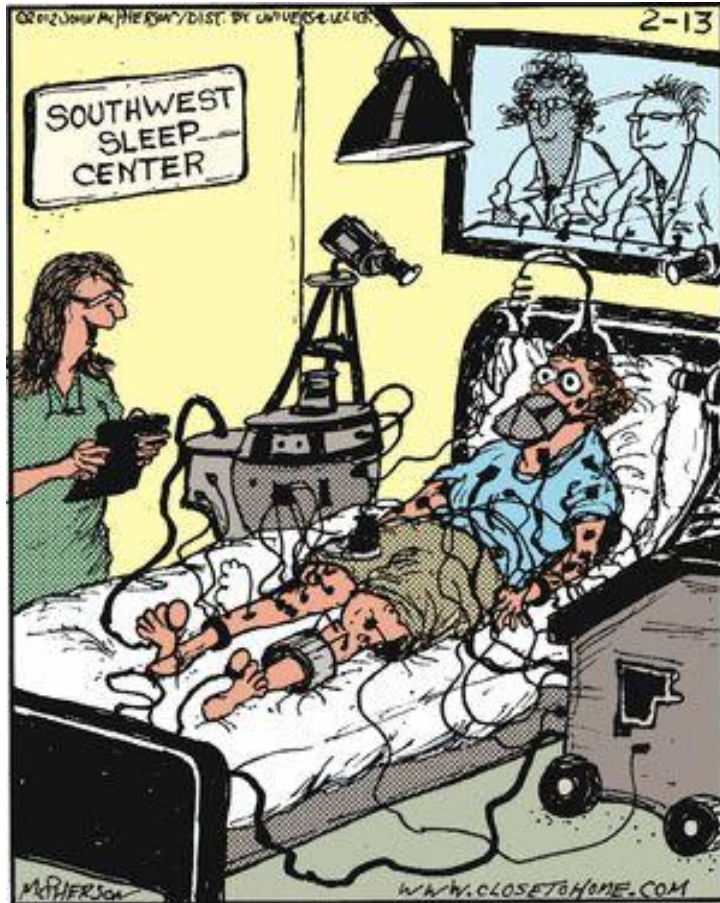
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How do we measure sleep? Polysomnography

Necessary for identifying sleep stages

Measures respiratory effort



"OK, Mrs. Tully. We want you to relax, get a good night's sleep, and we'll evaluate any sleep issues that you have."

- EEG
- EOG
- Chin EMG
- ECG
- Pulse oximetry
- Leg EMG

- Chest and abdominal bands
- Oral-nasal thermistor
- Nasal pressure sensor
- Snore channel

Measures air flow

Home Sleep Testing:



Home Sleep Study

- Pulse oximetry
- Air flow
- Respiratory effort
- Only indicated for diagnosis of patients with high probability of OSA

Can be inaccurate

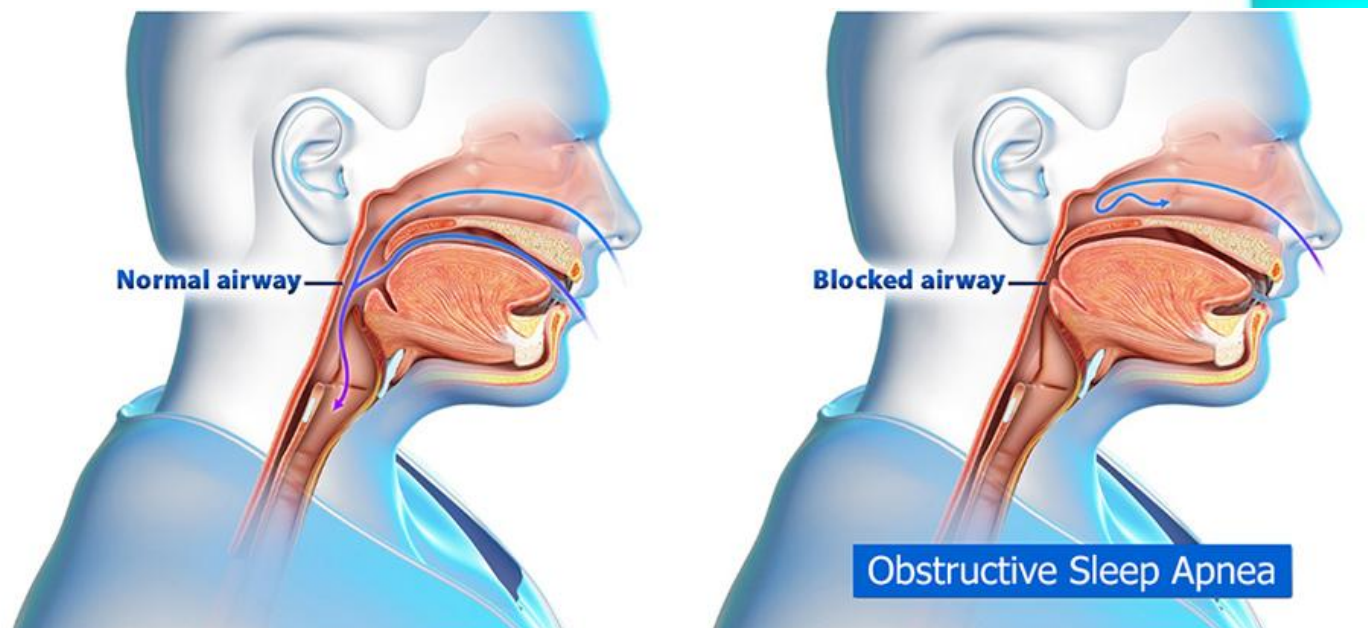
Allows sleep in normal environment

Can do multiple nights

Nyxoa

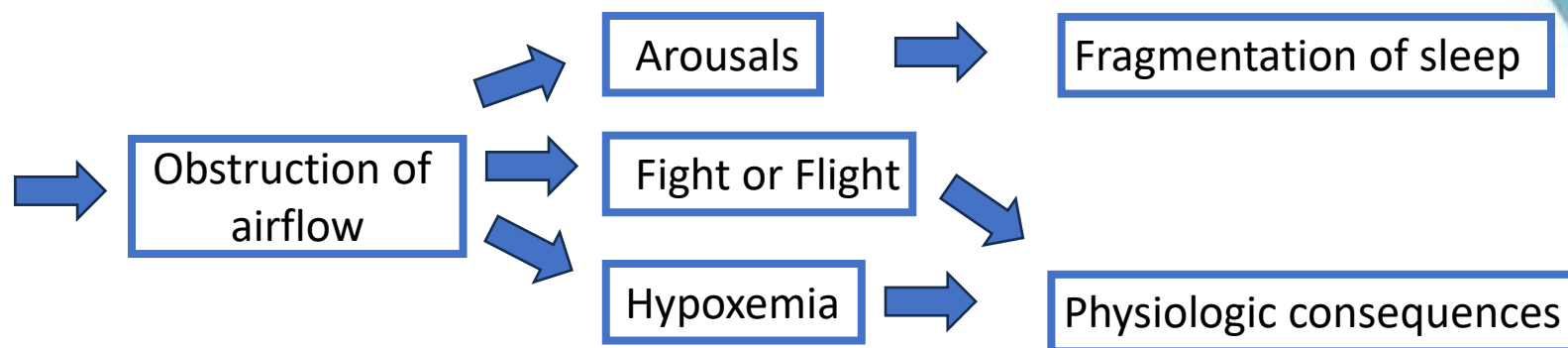


What is Obstructive Sleep Apnea (OSA):

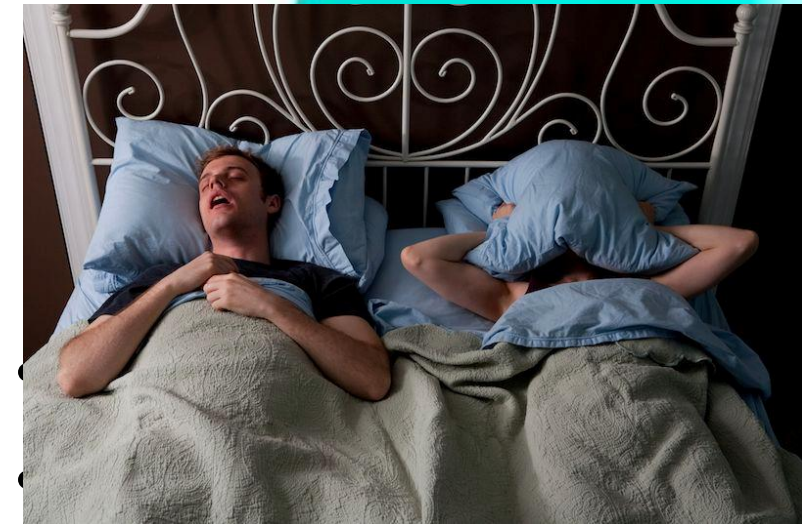


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Repetitive episodes of collapse
Of upper airway structures with
Continued respiratory effort



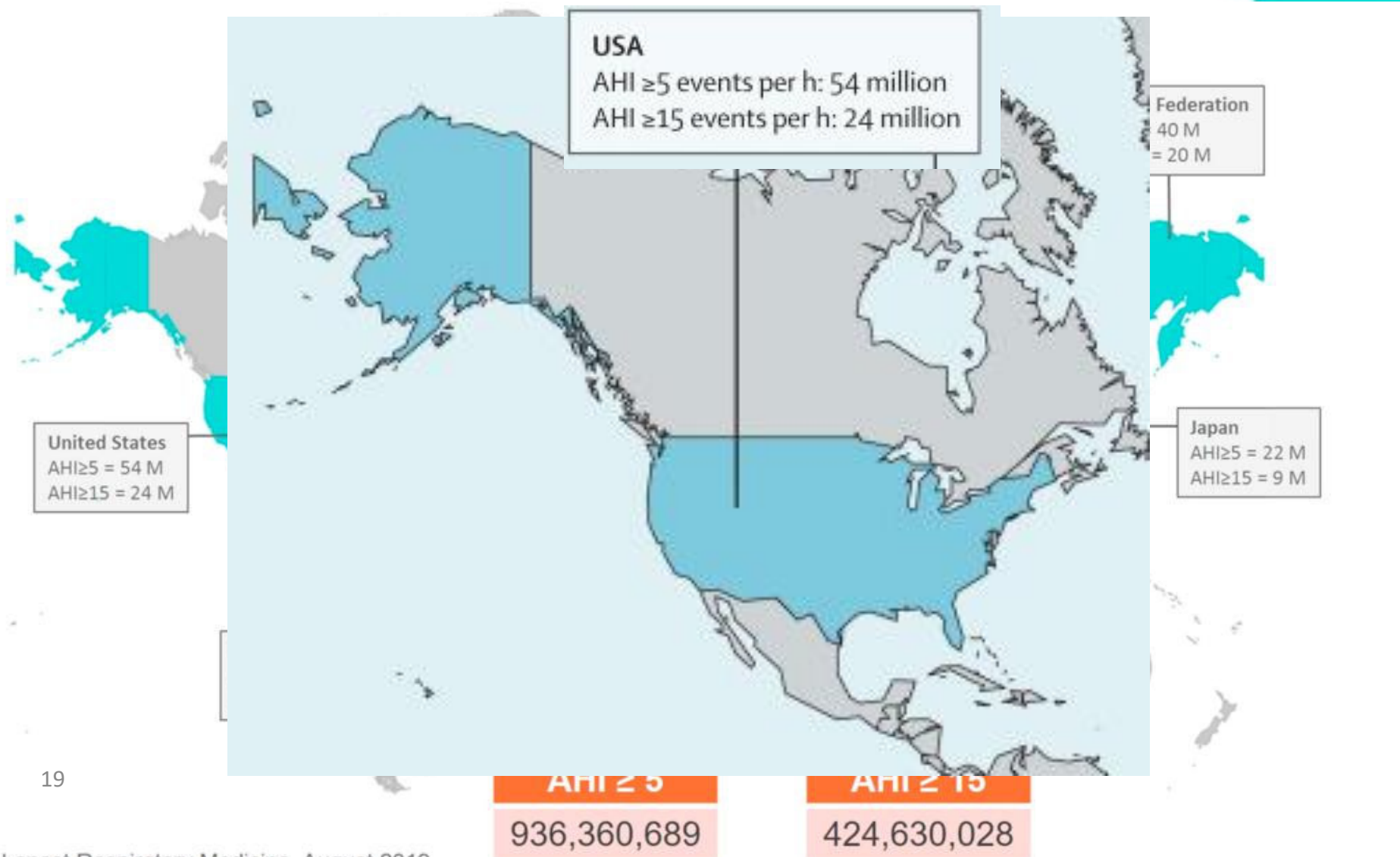
Why Do We Care About OSA



- Mood disorders (depression, anxiety)
- Work related accidents
- Motor vehicle accidents



OSA is a Big Problem



19

How Do We Characterize and Define OSA?



- Apnea: Complete cessation of airflow for 10 seconds or more
- Hypopnea: 2 rules
 - Reduction of airflow of 30% with 4% desaturation from baseline
 - Reduction of airflow of 30% with either 3% desaturation or arousal

Apnea Hypopnea Index = Average number of apneas + hypopneas
(AHI) Per hour

How Do We Characterize and Measure OSA



- Normal AHI: 0 – 5
- Mild: 5-15
- Moderate 15-30
- Severe: >30



Health Risks become significant

~~AHI~~



Hypoxic Burden

Measures of Hypoxic Burden



- Oxygen Nadir: lowest saturation measured during the sleep study
- Oxygen desaturation index (ODI) the average number of times the oxygen saturation reduces 3% (or 4%) from baseline
- T90: Amount of time that the saturation spends below 90% during the sleep study
- T88: Amount of time that the saturation spends below 88% during the sleep study

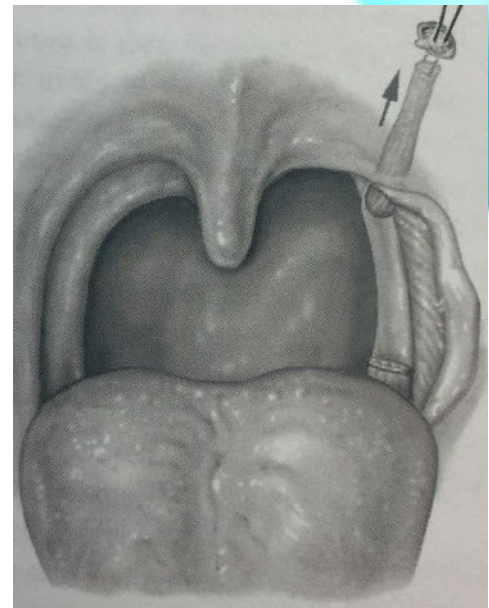
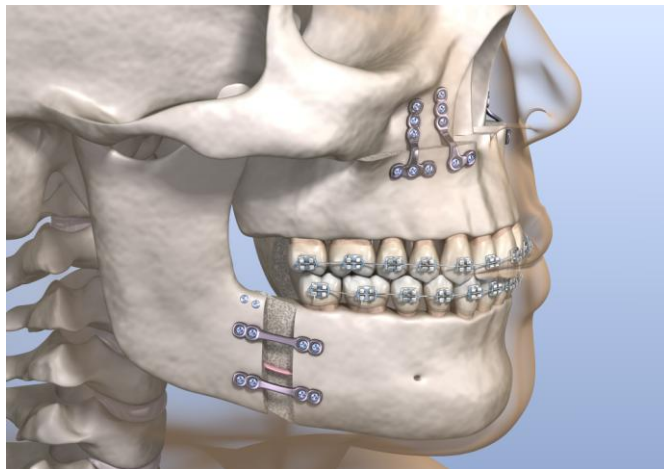
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Treating OSA



- Positive airway Pressure
- Alternative therapies

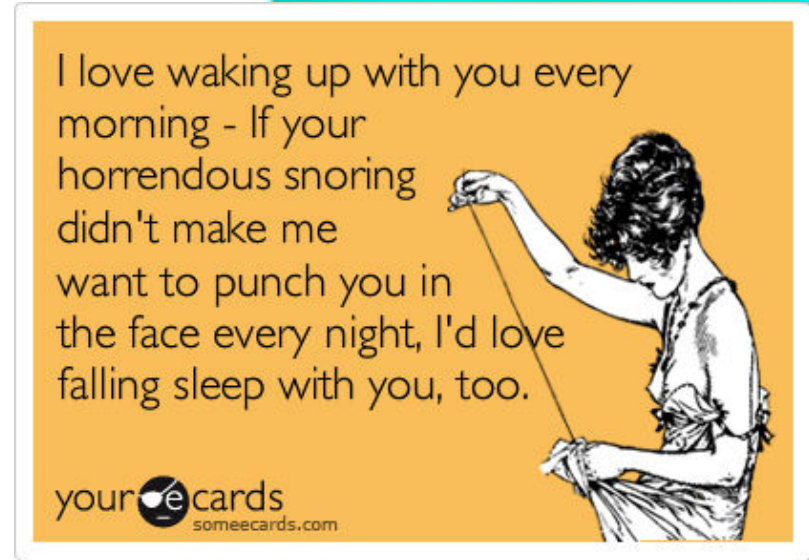


Treatment Goals?

- 1. Reduction in disease burden**
- 2. Improved quality of life for patient**

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- 3 Improved quality of life for bedpartner**



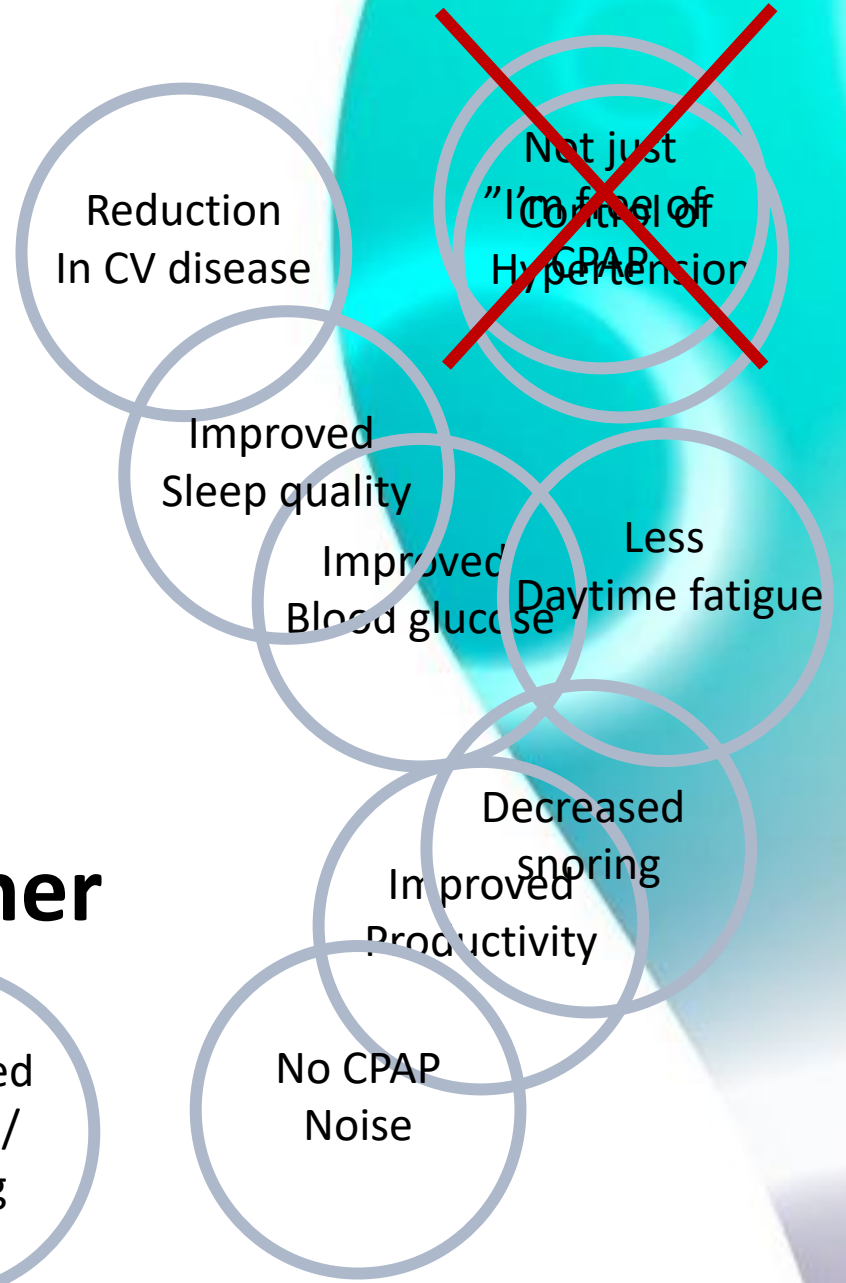
Treatment Goals?

1. Reduction in disease burden

2. Improved quality of life for patient



3 Improved quality of life for bedpartner



Lifestyle:

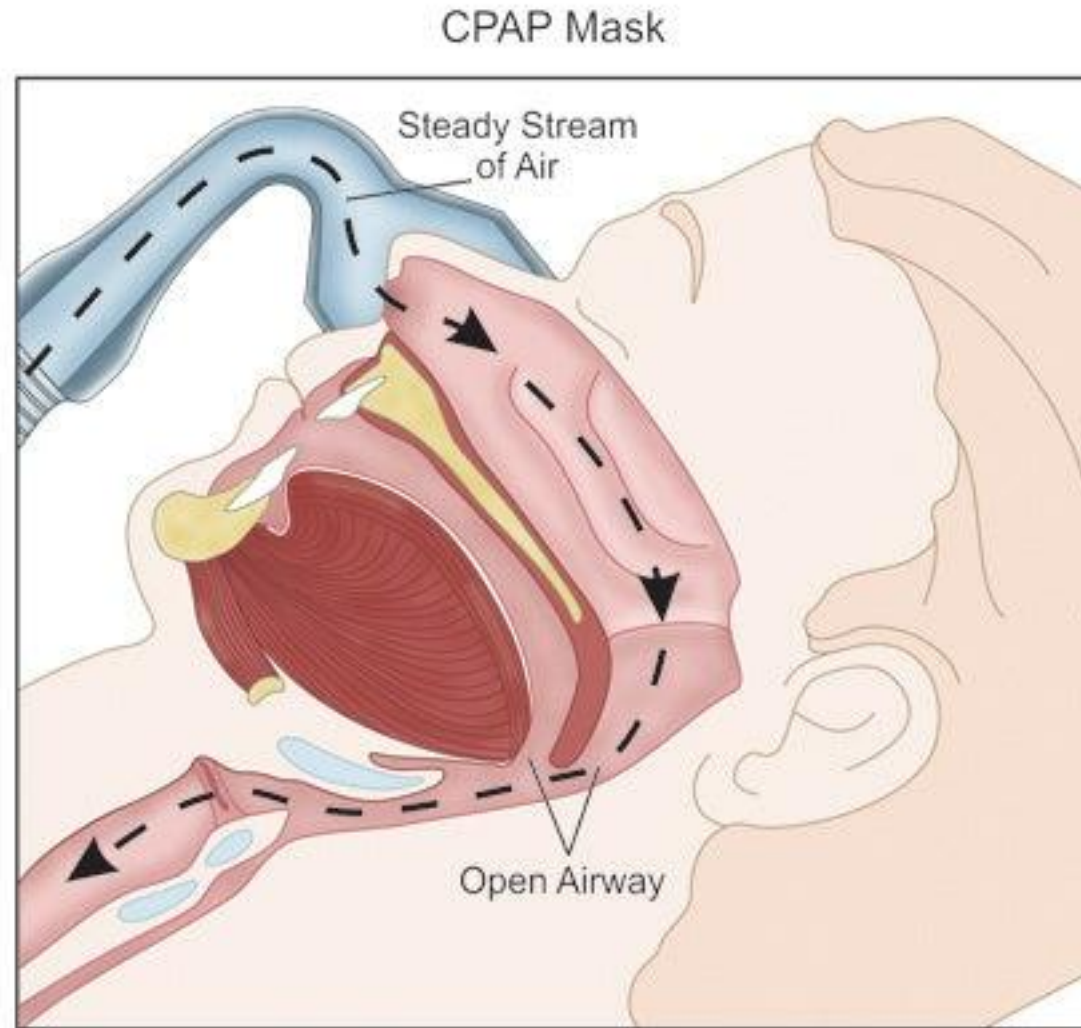


- Weight loss
- New drugs:
 - Metformin – mild weight change
 - Ozempic (semaglutide) – once weekly injection
 - For treatment of diabetes
 - Binds to GLP-1 and stimulates production of insulin to decrease blood glucose
 - Moderate weight change
 - Wegovy (semaglutide) – once weekly injection
 - Indicated for weight loss
 - Higher dose
 - Mounjaro (tirzepatide) - once weekly injection
 - Dual GLP-1 agonist and GIP agonist (increases sensitivity to insulin)

Indicated for Overweight or Obese with One or more Weight related Comorbid condition

CPAP: First Line Treatment

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BiPAP

CPAP Airflow

- Stands for **Continuous Positive Airway Pressure**
- Provides a **single set pressure** throughout your sleep
- Generally **more affordable**
- Not as great for accomodating changes in breathing

CONSTANT SET PRESSURE DURING INHALE



PRESSURE RELIEF DURING EXHALE

BiPAP Airflow

- Stands for **BiLevel Positive Airway Pressure**
- **Two distinct pressure settings** for inhale and exhale
- Often used to treat **more complex sleep and breathing disorders**

CONSTANT SET PRESSURE DURING INHALE



CONSTANT SET PRESSURE DURING EXHALE




46-83% Non Adherence



Weaver, TE et al. Adherence to Continuous Positive Airway Pressure Therapy: The Challenge to effective treatment. Proceedings of the American Thoracic Society. 5(2). 2008 Feb 173-8

Improving Adherence:

- Early follow up  1 week
- Heated Humidification
- Mask
- Ramp
- Monitoring and feedback
- BiPAP

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Alternative Therapies

- Personalized therapy based on:
 - Site of airway collapse
 - Mechanism of airway collapse
 - Patient phenotype
 - Patient preference

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DISE



- Attempt to reproduce airway collapse patterns seen during patient's normal sleep
- Sedative anesthesia
- Fiberoptic scope passed transnasally

NAME
ID
1

AGE SEX 11/11/2014
20:25:40



COMMENT
Facility

DR BOON

Nyx

NAME
ID
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AGE 02/24/2017
01:00:22

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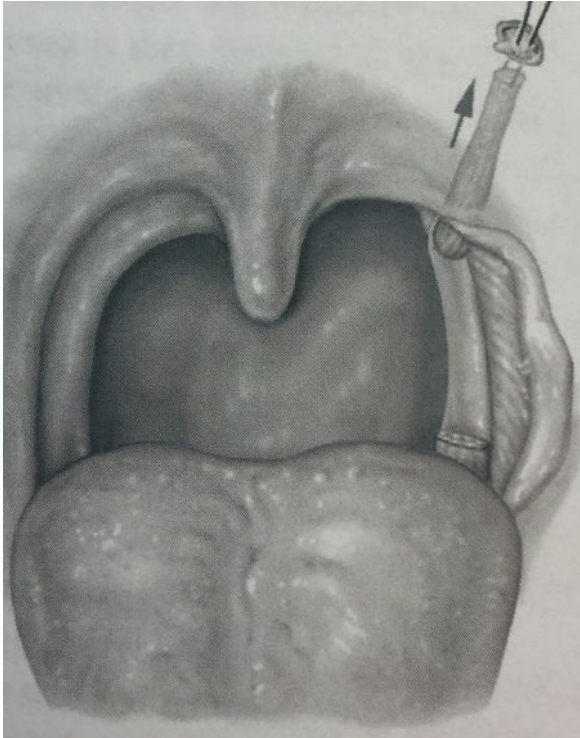
Oral Appliance Therapy



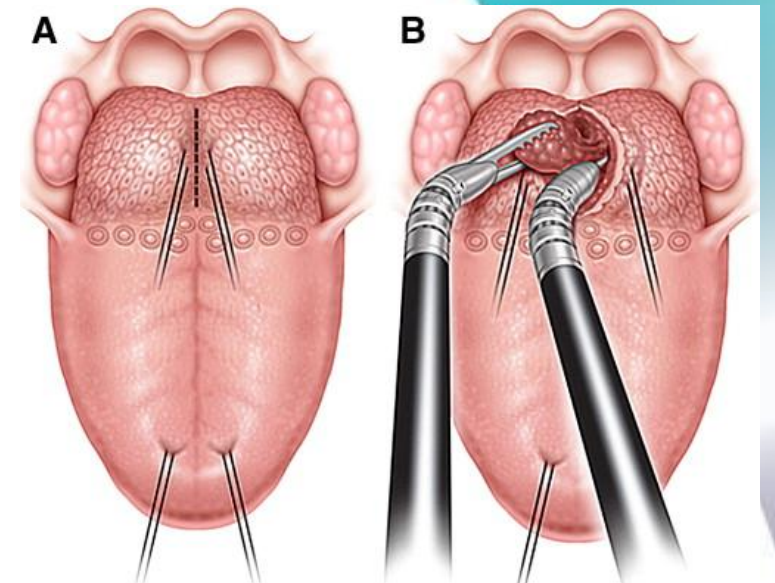
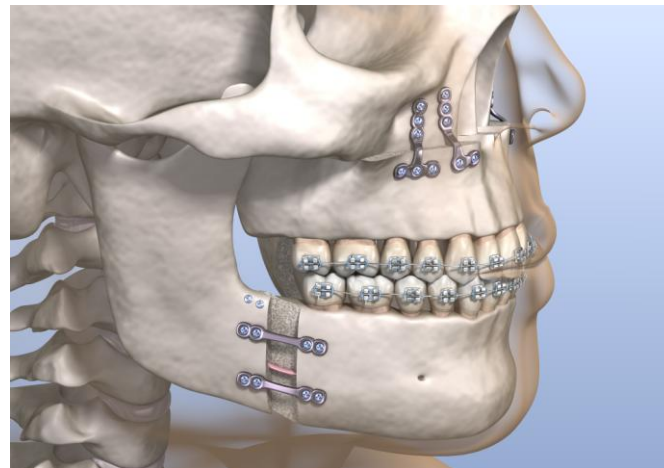
Several leading FDA-approved oral appliance designs

- Tongue retaining
- Mandibular advancement devices
- Pull lower jaw forward relative to upper jaw
- Better with mild to moderate OSA
- Lower BMI
- Better compliance than CPAP
- Lower overall reduction in AHI

Surgery for OSA:

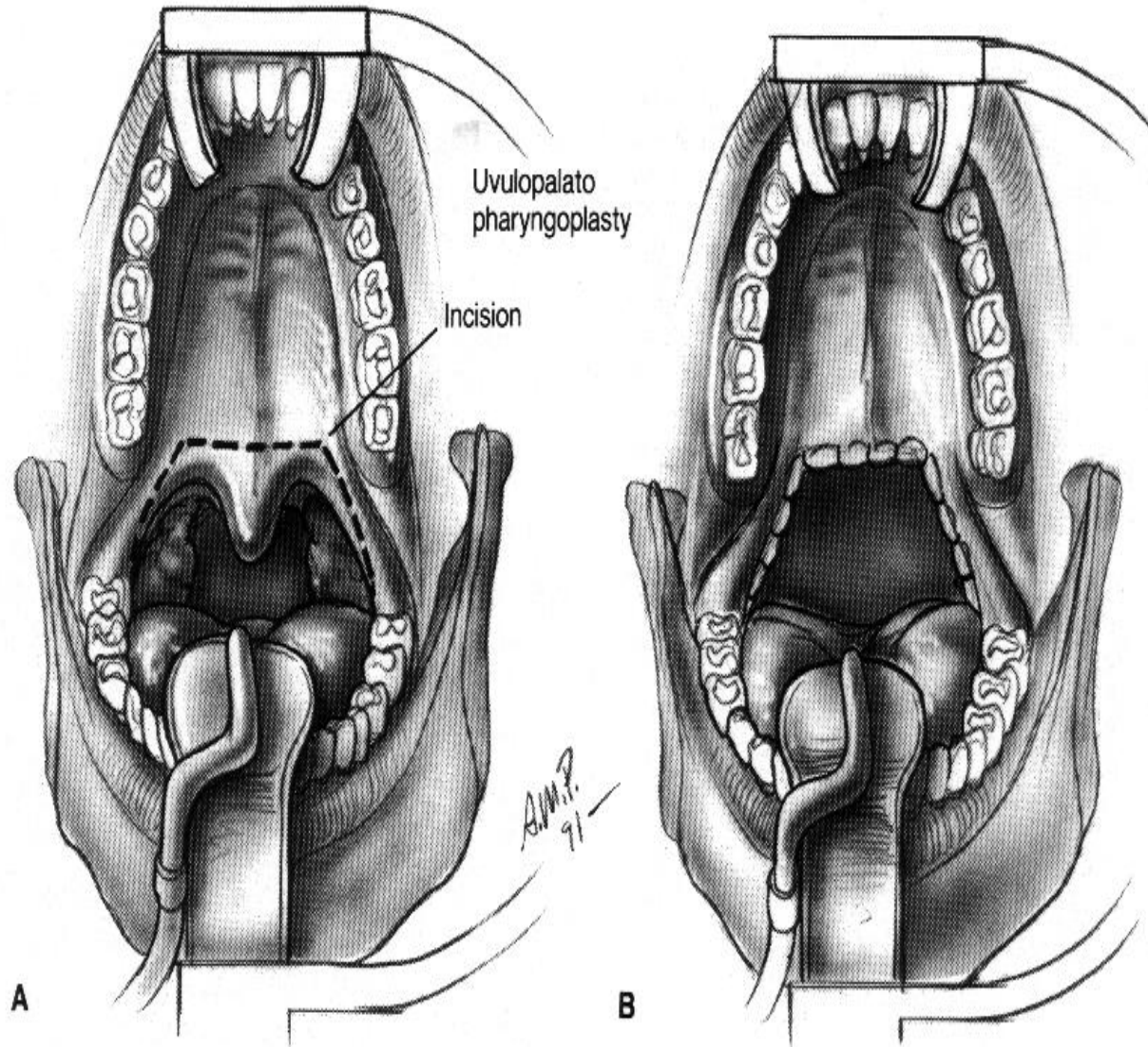


- Many different procedures
- Shift from ablative surgery to “reconstructive” efforts to
- Considered invasive
 - Risks associated with procedures

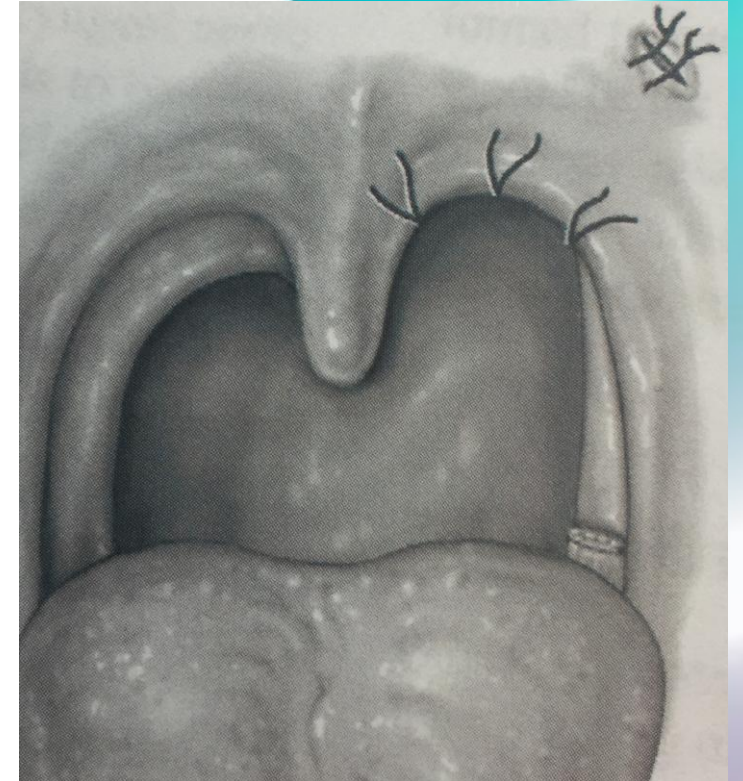
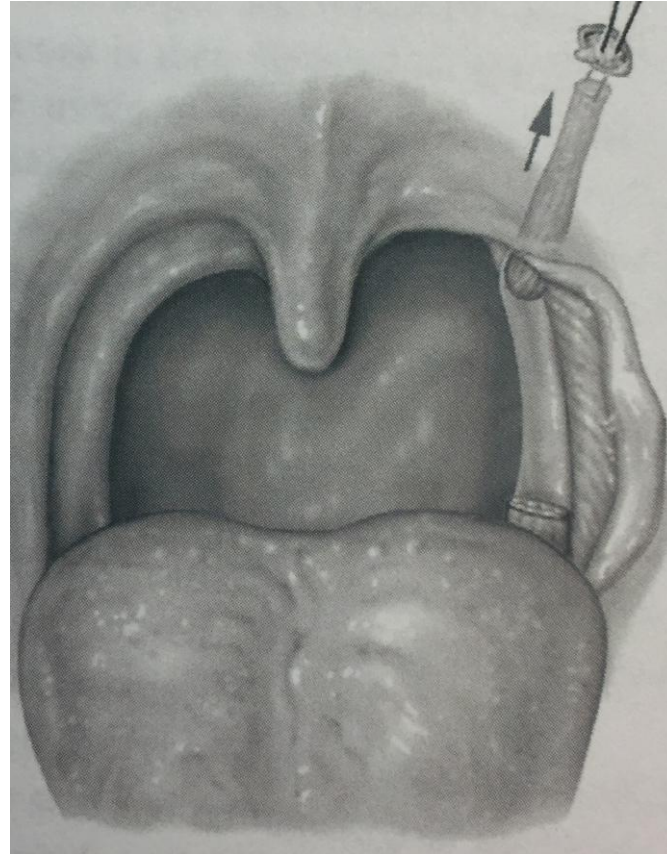
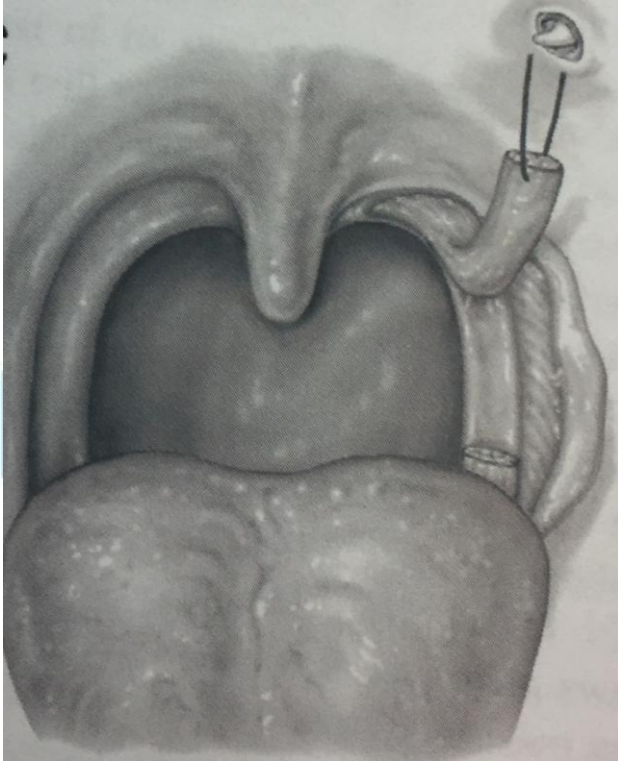


UPPP: Uvulopalatopharyngoplasty

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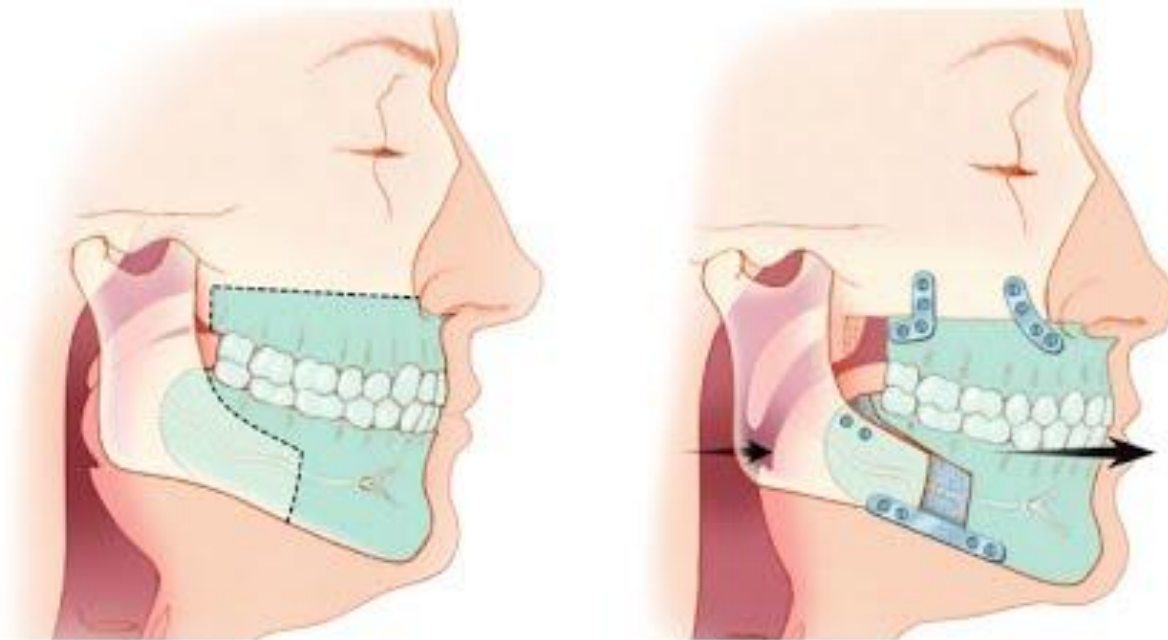
Anatomy Altering Surgery



Maxillo-mandibular Advancement (MMA):

MaxilloMandibular Advancement

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Measuring Surgical Success:



- Sher criteria
 - 50% reduction in AHI
 - Overall AHI < 20
- Modified Sher criteria
 - 50 reduction in AHI
 - Overall AHI < 15

MDA

Efficacy

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100

0

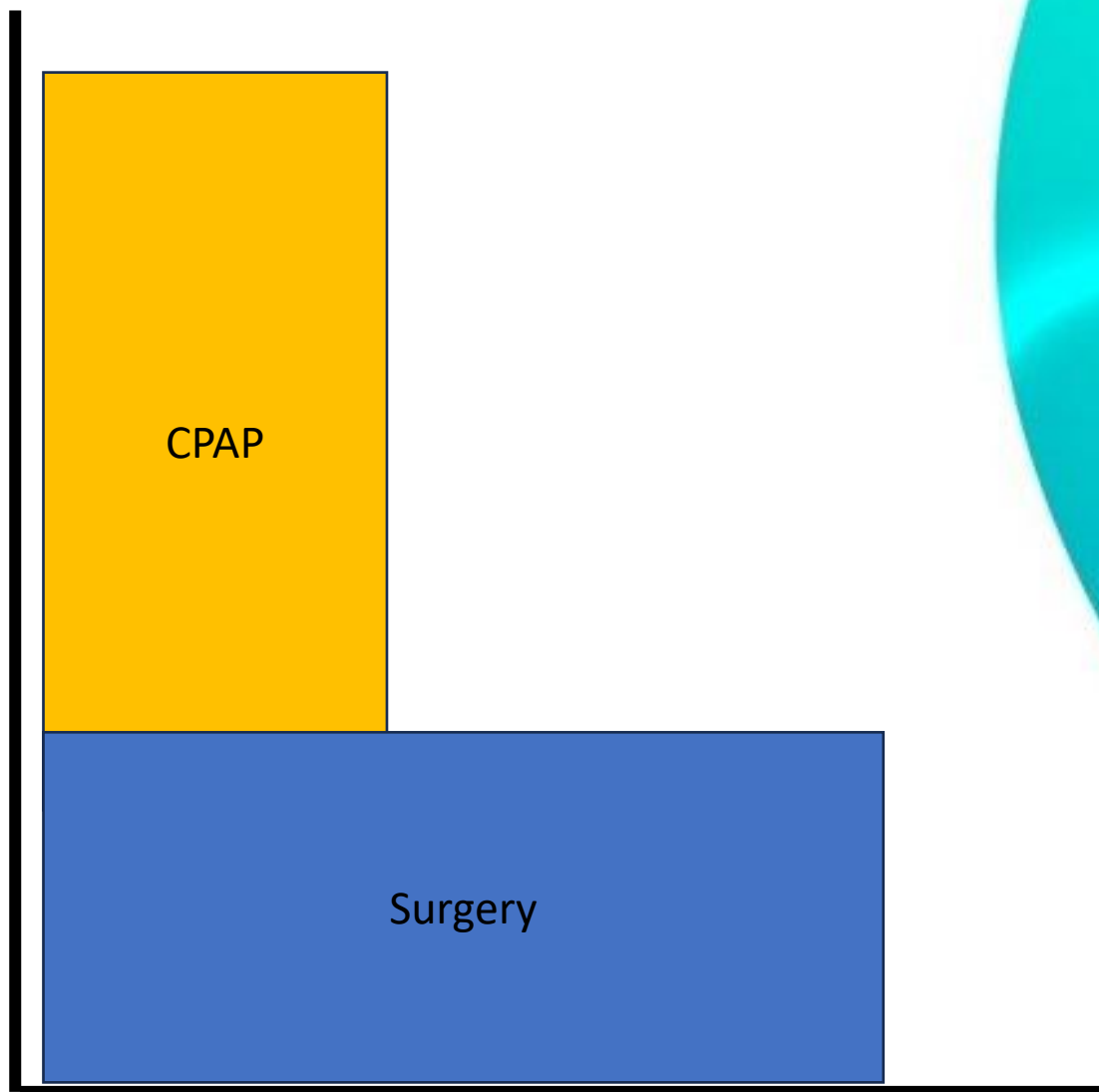
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Compliance

CPAP

Surgery

Commercially confidential. Not for distribution.



Effective AHI

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CPAP user

AHI baseline 40



With PAP therapy 0



Compliance 50%



Effective AHI: 20

Effective AHI



UPPP

AHI baseline 40



With Surgery 15



Compliance 100%

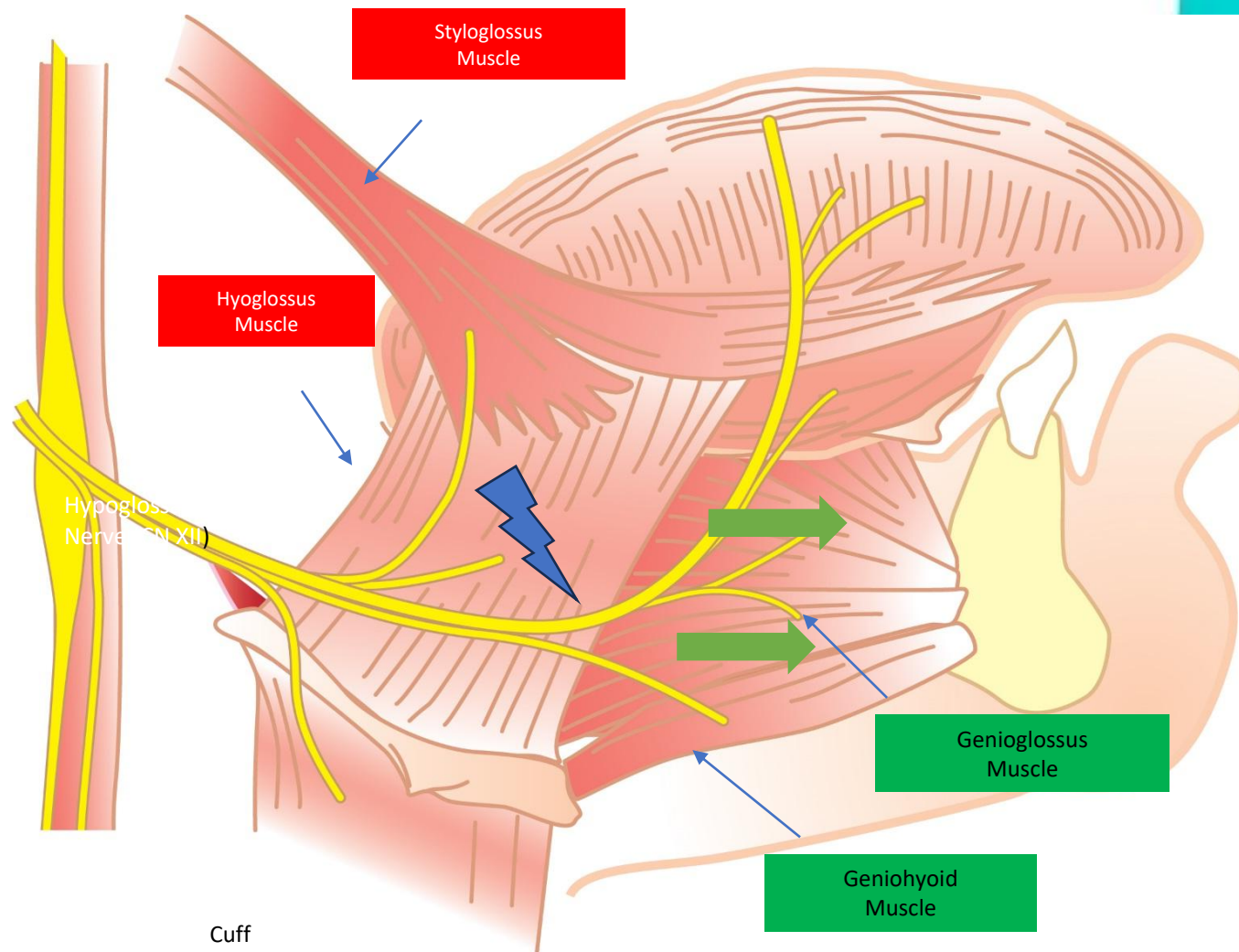


Effective AHI: 15

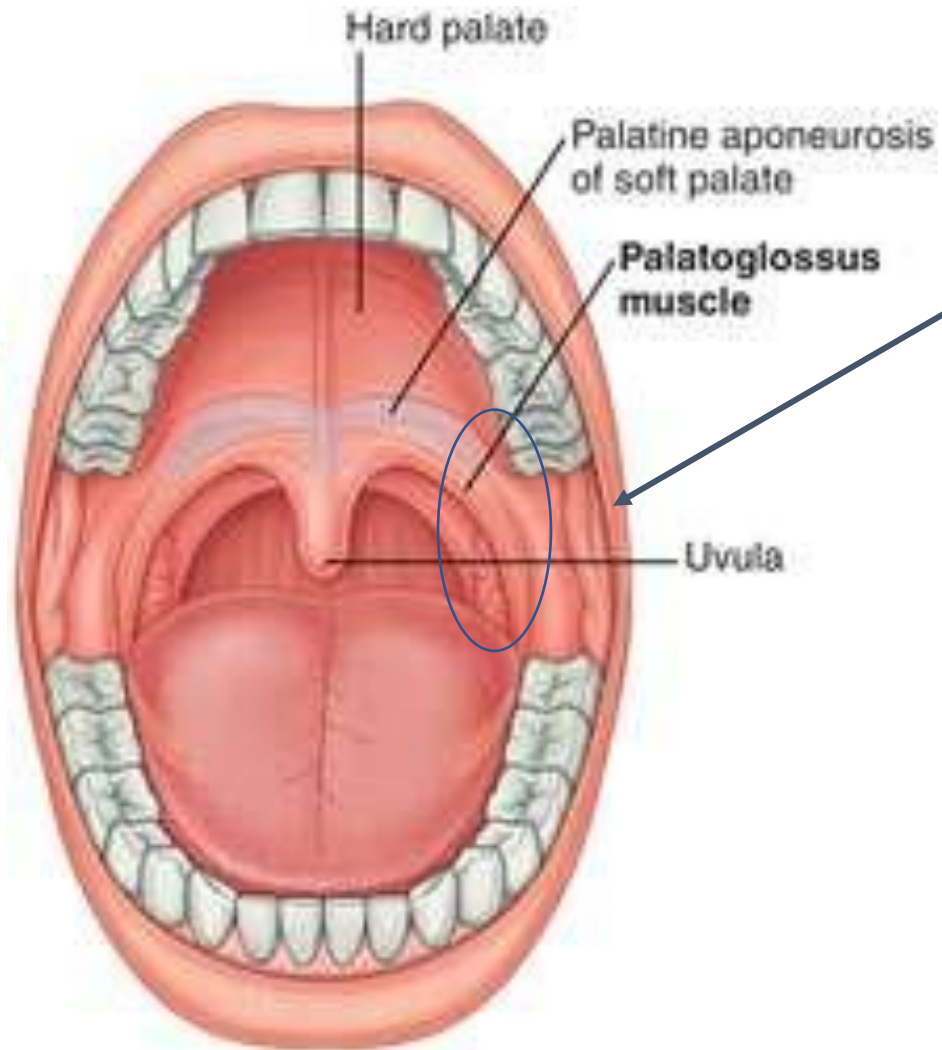


Hypoglossal Nerve Stimulation (HGNS)

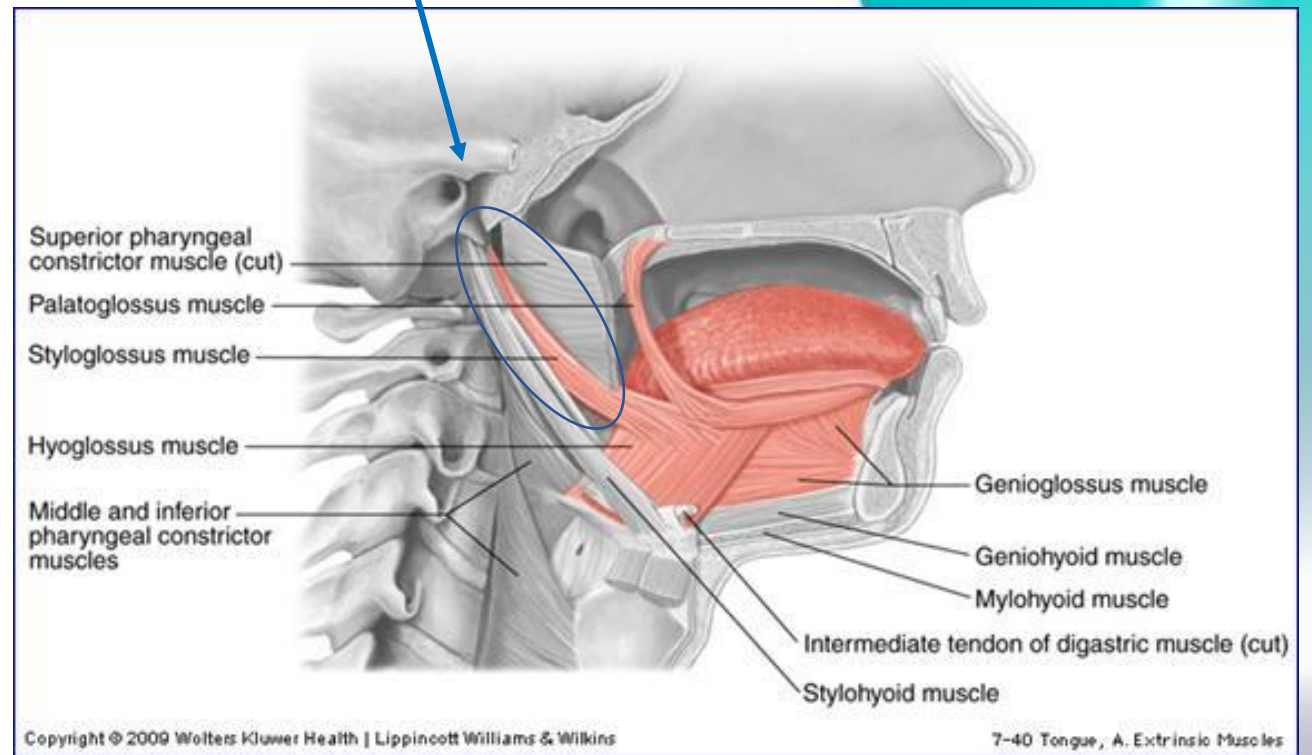
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Multilevel Opening with HGNS

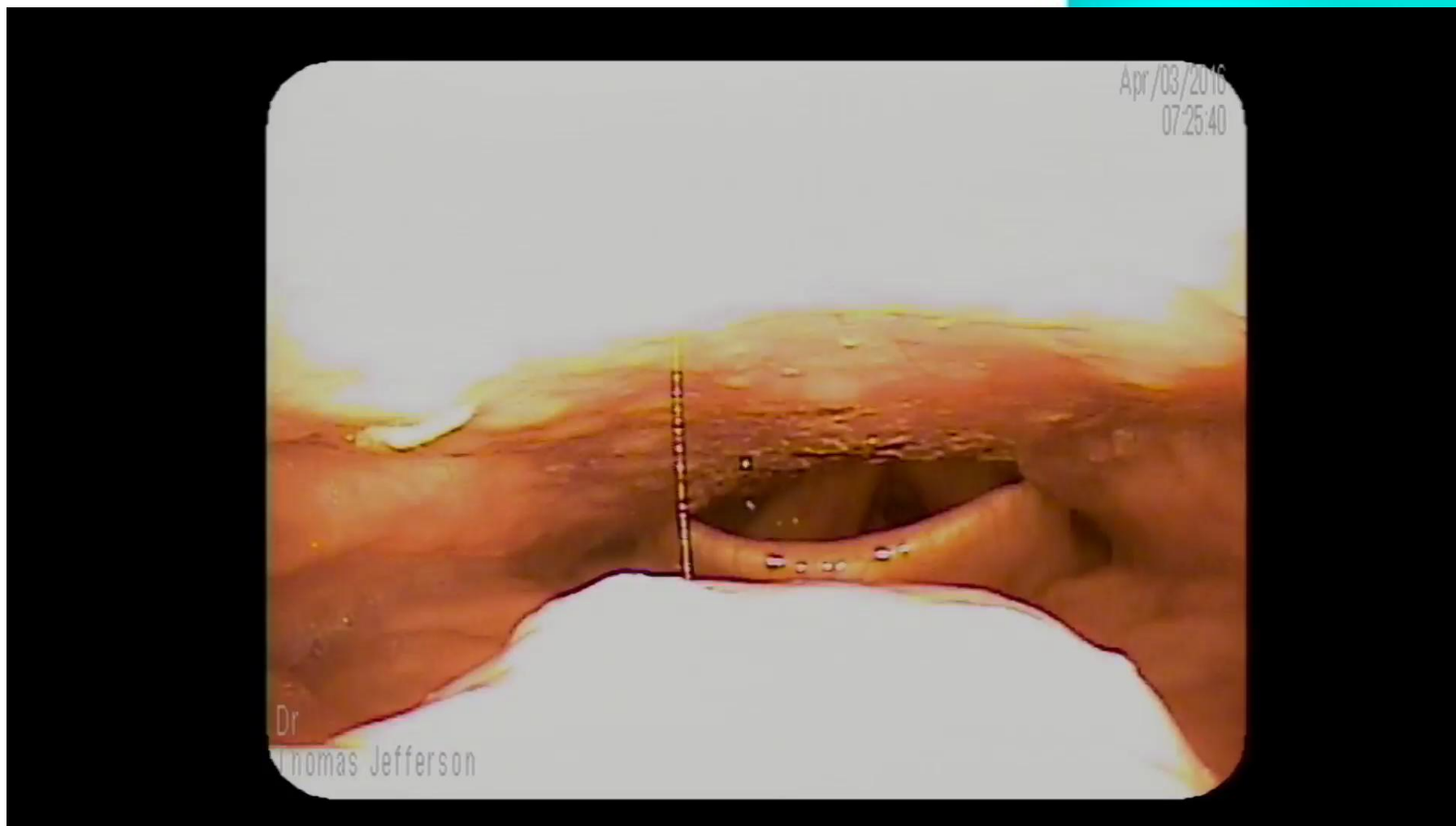


Palatoglossus Muscle



Hypoglossal Nerve Stimulation:

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STAR Trial: Stimulation Treatment for Apnea Reduction: NEJM 2014



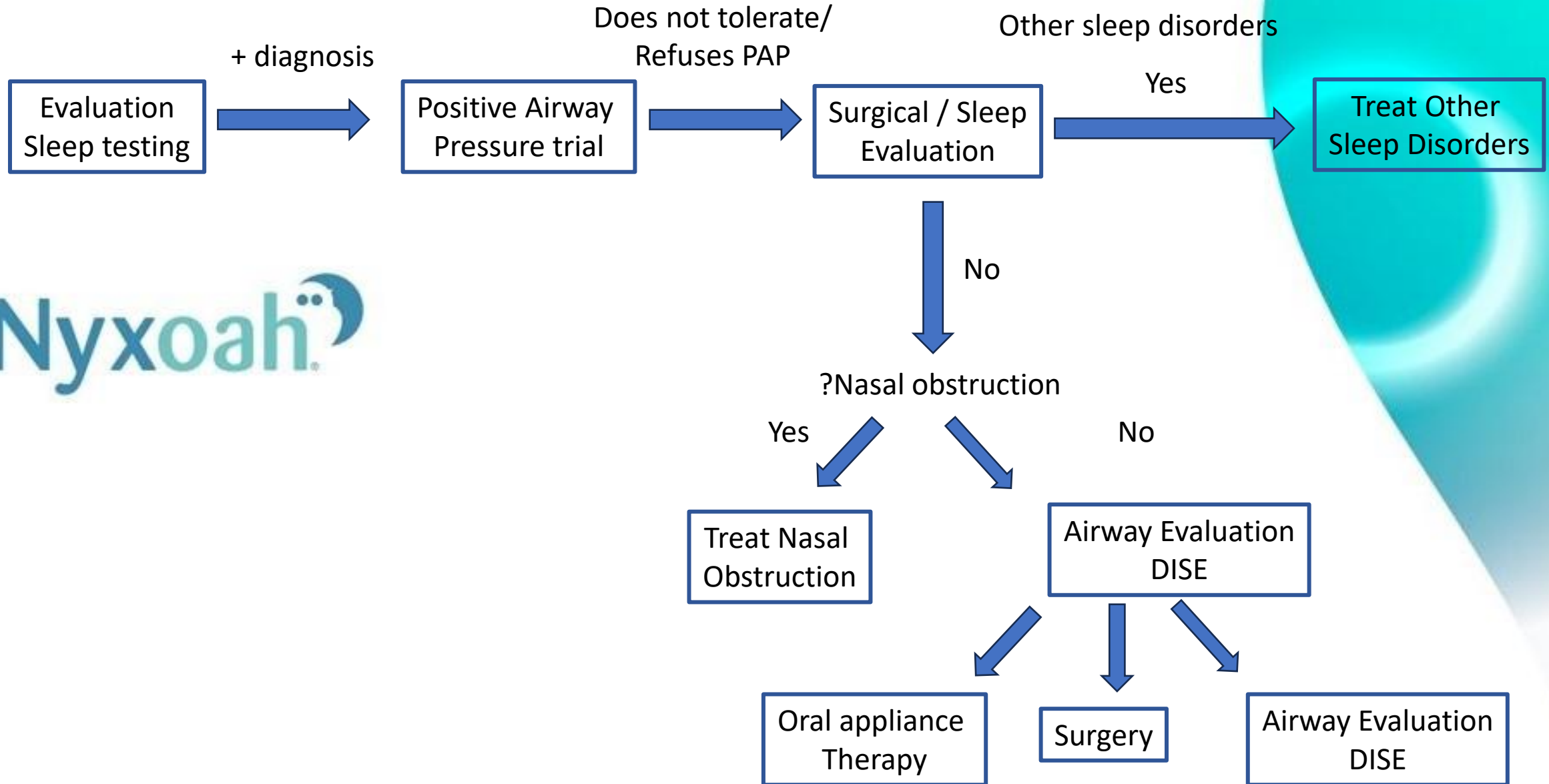
- 129 Patients
- Median AHI reduction 68%
- AHI Responder 66%
- ODI 75%

Indications:

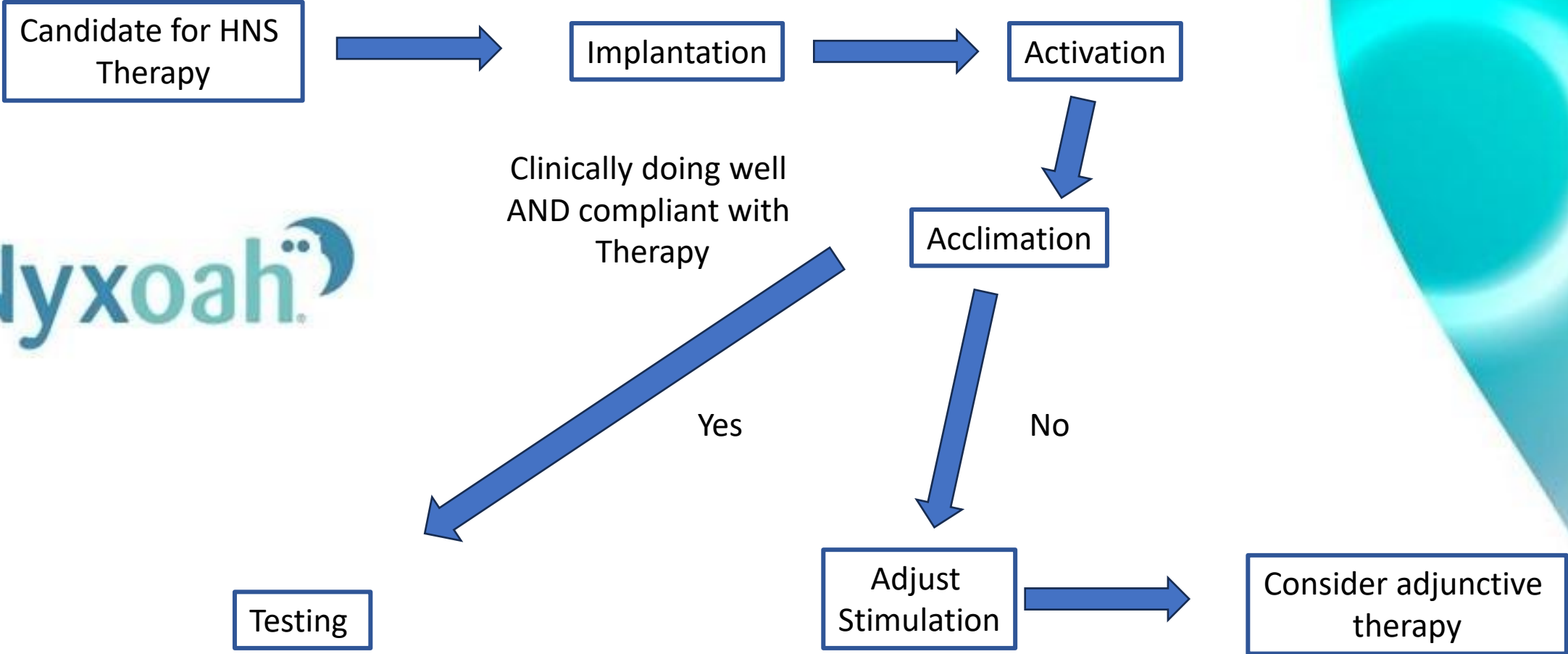
- BMI of 35 or less (for Genio 32 or less)
- AHI 15-65
- Less than 25% of events central
- Must attempt and either fail or don't tolerate CPAP

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Patient Journey and Monitoring: HNS Therapy



Patient Journey and Monitoring:



Post Activation Titration - Limitations

- Time during any amplitude is limited
- ?REM sleep
- Supine vs non-supine sleep
- Therapeutic amplitude may not be tolerable with at home use

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Efficacy Study:

- Single amplitude of therapy used all night
- Can be HST or multiple night HST
- Can consider different amplitudes on different nights

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SCIENTIFIC INVESTIGATIONS

How we measure hypoglossal nerve stimulator outcome matters: titration vs single amplitude efficacy sleep studies

Thomas M. Kaffenberger, MD^{1,2}; Elliott M. Sina, BA³; Bryce Hambach, BS³; Praneet Kaki, BS³; Antony Fuleihan, BS³; Maurits Boon, MD^{4,5}; Colin Huntley, MD^{4,5}

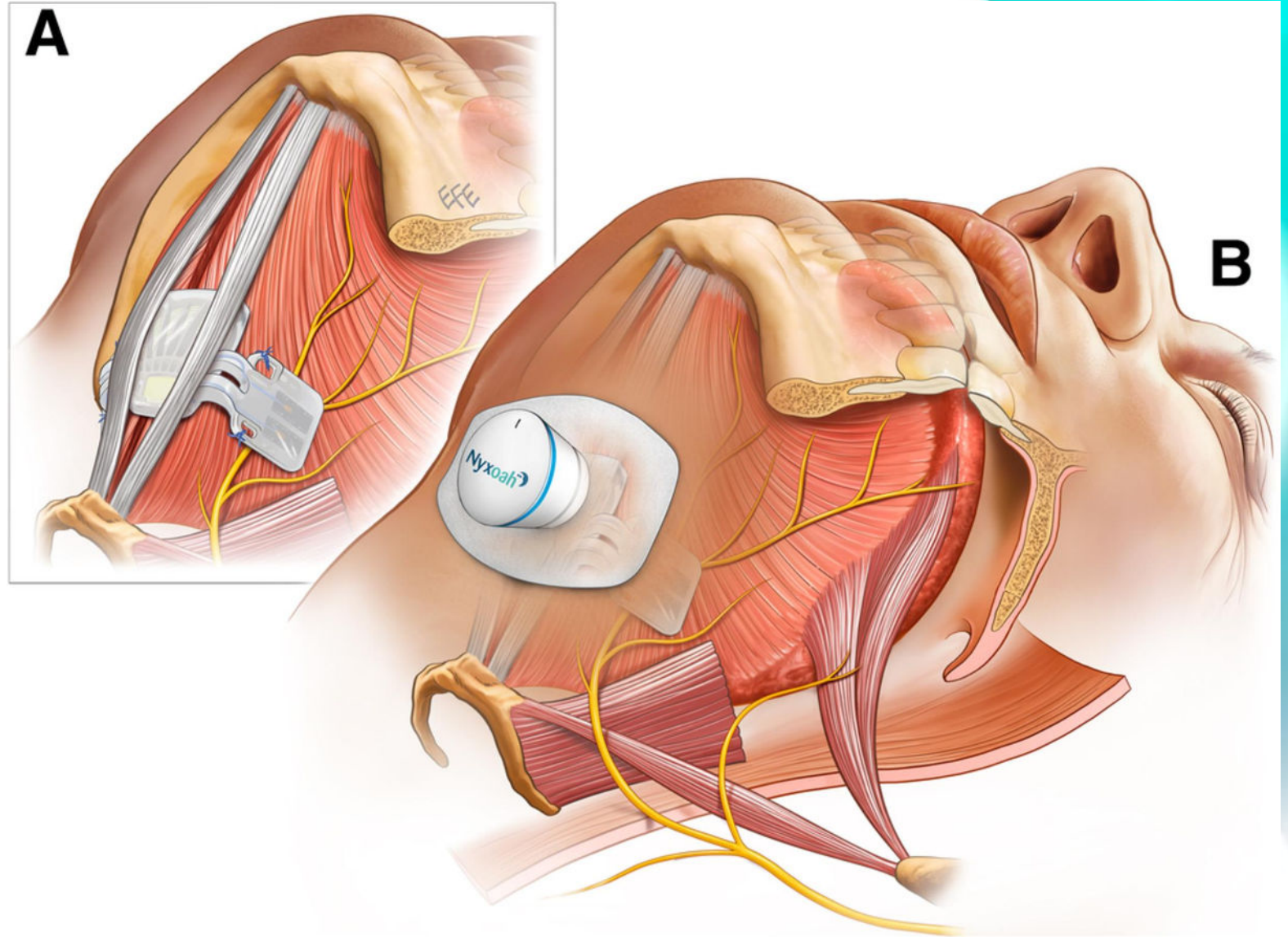


- AHI:
- Responder rate

	tAHI		eAHI
	8.8	→	17.8
	80.3%	→	45.9

Genio:

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Patient

- Evaluated in 2020
- Patient initial sleep study AHI 29, ESS 14
- Attempted and failed CPAP
- Initially evaluated for Inspire and insurance denied
 - Adjudicated in court and insurance decision upheld
- Evaluated for DREAM
- Implanted 2021
- Course over 1 year: PSG M12: AHI 1.7
- ESS 7
- “Genio has changed my life”



BLAST Study

TABLE 2 Outcome measures for modified intention-to-treat analyses

	Baseline	6 months	Mean difference (95% CI)	p-value
Subjects n	22	22		
Sleep disordered breathing				
AHI events·h ⁻¹	23.7±12.2	12.9±10.1	10.8 (14.6–7.0)	<0.0001
ODI events·h ⁻¹	19.1±11.2	9.8±6.9	9.3 (13.1–5.5)	<0.0001
S _{aO₂} <90% % time	5.0±6.0	2.1±3.0	2.9 (4.6–1.3)	0.0015
Apnoea index events·h ⁻¹	10.1±10.2	5.6±8.4	4.8 (9.2–0.4)	0.0334
Hypopnoea index events·h ⁻¹	12.5±8.9	7.6±6.2	4.9 (8.1–1.7)	0.0049
Symptoms				
ESS	11.0±5.3 [#]	8.0±5.4	3.0 (5.7–0.8)	0.0113
FOSQ-10	15.3±3.3	17.2±3.0	1.9 (0.4–3.4)	0.0157
Sleep architecture				
Sleep efficiency %	84.0±10.8	87.3±8.9	3.2 (0.01–6.4)	0.0494
NREM stage 1 %	13.1±7.9	8.2±4.0	5.0 (8.3–1.7)	0.0053
NREM stage 2 %	60.9±8.7	67.6±9.5	6.7 (2.2–11.3)	0.0058
NREM stage 3 %	8.2±6.9	3.5±4.3	4.7 (6.6–2.7)	<0.001
REM %	17.8±6.4	20.7±7.3	2.9 (–0.3–6.2)	0.0782
Arousal index events·h ⁻¹	28.7±11.5	16.0±8.0	12.7 (16.6–8.9)	<0.0001

DREAM (Dual sided NeRvE StimulAtion for the Treatment of Obstructive Sleep Apnea) :

115 Patients, 95 completed M12

- Median AHI reduction: STAR 68 vs DREAM 70.8
- AHI responder rate: STAR 66% vs DREAM 63.5
- ODI responder rate: STAR 75% vs DREAM 71.3%
- Adverse events: STAR 21% vs DREAM 9%



Genio Therapy:



- Single incision
- Passive device
- Bilateral stimulation
- Full body MRI conditional for 3 Tesla MRI
- Upgradable
- No battery

Genio therapy...

- Is safe and efficacious in treating patients OSA w/ or w/o CCC
- Improves QoL in patients suffering from OSA resulting in high levels of satisfaction
- Provides sustained symptom relief*
- Has strong therapy compliance**
- Results in comparable, if not better, super responders to INSP (AHI<10 and AHI<5)



*As measured by as measured by mean disease alleviation (MDA) and other relevant outcomes

** Use CPAP definition and/or ResMed's definition

