OSA Part 1 – Pathogenesis, Risk Assessment, Diagnostic options

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Learning objectives

- **What is obstructive sleep apnea (OSA)** in 2026?
- Who is at **risk** for OSA?
- How is OSA **diagnosed**?

Sleep apnea is… everywhere!

Global Adults Affected (30-69 years) ~1 Billion

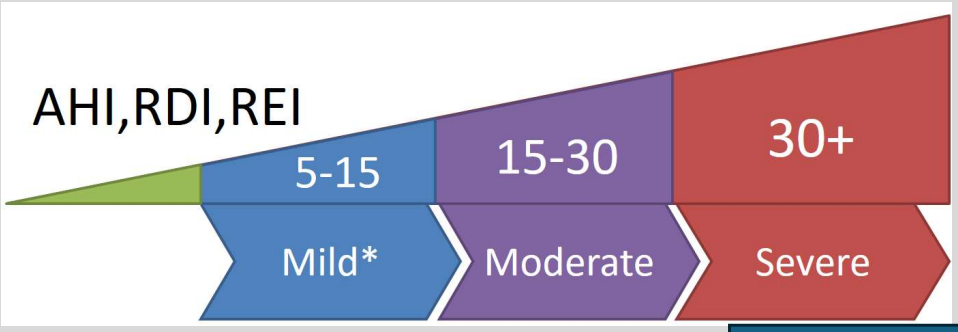
Benjafield et al. Lancet Respir Med. 2019

Current and future estimates in the United States

Boers et al. Lancet Respir Med. 2025

	2025	2050
AHI ≥ 5	60.7 million **35.6%**	76.6 million **46.2%**
AHI ≥15	41.0 million **23.9%**	52.9 million **32.0%**
AHI ≥ 30	20.6 million **12.1%**	28.1 million **17.0%**

Sleep study results



*AHI ≥ 5-15 with symptoms

Patient reported or observed:

- Sleepiness or fatigue
- Insomnia
- Nocturia
- Morning headaches
- Impaired concentration, memory, driving, social function, or work-productivity

Or observed:

- Waking up breath holding, gasping, or choking
- Habitual snoring or breathing interruptions during sleep
- Disruption of bedpartner's sleep

ICSD-3 Text Revision 2023

Comorbidities without symptoms **removed** from essential features:

HTN, ischemic heart disease, diabetes, or stroke

What is an event?

- Apnea
  - Airflow cessation
- Hypopnea (Rule 1B, or 4% criteria)
  - Reduced airflow
  - Associated 4% oxygen desaturation
- Hypopnea (Rule 1A, or 3% criteria)
  - Reduced airflow
  - Associated 3% oxygen desaturation
    or
  - Associated with an arousal caused by airflow

Each last at least 10 seconds

AHI (Apnea Hypopnea Index)

$$AHI = \frac{Apneas + Hypopneas}{Total\ sleep\ time}$$

RDI (Respiratory Disturbance Index)

$$RDI = \frac{Apneas + Hypopneas + RERAs}{Total\ sleep\ time}$$

REI (Respiratory Event Index)

$$REI = \frac{Apneas + Hypopneas}{Total\ Recording\ Time}$$

The tale of 2 patients:

Patient 1:

Presents with snoring, witnessed apneas, and excessive daytime sleepiness

Sleep study AHI=30

Patient 2:

Presents with snoring, witnessed apneas, and excessive daytime sleepiness

Sleep study AHI=30

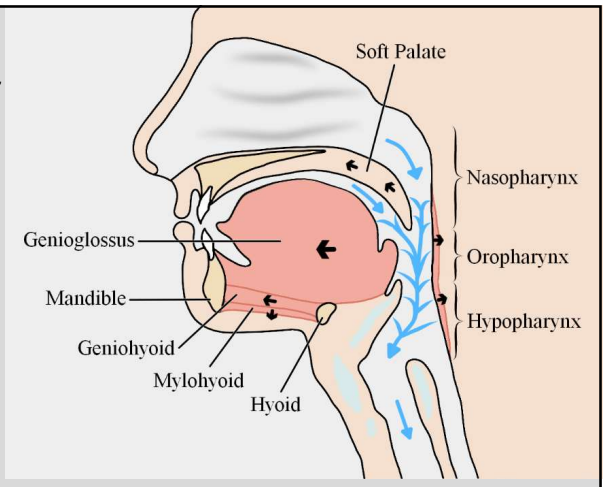
The PALM Framework for OSA Pathogenesis

Endotypes

J Carberry, J Amatoury, D Eckert. Chest 2018

1. Passive P_{crit} (Anatomy)
2. Arousal Threshold (Sleep Stability)
3. Loop Gain (Ventilatory Stability)
4. Muscle Responsiveness (Compensation)

PALM: Anatomy, Passive P_{crit}



Underlying risk for all endotypes.

How it causes OSA: Collapsing forces and structural support are insufficient

- Influenced by genetics, weight, fluid shifts and tissue compliance
- A collapsible upper airway is bad
- P_{crit} – Airway closes at this pressure
  - P_{crit} used in research, not clinically
- Smaller UA size, larger lateral pharyngeal walls, larger tongue, larger soft palette

What do we look for?

- BMI, neck circumference, crowded oropharynx, nasal/septal deviation

Mallampati Scoring

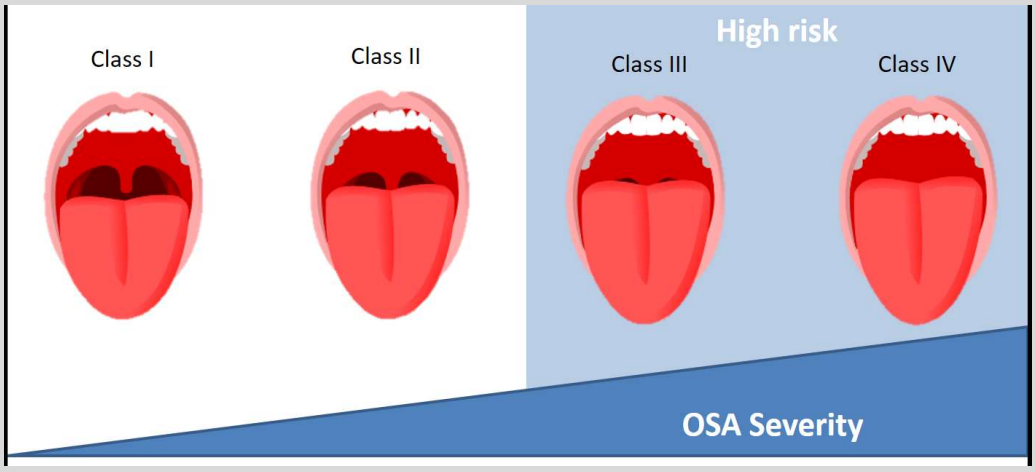


Image adapted from https://commons.wikimedia.org/wiki/File:Mallampati.svg - CC BY-SA 3.0

Miller, J. N., & Berger, A. M. (2016). Screening and assessment for obstructive sleep apnea in primary care. *Sleep medicine reviews*, *29*, 41-51.

So… what causes the initial collapse?

- Anatomy = ☑ Airway is collapsible
- Once asleep = Muscle tone decreases from baseline

Non-anatomical factors

1. Poor muscle responsiveness
2. Low arousal threshold
3. Unstable breathing (High loop gain)

Why is there stable breathing during parts of the night?

Answer: There are varying non-anatomic and compensating factors.

PALM: The Low Arousal Threshold

Arousal threshold = level of effort required to wake the brain.

How it causes OSA: A low threshold leads to early arousals, preventing dilator muscle recruitment.

Association: COMISA (COMorbid Insomnia and Sleep Apnea)

PALM: High Loop Gain (breathing instability)

Loop gain describes the ratio of $\frac{\text{Response}}{\text{Disturbance}}$

How it causes OSA: A high loop gain leads to periodic breathing.

What can you look for?

May be reported on sleep studies, under interpretation.
Has a recognizable desaturation pattern on the hypnogram.

Central sleep apnea

Absence of air-flow and respiratory effort

Examples:

- Cheyne-Stokes respiration in heart failure.

- Opiates causing ataxic (biot) breathing patterns

PALM: Poor Muscle compensation

The upper airway muscles, such as the Genioglossus, respond reflexively to negative pressure.

- Genioglossus EMG (main airway dilator) **decreases** during sleep[1]
- Wake pharyngeal muscle dilator activity is **higher** in OSA patients[2]
- OSA patients reduce muscle tone on sleep **more** than controls

How it causes OSA: Failure to respond to negative pressure or CO2

[1]Remmers et al. 1978, [2]Mezzanotte, 1992

The future?

POP - Polysomnography observed physiologic risk factors
PUP - endo-Phenotyping Using Polysomnography

Example:

PUP/PUPpy Algorithm, a breath-by-breath analysis of flow and effort.

Finnsson et al. Frontiers in Sleep. 2023.

OSA **Phenotypes** – symptom based

Phenotype	Features	Identification Metrics
Excessively Sleepy (ES)	Classical presentation of **excessive sleepiness** and **upper airway symptoms**	Epworth Sleepiness Scale (ESS) score > 10; high arousal index on PSG.
Disturbed Sleep (DS)	Potentially linked to a **low arousal threshold.**	Symptoms of insomnia (COMISA), frequent awakenings.
Minimally Symptomatic (MS)	May involve a **high arousal threshold** or lower chemosensitivity, allowing the patient to "tolerate" events without waking.	Lack of subjective sleepiness; often identified during screening for hypertension or atrial fibrillation.

Keenan et al. Sleep. 2018.

Risk Factors for Sleep-Disordered Breathing

Physical exam findings → **Cardio** → **Neuro** → **Endocrine** → **Obesity**

Anatomical Indicator	High-Risk Threshold or Finding
BMI	≥ 30
Neck circumference	>16” (Women), >17” (Men)
Mallampati Score	III or IV
Friedman Tongue position	III or IV
Jaw	Retrognathia or Micrognathia
Eyes	Floppy eyelid syndrome

Risk Factors for Sleep-Disordered Breathing

Physical exam findings | **Cardio** | Neuro | Endocrine | Obesity

Condition	Estimated prevalence
Atrial Fibrillation	>60% 50-90% are undetected [1]
Hypertension Resistant Hypertension	50% Up to 71% [2]
Heart Failure	71% 48% OSA, 23% CSA [3]
Pulmonary hypertension	American Heart Association consensus = screen all for OSA [4]

[1] Sousa et al. J Clin Med. 2025
[2] Tao et al. Front. Endocrinol. 2024
[3] Wang et al. Clin Cardiol. 2022
[4] McLaughlin et al. JACC. 2009

Risk Factors for Sleep-Disordered Breathing

Physical exam findings | Cardio | **Neuro** | Endocrine | Obesity

Condition	Estimated prevalence
TIA or Stroke	71% - 72% (AHI > 5) [1]
Hemorrhagic Stroke	82.7% (AHI > 5) [1]
US Testing Rate	~6% of stroke patients are screened [3]
Neuromuscular disease in children	>42% have sleep disordered breathing [4]

[1] Lio et al. J Stroke Cerebrovasc Dis. 2021
[2] Hoque, R. JCSM. 2016
[3] Brown et al. Sleep Med. 2019
[4] Chidambaram et al. Children (Basel). 2023

Risk Factors for Sleep-Disordered Breathing

Physical exam findings → Cardio → Neuro → **Endocrine** → Obesity

Condition	Estimated prevalence
Women with PCOS	37% [1]
Type 2 Diabetes	55-82% [2]
Acromegaly	44-87.5% [3]

[1] Jarfar et al. Front in Endo. 2025
[2] Huang and Chen, J Diabetes Investig. 2016 [3] Wolters et al. JCEM. 2019

Risk Factors for Sleep-Disordered Breathing

Physical exam findings → Cardio → Neuro → Endocrine → **Obesity**

Increased weight = increased OSA

10% weight ↑ ≈ ↑ AHI about 32%

10% weight ↓ ≈ ↓ AHI about 26%

Peppard, Paul E., et al. Jama. 2000

Pregnancy and maternal risk

Condition	Estimated prevalence
1st Trimester Prevalence	10.5% [1]
3rd Trimester Prevalence	26.7% [1]
Hypertensive disorders of pregnancy/ Preeclampsia	CPAP recommended [2]

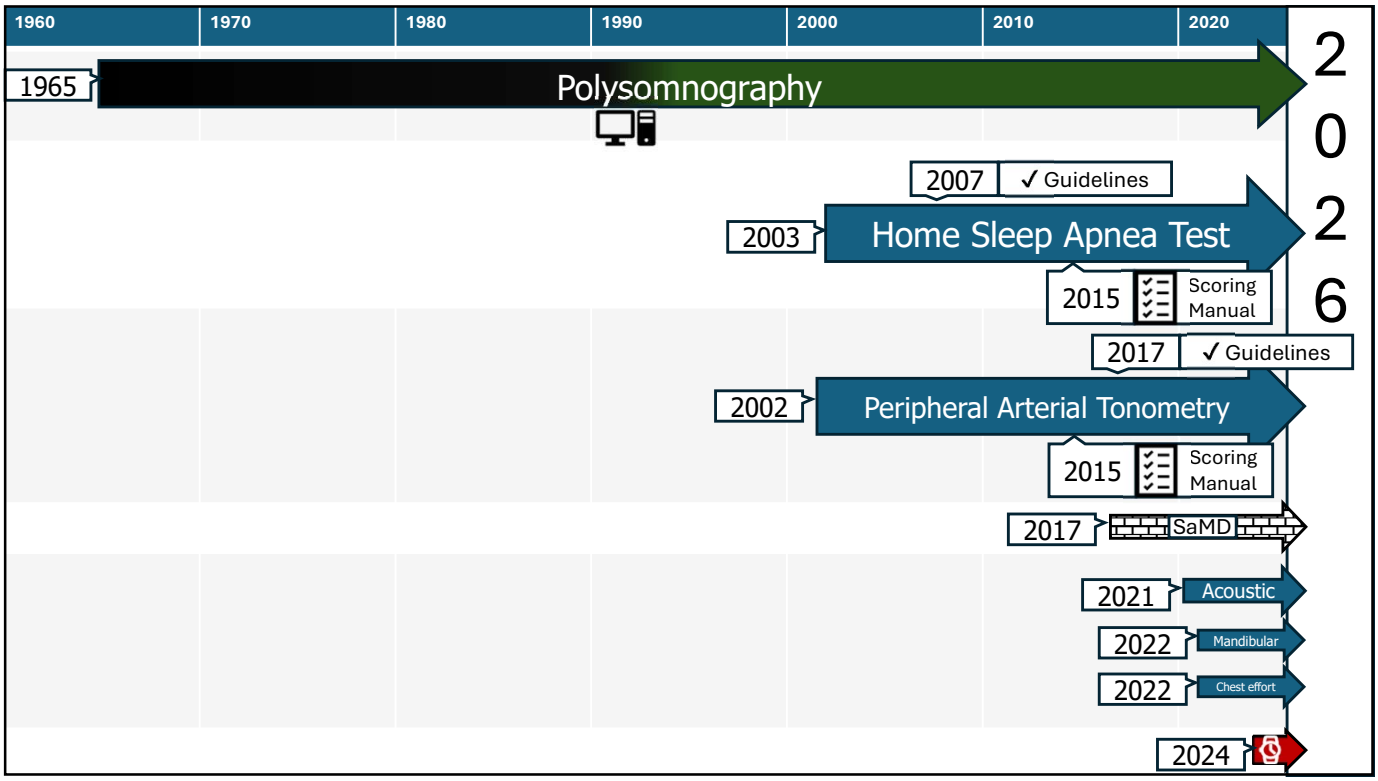
[1] Pien et al. Thorax. 2014

[2] Tang et al. Reprod Biol Endorcinol. 2025

Newer screening tools

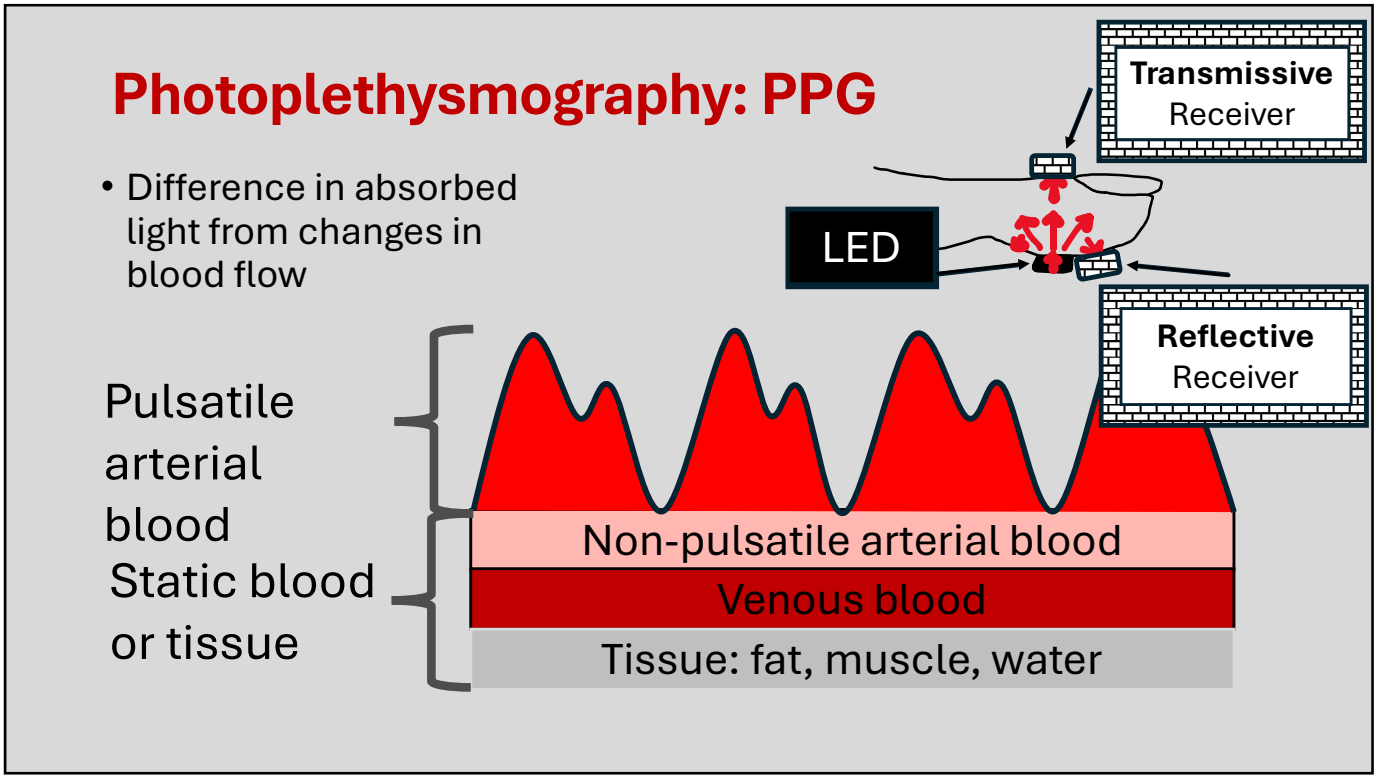
Screening Tool	Sensitivity (AHI ≥ 15)	Specificity (AHI ≥ 15)	LR+	LR-
STOP-Bang (Population estimate)	86%	44%	1.54	0.32
STOP-Bang (Sleep Clinic)	95%	27%	1.30	0.20
Samsung SAF	83%	88%	**6.72**	0.20
Apple SANF	66%	99%	**18.6**	0.36

STOP-Bang population estimate from Holfinger et al. CHEST. 2022



Photoplethysmography: PPG

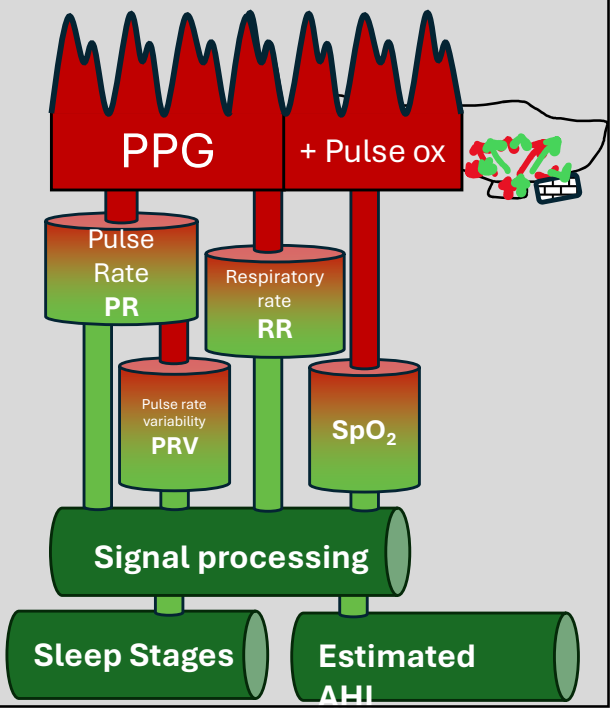
- Difference in absorbed light from changes in blood flow



PPG algorithm pipeline:

PPG changes:

- Respiratory effort
  - ↓ pulse wave amplitude during inspiration, ↑ during expiration
- Autonomic arousals
  - ↓ pulse wave amplitude drop
  - ↑ heart rate
- Apnea or hypopnea
  - ↓ pulse wave amplitude drop
  - ↑ heart rate
  - ↓ SpO_2



What is the intended use of each device?

Polysomnography

- ✓ Gold-standard OSA
- ✓ Gold-standard CSA
- ✓ Other conditions
  - Limb movements
  - REM behavior disorder
  - Other parasomnias
  - Part of narcolepsy/ hypersomnia evaluation
- ✓ PAP titration studies
- +/- CO2 monitoring

Home sleep apnea testing

- ✓ High risk for OSA
- +/- CSA

PAT, SaMD, acoustic, mandibular, chest effort devices

- ✓ High risk for OSA
- +/- CSA

Consumer devices

- +/- Some can alert user to very high risk for OSA

Traditional HSAT (Home Sleep Apnea Test)

- Airflow
- Respiratory effort
- Blood oxygenation

In-laboratory polysomnography

- Airflow
- Respiratory effort
- Blood oxygenation
- EEG → Sleep staging
- EOG → REM sleep
- ECG → Single lead
- EMG → Detect leg movements

+/- CO2 monitoring

Directly measured signals	**PPG +/- PAT** (Peripheral Arterial Tonometry)
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Pulse wave amplitude • Blood oxygenation
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	• PPG • Accelerometer (Most)

Examples:
WatchPAT, NightOwl, Belun Ring, SleepImage SaMD, TipTraQ, EnsoSleep PPG

Directly measured signals	PAT/PPG **+ ECG** (SANSA, ANNE Sleep)
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Pulse wave amplitude • Blood oxygenation
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	• PPG • Accelerometer • 1-lead ECG

Directly measured signals	PAT + **EEG, EOG** (Somfit)
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Pulse wave amplitude
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	• Blood oxygenation • Frontal EEG, EOG • Accelerometry

Directly measured signals	Acoustic
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Acoustic airflow
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	• Suprasternal pressure

Directly measured signals	**PPG** + Acoustic (AcuPEbble, BresoDX1)
• Airflow	• Acoustic airflow
⌂ • Respiratory effort	• Suprasternal pressure
• Blood oxygenation	• Blood oxygen
• EEG → Sleep staging	• PPG
• EOG → REM sleep	• Accelerometer
• ECG → Single lead	
• EMG → Detect leg movements	
+/- CO2 monitoring	

Directly measured signals	Mandibular Movements
• Airflow	
⌂ • Respiratory effort	• Respiratory effort
• Blood oxygenation	
• EEG → Sleep staging	• Marker for arousals
• EOG → REM sleep	
• ECG → Single lead	
• EMG → Detect leg movements	
+/- CO2 monitoring	

Directly measured signals	**PPG** + Mandibular Movements (Sunrise)
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Respiratory effort PPG: Blood oxygen
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	• PPG and MM (arousals) • Accelerometer, gyroscope

Directly measured signals	Chest effort
• Airflow ⌂ • Respiratory effort • Blood oxygenation	• Airflow • Respiratory effort
• EEG → Sleep staging • EOG → REM sleep • ECG → Single lead • EMG → Detect leg movements **+/-** CO2 monitoring	

Directly measured signals	**PPG** + Chest effort (Wesper Lab)
• Airflow	• Airflow
⌂ • Respiratory effort	• Respiratory effort
• Blood oxygenation	• Blood oxygen
• EEG → Sleep staging	• PPG
• EOG → REM sleep	• Accelerometer
• ECG → Single lead	
• EMG → Detect leg movements	
+/- CO2 monitoring	

Home devices to assess risk for sleep apnea

- Prescription options
  - Under-mattress mat: Withings Sleep Rx
  - Smartphone: Drowzle
- Available to consumers
  - Smartwatch apps:
    - Samsung Galaxy Watch: Sleep Apnea Feature
    - Apple Watch: Sleep Apnea Notification Feature

Considerations when using derived signals

- Performance varies by device, mechanism, signal processing
  - Some use “optimal device-AHI cutoffs”
  - Some report only the 3% or 4% criteria for hypopneas
  - Varying ability to detect central sleep apnea
  - Consider if the training and validation datasets match test population
- PPG:
  - Reliable in atrial fibrillation? Chronotropic medications?
  - PPG affected by skin tone
  - Incomplete reporting… positional sleep apnea?

Chiang A. et al. JCSM. 2024.

Take home points for OSA assessment

- Consumer or risk assessment devices
  - Detect risk, **NOT** a diagnosis
- Choice of diagnostic sleep testing should be based on the intended purpose
  - Newer, FDA-approved HSAT devices are designed for simple, high-risk obstructive sleep apnea evaluation
  - Awareness is needed regarding individual device limitations

Treatment Updates for Obstructive Sleep Apnea

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Treatment Options

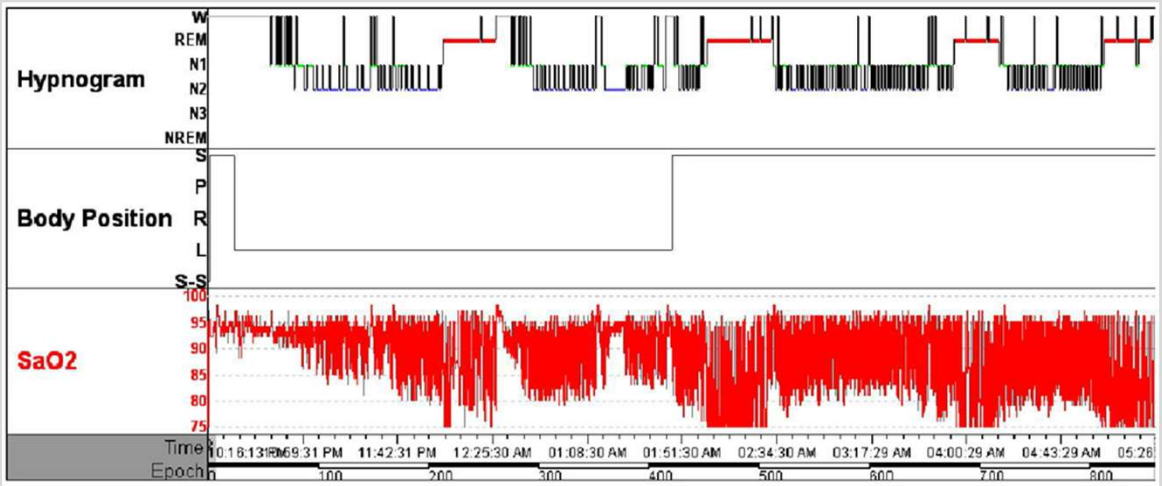
- Positive Airway Pressure
- Dental Devices
- Hypoglossal Nerve Stimulation
- Medications

Positive Airway Pressure

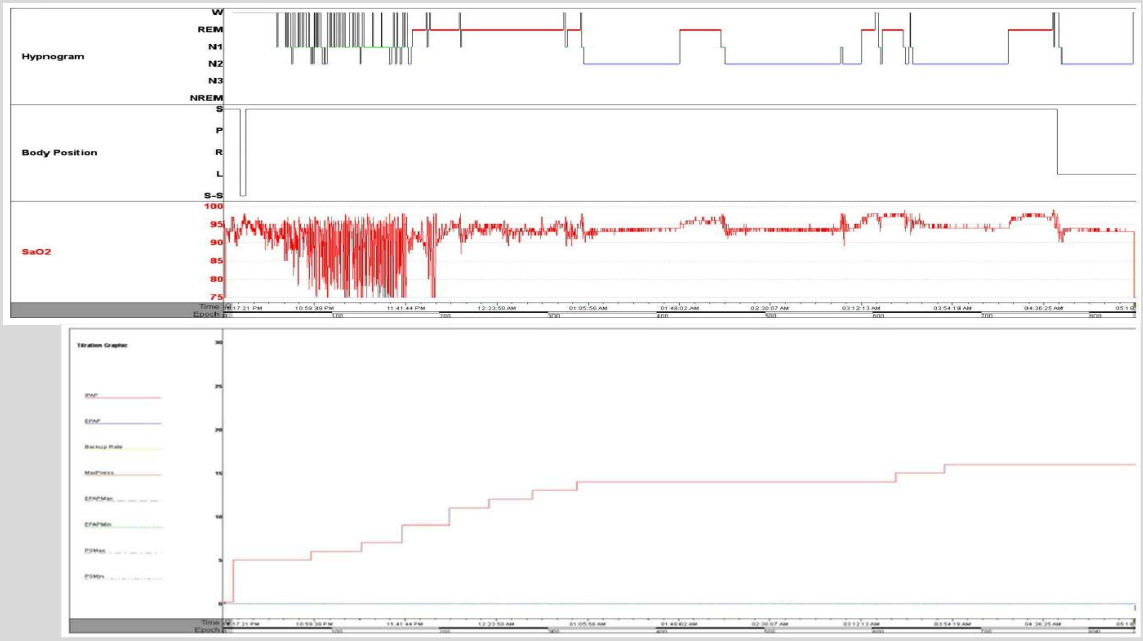
- Continuous
- Bilevel
- Kairos
  - End-expiration
    - Equal efficacy
    - Improved comfort
    - Less leak

https://swcofusa.com/sleep-apnea-osa-treatment/

Positive Airway Pressure



Positive Airway Pressure



Positive Airway Pressure

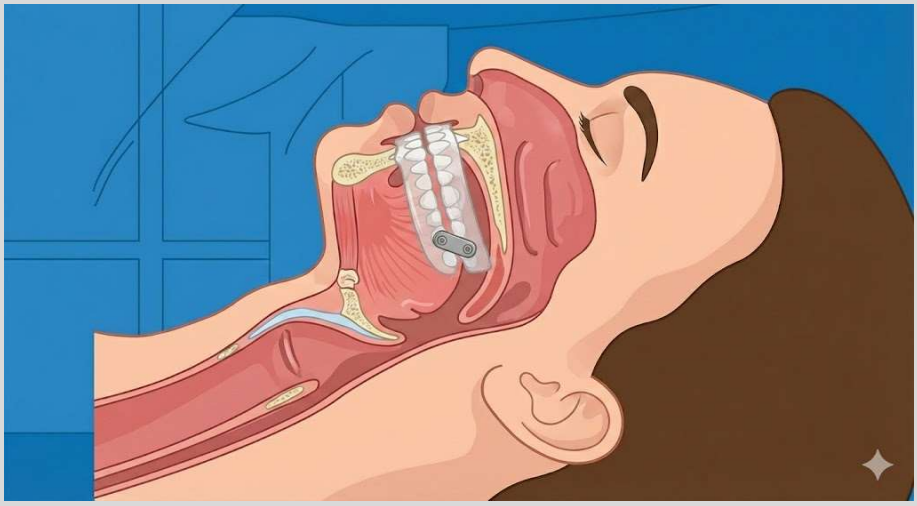
- Adherence
- Recall

Oral Appliances

https://www.doneskey.com/the-silent-partner/

https://chestnutdental.com/wp-content/uploads/2024/07/dental-appliance-treatment-for-sleep-apnea-1024x576.jpg

Oral Appliances



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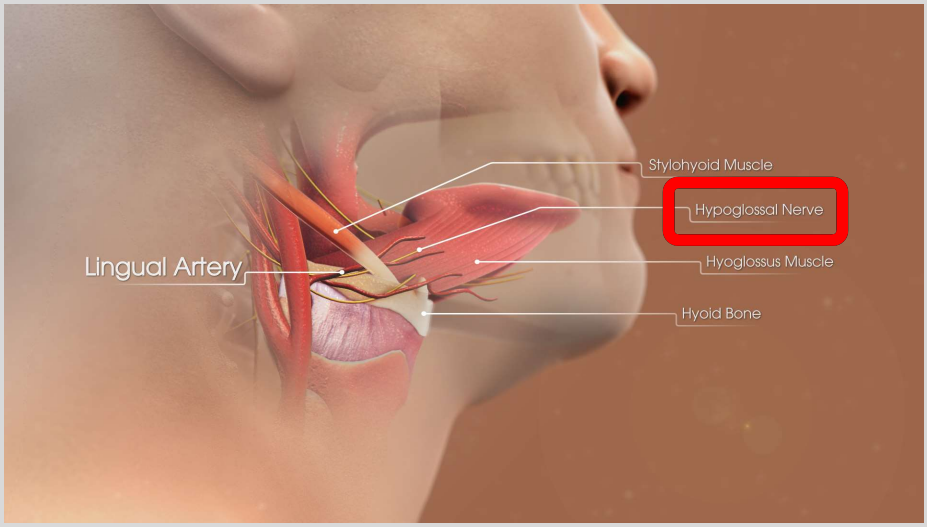
Hypoglossal Stimulation



Hypoglossal Stimulation

> Am Rev Respir Dis. 1989 Nov;140(5):1279-84. doi: 10.1164/ajrccm/140.5.1279.

Effects of electrical stimulation of the genioglossus on upper airway resistance in anesthetized dogs

H Miki [1], W Hida, C Shindoh, Y Kikuchi, T Chonan, O Taguchi, H Inoue, T Takishima

Affiliations + expand
PMID: 2817589 DOI: 10.1164/ajrccm/14

> Am Rev Respir Dis. 1993 May;147(5):1144-50. doi: 10.1164/ajrccm/147.5.1144.

Effect of electrical stimulation of the hypoglossal nerve on airflow mechanics in the isolated upper airway

A R Schwartz [1], D C Thut, B Russ, M Seelagy, X Yuan, R G Brower, S Permutt, R A Wise, P L Smith

Affiliations + expand
PMID: 8484623 DOI: 10.1164/ajrccm/147.5.1144

> Am Rev Respir Dis. 1992 Oct;146(4):1030-6. doi: 10.1164/ajrccm/146.4.1030.

The effects of transcutaneous electrical stimulation during wakefulness and sleep in patients with obstructive sleep apnea

L C Edmonds [1], B K Daniels, A W Stanson, P F Sheedy 3rd, J W Shepard Jr

Affiliations + expand
PMID: 1416392 DOI: 10.1164/ajrccm/146.4.1030

Hypoglossal Stimulation

Clinical Investigations: Sleep/Breathing: Articles

The Effect of Electrical Stimulation on Obstructive Sleep Apnea Syndrome

Christian Guilleminault MD [a], Nelson Powell MD [a], Bruce Bowman PhD [b], Riccardo Stoohs MD [b]

Show more

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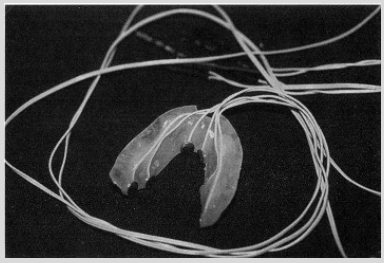

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Hypoglossal Stimulation

Arch Otolaryngol Head Neck Surg. 1997 Jan;123(1):57-61.
doi: 10.1001/archotol.1997.01900010067009.

Direct hypoglossal nerve stimulation in obstructive sleep apnea

D W Eisele [1], P L Smith, D S Alam, A R Schwartz

Affiliations + expand

PMID: 9006504 DOI: 10.1001/archotol.1997.01900

Clinical Trial

Arch Otolaryngol Head Neck Surg. 2001 Oct;127(10):1216-23.
doi: 10.1001/archotol.127.10.1216.

Therapeutic electrical stimulation of the hypoglossal nerve in obstructive sleep apnea

A R Schwartz [1], M L Bennett, P L Smith, W De Backer, J Hedner, A Boudewyns, P Van de Heyning, H Ejnell, W Hochban, L Knaack, T Podszus, T Penzel, J H Peter, G S Goding, D J Erickson, R Testerman, F Ottenhoff, D W Eisele

Affiliations + expand

PMID: 11587602 DOI: 10.1001/archotol.127.10.1216

Hypoglossal Stimulation

- Unilateral
- Bilateral

Unilateral Hypoglossal Stimulation

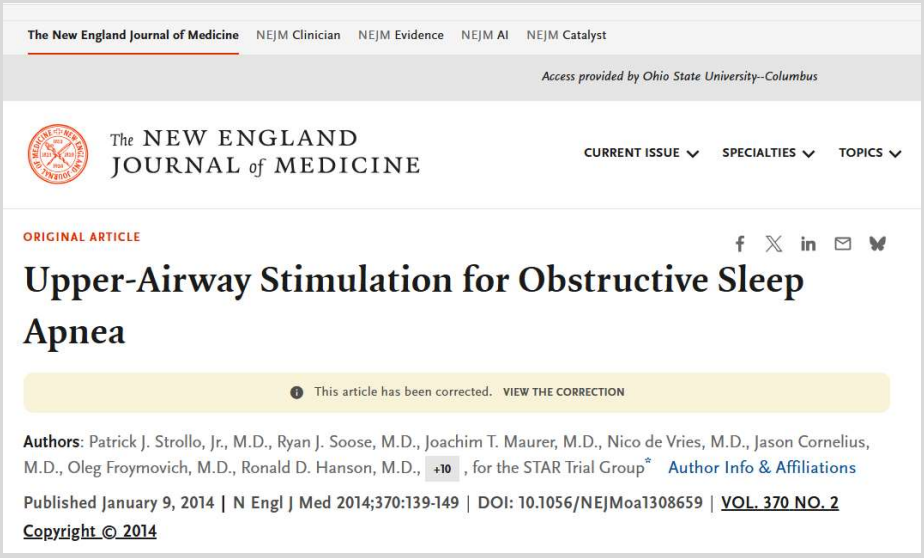
- Age >=18 yrs old
- Age 13-18, Down Syndrome

- AHI 15-100 (<25% central or mixed)
- AHI 10-50 (Down Syndrome)

- CPAP intolerance – Inability or unwillingness to use

- Body Mass Index ≤40 kg/m2
- Free of Complete Concentric Collapse (CCC) at the Palate

Hypoglossal Stimulation



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The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Upper-Airway Stimulation for Obstructive Sleep Apnea

This article has been corrected. VIEW THE CORRECTION

Authors: Patrick J. Strollo, Jr., M.D., Ryan J. Soose, M.D., Joachim T. Maurer, M.D., Nico de Vries, M.D., Jason Cornelius, M.D., Oleg Froymovich, M.D., Ronald D. Hanson, M.D., +10 , for the STAR Trial Group* Author Info & Affiliations

Published January 9, 2014 | N Engl J Med 2014;370:139-149 | DOI: 10.1056/NEJMoa1308659 | VOL. 370 NO. 2

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Hypoglossal Stimulation

- STAR (Stimulation Therapy for Apnea Reduction)
  - Inclusion criteria
    - AHI 20-50, BMI <32, CPAP intolerance
  - Exclusion criteria
    - Complete concentric collapse
- Median AHI reduction from 29.3 to 9.0 events per hour

Unilateral Hypoglossal Stimulation

Sleep Medicine

- Troubleshoot PAP device, alternative treatments
- Education about hypoglossal stimulation, process
- Update Sleep Study >2 years
  - Severity criteria, central sleep apnea
- Body Mass Index <=40 kg/m2

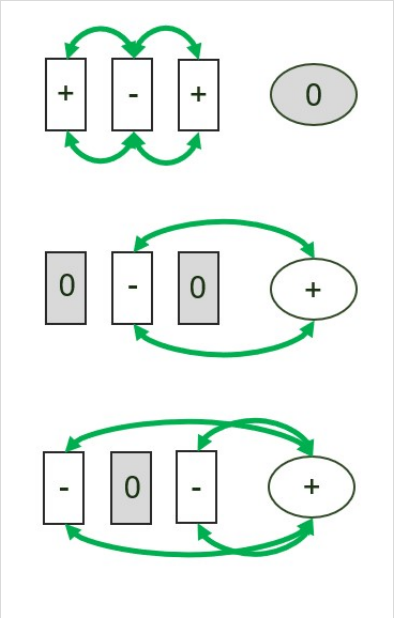
ENT

- Assessment
- Drug Induced Sleep Endoscopy

Implantation

- 2 incisions

- Implantable Pulse Generator
- Stimulating Lead



Activation

- Healing
  - Neurapraxia

https://commons.wikimedia.org/wiki/File:Unilateral_hypoglossal_nerve_injury.jpeg

Activation

- Settings
- Waveform Testing
- Education

Sleep Study

- Home Sleep Apnea Test
- In-laboratory Polysomnogram

Sleep Study

Hypoglossal nerve stimulation titration table

TX		SLEEP STAGES					RESPIRATORY EVENTS							AROUSALS		SAO2
HNS V	TIME AT LEVEL	TST (mins)	REM (mins)	REM SUPINE	NREM (mins)	SLEEP EFFIC.	APNEAS OA	APNEAS CA	APNEAS MA	HYP. (A1)	AHI (1A)	HYP. (1B)	AHI (1B)	RAI	TOTAL Arousals	LOWEST DESAT
0.0	110.9	78.6	0.0	0.0	78.6	0	0	0	0	82	62.6	63	48.1	19.86	26	85.0
2.0	37.1	24.5	0.0	0.0	24.5	0	16	0	0	13	71	11	66.1	48.98	20	83.0
2.1	40.5	33.5	0.0	0.0	33.5	0	8	0	0	43	91.3	36	78.8	28.64	16	84.0
2.2	31.9	29.4	0.0	0.0	29.4	0	4	0	0	38	85.7	31	71.4	12.26	6	87.0
2.3	37.3	35.3	0.0	0.0	35.3	0	8	0	0	39	79.9	29	62.9	20.40	12	84.0
2.4	30.8	29.8	0.0	0.0	29.8	0	17	0	0	22	78.5	22	78.5	30.17	15	84.0
2.5	20.4	17.7	0.0	0.0	17.7	0	1	0	0	24	84.7	20	71.2	20.32	6	85.0
2.6	38.9	33.9	0.0	0.0	33.9	0	11	0	0	26	65.5	21	56.6	3.55	2	87.0
2.7	107.2	100.8	21.5	21.5	79.3	0	0	0	0	12	7.1	4	2.4	0.00	0	88.0

Follow up

- Continue to assess tolerance/comfort
- Tongue Movement
- Waveform
- Usage Download

Bilateral Hypoglossal Stimulation

- Battery-Free stimulator implant (paddle)
- Single incision
- External sleep wearable battery (activation chip)
- MRI compatibility at 1.5T and 3T
- Continuous stimulation

Bilateral Hypoglossal Stimulation

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SCIENTIFIC INVESTIGATIONS

Bilateral hypoglossal nerve stimulation for obstructive sleep apnea: a nonrandomized clinical trial

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- 63.5% patients with >50% AHI reduction to <20 events/hr
- Mean AHI reduction 18.3 events/hr

Bilateral Hypoglossal Stimulation

- Eligibility criteria

- Age >22
- AHI 15-65
- CPAP intolerance
- BMI <32

Bilateral Hypoglossal Stimulation

- Contraindications
  - Central or Mixed AHI ≥ 25%
  - Compromised neurological control of the upper airway
- Warnings
  - Age < 22 or > 75
  - BMI > 32
  - AHI outside of 15-65
  - Complete Concentric Collapse

Medication

- Tirzepatide – Dual Agonist
  - Glucose-Dependent Insulinotropic Polypeptide (GIP) Receptor
  - Glucagon-like Peptide-1 (GLP-1) Receptor

Medication

The New England Journal of Medicine NEJM Clinician NEJM Evidence NEJM AI NEJM Catalyst

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CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

This article has been corrected. VIEW THE CORRECTION

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Medication

- SURMOUNT-OSA
  - Reduced AHI by 20-24 events per hour compared to placebo = 58.7% reduction in baseline
  - With and without CPAP
  - 50% of patients – AHI <5 or 5-14 with normal Epworth Sleepiness Scale
- FDA indication December 20, 2024

Medication

- Contraindications
  - Personal or family history of medullary thyroid cancer
  - Multiple endocrine neoplasia syndrome type 2 (MEN2)
- Cautions
  - Gastrointestinal side effects
  - Pancreatitis
  - Gallbladder disease
  - Acute Kidney Injury
  - Hypoglycemia