

# Arousal Threshold in Sleep Apnea Patients with Excessive Daytime Sleepiness

Pahnwat Tonya Taweeseedt, MD,  
Shyamsunder Subramanian, MD, FCCP,  
Sean Hesselbacher, MD,  
Salim R Surani, MD, MPH, MSHM, FACP, FCCP, FAASM

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**Pahnwat Tonya Taweeseedt, MD**  
**Bay Area Corpus Christi medical Center, TX**

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**Shyam Subramanian, MD, FCCP**  
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**Eastern Virginia Medical School, VA**  
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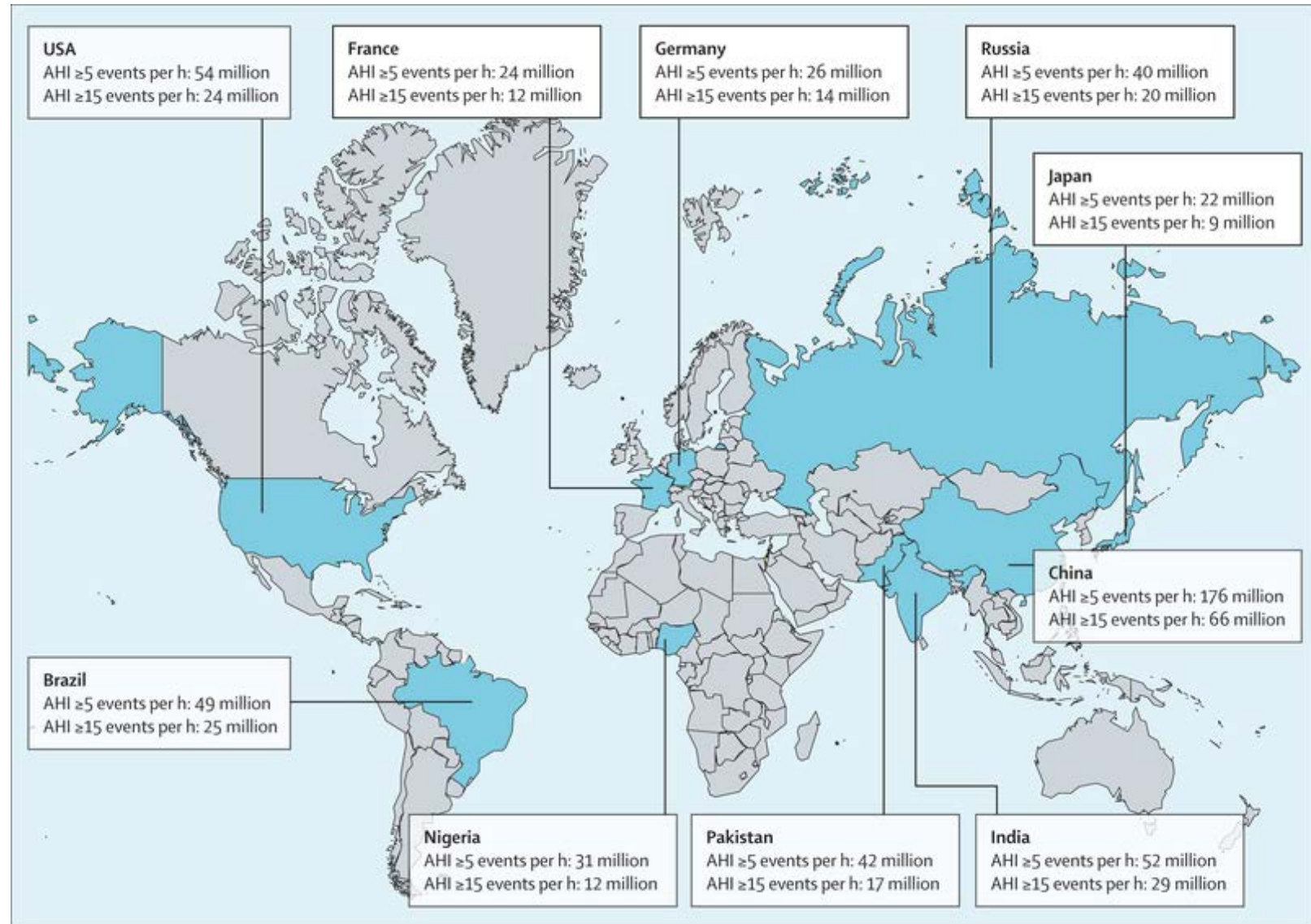
**Salim R Surani, MD, MPH, MSHM, FACP, FCCP, FAASM**  
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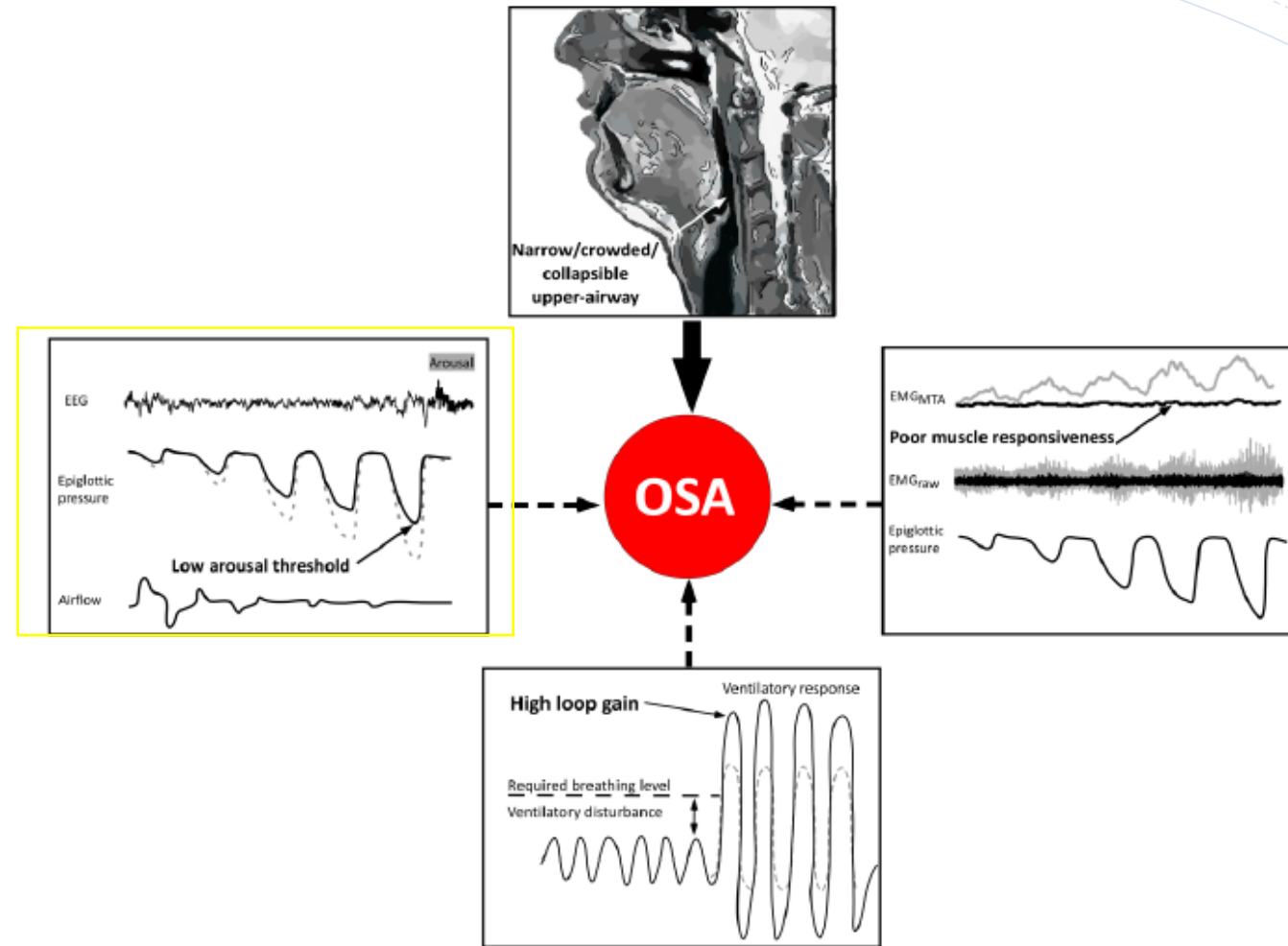
# Introduction

Nearly 1 billion people worldwide were estimated to have obstructive sleep apnea with prevalence >50% in some countries.



# Introduction

- Approximately 1/3 of patients with OSA was found to have a low respiratory arousal threshold (ArTH).
- A low ArTH is believed to contributed to OSA.

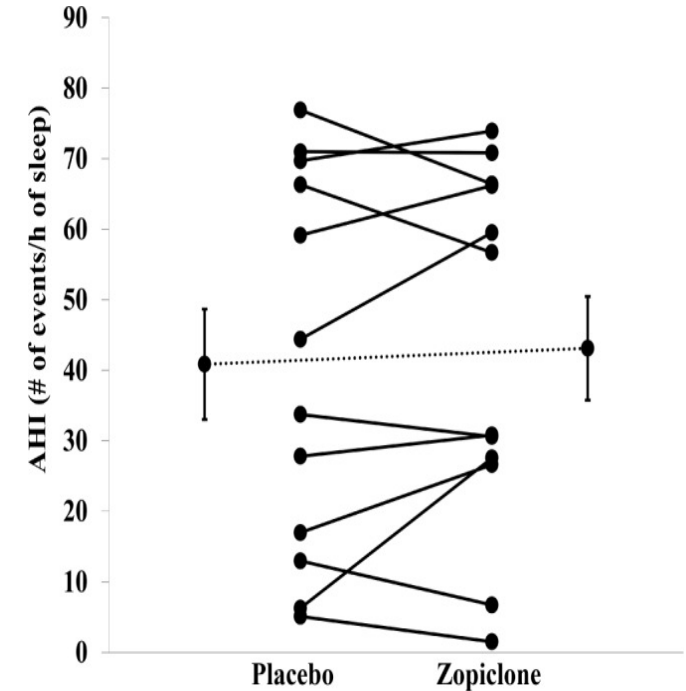
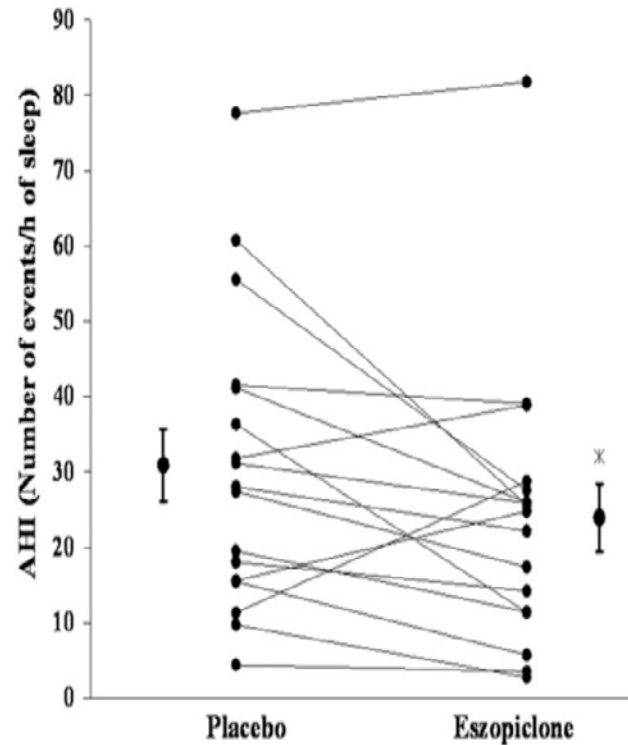
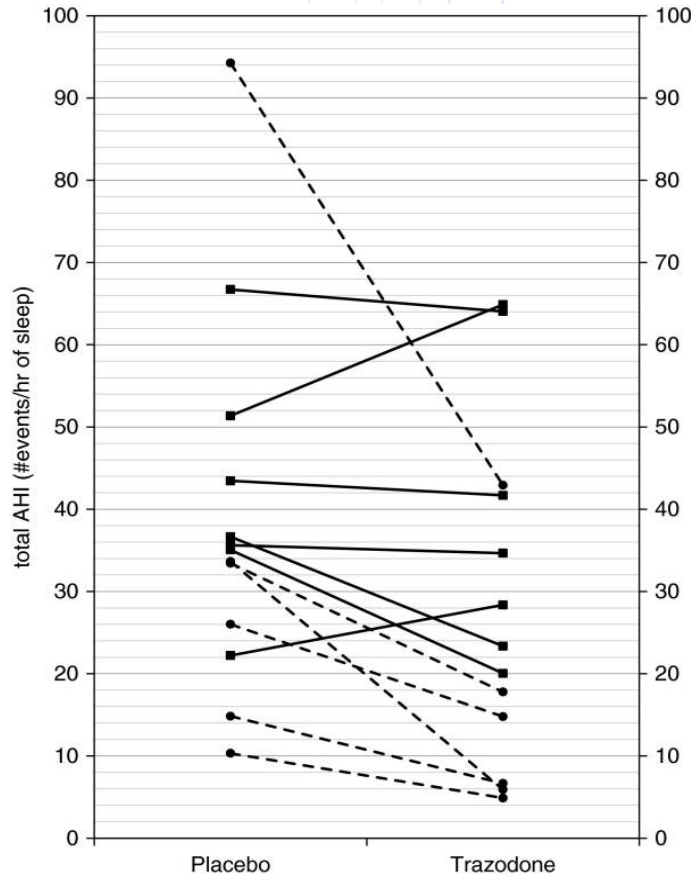


Schematic of the phenotypic traits that cause OSA. Some degree of “impaired” upper airway anatomy is a prerequisite for OSA (narrow/ crowded/collapsible upper airway) indicated by the thick solid arrow and MRI schematic. Impairment in the nonanatomical traits (ie, low arousal threshold, poor muscle responsiveness, high loop gain) also importantly contributes to the pathogenesis of OSA in the majority of patients (dashed arrows). Schematic representation of impairment in each of the nonanatomical traits (solid black lines with adjacent arrows) is given, along with a more desirable response for each nonanatomical trait (gray lines). EMG  $\frac{1}{4}$  genioglossus electromyographic activity; MTA  $\frac{1}{4}$  moving time average (100 ms) of the rectified EMG signal.



# Introduction

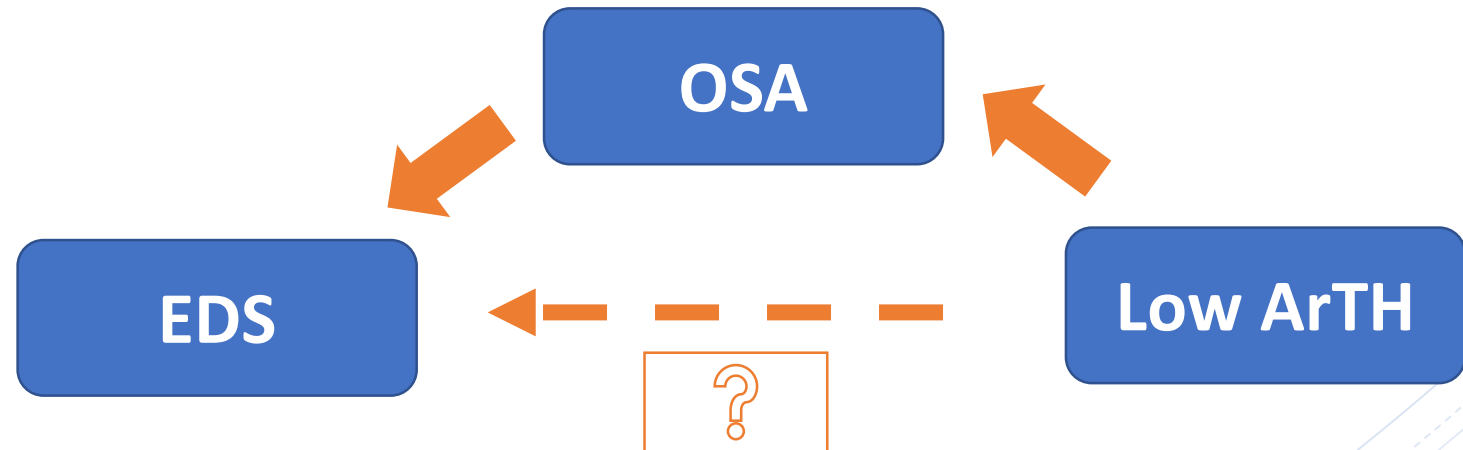
- Patients with OSA and low ArTH may benefit from hypnotic agents.
- Trazodone, eszopiclone and zolpidon increase the threshold of arousal and can reduce AHI by approximately 25-50%



Carter SG et. al. Sleep. 2016; 39(4): 757–766  
Eckert DJ et. al. Clin Sci (Lond). 2011; 120(12):505-14  
Smales ET et. al. Ann Am Thorac Soc. 2015; 12(5): 758–764

# Introduction

Although excessive daytime sleepiness (EDS) is commonly found in OSA patients, there are limited data regarding the association between a low ArTH phenotype and EDS.



# Objective

**To determine the association between arousal threshold and EDS in OSA patients**

# Materials and Methods

- **A retrospective chart review**
- **Adult patients who underwent in-lab full night PSG in Torr Sleep Center (Corpus Christi, TX) between 2/2007-4/2008**
- **Inclusion: Patients who meet the diagnosis of OSA**

# Materials and Methods

## Definitions

- OSA: AHI > 5
- EDS: ESS  $\geq$  10
- A low arousal threshold phenotype: Low ArTH score  $\geq$  2

**Low ArTH score = (AHI < 30 events/hr) + (nadir SpO<sub>2</sub> > 82.5%)  
+ ( Fhypopneas > 58.3%)**

(Edwards BA et. al. Am J Respir Crit Care Med. 2014 Dec 1;190(11):1293-300)

- **Baseline characteristics and polysomnography parameters were collected.**

**Odd ratio was calculated using logistic regression analysis**

# Results

**Patients with OSA  
(n = 470)**

**Non-EDS  
(n = 196)**

**EDS  
(n = 274)**

## Baseline characteristics

	ESS<10	ESS≥10	Total	P-value
Age, years	55 (18.5)	52 (18)	54 (19)	0.02
Male, n (%)	117 (60.3)	174 (63.5)	291 (62.2)	0.50
Race, n (%)				0.11
White	89 (45.4)	150 (54.7)	239 (50.9)	
Hispanic	103 (52.6)	117 (42.7)	220 (46.8)	
African American	4 (2.0)	7 (2.6)	11 (2.3)	
BMI, kg/m <sup>2</sup>	35.7 (8.9)	37.1 (8.6)	36.8 (8.7)	0.03
Neck circumference, inches	17 (2.5)	17 (2.5)	17 (2)	0.13
Mfriedman	3 (1)	3 (2)	3 (2)	0.16

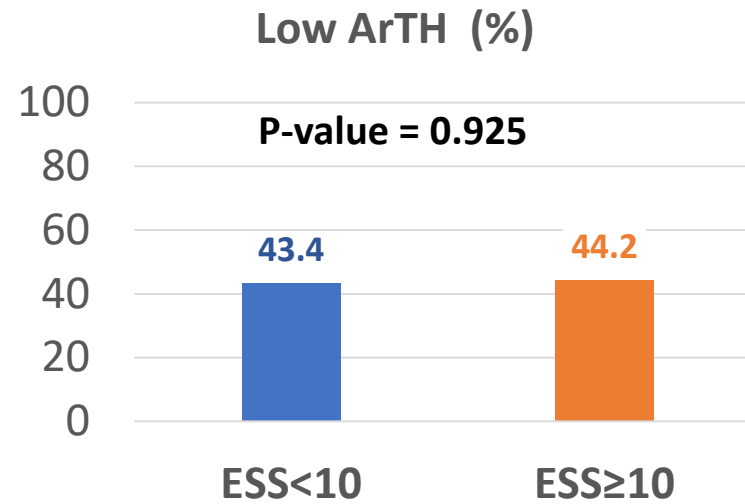
# Results

## Sleep indices

	ESS<10	ESS≥10	Total
TST, minutes*	349.5 (104.5)	376.3 (97.0)	366.0 (101.5)
SE*	78.7 (21)	83.6 (16.6)	81.5 (18.9)
REM, minutes*	54.5 (57.8)	57.3 (55.5)	55.5 (58.0)
REM %	14.9 (14.1)	15.8 (12.0)	15.2 (12.4)
REM AHI	37.0(45.3)	24.5 (41.5)	35.9 (42.8)
NREM AHI	22.2 (37.5)	26.2 (44.6)	24.0 (39.5)
Supine AHI	31.9 (49.9)	29.6 (43.4)	31 (45.9)
Arousal index	40.9 (32.7)	39.3 (36.2)	39.9 (35.1)
SaO2 Nadir*	79.6 (9.5)	77.0 (14.0)	78.0 (12.0)
AHI	26.7 (35.6)	27.6 (39.2)	27.2 (37.9)

\* P-value<0.05

# Results



	ESS < 10			ESS ≥ 10	
	Low ArTH	High ArTH		Low ArTH	High ArTH
Age*	52 (19)	57 (18)	Age	52 (18)	51 (18)
Male, n (%)	45 (53.6)	72 (65.5)	Male, n (%)	70 (57.9)	104 (68.0)
Neck circumference, inches *	16.5 (3.0)	17.3 (2.3)	Neck circumference, inches*	16.8 (2.5)	18 (2.25)
BMI, kg/m <sup>2</sup>	35.9 (9.4)	35.6 (7.5)	BMI, kg/m <sup>2</sup> *	35.2 (8.0)	37.7 (8.5)
Mfriedman	3 (1)	3 (1)	Mfriedman	3 (2)	3 (2)
Arousal Index*	28.3 (22.8)	52.3 (32.4)	Arousal Index*	29.3 (26)	52.2 (39.8)

\* P-value < 0.05



# Results

## Multivariate analysis

	OR	95%CI	p-value
<b>ESS <math>\geq 10</math></b>	<b>1.85</b>	<b>1.09-3.13</b>	<b>0.02</b>
Age, years	0.97	0.95-0.99	0.01
Female	1.55	0.79-3.05	0.20
BMI, kg/m <sup>2</sup>	1.02	0.98-1.06	0.32
Neck circumference, inches	0.95	0.79-1.14	0.56
TST, minutes	1.00	0.99-1.00	0.27
SE	0.99	0.95-1.02	0.44
Arousal index	0.95	0.94-0.97	<0.001
SaO <sub>2</sub> Nadir	1.24	1.18-1.30	<0.001
AHI	1.00	0.998-1.00	0.42

# Conclusion

- **Low ArTH phenotype of OSA is gaining importance as the pharmacological treatments to increase ArTH may benefit patients.**
- **Our data shows that in sleep apnea patients, EDS is associated with low ArTH phenotype.**
- **Our results support the role of using low ArTH score to define OSA phenotype particularly in patient with ESS  $\geq 10$**