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Residual Sleepiness after PAP Treatment of OSA

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Objectives



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- Understand mechanism of sleepiness in OSA
- How to proceed with workup of patient with residual sleepiness in patient with OSA treated with PAP therapy
- How to manage residual sleepiness in this group of patients

Conflicts of Interest



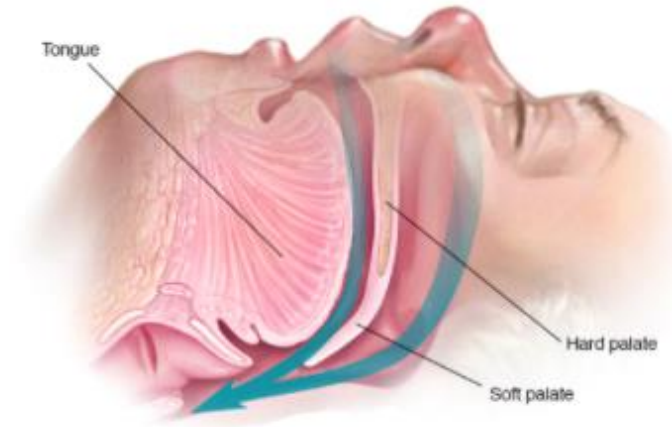
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- NONE related to this topic.

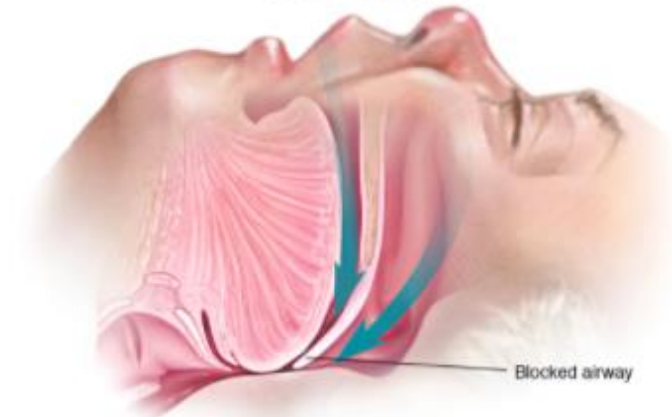
Obstructive Sleep Apnea



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Obstructive sleep apnea



Clinical Presentation of OSA



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- Snoring/ Witnessed Apneas
- Difficult to treat HTN/ A Fib
- Tiredness/ Sleepiness
- Pre/ Post operative – for any reason
- Employment related – DOT – due to neck circumference/ BMI

Current Diagnosis and Treatment of OSA



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- Clinical symptoms
 - Variable
- Diagnostic Study
 - Home Sleep Study
- Treatment
 - Auto Titrating PAP machine
 - CPAP
 - BPAP
 - Fixed Pressure PAP machine
 - CPAP
 - BPAP

Treatment of Obstructive Sleep Apnea



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- Positive Airway Pressure Therapy
 - CPAP
 - Fixed pressure
 - Auto Titrating
 - Bilevel
 - Fixed pressure
 - Auto Titrating
 - S/T – with backup rate
 - ASV
- Oral Appliance Therapy
- Upper Airway Surgery
- Maxillo-Mandibular Advancement
- Hypoglossal Nerve Stimulation

Inappropriate Sleepiness



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- Sleepiness when person should be awake
 - Inability to maintain wakefulness and alertness during major waking episode of day
 - Sleep occurring intentionally or at inappropriate times
- Risk for work related/ motor vehicle accidents
- Subjective – patient’s word
 - Falls asleep when not active
- Objective
 - Epworth Sleepiness Scale
 - Karolinska Sleepiness Scale
 - Multiple Sleep Latency Test – require PSG night before as well

Epworth Sleepiness Scale



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ESS is estimate of a person's 'average sleep propensity' across a wide range of activities in their daily lives

- No chance of dozing =0
- Slight chance of dozing =1
- Moderate chance of dozing =2
- High chance of dozing =3

Write down the number corresponding to your choice in the right hand column. Total your score below.

Situation	Chance of Dozing
Sitting and reading	•
Watching TV	•
Sitting inactive in a public place (e.g., a theater or a meeting)	•
As a passenger in a car for an hour without a break	•
Lying down to rest in the afternoon when circumstances permit	•
Sitting and talking to someone	•
Sitting quietly after a lunch without alcohol	•
In a car, while stopped for a few minutes in traffic	•

Total Score = _____

Karolinska Sleepiness Scale



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Karolinska Sleepiness Scale (KSS)

Extremely alert	1
Very alert	2
Alert	3
Rather alert	4
Neither alert nor sleepy	5
Some signs of sleepiness	6
Sleepy, but no effort to keep awake	7
Sleepy, but some effort to keep awake	8
Very sleepy, great effort to keep awake, fighting sleep	9
Extremely sleepy, can't keep awake	10

Functional Outcomes of Sleep Questionnaire (FOSQ)



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To assess impact of sleepiness

30 questions – assess in completing several tasks related to

- General Productivity
- Social Outcome
- Activity Level
- Vigilance
- Intimate Relationships and Sexual Activity

Sleepiness in Patients with OSA



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Many patients may not complain of sleepiness but may complain of

- Fatigue
- Lack of energy
- Lack of ambition
- Excessive consumption of caffeinated beverages

- May be related to patient's personality, chronic progression of symptoms
- May feel much better after starting to use PAP although never complained of sleepiness

Mechanism of Sleepiness in OSA



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- Not fully understood - Multifactorial
- Insufficient sleep duration – may not be related to OSA
- Intermittent nocturnal hypoxia – if persist over the years, may cause daytime cognitive dysfunction and damage wake-promoting neural networks.
- Sleep fragmentation and arousals
- Autonomic dysregulation
- Abnormal sleep architecture
- Chronic inflammation and cytokine production

EVERYONE WITH OSA IS NOT SLEEPY (SUBJECTIVELY AND BY EPWORTH SLEEPINESS SCALE) WHY?

Sleepiness is more common in people with symptoms of anxiety or depression.

Severity of OSA DOES NOT correlate with sleepiness.

Animal Experiments



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- Sleep 2004 Veasey et al: adult mice subjected to long term intermittent hypoxia (modeling hypoxia-reoxygenation model of OSA – experienced increased sleep time and objective sleepiness for weeks after back in normal oxygen conditions
- Zhu et al 2007: group of mice exposed to chronic sleep deprivation (modeling OSA) noted reduction in wake active neurons in Locus Coeruleus by 50% and orexinergic neurons by 25%

Human Studies



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- Sleep 2012 O'Donoghue et al: studies MRI changes in patients with OSA; noticed that changes in frontal lobes were not reversed after 6 months of PAP therapy although changes in hippocampus improved – some changes in brain due to OSA may be irreversible or at least slowly reversible
- Chest 2010 Aloia: Diffusion tensor imaging showed improvements in 3 months and complete reversal in 12 months of white matter abnormalities

Sleepiness in OSA



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Other Reasons for Sleepiness in patients with OSA

- Narcolepsy
- Idiopathic Hypersomnolence
- Insufficient Sleep Syndrome
- RLS/PLMD
- Frequent arousals due to pain/ GERD
- Medications

PAP Effect on Sleepiness in Patients with OSA



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- Can be literally transformed overnight
 - Wake up alert and be productive all day
 - Multicenter study (Launois 2013) patients with moderate to severe OSA and abnormal ESS – 66% had normal ESS scores at end of 3 months when using PAP for >5 hours
- Still sleepy (had sleepiness to begin with)
 - Despite AHI <5, sleeping at least 7 hours a night
 - About 10% (6-14%) will have excessive sleepiness after being optimally treated with PAP and excluding confounding causes of sleepiness

**SUBSTANTIAL PROPORTION OF PATIENTS WILL NOT NORMALIZE
NEUROBEHAVIORAL RESPONSES DESPITE ADEQUATE PAP THERAPY**

Meta-Analysis: 2003, Arch Int Medicine



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11 studies: used ESS to assess sleepiness before and after PAP therapy

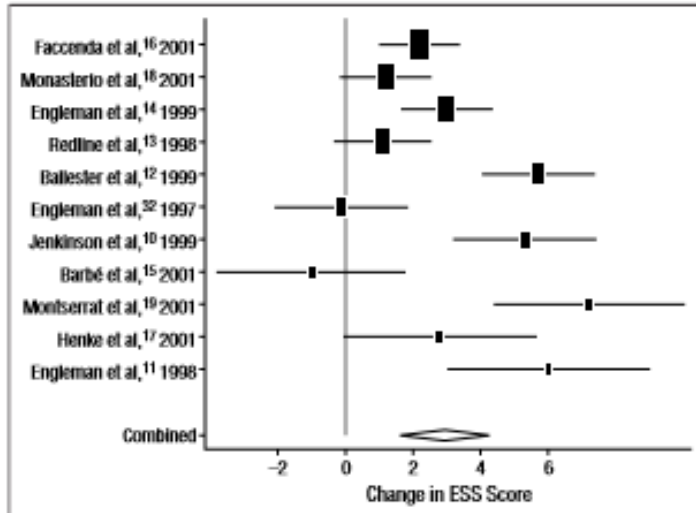


Figure 1. Effects of continuous positive airway pressure (CPAP) on change in Epworth Sleepiness Scale (ESS) score. Data are presented as means and 95% confidence intervals. A positive score indicates a more beneficial effect from CPAP than from placebo; i.e., the difference between change in ESS

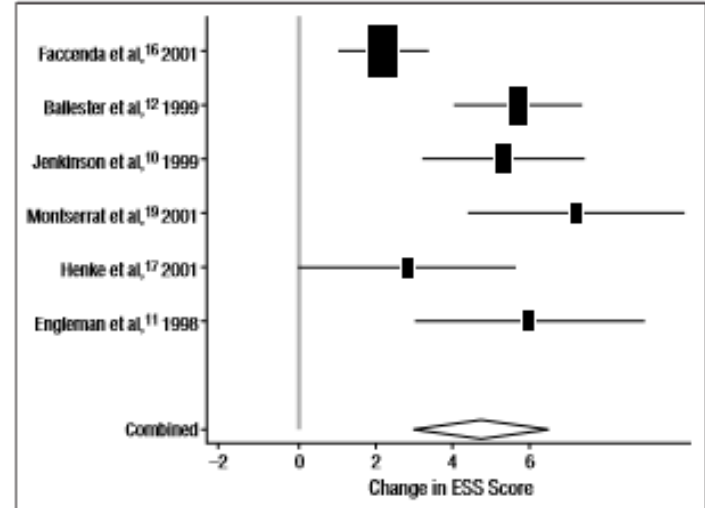


Figure 2. Effects of continuous positive airway pressure (CPAP) on change in Epworth Sleepiness Scale (ESS) score, limited to trials with a mean apnea-hypopnea index of 30 or greater and a mean ESS score of 11 or greater. Data are presented as means and 95% confidence intervals. The

Risk Factors for Residual Excessive Sleepiness (RES) in OSA



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Not well defined

- Severe EDS at diagnosis and low AHI at diagnosis
- Younger age - <55 years
- Lower mean duration of PAP use
- Depression
- Issues with PAP therapy – aerophagia / facial discomfort
- PSG features – reduced sleep latency; PLMD

Evaluation of RES



- Confirm diagnosis of OSA
 - Review PSG/HST
 - If initial diagnosis based on HST, consider PSG
- Consider other diagnoses that can cause excessive sleepiness
- confirm adherence to prescribed PAP therapy
 - Historical – patient, bed partner
 - PAP download data

PAP Download Data: Compliance Report



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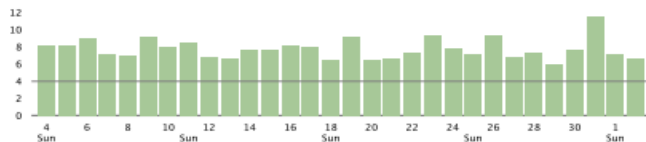
Compliance Report

Usage		10/04/2020 - 11/02/2020
Usage days	30/30 days (100%)	
>= 4 hours	30 days (100%)	
< 4 hours	0 days (0%)	
Usage hours	233 hours 30 minutes	
Average usage (total days)	7 hours 47 minutes	
Average usage (days used)	7 hours 47 minutes	
Median usage (days used)	7 hours 40 minutes	
Total used hours (value since last reset - 11/02/2020)	450 hours	

AirSense 10 AutoSet	
Serial number	23193278803
Mode	AutoSet
Min Pressure	6 cmH2O
Max Pressure	18 cmH2O
EPR	Fulltime
EPR level	1
Response	Standard

Therapy				
Pressure - cmH2O	Median: 6.3	95th percentile: 7.7	Maximum: 8.6	
Leaks - L/min	Median: 9.4	95th percentile: 19.6	Maximum: 25.3	
Events per hour	AI: 0.1	HI: 0.1	AHI: 0.2	
Apnea Index	Central: 0.0	Obstructive: 0.1	Unknown: 0.0	
RERA Index				0.0
Cheyne-Stokes respiration (average duration per night)				0 minutes (0%)

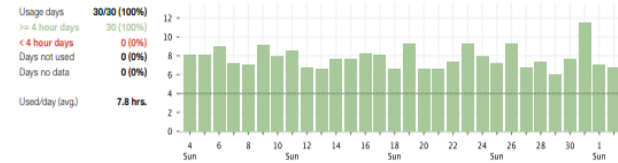
Usage - hours



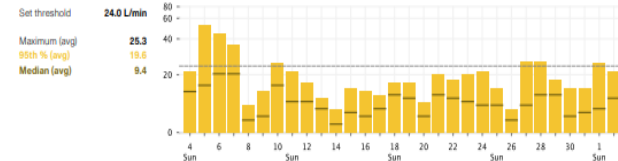
Therapy Report

AirSense 10 AutoSet SN: 23193278803

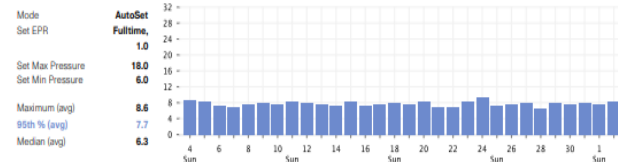
Usage (hours)



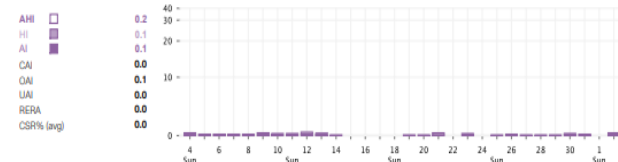
Leak (L/min)



Pressure (cmH2O)



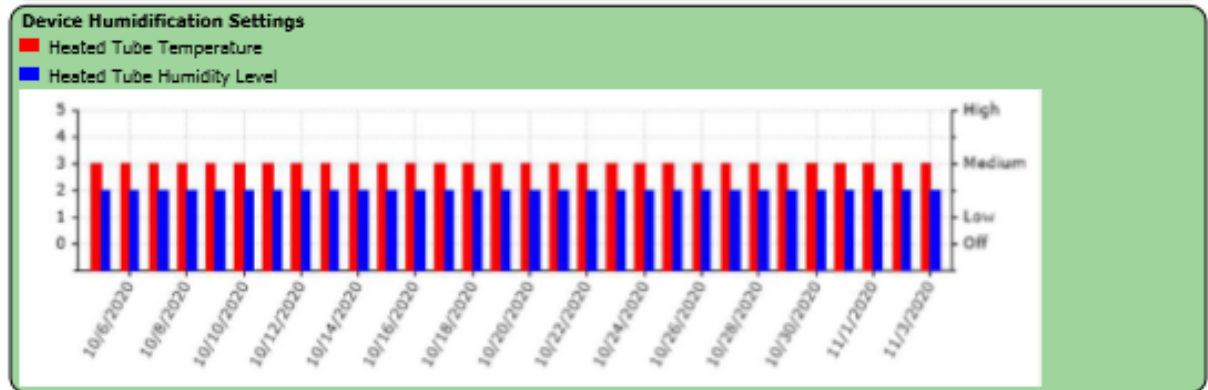
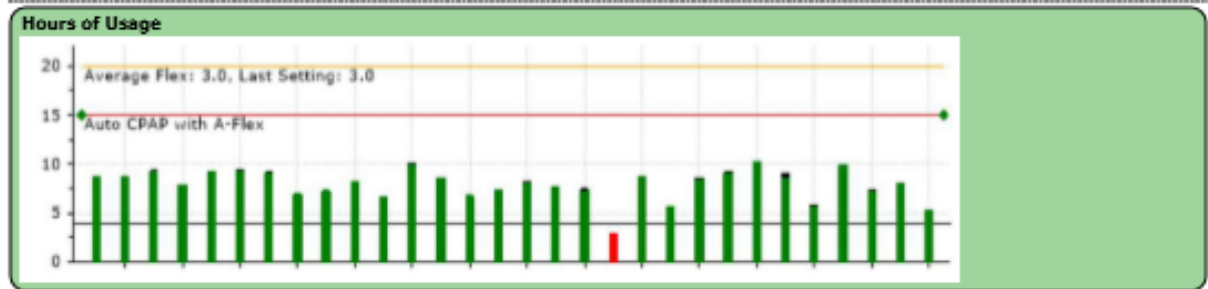
AHI (events/hour)



Device Mode AutoCPAP - A-Flex

Device Settings

Parameter	Value
Min Pressure	8 cmH2O
Max Pressure	15 cmH2O
A-Flex Setting	3
Auto Off	Off
Auto On	On
View Optional Screens	On
Ramp Type	Off
Mask Resistance	Off
Mask Resistance Lock	Off
Tubing Type	15 HT
Tubing Type Lock	Off
Opti-Start	Off
EZ-Start	Disabled
Tube Temperature	3
Humidifier	2
Humidification Mode on Heated Tube Disconnect	Adaptive



Information Obtained from PAP Download



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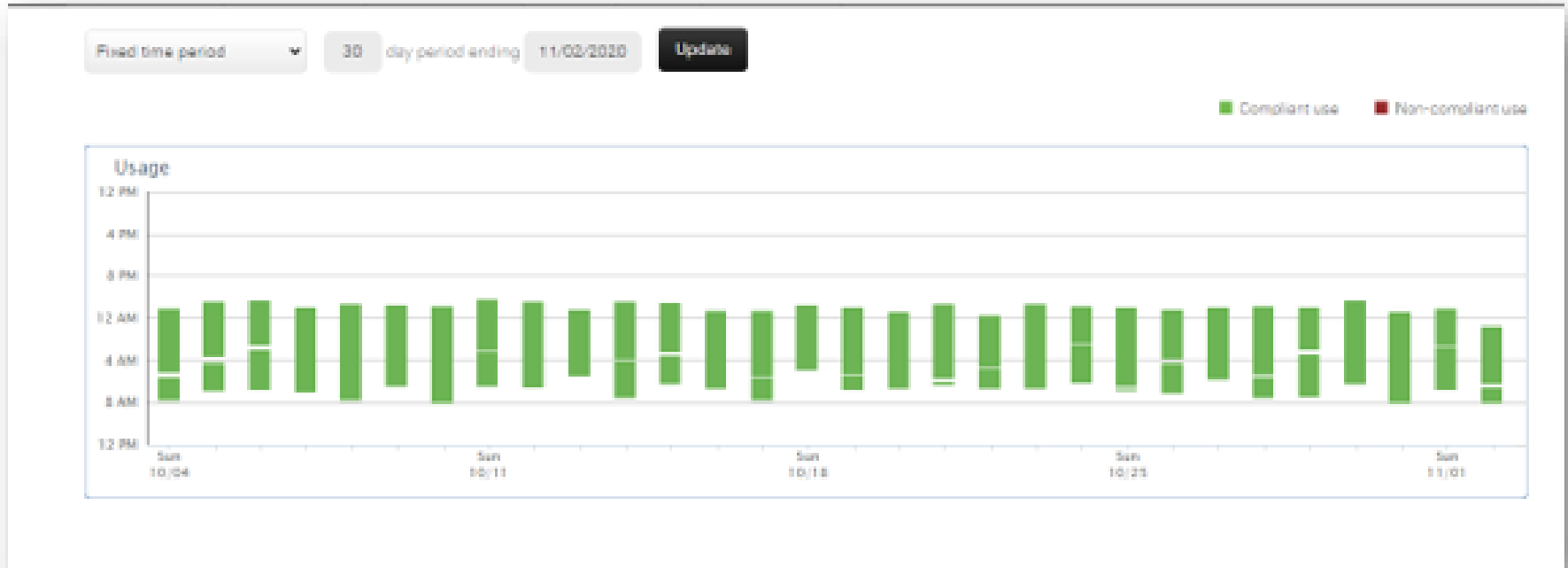
NOT UNIFORM

- Duration of Use – daily / up to one year
 - Not same as sleep time
 - Compliant not same as sufficient
- AHI - ? Significance
 - Not well correlated with sleep studies
- Leaks - ? Significance
 - Clinical correlation not there
 - Reported leaks from patient and report don't always match
- Main purpose of download – see if patient is compliant to ensure payment rather than making therapeutic decisions

PAP Download Data: Daily Data



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PAP Download Data: Detailed Report



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RES Evaluation



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- Exclude alternate etiologies of sleepiness
 - Sleep history
 - Bed time; sleep time; sleep journal; FITBIT / actigraphy
 - Insufficient Sleep – most likely reason
 - Medications
 - Thyroid function tests
 - Narcolepsy / Idiopathic hypersomnolence
 - PSG on PAP + MSLT

PSG on PAP + MSLT



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- PSG on PAP
 - How much pressure
 - Titration of pressure?
 - Sleep latency, PLMD, arousals
 - MSLT - ? PAP use

PAP Therapy Factors



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- Adjust pressure
- Mask factors – fitting/ change mask
- May consider hypnotic –to improve tolerance to PAP
- Consider treatment of RLS, PLMD
- Consider alternative Rx for OSA
 - Oral appliance therapy
 - Hypoglossal nerve stimulation
 - Maxillo Mandibular Advancement

Wakefulness Promoting Agents



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- Modafinil (Provigil) / Armodafinil (Nuvigil)
 - Promote wakefulness in early evening (reduce ESS by 2.5 with Modafinil)
 - Improved productivity, activity, and vigilance
 - Do not disrupt nighttime sleep
 - Side effect – headache 15-20%; rare CV effects – chest pain, palpitations
 - May reduce effectiveness of hormonal contraceptives (should be used in caution in women using hormonal contraception)
 - Act on CNS: exact mechanism not known; most likely enhance dopamine signaling

Wakefulness Promoting Agents



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Solriamfetol (Sunosi)

- Improve wakefulness
- Oral selective dopamine and NE reuptake inhibitor

Pitolisant (Wakix)

- Histamine receptor 3 antagonist
- Currently approved for use in patients with Narcolepsy
- Studies ongoing for approval in patients with OSA



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Questions?

