

# Mitä uutta uniapneasta?

Adel Bachour

LT, dosentti, keuhkosairauksien erikoislääkäri

Sydän ja keuhkokeskus, Uniapneapoliklinikka, Iho ja allergia sairaala



Clinical Review

# Efficacy of pharmacotherapy for OSA in adults: A systematic review and network meta-analysis

Thomas Gaisl <sup>a</sup>, Sarah R. Haile <sup>b</sup>, Sira Thiel <sup>a</sup>, Martin Osswald <sup>a</sup>, Malcolm Kohler <sup>a</sup>  

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<https://doi.org/10.1016/j.smr.2019.04.009>

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Pharmacotherapy:  
to raise the arousal threshold (eg. eszopicone )  
to enhance muscle responsiveness (eg. desipramine ),  
to dampen loop gain (eg. acetazolamide)  
are available, and proof-of-concept studies have been encouraging.



Clinical Review

# Efficacy of pharmacotherapy for OSA in adults: A systematic review and network meta-analysis

Thomas Gaisl <sup>a</sup>, Sarah R. Haile <sup>b</sup>, Sira Thiel <sup>a</sup>, Martin Osswald <sup>a</sup>, Malcolm Kohler <sup>a</sup>  

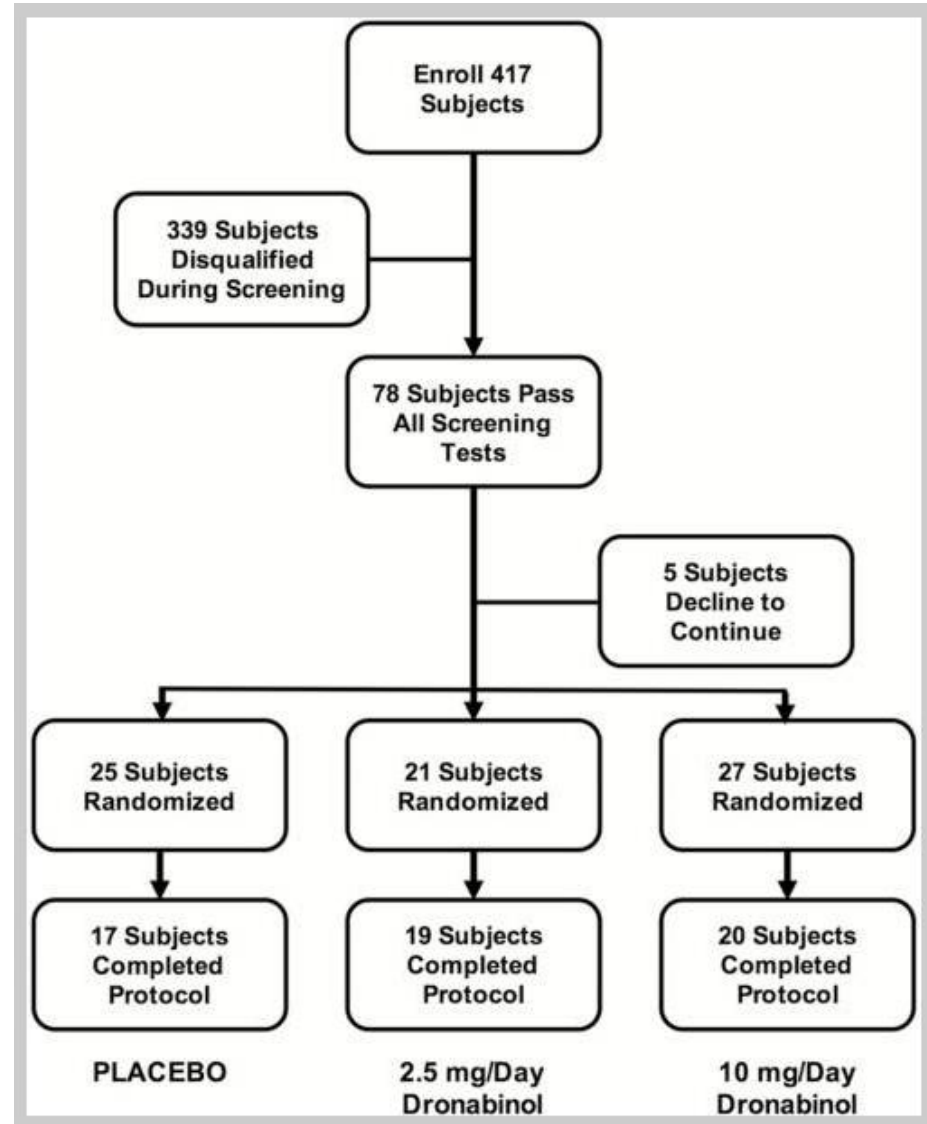
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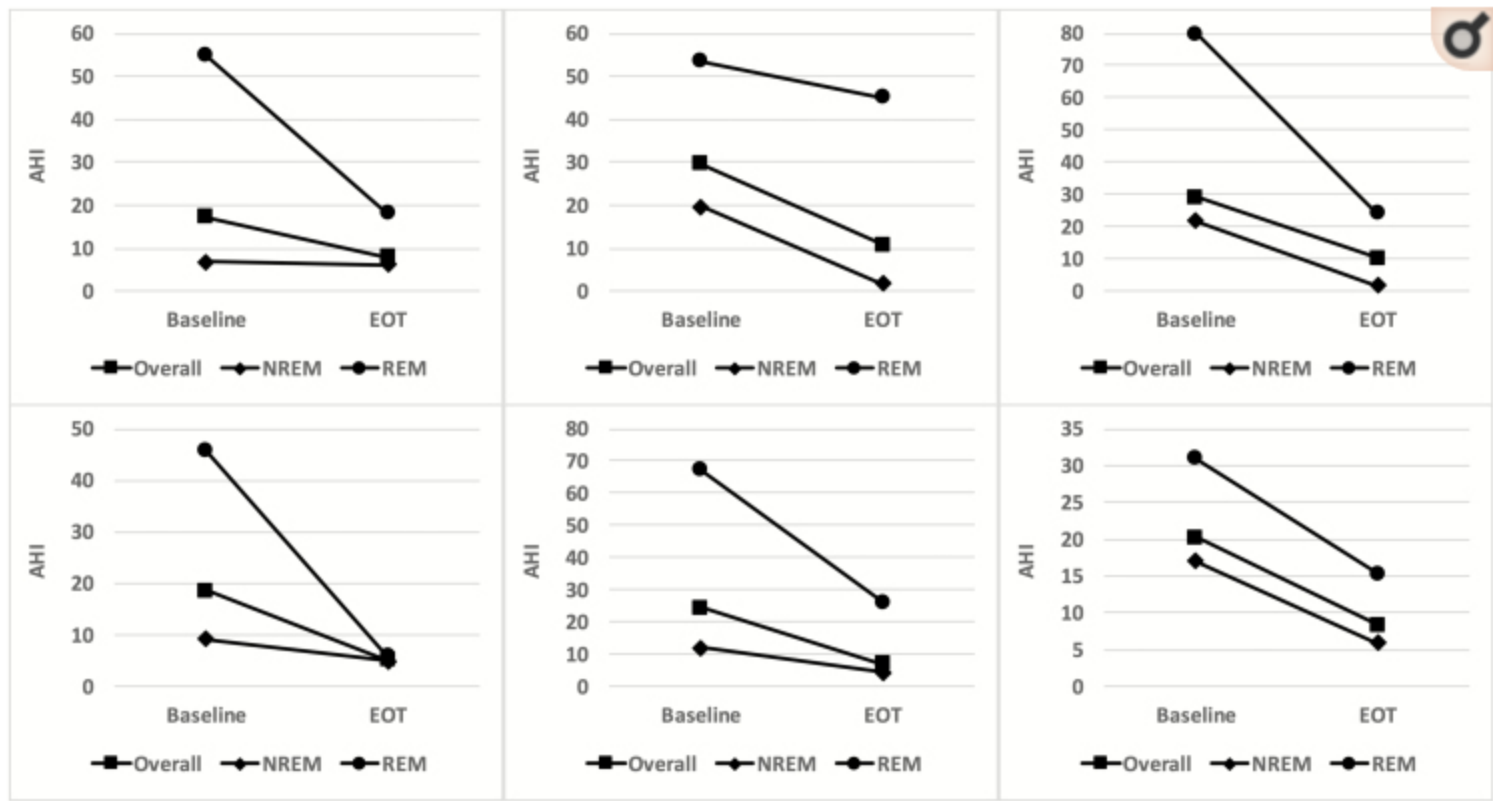
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Although some trials indicate favorable outcomes, these results are only valid for distinctive OSA-phenotypes or were not clinically significant. The effect sizes were small, the majority of trials were not adequately powered. There is currently insufficient evidence to recommend any pharmacotherapy for OSA and no phase-III trials are available.

Carley DW, et al. Pharmacotherapy of apnea by cannabimimetic enhancement, the PACE Clinical Trial: effects of **dronabinol** in obstructive sleep apnea. *Sleep*. 2018;41(1).





Treatment-related changes in AHI individual “responders.” Each panel depicts the AHI measured at baseline and at the end of treatment for a single responder (square symbols). In addition, AHI stratified according the NREM sleep (diamond symbols) and REM sleep (circle symbols) are depicted for each of these participants.

SPECIAL ARTICLES

## Medical Cannabis and the Treatment of Obstructive Sleep Apnea: An American Academy of Sleep Medicine Position Statement

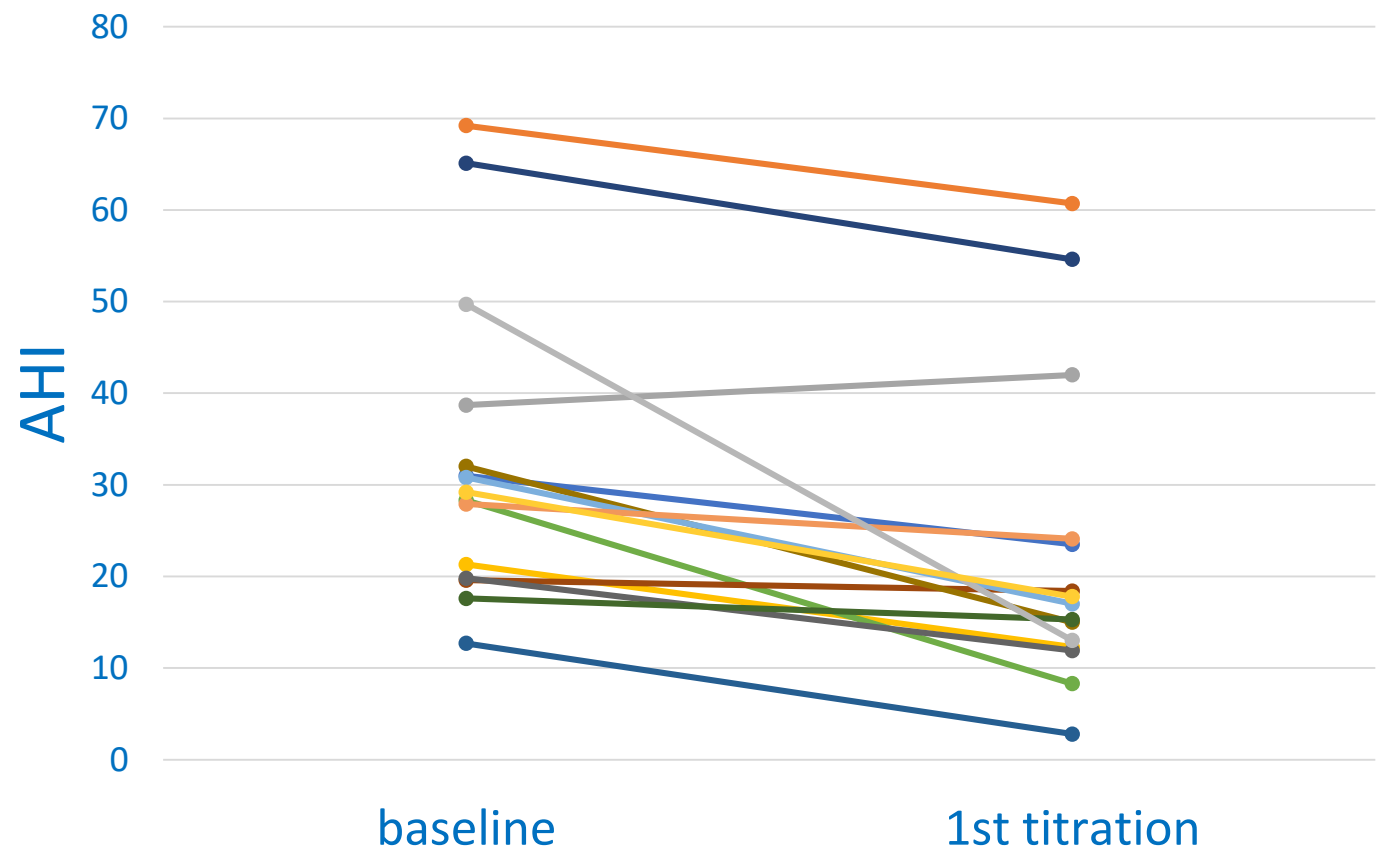
Kannan Ramar, MD<sup>1</sup>; Ilene M. Rosen, MD, MS<sup>2</sup>; Douglas B. Kirsch, MD<sup>3</sup>; Ronald D. Chervin, MD, MS<sup>4</sup>; Kelly A. Carden, MD<sup>5</sup>; R. Nisha Aurora, MD<sup>6</sup>; David A. Kristo, MD<sup>7</sup>; Raman K. Malhotra, MD<sup>8</sup>; Jennifer L. Martin, PhD<sup>9,10</sup>; Eric J. Olson, MD<sup>1</sup>; Carol L. Rosen, MD<sup>11</sup>; James A. Rowley, MD<sup>12</sup>; American Academy of Sleep Medicine Board of Directors

- The American Academy of Sleep Medicine states that “medical cannabis and/or its synthetic extracts **should not** be used for the treatment of OSA.

# Upper airway stimulation as treatment for sleep apnea



Difference in apnea and hypopnea index (AHI) in 15 patients treated for sleep apnea by an upper airway stimulator in Helsinki since September 2014







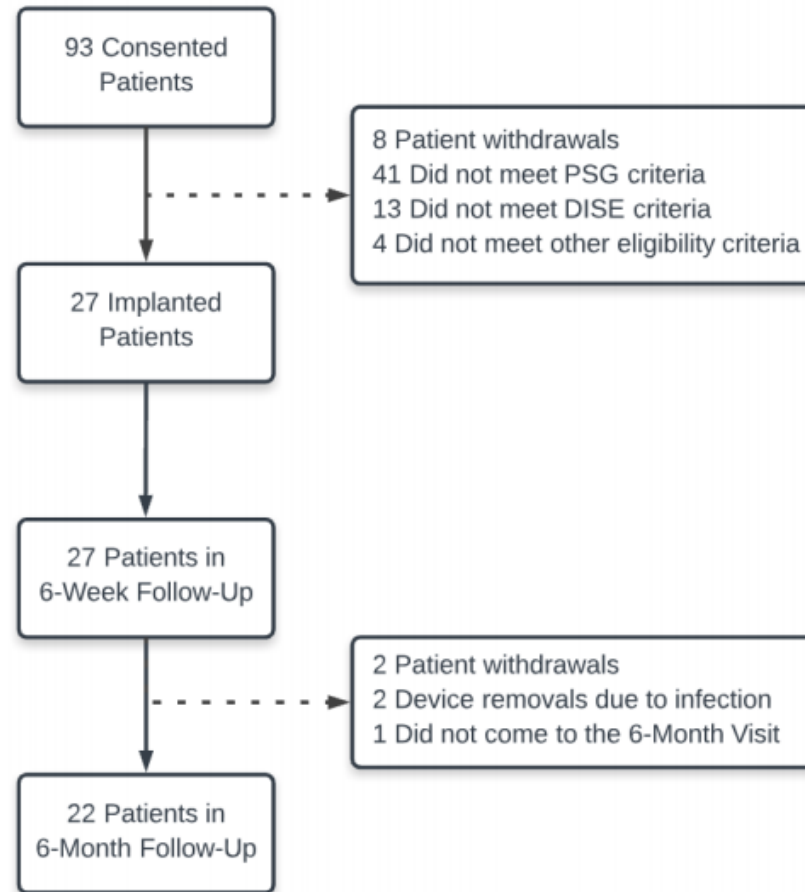
## Early View

Original article

### **Bilateral Hypoglossal Nerve Stimulation for Treatment of Adult Obstructive Sleep Apnea**

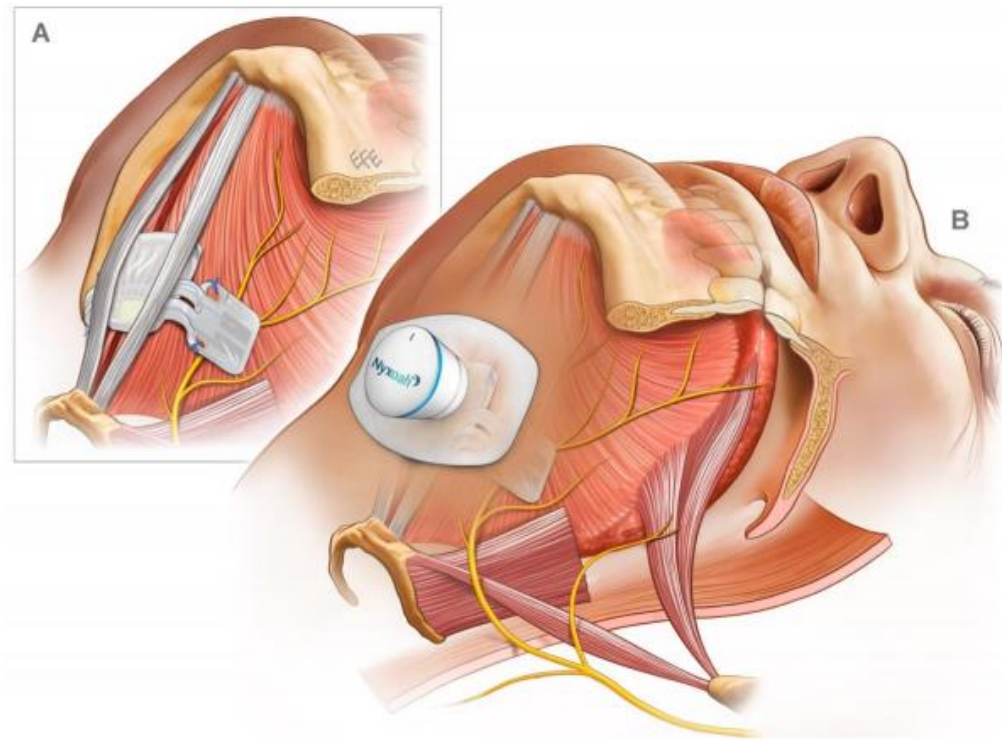
Peter R. Eastwood, Maree Barnes, Stuart G. MacKay, John R. Wheatley, David R. Hillman, Xuân-Lan Nguyễn, Richard Lewis, Matthew C. Campbell, Boris Pételle, Jennifer H. Walsh, Andrew C. Jones, Carsten E. Palme, Alain Bizon, Nicole Meslier, Chloé Bertolus, Kathleen J. Maddison, Laurent Laccourreye, Guillaume Raux, Katleen Denoncin, Valérie Attali, Frédéric Gagnadoux, Sandrine H. Launois

Please cite this article as: Eastwood PR, Barnes M, MacKay SG, *et al.* Bilateral Hypoglossal Nerve Stimulation for Treatment of Adult Obstructive Sleep Apnea. *Eur Respir J* 2019; in press (<https://doi.org/10.1183/13993003.01320-2019>).



**Figure 1.** Flow diagram showing study enrolment and participant progress

PSG=polysomnography; DISE=drug induced sleep endoscopy.

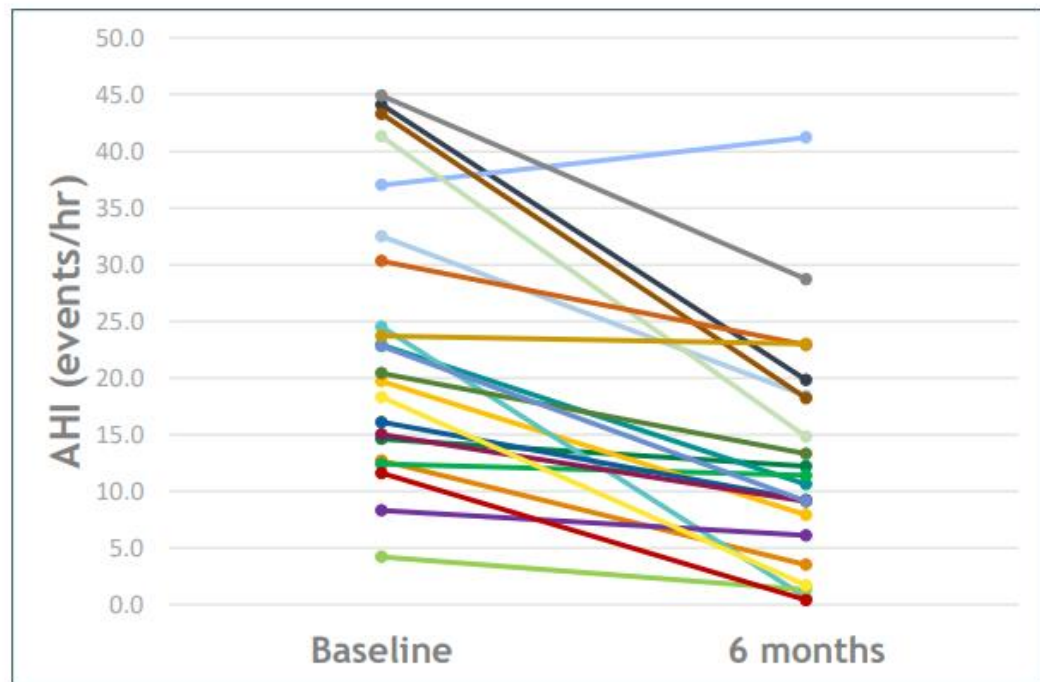


**Figure 2.** Submental musculature showing (A) the implanted stimulator straddling the genioglossus muscles and hypoglossal nerve branches bilaterally and (B) the disposable patch and activation unit. The images are for illustrational purposes only and it should be noted that the surgical anatomy might differ from person to person thereby requiring adjustment to the specific placement of the implanted stimulator over the hypoglossal nerves.

The implant is surgically inserted in at the back of the tongue, that electrically stimulates the tongue to move it out of the airway during breathing cycles. The neurostimulator is energized using an stick-on battery patch that is placed on the chin over the implant site, and the two work in unison through the night stimulating the nerves as needed to prevent OSA and snoring.



**Supplementary Figure 1.** Disposable patch and activation unit



**Figure 3.** Change in Apnea-Hypopnea Index (AHI) for each participant from baseline to 6 months post-implantation. Each coloured line represents an individual participant using modified intention-to-treat analyses (n=22).

**Table 2.** Outcome measures for modified intention-to-treat analyses.

Outcome	Baseline (N=22)	6 months (N=22)	Mean Difference (95% CI)	P-value
<b>Sleep Disordered Breathing</b>				
AHI, events/hr	23.7 (12.2)	12.9 (10.1)	10.8 (14.6 to 7.0)	<0.0001
ODI, events/hr	19.1 (11.2)	9.8 (6.9)	9.3 (13.1 to 5.5)	<0.0001
SaO <sub>2</sub> <90%, % time	5.0 (6.0)	2.1 (3.0)	2.9 (4.6 to 1.3)	0.0015
AI, events/hr	10.1 (10.2)	5.6 (8.4)	4.8 (9.2 to 0.4)	0.0334
HI, events/hr	12.5 (8.9)	7.6 (6.2)	4.9 (8.1 to 1.7)	0.0049
<b>Symptoms</b>				
ESS	11.0 (5.3)*	8.0 (5.4)	3.0 (5.7 to 0.8)	0.0113
FOSQ-10	15.3 (3.3)	17.2 (3.0)	1.9 (0.4 to 3.4)	0.0157

## THE OCCURRENCE OF SLEEP-DISORDERED BREATHING AMONG MIDDLE-AGED ADULTS

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STEVEN WEBER, PH.D., AND SAFWAN BADR, M.D.

**Abstract** *Background.* Limited data have suggested that sleep-disordered breathing, a condition of repeated episodes of apnea and hypopnea during sleep, is prevalent among adults. Data from the Wisconsin Sleep Cohort Study, a longitudinal study of the natural history of cardio-pulmonary disorders of sleep, were used to estimate the prevalence of undiagnosed sleep-disordered breathing among adults and address its importance to the public health.

*Methods.* A random sample of 602 employed men and women 30 to 60 years old were studied by overnight polysomnography to determine the frequency of episodes of apnea and hypopnea per hour of sleep (the apnea-hypopnea score). We measured the age- and sex-specific prevalence of sleep-disordered breathing in this group using three cutoff points for the apnea-hypopnea score ( $\geq 5$ ,  $\geq 10$ , and  $\geq 15$ ); we used logistic regression to investigate risk factors.

*Results.* The estimated prevalence of sleep-disordered breathing, defined as an apnea-hypopnea score of 5 or higher, was 9 percent for women and 24 percent for men. We estimated that 2 percent of women and 4 percent of men in the middle-aged work force meet the minimal diagnostic criteria for the sleep apnea syndrome (an apnea-hypopnea score of 5 or higher and daytime hypersomnolence). Male sex and obesity were strongly associated with the presence of sleep-disordered breathing. Habitual snorers, both men and women, tended to have a higher prevalence of apnea-hypopnea scores of 15 or higher.

*Conclusions.* The prevalence of undiagnosed sleep-disordered breathing is high among men and is much higher than previously suspected among women. Undiagnosed sleep-disordered breathing is associated with daytime hypersomnolence. (N Engl J Med 1993;328:1230-5.)

**Table 4. Age-Specific Estimates of Sleep-Disordered Breathing in the General Population, According to Apnea–Hypopnea Score and Sex.**

AGE (YR)	WOMEN			MEN		
	APNEA–HYPOPNEA SCORE			APNEA–HYPOPNEA SCORE		
	≥5	≥10	≥15	≥5	≥10	≥15
	<i>percent of subjects (95% confidence interval)</i>					
30–39	6.5 (1.4–11)	4.9 (0.6–9.8)	4.4 (1.1–7.3)	17 (9.6–25)	12 (5.4–19)	6.2 (1.9–10)
40–49	8.7 (4.2–13)	4.9 (1.7–8.1)	3.7 (1.0–6.5)	25 (18–32)	18 (11–24)	11 (6.7–16)
50–60	16 (5.2–26)	5.9 (0.0–12)	4.0 (0.0–10)	31 (21–40)	14 (7.5–20)	9.1 (5.1–13)
<b>30–60*</b>	<b>9.0 (5.6–12)</b>	<b>5.0 (2.4–7.8)</b>	<b>4.0 (1.5–6.6)</b>	<b>24 (19–28)</b>	<b>15 (12–19)</b>	<b>9.1 (6.4–11)</b>

\*Values are adjusted to the age distribution of the survey population.



# HHS Public Access

Author manuscript

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Published in final edited form as:

*Lancet Respir Med.* 2015 April ; 3(4): 310–318. doi:10.1016/S2213-2600(15)00043-0.

## Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

**R Heinzer, S Vat, P Marques-Vidal, H Marti-Soler, D Andries, N Tobback, V Mooser, M Preisig, A Malhotra, G Waeber, P Vollenweider, M Tafti\*, and J Haba-Rubio\***

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The prevalence of moderate-to-severe sleep-disordered breathing ( $\geq 15$  events per h) was 23.4% (95% CI 20.9–26.0) in women and 49.7% (46.6–52.8) in



## Summary

**Background**—Sleep-disordered breathing is associated with major morbidity and mortality. However, its prevalence has mainly been selectively studied in populations at risk for sleep-disordered breathing or cardiovascular diseases. Taking into account improvements in recording techniques and new criteria used to define respiratory events, we aimed to assess the prevalence of sleep-disordered breathing and associated clinical features in a large population-based sample.

**Methods**—Between Sept 1, 2009, and June 30, 2013, we did a population-based study (HypnoLaus) in Lausanne, Switzerland. We invited a cohort of 3043 consecutive participants of the CoLaus/PsyCoLaus study to take part. Polysomnography data from 2121 people were included in the final analysis. 1024 (48%) participants were men, with a median age of 57 years (IQR 49–68, range 40–85) and mean body-mass index (BMI) of 25·6 kg/m<sup>2</sup> (SD 4·1). Participants underwent complete polysomnographic recordings at home and had extensive phenotyping for diabetes, hypertension, metabolic syndrome, and depression. The primary outcome was prevalence of sleep-disordered breathing, assessed by the apnoea-hypopnoea index.

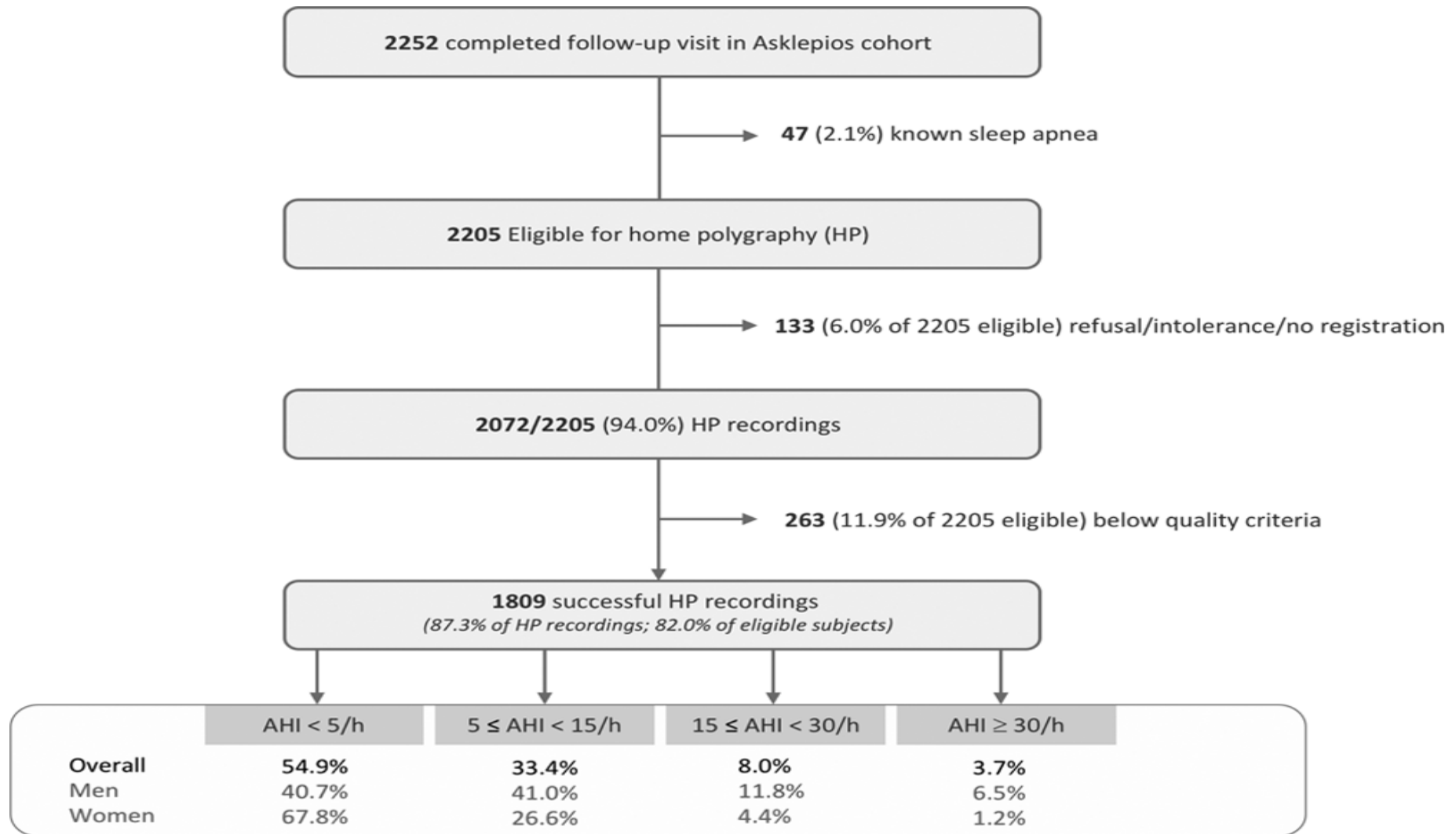
**Findings**—The median apnoea-hypopnoea index was 6·9 events per h (IQR 2·7–14·1) in women and 14·9 per h (7·2–27·1) in men. The prevalence of moderate-to-severe sleep-disordered breathing ( $\geq 15$  events per h) was 23·4% (95% CI 20·9–26·0) in women and 49·7% (46·6–52·8) in

# Phenotype and Risk Burden of Sleep Apnea A Population-Based Cohort Study

Fré A. Bauters, Katrien B. Hertegonne, Marc L. De Buyzere, Guy F. Joos, Julio A. Chirinos,  
Ernst R. Rietzschel

**Abstract**—Sleep apnea (SA) prevalence had increased. The socioeconomic burden is significant because of healthcare-related costs and adverse outcome, especially in moderate-to-severe SA. However, the population impact is unclear, particularly for mild SA. We aimed to assess the current prevalence and the cardiovascular risk associates of SA in the general population. We performed home polygraphy and extensive clinical, sociodemographic, and cardiovascular assessment in 2205 eligible subjects from a population-based cohort. Successful polygraphy was obtained in 1809 subjects (mean age, 56.0; SD, 5.9 years; 52.3% women). The prevalence was 41.0%, 11.8%, and 6.5% for mild, moderate, and severe SA in men and 26.6%, 4.4%, and 1.2% in women. Male sex, age, increasing BMI, and snoring were independently associated with SA, whereas sleepiness or tiredness were not. Compared with those without SA, mild SA was associated with (age- and sex-adjusted OR; 95% CI): diabetes mellitus (2.40; 1.52–3.80), hypertension (1.76; 1.42–2.19), left ventricular hypertrophy (1.36; 1.03–1.79), arterial plaques (1.19; 0.94–1.52), and increased IL-6 (interleukin-6) levels (1.37; 1.10–1.72). These associations were more pronounced in moderate-to-severe SA. To conclude, SA is highly prevalent in the middle-aged general population. It is largely undetected and undetectable using a symptom-based strategy. Yet, even the large group with mild SA shows a manifestly higher metabolic, inflammatory, and cardiovascular risk factor burden, with potential public health implications. (*Hypertension*. 2019;74:1052-1062. DOI: 10.1161/HYPERTENSIONAHA.119.13452.) • [Online Data Supplement](#)





# Phenotype and Risk Burden of Sleep Apnea

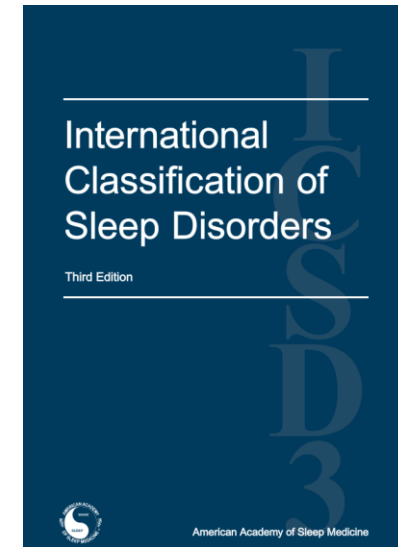
- Sleep apnea is highly prevalent in the general population. It is largely undetected and undetectable using a symptom-based strategy.
- One-third of the women and two-thirds of the men had some degree of OSA, as defined by an  $AHI \geq 5$ .

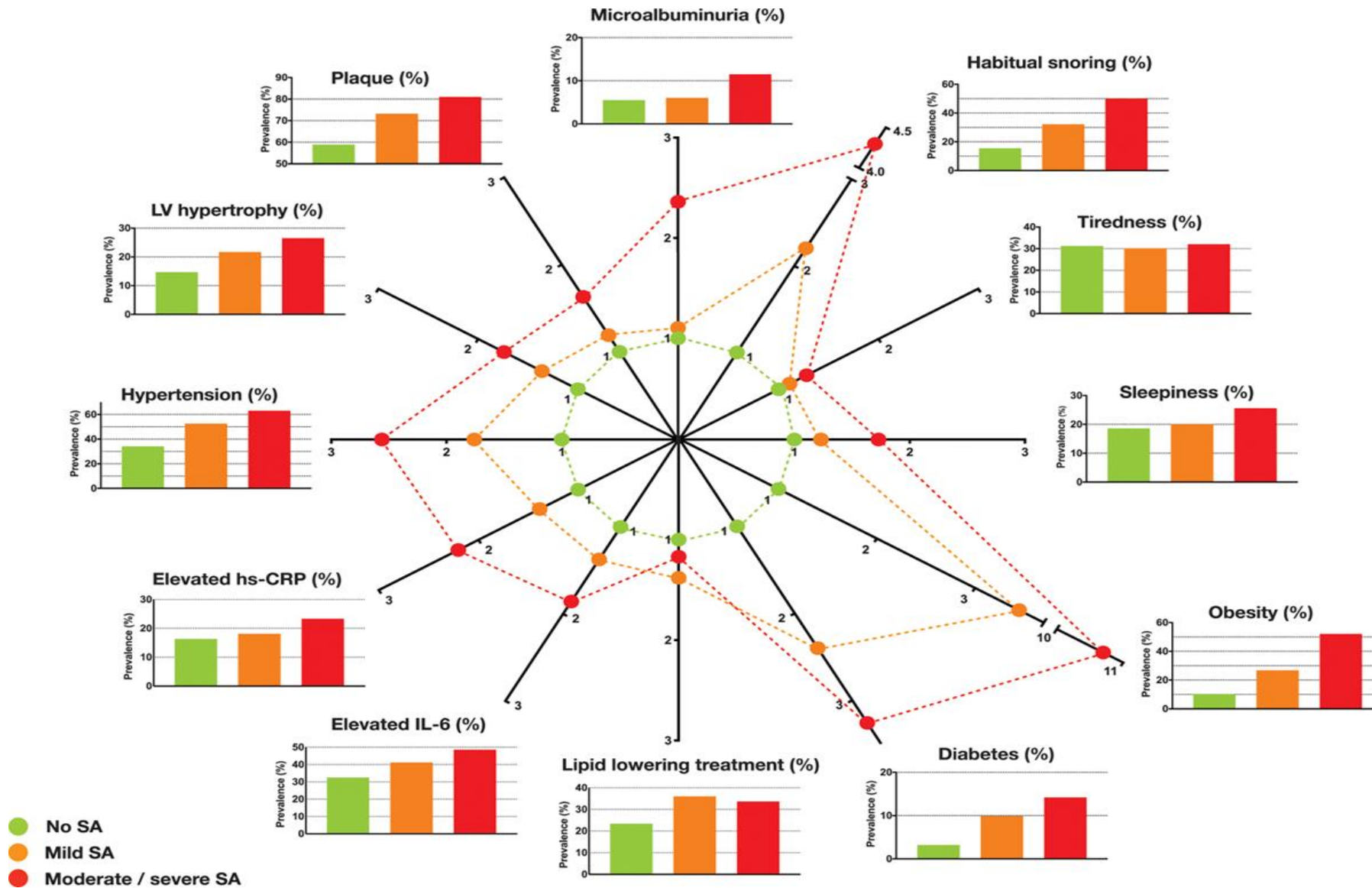


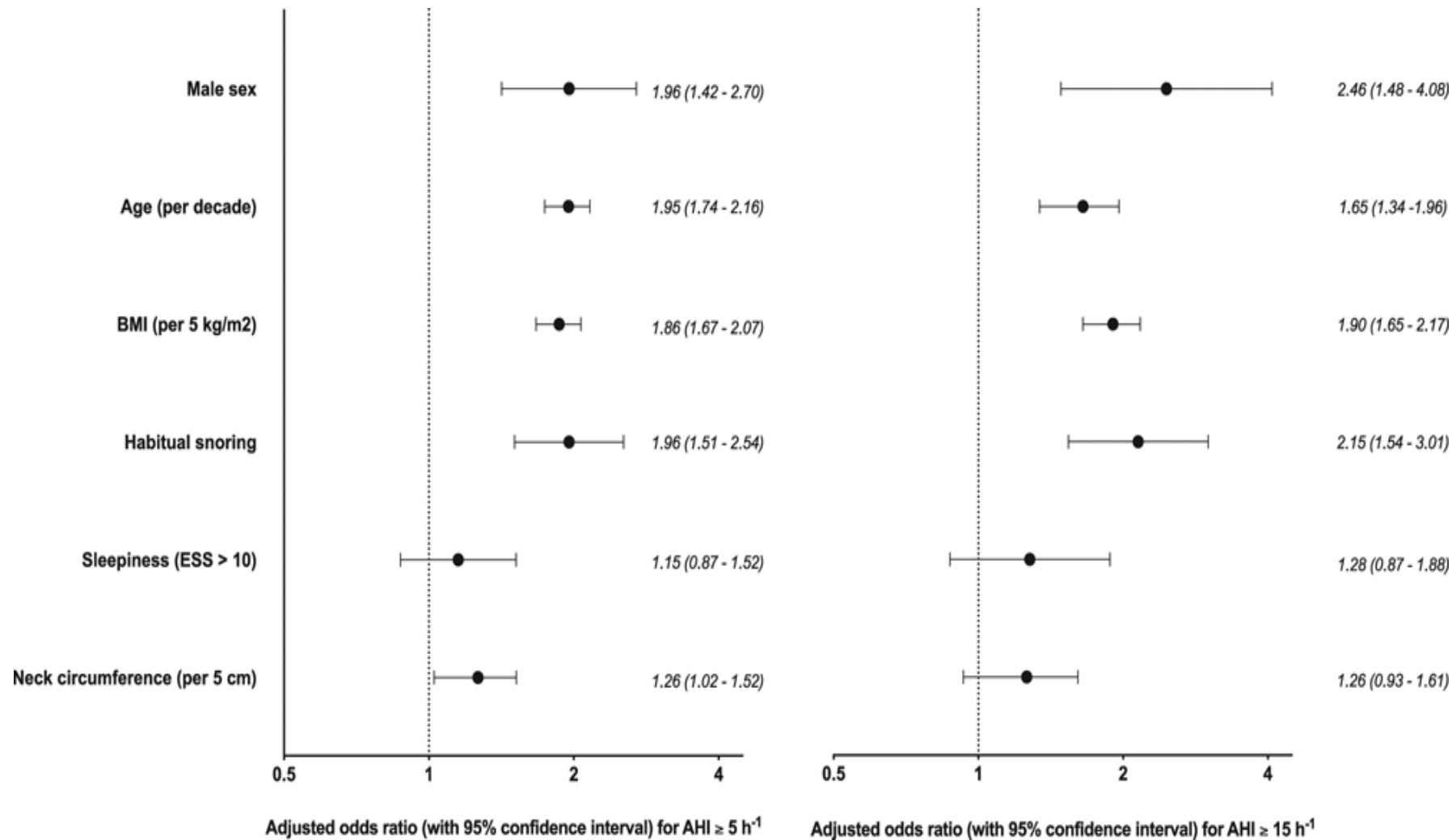
## Diagnostic Criteria

(A and B) or C satisfy the criteria

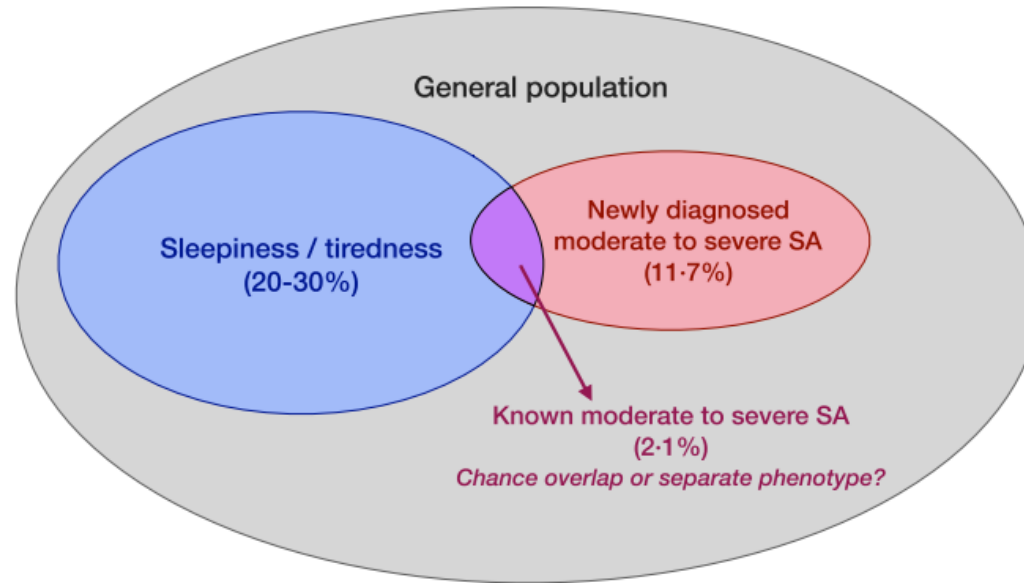
- A. The presence of one or more of the following:
1. The patient complains of sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms.
  2. The patient wakes with breath holding, gasping, or choking.
  3. The bed partner or other observer reports habitual snoring, breathing interruptions, or both during the patient's sleep.
  4. The patient has been diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus.
- B. Polysomnography (PSG) or OCST<sup>1</sup> demonstrates:
1. Five or more predominantly obstructive respiratory events<sup>2</sup> (obstructive and mixed apneas, hypopneas, or respiratory effort related arousals [RERAs])<sup>3</sup> per hour of sleep during a PSG or per hour of monitoring (OCST).<sup>1</sup>
- OR
- C. PSG or OCST<sup>1</sup> demonstrates:
1. Fifteen or more predominantly obstructive respiratory events (apneas, hypopneas, or RERAs)<sup>3</sup> per hour of sleep during a PSG or per hour of monitoring (OCST).<sup>1</sup>







**Figure S5: Known and newly diagnosed moderate-to-severe sleep apnea in the general population, and co-occurrence of sleepiness and tiredness**

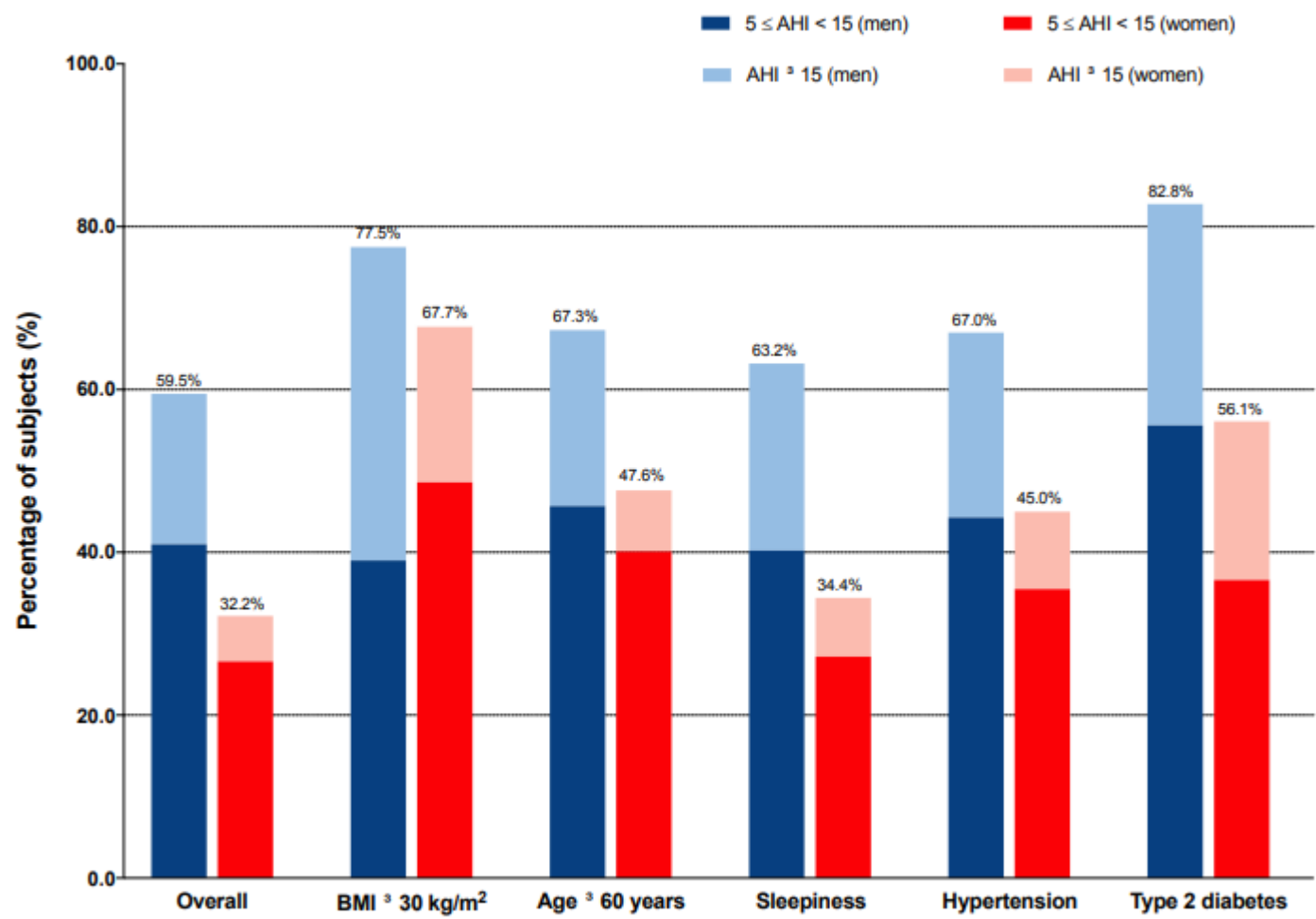


Tiredness and/or sleepiness and SA are both highly prevalent in the general population. SA: sleep apnea.





**Figure S3: Prevalence of mild and moderate-to-severe SA in specific clinical subgroups**



AHI: apnea/hypopnea index. BMI: body mass index. SA: sleep apnea.



# Kohonnut verenpaine

- Aikuisikäisistä suomalaista noin kahdella miljoonalla on kohonnut verenpaine.
- Noin miljoona suomalaista käyttää verenpainetta alentavia lääkkeitä, mutta heistä vain noin 40 %:lla verenpaine on hoitotavoitteessa

# Uniapnea (obstruktiivinen uniapnea aikuisilla)

Käypä hoito -suositus | Julkaistu: 15.06.2017 | Tila: [voimassa](#)

## Määritelmiä

- Aikuisen obstruktiivisella uniapnealla tarkoitetaan toistuvia, vähintään kymmenen sekunnin mittaisia hengityskatkoksia (apnea) tai hengityksen vaimentumia (hypopnea), jotka johtuvat ylähengitysteiden ahtautumisesta unen aikana.
- Apneoiden ja hypopneoiden keskimääräinen esiintyvyys tuntia kohden ilmaistaan apnea-hypopneaindeksinä (AHI).
- Osittaisella unenaikaisella ylähengitystieahtaumalla tarkoitetaan pitkiä, yli minuutin kestäviä jaksoja, joissa sisäänhengitysvirtauksen rajoittuminen ei johda hengityskatkokseen tai välittömään havahtumiseen vaan hengitysyrietykset, usein kovaääninen kuorsaus ja hiilidioksidipitoisuus lisääntyvät vähitellen.
- Hengityskatkoksiin liittyy veren happikyllästeisyyden pieneneminen, ja ne päättyvät tavallisesti lyhyisiin tiedostamattomiin havahtumisiin unesta.
- Kun uniapneaan liittyy oireita (taulukko **1**), puhutaan obstruktiivisesta uniapneaoireyhtymästä.
- Suosituksessa käytettävät lyhenteet esitellään lisätietoaineistossa **4**.



# Prevalence of sleep-disordered breathing and sleep apnoea syndrome, according to age and sex

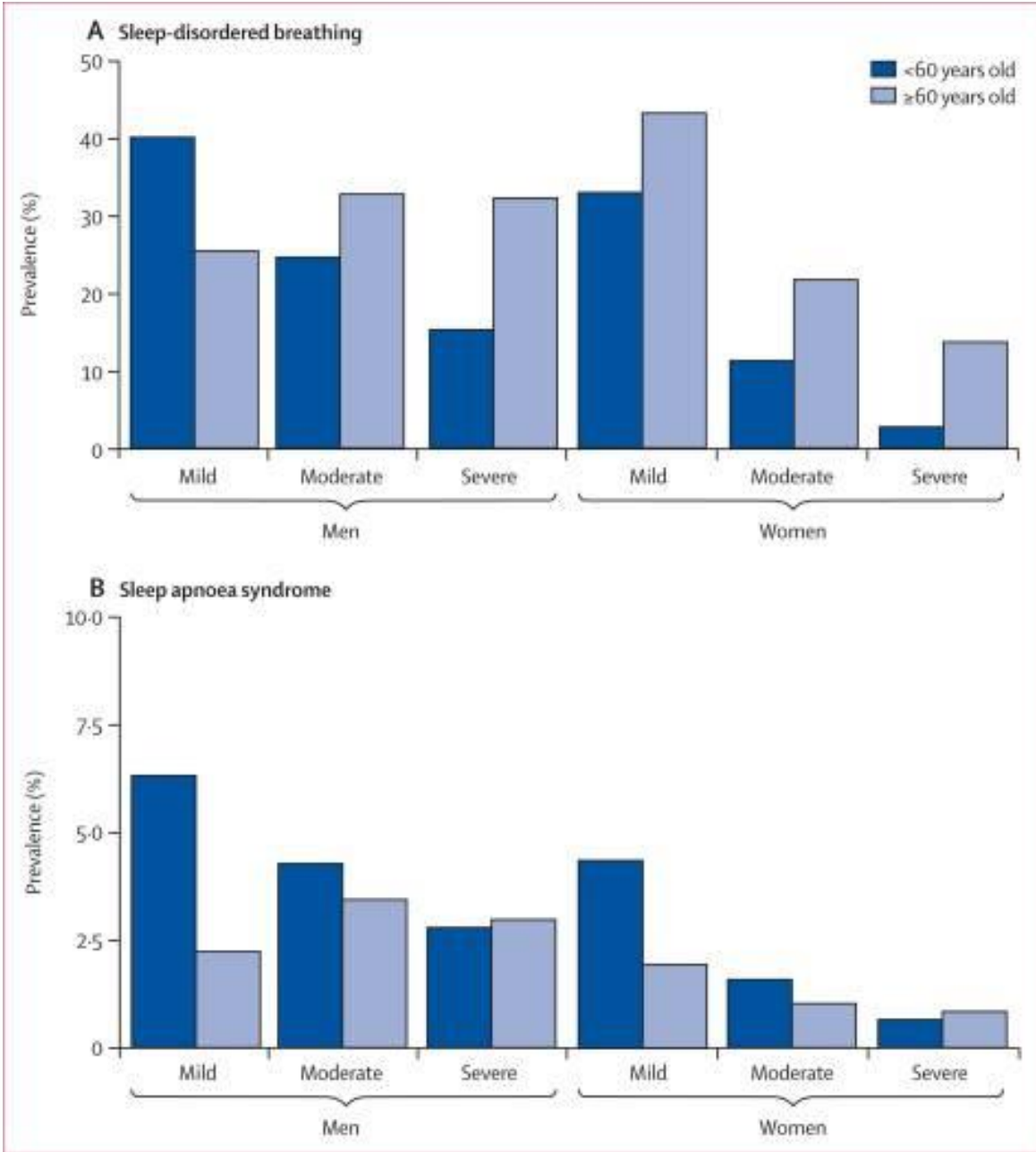
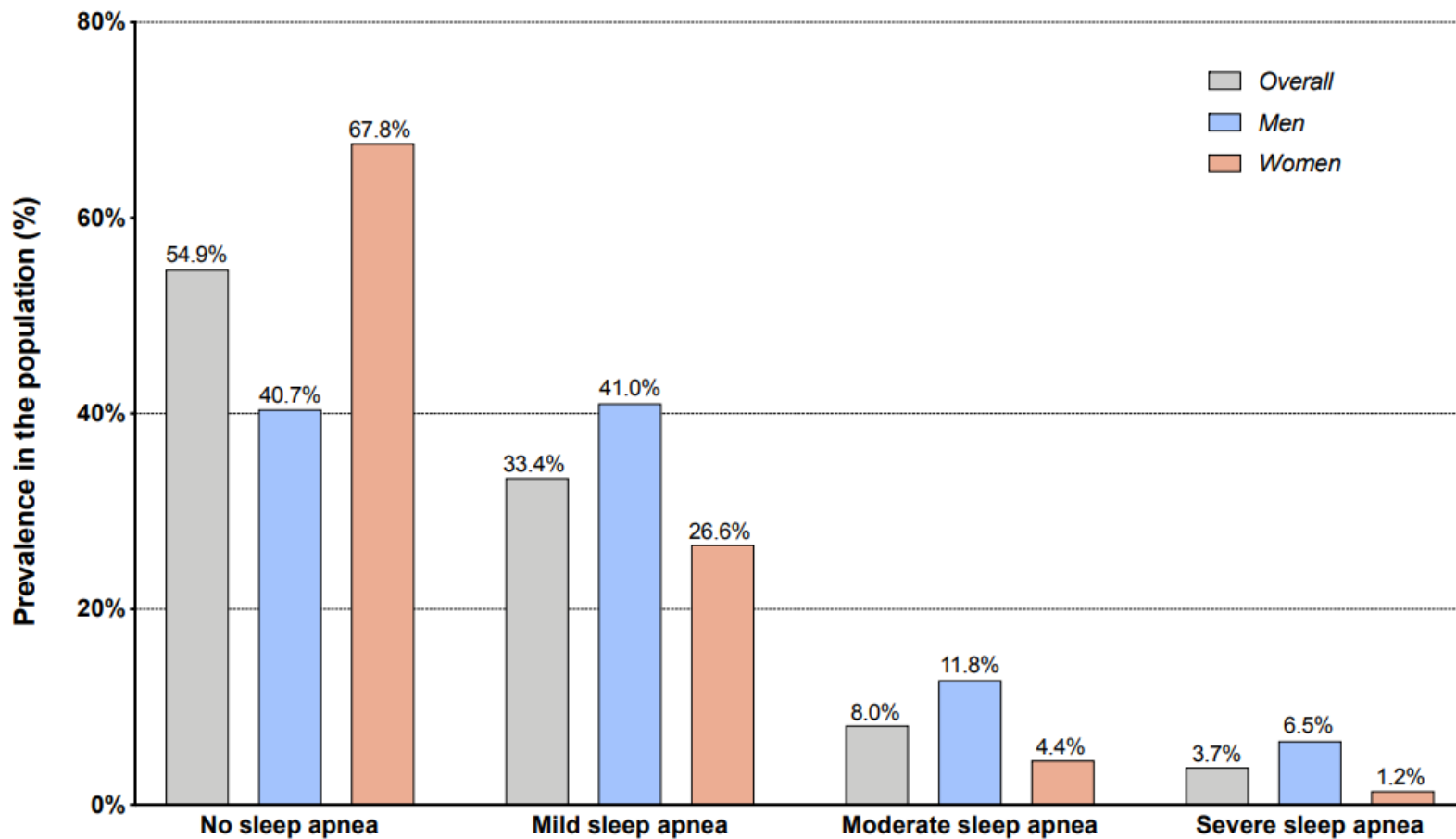


Figure S2: Prevalence of mild, moderate and severe sleep apnea in total population and in both sexes



No sleep apnea:  $AHI < 5h^{-1}$ . Mild sleep apnea:  $5 \leq AHI < 15 h^{-1}$ . Moderate sleep apnea:  $15 \leq AHI < 30 h^{-1}$ . Severe sleep apnea:  $AHI \geq 30 h^{-1}$ . AHI: apnea/hypopnea index.



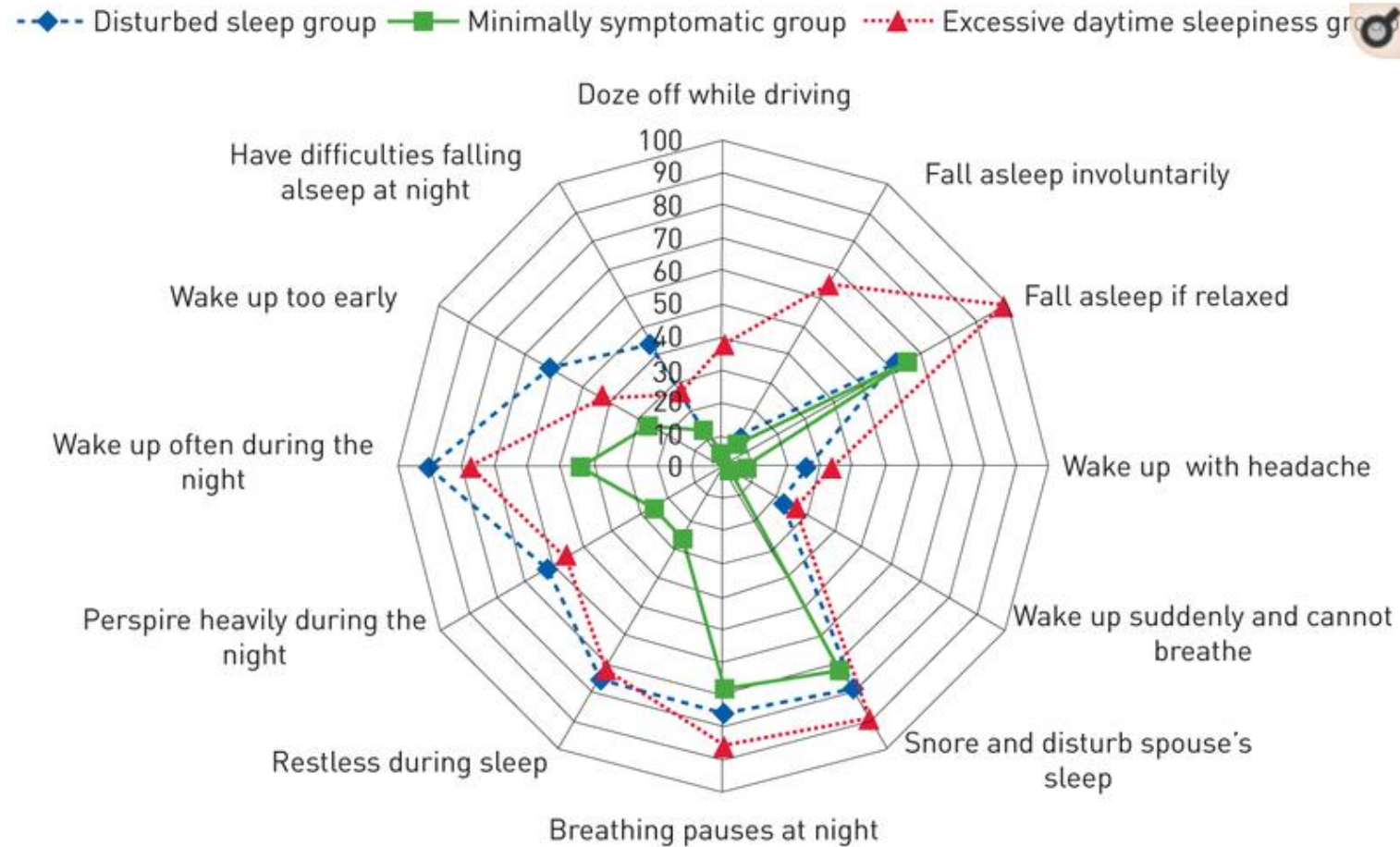
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Published online 2014 Sep 3. doi: [10.1183/09031936.00032314](https://doi.org/10.1183/09031936.00032314)

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## FIGURE 1



Probability of having a symptom within each cluster. The conditional probabilities of 12 symptoms (selected from the complete list in [Table 2](#)) are shown to highlight the major differences among clusters.

### Comparisons of PAP Adherence and Usage Among Symptom Clusters

Variable	Symptom clusters			P
	Disturbed sleep	Minimally symptomatic	Sleepy	
N (%)	229 (32.4)	170 (24.1)	307 (43.5)	—
Any PAP usage, n (%)	<b>140 (61.1)</b>	<b>102 (60.0)</b>	<b>215 (70.0)</b>	<b>.034*</b>
PAP usage group, n (%)				.085
Full user	112 (48.9)	84 (49.1)	165 (53.8)	
Partial user	28 (12.2)	18 (10.6)	50 (16.3)	
Nonuser	89 (38.9)	68 (40.0)	92 (30.0)	
Hours PAP usage <sup>a</sup>				
Mean ± SD	6.5 ± 2.3	6.2 ± 1.7	6.4 ± 1.9	.596
Median (Range)	6.9 (0.1, 10.4)	6.5 (0.3, 9.7)	6.9 (0.6, 10.4)	.160
Nights PAP used <sup>a</sup>				
Mean ± SD	24.2 ± 6.6	23.8 ± 6.2	24.5 ± 5.9	.720
Median (range)	28 (1, 28)	26 (1, 28)	27 (2, 28)	.183

\*Sleepy cluster significantly ( $p < .05$ ) more likely to use PAP compared with both DS and MS clusters in pairwise comparisons.

<sup>a</sup>Analyses on objective PAP usage data in 351 full or partial users with available data: 111 Disturbed Sleep, 72 Minimally Symptomatic, and 168 Sleepy.

PAP = positive airway pressure; DS = Disturbed Sleep; MS = Minimally Symptomatic; S = Sleepy; SD = standard deviation.

### Changing Faces of Obstructive Sleep Apnea: Treatment Effects by Cluster Designation in the Icelandic Sleep Apnea Cohort

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# Yhteenveto

- Turvallista lääkehoitoa uniapnealle ei ole vielä saatavilla
- Uusia hoitomenetelmiä uniapnealle kehitetään lähes vuosittain
- Uniapnean esiintyvyys on selvästi laajempi kuin on oletettu

Kiitos

