Sleep, Rhinitis, Asthma and Obesity

Timothy J. Craig
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Distinguished Educator
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Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do

Conflicts of interest with this presentation

- Merck- consultant and research
- GSK- research
- Genentech- research
- Novartis- research

Presentation Overview

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- What we need to do

Increase incidence of asthma correlates with?

- 1. High HDL
- 2. Waist Hip Ratio
- 3. Low triglycerides
- 4. Metabolic Syndrome

Answer:

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Answer: 4

R.V. Fenger[a,*], A. Gonzalez-Quintela[b], A. Linneberg[a], L.L.N. Husemoen[a], B.H. Thuesen[a], M. Aadahl[a], C. Vidal[b], T. Skaaby[a], J.C. Sainz[c], E. Calvo[c]

The relationship of serum triglycerides serum HDL, and obesity to the risk of wheezing in 85,555 adults

Respiratory Medicine (2013) 107, 816–824

Rhinitis symptoms		
Absent	9.3	(4561/48791)
Present	29.9	(10243/34295)
BMI		
<18.5 kg/m²	18.1	(257/1421)
18.5–25 kg/m²	16.0	(6239/38918)
25–30 kg/m²	18.1	(5816/32120)
≥30 kg/m²	24.1	(2999/12463)
WC		
Normal[b]	17.0	(11074/65329)
High[b]	24.5	(2701/11025)
S-Triglycerides		
<150 mg/dl	16.7	(11448/68472)
150–400 mg/dl	23.9	(3200/13416)
≥400 mg/dl	28.6	(269/942)
S-HDL		
Normal[b]	17.2	(11308/65728)
Low[b]	22.2	(3361/15167)
S-LDL		
Normal[b]	18.0	(13600/75564)
High[b]	18.3	(1829/9991)
S-glucose		
Normal[b]	17.8	(13456/75510)
High[b]	19.6	(1973/10045)
Blood pressure		
Normal[b]	17.5	(9098/52097)
High[b]	18.9	(6331/33458)
Metabolic syndrome		
Absent[b]	17.2	(10892/63149)
Present[b]	25.4	(2113/8334)

R.V. Fenger [a,*], A. Gonzalez-Quintela [b], A. Linneberg [a], L.L.N. Husemoen [a], B.H. Thuesen [a], M. Aadahl [a], C. Vidal [b], T. Skaaby [a], J.C. Sainz [c], E. Calvo [c]

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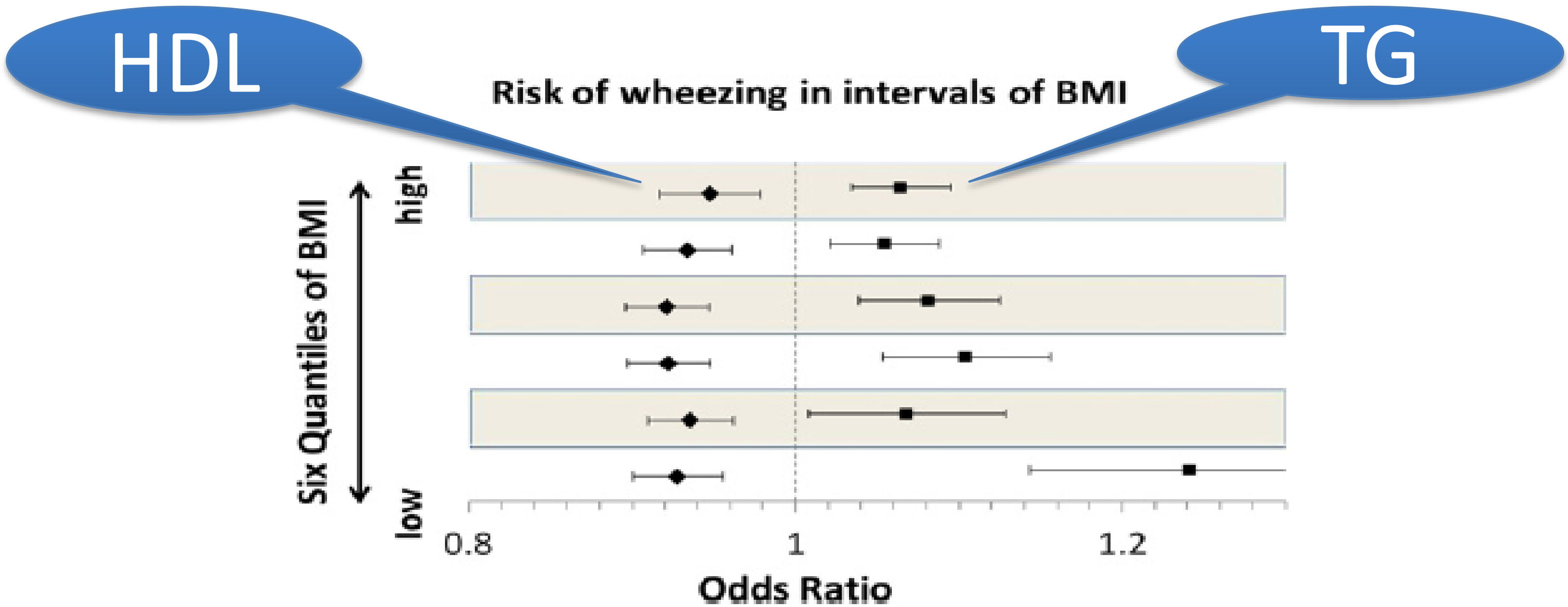

Figure 1 Risk of wheezing per standard deviation of s-HDL and s-TG by level of BMI. Diamonds: s-HDL; squares: s-TG. Odds ratio estimates with 95% confidence intervals indicated by error bars were obtained in one single logistic regression model adjusted for age, sex, adiposity, occupation, alcohol, and physical activity during working hours. S-TG, serum triglyceride; s-HDL, serum high density lipoprotein.

Respiratory Medicine (2013) 107, 816–824

Table 3 Association of adiposity (body mass index, upper panel, and waist circumference, lower panel), s-triglycerides and s-HDL with self reported wheezing in the rhinitis and non-rhinitis population.

Analyses with WC	Risk of wheeze		
	Rhinitis population	Non-rhinitis population	Interaction[b]
	OR[a] (CI)	OR[a] (CI)	*p*-value
Waist circumference			
Normal[d]	Reference	[illegible]	[illegible]
High[d]	1.47 (1.37–1.58)	[illegible]	[illegible]
S-Triglycerides			
Normal[d]	Reference	[illegible]	[illegible]
High[d]	1.21 (1.13–1.29)	[illegible]	[illegible]
S-HDL			
Normal[d]	Reference	[illegible]	[illegible]
Low[d]	1.11 (1.04–1.18)	[illegible]	[illegible]

Analyses with body mass index	Risk of wheeze		
	Rhinitis population	Non-r[illegible]	Interaction[b]
	OR[a] (CI)	OR[a] [illegible]	*p*-value
Body mass index			
<18.5 kg/m^2	1.20 (1.00–1.44)	0.89 (0.66–1.18)	
18.5–<25 kg/m^2	Reference	Reference	
25–<30 kg/m^2	1.16 (1.10–1.23)	1.22 (1.13–1.31)	
>30 kg/m^2	1.58 (1.47–1.71)	1.87 (1.72–2.05)	0.02[c]
S-Triglycerides			
Normal[d]	Reference	Reference	
High[d]	1.18 (1.10–1.26)	1.30 (1.20–1.41)	0.03
S-HDL			
Normal[d]	Reference	Reference	
Low[d]	1.09 (1.03–1.17)	1.23 (1.13–1.32)	0.02

With increase BMI there is increase asthma but only in those that do not have rhinitis

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In conclusion, we found that high s-TG and low s-HDL were significantly associated with the risk of wheezing in 85,555 Spanish workers and these associations persisted after adjusting in several ways for adiposity. The finding that these associations were mainly seen in individuals without rhinitis symptoms may support the notion that only specific types of asthma are associated with low-grade systemic inflammation.

Study of 351 asthma children in PR compared to 327 controls

Erick Forno, MD, MPH,a Edna Acosta-Perez, PhD, MSc,b John M. Brehm, M
Juan Celedon, MD,

	Asthma	Control
BMI	0.69 ± 1.19*	0.51 ± 1.12
PBF	0.29 ± 0.86§	0.22 ± 0.77
WC	0.03 ± 1.04§	−0.03 ± 0.95
WHR	0.001 ± 0.85	−0.001 ± 1.13
Pulmonary function tests, mean ± SD		
FEV_1 (L)	1.88 ± 0.67*	2.05 ± 0.74
FVC (L)	2.33 ± 0.82*	2.4[illegible] ± 0.88
FEV_1/FVC (%)	80.9% ± 9.0%*	83.5% ± 8.9%
Asthma severity		
No. of ED/UC visits for asthma†	10 (5-20)	NA
Severity scores, past year†		
Prednisone courses (0-4)	2 (1-2)	NA
Exercise symptoms (0-3)	1 (1-3)	NA
Missed school days (0-3)	1 (0-2)	NA
Atopy measures		
Total serum IgE level (IU/mL)†	346 (116-881)*	158 (44-600)
Allergic rhinitis (%)‖	53.6*	19.2
STR to (%)		
Dust mite	55.4*	41.6
Cockroach	39.4*	26.3

Increase obesity in asthma compared to controls

Lower FEV1

Increase allergies

J ALLERGY CLIN IMMUNOL
VOLUME 133, NUMBER 5

Conclusions:

- Adiposity indicators are associated with asthma, asthma severity/control, and atopy in Puerto Rican children.
- Atopy significantly mediates the effect of adiposity on asthma outcomes.
- Longitudinal studies are needed to further investigate the causal role, if any, of adiposity distribution and atopy on ‘‘obese asthma’’ in childhood.

J Allergy Clin Immunol 2014;133:1308-14.

Nathalie Leone[1]

Elderly????

9,059 Participants with completed respiratory questionnaire

8,020 Subjets with BMI and waist circumference measurements

7,643 Subjects with other covariates
N = 592 Prevalent asthma (7.7%)

6,915 Participants followed-up (90.5%)
Incident asthma status collected

...thma (n = 538),
...a unc... follow-up (n = 77)
...lung cance... -up (n = 33)

6,267 Participants
N = 67 Incident asthma (incidence rate: 3.0/1,000 person-year)

Followed 6,267 participants (elderly) for obesity and asthma

Obesity (2012) **20**, 628–635. doi:10.1038/oby.2011.308

Obesity (2012) **20**, 628–635. doi:10.1038/oby.2011.308

	Nonasthma *N* = 7,051	Asthma *N* = 592	*P* value[a]
	Mean ± SD or %		
Age, years	73.6 ± 4.9	73.5 ± 4.7	0.59
Women, %	60.0	62.7	0.19
Center, %			
Bordeaux	22.1	21.8	0.90
Dijon	51.2	53.9	
Montpellier	26.7	24.3	
Educational level, %			
No school or primary ± diploma[b]	32.6	33.6	0.14
Secondary without baccalaur[illegible]	30.2	26.7	
Baccalaureate or university[illegible]	37.2	39.7	
Smoking status, %			
Never	61.1	60.6	0.002
Former	33.0	36.5	
Current	5.9	2.9	
BMI, kg/m²	25.7 ± 4.0	26.1 ± 4.1	0.02
% Normal[c]	47.1	41.5	0.01
Overweight	39.8	42.6	
Obese	13.1	15.9	
Waist circumference, c[illegible]	88.7 ± 12.4	90.7 ± 12.5	<0.001
% <94/80[d]	39.7	31.6	<0.001
[94/80–102/88[	[illegible]	28.2	
≥102/88	[illegible]	40.2	
Metabolic syndrome, %[e]	[illegible]	39.1	0.25
Cardiovascular disease history, [illegible]	[illegible]	10.3	0.14
β-Blockers, %	17.6	11.3	<0.001
Dyspnea, %			
No troubled with breathlessness	45.7	26.5	<0.001
Troubled with shortness of breath when hurrying on the level ground or walking up a slight hill (strenuous exercise)	43.3	46.1	
Walks slower than people of the same age on the level ground because breathlessness	9.4	20.0	
Breathlessness when dressing or undressing or at rest	1.6	7.4	

Increase in BMI correlated with increase in asthma

Increase in waist circumference correlates with increase of asthma

Obesity (2012) 20, 628–635. doi:10.1038/oby.2011.308

In patients with the mean age of 72 years with asthma compared to without asthma there is:

1. Increase BMI
2. Increase waist size
3. Increase obesity
4. Increase dyspnea

	Nonasthma $N = 7,051$	Asthma $N = 592$	*P* value[a]
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% <94/80[d]	39.7	31.6	<0.001
[94/80–102/88[	29.2	28.2	
≥102/88	31.1	40.2	
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To conclude, abdominal overweight and obesity were found to be independently and strongly related to asthma prevalence and incidence in a large population-based study in the elderly. Given the parallel increase in the prevalence of elderly persons and of abdominal obesity in industrialized countries, an increasingly obese elderly population will undoubtedly require more attention by researchers and clinicians. Studies aiming to understand the origin of late-onset asthma and the mechanisms involved in the obesity–asthma link are needed.

Visceral adipose tissue secretes inflammatory mediations and results in which of the following?

- 1. Decrease levels of Leptin
- 2. Increase levels of adiponectin
- 3. Increase sputum eosinophils
- 4. Increase TNF, IL-1, IL-6 and IL-8

- Answer:

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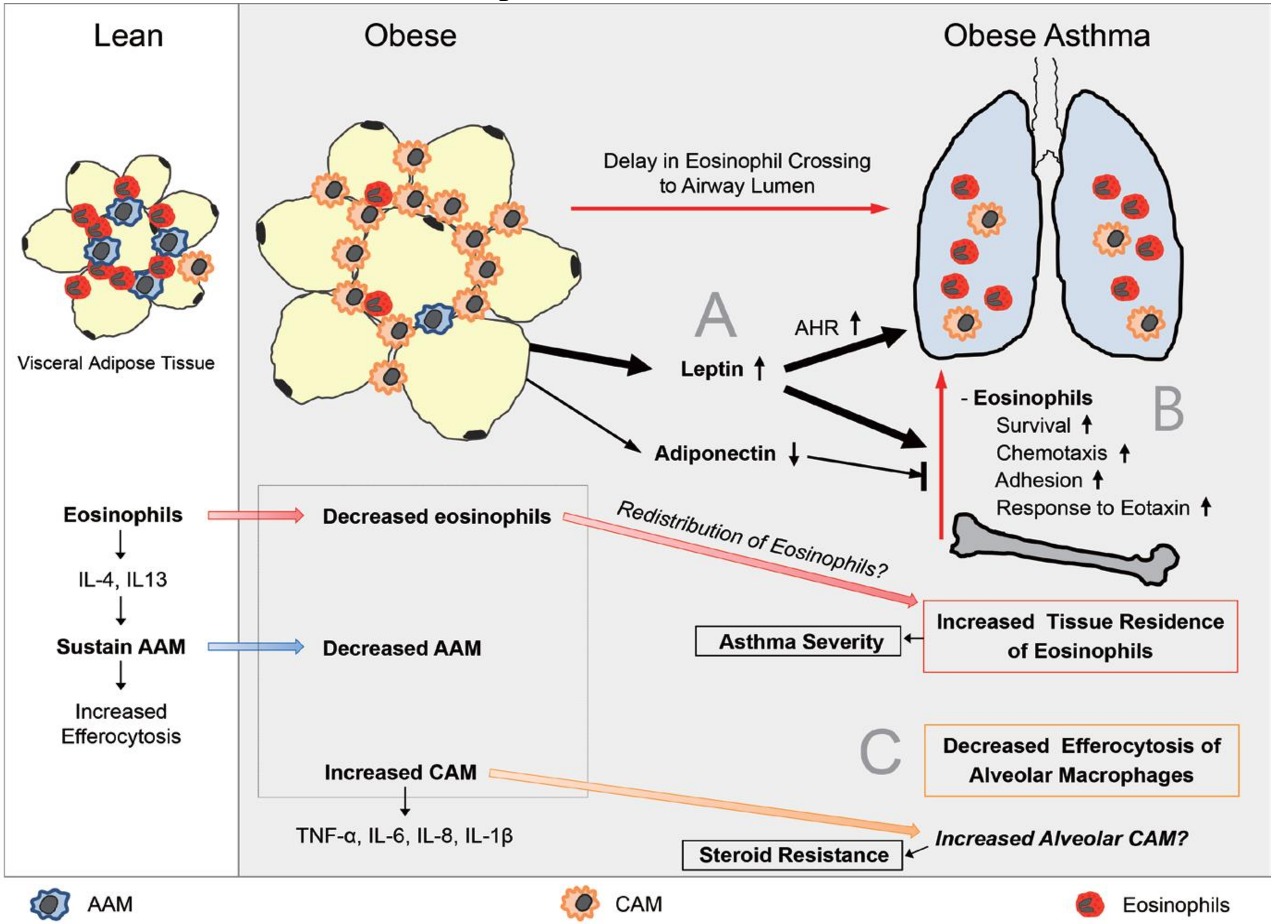
- Answer: 4

Obesity and Asthma



Allergy Asthma Immunol Res. 2014 May;6(3):189-195.

Sutherland- summary of asthma and obesity

Table 1. Notable characteristics of asthma in obese individuals

- In epidemiological studies, obesity significantly increases the risk for asthma.
- Obesity alters lung physiology in ways that mimic asthma, possibly confounding clinical evaluation of obese patients with respiratory symptoms.
- A substantial body of literature has identified potential inflammatory pathways by which obesity increases asthma risk, including increased allergic sensitization and airway hyperresponsiveness, redistribution of lung eosinophils, altered macrophage phenotype and function, and neurogenic pathways.
- Obese asthmatics have increased healthcare use and worsened health status.
- Cluster analyses have identified a number of important characteristics that differ between obese and lean asthmatics, including symptom severity, airway inflammation, age of asthma onset, sex, and treatment responsiveness.
- Both adult and pediatric studies indicate that obese asthmatics are less responsive to glucocorticoids, the mainstay of asthma controller therapy.
- Small studies have suggested that weight loss improves clinical and physiologic aspect of asthma, although the impact of weight loss on inflammatory pathways remains unknown.

Ann. N.Y. Acad. Sci. 1311 (2014) 31–41

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- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
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- What we need to do

The correlation of sleep apnea and asthma is mainly in?

- 1. men
- 2. females
- 3. children
- 4. independent of BMI

The correlation of sleep apnea and asthma is mainly in?

- 1. men
- 2. females
- 3. children
- 4. independent of BMI

- Answer: 2

Obstructive sleep apnea and asthma: Associations and treatment implications

Bharati Prasad[a,b,*], Sharmilee M. Nyenhuis[a], Terri E. Weaver[b]

Sleep Medicine Reviews 18 (2014) 165–171

Asthma and sleep apnea

B. Prasad et al. / Sleep Medicine Reviews 18 (2014) 165–171

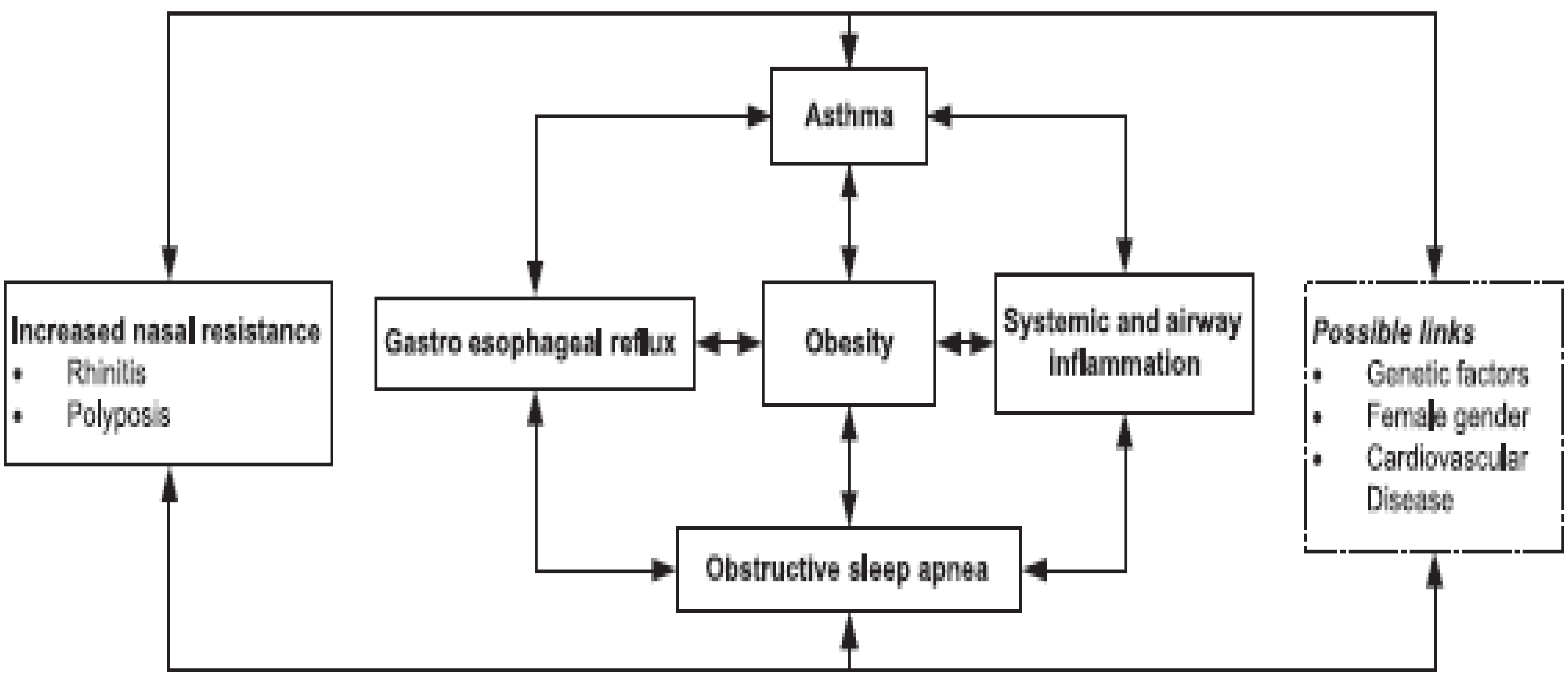


Fig. 1. Obstructive sleep apnea and asthma: pathophysiologic links.

Table 1
Selected studies on the association of OSA and asthma published in the last five years.

Study/year	Study design/sample (n)	Measurement of OSA and asthma	Result
Bhattacharya et al., 2012[101]	Cross-sectional/adult OSA related office visits to otorhinolaryngologist (4.1 ± 1.2 million visits)	OSA and asthma: International Classification of Diseases, Ninth Revision (ICD-9) codes	Increased risk for asthma (*OR 2.7; CI 1.6, 4.6) in OSA
Teodorescu et al., 2012[64]	Cross-sectional/adult asthma referral population (752)	OSA: SA-SDQ Asthma: frequency of daytime and nighttime symptoms (NAEPP classificatio[illegible]	Increased OSA risk with persistent daytime (OR 1.9; CI 1.3, 2.9) and nighttime (*OR 1.9; CI 1.3, 2.9) symptoms of asthma
Williams et al., 2011[102]	Cross-sectional/women before and during pregnancy (1335)	OSA: habitual snorin[illegible] Asthma: self-report [illegible]	Increased OSA risk in asthmatics [illegible]oth before (*OR 2.1; CI 1.1, 4.1) [illegible]d during (*OR 1.79; CI 1.1, 3) pregnancy
Teodorescu et al., 2010[2]	Cross-sectional/adult asthma referral population (472)	OSA: SA-SDQ Asthma control qu[illegible]	[illegible]thmatics at high risk for OSA had [illegible]creased risk for poorly-controlled asthma (*OR 2.9; CI 1.5, 5.3)
Alharbi et al., 2009[9]	Cross-sectional/OSA referral population (606)	OSA: AHI > 5/hou[illegible] Asthma: self-report of p[illegible]ma	35% prevalence of asthma, body mass i[illegible](BMI) was a significant predictor ([illegible]2.1; CI: 1.7, 2.4)
Teodorescu et al., 2009[13]	Cross-sectional/asthma referral population (244)	OSA: SA-SDQ Asthma: symptoms (NAEPP classification)	Predictor[illegible] high OSA risk in asthma were female gender (*OR 2.1; CI: 1.1, 4.0), asthma severity (*OR 1.6; CI: 1.2, 2.0), GERD (*OR 2.7; CI: 1.5, 4.8), use of ICS (*OR 4.0; CI: 1.5, 10.5)
Auckley et al., 2008[1]	Cross-sectional/asthma clinic population (177) vs. general medicine clinic population (GMC; 328)	OSA: Berlin sleep questionnaire Asthma: pulmonologist diagnosed, severity assessed by spirometry GMC: participants with history of OSA and asthma excluded	High OSA risk was more prevalent in asthma vs. GMC population (39.5% vs. 27.2%, @p = 0.004)

The OSA and asthma correlation was mainly in females

Sleep Medicine Reviews 18 (2014) 165–171

Practice points

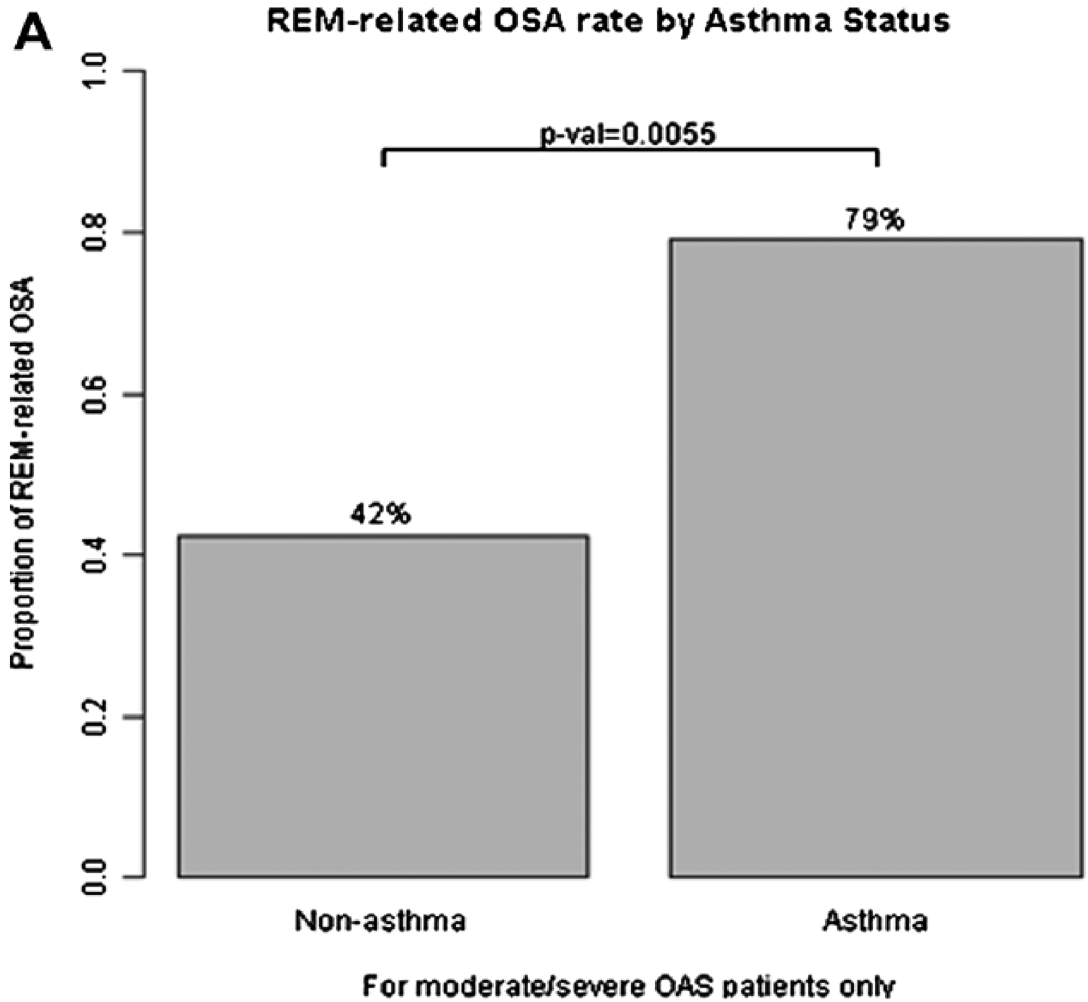
1) Obstructive sleep apnea (OSA) and asthma are highly prevalent respiratory disorders that frequently overlap in patients.
2) A high index of suspicion is warranted for overlap of OSA and asthma, particularly in the presence of obesity, rhinitis, gastroesophageal reflux (GER), and in patients poorly responsive to therapy.
3) Individualized therapy addressing moderating factors such as weight gain, GERD, nasal obstruction, and cardiovascular disease is warranted for optimal outcomes.

Sleep Medicine Reviews 18 (2014) 165–171

Nocturnal Phenotypical Features of Obstructive Sleep Apnea (OSA) in Asthmatic Children

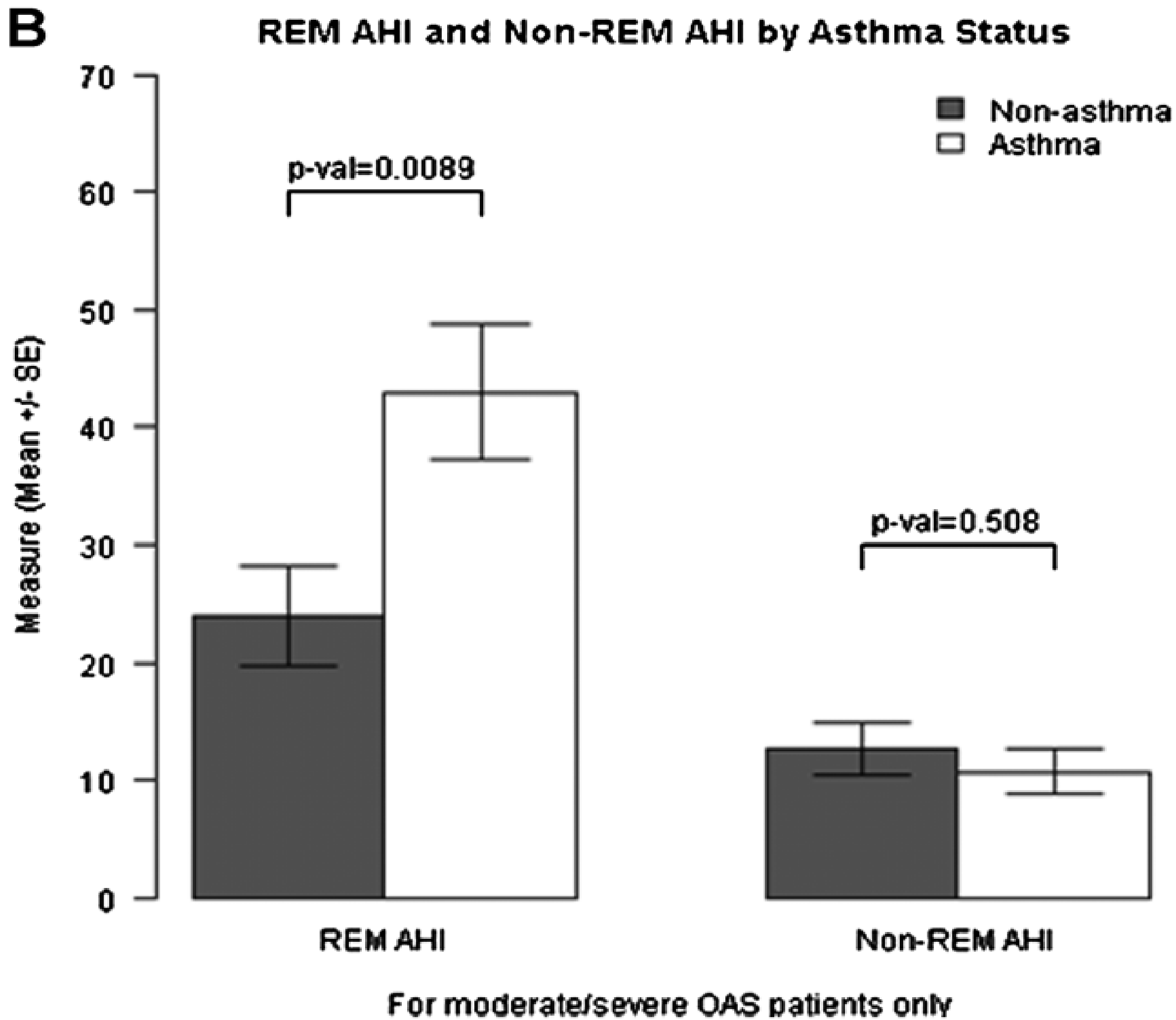
Maria J. Gutierrez, MD,[1,2] Junjia Zhu, PhD,[3] Carlos E. Rodriguez-Martinez, MD, MSc,[4,5,6] Cesar L. Nino, PhD,[7] and Gustavo Nino, MD[2,8*]

Moderate to severe OSA patients and the proportion with REM-related OSA



Pediatric Pulmonology 48:592–600 (2013)

AHI in and out of REM sleep in patients with OSA with and without asthma



Pediatric Pulmonology 48:592–600 (2013)

TABLE 4—Effect of Atopy and Rhinitis on REM-Related Breathing Abnormalities in Asthmatic Children

	Co-variables in asthmatic children with OSAS		
	Yes (n = 9)	No (n = 53)	*P*-value
Atopy			
Max% REM SAO2 desaturation mean (SE)	14.2 (1.2)	11.7 (0.8)	0.251
REM AHI mean (SE)	27.5 (10.6)	20.4 (3.3)	0.435
Non-REM AHI mean (SE)	3.9 (1.2)	5.3 (1.1)	0.381

	Co-variables in asthmatic children with OSAS		
	Yes (n = 33)	No (n = 29)	*P*-value
Rhinitis			
Max% REM SAO2 desaturation mean (SE)	11.7 (1.4)	12.4 (1.0)	0.654
REM AHI mean (SE)	24.3 (5.0)	19.7 (3.7)	0.234
Non-REM AHI mean (SE)	5.69 (1.3)	4.38 (1.3)	0.482

Pediatric Pulmonology 48:592–600 (2013)

sion: These results demonstrate that asthma is associated with REM-related breathing abnormalities in children with moderate–severe OSA. The link between asthma and REM-related OSA is independent of asthma control and obesity. Further research is needed to delineate the REM-sleep biological mechanisms that modulate the phenotypical expression of OSA in asthmatic children. **Pediatr Pulmonol. 2013; 48:592–600.**

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The true statement about obesity and rhinitis is?

- 1. no correlation
- 2. In obesity there is an increase in allergic rhinitis
- 3. In obesity there is an increase in chronic rhinosinusitis and allergic rhinitis
- 4. In obesity there is an increase in chronic rhinosinusitis

- Ans:

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- Ans: 3

Associations Between Obesity and Inflammatory Sinonasal Disorders

Neil Bhattacharyya, MD, FACS

Objectives/Hypothesis: Determine whether adult obesity is associated with chronic rhinosinusitis (CRS) and/or allergic rhinitis (AR).

Study Design: Cross-sectional analysis of medical panel survey.

Methods: The Medical Expenditure Panel Survey, a large-scale household-based survey of health care utilization in the United States (2008 and 2010) was examined, identifying adult cases of CRS and AR. The presence or absence of obesity (body mass index $\geq$ 30 kg/m^2) was determined. Adjusting for age, sex, race, geographic region, insurance coverage, and Charlson Comorbidity Index, odds ratios for the presence of CRS and/or AR in the presence of obesity were determined. The relations between body mass index as a linear variable and the presence of CRS and AR were determined.

Results: A total of 17.6 ± 0.6 million adults reported AR (7.7% ± 0.3%) and 13.0 ± 0.5 million reported CRS (5.7% ± 0.2%; weighted estimates). Additionally, 64.9 ± 1.4 million adults (29.0% ± 0.4%) were classified as obese based on body mass index. The adjusted odds ratio for AR when obesity was present was 1.22 (P <.001, 95% confidence interval = 1.12–1.33). The adjusted odds ratio for CRS when obesity was present was 1.31 (P <.001, 95% confidence interval = 1.18–1.45). Increasing body mass index as a continuous variable was significantly associated with the presence of both AR (odds ratio = 1.023, P <.001) and CRS (odds ratio = 1.022, P <.001).

Conclusions: The current data demonstrate an increased prevalence of adult obesity associated with both AR and CRS.

Key Words: Obesity, epidemiology, chronic rhinosinusitis, allergic rhinitis, prevalence, body mass index.

Level of Evidence: 2b

***Laryngoscope*, 123:1840–1844, 2013**

Associations Between Obesity and Inflammatory Sinonasal Disorders

ACS

17 million adults with allergic rhinitis and 13 million adults with chronic rhino-sinusitis. Also 64 million adults with obesity

Objectives/Hyp … ronic rhinosinusitis (CRS) and/or allergic rhinitis (AR).

Study Design: C …

Methods: The Me … sed survey of health care utilization in the United States (2008 and … and AR. The presence or absence of obesity (body mass index ≥ 30 kg/m … race, geographic region, insurance coverage, and Charlson Comorbidity Index, odds ra … /or AR in the presence of obesity were determined. The relations between body mass index as … variable and the presence of CRS and AR were determined.

Results: A total of 17.6 ± 0.6 … illion adults reported AR (7.7% ± 0.3%) and 13.0 ± 0.5 million reported CRS (5.7% ± 0.2%; weighted estimates). Additionally, 64.9 ± 1.4 million adults (29.0% ± 0.4%) were classified as obese based on body mass index. The adjusted odds ratio for AR when obesity was present was 1.22 (P < .001, 95% confidence interval = 1.12–1.33). The adjusted odds ratio for CRS when obesity was present was 1.31 (P < .001, 95% confidence interval = 1.18–1.45). Increasing body mass index as a continuous variable was significantly associated with the presence of both AR (odds ratio = 1.023, P < .001) and CRS (odds ratio = 1.022, P < .001).

Conclusions: The current data demonstrate an increased prevalence of adult obesity associated with both AR and CRS.

Key Words: Obesity, epidemiology, chronic rhinosinusitis, allergic rhinitis, prevalence, body mass index.

Level of Evidence: 2b

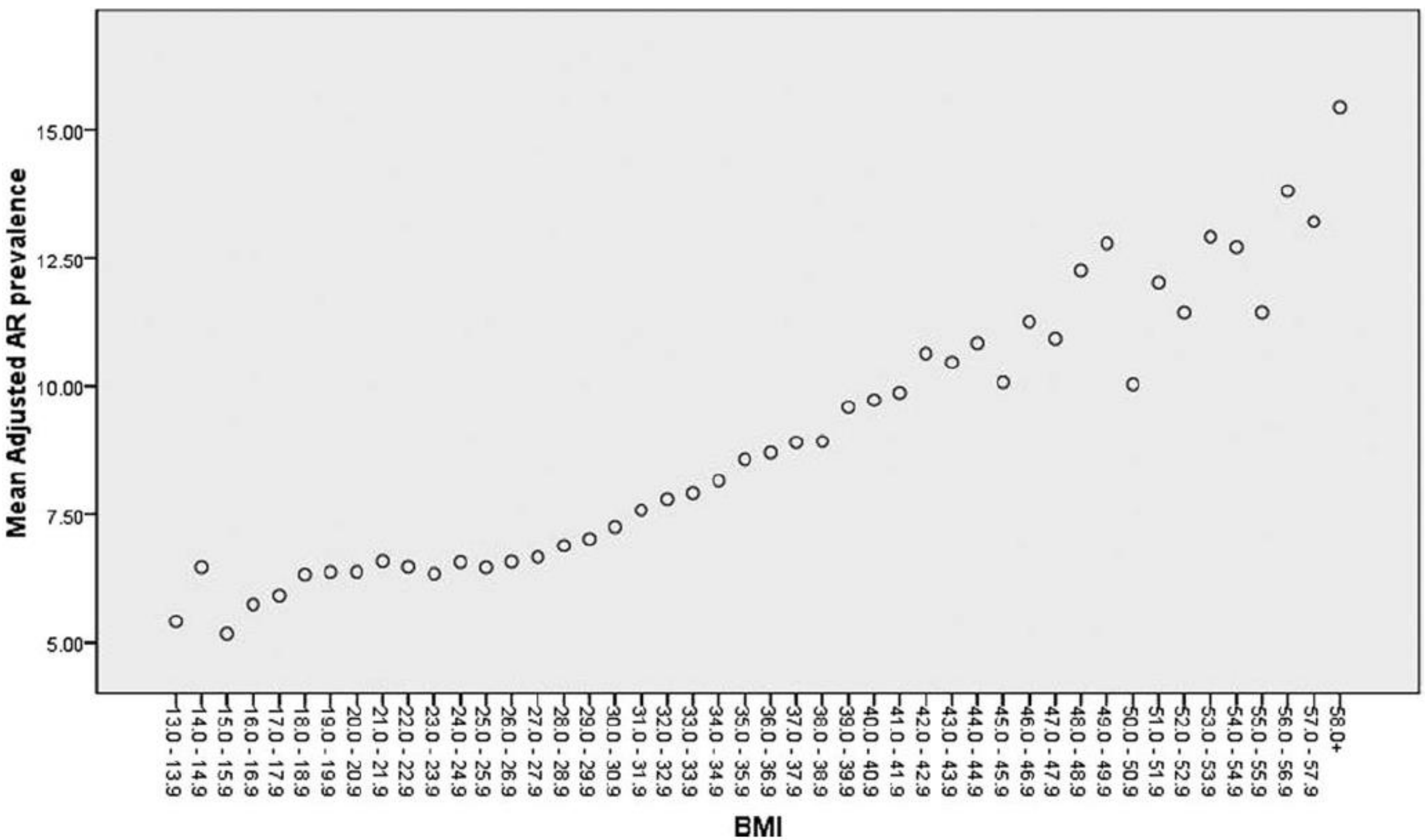
***Laryngoscope*, 123:1840–1844, 2013**

Multivariate Analysis Results for the Association Between Obesity and Allergic Rhinitis and Chronic Rhinosinusitis.

	Allergic Rhinitis			Chronic Rhinosinusitis		
Characteristic	Odds Ratio	95% CI	*P*	Odds Ratio	95% CI	*P*
Obese	1.218	1.117–1.328	<.001	1.309	1.184–1.448	<.001
Age, mean yr	1.001	0.998–1.003	.535	0.990	0.987–0.994	<.001
Gender						<.001
Male	0.601	0.550–0.657	<.001	0.538	0.482–0.601	
Female	Reference			Reference		
Race/ethnicity, %			<.001			<.001
Hispanic	0.889	0.775–1.042		0.396	0.312–0.502	
Black not Hispanic	0.614	0.521–0.723		0.484	0.396–0.592	
Asian	0.767	0.628–0.938		0.203	0.125–0.331	
Other not Hispanic	Reference			Reference		

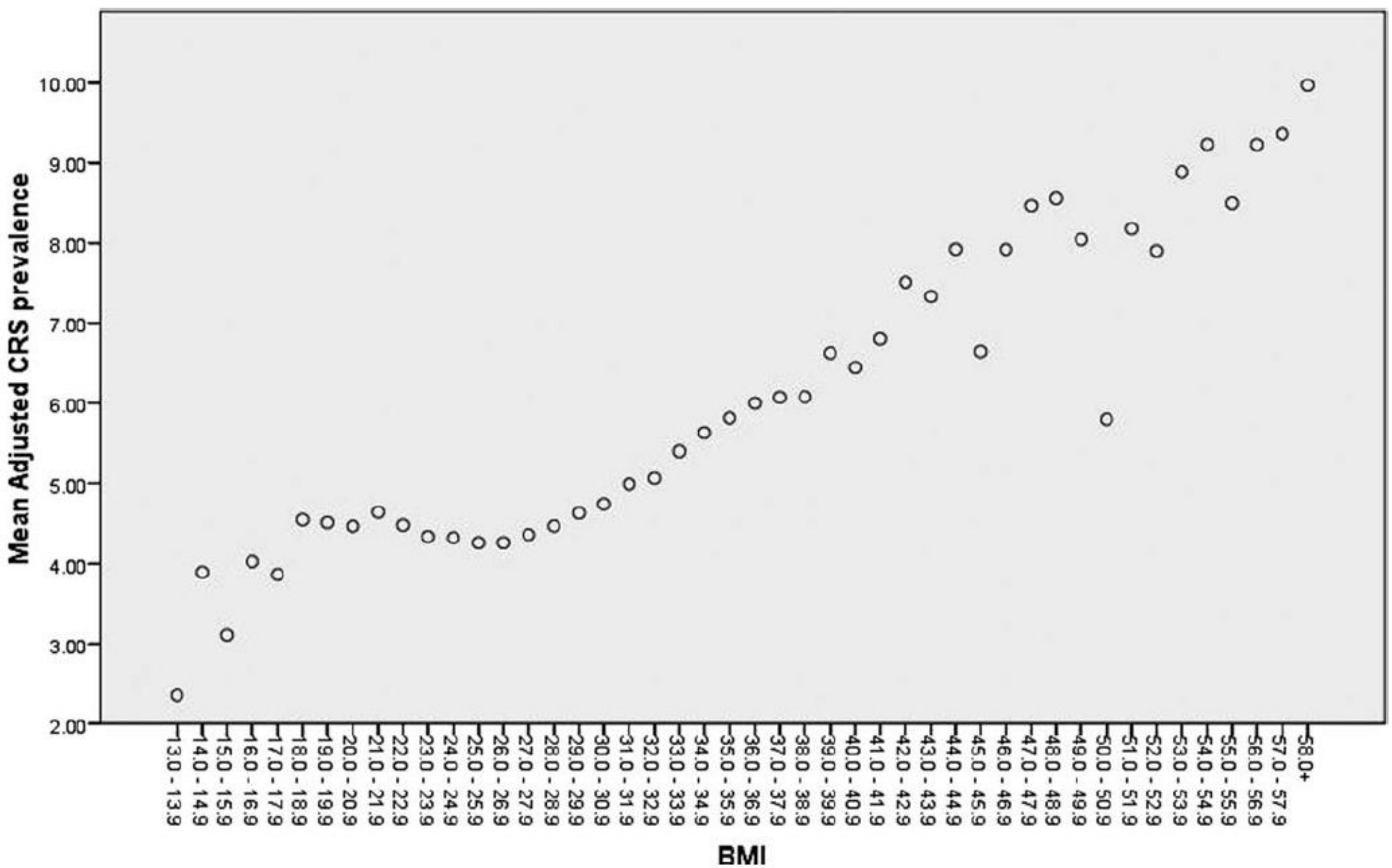
Bhattacharyya: Obesity and Sinonasal Disease

Allergic rhinitis vs. BMI



Bhattacharyya: Obesity and Sinonasal Disease

Chronic rhinosinusitis vs. BMI



Bhattacharyya: Obesity and Sinonasal Disease

CONCLUSION

The current data demonstrate an increased prevalence of obesity in the setting of CRS or ARS. Given the current findings, further research is warranted to determine if a potential causal relation between obesity and AR and CRS exists, especially given the projected future population demographics with respect to overweight and obese patients in the United States.

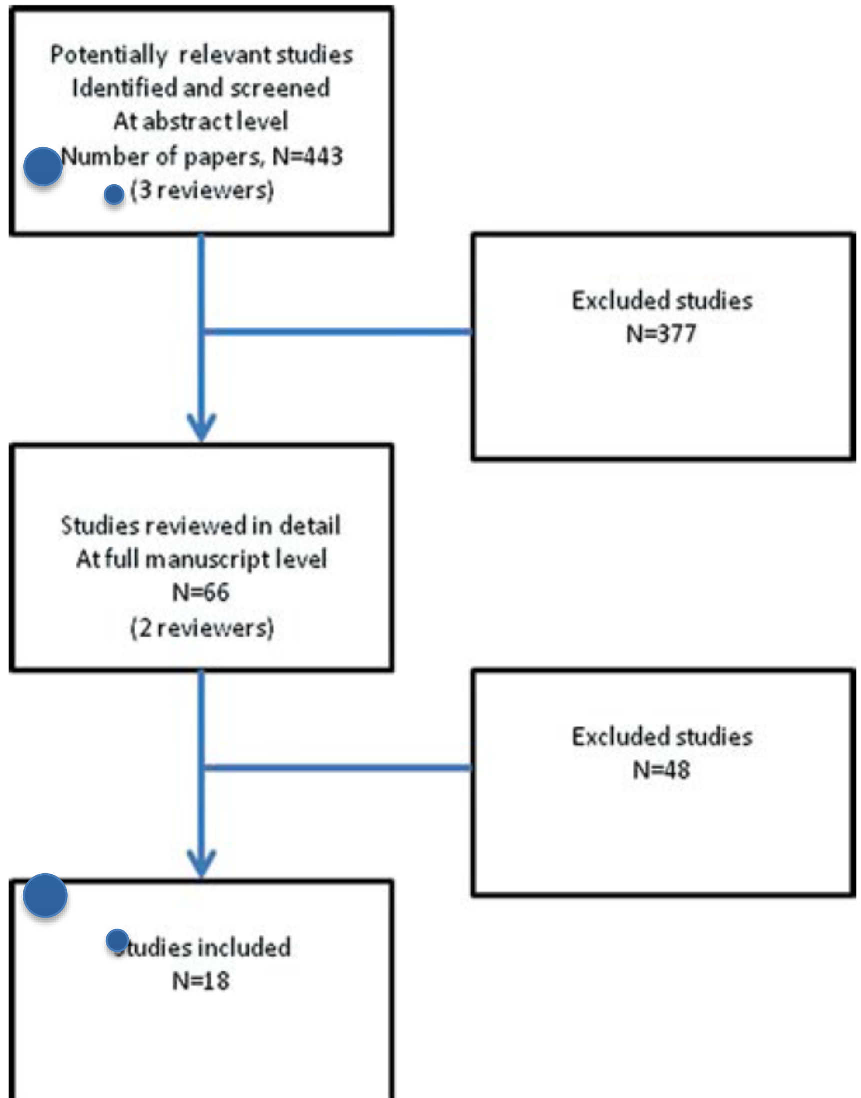
Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do

Lin SY, Melvin TA, Boss EF, Ishman SL. The association between allergic rhinitis and sleep-disordered breathing in children: a systematic review. *Int Forum Allergy Rhinol*, 2013; 3:504-509.

Lin SY, Melvin TA, Boss EF, Ishman SL. The association between allergic rhinitis and sleep-disordered breathing ...dren: a systematic review. *Int Forum Allergy Rhinol*, ...04-509.

Reviewed 443 manuscripts



18 articles met quality to include in the meta-analysis

Lin SY, Melvin TA, Boss EF, Ishman SL. The association between allergic rhinitis and sleep-disordered breathing in children: a systematic review. *Int Forum Allergy Rhinol*, 2013; 3:504-509.

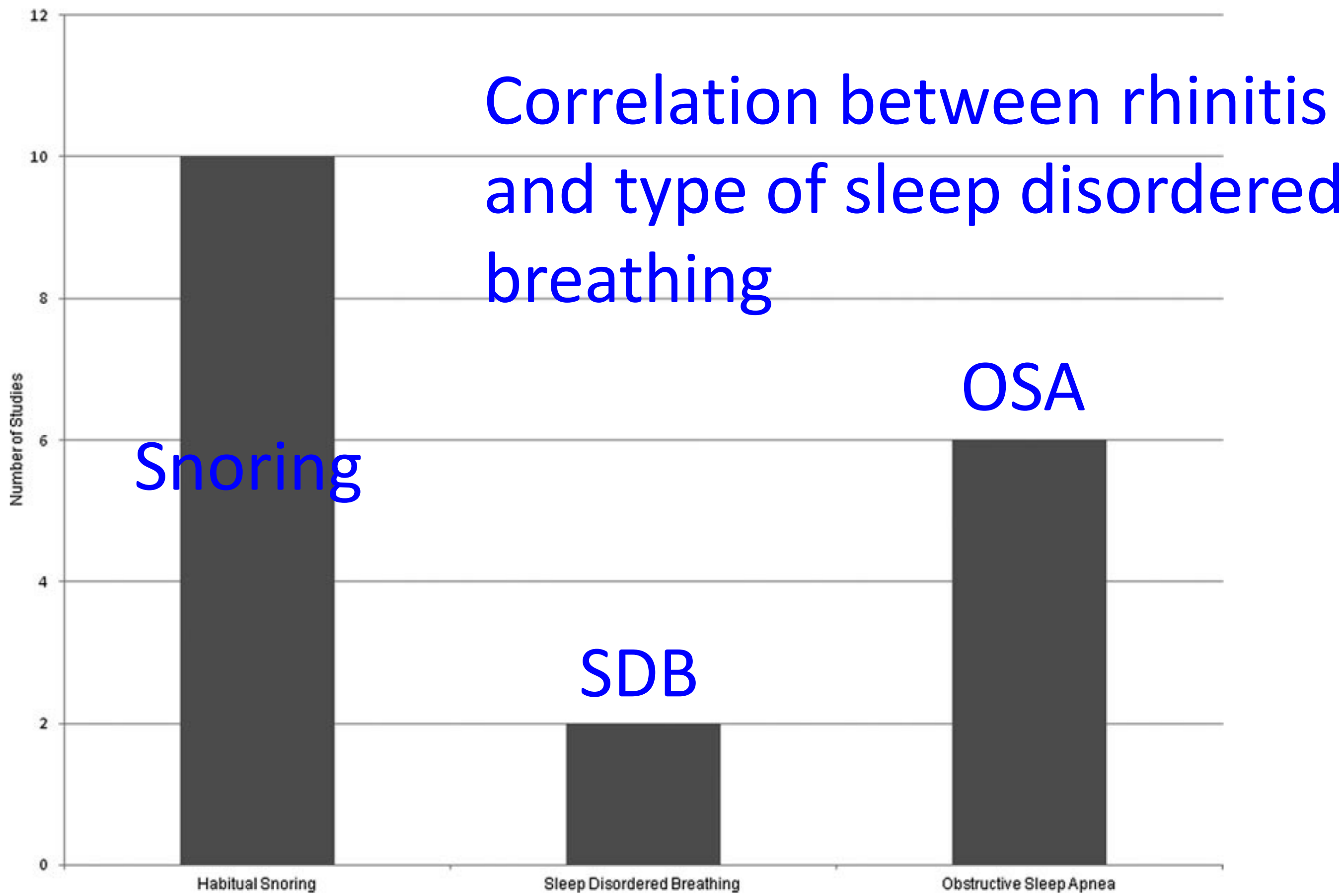


FIGURE 2. Sleep disorders assessed in included studies.

Lin SY, Melvin TA, Boss EF, Ishman SL. The association between allergic rhinitis and sleep-disordered breathing in children: a systematic review. *Int Forum Allergy Rhinol*, 2013; 3:504–509.

This report represents the first systematic review of existing literature on the association of AR and SDB. This review supports a correlation between AR and SDB. However, the majority of the studies included in this review had evidence Levels of 3 or 4. Further higher quality studies should be carried out in the future to better determine the relationship between AR and SDB in children.

The link between rhinitis and rapid-eye-movement sleep breathing disturbances in children with obstructive sleep apnea

Shehlanoor Huseni, M.D.,[1] Maria J. Gutierrez, M.D.,[2,3] Carlos E. Rodriguez, M.D., M.Sc.,[4,5,6]
Cesar L. Nino, Ph.D.,[7] Geovanny F. Perez, M.D.,[1] Krishna Pancham, M.D.,[1] and Gustavo Nino, M.D.[1,8]

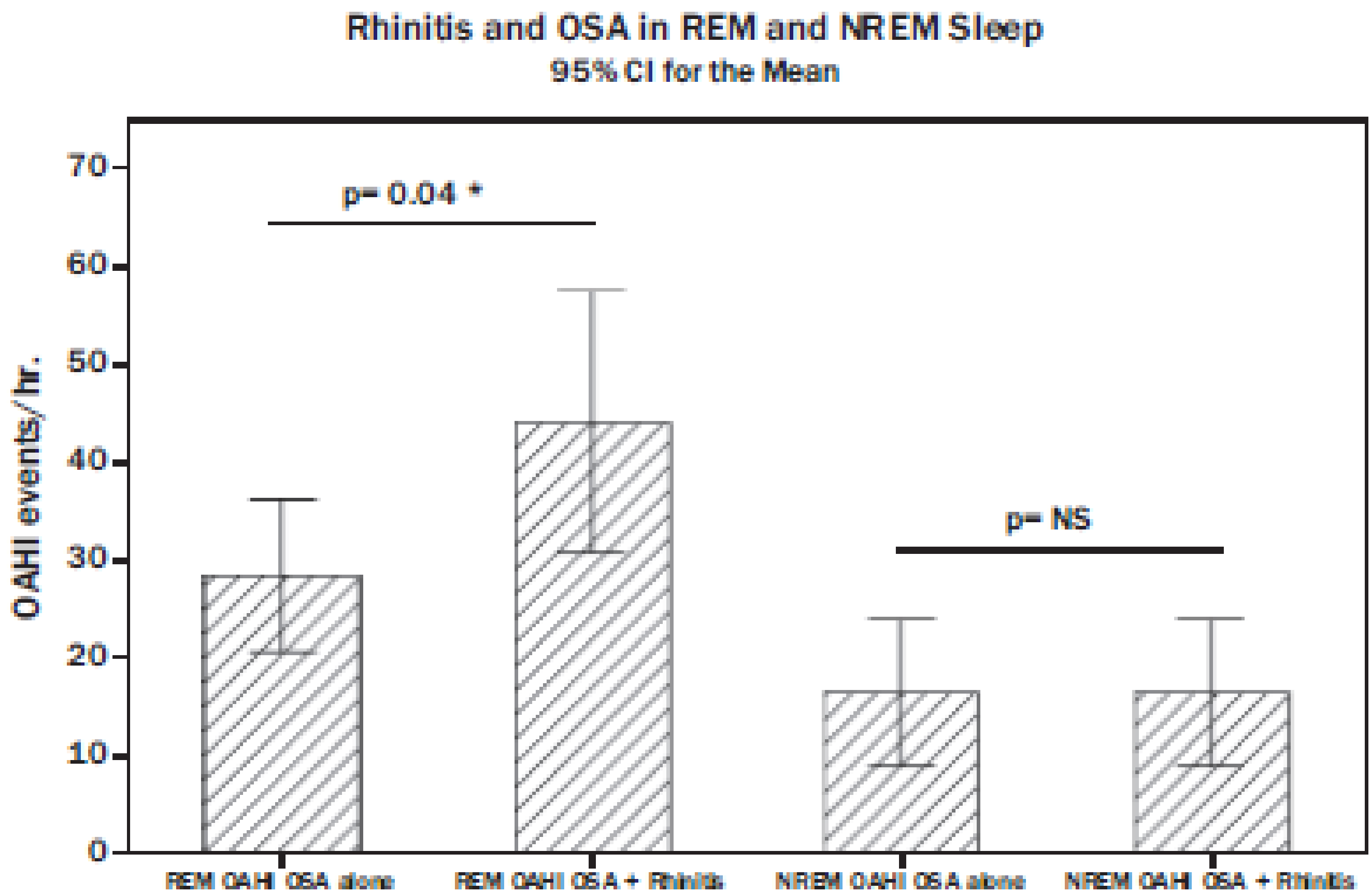
Conclusion: *Rhinitis is highly prevalent in children with OSA. Although OSA is not more severe in children with rhinitis, they do have a distinct OSA phenotype characterized by more REM-related OSA. Further research is needed to delineate the link between REM-sleep and the physiology of the nose during health and disease.*

(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)

Table 1 Demographic and polysomnographic profile of subjects

Factors/Variables	Total (n = 145)	OSA only (n = 82, 57%)	OSA with Rhinitis (n = 63, 43%)	p Value
Demographic variables				
Gender				0.57
Female	55 (38%)	34 (41%)	21 (33%)	
Male	90 (62%)	48 (59%)	42 (67%)	
Age, mean (SD)	6.26 (3.1)	6.14 (3.1)	6.4 (3.0)	0.61
Ethnicity				0.95
White	96 (62%)	55 (67%)	41 (65%)	
Other	49 (37%)	27 (33%)	22 (35%)	
BMI, mean (SD)	20.4 (6.3)	20.5 (6.3)	20.1 (6.5)	0.71
Sleep study parameters				
OSA severity				
Mean (SD) OAHI (mild)	2.62 (0.9)	2.65 (0.9)	2.58 (0.9)	0.70
Mean (SD) OAHI (moderate–severe)	18.8 (16.6)	18.04 (19)	20 (12.6)	0.61
TST, mean (SD)	518.6 (53)	515.7 (54)	522.6 (53)	0.50
TST supine, %; mean (SD)	41.0 (18.5)	44.6 (20.5)	38.8 (17)	0.24
REM (%), mean (SD)	19.6 (4.2)	19 (6)	20.1 (3.3)	0.38

(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)



(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)

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(Am J Rhinol Allergy 28, e56–e61, 2014; doi: 10.2500/ajra.2014.28.3994)

Ryan Soose

Key Points: Allergy and Sleep-Disordered Breathing

- Allergic rhinitis significantly contributes to sleep-disordered breathing through multiple mechanisms, with the greatest impact mediated primarily through nasal obstruction
- Sleep impairment is very common in patients with allergic rhinitis, chronic rhinosinusitis, and nasal polyposis, and has a significant impact on disease-specific and general health quality of life measures
- The degree of sleep disturbance is directly related to the severity of the allergic disease at a given time
- Nasal obstruction also demonstrates circadian rhythm and positional variability, with worsening in the overnight hours and in the supine position
- Nasal obstruction increases the likelihood of snoring, obstructive sleep apnea, and intolerance to medical device therapies for sleep apnea.

Otolaryngol Clin N Am 44 (2011) 625–635

Presentation Overview

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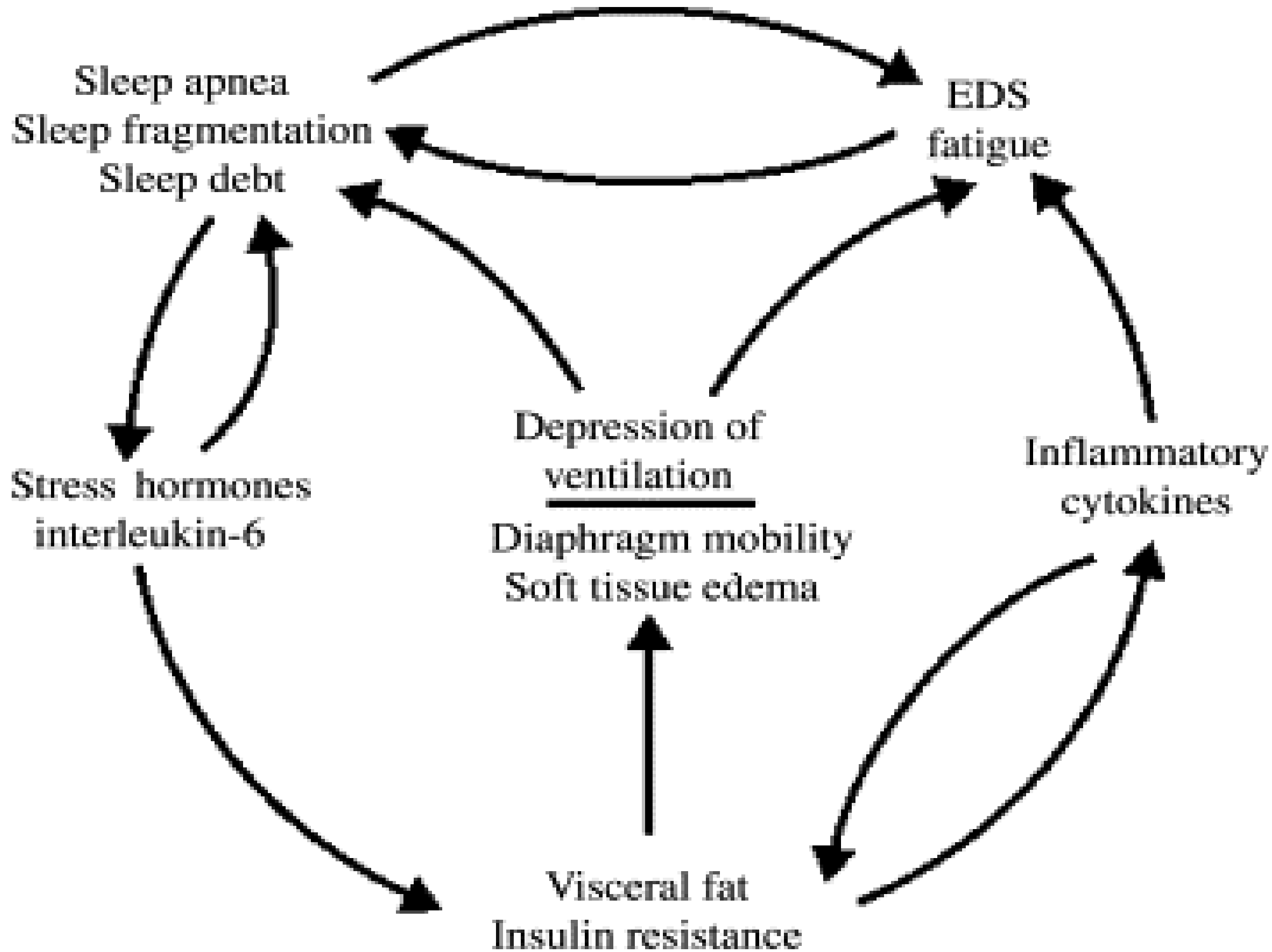
Sleep Disturbance and Inflammation



Vgontzas AN. Does obesity play a major role in the pathogenesis of sleep apnoea and its associated manifestations via inflammation, visceral adiposity, and insulin resistance?. [Review] [144 refs] [Journal Article. Review] Archives of Physiology & Biochemistry. 114(4):211-23, 2008 Oct.


YOUR GAME!

Similarities between the two

Obese man with severe OSA

- Increase in IL-1
- Increase in TNF
- Increase in Il-6
- Increase in T-helper 2 cytokines
- Decrease in T-helper 1 cytokines

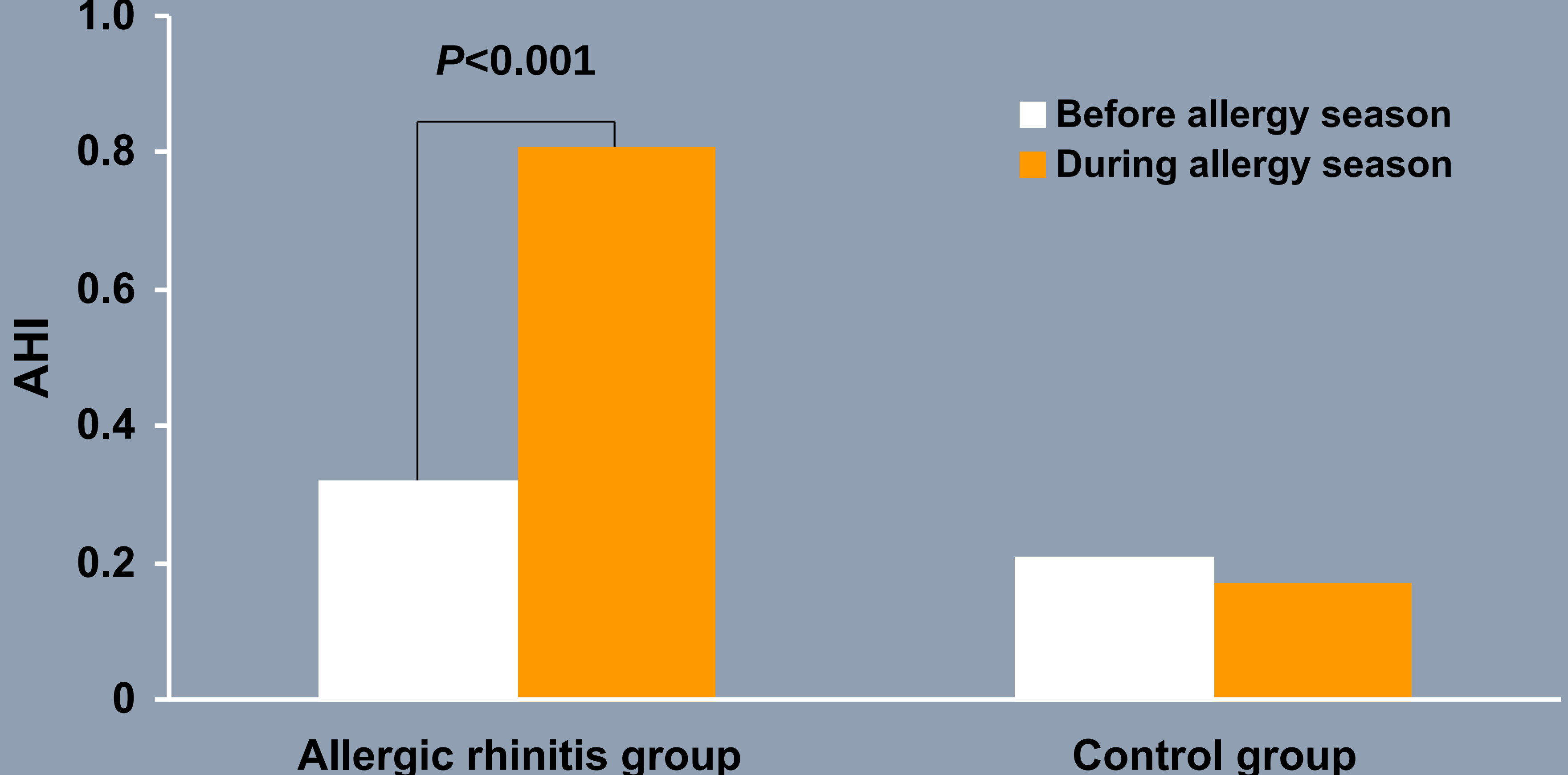
A young girl snoring and with rhinitis

- Increase in IL-1
- Increase in TNF
- Increase in Il-6
- Increase in T-helper 2 cytokines
- Decrease in T-helper 1 cytokines

Craig et al AAAI 2014

Allergic Patients Experience More Apnea/Hypopnea than Non-allergic Controls

Allergic patients had more apnea/hypopnea episodes than non-allergic controls

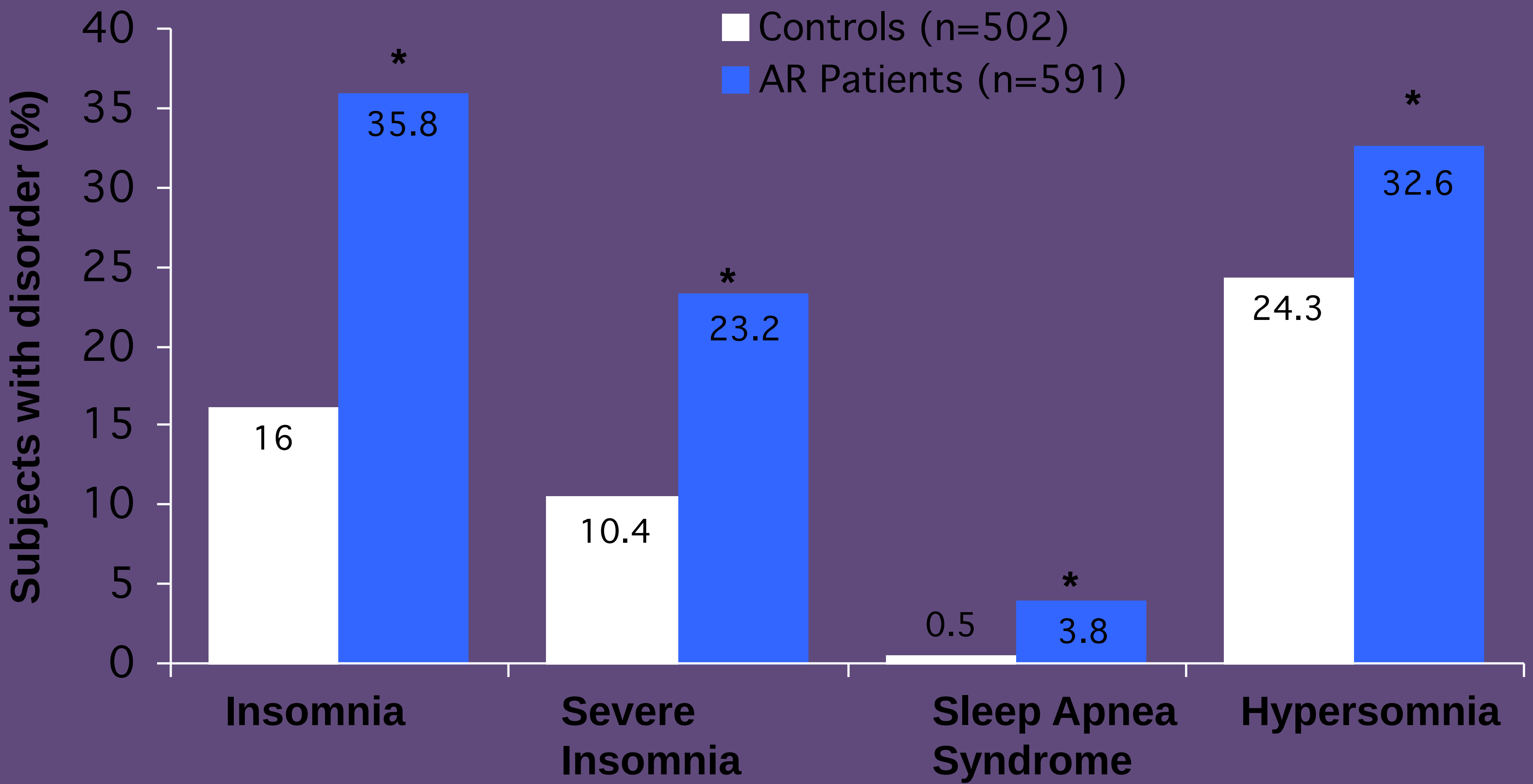


AHI=apnea/hypopnea index, determined as the total number of apnea and hypopnea episodes (assessed by polysomnography) divided by hours of sleep.

Stuck et al. *J Allergy Clin Immunol*. 2004;113:663.

Allergic Rhinitis Symptoms are Associated with *Sleep Disorders*

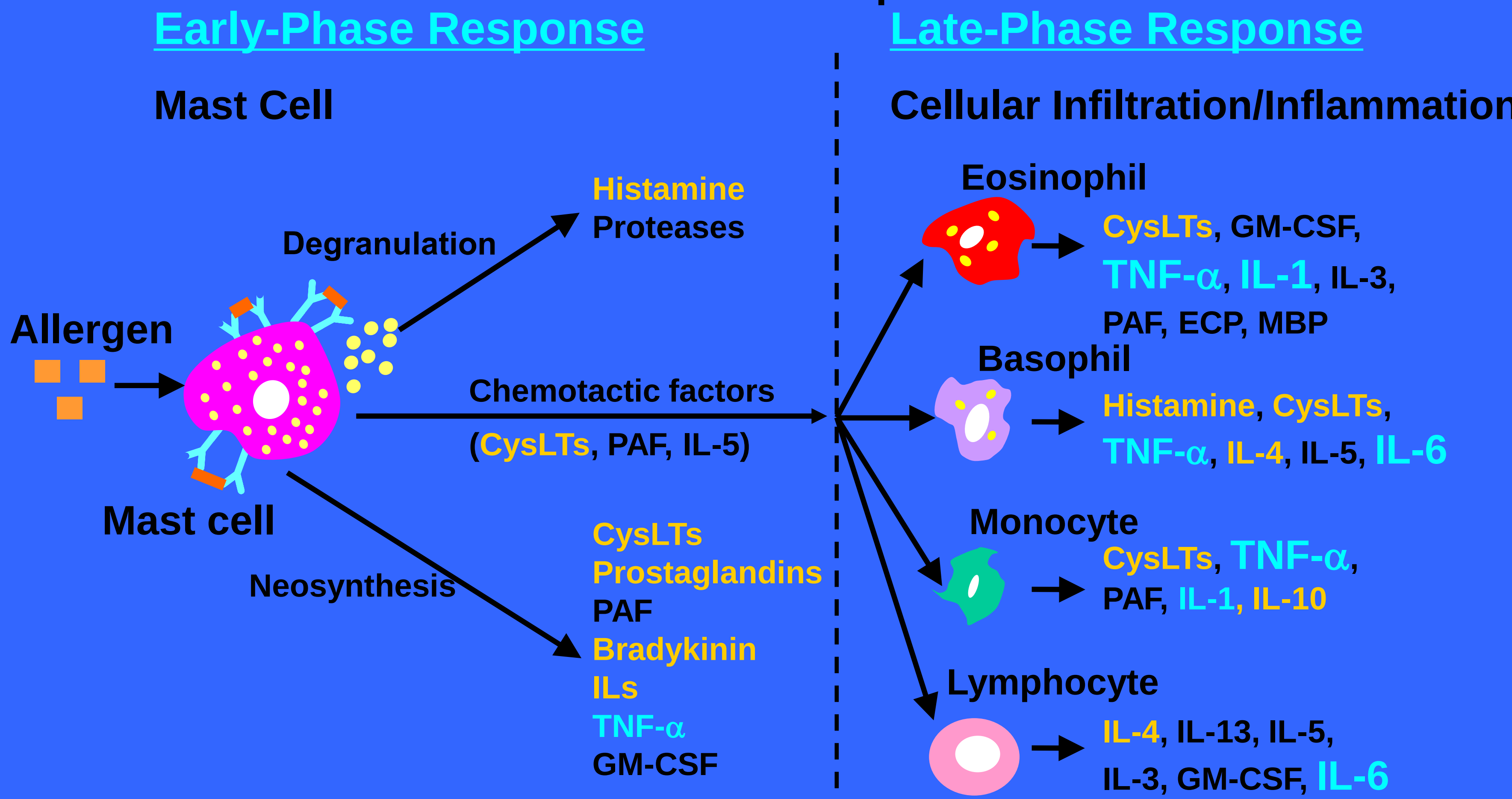
Prevalence of *Sleep Disorders* in Patients with Allergic Rhinitis and Controls



***P*≤0.003 vs controls.**

Leger et al. *Arch Intern Med.* 2006;166:1744.

Pathophysiology of Allergic Rhinitis and Impact on Sleep



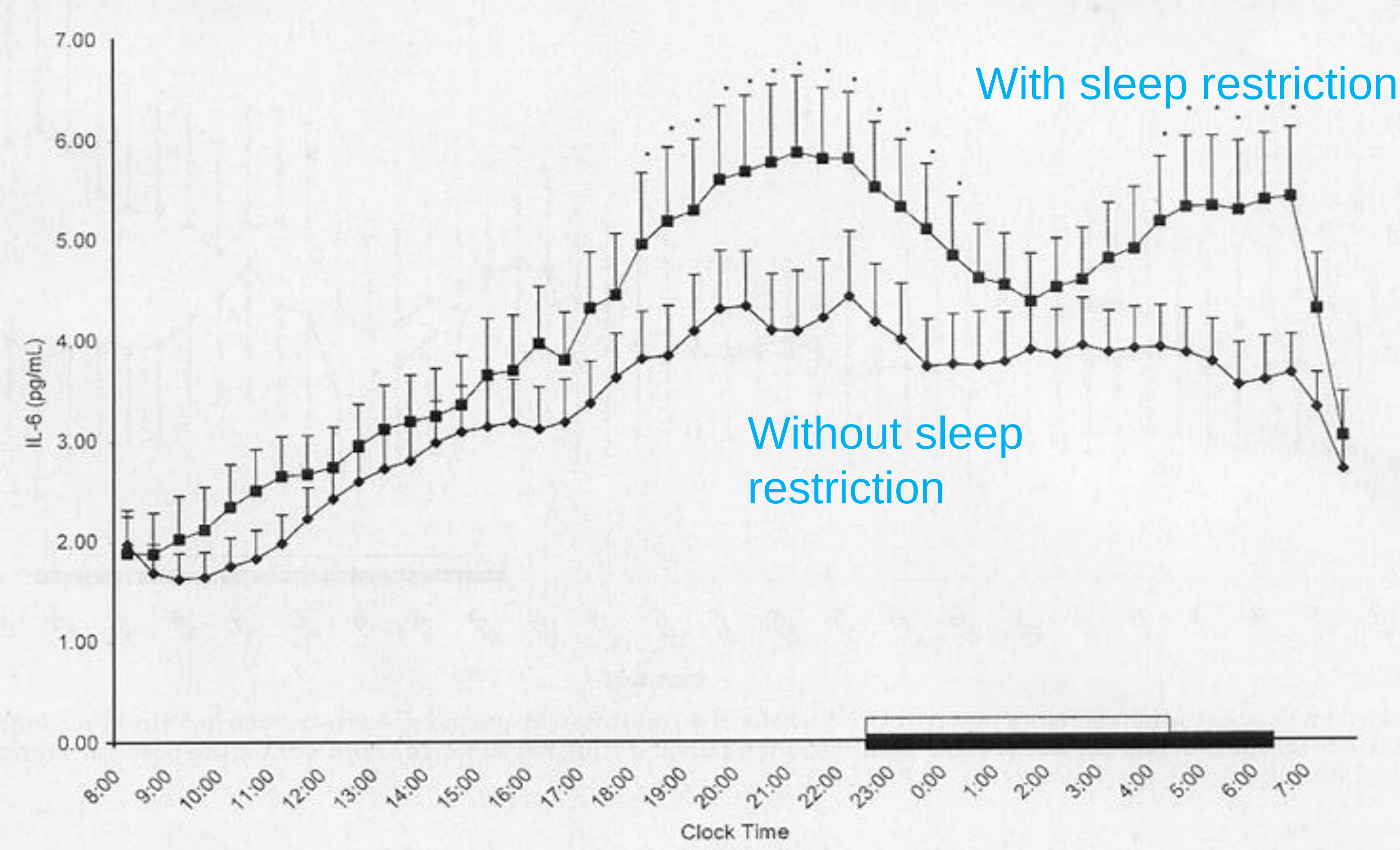
Bascom et al. *Am Rev Respir Dis*. 1988;138:406. Bascom et al. *J Allergy Clin Immunol*. 1988;81:580. Pearlman. *J Allergy Clin Immunol* 1999;104:S132. Quraishi et al. *J Am Osteopath Assoc.* 2004;104(suppl 5):S7.

Multiple Pro-Inflammatory Factors in Allergic Rhinitis Affect Sleep and Symptoms

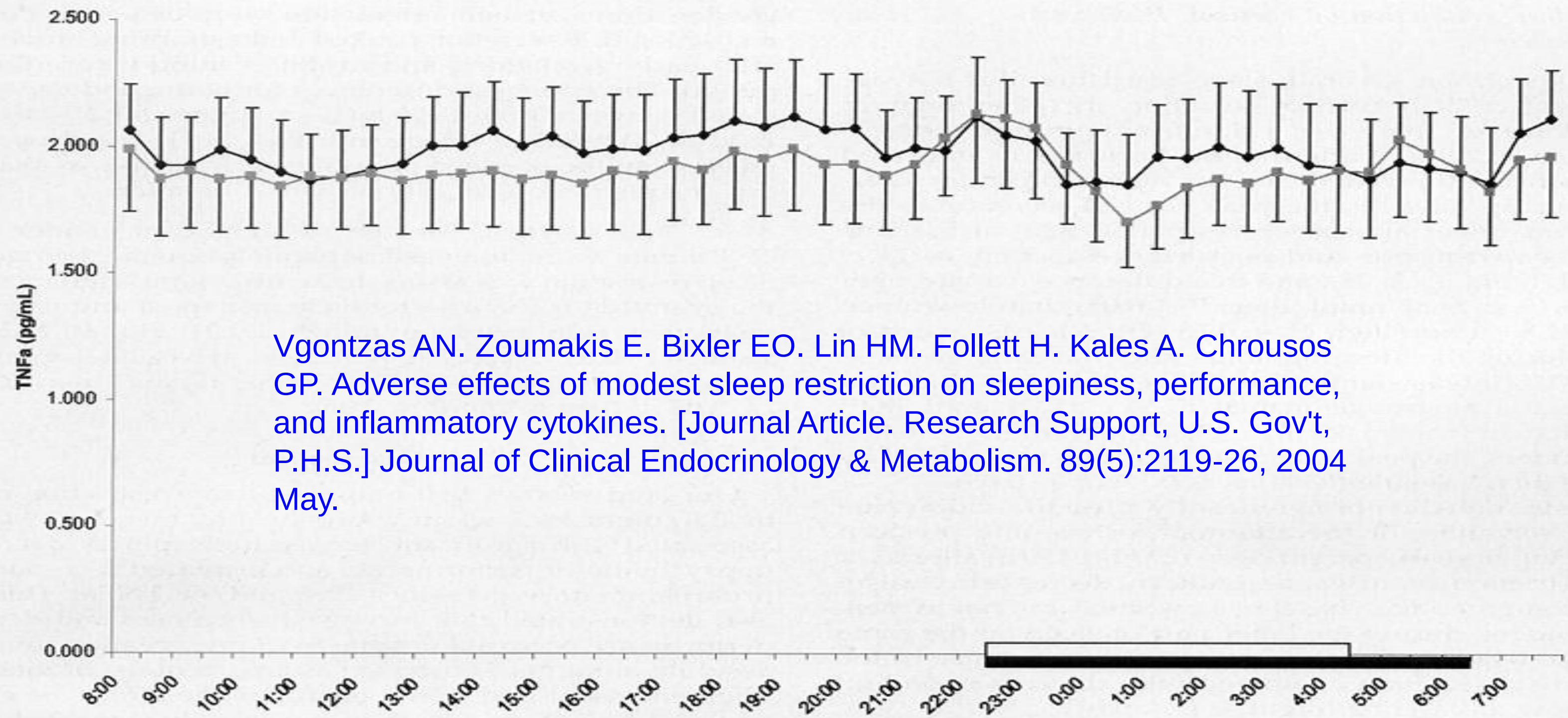
Mediator	Effect on Sleep
Histamine	Balance between wakefulness and sleep, arousal; ↑ nasal obstruction, rhinorrhea, & pruritus
CysLT	↑ Slow-wave sleep, ↑ Sleep-disordered breathing; ↑ Nasal obstruction, rhinorrhea
IL-1	↑ Latency to REM and ↓ REM duration
IL-4	
IL-10	
Bradykinin	↑ Sleep apnea; ↑ Nasal obstruction & rhinorrhea
Substance P	↑ Latency to REM, arousal; ↑ Nasal obstruction

Ferguson. *Otolaryngol Head Neck Surg*. 2004;130:617.

Effect of sleep restriction on IL-6

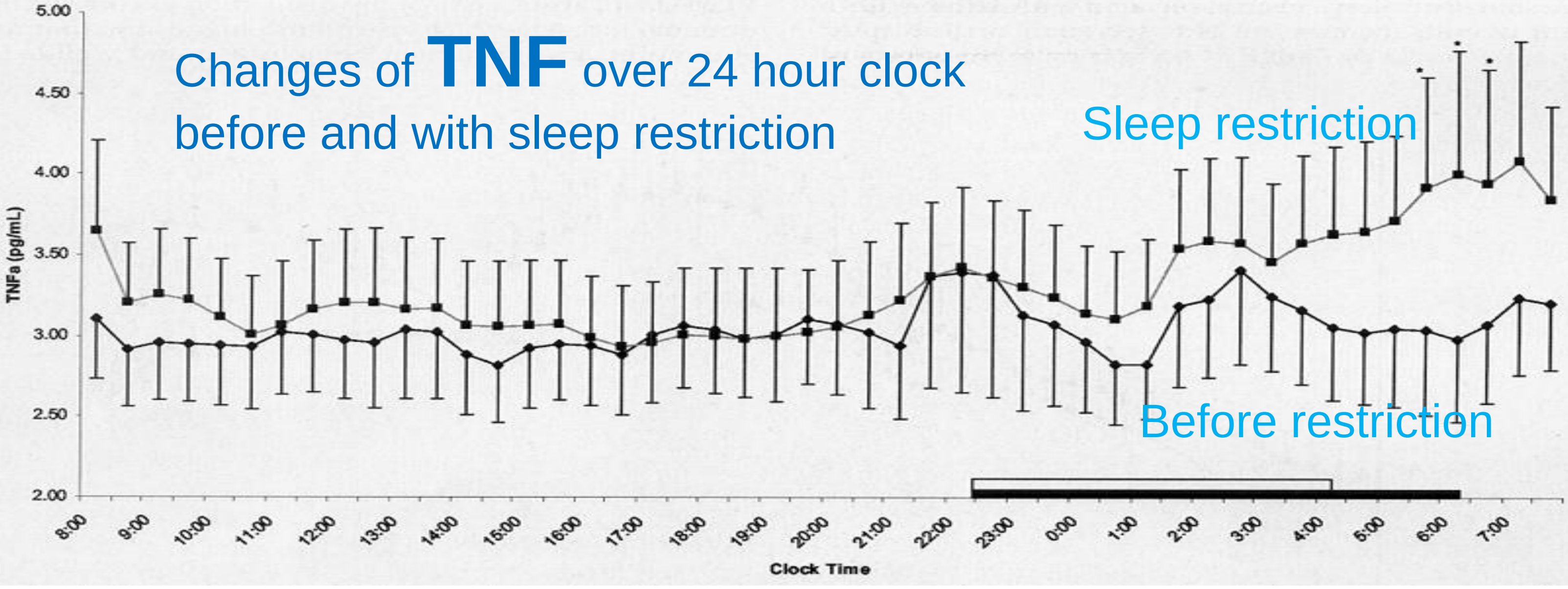


Vgontzas AN. Zoumakis E. Bixler EO. Lin HM. Follett H. Kales A. Chrousos GP. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. [Journal Article. Research Support, U.S. Gov't, P.H.S.] Journal of Clinical Endocrinology & Metabolism. 89(5):2119-26, 2004 May.



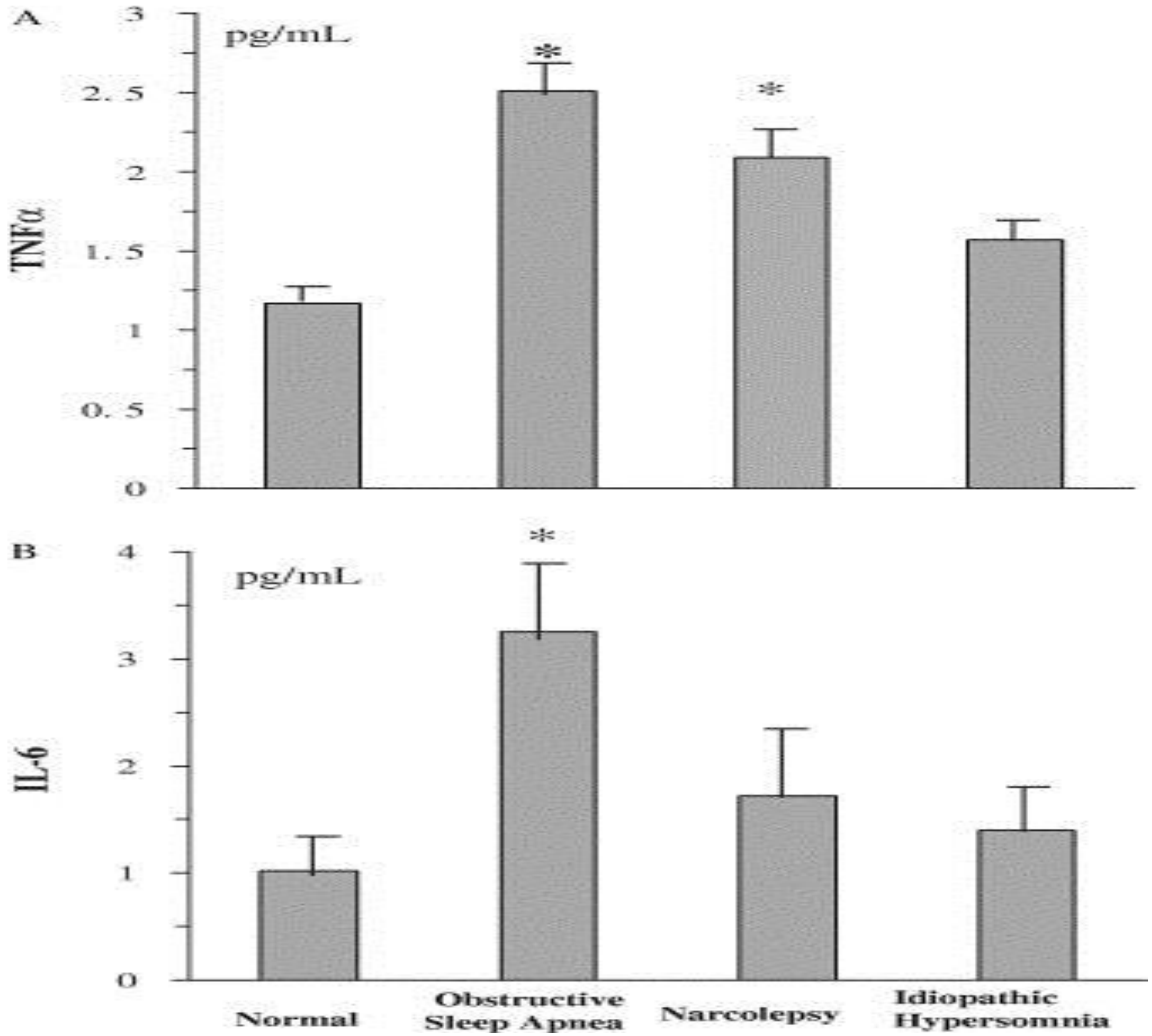
Vgontzas AN. Zoumakis E. Bixler EO. Lin HM. Follett H. Kales A. Chrousos GP. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. [Journal Article. Research Support, U.S. Gov't, P.H.S.] Journal of Clinical Endocrinology & Metabolism. 89(5):2119-26, 2004 May.

Changes of **TNF** over 24 hour clock before and with sleep restriction



Sleep restriction

Before restriction



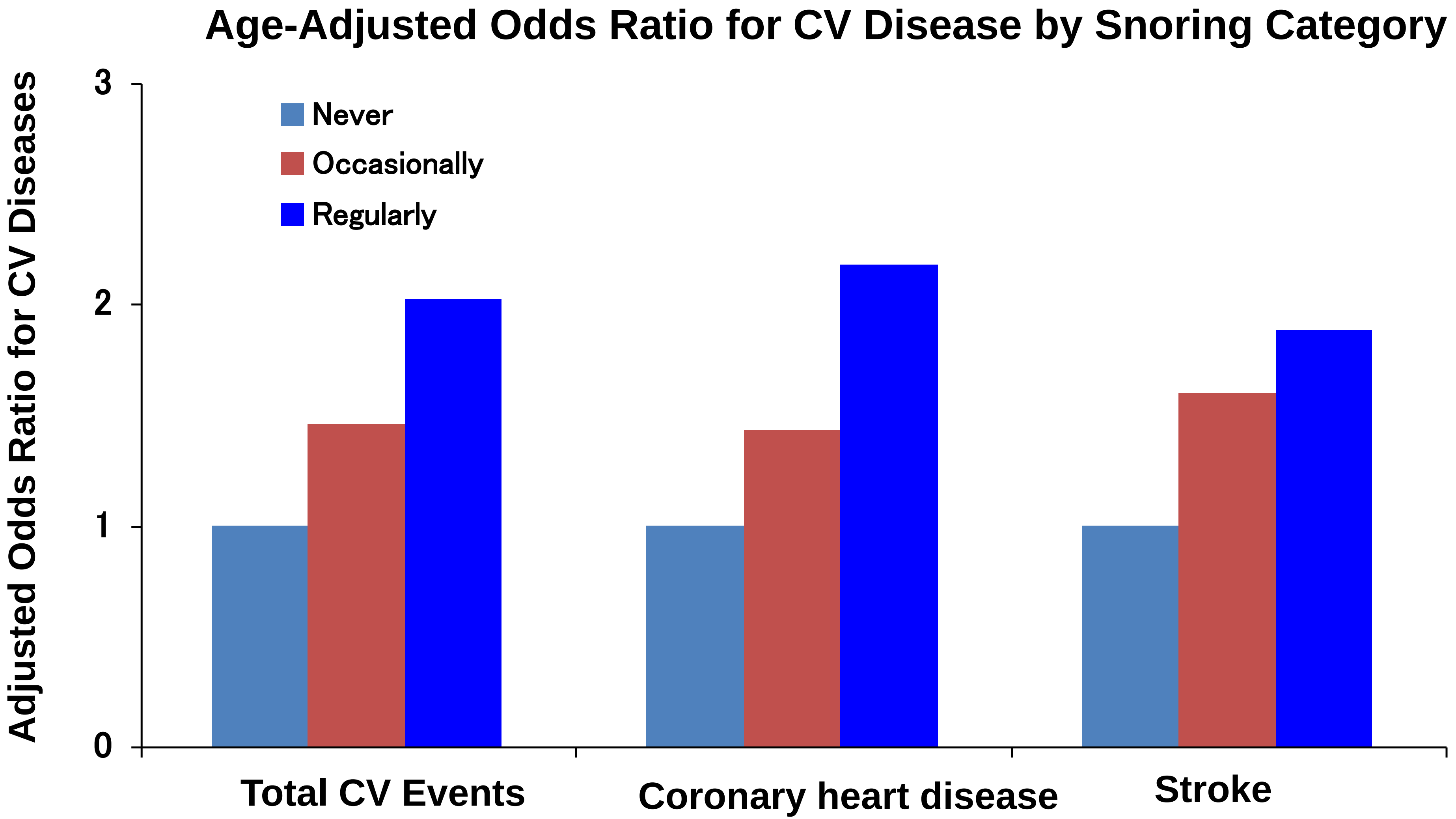
Vgontzas AN. Zoumakis M. Papanicolaou DA. Bixler EO. Prolo P. Lin HM. Vela-Bueno A. Kales A. Chrousos GP. Chronic insomnia is associated with a shift of interleukin-6 and tumor necrosis factor secretion from nighttime to daytime. [Clinical Trial. Controlled Clinical Trial. Journal Article] Metabolism: Clinical & Experimental. 51(7):887-92, 2002 Jul.

Nurses Health Study: Snoring Increases the Risk of Associated Diseases

Condition	Increased Risk with More Frequent Snoring
Coronary Heart Disease[1]	√
Stroke[1]	√
Hypertension[2]	√
Diabetes[3]	√

1. Hu et al. *J Am Coll Cardiol*. 2000;35:308.
2. Hu et al. *Am J Epidemiol*. 1999;150:806.
3. Al-Delaimy et al. *Am J Epidemiol*. 2002;155:387.

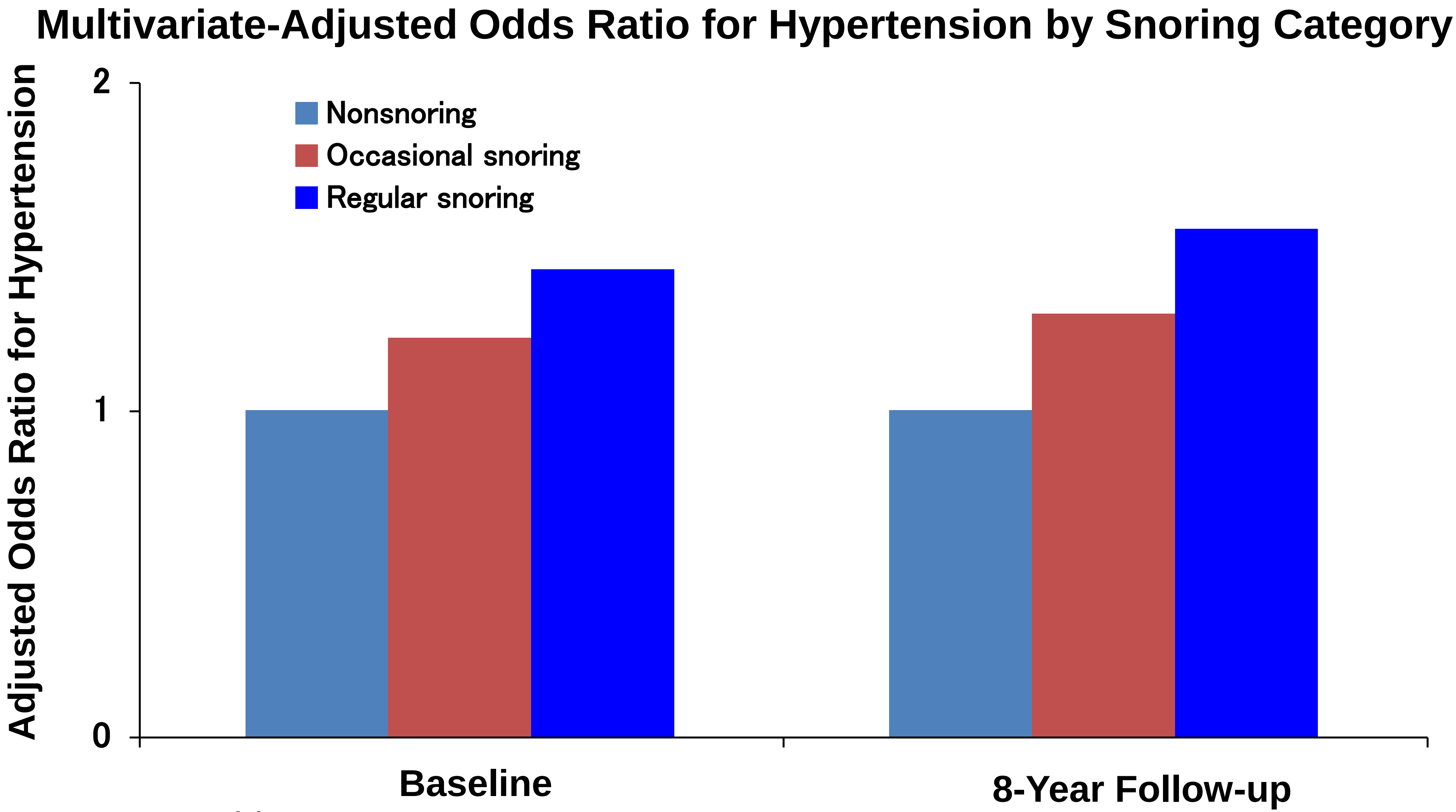
Nurses Health Study: Snoring Increases Risk of CV Disease



N=71,779 subjects.

Hu et al. *J Am Coll Cardiol*. 2000;35:308.

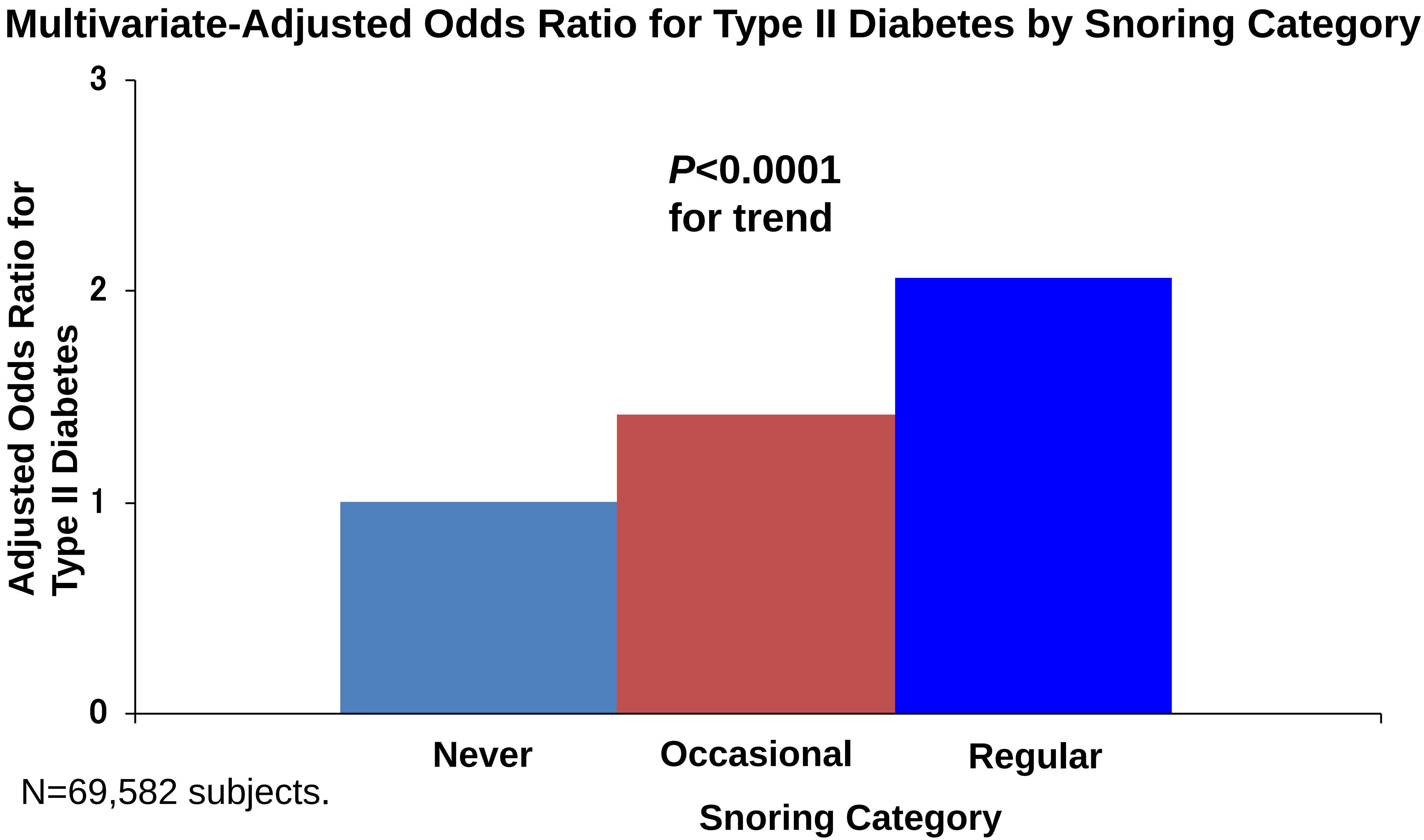
Nurses Health Study: Snoring Increases Risk of Hypertension



N=73,231 subjects.

Hu et al. *Am J Epidemiol*. 1999;150:806.

Nurses Health Study: Snoring Increases Risk of Type II Diabetes



N=69,582 subjects.

Al-Delaimy et al. *Am J Epidemiol*. 2002;155:387.

Presentation Overview

- Obesity and asthma
- OSA and asthma
- Obesity and rhinitis
- Rhinitis and OSA
- Sleep and inflammation
- What we need to do

For weight loss what is the recommendation in minutes per day?

- 1. 30 minutes
- 2. 45 minutes
- 3. 60 minutes
- 4. 90 minutes
- 5. 120 minutes

- ans

For weight loss what is the recommendation in minutes per day?

- 1. 30 minutes
- 2. 45 minutes
- 3. 60 minutes
- 4. 90 minutes
- 5. 120 minutes

- Ans: 3

2013 AHA/ACC/TOS Obesity Guideline

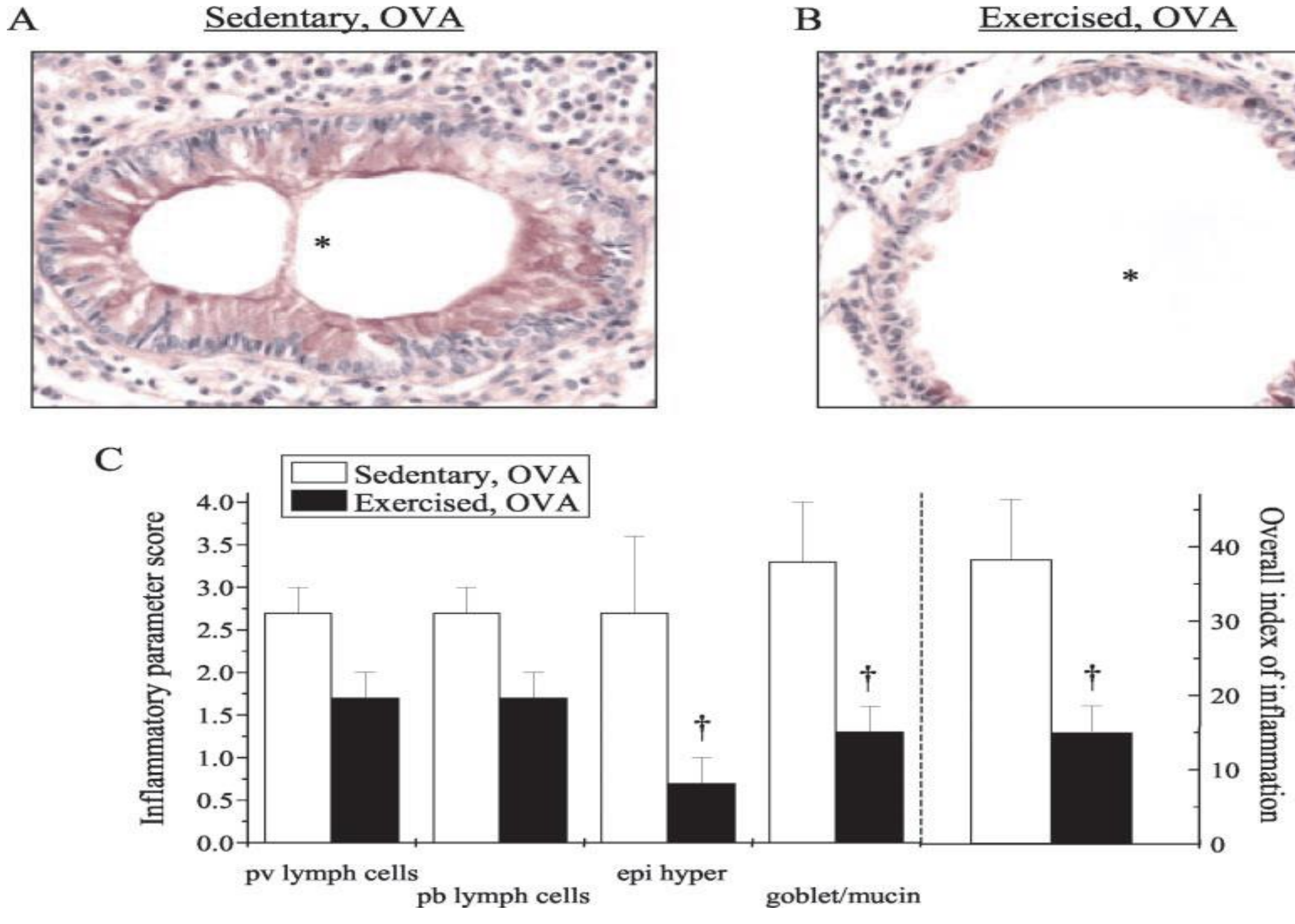
EXERCISE

Increased physical activity: Comprehensive lifestyle intervention programs typically prescribe increased aerobic physical activity (such as brisk walking) for ≥150 minutes/week (equal to ≥30 minutes/day, most days of the week). Higher levels of physical activity, approximately 200 to 300 minutes/week, are recommended to maintain lost weight or minimize weight regain long-term (>1 year).

30 minutes for healthy people
and 60 minutes for weight loss
and to maintain weight loss

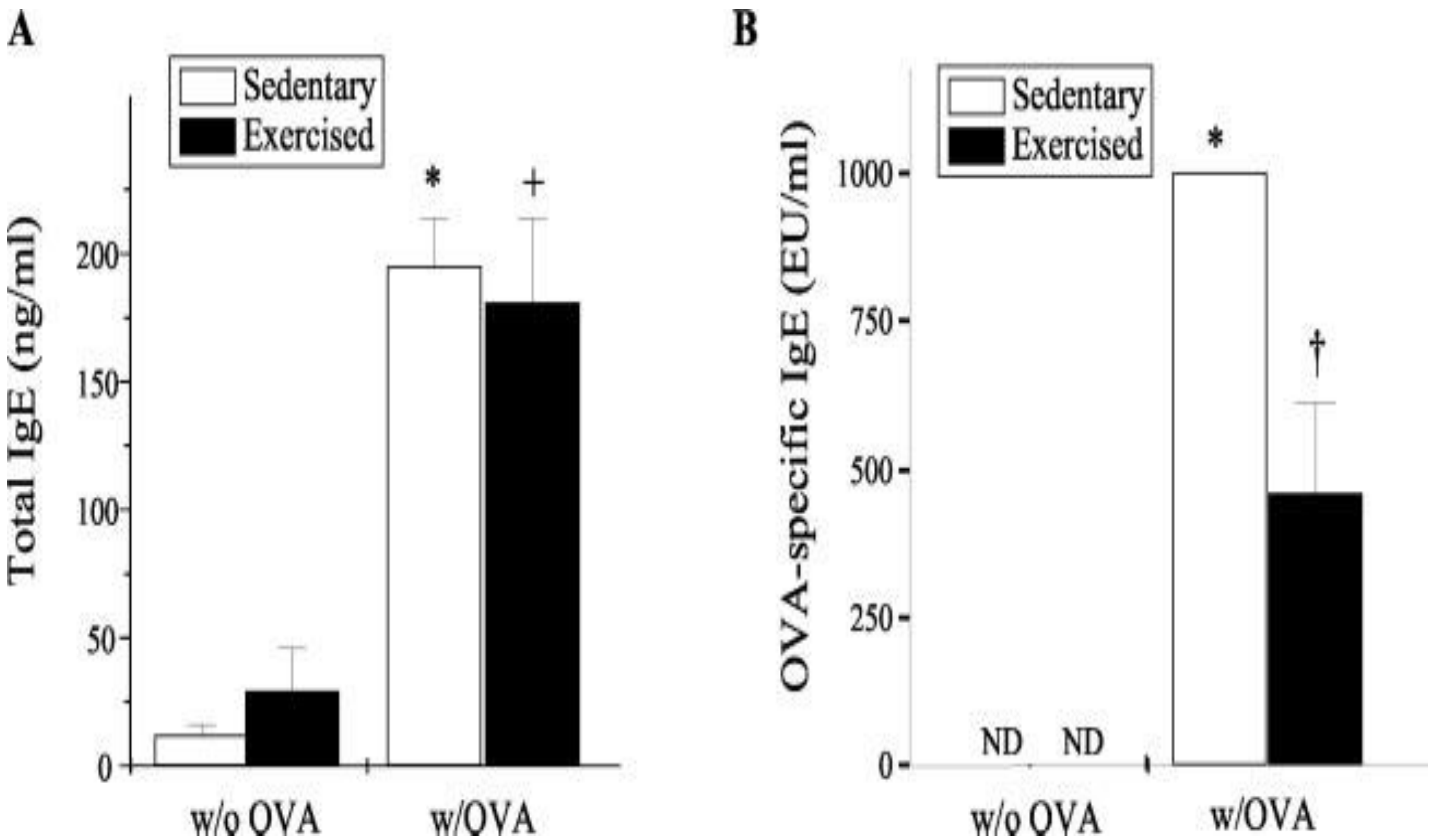
What is the importance of exercise in the mouse model with asthma

Effect of exercise on inflammatory mediators of asthma



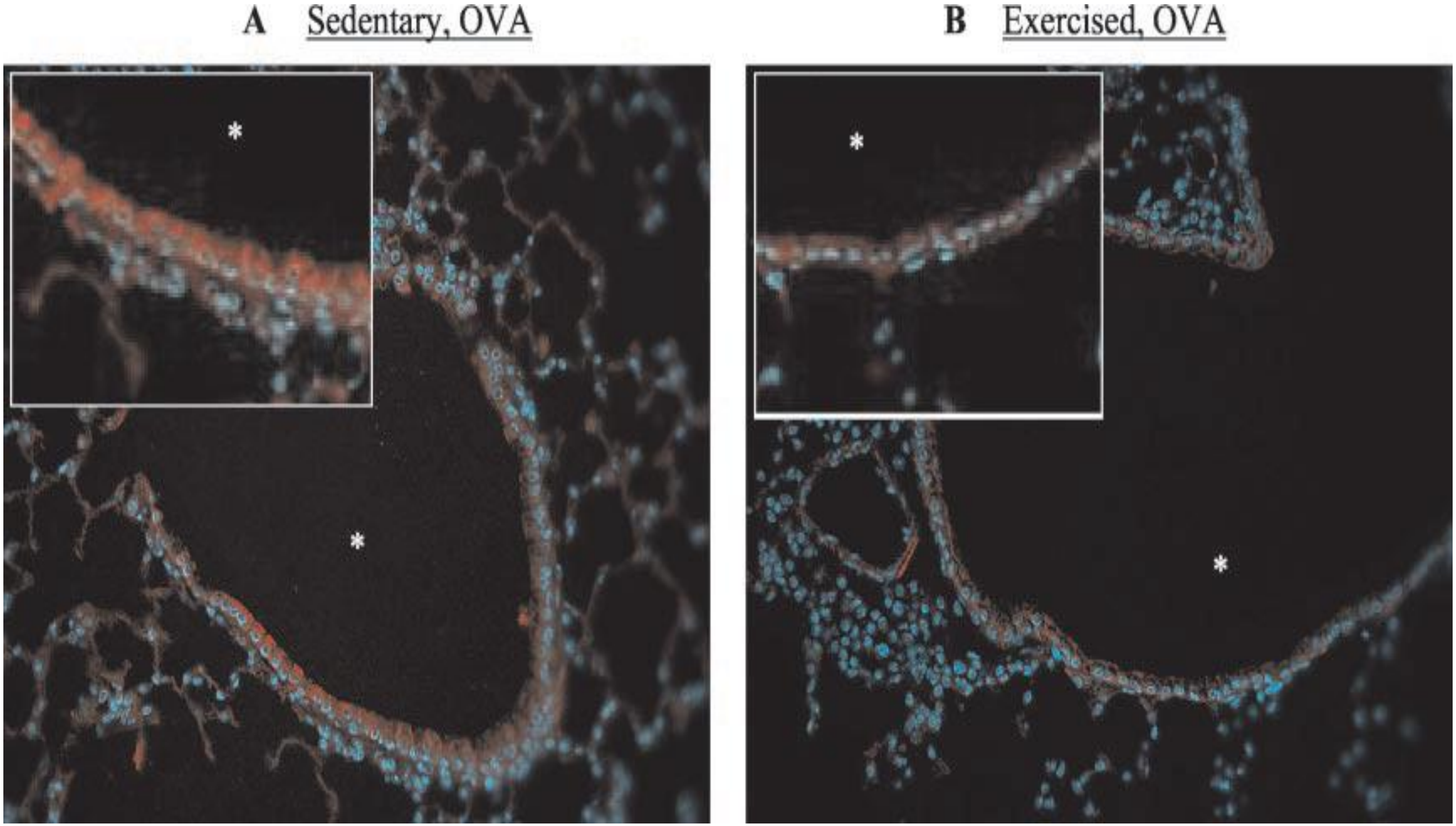
Pastva. J Immunol 2004;172;4520-4526

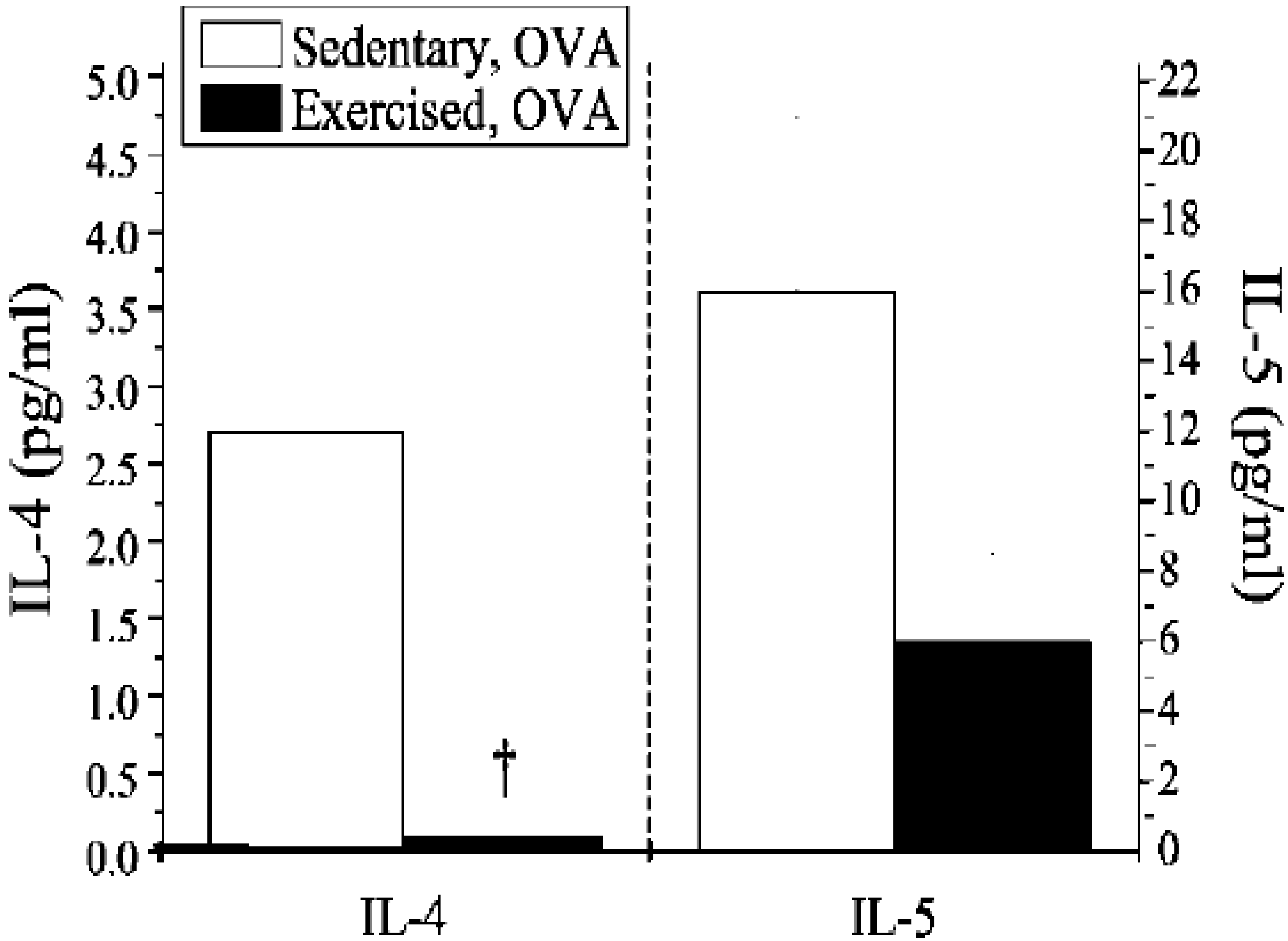
IgE production in sedentary and exercising mice



Pastva. J Immunol 2004;172;4520-4526

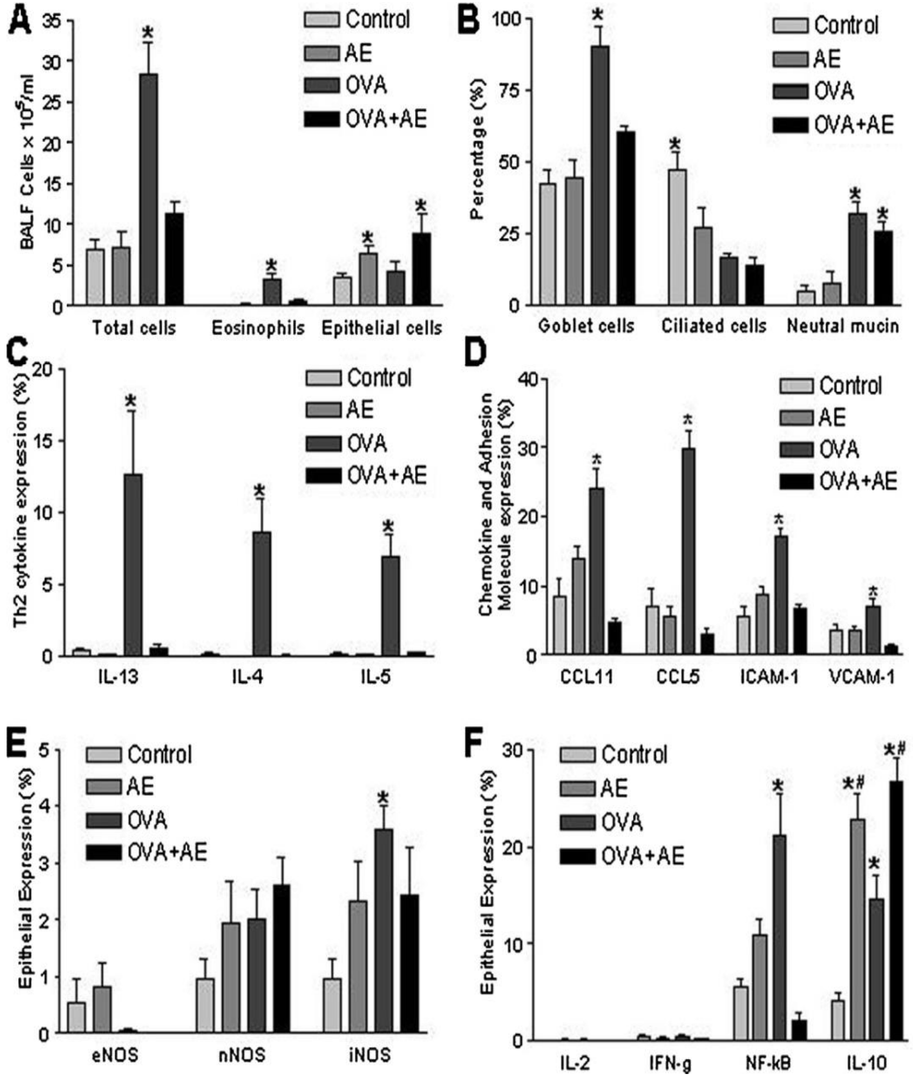
Exercise decreased VCAM-1 surface expression in the lungs of OVA-sensitized mice





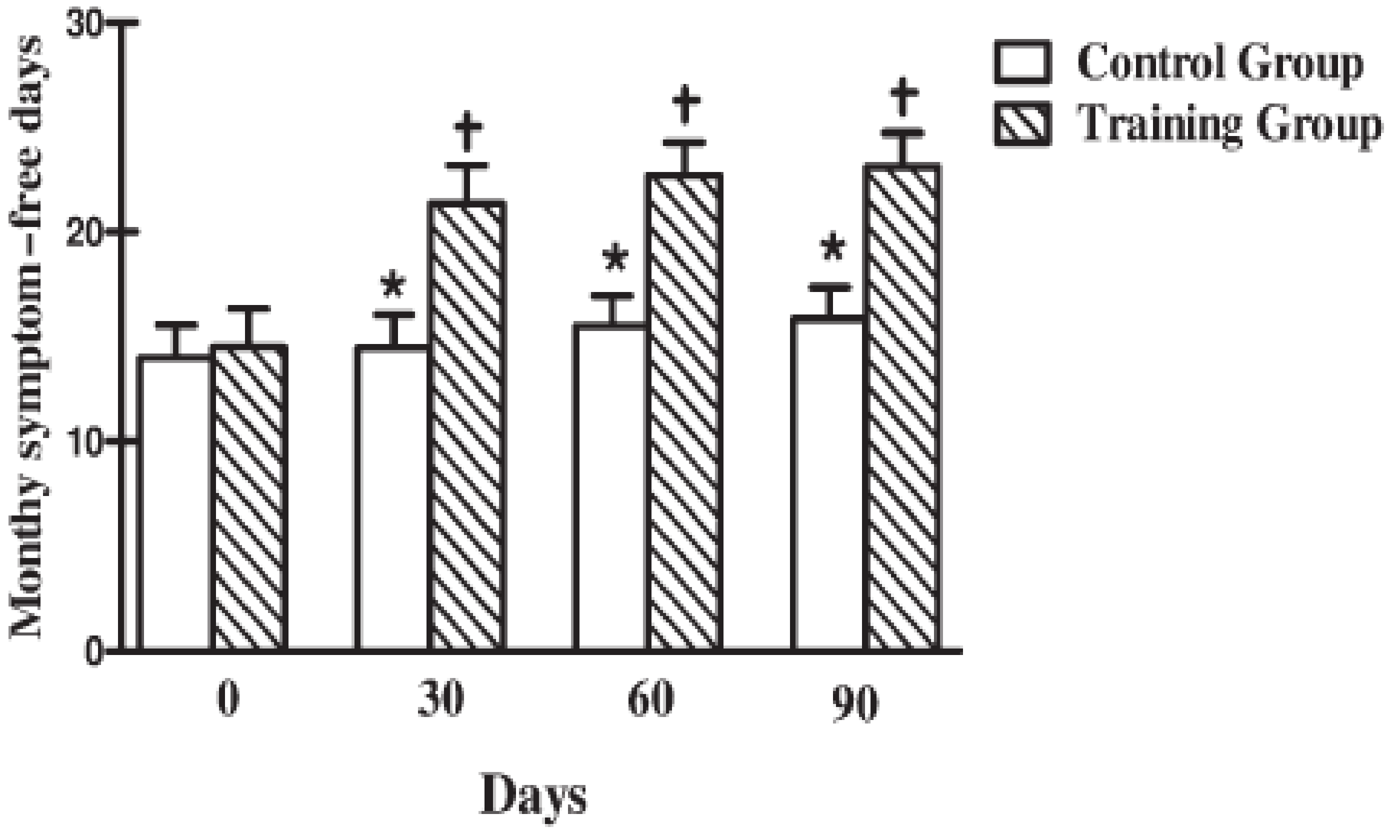
Pastva. J Immunol 2004;172;4520-4526

The number of total cells, eosinophils and epithelial cells in the bronchoalveolar lavage



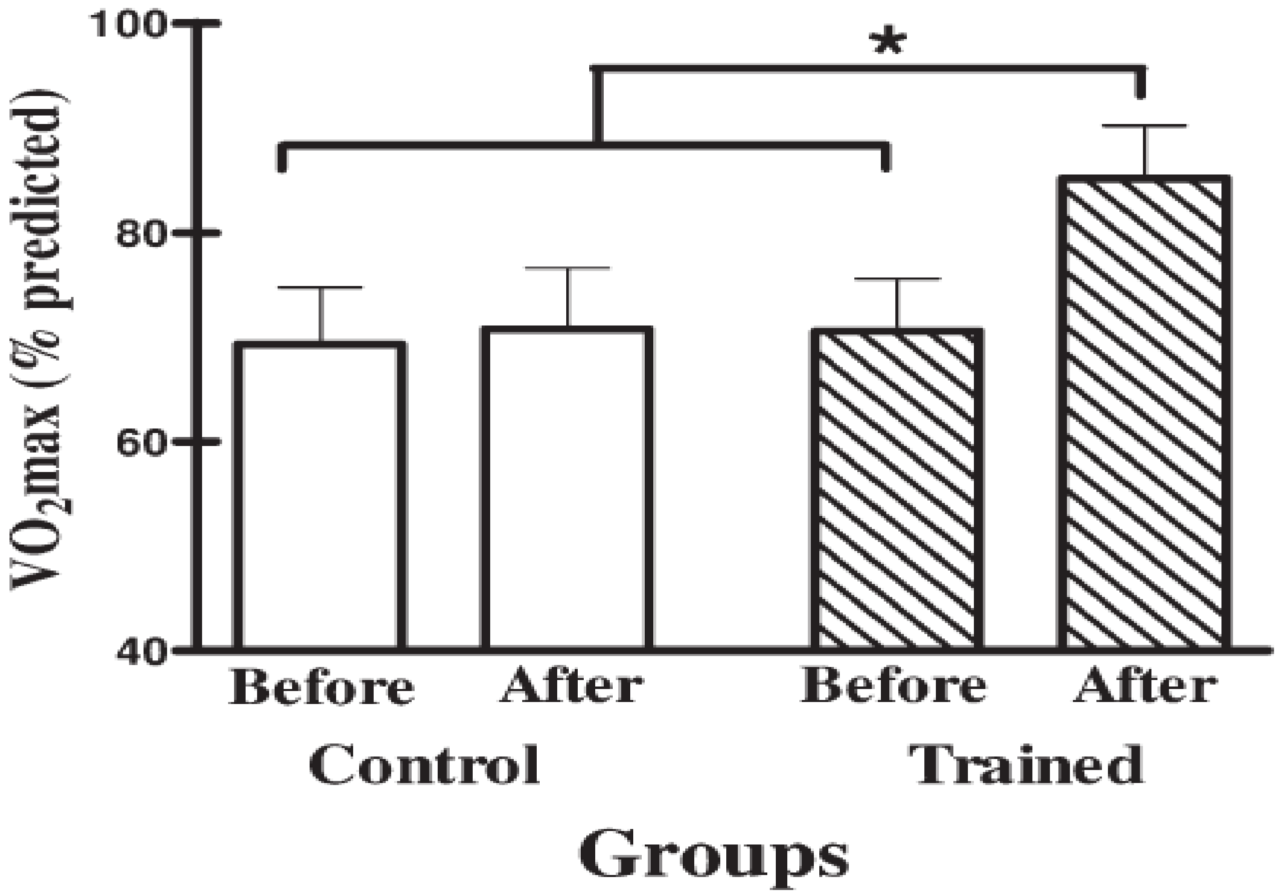
R.P. Vieira et al. / Respiratory Physiology & Neurobiology *175 (2011) 383–389*

Exercise Improves Asthma Outcomes
"Symptom Free Days"



Mendes. CHEST / 138 / 2 / AUGUST, 2010

Exercise Improves Asthma Outcomes
“ Oxygen consumption”



Mendes. CHEST / 138 / 2 / AUGUST, 2010

Exercise Improves Asthma Outcomes
"Quality of Life"

	Control Group		Exercise Group		
	Baseline (n=12)	**Week 12 (n=11†)**	**Baseline (n=18)**	**Week 12 (n=18)**	**Week 24 (n=15‡)**
ACQ Questionnaire	0.90±0.15	0.99±0.16†	1.30±0.19	0.72±0.10*	0.72±0.17‡***
ACQ with Spirometry	1.06±0.10#	0.80±0.14	1.37±0.21	0.95±0.11	1.02±0.18
Perceived Asthma Control	2.33±0.19	2.25±0.18†	2.56±0.15	1.94±0.10^	2.00±0.13‡***
Mini-AQLQ	5.79±0.15	5.90±0.17†	5.01±0.21	5.84±0.17	6.11±0.21‡**,***
Maximal VO_2	2.66±0.27	2.77±0.29	2.63±0.20	2.88±0.21	3.00±0.27***
Submaximal V_E/VO_2	23.21±0.73	23.64±0.80	24.89±1.08	23.78±0.74^	24.35±0.90
Maximal V_E/VO_2	28.46±0.88	28.65±1.39	28.84±1.02	27.44±0.78	28.48±1.17
Submaximal DI	0.42±0.03	0.42±0.02	0.45±0.02	0.48±0.03^	0.54±0.03***
Maximal DI	0.68±0.04	0.69±0.04	0.73±0.04	0.77±0.04	0.84±0.04

ACQ: Asthma Control Questionnaire; AQLQ: Asthma Quality of Life Questionnaire; VO_2: Oxygen uptake; V_E: Ventilation; DI: Dyspnea Index

†n=12 for paper measurements only; ‡n=17 for paper measurements only; # significant differences at baseline between control and exercise group; *p<0.05 between groups from T1 to T2; ** p< 0.05 within exercise group from T2 to T3; ***p<0.05 within exercise group from T1 to T3; ^ statistical trend from T1 to T2; p<0.10.

Dogra. ERJ June 7, 2010

Exercise in children: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Basaran 2006	2 months	1 hour, 3X a week	Aerobic, moderate	0.001 62
Fanelli 2007	4 months	1.5 hours, 2X a week	Aerobic to 70%	0.03 38
Flapper 2008	3 months	2.5 hours, 1 time a week	Aerobic	0.02 36
Moreira 2008	3 months	50 minutes, 2X weekly	Aerobic	0.004 34

D. Pacheco, J of Asthma, 2012

Exercise in adults: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Turner 2010	6 weeks	1.5 hour, 3X a week	Aerobic, moderate	0.04 34
Goncalves 2008	3 months	0.5 hours, 2X a week	Aerobic to 70%	0.001 20
Mendes 2010	3 months	0.5 hours, 2X a week	Aerobic to 70%	0.001 101

D. Pacheco, J of Asthma, 2012

Exercise in Adults, non aerobic: all compared to open label conventional treated group

author	duration	frequency	type	P value Subject #
Sabina 2005	1 month	1.5 hour, 2X a week	Yoga	NS 62
Thomas 2009	1 and 6 months	3 sessions	Breathing exercises	NS 183
Vempati 2009	2 months	1.5 hours, daily	Yoga	0.013 57

D. Pacheco, J of Asthma, 2012

Correct statement for treatment for OSA?

- 1. Weight loss is just as effective as CPAP
- 2. CPAP is better than weight loss
- 3. CRP is reduced more with CPAP than Weight loss
- 4. No one is adherent anyway so why try

- Ans:

Correct statement for treatment for OSA?

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- Ans:

Correct statement for treatment for OSA?

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- 2. CPAP is better than weight loss
- 3. CRP is reduced more with CPAP than Weight loss
- 4. No one is adherent anyway so why try

- Ans: 1

Adverse Impact of obesity on allergic diseases

- Obesity is associated with increase risk of asthma
- OSA and asthma overlap
- Obesity is associated with increased risk of rhinitis
- Rhinitis is associated with increase in OSA
- Impaired sleep causes an inflammatory state
- Sleep impairment in allergic diseases can be caused by
  - Inflammatory mediators
  - Symptoms, primarily ocular itch and rhinorrhea
  - Congestion
- Impaired sleep adversely affects performance, productivity and social functioning, and increases the risk of associated diseases and obesity
- Best treatment is weight loss and exercise

Thank you for your participation

- Stephanie Teets
- Stan Golden
- Josh Berlin
- Sujani Kukumanu
- Katherine Hughs
- Casey Glass
- Joel Torretti
- Faina Gurevich
- Wenxin Wei
- Jeff McCann
- Chris Hanks
- Carah Santos
- Niti Sardana

Thank you

Have a great day.