ERJ Express. Published on November 14, 2008 as doi: 10.1183/09031936.00075408

PROGRESSION OF SNORING AND OBSTRUCTIVE SLEEP APNEA: THE ROLE OF INCREASING WEIGHT AND TIME

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Run Title: Progression of snoring and obstructive sleep apnea

Abstract words: 199

Text words: 3192

Tables: 6

Figures: 3

References number: 27

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Disclosures: None of the authors have any financial interest or conflict of interest to disclose.

ABSTRACT

Objective: To examine the natural evolution of primary snoring and obstructive sleep apnea (OSA) in adult male patients.

Methods: A retrospective analysis on 160 untreated patients with primary snoring, mild, moderate and severe OSA who had two polysomnographic (PSG) recordings, mean time between recordings (TBR) was 5.1 ± 3 yrs.

Results: The mean Apnea-Hypopnea Index (AHI), Body Mass Index (BMI), lowest SaO_2 level during Rapid Eye Movement (REM) and Non-REM sleep showed a significant worsening effect. The change in AHI differed among the groups showing a similar significant increase in AHI for primary snoring, mild, and moderate OSA and an insignificant decrease for severe OSA patients. Stepwise linear regression showed that only ΔBMI and time were significant predictors for AHI change. A model for the mean AHI change showed that: ΔAHI = 4.33 X ΔBMI + 0.66 X TBR, R^2 =.322. After adjusting for confounders, multiple regression analysis indicated that age and high levels of BMI but not AHI were significant risk factors for developing hypertension and/or cardiovascular disease.

Conclusions: Patients with primary snoring, mild and moderate OSA had a similar increase in AHI over time which depended mainly on weight gain and to a lesser degree on time.

KEYWORDS: Apnea-Hypopnea Index, Body Mass Index, Natural Evolution of Disease, Obstructive Sleep Apnea, Polysomnography, Snoring.

INTRODUCTION

Lugaresi et al [1] were the first to theorize that prolonged snoring for years and even

decades antedated the appearance of overt Obstructive Sleep Apnea (OSA). Yet, owing to the sparse and conflicting data available to date, controversy arises whether OSA is a progressive disease. A number of longitudinal studies have dealt with the evolution and risk factors associated with snoring and OSA syndrome.[2-19] Several reports found that mild to moderate OSA have a tendency to worsen over time.[2-11] Other clinical trials found that apnea status is fairly stable across time[12, 14-19] or even improves.[13] Nine of these reports include subjects from the general population and four of them comprise a large number of participants (between 282 - 2968) and are relatively new studies. The other five are much older studies, include fewer participants and comprise mostly an elderly population. Nine of these 18 studies assessed patients seeking treatment, but most of them are relatively old studies including a small number of participants (between 11 and 55), not allowing meaningful subgroup comparisons. All but one included both genders.[6] In some, the time between the two polysomnographic (PSG) evaluations was relatively short,[4,5] or analysis was restricted to an older population (Table 1).[3,12,14,16,18]

The answer to the question of how to approach snoring and OSA has more than academic interest. A progressive nature of disease would dictate early and frequent follow up visits for patients with primary snoring and mild OSA and treatment planning at an early stage[20], whereas the opposite would hold true for a stable disease.

We followed up 160 untreated adult males over a mean period of 5 years, aiming to study the natural evolution of snoring and OSA in primary snorers, and in patients with mild, moderate, and severe OSA, and investigated the risk factors that may play a role in the progression of these conditions.

MATERIAL AND METHODS

Patient Selection

A retrospective longitudinal case study of untreated adult males who had primary snoring and various degrees of OSA were followed at our Sleep Disorders Unit, between 1989 and 2004. Only patients who had two overnight PSG for at least 4 sleep hours each on separate occasions, 6 months apart or longer were included. Patients using either continuous positive airway pressure (CPAP), bi-level positive airway pressure, an oral appliance or tennis ball technique and those who had nasal, oropharyngeal or bariatric surgery between recordings were excluded from the analysis. Also, patients who had split-night examinations and patients with predominant central apneas, with neuromuscular disorders or who were mentally retarded were excluded. After the exclusion criteria were applied 160 patients were left and comprised the research group.

Each patient completed a questionnaire for demographic, sleep habits and symptoms and general medical condition data. Further data on years of snoring, smoking habits, and concomitant diseases including hypertension (HT) and cardiovascular disease (CVD) were collected. Following initial PSG recordings, all patients were advised, when appropriate, to reduce weight and/or use CPAP, an oral device, or tennis ball technique, but either refused or had poor compliance. The request for a second PSG came from the referral physician who decided to ask for a reevaluation based on patients' symptoms. The patients were not paid to undergo the second examination. The patients belong to the Clalit Health Care Services (CHS) which is the largest Health Maintenance Organization (HMO) in Israel, providing medical services to about 60% of the total Israeli population and polysomnography is included in the medical services free of charge.

The study was approved by the local Institutional Review Board of the Sleep Disorders Unit, Loewenstein Hospital –Rehabilitation Center, Raanana.

Objective and Subjective Measurements

Complete PSG recordings were performed overnight. The recordings were carried out using

either Nihon Kohden polygraphs (models 4321 and 4414, Nihon Kohden, Tokyo, Japan) or Rembrandt Manager System (Medcare, Amsterdam, The Netherlands) and included conventional parameters [21]. The recordings were scored according to the standard criteria of Rechtschaffen and Kales.[22] Apnea was defined as an episode of complete breathing cessation of 10 sec or longer, and hypopnea as a reduction of more than 30% in oral/nasal airflow (oral / nasal thermistor) lasting 10 sec or longer, accompanied with arousal or by a drop of at least 3% in SaO_2. Pressure cannulas were not used during the study period. Snoring sounds were recorded by a microphone located above the patient's head at a distance of 1 meter and connected to a Sound Level Meter (SLM) (Quest Electronics - model 2700, Oconomowoc, WI). We use the dB A scale (A - weighting network that yields the response of the human ear), the 40 – 100 dB range and the fast response mode. This was a calibrated channel (40 - 80 db) of the PSG in order to evaluate the intensity of each snore event. The output from the SLM was also recorded in parallel on a calibrated (40 - 80 dB) chart recorder at a paper speed of 10 cm/hr**.** Subjective daytime sleepiness was assessed by using the Epworth Sleepiness Scale (ESS) [23]

Study Definitions

The patients were stratified by apnea-hypopnea index (AHI) severity to primary snoring (AHI < 5), mild OSA (AHI 5 – 15), moderate OSA (AHI 15 - 30), and severe OSA (AHI > 30). The snoring history was divided into 5 periods: < 5 years, 5 – 10, 10 - 20, and > 20 years. An ESS score > 10 was considered as abnormal daytime sleepiness. Improvement or worsening of initial AHI was defined as an increase or decrease of 25% or more of AHI^5 after assuring that there were at least10 events / h. A patient was defined as a nonsmoker if there was no history of cigarette smoking or smoking was stopped for at least 5 years.

Statistical Analysis

Since the Shapiro-Wilk test demonstrated that some of the parameters were not normally distributed, the nonparametric Wilcoxon Signed Rank test was used for comparing the mean baseline (time 1; T1) AHI, Body Mass Index (BMI, kg/m^2), Epworth Sleepiness Scale (EES) score (0 – 24), lowest oxygen saturation (SaO_2) during REM (Rapid Eye Movement) and Non-REM sleep, and maximum snoring sound levels (dB) in supine and lateral body positions with that of end of follow-up (time 2, T2). The non-parametric Kruskal-Wallis test was used to examine differences over time of the 4 AHI severity groups for a given demographic or sleep parameter (the Greek letter Δ indicates difference between T1 and T2). Stepwise linear regression was used to examine the correlations between ΔAHI as the dependent variable against ΔBMI, time between recordings (TBR), age, HT and/or CVD, and lowest SaO_2 levels during REM and Non-REM sleep. Stepwise logistic regression analysis determined the independent risk factors for HT and/or CVD. Only variables that were significant entered into the final multiple logistic regression model.

RESULTS

160 untreated adult males (mean age 51 ± 11 yrs) underwent full PSG recordings on two occasions (mean time between recordings (TBR), 5.1 ± 3 yrs, median 5 yrs, range 0.5 - 15 yrs). The mean sleep efficiency was 85.6 ± 8.9% for the first PSG and 85.5 ± 8.1% for the follow up evaluation.

Table 2 shows the mean + SD, median and range values of Age, AHI, BMI, ESS, lowest SaO_2 in REM and Non-REM sleep, and maximum snoring sound levels (dB) in supine and lateral body positions for T1 (baseline - PSG 1) and T2 (follow up - PSG 2) respectively. The significant increase in Age is obvious. Wilcoxon Signed Rank Test shows a significant increase for AHI and BMI levels, and a significant decrease (worsening) in lowest SaO_2 in REM and Non-REM sleep). There was also a significant increase in ESS score from T1 to

T2. The snoring intensity in the supine body position did not change significantly, however, in the lateral position a significant increased was observed.

Primary snoring was diagnosed in 26 (16.3%) patients, mild OSA in 47 (29.4%), moderate OSA in 41 (25.6%), and severe OSA in 40 (25%). The TBR was significantly different across these patients groups (6.2 ± 2.6, 5.4 ± 3.0, 4.9 ± 3.0 and 4.3 ± 3.1 yrs, respectively; p=.0.044). The ΔAHI differed significantly among the groups, showing two patterns (a significant increase for primary snoring, mild OSA, and moderate OSA and an insignificant decrease for severe OSA (Figure 1)). The difference for ΔBMI was also significant among the groups (p= 0.011). While primary snoring and mild OSA patients had a significant worsening in BMI, moderate and severe OSA patients did not show significant increases in BMI (Table 3). The lowest SaO_2 level in REM and Non-REM sleep showed significant differences among the groups but no significant interaction with time was observed. A significant deterioration was observed for lowest SaO_2 level in REM sleep for patients with mild and moderate OSA and for the lowest SaO_2 level in Non-REM sleep for primary snorers and mild OSA patients. Similar as for Δ AHI, patients with severe OSA showed an insignificant change in ΔSaO_2 for both REM sleep and Non-REM sleep (Table 3). Although severe OSA patients showed a significant increase in ESS score, the change in ESS score was not statistically significant neither across groups nor across time .The significant correlations between ΔAHI and ΔBMI (R^2 linear =.296) and ΔAHI and TBR (R^2 linear =.082) are displayed in Figure 2a and 2b respectively.

Stepwise linear regression analysis showed that ΔBMI and TBR were significant predictors for AHI change (95% CI, 2.72 - 4.92, p <.001; 95% CI, 0.6 - 2.66, p =.002; respectively, R^2 =.331), whereas baseline age, BMI, HT and/or CVD, lowest SaO_2 in REM and Non-REM sleep were not. Adjusting for these confounding factors, a model for the mean AHI change showed that: ΔAHI = 4.33 X ΔBMI + 0.66 X TBR, R^2 =0.322.

We used a cut-off point of 25%[8] for defining improvement or worsening of initial AHI (Table 4). Twenty three (14.4 %) patients improved their initial AHI score, 74 (46.2%) remained stable, and 63 (39.4%) worsened. No significant differences were found between

these 3 groups in terms of age and BMI. Patients who showed a worsening effect had a significantly lower AHI at T1 and patients who improved had a significantly higher AHI at baseline.

Table 5 shows that the incidence of HT and/or CVD increased from 54 (33.8%) at T1 to 65 (40.6%) patients at T2; also that 11 of 106 patients (10.4%) who had no HT at T1, developed this complication during follow-up period. In nine (81.8%) of them, there was an increase in BMI and AHI at follow up.

Analysis by age, BMI, and AHI at T2, duration of snoring, and smoking habits as independent risk factors for HT and/or CVD showed that age, BMI, and AHI were positively associated with HT and/or CVD (60.4 ± 11.6 vs. 52.8 ± 10.2, p =.017; 31.0 ± 4.7 vs. 29.2 ± 4.6, p =.026; and 31.8 ± 22.7 vs. 25.7,± 23.8, p =.038; respectively), whereas duration of snoring (p = .094) and smoking habits (p= .395) were not. Using the significant variables identified and adjusting for confounding factors, multiple regression analysis indicated that only age and higher levels of BMI remained significant risk factors for developing HT and/or CVD (Table 6).

DISCUSSION

The main finding of this study is that the outcome of untreated primary snorers and OSA patients in this adult male population is dependent mainly on weight increase and to a lesser degree on time. Of these two factors, weight increase exceeds the latter by almost 7 fold, having a major role in AHI progression. Age, hypertension, and lowest SaO_2 in REM and Non-REM sleep were not significant predictors for AHI progression.

Provided that ΔBMI and Time Between Recordings (TBR) are known, our model for calculating ΔAHI = 4.33 X ΔBMI + 0.66 X TBR may serve as a useful tool in sleep health care medicine for male patients aged about 50 yrs old, which are the vast majority of male patients seeking treatment for snoring and OSA at the sleep disorders units. It may be deduced from the model that with a stable body weight, it takes at least 6 years before the impact of TBR on ΔAHI perhaps becomes apparent (increased in 4 units). On the other hand, increasing weight in 1 BMI unit during one year, the AHI will increase in 5 units. Other authors have also shown the role of time in disease progression in the absence of concomitant weight increase [5, 24] and for some cases it is possible that AHI could be a risk factor for an increase in the BMI.

The number of patients included in the present study exceeds that of all publications available to date on the natural evolution of primary snoring and OSA for patients seeking treatment (Table 1), allowing us to establish a more meaningful statistical analysis for the 4 sub sets of disease severity.

A significant increase in AHI and BMI over time was shown in our 160 men with primary snoring and various degrees of OSA. Nevertheless, while snorers and those with mild and moderate OSA had an increase in AHI that correlated with the increase in BMI, patients with severe OSA had a non significant decrease in AHI suggesting a ceiling effect for OSA severity.

The correlation between ΔAHI and ΔBMI is demonstrated in several studies of patients

seeking treatment. In patients over 70 years of age, Ancoli-Israel et al.[18] showed that changes in AHI were associated with changes in BMI and, similar to our findings, this was independent of age. Furthermore, Sforza et al.[15] did not observe significant changes in apnea frequency or nocturnal hypoxemia in untreated OSA patients in the absence of changes in BMI. Likewise, no AHI changes were detected in untreated OSA patients who remained with stable weight, but those who reduced their weight had a significant decrease in AHI severity.[15]

Similar to others, [5,6,7] using a cut-off point of 25% for defining improvement or worsening of initial AHI [5], we showed no significant differences in the age of patients who improved, remained stable, or deteriorated (p =.478). Another study found a tendency for younger patients to deteriorate.[15]

The association between sleep disordered breathing and HT is well established.[25] Forty three of our 160 patients (26.9%) were initially diagnosed with HT. During the follow-up period, 10.4% of normotensive patients developed this complication, showing a more than two-fold increase in the incidence of HT than the expected incidence of newly diagnosed HT in the general population over a similar period.[26] Similar to others,[27] we found that age and high levels of BMI were significant predictors of HT and/or CVD while the progression in AHI itself was not the main factor in the development of CVD. Certainly, other cardiovascular risk factors not assessed in this study like dyslipidemia, insulin resistance, or endothelial dysfunction may have also participated in the development of cardiovascular morbidity.

Our study has several limitations. A retrospective design is of one the known limitations of studies covering the natural history of snoring and OSA. Yet it allowed us a better insight into the long-term trends of this syndrome in a relatively large group of untreated patients who had at least two PSG evaluations. A second limitation is that patients consist of a seek-treatment group and regardless of the mode of referral; they were assessed mainly because their sleep symptoms and/or daytime somnolence either continued or worsened. This may have induced a selection bias, as patients with severe or progressive symptoms are more eager to be reexamined. Nevertheless, it may have been balanced by the fact that most of

severe OSA patients are now successfully treated using CPAP, underwent surgery or use other devices and were all excluded from the analysis. Moreover, in our population, we have a similar number of patients with mild, moderate and severe OSA that had two PSG evaluations.

Using a cut-off point of 25% for defining improvement or worsening of initial AHI, although used in a previous study [5,] is arbitrary and could be affected by the night to night AHI variability. Also, since mild-moderate OSA patients are influenced mainly by the sleep posture, it is possible that part of the increase in AHI severity is related to an increase in time spent in the supine posture in the second PSG [21] However, since only a significant increase in Lateral AHI (19.4±19.6 vs.28.9 ±25.7, $p < 0.01$) was seen, without a significant change in Supine AHI (58.8±32.4 vs.59.4±27.4) from T1 to T2, this does not appear to be the case.

Unfortunately, we did not quantify the several reasons for seeking a repeated PSG evaluation in our patients, which could have provided valuable clinical information. However, based on our clinical experience, the main two reasons for a reevaluation were a suspected worsening of snoring and / or OSA and a subjective worsening in daytime sleepiness.. In some cases the trigger for a reevaluation came after reading a related article in a newspaper or magazine, after watching or listening to a television or radio program, or after the recommendations of a friend using CPAP successfully.

How do these data compare to data obtained from the general population?

The crucial role of weight gain on the progression of snoring and OSA shown in the present study in seeking-treatment patients is very similar to most of the studies that investigated the evolution of snoring and OSA in the general population. Population studies of the Wisconsin Sleep Cohort [7], from the Cleveland Family Study[9], or from the Sleep Heart Health Study[10] all found that weight gain is a crucial predictor of longitudinal changes in the incidence and severity of sleep disordered breathing. Although this association between increase in weight and the worsening in sleep disordered breathing has modifications according to gender, age, race and ethnicity, it is clear that excess weight is a critical contributor to the incidence and progression of this sleep related breathing disorder. Thus,

the results of this study of the largest untreated clinical population of seeking- treatment patients suffering from snoring and OSA agree completely with the result of the largest population study[10] and support the notion that avoiding weight gain for the prevention and encouraging weight loss for the treatment of this clinical entity are imperative purposes for public health.

In summary, in a follow up study (over a mean period of 5 years) of 160 untreated snorers and OSA adult male patients, we have found that patients with primary snoring and mild and moderate OSA had a similar significant increase in AHI over time while patients with severe OSA had an insignificant change in AHI suggesting a ceiling effect. The progression in AHI is mainly dependent on weight gain and to a lesser degree on time. Of these two factors, weight increase exceeds the latter by almost 7 fold, having a major role in AHI progression. Provided that ΔBMI and Time Between Recordings (TBR) are known, our model for calculating ΔAHI = 4.33 X ΔBMI + 0.66 X TBR may represent a useful tool in sleep health care medicine for male patients aged about 50 yrs old, which are the vast majority of male patients seeking treatment for snoring and OSA at the sleep disorders unit.

Legends of Figures:

Figure 1: The change across time in Apnea Hypopnea Index (AHI) in 160 untreated patients (mean interval between Time 1 and Time 2 = 5.1 ± 3 yrs) for 160 untreated patients divided into four groups according to the diagnosis at Time 1. Primary Snoring (AHI< 5), Mild Obstructive Sleep Apnea (OSA) (AHI 5-15) and Moderate OSA (AHI 15-30) patients have a similar significant increased in AHI, while Severe OSA patients (AHI>30) showed an insignificant decreased in AHI. Values are Mean ± SE

Figure 1. Changes in AHI across time in the four groups of patients

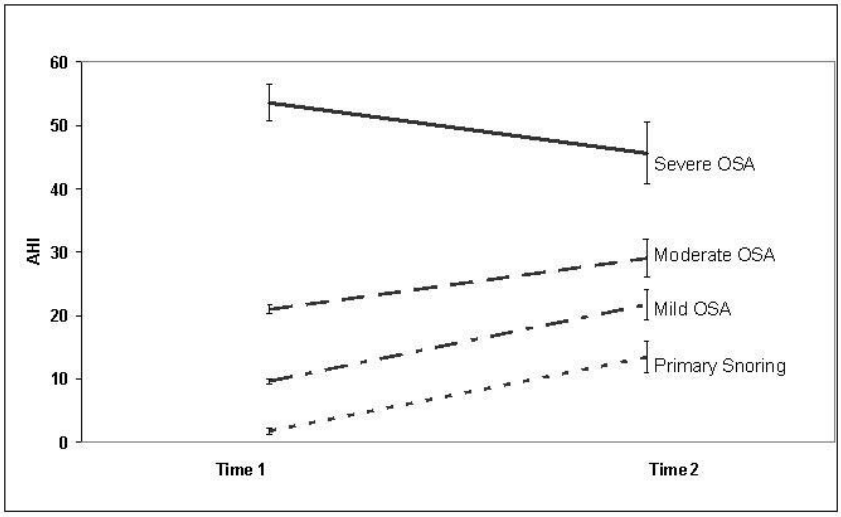


Figure 2a: The relationship between the change in AHI and the change in BMI for the all 160 untreated patients who had two complete polysomnographic evaluations during a mean period of about 5 years. $p < 0.001$

Figure 2a: Relationship between change in AHI and change in BMI

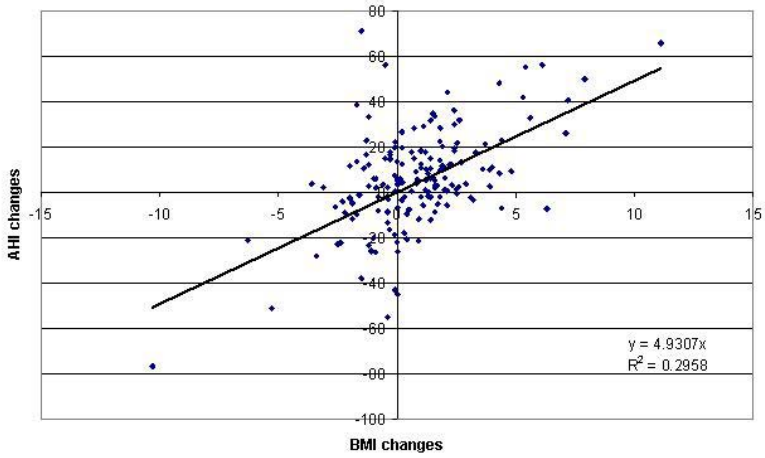
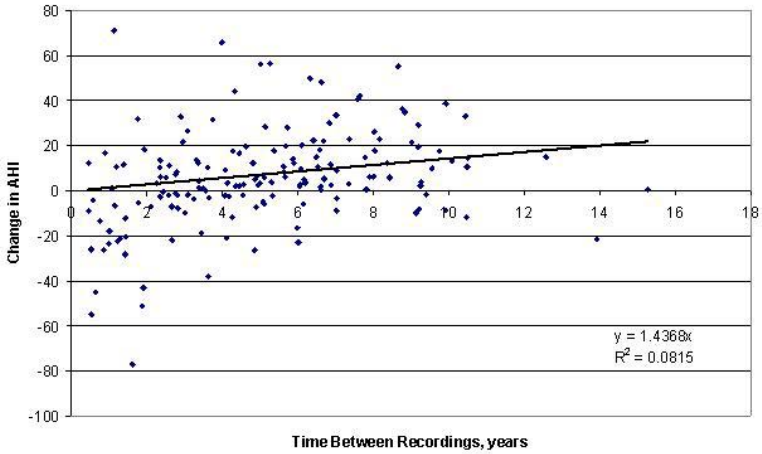


Figure 2b: The relationship between the change in AHI and Time Between Recordings for the all 160 untreated patients who had two complete polysomnographic evaluations during a mean period of about 5 years. $p < 0.001$

Figure 2b: Relationship between change in AHI and Time Between Recordings



REFERENCES

1. Lugaresi E, Cirignotta F, Gerardi R, et al. Snoring and sleep apnea: natural history of heavy snorers disease. In: Obstructive Sleep Apnea Syndrome. Clinical Research and Treatment. Guilleminault C, Partinen M, eds. New York, Raven Press, 1990:25-36.
2. Bliwise D, Carskadon M Carey E, et al. Longitudinal development of sleep – related respiratory disturbance in adult humans. J. Gerontology 1984;39:290-293
3. Phoha RL, Dickel MJ, Mosko SS. Preliminary longitudinal assessment of sleep in the elderly. Sleep 1990; 13:425-429.
4. Svanborg E and Larsson H. Development of nocturnal respiratory disturbance in untreated patients with obstructive sleep apnea syndrome. Chest 1993; 104:340-343.
5. Pendlebury ST, Pepin JL, Veale D, et al. Natural evolution of moderate sleep apnoea syndrome: significant progression over a mean of 17 months. Thorax 1997; 52:872-878.
6. Lindberg E, Elmasry A, Gislason T, et al. Evolution of Sleep Apnea Syndrome in Sleepy Snorers. A Population-based Prospective Study. Am. J. Respir. Crit. Care Med 1999; 159: 2024-2027.
7. Peppard PE, Young T, Palta M, et al. Longitudinal study of moderate weight changes and sleep-disordered breathing. JAMA 2000; 284;3015-3021
8. Young T, Peppard PE, Gotlieb DJ. Epidemiology of obstructive sleep apnea. Am J Respir Crit Care Med. 2002; 165:1217-1239.
9. Redline S, Schluchter MD, Larkin EK, et al. Predictors of longitudinal change in sleep-disordered breathing in a nonclinic population. Sleep 2003; 26:703-709.
10. Newman AB, Foster G, Givelber R, et al. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med 2005; 165:2408-2413.
11. Sahlman J, Pukkila M, Seppa J, et al. Evolution of mild obstructive sleep apnea after different treatments. Laryngoscope 2007; 117; 1107-1111.
12. Mason WJ, Ancoli Israel S, Kripke DF. Apnea revised: a longitudinal follow up. Sleep 1989; 12:423-429

13. Rosenthal LD, Roehrs TA, Roth T. Natural course of sleep apnea: a two years follow up. In: Kuna ST, Surrat PM, Remmers JE editors. Sleep and respiration in aging adults, New York: Elsevier, 1991. p 348.
14. Ancoli-Israel S, Kripke DF, Klauber MR, et al. Natural history of sleep disordered breathing in community dwelling elderly. Sleep 1993; 16:S25-29.
15. Sforza E, Addati G, Cirignotta F, et al. Natural evolution of sleep apnoea syndrome: a five year longitudinal study. Eur Respir J 1994; 7:1765-1770.
16. Hoch CC, Dew MA, Reynolds CF, et al. Longitudinal changes in diary and laboratory-based sleep measures in healthy "old old" and young old subjects: A three years follow up. Sleep 1997; 20: 192-202.
17. Quan SF. Evolution of OSA. Thorax 1998; 53: 532. (Letter).
18. Ancoli-Israel S, Gehrman P, Kripke DF, et al. Long-term follow-up of sleep disordered breathing in older adults. Sleep Med 2001; 2:511-516.
19. Fisher D, Pillar G, Malhotra A, et al. Long-term follow-up of untreated patients with sleep apnoea syndrome. Respir Med 2002; 96:337-343.
20. Lavie P. Sleep medicine – Time for a change. J Clin Sleep Med 2006; 2: 207–11.
21. Oksenberg A, Silverberg DS, Arons E, et al. Positional vs nonpositional obstructive sleep apnea patients. Anthropomorphic, nocturnal polysomnographic and multiple sleep latency test data. Chest 1997; 112: 629–639
22. Rechtschaffen A, Kales A. A manual of standardized terminology techniques and scoring system for sleep stages of human subjects. Los Angels: UCLA Brain Information Service, 1968.
23. Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1991; 14:540-5.
24. Pillar G, Peled R, Lavie P. Recurrence of sleep apnea without concomitant weight increase 7.5 years after weight reduction surgery. Chest 1994; 106:1702-1704.
25. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep disordered breathing and hypertension. N Engl J Med 2000; 342:1378-1384.

26. Bakx JC, van den Hoogen HJ, van den Bosch WJ, et al. Development of blood pressure and the incidence of hypertension in men and women over an 18-year period: results of the Nijmegen Cohort Study. J Clin Epidemiol 1999; 52:531-538
27. Lavie P, Lavie L, Herer P. All-cause mortality in males with sleep apnoea syndrome: declining mortality rates with age. Eur Respir J. 2005; 25): 514-520.

Table 1. Primary Snoring and Obstructive Sleep Apnea: Progressive or Stable

Author / Year*	N	Gender	Mean Age	Group Type	PSG settings	Follow-Up (years)
Progressive						
Bliwise et al, 1984[2]	10	M/F	51	GP	sleep lab	8.1
	15	M/F	73.6	GP	sleep lab	2.8
Phoha et al, 1990[3]	11	M/F	66	ST	sleep lab	3
Svanborg and Larsson,1993[4]	42	M/F	55	ST	SCSB/PSG	15.6 months
Pendlebury et al, 1997[5]	55	M/F	56	ST	sleep lab	17 months
Lindberg et al, 1999[6]	29	M	50	ST	sleep lab	10
Peppard et al, 2000[7]	690	M/F	46	GP	in-home	4
Young et al, 2002[8]	282	M/F	30-60**	GP	in-home	8
Redline et al, 2003[9]	486	M/F	32	GP	in-home	5.3
Newman et al, 2005[10]	2968	M/F	62	GP	in-home	5
Sahlman et al, 2007[11]	28	M/F	50.2	ST	In -home	3.9
Stable						
Mason et al, 1989[12]	32	M/F	70.3	GP	in-home	4.6
Rosenthal et al, 1991[13]	23	M/F	54.2	ST	sleep lab	2
Ancoli-Israel, 1993 [14]	24	M/F	70.1	GP	in-home	8.5
Sforza et al, 1994[15]	32	M/F	51	ST	sleep lab	5.7
Hoch et al, 1997[16]	50	M/F	61-87**	GP	sleep lab	3
Quan SF, 1998[17]	17	M/F	53	ST	sleep lab	6.9
Ancoli-Israel, 2001[18]	58	M/F	73	GP	in-home	18
Fisher et al, 2002[19]	40	M/F	47	ST	sleep lab	5

* Indicates reference number, ** age range

PSG= polysomnography, ST= seek-treatment, GP=general population. SCSB=static charge sensitive bed. NA= not available. Note that all studies used 2 polysomnographic recordings to compare progression of Apnea-Hypopnea Index (AHI).

Table 2. Demographic and sleep parameters data at baseline (T1) and at the end of follow-up period (T2).

Parameter		N	Mean ± SD	Median	Range	p value
Age (years)						
T1		160	50.6±11.4	50.8	19 – 83	
T2		160	55.8±11.4	56.9	26 – 84	
AHI (events/h)						
T1		160	23.0 ± 22.6	15.1	0.0 – 99.2	< 0.001
T2		160	28.9 ± 24.2	21.4	0.0 – 110.4	
BMI (kg/m^2)						
T1		160	29.3 ± 4.7	28.4	22.0 – 62.3	< 0.001
T2		160	30.1 ± 4.9	29.4	21.1 – 51.9	
ESS (units (0-24)						
T1		96	8.4±5.1	7.0	0 - 22	0.004
T2		98	10.2±5.4	10.0	0 - 23	
Lowest SaO_2 (%)	**REM**					
	T1	157	83.5 ± 11.2	86.0	35.0 – 96.0	0.004
	T2	157	80.7 ± 14.8	86.0	34.0 – 96.0	
	Non-REM					
	T1	156	86.1 ± 8.4	88.0	45.0 – 97.0	0.002
	T2	157	84.0 ± 9.5	84.0	42.0 – 97.0	
Maximum Snoring Intensity Level (dB)	**Supine**					
	T1	152	66.9 ± 9.0	68.0	40.0 – 91.0	0.587
	T2	144	66.9 ± 9.1	67.0	40.0 – 96.0	
	Lateral					
	T1	152	59.5 ± 10.1	60.0	40.0 – 82.0	0.044
	T2	157	61.0 ± 10.0	61.0	40.0 – 92.0	

AHI= Apnea Hypopnea Index, BMI= Body Mass Index, SaO_2= Oxygen Saturation, REM= Rapid Eye Movement. p values according to Wilcoxon Signed Rank Test analysis. The significance of Age is obvious.

Table 3. Change in Age, AHI, BMI, lowest SaO_2 during REM sleep and Non-REM sleep and ESS score over time for the four patient groups.

	AHI Severity Groups				
	Primary Snoring n=28	**Mild OSA n=49**	**Moderate OSA n=41**	**Severe OSA n=42**	**Differences among groups**
AGE					
T1	48.8±10.5	51.7±12.0	49.6±10.5	51.6±12.2	.657
T2	55.0±10.2	57.1±12.2	54.5±10.8	55.9±12.2	.731
Δ AGE	6.2 ± 2.6	5.4±3.0	4.9±3.0	4.3±3.1	.044
p value					
AHI					
T1	1.8±1.6	9.1±3.3	21±4.2	52.6±2	≤ 0.001
T2	13.4±12.9	21.7±16.7	29±19.3	45.6±30.2	≤ 0.001
Δ AHI	11.7±12.8	12.6±16.4	8.1±19.6	-7±28.2	≤ 0.001
p value	<.001	<.001	.025	.051	
BMI					
T1	26.6±3.3	28.7±3.3	28.8±3.4	31.4±4.3	≤ 0.001
T2	27.8±3.6	30.2±4.2	29.5±4.5	31.5±5.3	.003
Δ BMI	1.2±2.1	1.4±2	0.7±2.3	0.1±3.3	.011
p value	.005	<.001	.187	.995	
Lowest SaO_2/REM					
T1	91.3±3.4	87.±8.6	83±8	75±14.3	≤ 0.001
T2	90±4.1	83.4±12.3	78.1±15.2	73.7±17.9	≤ 0.001
Δ Lowest SaO_2/REM	-1.4±5.2	-3.5±11.2	-4.9±14.3	-1.3±14.2	.871
p value	.205	.046	.093	.339	
Lowest SaO_2/Non-REM					
T1	92±3	89.3.±4	85.2±5.6	79.4±11.8	≤ 0.001
T2	89.8±3.7	86.3±5	82.3±11.2	80±11.7	≤ 0.001
Δ Lowest SaO_2/Non-REM	-2.2±3.4	-3.1±5.5	-3±11.4	0.6±11.3	.057
p value	.006	<.001	.462	.728	
ESS					
T1	7.8±5.3	8.9±4.8	8.7±5.1	8.1±5.5	.919
T2	7.9±4.8	10.2±5.4	11.0±5.2	11.3±5.6	.174
Δ ESS	0.8±5.6	2.2±5.2	2.9±4.9	2.1±5.2	.775
p value	.594	.090	.050	.298	

AHI= Apnea Hypopnea Index, OSA= Obstructive Sleep Apnea, T1= baseline, T2= end of follow-up, BMI= Body Mass Index, SaO_2= Oxygen saturation, REM= Rapid Eye Movement, ESS=Epworth Sleepiness Scale. Primary Snoring (AHI < 5), Mild OSA (AH = 5 -15), Moderate OSA (AHI =15-30), Severe OSA (AHI = > 30). p values between groups according to Kruskal – Willis test and p values for differences between T1 and T2 according to Wilcoxon Signed Rank test.

Table 4. Age, BMI, and AHI of patients who improved, did not change, or worsened the AHI between baseline (T1) and follow-up (T2)

		Groups			p value
		Improved n = 23 (14.4%)	**Unchanged n = 74 (46.2%)**	**Worsened n = 63 (39.4%)**	
Age (yrs)	**T1**	52.8±13.7	50.9±10.5	49.5±11.5	.478
	T2	55.7±13.5	56±10.8	55.6±11.6	.978
BMI (kg/m^2)	**T1**	29.8±4.1	29.4±5.8	29±3.4	.782
	T2	28.3±3.5	30±5.4	30.8±4.8	.107
AHI (events/hr)	**T1**	40.9±19	22.4±26.4	16.2±14.4	<.001
	T2	13.2±8.9	23.2±24.7	41.4±21.6	<.001

BMI= Body Mass Index, AHI= Apnea Hypopnea Index. Improved, unchanged or worsened of AHI was defined as a 25% change or more of initial AHI[8]

Table 5. The number of patients with HT and CVD at baseline (T1) and end of follow-up (T2)

	No. of Patients (%) (n = 160)					
	HT Alone	**CVD Alone**	**HT and CVD**	**Total**		
				HT	**CVD**	**HT and/or CVD**
T1	32 (20)	11 (6.9)	11 (6.9)	43 (26.9)	22 (13.8)	54 (33.8)
T2	41 (25.6)	9 (5.6)	15 (9.4)	56 (35)	24 (15)	65 (40.6)
T2-T1	9 (5.6)	-2 (-1.3)	4 (2.5)	13 (8.1)	2 (1.3)	11 (10.4)

HT= hypertension, CVD= cardiovascular disease.

Note that components may not sum to totals because of rounding.

Table 6. Risk factors for developing HT and/or CVD*

	HT and/or CVD (n = 65)	No HT and/or CVD (n = 90)	OR (95%CI)
Age / T2 (year)	60.4±11.6	52.8±10.2	1.08 (1.04 - 1.12)
BMI / T2 (unit)	31±4.7	29.2±4.6	1.13 (1.04 - 1.22)

HT= Hypertension, CVD= Cardiovascular Disease, Confidence Interval = CI, T2= end of the follow-up period, BMI= Body Mass Index.

Note that the number of patients exceeds 160 because patients may have more than one disease.