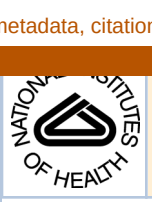

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Insomnia in untreated sleep apnea patients compared to controls

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Abstract

Insomnia and obstructive sleep apnea (OSA) often co-exist, but the nature of their relationship is unclear. The aims of this study were to compare the prevalence of initial and middle insomnia between OSA patients and controls from the general population as well as to study the influence of insomnia on sleepiness and quality of life in OSA patients.

Two groups were compared, untreated OSA patients (n=824) and controls ≥ 40 years from the general population in Iceland (n=762). All subjects answered the same questionnaires on health and sleep and OSA patients underwent a sleep study. Altogether, 53% of controls were males compared to 81% of OSA patients.

Difficulties maintaining sleep (DMS) were more common among men and women with OSA compared to the general population (52 vs. 31% and 62 vs. 31%, respectively, p<0.0001). Difficulties initiating sleep (DIS) and DIS+DMS were more common among women with OSA compared to women without OSA. OSA patients with DMS were sleepier than patients without DMS (Epworth Sleepiness Scale: 12.2 vs. 10.9, <0.001) while both DMS and DIS were related to lower quality of life in OSA patients as measured by the Short Form 12 (physical score 39 vs. 42 and mental score 36 vs. 41, p<0.001). DIS and DMS were not related to OSA severity.

Insomnia is common among OSA patients and has a negative influence on quality of life and sleepiness in this patient group. It is relevant to screen for insomnia among OSA patients and treat both conditions when they co-occur.

Keywords

Insomnia; sleep apnea; risk factors; population sample

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Introduction

Insomnia is a common and often persistent complaint and includes symptoms such as difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS). Studies of population-based samples have found the prevalence of insomnia to range between 10% and 48%, depending on the definition of insomnia that is used and the population studied (Roth *et al*., 2007; Morphy *et al*., 2007; LeBlanc *et al*., 2009). Insomnia can be an independent disorder (primary insomnia) or comorbid with another medical or psychiatric condition. Primary insomnia is estimated to affect about 25% of all patients suffering from chronic insomnia (Buysse *et al*., 1997). Female gender, age, poor self-rated health and snoring have been associated with increased rates of insomnia symptoms (Klink *et al*., 1992; Hartz *et al*., 2007).

Like insomnia, obstructive sleep apnea (OSA) is a prevalent disorder, often with serious adverse consequences. OSA is characterized by loud snoring and frequent breathing pauses during the night due to increased airway resistance which leads to partial (hypopnea) or complete (apnea) upper airway collapse (Pack and Gislason, 2009). These events lead to repeated drops in oxygen saturation and, over time, OSA can contribute to impaired daytime function including excessive daytime sleepiness (EDS), and increased behavioral, metabolic and cardiovascular morbidity and mortality. Although the most common symptoms of OSA are loud snoring and daytime sleepiness the condition is often undiagnosed (Young *et al*., 2007).

Complaints of insomnia are frequent among OSA patients (Benető *et al*., 2009) and in recent years there has been a growing interest in the co-existence of these disorders. When insomnia and OSA co-occur, it is likely that the interaction promotes overall greater illness severity (both in terms of OSA and insomnia) and increases cumulative medical and psychiatric morbidity (Krakow *et al*., 2001; Smith *et al*., 2004; Luyster *et al*., 2010).

Studies on the relationship between OSA and insomnia have estimated that between 40-60% of untreated OSA patients are suffering simultaneously from chronic insomnia, a rate which far exceeds the prevalence in the general population (Krell and Kapur, 2005; Wickwire and Collop, 2010; Chung, 2005; Subramanian *et al*., 2010). However, there has been a lack of studies directly comparing the prevalence of insomnia and its subtypes between untreated OSA patients and controls from the general population. Since insomnia is prevalent among OSA patients, it is also of interest whether people from the general population with symptoms of OSA are at increased risk for insomnia.

The aims of the study were a) to compare the prevalence of difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS) in untreated OSA patients vs. controls; b) to examine whether OSA symptoms are risk factors for insomnia symptoms in a general population sample from Iceland; c) to examine whether the co-existence of OSA and insomnia has an additional negative effect on quality of life compared to OSA alone.

Subjects and Methods

Participants

1) Patients diagnosed with OSA in Iceland and referred for treatment with continuous positive airway pressure (CPAP) to the Landspitali-The National University Hospital of Iceland from September 2005 - December 2009 were invited to participate in the study. They are part of the Icelandic Sleep Apnea Cohort (ISAC). Over 90% of the eligible subjects who were approached agreed to participate. Altogether 824 patients with OSA took

part in this study. Among OSA patients, 81% were males and 19% were females, and the mean age was 54.4 ± 10.7 years.

2) The controls were 762 individuals aged 40+, randomly sampled from the general population in Iceland with a response rate of 81% (Benediktsdottir *et al*., 2010). Among controls, 53% were males and 47% were females. The controls were on average two years older (56.4 vs. 54.4) than OSA patients ($p<0.001$).

Questionnaire and procedure

All participants (both OSA patients and controls) were invited to the outpatient clinic at the Landspitali-The National University Hospital of Iceland. After written informed consent was obtained, they answered standardized questionnaires about sleep, daytime sleepiness, health, lifestyle and quality of life. The protocol was approved by the National Bioethics Committee of Iceland.

Insomnia

Insomnia was defined using answers to two questions from the Basic Nordic Sleep Questionnaire: “I have difficulties falling asleep at night” (DIS) and “I wake up often during the night” (DMS) based on the past month (Partinen and Gislason, 1995). The answers were rated on a five point scale: never/almost never (1); less than once a week (2); once or twice a week (3); three to five times a week (4); every day or almost every day of the week (5). Those who scored ≥ 4 were defined as having insomnia. The prevalence of having both DIS and DMS at the same time (DIS+DMS) was also explored.

Daytime sleepiness, body mass index and snoring

Daytime sleepiness was evaluated with the Epworth Sleepiness Scale (ESS) (Johns, 1992) and excessive daytime sleepiness (EDS) was defined as ESS score ≥10. Standardized methods were used to measure height and weight. BMI was calculated as kg/m^2. Habitual snoring was defined as snoring ≥ 3 nights per week.

Quality of life

Assessment of quality of life was based on the SF-12 questionnaire, a short form of the SF-36, the most widely used health survey. Two summary component scores can be derived from the SF-12, both physical (PS) and mental (MS) health summary scores (Ware *et al*., 1996). These scores range from 0-100, where a zero score indicates the lowest life quality and 100 indicates the highest life quality.

Restless legs syndrome

Diagnostic criteria for restless legs syndrome was based on answers from the International Restless Legs Syndrome Study Group Questionnaire (IRLS) (Benediktsdottir *et al*., 2010; Allen *et al*., 2003). Those who answered the questionnaire as following were regarded as having RLS; they had a strong urge to move their legs often or very often. The discomfort in the legs was relieved by moving the legs or walking. The symptoms had to be most prominent in the evening, at bedtime or no difference of symptoms by the time of day.

Diabetes and hypertension

Participants were defined as having diabetes if they indicated that they had been diagnosed by a doctor and were using medication for diabetes. Similarly, they were considered to have hypertension if they had been diagnosed by a doctor and were on antihypertensive medication.

Smoking history

Participants were asked about their smoking history; subjects who smoked more than 20 packs of cigarettes in a lifetime or more than one cigarette each day for a year but were not current smokers were defined as being ex-smokers. Those who had never smoked or smoked less than 20 packs of cigarettes in their lifetime were defined as being never smokers, while subjects reporting still to be smoking were classified as current smokers.

Sleep apnea

All OSA subjects had a sleep study while untreated with an Embletta type 3 portable monitor or an Embla 12 channel system (Embla™; Flaga Inc., Reykjavik, Iceland) recording the same channels. The sleep recordings were scored in a uniform manner at the Sleep Study Reading Unit of the University of Pennsylvania. These data were used to calculate an apnea/hypopnea index (AHI). Events were scored according to the following definitions: a classification of hypopnea required a ≥30% or greater drop in flow with ≥ 4% oxygen desaturation or a ≥50% drop in flow for ≥10 seconds with a sudden increase in flow at the end of the event. A classification of an obstructive apnea required a ≥80% drop in flow for ≥10 seconds. The oxygen desaturation index (ODI) was calculated as the number of falls in oxygen of >4% per hour of sleep. The minimum SaO_2 was defined as the lowest oxygen saturation reached during the study. Controls did not have a sleep study.

OSA high and low risk controls

Controls were defined as OSA high risk or low risk based on the multivariable apnea index (MAP) (Maislin *et al*., 1993). The MAP score is based on self reported presence of apnea symptoms (snoring or gasping, breathing stops, choking or struggling for breath during night) as well as BMI and gender. The MAP score ranges between 0 and 1 where subject who score 0 are the least likely to have sleep apnea. A cut-off of 0.5 has been shown to have sensitivity of 0.88, specificity of 0.55 and positive predictive value of 0.75 in predicting OSA (Maislin *et al*., 1993). This cut-off has however mostly been used on patient groups and therefore a cut-off of 0.75 in the MAP index was used in this study to divide controls into OSA high and low risk groups.

Statistical analyses

All statistics were calculated with STATA 11.0 for Windows (Stata Corporation, College Station, Texas). Differences between the groups of subjects with and without OSA were first compared using the Chi-square test and unpaired t-test. Multiple logistic regression was then used to identify which risk factors had an independent association with the outcome variables. A p value < 0.05 was regarded as statistically significant.

Results

Study population characteristics

Table 1 shows that there were more males among the OSA patients and that they had a higher BMI, were sleepier and less likely to be never-smokers than controls. In addition, they had a higher prevalence of hypertension, diabetes and RLS compared to the control population. DMS was more common among men and women with OSA compared to the general population. DIS and DIS+DMS were more common among women with OSA compared to women without OSA (Table 1).

The prevalence of insomnia

The majority of the OSA patients (57.6%) reported difficulties maintaining sleep compared to 32% of the controls ($p<0.001$). The difference in the prevalence of difficulties initiating sleep (DIS) and DIS+DMS were however not significant between the two groups. DMS was similarly common among men and women while having DIS and DIS+DMS was more common among women ($p<0.05$). Overall, symptoms of insomnia were more frequently reported by women in both groups (Table 1 and Figures 1 and 2).

Associations with insomnia in controls and OSA patients

Table 2 shows that among the controls, poor mental and physical quality of life, hypertension and RLS were independent risk factors for both DIS and DMS. In addition, a high map score was an independent risk factors for DMS.

Among the OSA patients, female gender and smoking were independent risk factors for DIS while age and RLS were independent risk factors for DMS. Lower mental and physical qualities of life were associated with both DIS and DMS among controls and OSA patients (table 3).

DMS was significantly associated with OSA in men when this was tested by combining the patient population and the general population and adjusting for possible confounders (table 4). No significant association between OSA and DMS was found in women and no significant independent association between OSA and DIS was found in either gender.

Characteristics of OSA patients and controls with and without insomnia

Among the controls, subjects with DIS and DMS were older, had higher BMI, higher prevalence of hypertension and RLS and reported poorer mental and physical life qualities compared to controls without DIS and DMS. In addition, controls with DIS were less sleepy than controls without DIS (table 5).

Table 6 shows that there was no difference in age, BMI or daytime sleepiness between the OSA patients with and without DIS. However, the OSA patients with DIS reported poorer mental and physical quality of life and a higher prevalence of RLS compared to OSA patients without DIS. The OSA patients with DMS were older, with more daytime sleepiness, higher prevalence of RLS and poorer quality of life than the OSA patients without DMS (table 6). When considering the genders separately, the only difference was that men with DMS were older than men without DMS (54.8 years vs. 51.9 years; $p<0.001$) but no significant age difference was found among women. In addition, women with DIS did not report poorer physical health while that difference remained significant among men ($p<0.001$).

The prevalence of DIS and DMS was not related to OSA severity expressed as AHI, minimum SaO_2 or ODI.

OSA high risk and low risk controls

The OSA high risk definition was met by 92 (12.0%) controls with a mean MAP score of 0.81 ±0.05. The low risk controls were 672 (88.0%) individuals with a mean MAP score of 0.33±0.2.

DMS was reported among 39.7% of high risk controls compared to 31.1% of low risk controls ($p=0.135$). DIS was reported among 22.9% of high risk controls compared to 13.2% of low risk controls ($p=0.027$). Both DIS and DMS were most frequent among subjects with the highest MAP score (0.75-1.0). Symptoms of DIS are particularly common among

subjects with MAP score between 0.75-1.0 compared to subjects with a lower MAP score ($p<0.05$) (figure 3). High risk controls reported poorer physical life qualities compared to low risk controls ($p<0.001$) but the difference in mental life qualities was not significant.

Figure 3. Prevalence (%) of difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS) based on multivariable apnea index (MAP).

Discussion

In our study, the majority of the OSA patients (57.6%) had DMS compared to one third of controls. The prevalence of DIS and DIS+DMS was only significantly higher among women with OSA compared to women without OSA. This is not surprising since 80% of the OSA patients in this study were men and DIS is generally more common among women (Subramanian *et al*., 2010; Li *et al*., 2002).

The OSA patients with insomnia reported poorer physical and mental quality of life compared to patients without insomnia. Furthermore, the OSA patients with DMS were older and sleepier than other OSA patients. Patients with DIS were not sleepier than patients without DIS which is consistent with the idea of insomnia as a state of hyper-arousal.

Poor physical and mental health as measured by the SF 12, RLS and hypertension were significantly related to an increased risk of insomnia in the general population. Overall, 12% of the general population had a high risk for OSA when using the 0.75 cut-off point in the MAP index. This is a very high prevalence which might suggest that OSA is often undiagnosed. Being in high risk for OSA as measured by the MAP was an independent risk factor for DMS among controls.

Among the OSA patients, female gender, smoking history and poor mental and/or physical life qualities were independent risk factors for DIS, while age, RLS and poor mental life qualities were independent risk factors for DMS. It is important to note, however, that poor quality of life can be the result of insomnia rather than a predictor of the disorder. The association we have demonstrated does not allow us to distinguish between these possibilities. Some components of quality of life, such as pain and anxiety, are likely risk factors for the onset of insomnia while other components such as being inactive and depressed can be the result of insomnia (LeBlanc *et al*., 2009; Hartz *et al*., 2007). As there was no evaluation of depression and anxiety besides the Short Form 12 in this study the use of other tools would have been beneficial in order to understand this association better.

One explanation for the high rate of insomnia in patients with OSA is that the apnea may serve as a precipitating factor for DIS and DMS and may co-occur in such a manner as to exacerbate these conditions. It is possible that when falling asleep some OSA patients may be repeatedly disrupted from light sleep by an apnea event causing them not to perceive sleeping in between the disruptions. These events could recur many times before sleep is established and as a result the patient experiences long sleep latency. The same pattern could happen when patients wake up in the middle of the night and are having difficulties falling back to sleep. Alternatively, apneic events may lead to full awakenings from sleep, but then the individual is not able to fall back to sleep due to sleep-related anxiety and conditioned arousal.

Symptoms of insomnia may have a negative effect on CPAP treatment in that it is probably difficult for those insomnia patients who have DIS to spend a long time awake in order to adapt properly to the CPAP device. On the other hand, those OSA patients who wake up frequently because of apneic episodes and complain of difficulty maintaining sleep might experience more refreshing sleep and adjust favorably to CPAP. It would therefore be

interesting to study the prevalence of insomnia subtypes among OSA patients before and after CPAP.

It has been suggested that the best treatment results are obtained when patients are treated for both disorders separately (Wickwire and Collop, 2010). There is clearly a co-occurrence of these disorders which could have important clinical implications. Compliance to CPAP treatment is relatively poor but only around 50% of patients are compliant with treatment over time (Haynes, 2005). Insomnia could have a negative effect on CPAP compliance and therefore it could be important to adjust treatment of these conditions when they co-exist in order to minimize the negative impact on quality of life and avoid a vicious cycle where these conditions intensify the severity of each other.

Comparing the prevalence of insomnia among studies is often difficult due to the differences in the definition of insomnia and the different populations studied. Some studies have reported a similar prevalence of insomnia among sleep apnea patients (Krakow *et al*., 2001; Luyster *et al*., 2010; Krell and Kapur, 2005; Subramanian *et al*., 2010) as we did here, but others have found a slightly lower prevalence (Smith *et al*., 2004; Wickwire and Collop, 2010). However, it is a shared conclusion that symptoms of insomnia are more prevalent among OSA patients than in the general population. Theoretically, this is surprising since one of the main symptoms of OSA is daytime sleepiness and therefore one might think that these patients would be protected against insomnia. The fact that insomnia is so prevalent among OSA patients strongly hints to a mechanistic link between these conditions.

In our study, there was no relationship between OSA severity and insomnia even though having OSA was a strong risk factor for DMS. This is surprising and one possible explanation might be that patients with more severe sleep apnea have greater hypercapnia because of the severity of their disease, their increased weight and the possible co-occurrence of obstructive pulmonary disease (COPD). This could mean that they are sleepier at bedtime and less likely to wake up during the night (Kaw *et al*., 2009; Witzenblum *et al*., 2008). Similar results were found in a recent study (Hagen *et al*., 2009) which indicated that even though OSA and insomnia often co-exist, insomnia is still independent of the degree of OSA. Another study by Kapur and colleagues (2005) suggested that DMS and sleep apnea severity were independent of each other, but it is clear that prospective studies are needed to further clarify the issue.

Our study is the first one to look systematically at a high MAP index as an independent risk factor for insomnia in a general population sample. Having a high MAP index (≥0.75) was a significant predictor for DMS. This is not surprising given the high prevalence of DMS among OSA patients. However, having DMS was not more prevalent among high risk subjects compared to low risk subjects (p=0.135). DIS was on the other hand more prevalent among those in the high risk group (p=0.027).

The current study has several limitations. The insomnia definition was based on two questions answered in a self-report, whereas having a more accurate insomnia evaluation would have been beneficial. Subjects from the general population sample were all aged 40 years or older and therefore results from this study cannot be generalized to younger people. This study was cross-sectional and therefore we could not assess whether the variables associated with the presence of insomnia were risk factors or consequences of insomnia. Lastly, OSA was not objectively assessed in the control group so the prevalence and associations with insomnia in the general population cannot be accurately determined from these data.

In summary, we found that OSA and DMS frequently co-exist and patients with both conditions are older, sleepier and report poorer life qualities than other OSA patients. There

are a number of clinical implications of these results. First, providers should routinely screen for the presence of insomnia in OSA patients given that it is associated with greater impairment in quality of life than OSA alone and the possible negative impact on CPAP treatment. Assessment of insomnia should take into account the insomnia subtypes among these patients since different subtypes have different rates, consequences and risk factors. Providers should consider treating both conditions together when they co-occur in order to maximize clinical outcomes. This may lead to both direct improvement in symptoms by reducing the severity of insomnia, and indirectly, by influencing adherence to CPAP treatment. Further studies are needed to explore whether pharmacologic or cognitive behavioral treatment of insomnia optimizes outcomes in this population when combined with CPAP.

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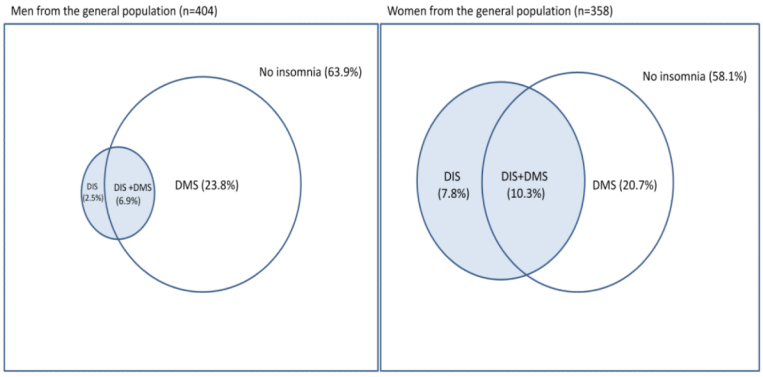

Figure 1.
Prevalence of difficulties initiating sleep (DIS), difficulties maintaining sleep (DMS) and DIS+DMS among men and women from the general population.

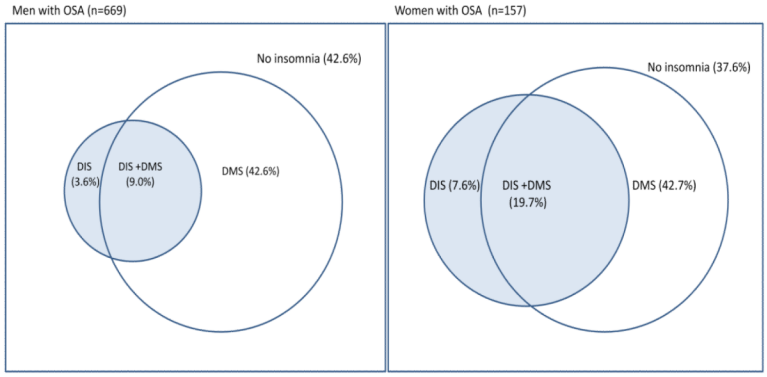

Figure 2.
Prevalence of difficulties initiating sleep (DIS), difficulties maintaining sleep (DMS) and DIS+DMS among OSA patients.

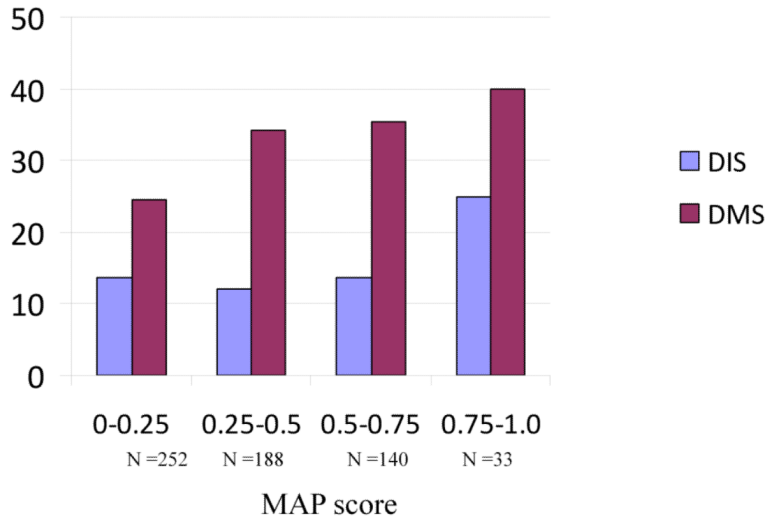

Figure 3.
Prevalence (%) of difficulties initiating sleep (DIS) and difficulties maintaining sleep (DMS) based on multivariable apnea index (MAP).

Table 1

Characteristics of study population

	Men			Women		
	Controls (n=404)	OSA (n=669)	P-value	Controls (n=358)	OSA (n=157)	P-value
Age (years)	56.4±11.5	53.5±10.8	**<0.0001**	57.7±12.2	58.4±9.1	0.903
BMI (kg /m^2)	28.3±4.4	33.4±5.6	**<0.0001**	27.5±5.5	34.1±6.3	<0.0001
Smoking history			**<0.0001**			0.160
Never smoker (%)	38.7	27.1	**<0.0001**	39.7	30.6	0.068
Ex-smoker (%)	45.8	51.4	0.074	38.9	50.3	**0.018**
Smokers (%)	15.5	21.5	**0.008**	21.4	19.1	0.914
Hypertension (%)	30.2	54.8	**<0.0001**	36.1	66.2	**<0.0001**
Diabetes (%)	4.6	10.7	**0.002**	5.3	11.5	**0.026**
RLS (%)	12.9	22.3	**<0.0001**	24.4	33.8	0.052
EDS (ESS≥10)	22.8	65.4	**<0.0001**	23.2	63.1	<0.0001
DIS (%)	9.4	12.6	0.221	18.1	27.3	**0.026**
DMS (%)	30.7	51.6	**<0.0001**	31.0	62.4	**<0.0001**
DIS+DMS (%)	6.9	9.0	0.412	10.3	19.7	**0.003**

BMI (body mass index), EDS (Excessive daytime sleepiness), ESS (Epworth sleepiness scale), RLS (restless leg syndrome), DIS (Difficulties initiating sleep), DMS (Difficulties maintaining sleep). Significance is marked as bold.

Table 2

Factors associated with DIS and DMS in the general population. The association expressed as adjusted odds ratio with a 95% confidence interval (OR (95% CI).

	DIS OR (95% CI)*	DMS (OR 95% CI)*
Smoking history	0.96 (0.69-1.33)	0.98 (0.77-1.24)
RLS	**2.69 (1.60-4.53)**	**2.08 (1.36-3.18)**
SF12 MS	**0.91 (0.87-0.95)**	**0.95 (0.92-0.99)**
SF12 PS	**0.93 (0.90-0.95)**	**0.97 (0.94-0.99)**
Diabetes	0.59 (0.21-1.66)	0.92 (0.44-1.95)
Hypertension	1.21 (0.74-1.96)	**1.64 (1.15-2.34)**
Map index	1.59(0.59-4.35)	**2.13 (1.02-4.43)**

*adjusted for all the variables in the table. RLS (restless leg syndrome), SF12 MS (Short form 12 mental score), SF12 PS (Short form 12 physical score), MAP (Multivariable apnea index). Significance is marked as bold.

Table 3

Factors associated with DIS and DMS among OSA patients. The association expressed as adjusted odds ratio with a 95% confidence interval (OR (95% CI).

	DIS OR (95% CI)*	DMS (OR 95% CI)*
Age per 10 years	0.89 (0.70-1.10)	**1.27 (1.08-1.48)**
Female gender	**2.43 (1.51-3.91)**	0.89 (0.60-1.31)
BMI by 5 units	1.04 (0.86-1.27)	1.14 (0.98-1.32)
Ex smoker	0.97 (0.56-1.68)	1.12 (0.80-1.63)
Current smoker	**2.40 (1.35-4.25)**	0.96 (0.63-1.47)
Snoring every day	0.64 (0.38-1.07)	1.29 (0.88-1.88)
RLS	1.11 (0.69-1.77)	**1.71 (1.18-2.46)**
SF12 MS	**0.96 (0.94-0.98)**	**0.98 (0.97-1.00)**
SF 12 PS	**0.97 (0.95-0.99)**	**0.98 (0.97-1.00)**
Diabetes	1.03 (0.54-2.00)	0.69 (0.42-1.13)
Hypertension	1.12 (0.70-1.78)	1.00 (0.72-1.38)

* adjusted for all the variables in the table. BMI (body mass index), RLS (restless leg syndrome), SF12 MS (Short form 12 mental score), SF12 PS (Short form 12 physical score). Significance is marked as bold.

Table 4

The association between OSA with DIS and DMS in men and women. The association expressed as adjusted odds ratio with a 95% confidence interval (OR (95% CI)).

	DIS (OR (95% CI)*	DMS (OR (95% CI)*
Men	0.55 (0.32-1.97)	**2.11 (1.52-2.93)**
Women	0.60 (0.26-1.23)	1.50 (0.83-2.69)

* Adjusted for population (patient vs. controls), age, BMI, smoking history, RLS, mental and physical life qualities, hypertension and diabetes. Significance is marked as bold.

Table 5

Age, daytime sleepiness, SF12 and BMI in controls without and with DIS and DMS. Data shown as mean ±SD.

	No DIS (n=635)	DIS (n=103)	P value	No DMS (n=503)	DMS (n=235)	P value
Age (years)	55.6±11.4	61.0±12.8	**<0.001**	54.9±11.4	59.1±11.5	**<0.001**
ESS	6.1±3.8	5.1±4.1	**0.026**	5.9±3.8	6.1±4.0	0.452
Short Form 12						
Mental score	51.6±4.4	49.9±6.3	**<0.001**	51.6±4.4	50.8±5.2	**0.038**
Physical score	51.7±7.1	47.0±10.0	**<0.001**	51.8±7.2	49.3±8.6	**<0.001**
BMI(kg /m^2)	27.7±4.8	28.9±5.6	**0.017**	27.6±4.8	28.5±5.1	**0.029**
Hypertension	31.9%	41.8%	**0.049**	28.6%	43.2%	**<0.001**
Diabetes	4.6%	5.8%	0.608	4.2%	5.9%	0.303
RLS	15.3%	34.6%	**<0.001**	14.7%	26.1%	**<0.001**

BMI (body mass index), ESS (Epworth sleepiness scale), RLS (restless leg syndrome). Significance is marked as bold.

Table 6

Age, daytime sleepiness, SF12 and BMI in OSA patients without and with DIS and DMS. Data shown as mean ±SD

	No DIS (n=695)	DIS (n=127)	P value	No DMS (n=343)	DMS (n=480)	P value
Age (years)	54.5±10.6	54.2±10.8	0.723	53.1±10.7	55.5±10.4	**0.002**
ESS	11.8±5.0	11.2±5.4	0.212	10.9±5.0	12.2±5.0	**<0.001**
Short Form 12						
Mental score	49.2±10.5	43.2±12.0	**<0.001**	49.4±10.7	47.6±11.0	**0.022**
Physical score	41.0±10.7	36.3±10.9	**<0.001**	42.2±10.5	38.9±11.0	**<0.001**
BMI(kg /m2)	33.4±5.8	33.9±5.3	0.349	33.1±5.3	33.7±6.0	0.116
Hypertension	56.1%	61.9%	0.224	54.6%	58.8%	0.227
Diabetes	10.7%	11.9%	0.696	11.4%	10.5%	0.673
RLS	22.9%	33.1%	**0.014**	17.2 %	29.7%	**<0.001**

BMI (body mass index), ESS (Epworth sleepiness scale), RLS (restless leg syndrome). Significance is marked as bold.