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ORIGINAL RESEARCH

Prevalence of sleep-related symptoms in a primary care population – their relation to asthma and COPD

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Abstract

Aims: The aim of this study was to clarify the association between obstructive sleep apnoea/hypopnoea syndrome (OSAHS)-related symptoms and physician-diagnosed asthma and COPD.

Methods: 1501 subjects aged 19-90 years completed a structured questionnaire and underwent spirometry and respiratory physician assessment in 10 primary care centres.

Results: Frequent snoring was reported in 45.6%, breathing pauses during sleep in 11.0%, and excessive daytime sleepiness in 6.7% of the sample. COPD patients were more likely to report frequent snoring (OR=1.34; 95% CI:1.04-1.71), breathing pauses (OR=1.46; 95% CI:1.01-2.10), and excessive daytime sleepiness (OR=2.04; 95% CI:1.33-3.14). In contrast, there was no significant association between asthma patients and OSAHS-related symptoms. Gender differences were recognised as well.

Conclusions: The increased likelihood for OSAHS-related symptoms in COPD patients, in contrast to patients with asthma, designates them as a target group for the screening of OSAHS in primary care.

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Keywords obstructive sleep apnoea/hypopnoea syndrome, asthma, chronic obstructive pulmonary disease, snoring, sleepiness

Introduction

The obstructive sleep apnoea/hypopnoea syndrome (OSAHS) is a condition characterised by recurrent episodes of upper airway obstruction during sleep.[1] The most common clinical presentations of OSAHS include snoring, breathing pauses observed by the patient's bed partner, and daytime sleepiness.[2] This syndrome is often underdiagnosed, since less than 10% of patients with significant OSAHS are recognised.[3] Reasons for the underdiagnosis include the limited education of doctors in sleep disorders and patients' inability to inform doctors about sleep problems.[4]

OSAHS has been associated with many medical problems. Lately, epidemiological studies have demonstrated a positive connection between obstructive sleep apnoea and cardiovascular diseases (CVD).[5] OSAHS often coexists with COPD, and this coexistence has been confirmed in epidemiological studies.[6] An association of snoring and breathing pauses in subjects with asthma-related symptoms has also been reported,[7,8] but these results were not confirmed in other studies.[9]

OSAHS – especially if there is excessive daytime sleepiness – has been associated with workplace problems and motor vehicle accidents, resulting in diminished quality of life and increased morbidity and mortality.[10] The early detection of OSAHS-related symptoms by primary care physicians may be essential in order to reduce co-morbidity and the burden on public health services. Only a few studies in the literature have focused on screening for OSAHS-related symptoms in primary

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care, and even less on the relation of such symptoms to other major respiratory disorders, such as asthma and COPD.

The aim of the present study was to estimate the prevalence of OSAHS-related symptoms and risk factors in a population of Greek adults visiting primary care offices, and to determine whether these symptoms were associated with a physician-confirmed diagnosis of asthma or COPD. The secondary aims of this study were to assess differences in OSAHS-related symptoms between different genders and in patients with a history of hypertension, CVD and stroke.

Materials and methods

The study was conducted over a 1-year period (from January 2004 to February 2005) in 10 primary care centres in Greece. Subjects included in the study were Greek residents, aged 19-90 years old, who visited primary care doctors for any reason. The study population was a random sample of the patients attending each primary care centre. The study co-ordinators visited each primary care centre on the first five working days of one month. Participation in the study was offered to 1821 patients who attended the primary care centres on these days and 1501 patients agreed to participate in the study – a response rate of 82.4%. A structured questionnaire was completed for all patients. Subsequently, all patients were subjected to spirometry, and assessment of body mass index (BMI) by measuring their weight and height and expressing it in kg/m^2. The demographic characteristics of the study participants are shown in Table 1.

Table 1. Demographic data of the study participants.

Characteristic	Data	(%)
Gender	1501	
Male	892	59.4
Female	609	40.6
Age (years)	60.7±14.3	
<45y	278	18.5
46-65y	522	34.8
>66y	701	46.7
BMI (kg/m^2)	28.9±4.7	
<30 kg/m^2	951	63.4
≥30kgr/m^2	550	36.6
Smoking status		
Current	537	35.8
Former	271	18.1
Never	693	46.2
Hypertension	716	47.7
Cardiovascular diseases*	270	17.1
Stroke	54	3.5
COPD	323	21.5
Stage I (FEV$_1$ ≥80%)	93	6.1
Stage II (FEV$_1$ 50-79%)	172	11.4
Stage III (FEV$_1$ 30-49%)	49	3.2
Stage IV (FEV$_1$ <30%)	9	0.5
Asthma	218	14.5

*Cardiovascular diseases include congestive heart failure, coronary artery disease, and arrhythmias

Study questionnaire

A questionnaire was used to collect demographic information and past medical history, including smoking habit, hypertension, CVD (congestive heart failure, coronary artery disease, and arrhythmias), and stroke, as well as other significant co-morbidities (e.g. diabetes, hypothyroidism, depression, and use of medication). Medical records and prescribing records were reviewed in the majority of the patients who participated in the study, in order to validate the presence of co-morbidities. Specific questions about symptoms related to asthma and COPD were also included; patients were asked if they had any of the following symptoms during the past year – cough, sputum production, shortness of breath while exercising or during sleep, or wheezing. Questions about asthma attacks or use of asthma medication, and allergic rhinitis, were also included.

Subsequently, participants underwent an interview by physicians specially trained in respiratory and sleep disorders. Two instruments were used for identification of OSAHS symptoms;

- symptoms related to OSAHS were assessed using the Berlin Questionnaire,[11] which has been previously used in epidemiological studies in primary care. This questionnaire has increased sensitivity and specificity for the identification of patients with clinically significant OSAHS, i.e. an apnoea/hypopnoea index >5 events/hour in a sleep study. It includes questions about snoring, witnessed apnoeas, tiredness, history of high blood pressure and/or BMI >30 kg/m^2. Positive answers to two of the three categories of the questionnaire indicate a high pre-test probability for OSAHS.
- subjective daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESS); scores ≥10 are consistent with excessive daytime sleepiness.[12]

Spirometry

Spirometry was performed with a dry spirometer (Koko Legend, Ferraris Louisville, CO, USA) according to American Thoracic Society (ATS) Guidelines.[13] Forced expiratory volume in one second (FEV$_1$), forced vital capacity (FVC), and their ratio (FEV$_1$/FVC), were measured. All subjects with FEV$_1$ <80% of the predicted value and/or FEV$_1$/FVC<70% were

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Table 2. Distribution of responses according to gender and age. Data are presented as actual numbers with percentages in the specific age group in parentheses.

	MEN				WOMEN			
Age Groups	19-45	46-65	66+	Total	19-45	46-65	66+	Total
Snoring Frequency								
Almost every day	34(18.4)	81(30.9)	149(33.4)	264(29.5)	10(10.6)	66(25.3)	71(31.5)	147(24.1)
3-4 times/wk	33(17.9)	61(23.2)	80(17.9)	174(19.5)	15(15.9)	40(15.3)	45(20.0)	100(16.4)
1-2 times/wk	21(11.4)	16(6.1)	33(7.3)	70(7.8)	5(5.3)	19(7.3)	21(9.3)	45(7.3)
1-2 times/mo	26(14.1)	31(11.8)	46(10.3)	103(11.2)	16(17.0)	32(12.3)	29(12.8)	77(12.6)
Never or almost never	70(38.0)	73(27.8)	138(30.9)	281(31.5)	48(51.0)	103(39.6)	89(39.5)	240(39.4)
ESS								
0-9	178(96.7)	240(91.6)	400(89.6)	818(91.7)	93(98.9)	249(95.7)	240(94.1)	582(95.5)
≥10	6(3.2)	22(8.3)	46(10.3)	74(8.2)	1(1.1)	11(4.2)	15(5.8)	27(4.4)
Witnessed apnoeas								
yes	19(10.3)	47(17.9)	57(12.7)	123(13.7)	5(5.3)	21(8.1)	17(6.7)	43(7.1)
no	165(89.6)	215(82.0)	389(87.2)	769(86.2)	89(94.6)	239(91.9)	238(93.3)	566(92.9)
BMI >30kgr/m^2								
yes	49(26.6)	90(34.3)	146(32.7)	285(31.9)	26(27.6)	126(48.5)	126(49.4)	278(45.6)
no	135(73.4)	172(65.6)	300(67.2)	607(68.1)	68(72.3)	134(51.5)	129(50.6)	331(54.3)
Hypertension								
yes	12(6.5)	93(35.4)	304(68.1)	409(45.8)	4(4.2)	112(43.0)	191(74.9)	307(50.4)
no	172(93.5)	169(64.5)	142(31.8)	483(51.4)	90(95.8)	148(56.9)	64(25.0)	302(49.6)
History of CVD*								
yes	0(0.0)	37(14.1)	147(32.9)	184(20.6)	0(0.0)	18(6.9)	68(26.6)	86(14.1)
no	184(100.0)	225(85.8)	299(67.0)	708(79.3)	94(100.0)	242(93.1)	187(73.3)	523(85.9)
History of stroke								
yes	1(0.5)	6(2.2)	35(7.8)	42(4.7)	0(0.0)	7(2.6)	5(1.9)	12(2.0)
no	183(99.5)	256(97.7)	411(92.1)	850(95.3)	94(100.0)	253(97.3)	250(98.0)	597(98.0)
COPD								
yes	19(10.3)	73(27.8)	205(80.3)	297(33.3)	3(3.2)	15(5.7)	8(3.1)	26(4.3)
no	165(89.6)	189(72.1)	241(94.5)	595(66.7)	91(96.8)	245(94.2)	247(96.8)	583(95.7)
Asthma								
yes	9(4.9)	17(6.5)	47(10.5)	73(8.2)	13(13.8)	62(23.8)	70(27.4)	145(23.8)
no	175(95.1)	245(93.5)	399(89.4)	819(91.8)	81(86.2)	198(76.1)	185(72.5)	464(76.2)

*CVD: cardiovascular diseases (including coronary artery disease, arrhythmias and congestive heart failure).

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subsequently subjected to bronchodilator reversibility testing, according to GOLD guidelines.[14]

Diagnosis of asthma and COPD

The diagnoses of COPD and asthma were confirmed by two respiratory physicians who were present throughout the study. The diagnosis of COPD was based on the presence of an obstructive pattern in spirometry (i.e. post-bronchodilator FEV_1/FVC <70%) in patients with a smoking history >30 pack-years, in accordance with the GOLD guidelines.[14] The differentiation of asthmatic and COPD patients was based on

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the following criteria:[15] (a) asthmatic subjects had a long-standing history of asthma from their childhood or adolescence whereas COPD patients had a later onset of symptoms which were closely related to smoking; (b) a history of atopy (e.g. seasonal symptoms, allergic rhinitis) was considered indicative of asthma; (c) significant reversibility of airway obstruction on spirometry (i.e. increase of at least 12% and 200 mL in baseline FEV_1 after administration of 400 μg salbutamol) was considered indicative of asthma.

Statistical analysis

Statistical analysis was performed by using SPSS (v.12.0; SPSS, Inc.; Chicago, IL). Normality of distribution of data was tested with the Kolmogorov-Smirnov test. Demographic data and prevalence rates of sleep-related symptoms and co-morbidities were described using frequency distributions and proportions, whereas quantitative variables were expressed as mean±SD. Comparison between categorical variables was performed with chi-square tests, whereas comparisons between continuous variables were performed with unpaired t-tests or Mann-Whitney U-tests, as appropriate. P values <0.05 were considered statistically significant.

For the evaluation of possible differences in BMI and sleep-related symptoms according to gender, respiratory (asthma or COPD), and cardiovascular (hypertension, coronary artery disease or stroke) co-morbidities, logistic regression was applied. Dichotomisation of variables was performed as follows: patients snoring "almost every day" and "3-4 times/week" were considered as "frequent snorers", whereas those snoring "1-2 times/week", "1-2 times/month" and "never or almost never" were considered as "occasional snorers"; subjective sleepiness (ESS <10 or ESS ≥10); BMI (<30 kg/m^2 or ≥30 kg/m^2); gender (male/female); hypertension (yes/no); CVD (yes/no); stroke (yes/no); COPD (yes/no); and asthma (yes/no). Age was divided using the following cut-off points: 19-45 years, 46-65 years, and ≥66 years; this was performed in order to obtain roughly equal groups. Rate differences between groups were calculated by odds ratios (OR) and the corresponding 95% confidence intervals (CI).

Results

Patients' demographics are presented in Table 1 and the distribution of responses among age and gender groups in Table 2. Males and females did not differ with respect to age (men, 60.9±15.4 years; women, 60.3±12.6 years; p=0.38). Men reported higher levels of current smoking (48.7% vs. 18.7%, respectively; p<0.001) and lower BMI (28.4±4.1 kg/m^2 vs. 29.6±5.3 kg/m^2; p<0.001) compared to women. A diagnosis of COPD was more common in men than women (33.3% vs. 4.3%, respectively; p<0.001), whereas a diagnosis of asthma was more common in women compared to men (23.8% vs. 8.2%, respectively; p<0.001). A history of hypertension did not differ between the two genders (45.8% vs. 50.4%, respectively; p=0.09), but men reported more frequently a history of CVD (20.6% vs. 14.1%; p=0.002) and a history of stroke (4.7% vs. 2.0%; p=0.008).

Figure 1. OR comparisons between COPD and non-COPD patients with regard to OSAHS-related symptoms and obesity. An OR >1 indicates greater likelihood for COPD patients. Bars represent 95% confidence intervals (CI).

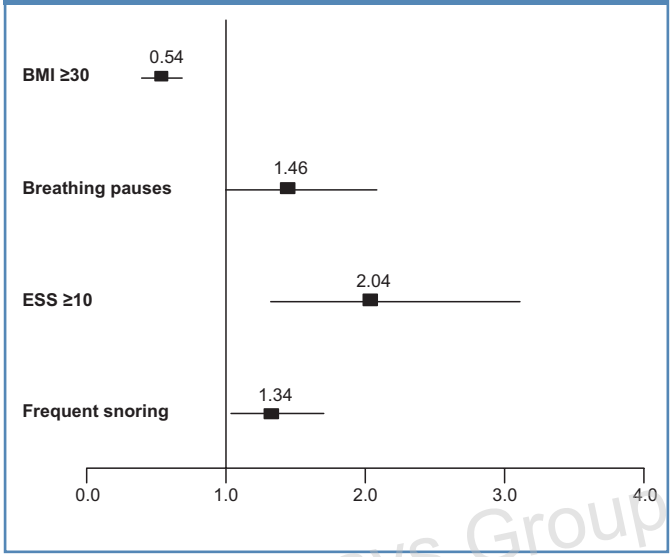

Figure 2. OR comparisons between asthmatics and non-asthmatics patients with regard to OSAHS- related symptoms and obesity. An OR >1 indicates greater likelihood for asthmatic patients. Bars represent 95% confidence intervals (CI).

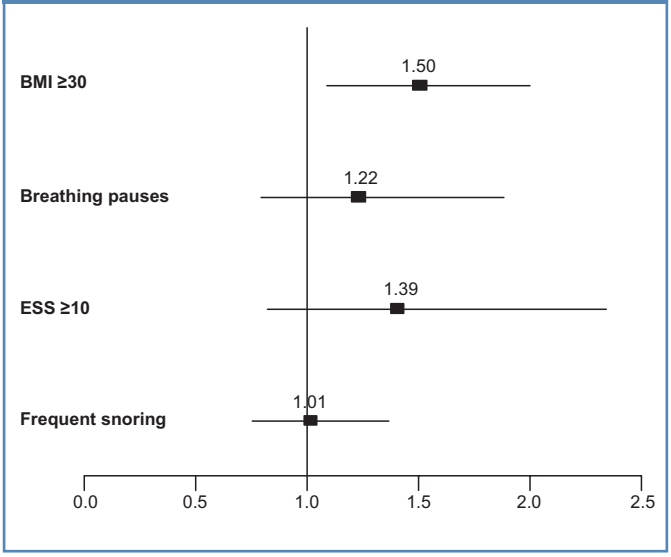

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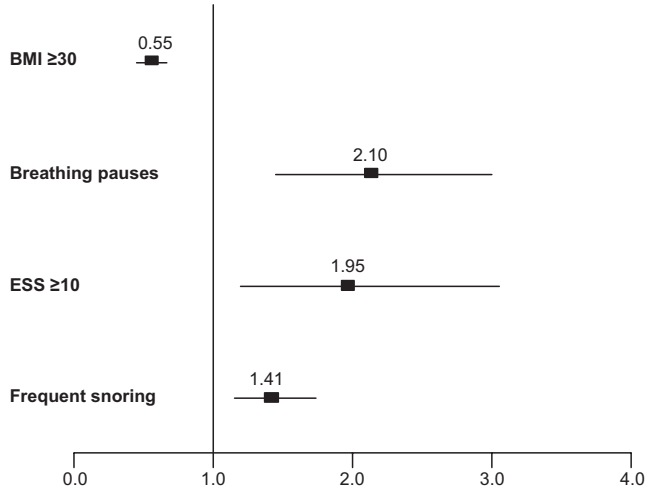
Figure 3. OR comparisons between men and women with regard to OSAHS-symptoms and obesity. An OR >1 indicates greater likelihood for men. Bars represent 95% confidence intervals (CI).



Frequent snoring (>3 nights/week) was reported in 45.6% of the study population, breathing pauses during sleep as witnessed by the participants' bed partners in 11.0%, and excessive daytime sleepiness (ESS ≥10) in 6.7% of the sample.

Sleep-related symptoms and obesity in patients with COPD

Sleep-related symptoms were more prevalent in COPD patients. Specifically, COPD patients were more likely to report frequent snoring (OR=1.34; CI: 1.04-1.71), breathing pauses (OR=1.46; CI: 1.01-2.10), and excessive daytime sleepiness (OR=2.04; CI: 1.33-3.14). These findings again were observed despite the fact that COPD patients were less likely to be obese (OR=0.54; CI: 0.41-0.71) – Figure 1. No differences were observed in the likelihood for sleep-related symptoms between COPD patients with different disease severities.

Sleep-related symptoms and obesity in patients with asthma

Subjects with a diagnosis of asthma were more likely to be obese (OR=1.50; CI: 1.12-2.04), but there was no association with snoring (OR=1.01; CI: 0.76-1.35), breathing pauses (OR=1.22; CI: 0.79-1.88), and excessive daytime sleepiness (OR=1.39; CI: 0.83-2.35) in these patients – Figure 2.

Sleep-related symptoms and obesity in patients with a history of hypertension, CVD, and stroke

Patients with a history of hypertension were almost twice as likely to present excessive daytime sleepiness (OR=1.81; CI: 1.19-2.74). They were also more likely to be frequent snorers (OR=1.72; CI: 1.40-2.11) and obese (OR=1.93; CI: 1.56-2.38). However, hypertension was not associated with breathing pauses (OR=1.02; CI: 0.74-1.41).

Patients with a history of CVD were twice as likely to present excessive daytime sleepiness (OR=2.04; CI: 1.30-3.19), and were more likely to present frequent snoring (OR=1.51; CI: 1.16-1.96) and obesity (OR=1.37; CI: 1.04-1.79). There was no association between CVD and breathing pauses (OR=1.25; CI: 0.83-1.86).

Patients with a history of stroke were more likely to present frequent snoring (OR=1.91; CI: 1.09-3.34). However, a history of stroke was not associated with excessive daytime sleepiness (OR=1.71; CI: 0.74-4.26), breathing pauses (OR=1.88; CI: 0.92-3.80), or obesity (OR=0.97; CI: 0.55-1.71).

Differences in sleep-related symptoms and obesity between genders

Differences in symptom frequencies between men and women are presented in Table 2. Men reported frequent snoring more often than women (OR=1.41; CI: 1.14-1.74); men were additionally twice more likely to present breathing pauses (OR=2.10; CI: 1.46-3.02) and excessive daytime sleepiness (OR=1.95; CI: 1.23-3.06) than women. These differences were observed despite the fact that men were less likely to be obese compared to women (OR=0.55; CI: 0.45-0.69 – Figure 3).

Discussion

In this cross-sectional study conducted in primary care centres in Greece we have shown that OSAHS-related symptoms (i.e. frequent snoring, excessive daytime sleepiness and breathing pauses) that present a high pre-test probability for the diagnosis of OSAHS are more frequent in patients with COPD, whereas no such association was observed in patients with asthma. Additionally, patients with a history of hypertension, CVD or stroke were more likely to present frequent snoring, whereas excessive daytime sleepiness was associated only with a past history of hypertension or CVD. Breathing pauses were not related to hypertension, CVD or stroke. Finally, OSAHS-related symptoms were more frequent in men compared to women. These results correspond to a large random sample of the population attending primary care centres in Greece, and given the relatively high response rate of 82.4%, they may reflect the prevalence of OSAHS-related symptoms in this population.

To our knowledge, this is the first study to assess OSAHS-related symptoms in patients with a diagnosis of asthma or COPD confirmed by respiratory physicians. COPD patients in our population presented a higher prevalence of OSAHS-related symptoms. These results are in accordance with the findings of a previous postal survey, reporting that OSAHS symptoms were more common in subjects with chronic bronchitis.[6] Numerous studies have shown that OSAHS patients diagnosed in a sleep laboratory often present with coexisting COPD, with a prevalence of overlap ranging from 11% to 16%.[16,17] The present study has shown that COPD patients are twice as likely to present daytime sleepiness and,

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additionally, are more likely to present frequent snoring or breathing pauses, compared to non-COPD subjects. The absence of any difference in the likelihood of sleep-related symptoms in patients with different COPD severities may be attributed to the fact that the majority of our patients had mild-to-moderate COPD. Interestingly, the increased prevalence of these symptoms was evident despite the fact that our COPD patients were less likely to be obese compared to the general population.

Possible explanations for the relationship between COPD and OSAHS-related symptoms include sleep-related hypoxemia that is often present in patients with COPD and could contribute to daytime sleepiness in such patients; alternatively, the coexistence of an underlying sleep disorder, most likely obstructive sleep apnoea, might account for these symptoms. Although many COPD patients complained of poor quality of sleep in the Sleep Heart Health Study,[18] in fact patients with mild COPD without sleep apnoea/hypopnoea syndrome had minimally perturbed sleep, indicating that mild COPD *per se* affects minimally the quality of sleep. In contrast, the coexistence of COPD and OSAHS was associated with increased sleep desaturations,[18] plausibly leading to more severe daytime symptoms. Smoking may represent a common risk factor for both conditions.[19]

In the present study, no significant association was found between sleep-related symptoms and physician-diagnosed asthma. These findings are inconsistent with the findings of a population-based cross-sectional study by Ekici and co-workers,[7] who reported a significant association of snoring and observed apnoeas in subjects with asthma-related symptoms. In another questionnaire study, Larsson *et al*.[8] reported that asthma was related to snoring and witnessed apnoeas, but not daytime sleepiness. These associations were not confirmed, however, in other population-based studies. Klink *et al*. did not find a significant association between excessive daytime sleepiness and asthma.[9,20] However, in questionnaire-based studies, non-specific symptoms such as cough and wheeze could have been attributed to different causes besides asthma, including COPD. Moreover, it is possible that the link between asthma and snoring might simply be due to the presence of upper airway inflammation that is common in asthmatic patients. The difference between our study and the aforementioned ones is that the diagnosis of asthma was based on strict criteria and the clinical judgement of a respiratory physician. The absence of a plausible common underlying pathophysiologic mechanism between asthma and OSAHS further supports the absence of association between the two conditions.

Patients with hypertension or CVD were more likely to present excessive daytime sleepiness and frequent snoring. Our data are in agreement with previous studies reporting association between OSAHS and hypertension, both in young and elderly patients.[21] Moreover, frequent snoring has also been associated with CVD in large epidemiologic studies, with similar odds ratios to the present study.[22] Patients with stroke were also more likely to present frequent snoring in our study, in agreement with data from the Sleep Heart Health Study.[5] Interestingly, breathing pauses in our study were not associated with a history of CVD, stroke and hypertension, in contrast with a recent study by Teculescu *et al*. which reported a significant association between breathing pauses and a history of stroke or hypertension.[23] However, the findings of the latter study were not based on a community sample but only in active men and only 5.4% reported breathing pauses. Furthermore, 46.6% of the studied sample was bus drivers and there could be an underestimation of their symptoms. In our study 13.7% of men and 7.1% of women presented breathing pauses. A potential limitation of our study might be the fact that the presence or absence of breathing pauses in a significant proportion of our patients was self-reported and not always confirmed by the bed-partner.

Another potential limitation of the present study was that polysomnography was not performed for OSAHS diagnosis. Although this is the gold standard for the diagnosis of sleep apnoea, it is a costly method not suitable for screening in primary care. In the era of increasing demand for sleep studies, the identification of target groups for the application of simple questionnaires for the screening of OSAHS in the primary care setting is invaluable. Our study provides evidence that, besides patients with cardiovascular disorders, COPD patients should also be screened for OSAHS-related symptoms in primary care.

Finally, another limitation of the present study is the fact that the presence of co-morbidities was self-reported by the patients. However, in the majority of cases the medical records of each patient and the medication that he or she was receiving were reviewed in order to confirm the corresponding diagnoses.

In summary, this is the first large epidemiological study conducted in Greece which reports the prevalence of symptoms related to sleep apnoea and assesses their correlation with physician-diagnosed asthma and COPD. Our study has obtained a rather high prevalence of snoring, witnessed breathing pauses and daytime sleepiness, symptoms which present a high pre-test probability for OSAHS. The increased likelihood for OSAHS-related symptoms in COPD patients, in contrast with asthmatic patients, designates them as another target group for the screening of OSAHS in the primary care setting.

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Conflict of interest statement

There were no conflicts of interest for the authors in the preparation of this paper.

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