# Gender Differences in Morbidity and Health Care Utilization Among Adult Obstructive Sleep Apnea Patients

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**Study Objective:** To explore gender differences in morbidity and total health care utilization 5 years prior to diagnosis of obstructive sleep apnea (OSA).

**Design:** Case-control study; patients were recruited between January 2001 and April 2003.

**Setting:** Two university-affiliated sleep laboratories.

**Patients:** 289 women (22–81 years) with OSA were matched with 289 men with OSA for age, body mass index (BMI), and apnea-hypopnea index (AHI). All OSA patients were matched 1:1 with healthy controls by age, geographic area, and primary physician.

**Measurements and Results:** Women with OSA compared to men with OSA have lower perceived health status and Functional Outcomes of Sleep Questionnaire score (54.5% vs. 28.4%, P <0.05 and 67.5±21.4 vs. 76±20.1, P <0.05, respectively). Compared to men with OSA, women with OSA have higher risk of hypothyroidism (OR 4.7; 95% CI, 2.3-10) and arthropathy (OR 1.6, 95% CI, 1.1-2.2) and lower risk for CVD (OR 0.7; 95% CI, 0.5-0.91). Compared to controls, both women and men with OSA had 1.8 times higher 5-year total costs (P <0.0001). Compared to men with OSA, expenditures for women with OSA are 1.3 times higher (P <0.0001). The multiple logistic regression (adjusting for BMI, AHI) revealed that age (OR 1.04; 95% CI, 1.01-1.07), antipsychotic and anxiolytic drugs (OR 2.3; 95% CI, 1.2-4.4), and asthma (OR 2.4; 95% CI, 1.1-5.6) are independent determinants for "most costly" OSA women.

**Conclusion:** Compared to men with similar OSA severity, women are heavier users of health care resources. Low FOSQ score and poor perceived health status in addition to overuse of psychoactive drugs are associated with high health care utilization among women with OSA.

**Keywords:** Gender differences, heath care utilization, obstructive sleep apnea

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## INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMMON DISORDER AFFECTING ABOUT 5% OF THE MIDDLE-AGED MALE POPULATION. EPIDEMIOLOGICAL STUDIES have shown a higher prevalence of OSA in men than women,[1,2] which may be the result of referral selection bias, which in part may be caused by differences in presentation of female and male cases. At the time of diagnosis, in contrast to men, women manifest different polysomnographic (PSG) findings: lower apnea hypopnea index (AHI) and more episodes of upper airway resistance; they are older, more obese, and report different symptoms, i.e., lack of energy, morning headaches, restless legs, depression, and insomnia.[3–14] Shepertycky et al[14] reported that, after matching women to men (by AHI, Epworth Sleepiness Scale [ESS], age, and body mass index [BMI]), women with OSA were more likely to be treated for depression, insomnia, and hypothyroidism.

In general, women use more health care services than men, even after correcting for the use of health care services, such as gynecology, that are specific for women.[15] Women tend to have more minor illnesses and nonfatal chronic diseases, while men have more fatal chronic diseases and higher mortality rates.[16] Health care utilization and gender are indirectly related through several pathways, such as mental distress, physical illness, symptom perception, and perceived health status.[15]

Patients with untreated OSA have greater health care utilization many years prior to diagnosis.[6,9,17] Health care utilization is a reliable index for morbidity in both adults[6,9] and children with OSA.[18] Little is known regarding sex differences in morbidity and health care utilization prior to OSA diagnosis.[19] At the individual level, women with typical symptoms may fail to get feedback from bed partners and thus be unaware of the need to seek care or, if aware, may feel uncomfortable about seeking help for a "male" problem.[11–14] In addition, clinicians who are unaware that OSA is common in women will likely fail to recognize the problem, and women without typical symptoms will also be missed.

We hypothesize that after adjusting for apnea-hypopnea index (AHI, index of OSA severity), age, and BMI between genders, clinical presentation and morbidity are different, resulting in higher health care utilization in women than men. In the present study we compared morbidity and health care utilization for women and men with OSA matched for age, BMI, and AHI. In addition, all patients were individually matched 1:1 with healthy controls from the general population (by age, sex, primary care physician, geographic location).

## METHODS

*Setting*: Case-control study conducted in two Sleep-Wake Disorders Centers in 2 districts – the Soroka University Medical Center and Loewenstein Hospital–Rehabilitation Center – in which >95% and >70% of patients, respectively, are enrollees of Clalit Health Care Services (CHS).[20]

Study population: Between January 2001 and April 2003, we consecutively recruited OSA patients aged 22 through 81 years,

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**Table 1**—Characteristics of Matched OSA Women and Men

| | Women n=289 | Men n=289 |
|---|---|---|
| Age (years) | 57.2±9.8 | 57.2±9.9 |
| BMI (kg/m$^2$) | 31.7±5 | 31.6±4.8 |
| Weight gain in last year (kg) | 5.1±5.8 | 5.1±5.4 |
| ESS (score) | 8.8±5.4 | 8.7±4.9 |
| Snoring (yes) | 95% | 98% |
| Tobacco smoking (packs/year) | 24.5±19.5 | 35.8±30.1* |
| Self-perceived poor health status | 54.5% | 28.4%* |
| Consumption of vitamins and food supplements (yes) | 45.6% | 17.7%# |
| FOSQ (score) | 67.5±21.4 | 76±20.1* |
| TST (min) | 314.4±82.2 | 293.2±101.6 |
| Sleep efficiency (%) | 79.6±16.3 | 80.1±15.8 |
| Arousal index (events/hr) | 37.3±42.9 | 27.2±22.8 |
| WASO (min) | 33.7±37.1 | 34.4±39.3 |
| AHI (events/hr) | 24.3±19.7 | 24.2±18.7 |
| AHI supine (events/hr) | 28.7±25.3 | 34.8±27.1* |
| AHI lateral (events/hr) | 21.3±22.3 | 22.1±25.6 |
| AHI NREM (events/hr) | 22.6±22.6 | 21.1±19.3 |
| AHI REM (events/hr) | 33.8±24.4 | 35.1±22.7 |
| $T_{90}$ (%) | 10.7±22.2 | 9±20.5 |

AHI – Apnea-Hypopnea Index, BMI – Body Mass Index, ESS – Epworth Sleepiness Scale, FOSQ – Functional Outcomes of Sleep Questionnaire, NREM – non-rapid eye movement, REM – rapid eye movement, $T_{90}$ – percent sleeping time in which oxygen saturation was below 90%, WASO – wake after sleep onset. Values are mean ± SD. *P < 0.05, #P < 0.0001.

with PSG-proven OSA. All patients had "typical" symptoms[1,6,9] of OSA and were referred for PSG evaluation by their primary care physicians after being evaluated by otolaryngology surgeons or pulmonologists (OSAS-related consultants). Each of the OSA patients was matched 1:1 by age, gender, geographic location, and primary care physician (P = 0.999) with healthy subjects selected randomly from the healthy general population in the CHS database.[9,20] All subjects are enrollees of CHS, the largest Health Maintenance Organization (HMO) in Israel, providing medical services to about 60% of the total Israeli population.

Patients and control subjects with chronic obstructive pulmonary disease (COPD), nocturnal hypoventilation, genetic disorders, cancer, or autoimmune disorders, and patients hospitalized more than 50 days during the 5 years of data collection were excluded.[6,9,20] Patients were not matched to control subjects for BMI because that information is not included in the CHS database. Due to ethical considerations, we were not able to contact the control subjects.[9,18,20] However, it is possible that on the average, about 5% of the controls might have undiagnosed OSA.[1]

During the 28-month study period, 2052 patients underwent PSG studies; of those, 155 were enrollees of other HMOs and/or were severely sick patients (hospitalized >50 days in the 5 years preceding the research); 118 (6.2%) patients refused to participate in the study. Following PSG, 290 subjects did not meet the inclusion criteria of OSA diagnosis. The final database included 1489 OSA patients (AHI >5; n=349 women) eligible for this study. Of those, we were able to match 289 women with 289 men only for age, BMI, and AHI.

The Soroka University Medical Center and Loewenstein Hospital–Rehabilitation Center Ethics Committees approved the protocol. Informed consent was obtained from all OSA subjects.

Data resources for the OSA patients included:

- PSG recording.[20] Obstructive apnea was defined as an episode of complete cessation of breathing (airflow reduction of >80%) of ≥10 seconds with continuing inspiratory effort. A hypopnea was scored when continuing inspiratory effort was accompanied by a reduction of at least 50% in airflow, resulting in either an arousal or oxygen desaturation of at least 4%. The AHI was calculated as the number of respiratory events (apnea/hypopnea) per hour of sleep.
- Sleeping habits, ESS.[21]
- Functional Outcomes of Sleep Questionnaire (FOSQ)[22]

All these data were collected as previously described.[20]

Self-rated health status was evaluated by asking a single question ("Define the level of satisfaction with your health status.") with 5 possible answers, ranging from "very satisfied" to "very much not satisfied." A high score reflects poor perceived health.[15]

We defined the variable of self-reported consumption of vitamins and food supplements as an index for health consciousness.[23] Medical diagnoses for all subjects were obtained from the CHS databases, documented only by physicians during patients visits (community and hospital) using the International Classification of Diseases, Ninth Revision (ICD-9) codes.

Information regarding health care utilization was obtained from the CHS computerized databases.[9,18,20] All costs were combined for the 5 years prior to the PSG diagnosis, and similar time periods were used for the control subjects. Indicators of health care utilization included hospitalization (days and costs), emergency department visits (number and costs), visits to specialists (category of specialty, number, and cost per encounter), and prescriptions supplied (number, category,[24] and cost). Drug category was classified according to World Health Organization statistics methodology guidelines.[24] Costs of hospitalization and emergency department visits and to specialists are based on the price list published by the Israeli Ministry of Health in 2005. Cost per prescribed drug is according to the CHS price list. Cost of the PSG study was not included in data analysis. All costs are expressed in $US; exchange rate was NIS 4.5 per $1US.

### Data and Statistical Analysis

Health care utilization was analyzed for 289 women and 289 matched men with OSA by combining the 5 years prior to PSG diagnosis. This was performed to minimize seasonal effects. Data were analyzed as previously described[18,20] using SPSS software (v 14.0). We applied a 3-group design i.e., female OSA patients compared to pair-matched female controls and to pair-matched males with OSA. In addition, we included a fourth comparison group of healthy pair-matched males. Continuous variables are presented as mean with standard deviation, unless otherwise specified. Mann-Whitney and Wilcoxon tests were used to determine the statistical significance of cost elements between women and men OSA patients and between controls and OSA subjects. Chi-square ($\chi^2$) was used to compare the "most costly" to "least costly" OSA patients and differences in morbidity. Spearman correlation was performed to correlate between "self-perceived

**Table 2**—Comparison of Total Cost Elements During 5 Years Prior to Diagnosis Between Subjects with OSA and Matched Controls

| Parameter | Women | | P value | Men | | P value |
|---|---|---|---|---|---|---|
| | Control n=289 | OSA n=289 | | Control n=289 | OSA n=289 | |
| **Hospitalization** | | | | | | |
| Costs ($US/person/5 years) | 462.5±75 | 953±135.2 | 0.002 | 441±73 | 793.3±97 | 0.001 |
| Median (range) | 0 (0–10,266) | 0 (0–15,930) | | 0 (0–7,788) | 0 (0–9,912) | |
| Days/person/5 years | 1.3±0.2 | 2.7±0.4 | 0.002 | 1.2±0.2 | 2.3±0.3 | 0.001 |
| Median (range) | 0 (0–29) | 0 (0–45) | | 0 (0–22) | 0 (0–28) | |
| **Emergency department** | | | | | | |
| Costs ($US/person/5 years) | 92.3±11.3 | 175±14.8* | <0.0001 | 81.3±7.7 | 114±9.2 | 0.003 |
| Median (range) | 0 (0–2,107) | 111 (0–1,442) | | 0 (0–887) | 111 (0–998) | |
| Visits/person/5 years | 0.8±0.1 | 1.6±0.13* | <0.0001 | 0.7±0.07 | 1.02±0.08 | 0.003 |
| Median (range) | 0 (0–19) | 1 (0–13) | | 0 (0–8) | 1 (0–9) | |
| **Consultations** | | | | | | |
| Costs ($US/person/5 years) | 318±18.7 | 521±23.7# | <0.0001 | 156±12.2 | 328±18 | <0.0001 |
| Median (range) | 236 (0–1,613) | 433 (0–2,321) | | 79 (0–1,062) | 236 (0–1,770) | |
| Visits/person/5 years | 8.1±0.5 | 13.3±0.6# | <0.0001 | 4±0.3 | 8.3±0.5 | <0.0001 |
| Median (range) | 6 (0–41) | 11 (0–59) | | 2 (0–27) | 6 (0–45) | |
| **Drugs** | 394±41.5 | 602±47.6# | <0.0001 | 217±24 | 459±38 | <0.0001 |
| Costs ($US/person/5 years) | 190 (0–9,130) | 355 (0–6,555) | | 57 (0–3,252) | 201 (0–5,236) | |
| **Total Costs** ($US/person/5 years) | 1267±100 | 2251±179# | <0.0001 | 896±90 | 1694±124 | <0.0001 |
| Median (range) | 682 (0–13,250) | 1,252 (39–23,494) | | 290 (0–9,432) | 799 (0–11,129) | |

Values are presented as mean ± SEM, median (range) summing costs and health care utilization per patient during the five years prior to OSA diagnosis. Comparison between OSA patients and matched controls was performed by Wilcoxon test. Comparison between women and men OSA patients performed by Mann-Whitney test (* $P < 0.05$, # $P < 0.0001$).

health status" and FOSQ scores. Two-way analysis of variance (Anova II) was used to determine the significance of total 5-year costs between all women and men and between OSA groups.

Previously[9] we found that costs are not normally distributed among OSA patients. Therefore, we arbitrarily divided the OSA group by cost. We defined 2 subgroups: the upper 25% (n=72) "most costly" OSA patients and 75% (n=217) "least costly" patients. The multiple logistic regression analysis was used to establish the primary determinants of the "most costly" women and men OSA patients (dependent variable). Independent variables included age, BMI, ICD-9 codes, supplied drugs, smoking history, PSG findings, ESS, FOSQ score, AHI, and duration of oxygen saturation below 90% during sleep ($T_{90}$). The null hypothesis was rejected at the 5% level with Bonferroni correction for multiple between-group comparisons.

## RESULTS

### Subjects

A total of 289 women and 289 men (Table 1) were similarly matched with respect to age (P = 0.99), BMI (P = 0.83), and AHI (P = 0.97). Both sexes with OSA have similar $T_{90}$, ESS, and sleep efficiency, wake after sleep onset, arousal index, weight gain of 5 kg in the 12 months prior to PSG study, and prevalence of habitual snoring. Men had more packs/year of tobacco smoking compared to women (35.8±30.1 vs. 24.5±19.5, respectively, P <0.024). More women with OSA self-perceive their health status as poor compared to men (P <0.05). Compared to men with OSAS, women consumed more vitamins and food supplements. Self-perceived health status inversely correlated with FOSQ score (r = -0.367, P <0.0001; and r = -0.268, P = 0.01) in women and men with OSA, respectively.

Of the 349 women identified during the study period, we were not able to individually match 60 women with OSA to men. Compared to the 289 women with OSA included in the study (Table 1), those women were considerably obese (BMI=42.5±7.4 (kg/m$^2$); P < 0.0001), 80% reported poor perceived health status (P <0.05), lower FOSQ score (55.3±24.1; P < 0.05), higher AHI (32.8±26.7 (events/hr); P <0.05), and $T_{90}$ (19±27.3; P <0.05). The 5-year total health care total cost prior to OSA diagnosis was $3224 ± 515 (median, range [$1690, 7–17951], P = 0.057) compared to $2251±179 ($1252, 39–23494) in the 289 women with OSA.

Of the 1140 men with OSA identified during the study period, we did not include 851 men in our data analysis. Compared to the 289 OSA men included in the study (Table 1), those 851 men were less obese (BMI= 30.6±6.1 (kg/m$^2$); P < 0.01), 39% reported poor perceived health status (P < 0.05), had similar FOSQ scores

**Table 3**—Prevalence and Odds Ratios of Comorbid Diagnoses of Women and Men OSA Patients vs. Paired Matched Control Subjects

| Diagnosis | Women | | | Men | | | Women vs. Men |
|---|---|---|---|---|---|---|---|
| | Control n | OSA n | OR (95% CI) | Control n | OSA n | OR (95% CI) | OR (95% CI) |
| CVD | 84 | 108 | 1.4 (1.02–2.04) | 94 | 138 | 1.9 (1.4–2.7) | 0.7 (0.5–0.91) |
| Hyperlipidemia | 103 | 132 | 1.5 (1.1–2.1) | 93 | 145 | 2.1 (1.5–3) | 0.8 (0.6–1.2) |
| Diabetes | 32 | 49 | 1.6 (1.01–2.6) | 26 | 48 | 2.0 (1.2–3.3) | 1.03 (0.7–1.6) |
| Asthma | 15 | 30 | 2.1 (1.1–4) | 8 | 21 | 2.8 (1.2–6.3) | 1.5 (0.8–2.7) |
| Hypothyroidism | 28 | 42 | 1.6 (0.95–2.6) | 4 | 10 | 2.6 (0.79–8.2) | 4.7 (2.3–10) |
| Arthropathy | 73 | 103 | 1.6 (1.1–2.3) | 54 | 76 | 1.6 (1.05–2.3) | 1.6 (1.1–2.2) |
| Reflux/Esophagitis/ Gastritis | 7 | 17 | 2.5 (1.02–6.1) | 7 | 11 | 1.6 (0.61–4.2) | 1.6 (0.7–3.4) |

Arthropathy (codes 713, 716.9), asthma (codes 491, 493, 496), CVD – cardiovascular disease (codes 401–405, 410–414, 426–438, 443), diabetes mellitus (code 250), hyperlipidemia (code 272), hypothyroidism (code 244.9), reflux/esophagitis/gastritis (codes 530, 535, 593, 716.9 are combined in the CHS data bases).
Values are prevalence number subjects, Odds Ratio (OR), and 95% confidence interval (95% CI).

(76.2±19.2; P = 0.88), higher AHI (34.9±26.7 (events/hr); P < 0.0001), and $T_{90}$ (13.5±24.6; P <0.006). Comparing the included and non-included OSAS patients, the 5-year total health care costs prior to OSA diagnosis were similar, 1694±124 ($799, 0–1129) and $1616 ± 104 (median, range [$631, 0–49945] respectively.

### Comorbidity

Compared to their controls, women with OSA have higher odds (Table 3) of being diagnosed with CVD, hyperlipidemia, diabetes, asthma, arthropathy, and reflux/esophagitis/gastritis. Compared to their controls, men with OSA have higher odds of being diagnosed with CVD, hyperlipidemia, diabetes, asthma, and arthropathy. Compared to men with OSA, women with OSA have a higher risk of being diagnosed with hypothyroidism (OR 4.7; 95% CI, 2.3-10) and arthropathy (OR 1.6; 95% CI, 1.1-2.2) and lower risk for CVD (OR 0.7; 95% CI, 0.5-0.91).

### Health Care Utilization

Compared to healthy controls, women and men with OSA had 1.78 and 1.89 times higher 5-year total health care costs, respectively (P <0.0001; Table 2). Five-year total costs in women were significantly higher than men in both control and OSA groups (P <0.0001, Anova II). No interaction (P = 0.47) was found between gender and OSA/control groups. The 5-year total health care costs were 1.3 times higher in women compared to men with OSA (P <0.0001).

Both sexes with OSA had significantly more consultations with specialists compared to controls. Women with OSA had 25%–50% more visits (P <0.05) and recurrent visits (P <0.05) compared to men to the following specialists: otolaryngology surgeons, ophthalmologists, pulmonologists, and gastroenterologists. Compared to controls, the total 5-year costs for drugs among women and men OSA patients were 1.52 and 2.12 times higher (P <0.0001), respectively. Costs for drugs are 1.3 times higher among women compared to men with OSA (P <0.0001). The supplied drug categories are summarized in Table 4; included are all drug categories in which significant differences were found in one sex. Odds for supplying drugs treating peptic ulcer and gastroesophageal reflux disease (A02B), antibacterials for systemic use (J01), analgesics (N02), anti-inflammatory and anti-rheumatic products (M01), respiratory system drugs (R), and psycholeptics and psychoanaleptics (N05, N06) were 2 to 3 times higher in women with OSA than men with OSA. Women were supplied 2.86 times more with vitamins than men with OSA (P < 0.0001). Women compared with men with OSA were supplied 3.16 times more with antidepressants (3.8±0.7 vs. 1.2±0.3, P <0.0001), 1.63 times more with hypnotics and sedatives (1.8±0.3 vs. 1.1, P <0.0001), and 1.62 times more with anxiolytics (1.14±0.2 vs. 0.7±0.2, P < 0.0001). Self-perceived poor health status increased odds to be supplied with psycholeptic and psychoanaleptic drugs (OR 2.2; 95% CI, 1.01-4.7) in women with OSA but not in men (OR 1.4; 95% CI, 0.59–3.2). Compared to their controls, all 6 respiratory subcategories (R) were supplied significantly more to both sexes with OSA. However, compared with men, women with OSA were supplied 1.3 to 2.3 times more with all respiratory subcategory drugs (P <0.05).

### Characteristics of the "Most Costly" OSA Patients

When arbitrarily dividing the OSA groups by cost, the upper quarter (n=72) "most costly" patients consumed 65% and 69% of all costs among women and men, respectively (Table 5). The "most costly" compared to the "least costly" women are significantly older, have higher $T_{90}$, are diagnosed more frequently with hyperlipidemia, CVD, arthropathy, and asthma, and more frequently reported poor perceived health status.

The "most costly" men with OSA compared to the "least costly" male patients are older, have higher AHI and $T_{90}$, are diagnosed more frequently with hyperlipidemia, CVD, asthma, diabetes, and hypothyroidism, and more frequently reported poor self-perceived health status.

The univariate and multivariate (logistic regression) odds determinants of the "most costly" OSA women and men are presented in Table 6A and B. After adjusting for BMI and AHI, multiple logistic regression analysis revealed that age (OR 1.04; 95% CI, 1.01-1.07), supplied antipsychotic and anxiolytic drugs (OR 2.2; 95% CI, 1.3-4), and asthma diagnosis (OR 2.3; 95% CI, 1.01–5.3) are the independent determinants for "most costly" women with OSA. None of the PSG objective findings i.e., AHI, $T_{90,}$ and ESS, added to the prediction of "most costly" women

**Table 4**—Total Mean Number of Supplied Drugs During the 5 Years Prior to OSA Diagnosis

| Parameter | Women (n=289) | | | Men (n=289) | | |
|---|---|---|---|---|---|---|
| | Mean number of supplied drugs±SEM of OSA patients (Median, range) | Mean Difference ±SEM | P value | Mean number of supplied drugs±SEM of OSA patients (Median, range) | Mean Difference ±SEM | P value |
| Cardiovascular system (C) | 25.7±2.7 (2, 0–253) | 6.7±3.1 | 0.096 | 31.8±2.7 7 (0-308) | 15.9±3.3 | <0.0001 |
| Respiratory system (R) | 13.5±1.1# (8, 0–159) | 5.7±1.4 | <0.0001 | 8.8±0.8 (5, 0–110) | 2.4±1.8 | <0.0001 |
| Analgestics (N02) | 9.3±0.8# (4, 0–87) | 2.0±1 | 0.004 | 5.6±0.5 (2, 0–54) | 2.1±0.7 | <0.0001 |
| Antibacterials for systemic Use (J01) | 7.2±0.4# (5, 0–50) | 1.9±0.5 | <0.0001 | 4.5±0.3 (3, 0–41) | 1.7±0.4 | <0.0001 |
| Psycholeptics and psychoanaleptics (N05, N06) | 7.6±1.1# (1, 0–228) | 2.7±1.4 | <0.0001 | 3.8±0.6 (0, 0–94) | 1.2±0.8 | <0.0001 |
| Anti-inflammatory and anti-rheumatic products (M01) | 5.8±0.5# (3, 0–50) | 1.5±0.6 | 0.002 | 3.6±0.4 (2, 0–62) | 2.1±0.4 | <0.0001 |
| Peptic ulcer and gastroesophageal reflux disease (A02B) | 4.5±0.6* (1, 0–69) | 1.7±0.7 | 0.001 | 3.3±0.5 (0, 0–62) | 1.6±0.6 | 0.001 |
| Vitamins (A08, A11) | 4.3±0.6# (1, 0–96) | 1.7±0.7 | 0.002 | 1.5±0.3 (0, 0–42) | 0.04±0.4 | 0.134 |

Supplied medications are the mean ± SEM (median, range) number of drugs per patient per 5 years. Presented are all pharmacological groups in which differences were found (Difference – mean difference between cases and controls in the number of times per five years the drug was prescribed).
Cardiovascular categories include: Therapy and Selective Calcium Channel Blockers with Direct Cardiac Effect (C01, C08D); Antiadrenergic Agents, Centrally Acting and Antiadrenergic Agents, Peripherally Acting (C02A,C02C); Arteriolar Smooth Muscle, Agents Acting On (C02D); Low Ceiling Diuretics, Thiazides and Low Ceiling Diuretics, Excluding Thiazides and Potassium Sparing Agents and Diuretics and Potassium Sparing Agents in Combination (C03A, C03B,C03D, C03E); High Ceiling Diuretics (C03C); Peripheral Vasodilators (C04); Vasoprotectives (C05); Beta Blocking Agents (C07); Selective Calcium Channel Blockers with Mainly Vascular Effects (C08C); ACE-Inhibitors, Plain and ACE-Inhibitors, Combinations (C09A,C09B); Angiotensin II Antagonists and Angiotensin II Antagonists, Combinations (C09C,C09D); Cholesterol and Triglyceride Reducers (C10A).
Cardiovascular system drugs was analyzed according to methods described by Otake et al.[25] Comparison between OSA patients and controls was performed by Wilcoxon test. Comparison between women and men OSA patients was performed by Mann-Whitney test (*P < 0.05, #P < 0.0001). P value comparing OSA patients to their paired matched controls.

with OSA. The area under the receiver operating characteristic = 70%. After adjusting for age, BMI, and AHI, multiple logistic regression analysis revealed that CVD diagnosis (OR 5.7; 95% CI, 2.7–12), asthma (OR 5; 95% CI, 1.7–15), and supplied antipsychotic and anxiolytic drugs (OR 2.5; 95% CI, 1.3-4.8) are the independent determinants for "most costly" men with OSA. None of the PSG objective findings i.e., AHI, $T_{90,}$ and ESS, added to the prediction of most costly men with OSA (Table 6). The area under the receiver operating characteristic = 80%.

## DISCUSSION

Prior to diagnosis, the total 5-year consumption of health care services among all OSA patients and OSA women was higher, compared to both healthy and control men, respectively. Multiple logistic regression analysis revealed that supplied antipsychotic and anxiolytic drugs and asthma diagnosis are independent determinants for "most costly" women with OSA.

In this study we explored "typical" symptomatic women and men with OSA recruited from 2 geographic locations, as previously described by our group.[20] Our data represent a health care system similar to others such as that in Canada,[6,14,17,19,25] reflecting "true" consumption of health care resources.[9,18,20]

Although we matched OSA patients and control subjects, we were not permitted to contact the control subjects or obtain their BMI and symptoms from the medical records because of legislation protecting patient confidentiality.[9,18,20] It is possible that a comparison between patients and controls regarding comorbidities is

**Table 5**—Characteristics of the Upper Quarter Most Costly OSAS Patients

| | Women n=289 | | | Men n=289 | | |
|---|---|---|---|---|---|---|
| | **Upper quarter (n=72)** | **Least costly (n=217)** | **P value** | **Upper quarter (n=72)** | **Least costly (n=217)** | **P value** |
| Total costs (per person/5 years) | $5,872±509 | $1,050±45.6 | <0.0001 | $4,660±268 | $710±36.2 | <0.0001 |
| Age (years) | 60.5±1 | 56.1±0.7 | 0.001 | 62.1±1 | 55.6±0.7 | <0.0001 |
| BMI (kg/m$^2$) | 32.2±0.7 | 31.5±0.3 | 0.452 | 32.2±0.6 | 31.4±0.3 | 0.137 |
| AHI (events/hr) | 26.7±2.6 | 23.5±1.3 | 0.391 | 27.5±2.2 | 23.2±1.3 | 0.029 |
| $T_{90}$ (%) | 17.6±3.6 | 8.2±1.3 | 0.001 | 14.1±3.4 | 7.2±1.3 | 0.012 |
| **Medical diagnosis** | | | | | | |
| Hyperlipidemia (yes) | 58.3% | 41.5% | 0.013 | 70.8% | 43.3% | <0.0001 |
| CVD+HTN | 54.2% | 31.8% | 0.001 | 80.6% | 36.9% | <0.0001 |
| Arthropathy (yes) | 45.8% | 32.3% | 0.037 | 34.7% | 23.5% | 0.061 |
| Diabetes (yes) | 23.6% | 14.7% | 0.082 | 26.4% | 13.4% | 0.01 |
| Asthma (yes) | 16.7% | 8.3% | 0.044 | 13.9% | 5.1% | 0.012 |
| Hypothyroidism (yes) | 16.7% | 13.8% | 0.553 | 8.3% | 1.8% | 0.009 |
| Self-perceived poor health status | 68.2% | 47.8% | 0.026 | 41.2% | 22.7% | 0.047 |

P value – comparing OSA patients to their paired matched controls.

problematic when BMI data are not available for controls. This is a limitation when analyzing utilization in a health care system in which legislation protecting patient confidentiality exists. Obesity may lead to some increased medical utilization.[26] However, people with or without OSA who are obese are not necessarily heavy users of health care resources. "Healthy" obese individuals who participated in a Canadian population-based study[27] had quite similar utilization compared to a group of individuals chosen from the general population matched for age, gender, and postal code. Even within the OSA obese population there is no a priori reason why BMI should influence greater expenditure in a patient.[6]

We were not able to match 60 (17%) women with OSA to men. Those women are not "typical" representatives of our OSA patients, since they were extremely obese (Class 3, BMI >40). We found that those women with OSA and class 3 obesity reported the lowest perceived health status and FOSQ score and had considerable elevation of health care utilization (1.4 times more) compared to "typical" women with OSA. Further studies are needed to explore this subgroup of patients.

According to our matching criteria, 851 men were not included in the study. These men were less obese, and had higher AHI and $T_{90}$ compared to the included 298 men with OSA. However, the significant differences in objective PSG findings did not affect the 5-year total health care cost between both groups. This finding supports the thought that objective PSG findings such as AHI and oxygen saturation have little effect on utilization of health care services (see below).[6,20]

Our matching methodology, similar to that in previous reports,[14] allowed us to investigate the independent effect of sex on health care utilization, controlling for age, BMI, and AHI. In the present study we did not find differences between the sexes regarding snoring and excessive daytime sleepiness, recall of duration of sleep symptoms, or weight gain prior to the PSG study, in accordance to earlier reports.[4,14,28,29]

In the present study the main differences between sexes were self-perceived poor health status and FOSQ score, both of which were significantly low among OSA women, supporting earlier reports.[30] Our OSA women have higher health consciousness as indicated by self-reported purchase of and supplied vitamins and food supplements. It was reported[15] that these findings result in greater utilization of somatic health care. Sex-based health care inequities are associated with many disorders.[15] It has been demonstrated that, compared to men, women in general have greater awareness of physical symptoms that will trigger seeking more medical help.[31] As previously reported,[12,13,32,33] we found that prior to OSA diagnosis, women were being treated for secondary manifestations and nonspecific symptoms.

Compared to men, women with OSA have significantly higher health care consumption. Women with OSA reported significantly lower perceived health status, which correlated with FOSQ scores, and were supplied 2.7 times more with psycholeptic and psychoanaleptic drugs than men with OSA. Supplied antipsychotics, anxiolytics (multivariate analysis), and antidepressants (univariate analysis) are independent variables associated with increased odds to be included in the "most costly" OSA women, suggesting that these patients may experience insomnia, anxiety, and depression.[11-14,33,34] Ninety-three percent of women with moderate to severe OSA have not been clinically diagnosed.[35] Women with OSA report "atypical" OSA symptoms,[11-14] which may lead physicians to other diagnostic options. It is possible that our physicians have interpreted nonspecific symptoms to be related to multiple morbidities, distracting them from documenting a specific ICD-9 code (i.e., insomnia, anxiety, depression).

Obesity[14] and depression[33] are commonly seen in women with OSA. Both are associated with increased odds for poor quality of life and self-perceived poor health status in other illnesses.[36] After adjusting for obesity, women more frequently reported depressive symptoms than did men.[37] Patients with symptoms of depression or mental distress have high health care costs for somatic health reasons that may lead to more office visits,[15,27,35-41] as noted in our study.

In the present study none of the PSG objective findings add to the prediction of most costly women or men with OSA (Table 6), supporting earlier reports.[6,20] AHI is probably an imperfect linear measure of OSA severity and obesity is not necessarily a cause for health-care consumption.[27] CVD is a risk factor for "most costly" and ill OSA men.[6,20] Interestingly, in our study, supplied psychoactive drugs and not CVD predicted the "most costly and

**Table 6**—Determinants of Most Costly Quarter OSA Patients

a. Women with OSA (n=289)

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | **OR (95% CI)** | **P value** | **OR (95% CI)** | **P value** |
| Age (+1 yr) | 1.05 (1.02–1.1) | 0.001 | 1.04 (1.01–1.07) | 0.047 |
| BMI (+1 kg/m$^2$) | 1.03 (0.97–1.1) | 0.263 | 1.02 (0.95–1.08) | 0.577 |
| AHI (+1 event/hr) | 1.01 (0.99–1.02) | 0.233 | 1.001 (0.98–1.02) | 0.865 |
| CVD (1 – yes/0 – no) | 2.5 (1.5–4.4) | 0.001 | 1.7 (0.94–3.3) | 0.080 |
| Supplied antipsychotic and anxiolytic drugs (N05A, N05B) | 2.6 (1.4–4.9) | 0.002 | 2.2 (1.3–4) | 0.006 |
| Asthma (1 – yes/0 – no) | 2.2 (1.01–4.9) | 0.048 | 2.3 (1.01–5.3) | 0.048 |
| Antidepressants (NO6A) | 1.9 (1.1-3.3) | 0.024 | Not included | |

b. Men with OSA (n=289)

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | **OR (95% CI)** | **P value** | **OR (95% CI)** | **P value** |
| Age (+1 yr) | 1.08 (1.05–1.12) | <0.0001 | 1.03 (0.99–1.1) | 0.088 |
| BMI (+1 kg/m$^2$) | 1.04 (0.98–1.1) | 0.189 | 1.03 (0.96–1.1) | 0.384 |
| AHI (+1 event/hr) | 1.01 (0.99–1.03) | 0.090 | 1.002 (0.98–1.02) | 0.836 |
| CVD (1 – yes/0 – no) | 7.1 (3.7–13.5) | <0.0001 | 5.7 (2.7–12) | <0.0001 |
| Asthma (1 – yes/0 – no) | 3.0 (1.2–7.4) | 0.016 | 5.0 (1.7–15) | 0.003 |
| Supplied antipsychotic and anxiolytic drugs (N05A, N05B) | 4.6 (2.6–8.3) | <0.0001 | 2.5 (1.3–4.8) | 0.007 |
| Hypothyroidism (1 – yes/0 – no) | 4.8 (1.3–17.7) | 0.017 | Not included | |
| Antidepressants (NO6A) | 2.5 (1.3-4.9) | 0.006 | Not included | |

P value – comparing OSA patients to their paired matched controls.
Univariate and multiple logistic regression models were used to calculate odds ratios (ORs) with 95% confidence intervals (CI) and establish the primary determinants of most costly OSA patients.
AHI – Apnea-Hypopnea Index, BMI – body mass index, CVD – Cardiovascular Disease. The area under the receiver-operating characteristic is 70% and 80% for women and men, respectively.

ill" women with OSA. Our findings further support the concept that women tend to have more minor illnesses and "atypical" symptoms while men have more chronic and fatal diseases.[15]

Conclusions: Women with OSA are heavy users of health care compared to men with similar OSA severity. Poor perceived health status and low FOSQ score among women with OSA probably leads to minor illnesses and "atypical" symptoms that could explain the increase in health care utilization.

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