

SCIENTIFIC INVESTIGATIONS

Comorbidities and quality of life in Australian men and women with diagnosed and undiagnosed high-risk obstructive sleep apnea

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Study Objectives: In a population-based survey, we determined sex differences in health profiles and quality of life between individuals who have a confirmed diagnosis of obstructive sleep apnea (OSA) and those who are at high risk of OSA yet remain undiagnosed.

Methods: An online survey of Australian adults ≥ 18 years ($n = 3,818$) identified participants with self-reported diagnosed OSA ($n = 460$) or high-risk, undiagnosed OSA (OSA50 score ≥ 5 , $n = 1,015$). Ever-diagnosed comorbidities, sociodemographics, and quality of life (EQ-5D-5L, Functional Outcomes of Sleep Questionnaire-10) were assessed.

Results: Women were more frequently represented in the high-OSA-risk group compared with those with diagnosed OSA (55.5%, $n = 563$, versus 43%, $n = 198$; $P < .001$). In sex-specific logistic regression analyses, diagnosed OSA was associated with increased likelihoods of ≥ 1 cardiovascular condition (odds ratio: 3.0; 95% confidence interval: 2.0–4.5), hypertension (1.9; 1.3–2.8), gout (1.8; 1.1–2.9), and chronic obstructive pulmonary disease (3.8; 2.1–6.9) in men. In women, an association with asthma (2.0; 1.3–3.0) was seen. Diabetes, arthritis, mental health conditions (ever-diagnosed), and all EQ-5D-5L dimensions were associated with an OSA diagnosis regardless of sex, except for EQ-5D-5L anxiety/depression, which was only associated with an OSA diagnosis in women. A diagnosis of OSA was associated with sleepiness-related impairment (lowest quartile of Functional Outcomes of Sleep Questionnaire-10) in men (1.6; 1.01–2.5) and women (2.2; 1.4–3.6).

Conclusions: Sex-specific health conditions may drive diagnosis of OSA; however, clinical suspicion of OSA needs to be increased in men and women. The impaired quality of life and persistent sleepiness in participants with diagnosed OSA observed at a population level requires greater clinical attention.

Keywords: obstructive sleep apnea, sex, diagnosis, OSA50, comorbidities, epidemiology

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea (OSA) is highly prevalent and associated with significant mental and physical health impacts, yet remains undiagnosed in a large proportion of adults. Identifying factors that facilitate a diagnosis may lead to early and targeted diagnoses; however, sex-specific health correlates of a diagnosis of OSA are unknown.

Study Impact: Men and women at high risk of OSA on the OSA50 questionnaire without an OSA diagnosis experienced a high burden of morbidity. Compared with participants at high risk of OSA, diagnosed participants were significantly more likely to report major morbidity and sleepiness-related impacts despite most having received a diagnosis 1–2 years prior to the survey and recommendations for treatment. These findings suggest that increased diagnostic and therapeutic efforts for OSA are required.

INTRODUCTION

Obstructive sleep apnea (OSA) is a condition characterized by repetitive partial or complete closure of the airway during sleep, resulting in hypoxemia, sleep fragmentation, and intrathoracic pressure swings. OSA is associated with a significant comorbid physical and mental health burden,^{1,2} including an increased cardiovascular and cerebrovascular risk.³ Contemporary population studies in different countries have shown that the prevalence of moderate to severe OSA ranges from 10% to 50% in men, which is at least double that of women, which ranges from 3% to 23.4%.^{1,4–6} These figures have led the condition to be perceived largely as a disorder of men, although OSA of any severity can be present in up to 50% of adult women.^{1,7}

Despite the high prevalence of OSA, it may remain undiagnosed in individuals who are at high risk.^{8–12} Furthermore, a higher index of clinical suspicion for OSA may be required in women to increase equity in health outcomes.⁸ Women with OSA are more likely to report atypical symptoms, such as fatigue, insomnia, and mood disturbance compared to men and experience greater impairment in quality of life.¹³

Previous studies have explored sex differences in health factors (including conditions and health service use) associated with diagnosed and undiagnosed OSA compared to those without the disorder.^{13–16} Other recent studies have determined health factors and comorbidities in relation to the level of risk of OSA (ascertained by screening questionnaires).^{11,12} This literature has been critical in highlighting the need for improved

diagnosis and management of the condition for men and women. However, within the population of adults with OSA, our understanding of factors that facilitate a diagnosis is lacking. It is also unclear how a diagnosis of OSA improves health and quality of life for those with OSA. It is important to understand how clinical presentation can differ between the sexes, as this knowledge could lead to early and targeted diagnosis and treatment of this condition to reduce morbidity. To our knowledge, there have been no studies comparing adults diagnosed with OSA with those identified as undiagnosed, but at high risk of having OSA, with sex-specific sociodemographic, comorbidities, and quality of life comparisons.

Using an online survey of Australian adults, we aimed to identify sex-specific demographic and health correlates of participants with a diagnosis of OSA compared to those identified with a screening questionnaire as being at high risk of OSA but who remain undiagnosed. We also examined if high-risk but undiagnosed OSA is associated with poorer health-related quality of life in men and women.

METHODS

Survey sampling methods

A cross-sectional web-based survey was undertaken of adults (≥ 18 years) recruited from an online panel of over 500,000 Australian adults by Dynata, an international survey and market research company. The primary aim of this survey was to investigate the various diagnostic pathways experienced by the participants to receive an OSA diagnosis. The survey was conducted between September and November 2019 using a 3-stage randomization process to minimize the risk of bias to match a potential participant with a survey they are likely to be able to complete as follows.¹⁷ First, the panel was randomly sampled and participants were invited to take a survey, combined with others entering the Survey Sampling International Dynamix sampling platform after responding to online messaging. Second, a set of profiling questions was randomly selected (these were not affirmation questions), and, upon completion, participants were matched with a survey they were likely to be able to take using the third element of randomization of participants to a survey they may be eligible to undertake. Participants were invited to participate through invitations via email, telephone alerts, banners, and messaging to the Dynata membership panel community. The messages were varied, including invitations to provide an opinion and earn cash or prizes (value of this is approximately \$1). To avoid self-selection bias, specific project details were not generally included in the invitation. Rather, participants were invited to “take a survey”. The panel was sampled to generate a study sample that broadly matches Australian Bureau of Statistics estimates on sex, state, and regional representation. The survey was initially set up to sample from participants 18–65+ years of age; however, the sampling criteria was modified 3 days after the survey was launched to enrich the sample for high-risk and diagnosed OSA. This included imposing a limit for age of invited participants toward an older age (> 35 years) due to higher risk and prevalence of OSA in older adults. Prior to this modification, 100 participants in the age range of 18–34 years responded to the survey and were included in the analyses. Ethical

approval for the conduct of the study was obtained from Social and Behavioral Research Ethics Committee at Flinders University, protocol number 8435.

Diagnosed OSA and high-risk (undiagnosed) OSA

The independent variable, OSA, was identified with the question “Have you ever been diagnosed or investigated for obstructive sleep apnea (OSA)?” Those answering “No” were administered the OSA50 screening questionnaire (score range of 0–10), which was developed and validated in an Australian primary care population.¹⁸ A score of ≥ 5 identified patients at high risk of having moderate to severe OSA as follows:

- Waist circumference greater than 102 cm (or pants waist size 40) for men; or greater than 88 cm (or a pants waist size 16/XL) for women (yes = 3).
- In snoring participants, has your snoring ever bothered other people? (yes = 3)
- Has anyone ever told you that you stop breathing during your sleep? (yes = 2)
- Aged 50 years or older? (yes = 2)

Diagnosed health conditions and chronic disease risk factors

Data were collected regarding common health conditions (“Have you *ever* been told by a doctor that you have ...?”), including heart disease; angina or coronary artery disease; previous heart attack; stroke or transient ischemic attack; atrial fibrillation/irregular heart beat (also categorized as at least 1 cardiovascular condition); depression; anxiety or panic disorder (also categorized as at least 1 mental health disorder); diabetes; high blood pressure; arthritis, gout; asthma; nasal obstruction/hay fever/rhinitis; other lung disease, eg, chronic obstructive pulmonary disease (COPD), heartburn or reflux disease, prostate disease/bladder problems.

Health-related quality of life

The EuroQol (European Quality of Life) 5-dimension, 5-level scale (EQ-5D-5L) is a validated, extensively used instrument (in a wide range of clinical conditions and population samples) that assesses 5 dimensions of current function (ie, today), including mobility, personal care, usual activities, pain/discomfort, depression/anxiety.¹⁹ There were too few participants reporting severe and extreme levels of impairment for robust modeling, and therefore we combined the highest 3 levels of impairment as follows: 1) no problem, 2) slight problem, and 3) moderate, severe, extreme/unable. The EQ-5D-5L has a visual analog scale scored 0–100, in response to the question “We would like to know how good or bad your health is TODAY,” where “100 means the best health you can imagine” and “0 means the worst health you can imagine”. EuroQol approval was obtained for the use of the instrument.

The Functional Outcomes of Sleep Questionnaire (FOSQ)-10 (FOSQ-10) is the shortened version of the FOSQ-30, an OSA-specific questionnaire designed to measure the impact of daytime sleepiness on activities of daily living.²⁰ The 10-item instrument, with scores in the range of 5–20, contains questions relating to 5 dimensions of vigilance, activity level, general productivity,

intimacy, and social outcomes. No formal cut-off values have been published for the FOSQ-10. The mean FOSQ-10 score was reported as 12.5 (standard deviation [SD] = 3.2) in moderate to severe OSA compared with 17.8 (SD = 3.1) in a normal control group.²⁰ This value of 17.8 for a normal/healthy sleeper group is not dissimilar to data published for the FOSQ-30, where the mean for a group of adults free of polysomnography-assessed sleep disorders was 17.9²¹ and equates to 1 SD above the mean score (14.1 [SD = 3.7]) of a clinical sample with moderate to severe OSA.²¹

Covariates

Standard sociodemographic factors included sex, age, location of residence (metropolitan or regional/rural), main language spoken at home, gross household income, and highest educational attainment. Participant area-level economic and social status was considered using the Socio-Economic Indexes for Areas Index of Relative Socioeconomic Disadvantage matched to participants' postcodes based on the 2106 Australian Census of Population and Housing,²² taking into account 16 measures of disadvantage. Current smoking was defined as smoking every day or sometimes. Body mass index (BMI; kg/m²) was calculated from self-reported height and weight and classified according to World Health Organization criteria.

Treatment of OSA

Recommended common treatments of OSA and their uptake were assessed with the questions: 1) What treatments have you been recommended for your sleep apnea? (response options included continuous positive airways pressure [CPAP] therapy/[mask], mouthguards, throat surgery) and 2) Did you start the therapy that was recommended to you?

Statistical analysis

Data were analyzed using IBM SPSS version 25.0 (IBM Corporation, Armonk, NY). Sex-specific differences in distribution of outcomes, including ever-diagnosed health conditions and EQ-5D-5L dimensions across OSA diagnosis status, the independent variable, were determined using Pearson χ^2 tests. Differences in distribution by sex within participants with high-risk (undiagnosed) OSA and diagnosed OSA were also determined using Pearson χ^2 tests. The Mann-Whitney test determined differences in distribution of FOSQ-10 scores by OSA status.

The associations of ever-diagnosed health conditions (dependent variables) with a diagnosis of OSA were determined with sex-specific multivariable binary logistic regression analysis. Models for all health conditions were adjusted for age, BMI, and smoking. Models for 1 or more ever-diagnosed cardiovascular disease (CVD) condition were additionally adjusted for hypertension, diabetes, and depression. Inclusion of an interaction term in models in all participants determined the moderation of associations of OSA status by sex.

Ordinal logistic regression analyses were used to determine associations of 3-level EQ-5D-5L dimensions (dependent variables) with a diagnosis of OSA with adjustment for age and BMI and additional ever-diagnosed conditions that are chronic in nature as informed by the literature and our own univariate analyses as applicable, as follows—Mobility: at least 1 cardiovascular

condition, lung disease/COPD, arthritis; Personal Care: depression and or anxiety/panic disorder, lung disease/COPD, arthritis; Usual Activities: depression and or anxiety/panic disorder, lung disease/COPD, arthritis, and at least 1 cardiovascular condition; Pain/Discomfort: cancer (not skin); Depression/Anxiety: asthma, lung disease (COPD), nasal obstruction/rhinitis. For Usual Activities in men, a multinomial logistic regression was conducted because the model failed the proportional odds assumptions in ordinal logistic regression.

Multiple linear regression analyses determined the sex-specific association of EQ-5D-5L visual analog scale (VAS) score with a diagnosis of OSA, with adjustment for age, BMI, and household income.

FOSQ-10 scores in our sample were highly skewed, suggesting a low impact of daytime sleepiness on activities of daily living. Multivariable logistic regression analysis determined sex-specific associations of an OSA diagnosis with FOSQ-10 scores in the lowest quartile of the distribution for men ≤ 16.33 and women ≤ 15.67 . These values are equivalent to the mean of a clinical population undergoing surgery for moderate or severe OSA who failed conventional therapy.²³ Logistic regression models were adjusted for age, BMI, and comorbidities that may disrupt sleep, including EQ-5D-5L dimensions of pain discomfort, depression/anxiety ever diagnosed airways disease, and bladder problems.

RESULTS

Study sample

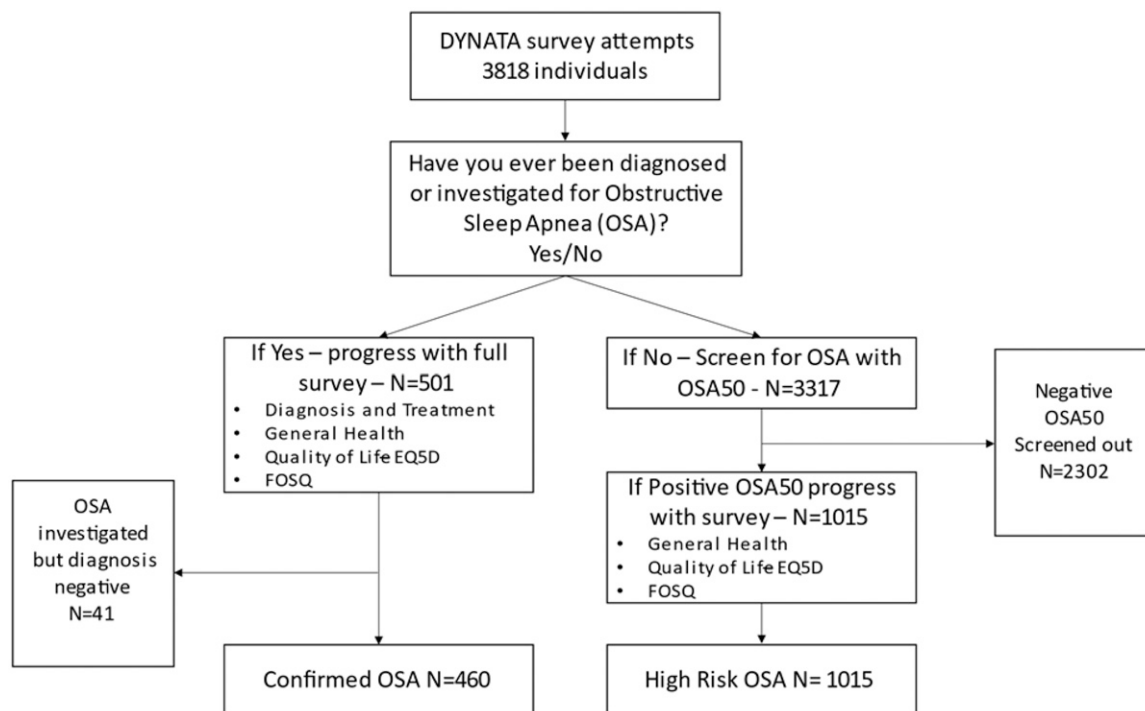
As shown in **Figure 1**, of 3,818 adults who commenced the survey, the sampling process generated a sample of participants with diagnosed OSA (n = 460, 12%) or probable/high risk of OSA (n = 1,015) based on OSA symptom screening. Of diagnosed participants, 75.2% reported being diagnosed at least 1–2 years ago, and only 12.4% reported that their diagnosis occurred in the last 6 months.

Sample characteristics

The sociodemographic and biomedical characteristics of the sample overall and in relation to a diagnosis of OSA are presented in **Table S1** in the supplemental material. Compared to Australian Bureau of Statistics and National Health Survey estimates,²⁴ survey participants were older (29% ≥ 65 years versus 16%) and demonstrated higher rates of overweight or obesity (81% versus 63%, consistent with a survey designed to capture participants with OSA) and showed higher levels of tertiary qualifications (29% versus 22%) and Australian place of birth (78% versus 67%), but otherwise were similar to Australian 2016 Census estimates in terms of sex, metropolitan or rural/regional residence, and extremes of annual household income (< \$20,000 or > \$150,000 per year).²⁵

Sociodemographic characteristics associated with a diagnosis of OSA

Of those at high risk of OSA, 55.5% (n = 563) were women, while women comprised 43% of the diagnosed OSA group (n = 198,

Figure 1—Study flow diagram.

FOSQ = Functional Outcomes of Sleep Questionnaire, OSA = obstructive sleep apnea.

$P < .001$) (**Table S1**). **Table 1** shows sociodemographic characteristics of those with diagnosed OSA compared with high-risk (undiagnosed) OSA in relation to sex. Compared to high-risk OSA, those with a diagnosis of OSA were more likely to be in the younger age group regardless of sex ($P < .001$) and women with a diagnosis were more likely to report higher levels of education ($P = .012$) and household income ($P = .034$). No significant associations with area-level socioeconomic disadvantage, regional/metropolitan location of residence, or speaking English at home were seen.

Ever-diagnosed chronic conditions associated with a diagnosis of OSA

In men, self-reported, ever-diagnosed cardiovascular conditions, high blood pressure, COPD, and gout were significantly more prevalent in those with a diagnosis of OSA compared to participants at high risk of OSA but not diagnosed (**Table 2**). In women, ever-diagnosed asthma and a healthy body weight (based on BMI) were more prevalent in those with a diagnosis of OSA (**Table 2**). Ever-diagnosed diabetes, mental health conditions, arthritis, and reflux were significantly more prevalent in both male and female participants with a diagnosis of OSA compared to those at high risk of OSA but not diagnosed.

These associations persisted after adjusting for age, BMI, and smoking (at least 1 CVD condition was additionally adjusted for ever-diagnosed hypertension, depression, and diabetes). In logistic regression models in the sample not stratified by sex, interaction terms (OSA diagnosis \times sex) indicated that associations of an OSA diagnosis with 1 or more CVD conditions were significantly

stronger in men and that sex is likely to influence relationships with COPD (in males) and healthy weight (in females). The prevalence of individual CVD conditions in relation to OSA diagnosis and sex is shown in **Table S2** in the supplemental material.

In univariate analyses in participants with diagnosed OSA, women were significantly less likely to report ever being diagnosed with CVD conditions, COPD, or gout, but more likely to report a diagnosis of asthma, depression, and anxiety and be of healthy weight ($\text{BMI} < 25 \text{ kg/m}^2$) than men.

Similarly, in participants with high-risk (undiagnosed) OSA, women reported significantly less gout and more ever-diagnosed mental health conditions, arthritis, and nasal symptoms than their male counterparts.

EQ-5D-5L current health status dimensions associated with a diagnosis of OSA

In both men and women, a diagnosis of OSA was significantly associated with a report of current moderate to extreme problems/unable in all 5 EQ-5D-5L dimensions compared to those at high risk of OSA (**Table 3**). This finding persisted in covariate-adjusted models with 1 exception where the association of diagnosed OSA with currently feeling anxious or depressed was attenuated in men.

Mean (SD) EQ-5D-5L VAS scores were significantly lower in men [63.7 (21.9) versus 67.7 (21.0)] and women [62.1 (23.5) versus 66.2 (21.5)] with a diagnosis of OSA compared to those at high risk of OSA. The association of a diagnosis of OSA with impaired VAS scores persisted after adjustment for age and BMI in female (unstandardized B: -4.0 ; 95% confidence

Table 1—Sex-specific sociodemographic and biomedical characteristics of participants according to OSA status.

Characteristic	Men, % (n)			Women, % (n)		
	High-Risk* OSA (n = 452)	Diagnosed OSA (n = 262)	$\chi^2 P$	High-Risk* OSA (n = 563)	Diagnosed OSA (n = 198)	$\chi^2 P$
Age, years						
18–34	6.4 (29)	16.8 (44)	< .001	2.8 (16)	16.2 (32)	< .001
35–54	29.0 (131)	35.1 (92)		41.0 (231)	41.4 (82)	
55–64	26.5 (120)	17.6 (46)		31.1 (175)	23.7 (47)	
65+	38.1 (172)	30.5 (80)		25.0 (141)	18.7 (37)	
< 55	35.4 (160)	51.9 (136)	< .001	43.9 (247)	57.6 (114)	< .001
≥ 55	64.6 (292)	48.1 (126)		56.1 (316)	42.4 (84)	
Area of residence metropolitan	65.9 (298)	69.8 (183)	.282	60.4 (340)	67.2 (133)	.091
Annual gross household income			.919			.034
< \$20,000	3.3 (15)	3.4 (9)		6.2 (35)	8.1 (16)	
\$20,001–\$60,000	39.4 (178)	37.4 (98)		41.4 (233)	34.8 (69)	
\$60,001–\$100,000	25.9 (117)	28.2 (74)		21.8 (123)	24.2 (48)	
> \$100,000	23.2 (105)	24.0 (63)		19.4 (109)	26.8 (53)	
Don't know/refused	8.2 (37)	6.9 (18)		11.2 (63)	6.1 (12)	
Highest education			.075			.012
High school or less	32.1 (145)	31.7 (83)		38.5 (217)	28.8 (57)	
Certificate, diploma, trade qualification	37.6 (170)	30.5 (80)		37.5 (211)	38.4 (76)	
Bachelor's degree or higher	30.3 (137)	37.8 (99)		23.4 (132)	32.8 (65)	
SEIFA quintiles			.313			.336
1 - most disadvantaged	15.5 (70)	15.3 (40)		18.1 (102)	14.2 (28)	
2	22.8 (103)	20.2 (53)		21.4 (120)	21.3 (42)	
3	18.6 (84)	19.8 (52)		20.5 (115)	21.8 (43)	
4	17.5 (79)	23.3 (61)		23.3 (131)	20.3 (40)	
5 - least disadvantaged	25.7 (116)	21.4 (56)		16.7 (94)	22.3 (44)	
Language spoken at home, English	93.4 (422)	89.7 (235)	.081	94.1 (530)	91.4 (181)	.183
BMI, kg/m ² (mean, SD)	30.4 (6.9)	31.1 (7.9)	.268	32.1 (8.1)	30.4 (8.9)	.019
Current smoker	25.0 (113)	34.7 (91)	.006	25.0 (141)	26.8 (53)	.632

*OSA-50 score of ≥ 5 identified patients at high risk of having moderate to severe OSA. Statistical difference by OSA status determined by Student's *t* test. BMI = body mass index, OSA = obstructive sleep apnea, SD = standard deviation, SEIFA = Socio-Economic Indexes for Areas.

interval: $-7.8, -0.2$) but not in male ($-2.9; -6.3, 0.4$) participants. Additional adjustment for household income attenuated these results, and significant impairment persisted in women ($-3.5; -0.7, -0.4$) but not men ($-2.1; -5.5, 1.4$).

Impact of daytime sleepiness on activities of daily living in relation to a diagnosis of OSA

Both men and women with a diagnosis of OSA were significantly more likely to demonstrate FOSQ-10 scores below the 25th percentile compared to their high-risk OSA counterparts. These associations persisted in covariate-adjusted logistic regression analyses (Table 3). The relationship of OSA treatment and sleepiness-related impairments in activities of daily living (FOSQ-10 scores) is shown in Table 4. Of 262 male and 198 female participants with diagnosed OSA, 76.7% of men ($n = 201$) and 74.6% of women ($n = 148$) were recommended to

receive treatment with one or more of CPAP, mandibular advancement devices, or surgery. Of those recommended treatments, 87.6% of men and 83.8% of women commenced treatment. Across OSA treatment categories, there were no significant differences in the proportion of participants with diagnosed OSA demonstrating FOSQ-10 scores in the lowest quartile (indicating more impairment related to daytime sleepiness).

DISCUSSION

Given the documented influence of sex on the pathophysiology and presentation of OSA,^{8,13–16} we a priori sought to identify sex-specific differences in the associations of health conditions and quality-of-life measures with a diagnosis of OSA in a sample of Australian adults, including those identified by a screening

Table 2—Prevalence of ever-diagnosed chronic conditions in relation to OSA diagnosis and sex and adjusted OR and 95% CI for chronic conditions associated with a diagnosis of OSA.

	Men, % (n)			Women, % (n)			P†
	High-Risk# OSA	Diagnosed OSA	χ^2 P	High-Risk# OSA	Diagnosed OSA	χ^2 P	
≥ 1 Cardiovascular condition	17.9 (81)	40.1 (105)	< .001	17.1 (96)	20.7‡ (41)	.25	
OR (95% CI)	1.0	3.0 (2.0–4.5)		1.0	0.9 (0.6–1.6)		.001
Cardiometabolic conditions							
High blood pressure	42.9 (194)	50.8 (133)	.043	43.0 (242)	41.9 (83)	.794	
OR (95% CI)	1.0	1.9 (1.3–2.8)		1.0	1.4 (0.9–2.1)		.532
Diabetes	14.6 (66)	28.2 (74)	< .001	15.1 (85)	21.7 (43)	.032	
OR (95% CI)	1.0	2.6 (1.7–3.9)		1.0	2.2 (1.3–3.5)		.520
BMI, kg/m ²							
Overweight or obese ≥ 25.0	84.3 (350)	79.8 (182)	.147	83.4 (398)	68.5 (111)	< .001	
OR (95% CI)	1.0	0.96 (0.6–1.5)		1.0	0.5 (0.3–0.8)		.063
Mental health conditions							
Depression	27.4 (124)	35.5 (93)	.024	36.1* (203)	50.5‡ (100)	< .001	
Anxiety/panic disorder	15.0 (68)	22.1 (58)	.017	27.9* (157)	39.9‡ (79)	< .001	
≥ 1 condition	30.3 (137)	40.2 (110)	.002	43.0* (242)	59.1‡ (117)	< .001	
OR (95% CI)	1.0	1.6 (1.1–2.3)		1.0	2.5 (1.7–3.7)		.462
Airways diseases							
Asthma	15.3 (69)	18.7 (49)	.233	18.7 (105)	32.8‡ (65)	< .001	
OR (95% CI)	1.0	1.2 (0.8–1.8)		1.0	2.0 (1.3–3.0)		.167
Lung disease, eg, COPD, emphysema	4.9 (22)	15.6 (41)	< .001	5.0 (28)	8.1‡ (16)	.107	
OR (95% CI)	1.0	3.8 (2.1–6.9)		1.0	1.7 (0.8–3.8)		.091
Nasal obstruction/hay fever/rhinitis	18.6 (84)	23.7 (62)	.105	25.8* (145)	31.8 (63)	.100	
OR (95% CI)	1.0	1.4 (0.9–2.0)		1.0	1.3 (0.8–2.0)		.816
Pain disorders							
Arthritis	27.4 (124)	37.8 (99)	.004	38.0* (214)	46.5 (92)	.037	
OR (95% CI)	1.0	2.0 (1.4–2.9)		1.0	1.9 (1.3–2.9)		.709
Gout	10.8 (49)	17.2 (45)	.016	5.2* (29)	6.1‡ (12)	.626	
OR (95% CI)	1.0	1.8 (1.1–2.9)		1.0	1.0 (0.5–2.4)		.363
Heartburn/reflux	27.2 (123)	33.2 (87)	.090	32.7 (184)	38.9 (77)	.114	
OR (95% CI)	1.0	1.5 (1.02–2.1)		1.0	1.6 (1.05–2.3)		.913
Bladder problems	14.4 (65)	16.8 (44)	.387	4.8* (27)	13.1 (26)	< .01	
OR (95%CI)	1.0	1.4 (0.9–2.0)		1.0	1.2 (0.8–1.8)		.841

All binary logistic regression models were adjusted for age, smoking, and BMI, except for reflux and bladder problems (age and BMI only); at least 1 cardiovascular condition additionally adjusted for hypertension, diabetes, and at least 1 mental health condition; overweight or obesity (age and smoking only). †P for the interaction of OSA status with sex in separate models for chronic conditions. Each comorbidity was analyzed as the dependent variable in separate models. #OSA-50 score of ≥ 5 identified patients at high risk of having moderate to severe OSA. Cardiovascular conditions included heart disease, angina or coronary artery disease, previous heart attack, stroke or transient ischemic attack (TIA), atrial fibrillation/irregular heartbeat. *P < .05 for difference in distribution of chronic condition between men and women within undiagnosed OSA. ‡P < .05 for difference in distribution of chronic condition between men and women within diagnosed OSA. BMI = body mass index, CI, confidence interval, COPD = chronic obstructive pulmonary disease, OR = odds ratio, OSA = obstructive sleep apnea.

Table 3—EQ-5D health-related quality of life in relation to diagnosis of OSA and sex, and adjusted OR and 95% CI for increasing functional impairment associated with a diagnosis of OSA.

	Men, % (n)			Women, % (n)		
	High-Risk# OSA	Diagnosed OSA	P	High-Risk# OSA	Diagnosed OSA	P
Mobility			< .001			< .001
No problem	65.7 (297)	43.5 (114)		59.3 (334)	44.9 (89)	
Slight problem	21.2 (96)	30.5 (80)		24.5 (138)	25.3 (50)	
Moderate, severe difficulty, unable	13.1 (59)	26.0 (68)		16.2 (91)	29.8 (59)	
Model 1 OR (95% CI)	1.0	2.4 (1.7–3.3)		1.0	1.9 (1.3–2.8)	
Model 2 OR (95% CI)	1.0	1.9 (1.3–2.6)		1.0	1.7 (1.1–2.4)	
Personal care			< .001			< .001
No problem	88.9 (402)	70.2 (184)		89.3 (503)	73.2 (145)	
Slight problem	8.0 (36)	18.7 (49)		7.6 (43)	17.7 (35)	
Moderate, severe difficulty, unable	3.1 (14)	11.1 (29)		3.0 (17)	9.1 (18)	
Model 1 OR (95% CI)	1.0	2.6 (1.7–4.1)		1.0	2.3 (1.4–3.8)	
Model 2 OR (95% CI)	1.0	2.1 (1.3–3.3)		1.0	1.8 (1.1–3.1)	
Usual activities			< .001			< .001
No problem	70.6 (319)	52.7 (138)		65.5 (369)	49.5 (98)	
Slight problem	22.1 (100)	25.6 (67)		23.1 (130)	23.7 (47)	
Moderate, severe difficulty, unable	7.3 (33)	21.8 (57)		11.4 (64)	26.8 (53)	
Model 1 OR (95% CI)	1.0	3.3 (2.0–5.6)†		1.0	2.4 (1.7–3.5)	
Model 2 OR (95% CI)	1.0	2.0 (1.1–3.6)†		1.0	2.0 (1.4–3.0)	
Pain/discomfort			.026	*	‡	< .001
No problem	33.0 (149)	26.3 (69)		23.6 (133)	23.2 (46)	
Slight problem	41.4 (187)	38.9 (102)		45.8 (258)	30.3 (60)	
Moderate-extreme problem	25.7 (116)	34.7 (91)		30.6 (172)	46.5 (92)	
Model 1 OR (95% CI)	1.0	1.4 (1.03–1.9)		1.0	1.6 (1.1–2.2)	
Model 2 OR (95% CI)	1.0	1.4 (1.04–2.0)		1.0	1.5 (1.1–2.2)	
Anxiety/depression			.005	*	‡	< .001
No problem	56.6 (256)	46.6 (122)		46.4 (261)	27.3 (54)	
Slight problem	24.3 (110)	24.4 (64)		30.2 (170)	38.4 (76)	
Moderate-extreme problem	19.0 (86)	29.0 (76)		23.4 (132)	34.3 (68)	
Model 1 OR (95% CI)	1.0	1.2 (0.9–1.7)		1.0	1.9 (1.3–2.6)	
Model 2 OR (95% CI)	1.0	1.1 (0.8–1.5)		1.0	1.8 (1.2–2.5)	
FOSQ-10 quartiles			< .001			< .001
1 - most impaired	17.1 (77)	32.7 (85)		19.4 (109)	42.4 (84)	
2	29.0 (130)	28.8 (75)		25.1 (141)	22.7 (45)	
3	23.6 (106)	17.3 (45)		25.8 (145)	17.7 (35)	
4 - least impaired	30.3 (136)	21.2 (55)		29.7 (167)	17.2 (34)	
Model 1 OR** (95% CI)	1.0	1.8 (1.2–2.6)		1.0	2.7 (1.8–4.1)	
Model 2 OR** (95% CI)	1.0	1.6 (1.01–2.5)		1.0	2.2 (1.4–3.6)	

Ordinal logistic regression except for usual activities in men that did not meet assumptions for proportional odds (test of parallel lines $P < .05$). Model 1 adjusted for age and BMI. Model 2 adjusted for age and BMI and ever-diagnosed conditions as follows: Mobility additionally adjusted for at least 1 cardiovascular condition, lung disease/COPD, arthritis; Personal care additionally adjusted for depression and or anxiety/panic disorder, lung disease/COPD, arthritis; Usual activities additionally adjusted for depression and or anxiety/panic disorder, lung disease/COPD, arthritis and at least 1 cardiovascular condition; Pain/discomfort additionally adjusted for cancer (not skin); Depression/anxiety additionally adjusted for asthma, lung disease (COPD), nasal obstruction/rhinitis. †Multinomial logistic regression analysis, OR for moderate to extreme difficulty with usual activities (compared to no problem) associated with diagnosed OSA. OR (95% CI) for slight problem with usual activities (compared to no problem) associated with diagnosed OSA: Model 1: 1.6 (1.04–2.3); Model 2: 2.0 (1.1–3.6). FOSQ-10 cutoffs: Males: 0–25th \leq 16.33; 26th–50th 16.34–18.67; 51st–75th 18.68–19.67; 75th–100th $>$ 19.67. Females: 0–25th \leq 15.67; 26th–50th 15.68–18.17; 51st–75th 18.18–19.58; 75th–100th $>$ 19.58. #OSA-50 score of \geq 5 identified patients at high risk of having moderate to severe OSA. * $P < .05$ for difference between men and women within undiagnosed OSA. ‡ $P < .05$ for difference between men and women within diagnosed OSA. **Logistic regression analyses of association of an OSA diagnosis with FOSQ-10 score in the lowest quartile compared to the quartiles 2, 3, and 4 with adjustment for age, BMI, EQ-5D current pain/discomfort and anxiety/depression, ever-diagnosed airways disease, bladder problems (female model) in Model 2. BMI = body mass index, CI = confidence interval, COPD = chronic obstructive pulmonary disease, EQ-5D = EuroQol (European quality of life) five dimension five level scale (EQ-5D-5L), FOSQ = Functional Outcomes of Sleep Questionnaire, OR = odds ratio, OSA = obstructive sleep apnea.

Table 4—Prevalence of FOSQ-10 scores in the lowest quartile of sex-specific distributions in relation to treatment of OSA.

	Lowest Quartile of FOSQ-10*	
	% (n)	OR (95% CI)
Women (n = 193)		
Recommended MAS, CPAP, or surgery <i>and</i> started treatment (n = 124)	44.4 (55)	1.0 (reference)
Did not start recommended treatment (n = 24)	41.7 (10)	0.9 (0.4–2.2)
No MAS, CPAP, or surgery recommended (n = 50)	38.0 (19)	0.8 (0.4–1.5)
High risk OSA# untreated (n = 562)	19.4 (109)	0.3 (0.2–0.5)
Men (n = 162)		
Recommended MAS, CPAP, or surgery <i>and</i> started treatment (n = 175)	31.4 (55)	1.0 (reference)
Did not start recommended treatment (n = 24)	33.3 (8)	1.1 (0.4–2.7)
No MAS, CPAP, or surgery recommended (n = 61)	36.1 (22)	1.2 (0.7–2.3)
High risk OSA# untreated (n = 449)	17.1 (77)	0.5 (0.3–0.7)

*FOSQ-10 score females < 15.67, males < 16.33; assesses sleepiness related impairments in activities of daily living. #OSA-50 score of ≥ 5 identified patients at high risk of having moderate to severe OSA. Treatments considered included MAS, CPAP therapy, or surgery. CI = confidence interval, CPAP = continuous positive airway pressure, FOSQ = Functional Outcomes of Sleep Questionnaire, MAS = mandibular advancement splint/device, OSA = obstructive sleep apnea.

questionnaire as being at high risk of having the condition but who had not undergone previous investigation for OSA. Our study is the only one we are aware of that has considered this important question. Compared to those classified as being at high risk of OSA but not previously diagnosed, correlates of diagnosed OSA included a number of ever-diagnosed health conditions that were independent of sex, including mental health conditions, diabetes, reflux disease, and arthritis, while associations with some conditions varied by sex, including airways diseases, gout, hypertension, and CVDs. Importantly, we were able to demonstrate that the association of 1 or more CVDs with a diagnosis of OSA was significantly stronger in men than women. These findings suggest the existence of different diagnostic pathways for men and women with OSA.

Our findings may reflect a diagnosis of OSA that occurred due to optimal clinical decision making based on excluding differential diagnoses and secondary prevention activities. Men with a diagnosis of OSA were significantly more likely to have been ever-diagnosed with CVD, COPD, and gout compared to those at high risk but not yet diagnosed. This is likely the result of secondary prevention activities to minimize additional CVD risk by active surveillance of OSA symptoms and assessment of OSA/COPD overlap syndrome as recommended by guidelines.^{26,27}

In women, compared to those at high risk of having OSA, an OSA diagnosis was associated with younger age, being of healthy weight (BMI < 25.0 kg/m²), and an increased likelihood of ever being diagnosed with asthma and a mental health condition. Clinical cohort studies show that women likely underreport snoring and its intensity²⁸ and present with differing symptom profiles to men²⁹ (snoring, apneas) that include fatigue, tiredness, headache, and mood disturbance that may relate to or be misinterpreted as depression.²⁹ OSA and asthma are highly comorbid and some evidence suggests that OSA results in worse asthma control.³⁰ Persistent nocturnal asthma symptoms despite optimal controller

therapy may have driven sleep study referrals.³¹ Importantly, guidelines also recommend assessment of OSA for recurrent symptomatic atrial fibrillation,³² pharmacotherapy-resistant hypertension,³³ and investigating type 2 diabetes etiology.³⁴

Ostensibly, our findings may suggest that a diagnosis of OSA is associated with worse health, although the presence of comorbidities is likely to have contributed to the OSA diagnosis. However, the increased likelihood of health status impairment and activity limitation in those with a diagnosis should not detract from the significant impairment observed in those identified at high risk of OSA (as evident by the prevalence of morbidity and low level of EQ-5D-5L VAS scores) or argue against improving early diagnosis and treatment.

Men and women with diagnosed OSA reported higher levels of university-level education, which may impact health literacy and help-seeking behaviors. We have shown that men with doctor-diagnosed OSA were more likely to have better health literacy (and ever diagnosed CVD) than men with polysomnography-determined previously undiagnosed OSA.³⁵ Regardless of sex, those aged 18–34 years were more likely to report a diagnosis of OSA. As our survey targeted respondents who were at a higher risk of having OSA, only a small percentage (8.2%, n = 121) of our study population consisted of adults aged 18–34 years. Within this small sample size, the young respondents were more likely to have been diagnosed with OSA, and McArdle et al³⁶ described a prevalence of OSA (apnea-hypopnea index ≥ 5 events/h) of 20.8% in 22-year-old participants of the Raine Study. More research into the prevalence and diagnosis of OSA in young adults is needed to provide more insight into these findings.

In Australia, access to treatment and support for sleep disorders can be limited outside metropolitan areas and major regional centers. There has been increasing awareness of the need to address sleep health disparities to optimize physical and mental well-being.³⁷ We observed no sociodemographic or economic disparities in screening and diagnosis of OSA, with no significant

associations with household income, area level socioeconomic disadvantage, regional/metropolitan location of residence, or speaking English at home. This is an important finding considering nearly one-third of our sample was born overseas and 7.3% speak a language other than English at home. It is also a testament to the universal health coverage (Medicare) program that introduced publicly funded in-home PSG available to all Australians citizens in 2008.³⁸ The online nature of our survey may have influenced these results; however, 88% of homes in major cities and 77% in remote regions of Australia have access to the internet.³⁹

A previous diagnosis of depression or anxiety was associated with a diagnosis of OSA regardless of sex. Multiple previous studies show similar associations when comparing OSA populations to those without the disorder.² Quality-of-life impairments in OSA have been observed in both men and women with diagnosed OSA and those with OSA symptoms.⁴⁰ Similarly, our study population (both diagnosed OSA and high-risk OSA groups) demonstrated considerably lower mean VAS scores (~10 percentage points lower) than recently reported for the South Australian population [men 78.9 (SD 15.7), women 78.2 (SD 17.4)].⁴¹ When comparing EQ-5D-5L dimensions between the 2 groups, a diagnosis of OSA was significantly associated with increased impairments in all components regardless of sex, except for current feelings of anxiety or depression, which was associated with a diagnosis of OSA in women only. Although the reason for this is unclear, it supports our previous findings demonstrating that women with OSA symptoms and women with an OSA diagnosis had lower SF-36 (Short Form-36) questionnaire mental component summary scores when compared to male counterparts.⁴⁰

Our findings highlight a possible management problem. A recommendation for treatment with mainstream CPAP therapy or mandibular advancement devices was reported by 72% of diagnosed women in our study (similar to findings of CPAP use in 65% reported in a recent US study of women veterans¹¹) and by 74% of diagnosed men. However, FOSQ-10 scores indicate that some participants with diagnosed OSA were more likely to experience sleepiness-related impairments in activities of daily living than those participants at high risk of OSA. In addition, both men and women reporting commencement of therapy (surgery, CPAP, or mandibular advancement splint) demonstrated similar sleepiness-related impairment as those participants not starting recommended treatment. Clearly, excessive daytime somnolence is likely to have been a key factor contributing to referral for investigation for OSA. However, three-quarters of diagnosed people received their diagnosis 12 months or more ago, suggesting that their somnolence has not been completely addressed. Potential explanations include 1) conditions other than OSA that contribute to excessive daytime sleepiness such as depression and nocturia;⁴² 2) inadequate treatment or reduced compliance to recommended therapy for OSA;⁴³ and 3) residual sleepiness that has been reported in CPAP-adherent patients.⁴⁴ The mainstay of therapy for OSA is CPAP,⁴⁵ but nonadherence rates are between 30% and 40%.⁴³ Behavioral therapy, regular follow-up, and early troubleshooting of side effects can promote CPAP adherence,⁴⁶ and referral to the appropriate specialist or allied health service after diagnosis of OSA may be necessary for those with persistent symptoms. The low EQ-5D-5L VAS scores

and persistent daytime somnolence in participants with diagnosed OSA suggest that, at a population level, opportunities to reduce avoidable morbidity in current sleep health services are being missed. Recent economic analyses⁴⁷ also suggest that greater investment to identify better and treat OSA is justified.

The strengths of our study include the sampling procedure that allowed us to generate a sample of adults across a broad age range and comprising 50% women, unlike previous work where female participants are underrepresented, particularly in clinical populations.⁴⁸ Furthermore, despite targeting older participants, we have sampled participants across a wide age range, and the sample broadly matches Australian Bureau of Statistics estimates on sex, state, and regional representation.

The study has some limitations. The OSA50 score ≥ 5 has a positive predictive value of 48% for moderate to severe OSA in the primary care setting¹⁸ to define the high-risk population. This means that a significant proportion of the high-risk population could have mild or no OSA, which needs to be taken into account when interpreting the comparison data. The OSA50 was not administered to participants reporting a diagnosis of OSA. This lack of specific information pertaining to the symptoms such as snoring and witnessed apneas has prevented a comparison symptom burdens between the groups. The diagnosis of OSA was self-reported without review of polysomnography data; however, self-reported OSA has been previously validated.¹⁶ Last, although 65% of the diagnosed group initiated clinician-recommended OSA treatment or had surgery, we did not have data regarding CPAP or mandibular advancement splint compliance and thus cannot relate this to the persistent sleepiness and quality-of-life parameters that can be alleviated with OSA treatment.^{45,49} Furthermore, the cross-sectional nature of the study prevents conclusions regarding the direction of the observed associations with chronic conditions and quality of life.

CONCLUSIONS

Our study highlights the potential missed opportunities of current OSA screening, diagnosis, and management pathways. There is a population of men and women with possible undiagnosed OSA in the community with major health conditions that require investigation. A stronger emphasis on the importance of general sleep health and identification of sleep disorders in primary care will be needed to identify these adults. Importantly, persisting physical and mental morbidity and limitations in activities of daily living were observed in those who sought a diagnosis for OSA, of whom around two-thirds had initiated therapy. Future research should focus on reviewing current diagnostic pathways for OSA and comparing quality-of-life and treatment outcomes to determine the best model of OSA care for Australian men and women.

ABBREVIATIONS

BMI, body mass index
EQ-5D-5L, EuroQol (European quality of life) 5-dimension
5-level scale

COPD, chronic obstructive pulmonary disease
 CPAP, continuous positive airway pressure
 CVD, cardiovascular disease
 FOSQ, Functional Outcomes of Sleep Questionnaire
 OSA, obstructive sleep apnea
 SD, standard deviation
 VAS, visual analog scale

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