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ORIGINAL ARTICLE

Undiagnosed obstructive sleep apnea is independently associated with reductions in quality of life in middle-aged, but not elderly men of a population cohort

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Abstract
Purpose Obstructive sleep apnea (OSA) is now highly prevalent but largely undiagnosed. Quality of life is an indicator of both the impact of undiagnosed OSA and the need for strategies to increase OSA diagnosis. We determined age-related impacts of undiagnosed OSA on health-related quality of life (HRQL) and whether this was independent of sleepiness and comorbidities.
Methods In 2010–2012, 837 participants from the Men Androgen Inflammation Lifestyle Environment and Stress Study (population cohort $n=1869$, ≥40 years, Adelaide, Australia), without a prior OSA diagnosis underwent full in-home polysomnography (Embletta X100) and completed the Epworth Sleepiness Scale and SF-36 questionnaire. The effects of the apnea-hypopnea index (AHI) on SF-36 physical (PCS) and mental (MCS) component summary scores and standardized SF-36 scale z-scores were estimated using multiple linear regression adjusted for major comorbidities and sleepiness, stratified by age.
Results Men ≤69 years demonstrated significant ($p<0.05$) decrements/event increase in AHI in PCS score [unstandardized B coefficient (SE)=−0.068 (0.023)], physical functioning, role physical, general health, and vitality z-scores in fully adjusted models. Severe OSA (AHI ≥30) was associated with significant reductions in PCS [B=−4.1 (1.1)] and MCS score [B=−3.6 (1.2)] independent of sleepiness and comorbidities which were attenuated but persisted in men <69 years without depression. In men aged ≥70 years, statistically significant AHI-associated impairments were generally not seen.
Conclusions Undiagnosed OSA was a major independent contributor to HRQL impairments in men <69 years. Improved strategies to identify undiagnosed OSA are indicated that may require a reduced focus on daytime sleepiness.

Keywords SF-36 health-related quality of life · Obstructive sleep apnea · Excessive daytime sleepiness · Depression · Cohort study · Men

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Introduction

The prevalence of obstructive sleep apnea (OSA) has increased in the last two decades in parallel with increasing obesity. Recent data from the Wisconsin Sleep Cohort [1] estimates a prevalence of 34 % for OSA [apnea-hypopnea index (AHI)≥5] in men aged 50–70 years as compared to

26 % in 1988–1994. The presence of excessive daytime sleepiness (EDS) generally guides OSA diagnosis and treatment. EDS resulting from OSA is associated with a two to threefold increase in motor vehicle accidents [2] and significant impairments of health-related quality of life (HRQL) [3] that can be improved with CPAP [4]. However, community-based studies have shown that 50–80 % of those identified with OSA, even those with a very high frequency of apneas, do not complain of EDS [5] and this may partly account for 75–80 % of OSA remaining undiagnosed [6]. OSA is also associated with a number of other symptoms (e.g., nocturia, headache, reduced libido, erectile dysfunction, and impaired neurocognition) and comorbid conditions such as diabetes, depression and may trigger premature strokes and coronary events [7]. Thus, the full importance of OSA to community health may not be fully appreciated simply by focusing on EDS.

HRQL, a broad multidimensional concept encompassing physical, mental, emotional, and social functioning, may capture the multilayered impacts and experiences of OSA on health beyond the AHI and could be important for future service planning. HRQL supplements traditional measures of morbidity and mortality, is a valid indicator of service needs/intervention [8], and is an important component of health surveillance [9]. There is considerable uncertainty at the present time regarding the impact of OSA on HRQL. The extent to which associations between OSA and HRQL are dependent on comorbidities, and the presence of EDS is unclear. Clinic studies have shown reduced HRQL in OSA patients compared to population norms [10], but such studies are likely confounded by referral bias. Population-based studies examining HRQL in OSA have shown conflicting results. Significant reductions in six of eight SF-36 scales were observed in subjects with even very mild OSA in the Wisconsin Sleep Cohort [11]. The Sleep Heart Health Study (SHHS) found that only severe OSA was associated with impaired SF-36 physical component summary (PCS) [12] and "poor" QoL (score <25th percentile) on physical functioning, general health, vitality, and social functioning scales [3] and that increased EDS, but not progression of OSA, was accompanied by worsening of both physical and mental health [13]. Furthermore, studies in samples of only older men [14] or OSA patients [15] suggest that OSA is not the major influence on HRQL in men aged over 65 years, but this has not been systematically explored. Elderly patients have more central apneas [16], and HRQL impacts caused by deleterious end organ effects of OSA may be mitigated in this age group by hypoxic preconditioning [17].

The aim of this study was to assess the effects of undiagnosed OSA on HRQL in a cohort of community-dwelling men and determine to what extent this is mediated by EDS and a wide range of comorbidities including depression, erectile dysfunction, and lower urinary tract symptoms, which have not previously been considered. We have examined whether age modulates the effects of OSA on HRQL since there is increasing evidence that OSA may be a different disease in elderly compared with middle aged adults [16, 18, 19].

Methods

Study participants

The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study is comprised of randomly selected, urban community-dwelling men aged 40 years and over, and has been described previously [20]. Initial random recruitment by electronic white pages and computer-assisted telephone interviews (CATI) occurred in 2000–2002. Biomedical assessments were conducted in hospital-based clinics, using standardized and reproducible study protocols. Data for the current analyses were derived from follow-up assessments in 2010–2012. Body mass index (kg/m^2) was categorized according to international criteria: underweight/normal ≤24.9, overweight 25.0–29.9, and obesity ≥30.0. Self-completed questionnaires assessed demographic, biographical, self-reported comorbidities, behavioral risk factors, SF-36 HRQL, depression (score of >12 on the Beck Depression Inventory or ≥21 on the Center for Epidemiological Studies Depression Scale or treatment), total lower urinary tract symptoms (LUTS, International Prostate Symptom Scale), and significant erectile dysfunction (ED, Global Impotence Rating with moderate and severe combined). Diabetes was determined by self-report of doctor diagnosis, fasting plasma glucose ≥7.0 mmol/l or hemoglobin A1c ≥6.5 %. Cardiovascular disease (CVD) included self-reported doctor diagnosed myocardial infarction, stroke, transient ischemic attack, or angina. Hypertension was identified by systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or self-reported antihypertensive medication use. High total cholesterol was defined as total cholesterol ≥5.5 mmol/l.

Sleep data

MAILES study participants completed a CATI survey in August 2010 (n=1629). Of these, 184 responded "yes" to "Have you ever been diagnosed with obstructive sleep apnea with a sleep study?" The 1445 men reporting "no" were invited to undergo a sleep study, with 75.2 % agreeing. In 2010–2012, 857 subjects underwent eight-channel in-home unattended polysomnography (PSG, Embletta X100, Embla Systems, CO) which measured EEG, EOG, EMG, nasal pressure, thoracic and abdominal effort, oximetry, body position, and limb movements. Trained staff visited study participants in their homes to set up the PSG equipment. The Epworth Sleepiness Scale (ESS) [21] was administered, and anthropometric measures and current medications, including sedatives and antidepressants, were recorded. A physician investigator

coordinated any necessary clinical follow-up. The study flow is shown in Fig. 1.

A single experienced sleep technician performed manual scoring of all home PSGs according to the 2007 American Academy of Sleep Medicine (AASM alternate) criteria [22]. Studies were considered acceptable (n=837) with 3.5 h of sleep recorded and 5.5 h of total recorded study time. Apneas were defined as cessations of nasal flow lasting ≥10 s and hypopneas as a >50 % decrease in nasal flow (or in both thoracic and abdominal excursions) and associated ≥3 % oxygen desaturation or an EEG arousal. OSA was defined as an AHI ≥10/h, with further categorization: mild, AHI of 10–19/h; moderate, 20–29; and severe, ≥30/h. The cutoffs for classification were chosen because Ruehland et al. [23] have shown that an AHI of 5/h of sleep used to define sleep-disordered breathing scored by the 2007 *recommended* AASM criteria is equivalent to an AHI of 10/h of sleep using the *alternate* AASM definition, and 15/h using the older 1999 *Chicago* criteria. In order to maintain comparability with previous work a cutoff of 10/h was chosen [23]. EDS was identified by ESS ≥11.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 19.0 (SPSS Inc., Chicago, IL, USA).

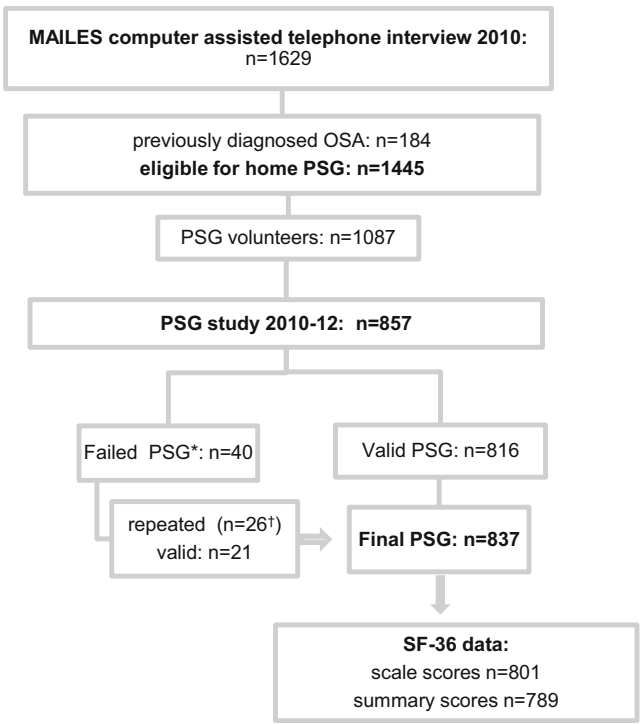

Fig. 1 The MAILES study flow diagram: polysomnography recruitment, successful studies, and SF-36 questionnaire completion. * n=21 total sleep time (TST) not ≥3.5 hours from ≥5 hours recording; n=3 poor respiratory signals; n=2 poor EEG; n=14 no oxygen saturation (SAO_2); n=3 all traces/recording failed. †Includes 20 successful and 3 failed second PSG of which one was successfully repeated a third time

PCS and mental component summary (MCS) scales are scored to generate a mean of 50 with a SD of 10. SF-36 scale scores are presented as standardized z-scores, i.e., the number of standard deviations from the mean scale score of the population (e.g., z-score of −1.0 or less equates to the lowest scoring 16 % of the population).

t Tests and ANOVA determined mean SF-36 scores in relation to OSA, ESS scores, and comorbidities. Multiple linear regression models were conducted with AHI as the primary independent variable to predict SF-36 scores with adjustment for confounders where appropriate including age, BMI, sleepiness, LUTS, CVD, hypertension, total cholesterol, smoking, diabetes, joint pain, sedative use, ED, and depression. Analyses were conducted to examine age-specific effects of the AHI and OSA on HRQL in the study population stratified by age ≤69/≥70 years (consistent with reported increased risk of death associated with severe OSA in men aged 40–70 years [19]) and presence of depression. Furthermore, in the total sample, interactions of age (dichotomized ≤69/≥70 years) with AHI with $p<0.10$ were seen for physical functioning ($p=0.08$), general health ($p=0.08$), and role emotional ($p<0.05$).

Subgroup analysis in men free of depression was conducted to identify the effects of OSA on mental health scores not influenced by effects of depression given that low scores on the MCS, mental health, and vitality scales identify depressive/psychiatric disorders [24]. Accordingly, models for MCS and mental scales in all men were not adjusted for depression. In men without depression, significant interactions of age (dichotomized ≤69/≥70 years) with AHI were detected for PCS ($p=0.04$), physical functioning ($p=0.003$), role physical ($p=0.05$), and general health ($p=0.04$). Linear regression covariates missing data were imputed if necessary. Multiple linear regression models were also conducted with the AHI dichotomized to OSA clinical categories including mild (10–19 events/h) at least moderate OSA (≥20 events/h) or severe OSA (≥30 events/h) compared with AHI <10.

The study was approved by the North West Adelaide Health Service and the Royal Adelaide Hospital institutional ethics committees, and all subjects gave written informed consent for each study component.

Results

Complete valid PSG data were obtained in 837 men. SF-36 component summary scores were determined in 789 (94 %), and scale scores were determined across the eight scales in 801–809 (97 %) men. Table 1 shows unadjusted mean (SD) PCS and MCS scores in relation to OSA, OSA severity, daytime sleepiness (ESS≥11), and sedative medication use stratified by age. In men aged 40–69 years only, significant reductions in mean PCS scores occurred in participants with previously undiagnosed OSA, with more marked reductions with

Table 1 Participant characteristics [% (*n*)] and mean (SD) SF-36 physical component summary (PCS) and mental component summary (MCS) scores in relation to age and obstructive sleep apnea (OSA) criteria, sleepiness, and sedative use in men undergoing sleep studies

	Age 40–69 years (*n*=619)			Age ≥70 years (*n*=170)		
	% (*n*)	PCS 50.4 (8.3)	MCS 50.8 (9.0)	% (n)	PCS 47.5 (10.5)	MCS 50.5 (9.7)
No OSA (AHI <10)	50.6 (313)	51.6 (6.9)	51.7 (7.6)	37.6 (64)	47.7 (10.1)	51.8 (7.9)
OSA (AHI ≥10)	49.4 (306)	49.1[a] (9.4)	49.8[a] (10.1)	62.4 (106)	47.4 (10.9)	49.8 (10.7)
OSA severity (AHI)						
10–19 (mild)	25.4 (157)	50.0 (8.7)	50.2 (9.7)	31.2 (53)	48.6 (9.8)	51.0 (9.2)
20–29 (moderate)	13.4 (83)	50.1 (9.0)	50.4 (9.6)	14.7 (25)	46.7 (9.9)	50.5 (8.9)
≥30 (severe)	10.7 (66)	45.8[b] (10.9)	48.0[b] (11.5)	16.5 (28)	45.7 (13.4)	46.8 (14.1)
Sleepiness						
ESS ≤10	86.8 (531)	50.9 (8.0)	51.4 (8.3)	89.8 (149)	47.4 (10.5)	50.8 (9.3)
ESS ≥11	13.2 (81)	46.8[a] (10.1)	46.6[a] (11.4)	10.2 (17)	47.0 (12.2)	48.7 (13.4)
No OSA						
ESS <11	45.4 (278)	51.8 (6.9)	52.1 (7.4)	34.3 (57)	47.8 (9.5)	51.9 (7.8)
ESS ≥11	5.6 (34)	50.0 (7.3)	48.8 (8.6)	4.2 (7)	47.1 (14.8)	51.4 (9.4)
OSA						
ESS <11	41.3 (253)	49.9 (8.9)	50.6 (9.2)	55.4 (92)	47.4 (10.9)	50.1 (10.1)
ESS ≥11	7.7 (47)	44.8[b] (11.1)	45.3[b] (13.1)	6.0 (10)	46.8 (11.0)	46.7 (15.7)
No sedative use	98.1 (607)	50.4 (8.3)	50.8 (9.0)	91.9 (155)	48.2 (10.3)	51.4 (9.1)
Sedative use	1.9 (12)	49.2 (10.1)	49.8 (9.2)	8.8 (15)	40.4[a] (11.1)	41.5[a] (11.6)

PCS and MCS scales are scored so that their means are set at 50 with a SD of 10

ESS Epworth Sleepiness Scale, scores were only available in 612 of 619 of men 40–69 years and in 166 of 170 men aged ≥30

[a] $p<0.01$; [b] p of differences between groups <0.05 by ANOVA

severe OSA. The reduction in PCS scores observed in younger men (40–69 years) with severe OSA compared with no OSA was 5.8 units (equivalent to 0.58 of a standard deviation). The reduction in MCS scores with severe OSA was similar across age groups. Among those with both OSA and sleepiness, the reduction in PCS scores compared to those without either was greater in younger men (7.0) than older men (1.0), while reductions in MCS scores were similar across age groups. In older men only, major reductions in PCS and MCS scores in current sedative medication users were observed. The HRQL impacts of major conditions and risk factors are shown in Online Resource Table 1, with effects of depression, LUTS, ED, and CVD seen in both age groups.

The reductions in PCS and MCS scores reported in Table 1 are reflected in the mean (SD) standardized SF-36 scale z-scores (Online Resource Table 2). Among the younger men with OSA, large reductions were seen in the domains relating to physical health, and in general health and vitality, whereas in older men impairments were more prominent in domains relating mental health, such as emotional role functioning. Severe OSA was associated with around twofold greater reductions in domains of physical health, general health, and vitality in younger men compared to men aged ≥70 years who tended to come off a lower baseline.

Multiple linear regression analysis (Table 2), in the whole sample aged ≥40 years, showed significant reductions in both PCS and MCS scores per event increase in AHI, independent of age, ESS scores, BMI, and major comorbidities. However, when the effects of age and depression are considered, age-specific impairments in PCS scores were confined to the younger men (aged 40–69) and persisted in men without depression. Furthermore, in this younger group free of depression, reductions of borderline significance were observed for MCS ($p=0.053$). In men aged ≥70 years, significant independent impairments in MCS scores per event increase in AHI occurred that did not persist when men with depression were excluded from the analysis. Online Resource Fig. 1 illustrates the adjusted age-specific effects of the AHI on PCS and MCS scores in men without depression.

In relation to SF-36 scale scores (Online Resource Table 3), multiple linear regression analysis showed that men aged 40–69 years experienced significant impairments in physical functioning, role physical, general health, and vitality per one unit increase in AHI after adjustment for age, ESS scores, BMI, and major comorbidities. When those with depression were excluded, significant impairments persisted in role physical and general health scales and a reduction of borderline significance was observed for vitality ($p=0.06$). In men

Table 2 Age stratified linear regression analyses of the association of the apnea hypopnea index (AHI) with SF-36 summary scores in all MAILES participants and those free of depression

	Unstandardized B coefficients (SE)				
	All men			Men without depression	
	Age ≥40 years	Age 40–69 years (n=619)	Age ≥70 years (n=170)	Age 40–69 years (n=530)	Age ≥70 years (n=152)
PCS	−0.055[a] (0.021)	−0.068[a] (0.023)	−0.017 (0.050)	−0.053[b] (0.023)	0.052 (0.055)
MCS	−0.064[a] (0.023)	−0.045 (0.026)	−0.119[b] (0.046)	−0.041 (0.021)	−0.003 (0.046)

Coefficients reflect change in physical component summary (PCS) or mental component summary (MCS) scores per event increase in AHI. Models adjusted for age, body mass index, Epworth Sleepiness Scale scores, lower urinary tract symptoms, CVD, hypertension (age≤69, PCS scores only), diabetes, joint pain, sedative use, smoking, erectile dysfunction and depression (only for PCS, physical functioning, role physical, bodily pain, general health scores in all men)

[a] Model B coefficient $p<0.01$; [b] model B coefficient $p<0.05$

≥70 years, impairments in social functioning and role emotional were evident, but after men with depression were excluded from the analysis, these effects were lost, and a significant improvement in the physical health scale was observed. The results for the whole sample aged ≥40 years were similar to those for men aged 40–69 years with exceptions that obscured the impairments in physical scales confined to the younger men, and impairments in mental scales that occurred in older men (as described above).

The effects of OSA clinical severity categories on PCS and MCS scores determined using multiple regression are shown in Table 3. In men aged 40–69 years, significant independent effects of all OSA (AHI≥10), mild (AHI 10–19, PCS p=0.05), moderate-severe (AHI≥20), and severe OSA on PCS and MCS scores were seen in fully adjusted models. Compared to no OSA (AHI<10), the decrements in severe OSA (AHI≥30) represent reductions in PCS and MCS scores of 0.41 and 0.36 of a SD, respectively. No significant reductions in summary scores were observed in men aged ≥70 years.

When analyses were limited to men without depression, in 40–69-year-old men, impairments in PCS and MCS scores associated with moderate-severe OSA and severe OSA were attenuated but persisted. However, in the older men, severe OSA was associated with an improvement in PCS score (equating to an increase 0.44 of a SD compared to men with no OSA) which approached statistical significance (p=0.059).

Discussion

In middle aged men aged 40–69 years in our community-dwelling population, undiagnosed OSA was associated with impaired HRQL in both physical and mental health, independent of sleepiness and other traditional comorbidities. There was an apparent "dose-response" relationship, with incremental impacts observed with increasing OSA severity on both physical and mental functioning, with a moderate level reduction [25] in PCS scores (0.4 SD) observed with severe undiagnosed OSA. In contrast, in older men aged ≥70, even severe undiagnosed OSA was not associated with independent HRQL impairments.

Table 3 Age stratified linear regression analyses of the association of obstructive sleep apnea severity with SF-36 summary scores in all MAILES participants and those free of depression

	Unstandardized B coefficients (SE)			
	All men		Men without depression	
	Age ≤69	Age ≥70	Age ≤69	Age ≥70
OSA (AHI ≥10)				
PCS	−1.82[a] (0.63)	1.79 (1.49)	−1.21 (0.63)	1.88 (1.50)
MCS	−2.05[a] (0.73)	−0.52 (1.43)	−1.28[b] (0.57)	0.56 (1.25)
Mild OSA (AHI 10–19)				
PCS	−1.40 (0.71)	2.45 (1.78)	−1.01 (0.73)	2.41 (1.80)
MCS	−2.00[b] (0.81)	0.05 (1.49)	−0.97 (0.64)	0.80 (1.47)
Moderate-severe OSA (AHI ≥20)				
PCS	−2.56[a] (0.79)	1.24 (1.81)	−1.58[b] (0.78)	1.50 (1.87)
MCS	−2.57[b] (0.91)	−1.54 (1.76)	−1.82[b] (0.72)	−0.003 (1.58)
Severe OSA (AHI ≥30)				
PCS	−4.13[a] (1.06)	2.68 (2.17)	−2.95[b] (1.09)	4.37 (2.28)
MCS	−3.59[a] (1.23)	−2.35 (2.26)	−2.29[b] (0.96)	1.35 (2.02)

Coefficients reflect the SD change in physical component summary (PCS) or mental component summary (MCS) score associated with a change from no OSA to OSA, mild OSA, moderate-severe or severe OSA. PCS and MCS scales are scored to produce a mean set at 50 with a SD of 10; thus, for all men aged ≤69 years, a coefficient of −4.13 for severe OSA represents a reduction in PCS score of 0.41 of a standard deviation for men with severe OSA compared to no OSA. Models adjusted for age, body mass index, Epworth Sleepiness Scale scores, lower urinary tract symptoms, CVD, diabetes, joint pain, sedative use, smoking, erectile dysfunction, hypertension (age≤69, PCS scores only) and depression (PCS scores only in all men)

[a] Model B coefficient $p<0.01$; [b] model B coefficient $p<0.05$

The triad of OSA, sleepiness, and depression is complex due to the inter-relatedness of these factors. Our findings suggest the impact of OSA on HRQL is mediated in part by depression. If OSA causes depression as some findings suggest [26], then the true impact of OSA on HRQL may be underestimated when adjusting for depression. Nevertheless, when the younger men with depression were excluded from the analysis, impairments in relation to AHI persisted for PCS scores and the impact of severe OSA on both PCS and MCS persisted at a mild level (0.2–0.3 SD reduction) [25], independent of sleepiness and comorbidities. In older men without depression, negative mental health impacts were not evident, and we observed a moderate positive effect of severe OSA on PCS scores that approached statistical significance ($p=0.059$). While this may also partly represent a survivor effect in the older men, these findings support the argument that OSA in the elderly may be a different disease entity [16] and that age alters risks for manifestations of OSA [16, 19, 27].

Impairments in the younger undiagnosed men may have implications for ongoing workforce participation in those of working age [28] and emphasizes the need to identify this group with a strategy that does not rely on the presence of daytime sleepiness. Severe undiagnosed OSA was highly prevalent in our sample (12 %), and relatively few (13 %) of these subjects reported excessive daytime sleepiness. Therefore, a focus on daytime sleepiness may limit the potential for gains in HRQL given that CPAP treatment has been shown to improve SF-36 physical function and general health domains; however, results are conflicting for other domains [4]. Importantly, two randomized controlled trials of CPAP have demonstrated improvements in SF-36 scales in minimally symptomatic OSA patients [29, 30].

The SHHS have reported significant decrements in SF-36 scale scores of physical health in OSA patients (63±11 years) mainly confined to severe disease [3], and the Wisconsin Study of younger state employed male and female participants (30–60 years) identified significant decrements in six of eight SF-36 scale scores for even mild OSA (AHI≥5) [11], after adjusting for some confounders including cardiovascular disease. Khan et al. found that in a community-based sample of older adult men ≥65 years, REM-predominant OSA was not associated with impairment in HRQL, assessed by the SF-12 [14]. We extend these findings by showing that in contrast with older men, in younger, mostly working age men from a representative population cohort, moderate-severe OSA is independently associated with impaired physical health domains of HRQL, after adjusting for important predictors of HRQL such as ED, depression, LUTS, and chronic joint pain, that have not been accounted for in previous studies.

The mechanism through which OSA may operate to negatively impact on HRQL is unclear, given we adjusted for factors that influence HRQL including sleepiness [3]. Many people with OSA do not report excessive daytime sleepiness [5], and sleepiness often does not resolve with CPAP treatment, indicating sleepiness may be due to other causes [31]. While OSA and ESS assessed sleepiness had independent effects upon physical domains of HRQL in younger men, we did not assess as a separate construct tiredness or fatigue which may not result in daytime sleepiness or inadvertent napping, but may nevertheless be detrimental to HRQL. The use of fatigue, as distinct from daytime sleepiness, as a clinical trial outcome requires consideration in order to potentially reduce the significant burden of HRQL impairments in OSA. Further work is required to investigate hormonal, inflammatory and neurocognitive consequences of OSA that may independently impact upon general well-being and HRQL which were not studied here.

A possible limitation of this study is the use of the SF-36, a generic HRQL questionnaire. However, the SF-36 assesses domains of functional health and well-being relevant to OSA patients and has similarities to the Functional Outcomes of Sleep Questionnaire. The SF-36 allows comparisons with general population norms, across different populations and conditions, and with other major studies that have used it in OSA [3, 11]. A limitation of the SF-36 is that it generates multiple endpoints (eight scale scores and two summary scores) and our findings may be weakened due to multiple testing. Our study was confined to men and our findings may not be generalizable to women. However, strengths of our study include the population-based sampling which did not oversample snorers, including men not in the workforce, unlike prior studies [11], and adjustment for multiple common confounders that can affect sleep and HRQL in men (including depression, joint pain, ED, and LUTS) not accounted for in previous studies [3, 11].

In conclusion, in men aged 40–69 years from a community sample, previously undiagnosed OSA is associated with impairments in HRQL, particularly in physical health, independent of sleepiness and major comorbidities. Our findings highlight that the HRQL burden is not limited to only symptomatic sleepy patients normally referred for clinical investigation. Significant quality of life gains may be possible upon commencement of CPAP irrespective of the presence of sleepiness [29, 30], if a diagnosis can be made. However, appropriately designed randomized controlled studies are needed to demonstrate convincingly that there is a HRQL benefit in this group. In particular, there is a need for treatment trials examining fatigue as a study outcome. Better identification of working-age men who have severe OSA without sleepiness would also then become an important clinical goal. Although impairments in mental health scales were seen in older men with OSA, these were related to depression and physical health benefits were seen in older men without depression. Prospective studies examining differences in OSA outcomes

across age groups are needed particularly in older subjects where the notion of hypoxic conditioning requires additional investigation.

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SM, JG, and SA have no conflicts of interest to declare.

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