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Obstructive Sleep Apnea Is Treatable With Continuous Positive Airway Pressure in People With Schizophrenia and Other Psychotic Disorders

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Obstructive sleep apnea (OSA) is a highly prevalent condition in people living with schizophrenia or other psychotic disorder. Its treatment with continuous positive airway pressure therapy (CPAP) can dramatically improve daytime and physical health function. People with a psychotic disorder, however, are rarely diagnosed and treated and there are no large-scale studies showing evidence of successful treatment with CPAP. Using a retrospective case-control study approach ($N = 554$), we examined adherence to and effectiveness of a CPAP trial in individuals with comorbid psychotic disorder and OSA (psychosis group, $n = 165$) referred for a CPAP trial at the West Australian Sleep Disorders Research Institute. Given that antipsychotic medication is an important confounder, we included a psychiatric (non-psychosis) comparison group taking antipsychotic medication (antipsychotic group, $n = 82$), as well as a nonpsychiatric control group (OSA control group, $n = 307$) also diagnosed with OSA and referred for CPAP. Variables included OSA symptom response, CPAP engagement, and usage at 3 months. The Psychosis group had the most severe OSA at baseline and they attended fewer clinic appointments overall. However, there were no other group differences either in CPAP adherence or treatment response. CPAP was equally effective in normalizing OSA symptoms and daytime sleepiness in all groups. CPAP usage was longer per night in the Psychosis and Antipsychotic groups, perhaps suggesting a role of sedation from antipsychotic medications. In conclusion, OSA is treatable and CPAP feasible in people with severe mental illness and antipsychotic medications are not a barrier to treatment response.

Key words: sleep apnea/OSA/snoring/physical health/mental illness/apneic hypopneic/schizophrenia

Introduction

Obstructive sleep apnea (OSA) is a common, sleep-related breathing disorder characterized by repetitive collapse of the upper airway during sleep. Symptoms include loud snoring, apneic events, disturbed sleep and excessive daytime sleepiness.[1,2] OSA is associated with severe adverse health outcomes including impaired cardiovascular health, weight gain, diabetes, cognitive impairment, and reduced quality of life.[3–5] The most effective treatment for OSA is continuous positive airway pressure (CPAP) therapy[6,7] which utilizes a mask applied to the nose and/or mouth to deliver air pressure to the upper airway and prevent airway collapse during sleep.[8] CPAP reduces the risk of metabolic syndrome, improves cardiovascular outcomes and daytime function,[9–12] and is associated with large healthcare economic benefits by way of reductions in specialist visits and medications.[13,14]

OSA is highly prevalent in people diagnosed with schizophrenia or another psychotic disorder (20%–60%).[15–18] In those individuals, OSA has been linked to the development of physical health comorbidities including diabetes, cardiovascular and respiratory diseases[19,20] and to a greater severity of psychiatric symptoms.[21] Despite the potential benefits of CPAP, studies reporting on the diagnosis and treatment of OSA in psychosis are rare.[15,22,23] One contributing factor may be the lack of awareness of OSA and routine screening for apnea symptoms in

mental health settings.[19] In addition, there is a common notion that amotivation, poor adherence, or lack of tolerance in people with a psychotic disorder may lead to treatment failure.[19,24–26]

OSA treatment studies in psychosis are limited to case studies and small sample sizes. These show that OSA treatment with CPAP can reduce psychiatric symptom severity,[27,28] improve sleep quality,[29–31] and daytime function.[29,32]

However, there is a lack of evidence about the outcomes of OSA referrals that might support the use of CPAP. For confidence to grow about incorporating sleep clinic referrals in the care of people with psychosis, more evidence is required about the tolerability and effectiveness of CPAP therapy trials.

Another question is about the interaction between antipsychotic medications and the mechanisms of CPAP improvements. Antipsychotics are used to control the symptoms of psychosis but they are also linked to OSA via their effects on weight gain and the metabolic syndrome.[33–35] Because of their disruptive effects on bioenergetic and neuroendocrine function,[36] antipsychotic medications may limit the normalization of metabolic effects and the symptomatic benefits that may be gained from CPAP.[37]

Teasing-out the effects of antipsychotics from the psychotic illness is difficult because few patients are unmedicated. However, it is possible to include a comparison group who were prescribed antipsychotics for symptom management but with a psychiatric disorder other than psychosis.[38] This comparison group can assist in differentiating CPAP outcomes specific to a psychotic disorder from those linked to antipsychotic medication.

The aim of this study was to examine levels of engagement, adherence, and effectiveness to a CPAP initiation trial in people diagnosed with a psychotic disorder. Using a retrospective observational matched case-control design, we identified 3 groups diagnosed with OSA and recommended for CPAP in a large public sleep disorders clinic: (1) individuals with psychotic disorders taking antipsychotic medication (the "Psychosis" group), (2) a non-psychiatric/non-psychotic OSA control group ("OSA-Controls"), and (3) a psychiatric comparison group treated with antipsychotic medication for reasons other than a psychotic illness ("Antipsychotic" comparison group). The primary hypothesis was that, compared to OSA-controls, the Psychosis group would show lower CPAP trial engagement and adherence and lower symptomatic response to CPAP because of the influence of antipsychotic medications, after adjusting for key baseline covariates known to influence CPAP success. The secondary hypotheses were that the Antipsychotic comparison group would have similar CPAP trial engagement and adherence to OSA Controls, but less improvement in CPAP symptomatic response due to their antipsychotic medication.

Methods

Participants

All patients underwent a clinical evaluation by a specialist sleep physician at the West Australian Sleep Disorders Research Institute (WASDRI), a large tertiary sleep disorders clinic located in Perth, Western Australia.[39] Inclusion criteria were (1) age 18+, (2) OSA diagnosis, (3) Apnea-Hypopnea Index AHI ≥ 5, and (4) recommended for CPAP therapy by a sleep specialist. Exclusion criteria[40] included a significant sleep disorder other than OSA (including narcolepsy, idiopathic hypersomnolence, periodic limb movements during sleep >15 h); predominant central sleep apnea (>50% apneas were central) or Cheyne-Stokes breathing; significant neurological, neuromuscular, degenerative, or respiratory disease, stroke, unstable or severe cardiovascular disease, Class 3 or 4 heart failure[41]; unable to undertake standard CPAP initiation procedure due to living in a remote location; privately managed patients; and not CPAP naïve. Insomnia commonly co-occurs with OSA and was not excluded.

OSA-Controls represented a sample of consecutive WADSRI patients booked in for a CPAP trial between September 2009 and March 2010 (exclusion criteria as above). Patients with history of a psychiatric or psychotic disorder or taking antipsychotic treatment at PSG were also excluded. Ascertainment for the *Psychosis* and the *Antipsychotic* groups required the use of linked administrative hospital data. We utilized a pre-existing dataset which combined WASDRI records between 1989 and 2014 for people aged 18+, OSA diagnosis, and AHI ≥5 with Mental Health Information System hospital records. For the current study, patients were selected if they had a PSG after August 2002, had OSA and were recommended for CPAP, and were taking antipsychotic medication at the time of PSG. All were outpatients, and the exclusion criteria were the same as described above. The Psychosis group was defined as people diagnosed with schizophrenia, schizoaffective disorder, bipolar disorder with psychotic features, depressive psychosis and other non-organic psychoses,[42,43] and the Antipsychotic group included psychiatric disorders other than psychosis (e.g. autism, major depression, anxiety disorders, post-traumatic stress disorder) and taking antipsychotic medication.

OSA Diagnosis and CPAP Procedures

Procedures have been described in detail elsewhere.[44–46] Briefly, OSA diagnosis was conducted in-laboratory by polysomnography (PSG) using the Compumedics Grael system (Compumedics Ltd, Abbotsford, Australia) and defined by an Apnea-Hypopnea Index (AHI) of ≥5 events/h of sleep. Methods for scoring sleep stages and respiratory events followed Chicago criteria[47] (until 2013) and the Academy of Sleep Medicine (AASM)

2012 criteria thereafter,[48] which is a standard procedural change in the field and unlikely to influence the study's conclusion. Standard PSG measurements included nasal and oral airflow, oximetry, chest wall motion (inductive plethysmography), submental and bilateral anterior tibial electromyograms, electrooculogram, electrocardiogram, body position, and sound intensity.

Patients with OSA and prescribed CPAP therapy were booked for an initial CPAP trial appointment where they were provided with education and offered a home trial of CPAP therapy usually lasting 3–6 weeks. CPAP masks were individually fitted to maximize comfort and minimize leak. Prior to 2006, in-laboratory manual CPAP titration was used, performed based on PSG monitoring signals with the addition of mask pressure, leak and flow signals. CPAP pressure was increased in 1–2 cm H_2O increments to abolish snoring and respiratory events, and to minimize EEG arousals in all sleep stages and postures. Studies were analyzed overnight and the sleep physician determined a fixed pressure before the patient was discharged home in the morning. From 2006 onwards, automatic positive airway pressure (APAP) titration replaced PSG-based titration to standardize current practice with international guidelines with no known influence on research outcomes.[49] Patients were instructed to use the device during sleep and return for review weekly, during which CPAP device download data were evaluated to determine an appropriate fixed pressure setting. CPAP trial appointments included weekly or fortnightly reviews by an accredited sleep physician and scientist. The Epworth Sleepiness Scale (ESS) was collected at PSG and at the end of the trial. The score ranges from 0 to 24 and scores ≥11 indicate excessive sleepiness.[50]

Data Extraction and Outcome Measures

Data were manually extracted from the WADSRI databases through a review of referral and discharge letters, PSG/CPAP summaries and reviews, clinic appointments from the time of PSG (Psychosis and Antipsychotic groups), and from CPAP booking (OSA-Controls). The same data extraction and cleaning methodology was applied across all samples. Data integrity and quality control protocols included inter-rater reliability checks on a random 10% sample and independent verifications until 90^{+}% inter-rater intra-class correlations were achieved.

Patient variables included demographics, diagnostic information, and medications at baseline PSG (including antipsychotics, antidepressants, anxiolytics, mood stabilizers). *OSA severity* was assessed with AHI, ESS score and Hypoxemia during PSG (oxygen saturation levels—SpO_2—less than 90%). *CPAP Trial characteristics* included total trial duration; number of therapy clinic visits including initial issue appointment and reviews; outcomes at the following clinical stage (1) Initial trial issue (did not attend appointment; declined or accepted a CPAP trial); (2) end of trial outcomes (completed a full trial; accepted or declined CPAP for long term use); (3) 3 months review to determine continued usage (available for clinical groups only); and funding sources for acquiring CPAP machines after the trial for long-term use. *CPAP trial adherence* was assessed using end of trial nightly CPAP use (total hours of use divided by number of nights used, and final CPAP pressure). *CPAP treatment effectiveness* was assessed in terms of OSA and sleepiness indicators by comparing AHI and ESS score at the end of the CPAP trial to baseline.

Statistical Analysis

SPSS v25[51] was used to analyze the data. Group comparisons for discrete variables were conducted using chi-square analyses with significance thresholds adjusted for multiple comparisons using Bonferroni adjustment. Comparisons for continuous variables involved analyses of variance with Tukey's HSD post hoc analyses. Post-treatment outcomes were examined with regression analyses incorporating post-trial measurements, baseline values where appropriate, groups and covariates.[52] Selected group membership contrasts were used to isolate the independent contribution of psychosis (Psychosis group, vs Antipsychotic and OSA-Controls) and antipsychotics (OSA-Controls, vs Psychosis and Antipsychotic group). Separate step-wise regressions were conducted using average end of CPAP use, end CPAP pressure, final ESS and AHI scores as dependent variables. Independent variables included baseline ESS or AHI scores (CPAP response indicators), group membership, and covariates entered into separate regression steps. Age, sex and BMI were added as covariates based on group differences and the potential influence of these variables on CPAP outcomes. The effect of psychotropic medication was explored as a covariate coded in a binary way (taking/not taking).

To explore the impact of CPAP on treatment outcomes (AHI, ESS) repeated-measures ANOVA were conducted to determine the overall treatment effect on outcomes, followed by hierarchical multiple regression to control for baseline values in exploring group differences in treatment outcomes. These regressions were conducted with and without covariates of age, sex, and BMI. A 3-stage hierarchical multiple regression was conducted with post-CPAP ESS scores as the dependent variable. Pre-CPAP ESS was entered at Step 1 of the regression to control for possible baseline differences. The covariates age, sex, and BMI were entered at Step 2 because of significant group differences, and group membership was entered at Step 3. Grouping variable 1 (Psychosis and Antipsychotic groups combined into 1 sample coded 1 and OSA-Controls coded 0), and Grouping variable 2 (Psychosis group coded 1, and the Antipsychotic group

and OSA-Controls coded 0) to explore the effects of group on CPAP outcomes.

Ethics Committee Approval

All WASDRI patients provided informed consent. This project received human research ethics committee approval from the Department of Health Data Linkage Branch and the University of Western Australia Research Ethics Committees (RA/4/20/5037; 2016/33 CPI Dr B. Singh).

Results

Baseline Characteristics

The total sample consisted of 554 participants with OSA, with AHI ≥5 and recommended for CPAP. There were 307 OSA-Controls matching all selection criteria. For the psychiatric groups, 458 participants were identified from the linked dataset with a diagnosis of OSA with PSG after 2002, AHI ≥5, and taking antipsychotic medication at the time of PSG. After applying all selection criteria, there were 247 psychiatric patients, comprising 165 diagnosed with a psychotic disorder ("Psychosis" group) and 82 with a psychiatric disorder other than psychosis ("Antipsychotic" comparison group) (figure 1).

Table 1 shows the characteristics of the matched samples. The Psychosis group had a higher BMI compared to Controls ($P < .001$). The Antipsychotic group had a higher female/male ratio compared to the OSA-control ($P = .003$) and Psychosis groups ($P = .04$), and they used more antidepressant and anxiolytic medication than the Psychosis group. OSA-Controls tended to be older than the other groups ($P = .04$). Amongst the Psychosis sample, the most common diagnoses were schizophrenia (45.5%) and bipolar disorder (35.2%). There were more males in those diagnosed with schizophrenia ($P < .001$), but there were no other significant differences between subgroups in age, BMI, and pre-CPAP AHI and ESS scores (see Supplementary Material 1). Characteristics of

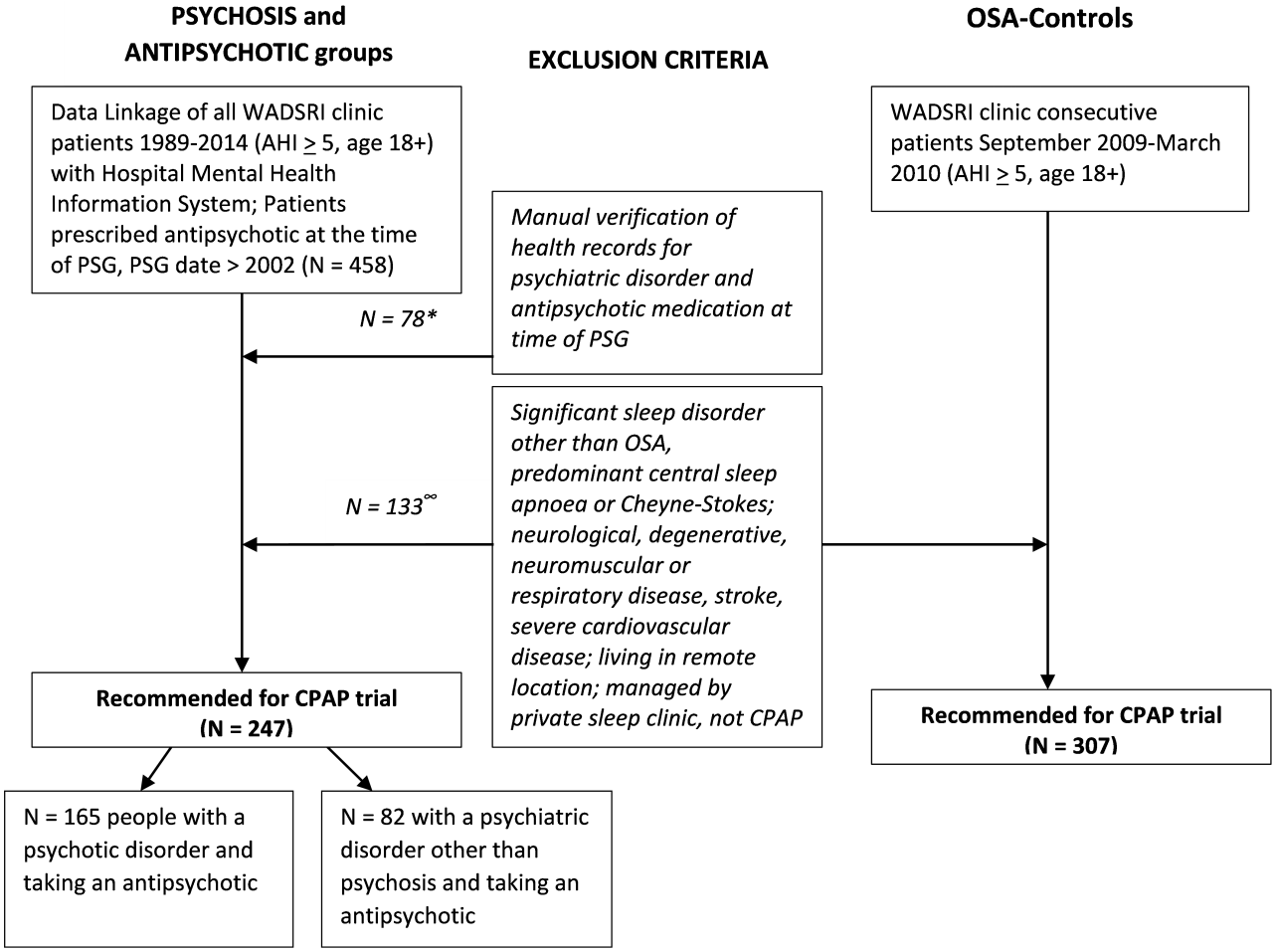

Fig. 1. Flow diagram for the case selection of patients in the Psychosis and Antipsychotic comparison groups. *Excluded ($n = 78$) due to: under 18 years old ($n = 1$), no psychiatric diagnosis ($n = 26$), organic or non-psychiatric disorder ($n = 26$), no details in sleep clinic health records ($n = 25$). °Excluded ($n = 133$) due to: significant other medical disease ($n = 29$); managed by private sleep clinic ($n = 22$); sleep disorder other than OSA ($n = 20$); PSG before 2002 ($n = 28$); rural referral ($n = 3$); CPAP not recommended ($n = 36$) (criteria are not mutually exclusive and may not add to 100%).

Table 1. Characteristics of Patients Diagnosed With OSA and Recommended for CPAP: Pre- and Post-CPAP Measures (Unadjusted Mean + Standard Deviation, Range or Count and Percentages)

	Psychosis (n = 165)	Antipsychotic Comparison (n = 82)	OSA-Controls (n = 307)	Statistical Test
Age (years)	42.9 ± 11.4 (19–81)	46.0 ± 11.9 (19–77)	49.9 ± 13.7 (18–85)	$F(2, 552) = 16.86$, $P < .001$
BMI	37.2 ± 6.9 (22–63)	36.0 ± 8.9 (22–71)	33.7 ± 8.3 (15–71)	$F(2, 550) = 10.80$, $P < .001$
Sex (male %)	100 (60.6%)	39 (47.9%)	199 (64.8%)	$\chi^2 = 8.73$, $P = .01$
Diagnosis				
Schizophrenia	75 (45.5%)	—	—	n/a
Schizoaffective disorder	14 (8.5%)	—	—	n/a
Bipolar disorder with psychotic features	58 (35.2%)	—	—	n/a
Depressive psychosis, other psychosis	18 (10.9%)	—	—	n/a
Medications				
Antipsychotic (oral)	160 (97.0%)	81 (97.6%)	—	$\chi^2 = 0.08$, $P = .78$
Antipsychotic (injection)	9 (5.5%)	0 (0%)	—	$\chi^2 = 4.70$, $P = .03$
Antidepressants/mood stabilizers	120 (72.7%)	71 (85.5%)	—	$\chi^2 = 5.12$, $P = .02$
Anxiolytic/hypnotic/sedatives	45 (20.6%)	38 (33%)	—	$\chi^2 = 4.73$, $P = .03$
Sleep measurements				
PSG SaO_2 <90% (min)	61.3 ± 92.3	48.1 ± 74.2	32.5 ± 63.2	$F(2, 552) = 8.18$, $P < .001$
ESS[a] pre-CPAP scores	10.3 ± 5.8	10.7 ± 6.4	10.5 ± 5.7	$F(2, 542) = 0.12$, $P = .89$
ESS[a] post-CPAP scores	6.0 ± 4.7	6.7 ± 5.3	6.4 ± 4.8	$F(2, 431) = 0.52$, $P = .59$
ESS[a] pre-CPAP % ≥10[a]	53.3%	53.7%	54.1%	$F(2, 295) = 1.74$, $P = .17$
ESS[a] post-CPAP % ≥10	14.5%	19.5%	18.9%	$F(2, 231) = 0.17$, $P = .84$
AHI[b] pre-CPAP	53.5 ± 42.4	43.1 ± 35.9	41.8 ± 27.6	$F(2, 552) = 6.57$, $P < .01$
AHI[b] post-CPAP	7.9 ± 9.7	8.3 ± 16.6	8.0 ± 6.7	$F(2, 437) = 0.02$, $P = .97$

[a]ESS = The Epworth Sleepiness Scale which ranges from 0 to 24 with scores ≥11 or above indicating excessive sleepiness.
[b]AHI = Apnea-Hypopnea Index.

the samples prior to matching showed a similar profile as above (see Supplementary Material 1).

With regards to OSA characteristics at baseline, the Psychosis group had the most severe OSA with significantly higher AHI ($P = .001$) and longer time spent in hypoxemia (29 minutes longer on average, $P < .001$) when compared to OSA-Controls. The difference in hypoxemia remained after adjusting for age, sex and BMI, $F(2, 547) = 4.62$, $P = .010$, $\eta^2 = 0.02$, but AHI differences did not remain after adjustments $F(2, 547) = 2.01$, $P = .135$. There were no significant differences between the Psychosis and Antipsychotic groups in OSA characteristics, and no differences between any groups in ESS scores baseline scores before or after adjustments.

CPAP Trial Characteristics

Both Psychosis and Antipsychotic groups visited the clinic significantly less often than OSA-Controls, before and after adjusting for age, sex and BMI, $F_{adjusted}(2, 490) = 3.26$, $P = .039$, $\eta^2 = 0.01$. However, the groups did not differ on other engagement indicators across the different triage stages. At the initial appointment, there were no significant differences in the proportion of patients who decided not to attend to their OSA diagnosis with CPAP (table 2). For all groups, the most common reason for not proceeding to the next CPAP trial stage was a failure to attend the initial appointment (10.9%, 17.1%, and 7.2% for the Psychosis, Antipsychotic, and OSA-Controls, respectively); amongst those who turned up for the initial trial visit, only a small percentage declined the CPAP offer or cancelled the trial appointment (1.3%, 0%, and 1.8%). Approximately 79% of patients completed a full trial, with all 3 groups showing similar total trial duration (39–40 days).

At the end of the trial, there were no group differences in the proportion of patients who accepted CPAP for long-term use, $\chi^2(2) = 0.56$, $P = .71$; OSA-Controls were significantly more likely to reject CPAP than the other groups ($P = .002$), whereas the Psychosis group was more likely to be undecided ($P = .004$) (post hoc chi-square tests with Bonferroni correction with alpha set at 0.006). The Antipsychotic comparison group did not differ from the other groups.

When acquiring CPAP machines after the trial for long-term use, the Psychosis group was significantly more likely to use public funds (government assistance) compared to the other 2 groups, $\chi^2(6, N = 347) = 58.9$, $P < .001$, while the OSA-control group were more likely to purchase CPAP equipment privately (figure 2). At the 3 month-review, 53% and 44% of the Psychosis and Antipsychotic group who were initially referred (66% and 64% of those who completed the CPAP trial) were still using CPAP, though this difference was not significant, $\chi^2(2, N = 167) = 0.72$, $P = .699$ (table 2).

Table 2. CPAP Trial Visits and Adherence Patients in the Psychosis, Antipsychotic, and OSA-Control Groups Who Were Referred for a CPAP Trial Across Differences CPAP Stages (Unadjusted Mean ± Standard Deviation, Range or Count, and Percentages)

	Psychosis (n = 165[a])	Antipsychotic Comparison (n = 82[a])	OSA-Controls (n = 307[a])	Statistical Test
CPAP visits (n)				
Therapy clinic visits during trial	2.6 ± 1.7	2.6 ± 1.4	2.9 ± 1.3	F = 3.14, P = .04
CPAP trial issue outcome (n)				
Did not attend appointment, declined or ended trial prematurely	32 (19.4%)	23 (28.1%)	62 (20.2%)	χ^2 = 8.26, P = .08
CPAP trial completion outcomes[b]				
Started and completed full CPAP trial (n,%)[c]	133 (80.6%[a])	59 (72.9%[a])	245 (79.8%[a])	χ^2 = 3.47, P = .17
Trial duration (days)	39.7 ± 37.2	40.4 ± 30.7	37.7 ± 28.6	F = 0.31, P = .73
Final nightly CPAP usage (h)	5.7 ± 2.5	6.0 ± 2.4	4.8 ± 2.3	F = 10.24, P < .001
Final CPAP pressure (cmH_2O)	11.8 ± 2.4	11.4 ± 1.6	11.4 ± 1.6	F = 2.02, P = .13
End of trial decision (n, %)				χ^2 = 16.4, P = .02
Accept CPAP for long-term use	105 (78.9%[b])	52 (88.1%[b])	185 (75.5%[b])	
Reject CPAP for long-term use	19 (14.2%[b])	6 (10.2%[b])	56 (22.8%[b])	
Undecided	9 (6.8%[b])	1 (1.7%[b])	4 (1.6%[b])	
CPAP use at 3 months review[d]				P = .002
Continued CPAP use at 3 months (n, %)	88 (53.3%[a], 66.5%[b])	38 (46.3%[a], 64.4%[b])	n/a	

[a]Number of participants referred for a CPAP trial.
[b]Number of participants who started and completed a full CPAP trial.
[c]Total N who started the CPAP trial = 144 (87.2%), 68 (82.9%) and 281 (91.5%) for the Psychosis, Antipsychotic, and OSA-Controls groups, respectively.
[d]Total N who accepted or were undecided end of CPAP trial = 114 and 53 for the Psychosis and Antipsychotic groups, respectively.

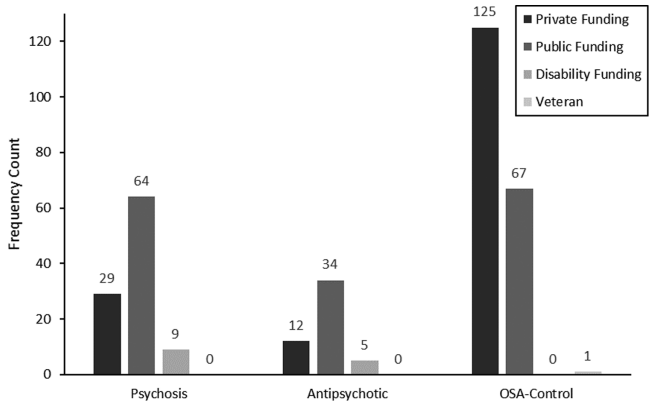

Fig. 2. Funding source for the purchase of a long-term CPAP device (frequency count) (privately funded, public funded, disability benefits, and veteran funding).

CPAP Trial Adherence

Contrary to our hypotheses, the Psychosis and Antipsychotic groups used CPAP for longer at night compared to OSA-Controls (η^2 = 0.05, table 2), with an upper range duration of 13 and 14 h for the Psychosis and Antipsychotic groups respectively, compared to 9 h for OSA-Controls. Among the regression covariates, higher BMI was associated with greater average CPAP usage F(3, 427) = 3.76, P = .011 (table 3), and the results remained significant after adjustments, F(2, 425) = 8.13, P < .001, η^2 = 0.04. Group variable 1 (Psychosis and Antipsychotic groups combined) explained a further 4% variation which was significant, F(2, 425) = 8.14, P < .001, confirming longer duration of CPAP usage at night in these 2 groups compared to OSA-Controls. The effects of other medications as a separate predictor did not explain further variation in average CPAP usage. Finally, there were no significant group differences in end-trial average CPAP Pressure. Male sex and higher BMI both explained 7% of variation in average end of trial CPAP pressure F(3, 376) = 9.80, P < .001, but the other grouping variables (at Step-2) added no additional variability despite age becoming a significant predictor.

CPAP Treatment Effectiveness

All 3 groups showed improvements in AHI levels and daytime sleepiness (ESS) following CPAP therapy (table 3). AHI improved significantly with CPAP treatment, F(1, 438) = 480.91, P < .001, η^2 = 0.52. Baseline pre-CPAP AHI was a significant predictor of post-CPAP AHI scores, F(1, 439) = 13.54, P < .001. The other variables were not significant predictors (group membership F(2, 434) = 0.10, P = .90; age, sex, BMI F(3, 436) = 1.56, P = .19). There were significant reductions in sleepiness (ESS) over time F(1, 427) = 175.95, P < .001, η^2 = 0.29, but no group differences in improvements in sleepiness. Pre-CPAP ESS scores were a significant predictor of post-CPAP scores. After adding sex, age, and BMI into the model, an additional and significant 3.4% of variation in ESS was explained although age was not a significant predictor.

Table 3. Hierarchical Multiple Regression: Post-CPAP (A) End of Trial Average Number of Hours CPAP Use (B) ESS Scores, and (C) AHI Scores

	Step 1			Step 2			Step 3		
	B (SE *B*)	95% CI	*B*	*B* (SE *B*)	95% CI	*β*			
(A) End of trial CPAP use (h)									
Age	−0.01 (0.01)	−0.03 to 0.01	−0.05	−0.00 (0.01)	−0.02 to 0.02	−0.00			
Sex	0.10 (0.26)	−0.40 to 0.60	0.02	0.15 (0.25)	−0.35 to 0.64	0.03			
BMI	0.05 (0.02)	0.02 to 0.08	0.15†	0.04 (0.02)	0.01 to 0.07	0.13‡			
Grouping 1	—	—	—	1.17 (0.34)	0.49 to 1.84	0.24‡			
Grouping 2	—	—	—	−0.32 (0.37)	−1.05 to 0.41	−0.06			
Model statistics R^2		0.03†			0.06‡				
R^2 change		—			0.03				
F change in R^2		3.76			8.14				
	B (SE)	95% CI	*β*	*B* (SE)	95% CI	*β*	*B* (SE *B*)	95% CI	*β*
(B) Post-CPAP ESS scores									
Pre-CPAP ESS	0.40 (0.04)	0.33 to 0.47	0.47‡	0.40 (0.04)	0.33 to 0.47	0.47‡	0.40 (0.04)	0.33 to 0.47	0.47‡
Age	—	—	—	−0.01 (0.02)	−0.04 to 0.02	−0.02	−0.01 (0.02)	−0.04 to 0.03	−0.02
Sex	—	—	—	−1.27 (0.45)	−2.16 to 0.39	−0.13‡	−1.26 (0.45)	−2.15 to 0.37	−0.13‡
BMI	—	—	—	−0.11 (0.03)	−0.17 to −0.06	−0.19‡	−0.11 (0.03)	−0.17 to 0.06	−0.19‡
Grouping 1	—	—	—	—	—	—	0.20 (0.63)	−1.04 to 1.44	0.02
Grouping 2	—	—	—	—	—	—	−0.26 (0.68)	−1.60 to 1.08	−0.02
Model statistics R^2		0.22‡			0.26‡			0.26	
R^2 change		—			0.03			0.00	
F for R^2 change		122.20			6.54			0.07	
	B (SE *B*)	95% CI	*β*	*B* (SE *B*)	95% CI	*β*	*B* (SE *B*)	95% CI	*β*
(C) Post-CPAP AHI scores									
Pre-CPAP AHI	0.05 (0.01)	0.02 to 0.08	0.17‡	0.05 (0.01)	0.02 to 0.08	0.17‡	0.05 (0.01)	0.02 to 0.08	0.18‡
Age	—	—	—	0.07 (0.04)	−0.00 to 0.14	0.09	0.07 (0.04)	−0.01 to 0.14	0.09
Sex	—	—	—	−1.10 (1.02)	−0.91 to 3.11	0.06	−1.12 (1.03)	−0.90 to 3.11	0.06
BMI	—	—	—	0.01 (0.07)	−0.12 to 0.14	0.01	0.01 (0.07)	−0.12 to 0.14	0.01
Grouping 1	—	—	—	—	—	—	0.40 (1.36)	−2.27 to 3.07	0.02
Grouping 2	—	—	—	—	—	—	−0.67 (1.47)	−3.56 to 2.23	−0.03
Model statistics R^2		0.03‡			0.04			0.04	
R^2 change			—		0.01			0.00	
F change in R^2		13.54			1.56			0.10	

Note: 95% CI, 95% confidence interval for *B*; *B*, unstandardized beta; *β*, standardized beta coefficient; SE *B*, standard error of unstandardized beta; Grouping 1 = Psychosis and Antipsychotic groups combined; Grouping 2 = Psychosis group.
†$P < .05$.
‡$P < .01$.

Discussion

This is the first large-scale study reporting on the outcomes of a CPAP trial in people diagnosed with psychosis and the contribution of antipsychotic medication. The results showed that CPAP is feasible and effective in people in this clinical population and that antipsychotic medication is not a barrier to OSA treatment response.

At baseline, the Psychosis group had the most severe OSA disease profile. They spent twice as long (61 vs 32 min) below critical oxygen saturation levels compared to OSA-Controls and had significantly higher AHI scores. Other than small samples or case studies,[27–31] there have been no previous comparisons of the PSG-derived OSA profile of people with psychotic disorders and therefore these results await replication. The findings however confirm a previously reported assessment gap in this group.[19] This suggest that more patients with psychotic disorders might be missed who could benefit from CPAP treatment and that unnecessary delays are incurred before formal referrals are made and which act to prolong the duration of untreated sleep apnea.

The Psychosis group showed few differences from OSA Controls on treatment indicators of CPAP trial engagement and adherence. They attended fewer clinic appointments overall, but both groups had similar CPAP trial acceptance and completion rates. Patients with Psychosis were no less adherent to CPAP compared to controls, and their adaptability to CPAP equipment during the trial extends results shown in mixed groups of patients with mental health disorders.[53,54] These positive findings argue against the notion that apathy, fearfulness, or illness-related factors in psychosis such as symptom severity, lack of insight or cognitive problems get in the way of engaging with and benefiting from treatment.[17,24,26,55]

At the end of the trial, an equivalent proportion of the Psychosis sample accepted CPAP for long-term use compared to Controls (79% vs 75%). Public health funds for CPAP are available to people with disability in Australia and our results demonstrate the successful use of these funds to meet the needs of people disadvantaged because of their mental and physical health problems.

After 3 months, half of the original sample who were referred were still using CPAP, which is a good indicator of probable long-term CPAP use.[56] The only other data available on a schizophrenia sample, although considerably smaller than our sample, is keeping with our findings of similar adherence to CPAP in those with schizophrenia to a control group (36% and 42% device use after 1 and 3 years)[57] signifying a need for research to find solutions to sustain adherence post CPAP trial completion.

Our findings show that both Psychosis and Antipsychotic groups had significantly longer average nightly CPAP use compared to OSA-Controls. Given that both groups were taking antipsychotic medication, it is possible that the sedative effects of antipsychotics facilitated CPAP tolerance and overnight compliance. In support, studies show that antipsychotic use can assist with sleep difficulties by producing sedation[58] and that sedative medication can increase long-term CPAP adherence.[59] Our regression analyses showed a non-significant role of antidepressants and hypnotics, although it is possible that dosage or interaction with the antipsychotics contributed in a way which we could not examine. In any case, the role of antipsychotic medication towards CPAP adherence is a new finding which deserves further investigation. Its role in producing higher AHI also needs to be investigated.

Another important and unexpected finding was that CPAP treatment response was as favorable in people with severe mental illness as for other OSA patients. Despite greater severe OSA severity at baseline, the Psychosis group showed OSA symptomatic relief after CPAP, as indicated by significant reductions in AHI and ESS scores, which did not differ from OSA-Controls. This demonstrates that people with OSA and psychotic or psychiatric disorders taking antipsychotic medication are well controlled and gain significant symptom benefit from CPAP. Further research is now needed to examine whether CPAP can contribute to reductions in other symptoms such as sleep disruption, cognitive performance, functional deficits, quality of life, weight, and other cardiometabolic risk factors.[19]

A limitation of this study includes the use of linked data for mental health diagnosis and medication information. While this was the most reliable way of selecting sleep clinic patients with a psychiatric diagnosis, those who were not in contact with public health services are not represented. Furthermore, psychiatric diagnoses were extracted from medical records and referral letters and were not independently verified, and this did not allow for an examination of CPAP treatment effects on psychiatric symptoms.[27–31]

Another limitation included data comparison from the point of CPAP referral onwards instead of sleep study referral. This was necessary to assist with the case-selection matching process with the OSA-Controls whose data had already been extracted and who were representative of the average characteristics of clinic patients in this and other sleep clinic cohorts.[12,53] This process however limited our ability to make accurate comparisons from the point of referral about overall attrition and adherence and there remains an important gap in knowledge about the patients' service journey prior to CPAP referral. Finally, baseline AHI scores were extracted from PSG readings, whereas end of trial AHI scores was extracted from the CPAP device download. However, CPAP device-estimated AHI is widely used to assess control of OSA from CPAP and is performs similar to PSG AHI in predicting important clinical outcomes from treatment trials.[49]

In summary, this research highlighted the potentially large benefit from referrals for OSA and gives an

encouraging depiction of adherence and symptomatic relief in people with chronic and severe psychiatric disorders. A lack of awareness of sleep apnea in mental health settings has previously been noted.[19] More systematic screening for OSA symptoms,[60] referrals to sleep clinics and more coordinated care pathways will assist in removing obstacles to obtaining the right medical care and hopefully will give clinicians confidence in making clinical management decisions involving CPAP referrals. Further studies should document the personal experience and care pathways that people with mental health issues face when their OSA symptom are first identified with a view to removing barriers to receiving the correct diagnosis and treatment.

Supplementary Material

Supplementary material is available at *Schizophrenia Bulletin* online.

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