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Cohort profile: The Western Australian Sleep health study, a prospective sleep clinic cohort study

Bindiya Shenoy[a,b], Bhajan Singh[a,b], Satvinder S Dhaliwal[c,d], Stuart King[a], Siobhan C Rea[a], Ivan T Ling[a], Peter R Eastwood[e], David R Hillman[a,b], Sutapa Mukherjee[f], Lyle J Palmer[g], Nigel McArdle[a,b,*]

[a] West Australian Sleep Disorders Research Institute, Department of Pulmonary Physiology and Sleep Medicine, Sir Charles Gairdner Hospital, Perth, Australia
[b] Centre for Sleep Science, School of Human Sciences, University of Western Australia, Perth, Australia
[c] Curtin Health Innovation Research Institute, Faculty of Health Sciences, Curtin University, Perth, Australia
[d] Duke-NUS Medical School, National University of Singapore, Singapore
[e] Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Adelaide, Australia
[f] Adelaide Institute for Sleep Health, Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Adelaide, Australia
[g] School of Public Health, University of Adelaide, Adelaide, Australia

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AASM, American Academy of Sleep Medicine
AHI, apnoea-hypopnoea index
ArI, arousal index
BMI, body mass index
CAI, central apnoea index
CPAP, continuous positive airway pressure
CSA, central sleep apnoea
CVD, cardiovascular disease
DEXA, dual energy X-ray absorptiometry
ESS, Epworth sleepiness score
ODI3%, oxygen desaturation index of 3%
OSA, obstructive sleep apnoea
PLMSI, periodic leg movements in sleep index
PSG, polysomnography
SEIFA, Socio-Economic Index for Areas
SpO2, oxygen saturation
TST, total sleep time
T90, study recording time spent with SpO2<90%
WADLS, Western Australian Data Linkage System
WASDRI, West Australian Sleep Disorders Research Institute
WASHS, Western Australian Sleep Health Study

ABSTRACT

Genetic and epidemiologic investigations into obstructive sleep apnoea (OSA) have been limited by a scarcity of sizeable well-characterised sleep clinic cohorts with laboratory-based polysomnography (PSG). This profile reports the characteristics of a prospective clinic cohort study exploring the genotypic and phenotypic features of OSA with ongoing patient follow-up to assess long-term health outcomes. The Western Australian Sleep Health Study (WASHS) recruited patients at a large tertiary hospital sleep clinic in Perth, Australia. Between 2006 and 2010, 5948 consecutive new adult patients attended the clinic and 4914 were eligible to participate following consent and screening. Among eligible patients, 98.5% (n = 4839) had diagnostic PSG available, and 86.0% (n = 4226) were comprehensively phenotyped by clinical questionnaire and anthropometric measurements. Among those comprehensively phenotyped, blood biospecimens for biochemistry and DNA were obtained in 2759 (65.2%), and linked health administrative data was requested in 2017 for 4067 patients (96.2%). The group of most interest, the comprehensively phenotyped patients (n = 4226), were predominantly male (60.6%), middle-aged (mean±SD: 50.5 ± 14.0 years), and obese (32.7 ± 7.7 kg/m^2). The majority of this group were diagnosed with OSA (93.8%). The WASHS Prospective Sleep Clinic Cohort is amongst the largest OSA cohorts globally with PSG and long-term morbidity and mortality data. Comprehensive phenotype and genotype data have contributed to numerous publications on the epidemiology and genetics of OSA. Patients have been monitored by ongoing clinic review, where OSA treatment data is collected, and by follow-up studies, such as an Australian National Health and Medical Research Council funded project (2018–2021) investigating cardiovascular outcomes in OSA.

* Corresponding author at: West Australian Sleep Disorders Research Institute, Department of Pulmonary Physiology and Sleep Medicine, Sir Charles Gairdner Hospital, Nedlands, WA 6009, Australia.
E-mail address: Nigel.McArdle@health.wa.gov.au (N. McArdle).

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1. How did the study come about?

The Western Australian Sleep Health Study (WASHS) Prospective Sleep Clinic Cohort is a study of obstructive sleep apnoea (OSA) patients who attended the West Australian Sleep Disorders Research Institute (WASDRI). The primary objective of this study is to investigate OSA and its associated health consequences.

OSA is characterised by recurrent collapse of the pharyngeal airway during sleep, causing intermittent reduction or cessation in airflow (i.e. a hypopnoea or apnoea event, respectively). The gold-standard diagnostic tool for OSA is an in-laboratory attended overnight sleep study known as polysomnography (PSG). The primary PSG metric used to define OSA severity is the apnoea-hypopnoea index (AHI), a measure of the number of obstructive breathing events per hour of sleep. In adults, an AHI of ≥5 events/hour is required to diagnose OSA.

OSA is a complex heterogeneous disorder with variations in its pathogenesis and symptom manifestation. Immediate physiological consequences of OSA include sleep fragmentation, intermittent hypoxaemia and hypercapnia, large negative intrathoracic pressure swings, and increases in sympathetic nervous system activity [1, 2].

Clinical features of OSA include excessive daytime sleepiness, snoring, witnessed apnoeas, waking unrefreshed, cognitive impairment, and diminished mood and quality of life. Long-term sequelae associated with untreated OSA include metabolic, neurocognitive, and cardiovascular disorders such as hypertension[3], coronary disease[4], stroke [5, 6], and heart failure[7]. Continuous positive airway pressure (CPAP) therapy, which provides a low positive pressure of air to the pharyngeal airway and acts as a pneumatic splint to maintain airway patency, is the most efficacious treatment for OSA [8, 9].

The global prevalence of OSA is high. Although estimates vary due to differences in methodology and diagnostic criteria, a recent study estimated that 936 million individuals (aged 30–69 years) globally have OSA, based on the current (American Academy of Sleep Medicine [AASM] $_{2012}$) scoring criteria[10]. Due to its prevalence and adverse long-term outcomes, OSA represents a major burden with an estimated total economic cost of $18.9 billion in Australia in 2019–2020[11].

Population-based epidemiological investigations have sought to objectively evaluate OSA and its associated outcomes in recent decades. However, at the time the WASHS protocol was developed in 2005, there was, and remains today, a paucity of sizeable well-characterised sleep clinic cohorts with in-laboratory PSG. Further, there is considerable uncertainty regarding the underlying genetic basis for OSA and its associated consequences.

WASHS was designed as a large extensively phenotyped OSA cohort with PSG by researchers (D.R.H., L.J.P., and S.M.) at WASDRI, in collaboration with Sir Charles Gairdner Hospital and the University of Western Australia. Since its establishment in 1988, in partnership with Sir Charles Gairdner Hospital, WASDRI has operated the largest public sleep clinic in Western Australia. The majority of patients are referred for suspected OSA and subsequently complete an in-laboratory diagnostic PSG.

The objective of WASHS was to assess the clinical and genetic epidemiology of OSA and investigate its long-term sequelae by prospectively phenotyping over 4000 consecutive new patients attending the clinic. This cohort profile is an update of a previous interim report detailing this cohort and related research projects, which was published in 2012 prior to completion of data collection[12]. It provides a detailed report of the developments in the WASHS Prospective Sleep Clinic Cohort study in the last decade.

2. Who is in the cohort?

The WASHS Prospective Sleep Clinic Cohort is comprised of patients referred to WASDRI for a possible sleep disorder. These referrals were from the main metropolitan centre of Perth, as well as rural and regional areas in Western Australia. In 2006, Western Australia had an adult population of 1477,239 (49.3% males) with a mean (±SD) age of 45.7 ± 17.6 years, predominantly of European-Australian ancestry (82.6%)[13]; the mean adult BMI, as reported in the 2011–12 Australian National Health Survey, was 27.7 kg/m^2[14].

Consecutive new adult patients attending the clinic during the study period were asked to consent to the use of their clinical data for research purposes. Consenting patients were ruled out for participation if they did not undertake a diagnostic PSG at WASDRI during the study period (Fig. 1). Those with neuromuscular diseases likely to impair respiratory function were not considered to be representative of typical OSA patients and were considered ineligible for the study. Following screening, 4914 patients were eligible for the WASHS cohort.

Key socio-demographic and PSG variables for eligible patients are presented in Tables 1 and 2, respectively. Patients eligible for the WASHS cohort (n = 4914) were predominantly male, middle-aged, and obese (≥30 kg/m^2) (Table 1) – a profile typical of sleep clinics in other developed countries. The Socio-Economic Index for Areas (SEIFA), a measure constructed by the Australian Bureau of Statistics using population census data, provides an index ranging from 0 to 10 units of the relative socio-economic advantage and disadvantage of a specific postal area[15]. Eligible patients had a mean SEIFA index score of 6.7 units, indicating a moderately high level of socio-economic advantage compared to other regions in Australia. These patients had, on average, severe OSA (AHI ≥30 events/hour), with severely fragmented sleep and moderately severe hypoxemic burden. amongst eligible patients, those with sub-optimal sleep measures (i.e. a total sleep time of fewer than 120 min on a full-night PSG) or incomplete PSG records were excluded from further analysis (n = 75). The remainder (n = 4839) constitute the WASHS baseline cohort (Fig. 1).

The baseline cohort was further separated into two sub-groups – patients with only PSG data available (n = 613) and others with PSG and comprehensive phenotypic data (including clinical questionnaire and anthropometric measurements) (n = 4226). The latter sub-group of the baseline cohort, the comprehensive cohort, is the particular cohort of most utility within the WASHS, as they have detailed information about their OSA, sleep behaviours, lifestyle risk factors, and co-morbidities.

Within the comprehensive cohort, in addition to the collection of clinical data, patients were also separately consented for the collection of blood-derived data (i.e. biochemistry and DNA/serum) and the storage of blood samples (for prospective analysis). Serum biochemistry is available in 2759 patients within the comprehensive cohort who completed these requirements.

Linked health administrative data is also available in a subset of the comprehensive cohort. The Western Australian Data Linkage System (WADLS) provides access to high-quality population-based health administrative datasets within Western Australia[16]. Records of 4067 patients in the comprehensive cohort were sent for linkage.

3. Representativeness of the cohort

The objective of the WASHS is to investigate the epidemiology of OSA and associated long-term outcomes in a clinically representative cohort of OSA patients. Therefore, it is important to assess the representativeness of the WASHS study cohorts in relation to all eligible clinic patients and determine the presence of any selection biases. Recruitment rate to the WASHS baseline cohort was high with 98.5% of all eligible patients recruited to and included in the cohort. We assessed representativeness of the cohorts using key demographic and PSG data available on all eligible WASDRI patients, as discussed below.

Firstly, to assess the representativeness of the WASHS baseline cohort (n = 4839) to all eligible patients (n = 4914), we compared the former group with eligible patients who were excluded (n = 75) (Table A.1). An independent samples t-test indicates that the group of excluded patients were, on average, four years older than the baseline cohort; however, this small difference, while statistically significant, is unlikely to be clinically meaningful. As the excluded group were defined on the

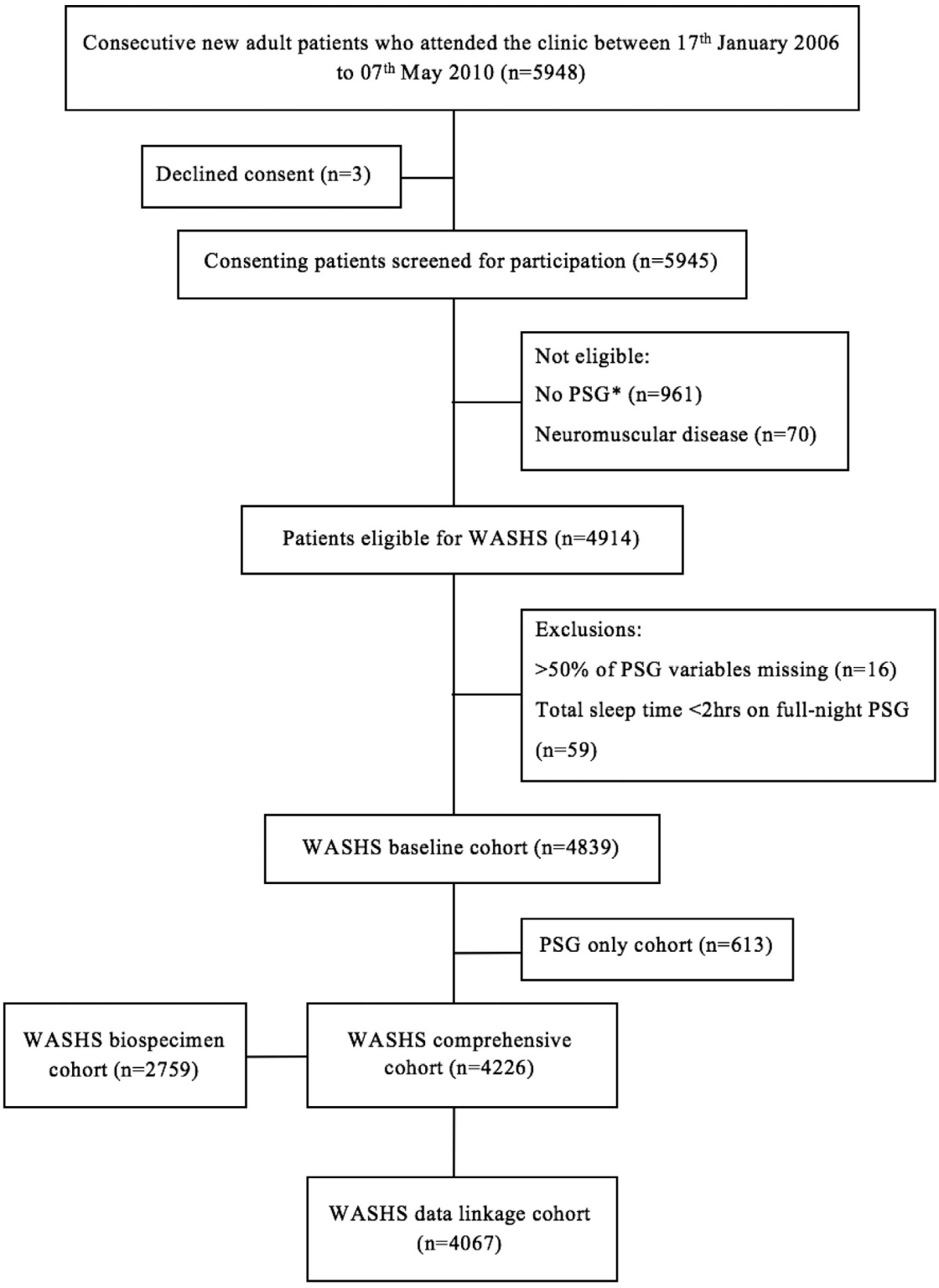

Fig. 1. Flow diagram of recruitment into the WASHS Prospective Sleep Clinic Cohort.
*Patients may not have undertaken a diagnostic PSG at the clinic for various reasons, including: the physician did not recommend a diagnostic PSG, booked in for a PSG at the clinic but declined or cancelled the appointment, PSG appointment was postponed to a period following the completion of the WASHS, or completed a diagnostic PSG through another sleep laboratory.

Table 1
Demographic characteristics of all eligible patients and the WASHS cohort sub-groups.

Characteristic*	Eligible for WASHS (*n* = 4914)	WASHS baseline cohort (*n* = 4839)	WASHS comprehensive cohort (*n* = 4226)	WASHS biospecimen cohort (*n* = 2759)	WASHS data linkage cohort (*n* = 4067)
Age, years	50.5 ± 14.1	50.4 ± 14.0	50.5 ± 14.0	51.3 ± 13.5	50.6 ± 14.0
Sex, male	2991 (60.9)	2943 (60.8)	2561 (60.6)	1660 (60.1)	2472 (60.8)
BMI, kg/m^2	32.8 ± 7.8 *(missing=57)*	32.8 ± 7.7 *(missing=40)*	32.7 ± 7.7 *(missing=31)*	32.6 ± 7.6 *(missing=17)*	32.7 ± 7.7 *(missing=28)*
SEIFA, units	6.7 ± 2.6 *(missing=57)*	6.7 ± 2.6 *(missing=57)*	6.7 ± 2.6 *(missing=46)*	6.7 ± 2.6 *(missing=26)*	6.7 ± 2.6 *(missing=44)*
Post-Secondary Education	—	—	1639 (38.8)	1074 (38.9)	1565 (38.3)
Employment, full-time	—	—	1726 (40.8) *(missing=12)*	1104 (40.0) *(missing=6)*	1669 (40.9) *(missing=12)*
Marital Status, married	—	—	2672 (63.0) *(missing=13)*	1763 (63.8) *(missing=7)*	2566 (62.9) *(missing=13)*
Ethnicity**, European-Australian	—	—	3825 (90.5)	2514 (91.1)	3685 (90.6)

*Data are presented as mean ± SD or n (%).
**Definition of ethnicity (European-Australian) – reporting a family ancestry of at least one parent who identifies as European-Australian. Note: details on post-secondary education, employment status, marital status, and ethnicity are only available in patients within the comprehensive cohort and its sub-cohorts as they completed the WASHS clinical questionnaire.

Table 2
Diagnostic polysomnography variables across all eligible patients and the WASHS cohort sub-groups.

Characteristic (mean ± SD)	Eligible for WASHS (*n* = 4914)	WASHS baseline cohort (*n* = 4839)	WASHS comprehensive cohort (*n* = 4226)	WASHS biospecimen cohort (*n* = 2759)	WASHS data linkage cohort (*n* = 4067)
TST, mins	340.0 ± 98.6 *(missing=16)*	343.4 ± 94.4	345.6 ± 92.1	347.5 ± 89.9	344.5 ± 90.7
Sleep efficiency,%	73.3 ± 15.1 *(missing=15)*	73.9 ± 14.1	74.0 ± 14.0	73.9 ± 13.9	74.0 ± 13.8
Sleep latency, mins	24.8 ± 32.1 *(missing=20)*	24.1 ± 29.8	23.9 ± 29.2	24.5 ± 29.9	23.7 ± 28.7
AHI, events/hour	36.6 ± 31.1 *(missing=17)*	36.4 ± 30.9	36.0 ± 30.3	35.6 ± 29.7	35.9 ± 30.3
CAI, events/hour	0.6 ± 3.5 *(missing=19)*	0.6 ± 3.5	0.6 ± 3.0	0.6 ± 3.0	0.6 ± 3.1
ArI, events/hour	39.2 ± 25.0 *(missing=18)*	39.0 ± 24.7	38.6 ± 24.1	38.4 ± 23.3	38.6 ± 24.1
PLMSI, events/hour	5.0 ± 14.0 *(missing=19)*	5.0 ± 14.0	4.9 ± 13.6	5.3 ± 14.5	5.0 ± 13.6
T90, mins	25.6 ± 58.5 *(missing=28)*	25.6 ± 58.5 *(missing=27)*	24.8 ± 57.0 *(missing=8)*	23.8 ± 55.3 *(missing=5)*	24.6 ± 56.4 *(missing=4)*
ODI3%, events/hour	26.9 ± 27.1 *(missing=64)*	26.8 ± 27.1 *(missing=47)*	26.1 ± 26.0 *(missing=15)*	25.9 ± 25.7 *(missing=10)*	26.0 ± 26.0 *(missing=7)*

TST, total sleep time; AHI, apnoea-hypopnoea index; CAI, central apnoea index; ArI, arousal index; PLMSI, periodic leg movements in sleep index; T90, recording time spent with oxygen saturation below 90%; ODI3%, oxygen desaturation index of ≥3%.

Table 3
Demographic and polysomnographic characteristics of the comprehensive cohort (*n* = 4226) as compared with all other eligible patients (*n* = 688) in the WASHS cohort.

Characteristic*	WASHS comprehensive cohort (*n* = 4226)	All other eligible patients (*n* = 688)	P-value	Mean difference**	95% CI of the difference
Age, years	50.5 ± 14.0	50.5 ± 14.7	0.943	−0.041	−1.175, 1.093
Sex,% male	2561 (60.6)	430 (62.5)	0.341	−0.019	−0.058, 0.020
BMI, kg/m^2	32.7 ± 7.7 *(missing=31)*	33.3 ± 8.2 *(missing=26)*	0.122	0.526	−0.140, 1.193
SEIFA, units	6.7 ± 2.6 *(missing=46)*	6.8 ± 2.7 *(missing=11)*	0.557	0.064	−0.148, 0.275
TST, mins	345.6 ± 92.1	305.4 ± 127.0 *(missing=16)*	**< 0.001**	−40.184	−50.197, −30.172
Sleep efficiency,%	74.0 ± 14.0	69.0 ± 20.2 *(missing=15)*	**< 0.001**	−4.965	−6.550, −3.379
Sleep latency, mins	23.9 ± 29.2	30.5 ± 46.1 *(missing=20)*	**< 0.001**	6.583	2.973, 10.192
AHI, events/hour	36.0 ± 30.3	40.6 ± 35.5 *(missing=17)*	**0.001**	4.677	1.838, 7.517
CAI, events/hour	0.6 ± 3.0	0.9 ± 5.8 *(missing=19)*	0.192	0.227	−0.149, 0.744
ArI, events/hour	38.6 ± 24.1	43.1 ± 29.8 *(missing=18)*	**< 0.001**	4.499	2.128, 6.871
PLMSI, events/hour	4.9 ± 13.6	5.7 ± 16.6 *(missing=19)*	0.267	0.749	−0.575, 2.072
T90, mins	24.8 ± 57.0 *(missing=8)*	31.0 ± 67.4 *(missing=20)*	**0.022**	6.300	0.899, 11.700
ODI3%, events/hour	26.1 ± 26.0 *(missing=15)*	32.1 ± 33.3 *(missing=49)*	**< 0.001**	6.038	3.337, 8.740

*Data are presented as mean ± SD or n (%).
**The effect sizes – TST (0.362), sleep efficiency (0.288), sleep latency (0.171), AHI (0.139), ArI (0.166), T90 (0.099), and ODI3% (0.201).

basis of incomplete PSG data or sub-optimal sleep on a full-night PSG, there were expected differences in PSG indices.

The study cohort of most interest for future analysis is the comprehensive cohort (*n* = 4226). As shown in Table 3, there were no important demographic differences between this cohort and all other eligible patients for WASHS (*n* = 688, comprised of the PSG only cohort [*n* = 613] and excluded patients [*n* = 75]). Other eligible patients had a lower sleep time and sleep efficiency, and greater sleep latency, AHI, ArI, T90, and ODI3% compared to the comprehensive cohort. Although statistically significant, these differences are small, as reflected in the effect sizes, and are unlikely to be clinically important. Comparisons between the WASHS comprehensive cohort and the PSG only cohort (*n* = 613) showed similar findings and data (Table A.2). Hence, the comprehensive cohort are similar on demographic and PSG characteristics to all other patients who were eligible to participate in WASHS.

Overall, these data indicate that the WASHS baseline and the comprehensive cohorts are closely representative of consecutive eligible clinic patients attending WASDRI between 2006 and 2010. Furthermore, it is evident that sub-groups of the comprehensive cohort (i.e. those with biospecimens and linked health data) are very similar to the overall comprehensive cohort with respect to key socio-demographic and PSG characteristics (Tables 1 and 2).

4. What has been measured?

A wide range of clinically relevant phenotypic measures were obtained in the comprehensive cohort; Table 4 summarises some examples of the available phenotypic information.

Consenting patients were asked to complete a detailed clinical questionnaire prior to or at their first clinic appointment with a sleep

Table 4
Key characteristics of the comprehensive cohort according to sex (n = 4226).

Key characteristics	N (%)		Missing, total N (%)
	Male (n = 2561)	**Female (n = 1665)**	
Age group, years			—
18–29	184 (7.2)	139 (8.3)	—
30–44	723 (28.2)	399 (24.0)	—
45–64	1206 (47.1)	834 (50.1)	—
65+	448 (17.5)	293 (17.6)	—
BMI, kg/m^2			—
Underweight: BMI <18.5	26 (1.0)	19 (1.1)	—
Normal: 18.5≤BMI<25.0	243 (9.5)	237 (14.2)	—
Overweight: 25.0≤BMI<30.0	834 (32.6)	374 (22.5)	—
Obese: BMI ≥30.0	1458 (56.9)	1035 (62.2)	—
Snoring, yes	2441 (95.3)	1511 (90.8)	—
ESS total (0–24), units			7 (0.17)
Normal: ESS <11	1426 (55.7)	953 (57.2)	—
Excessively Sleepy: 11≤ESS<16	693 (27.1)	436 (26.2)	—
Severely sleepy: ESS≥16	438 (17.1)	273 (16.4)	—
OSA, severity			—
No OSA: AHI <5	94 (3.7)	168 (10.1)	—
Mild: 5≤AHI<15	428 (16.7)	487 (29.2)	—
Moderate: 15≤AHI≤30	686 (26.8)	460 (27.6)	—
Severe: AHI>30	1353 (52.8)	550 (33.0)	—
Smoking status, self-reported			15 (0.35)
Current	564 (22.0)	329 (19.8)	—
Ex-smoker	1046 (40.8)	506 (30.4)	—
Never	942 (36.8)	824 (49.5)	—
Depression doctor-diagnosed, self-reported	851(33.2)	882 (53.0)	16 (0.38)
Diabetes doctor-diagnosed, self-reported	420 (16.4)	333 (20.0)	12 (0.28)
Myocardial infarction doctor-diagnosed, self-reported	152 (5.9)	37 (2.2)	19 (0.45)
Lung disease doctor-diagnosed, self-reported	297 (11.6)	347 (20.8)	—

physician. The questionnaire collected information on various characteristics, including socio-demographic variables, lifestyle factors, sleep behaviours and sleep disorder symptoms, Epworth Sleepiness Score (ESS) [17], smoking and alcohol consumption, and doctor-diagnosed medical conditions (see Appendix B). All questionnaires were completed within six-months of the PSG.

During the initial outpatient appointment, a manual measurement of blood pressure was completed using calibrated devices. Anthropometric measurements predictive of OSA were also obtained; these included neck circumference (measured at the level of the cricoid cartilage) and oropharyngeal-related assessments such as Mallampati score[18] and pharyngeal grade[19].

During this appointment with a sleep physician, WASHS patients were consented for blood specimen collection and storage and provided a referral to a pathology laboratory for a blood draw. Biochemical assessments included serum lipids, C-reactive protein, fibrinogen, glucose, insulin, and thyroid function. Fasting samples were requested but fasting status could not be verified. DNA, serum, and plasma were extracted and stored at −80C in the Western Australian DNA Bank (Perth, Australia) for future analyses. A whole genome scan using the Illumina Quad chip was undertaken on 2318 patients in the WASHS comprehensive cohort.

All patients within the comprehensive cohort completed a diagnostic in-laboratory attended PSG, at which measurements of height (stadiometer) and weight (calibrated scales) were collected and BMI was calculated (kg/m^2). Standard placement of PSG sensors was completed by trained sleep scientists. Electroencephalographic information was collected according to AASM guidelines[20]. Respiratory airflow was monitored using nasal pressure cannulae and an oronasal thermistor, and inductance plethysmography was used to assess respiratory effort. Pulse oximetry was used to measure peripheral arterial oxygen saturation. Snoring was detected and quantified using a sound level metre. Body position was monitored using a mercury switch positioned at chest level. Additional measurements of blood pressure were completed by the sleep scientist at the patient's bedside in the evening before and the morning after sleep.

PSG data was acquired digitally using the PSG Series E (Compumedics, Melbourne, Australia). All PSGs were scored by sleep scientists according to the AASM 'Chicago' scoring criteria[20], and all reports were reviewed, interpreted, and reported on by sleep physicians. Oxygen saturation (SpO_2) data were calculated using a proprietary script developed at WASDRI, which measured SpO_2 variables during the total recording time of the PSG.

The majority of patients in the comprehensive cohort (n = 3964, 93.8%) were diagnosed with OSA (AHI ≥5 events/hour). CPAP use data analysed in the WASHS data linkage cohort (n = 4067) shows that 51.7% (n = 2101) completed the first week of a therapy clinic trial at WASDRI; CPAP device downloads from this first week show an average nightly use of 4.6 ± 2.6 h. Many of the patients who accepted CPAP therapy at the conclusion of their trial have continued to be monitored at WASDRI with semi-regular follow-up assessments made by sleep physicians and scientists.

A proportion of patients in the comprehensive cohort (n = 4124, 97.6%) also completed spirometry within a year of their diagnostic PSG, measured before and after bronchodilator by trained respiratory technicians according to standard guidelines[21].

In the initial study period, a subset of recruited WASHS patients (n = 96) completed a measurement of regional body fat distribution using a full-body dual energy X-ray absorptiometry (DEXA) scan (GE Lunar Prodigy, Waltham, MA). The DEXA scan was completed within four weeks of the diagnostic PSG, and measurements included the percentage of fat and lean tissue as well as bone density.

Linked health administrative data from the WADLS provides details on long-term health outcomes in the WASHS cohort. Available information includes state-wide hospital separations, cancer diagnoses, utilisation of mental health services, motor vehicle insurance data, and mortality. The WADLS has contributed to significant research output since its establishment and is an important resource to support longitudinal studies[22].

A data quality assurance check has been completed to assess whether the WASHS database accurately reflects the original source data. Vari-

ables reviewed included age, sex, BMI, neck circumference, AHI, total ESS, snoring status, smoking status, diagnosis of myocardial infarction, and employment status. A random sample of 221 patients (5.2%), without missing values across any of the listed variables, was selected from the database. An independent researcher then recorded values for all listed variables from the source data, blind to the database values. Acceptable agreement between the source data and the WASHS database for continuous variables was defined as a threshold of ±1 unit, e.g. age within 1 year and AHI within 1 event/hour, to allow for rounding errors. Based on this random sample, the mean non-agreement rate within the WASHS database was 0.32% (Table A.3).

5. What has been found? key findings and publications

The WASHS study data has contributed to numerous publications related to OSA in the last decade. Genomic data collected from the WASHS cohort has contributed to various analyses[23–34]. Genome-wide association analyses have also been used to explore the genetic basis of OSA, including the identification of the RAI1 gene as a probable quantitative trait locus for OSA in men[35] and the various single-nucleotide polymorphisms, associated with inflammation, that may play a role in susceptibility to OSA[36].

WASHS data has contributed to various explorations of novel aspects of the OSA phenotype. By assessing physical activity as a modifiable risk factor for OSA and its symptoms, increased levels of occupational activity and physical exercise were found to be linked to a decreased risk of moderate-severe OSA[37]. With regards to obesity and OSA, centrally located fat distribution was found to be associated with OSA in both men and women in the WASHS cohort; in particular, neck fat was more closely associated with OSA severity in women whereas abdominal fat deposition played a greater role in men[38].

In a subset of recruited patients (n = 222) that completed the patient health questionnaire (PHQ-9) to assess depressive symptoms, it was found that these symptoms are highly prevalent in patients referred for suspicion of OSA and appear to be independently associated with OSA severity; depressive symptoms were effectively improved by CPAP treatment in both men and women[39].

The consequences of cognitive impairments associated with OSA, such as excessive daytime sleepiness, have also been examined. Data from WASHS indicates that patients with untreated OSA experience a high risk of motor vehicle accidents; in particular, those with increased daytime sleepiness, irrespective of OSA severity, are at highest risk of near-misses and crashes[40].

The WASHS cohort continues to be an important resource for ongoing research into OSA and its comorbidities. Currently, a National Health and Medical Research Council of Australia funded project is underway to investigate the relationship between OSA and cardiovascular disease (CVD) in the WASHS cohort (The interaction between obstructive sleep apnoea and cardiovascular risk factors on cardiovascular disease. Project grant: APP1145970).

This project, the West Australian cardioVascular Endpoints in obstructive Sleep apnoea or WAVES study, aims to assess the interaction between OSA-related physiological derangements in sleep and coexisting risk factors on the development of CVD in the WASHS Prospective Sleep Clinic Cohort. This longitudinal follow-up of living, consenting WASHS comprehensive cohort patients, includes follow-up clinical questionnaires, OSA treatment data, and further measurement of sleep and health parameters.

6. What are the main strengths and weaknesses?

The WASHS is one of the largest OSA clinic cohort studies globally with comprehensive phenotypic data, including in-laboratory diagnostic PSG. A major strength of the cohort is its high recruitment rate, with 86.0% of eligible patients providing comprehensive phenotypic information. As a result, the study sample is highly representative of typical (non-neuromuscular disease) sleep patients referred to the clinic who subsequently undertook diagnostic PSG. A further strength is the genotyping data available in a large proportion of the cohort, which can be used to investigate the genetic determinants of OSA and its associated comorbidities.

WASHS is unique among sleep clinic cohorts due to the long follow-up with comprehensive measures of morbidity and mortality. Western Australia has low migration rates and a highly stable population, which provides ideal conditions to conduct epidemiological research[16]. Patients are predominantly from the metropolitan area of Perth; however, as WASDRI is the primary public sleep clinic serving the state of Western Australia, many rural patients are referred to this clinic and continue to be represented in this cohort.

WASDRI actively follows up all attending patients and provides ongoing clinical review, including collection of treatment data. Another key strength of the study is the ability to undertake a large scale follow-up of the cohort, as evidenced by the current Australian National Health and Medical Research Council funded follow-up focusing on CVD outcomes.

The WASHS cohort comprises a predominantly European-Australian ancestry population, which means the study cannot be readily generalised to other ethnic groups. Other weaknesses include potential recall errors in the self-reported data and an inadvertent omission to request data linkage in a small number of the cohort (n = 159). However, this group were demographically similar to those who were sent for linkage (n = 4067), without evidence of systematic bias (Table A.4).

A strength of this study is the use of the same scoring criteria (AASM 'Chicago') consistently throughout the study period. However, scoring criteria have changed over time since the WASHS, which may make it difficult to compare our findings directly with later studies or to apply our findings in clinical settings where the current ($AASM_{2012}$) scoring criteria are used. In particular, the changes in rules for scoring hypopnoeas has been shown to significantly affect the AHI and the measured prevalence of OSA[41]. In comparison to the $AASM_{2007}$ and $AASM_{2012}$ diagnostic criteria, the 'Chicago' criteria results in a higher and similar prevalence estimate for OSA, respectively [41, 42].

Patients with predominant central sleep apnoea (CSA) were not excluded from this cohort; however, using criteria of central apnoea index (CAI) >5 events/hour and a CAI >50% of the obstructive apnoea index, 1.6% of the comprehensive cohort met criteria for predominant CSA. Disordered central control of breathing can be present in OSA, particularly in those with severe disease; hence, patients with predominant CSA pathophysiology were retained in the cohort.

Declarations of interest

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.sleepe.2021.100010.

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