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RESEARCH ARTICLE

# Isolated rapid eye movement sleep behaviour disorder (iRBD) in the Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study: protocol and baseline characteristics

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## Summary

Isolated rapid eye movement (REM) sleep behaviour disorder (iRBD) is a sleep disorder that is characterised by dream enactment episodes during REM sleep. It is the strongest known predictor of α-synuclein-related neurodegenerative disease (αNDD), such that >80% of people with iRBD will eventually develop Parkinson's disease, dementia with Lewy bodies, or multiple system atrophy in later life. More research is needed to understand the trajectory of phenoconversion to each αNDD. Only five 'gold standard' prevalence studies of iRBD in older adults have been undertaken previously, with estimates ranging from 0.74% to 2.01%. The diagnostic recommendations for video-polysomnography (vPSG) to confirm iRBD makes prevalence studies challenging, as vPSG is often unavailable to large cohorts. In Australia, there have been no iRBD prevalence studies, and little is known about the cognitive and motor profiles of Australian people with iRBD. The Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study will investigate the prevalence of iRBD in Tasmania, an island state of Australia, using validated questionnaires and home-based vPSG. It will also explore several cognitive, motor, olfactory, autonomic, visual, tactile, and sleep profiles in people with iRBD to better understand which characteristics influence the progression of iRBD to αNDD. This paper details the ISLAND Sleep Study protocol and presents preliminary baseline results.

**KEYWORDS**
neurodegenerative disease, Parkinson's, prodromal, rapid eye movement (REM), sleep

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## 1 | INTRODUCTION

Rapid eye movement (REM) sleep behaviour disorder (RBD) is characterised by enactment of motor behaviours correlating with vivid dreams in REM sleep and demonstrated loss of the normal REM atonia (Boeve, 2010). This disorder can be associated with other conditions, such as α-synuclein-related neurodegenerative disease (αNDD) including Parkinson's disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA), as well as narcolepsy, alcohol withdrawal, certain antidepressant medications, and recreational substance use (Roguski et al., 2020). There has been an increasing interest in identifying people with the isolated form of RBD (iRBD), as it is now recognised as an early stage, or 'prodromal phase', of αNDD. Approximately 80% of people with iRBD will progress to clinically defined PD or DLB within 15 years of first diagnosis (Schenck et al., 2013). This relationship was first reported by Schenck et al. (1996) who studied a group of 29 older men aged >50 years with iRBD and found that 38% developed an αNDD after a mean interval of 13 years from initial iRBD onset. A 16-year longitudinal follow-up of this cohort eventually found an 81% phenoconversion rate after a mean interval of 14 years from iRBD onset (Schenck et al., 2013). The majority of these cases progressed to PD and DLB, and a small number to MSA. It is noteworthy that two patients had been clinically diagnosed with Alzheimer's disease (AD), but autopsy found mixed AD and α-synuclein pathology.

The isolated form of RBD is now considered the strongest predictor of conversion to idiopathic αNDD (Postuma et al., 2019), and iRBD cohorts provide an important opportunity to implement neuroprotective trials and focussed lifestyle risk reduction strategies at an early stage of the disease course. Despite this, it is well-recognised that iRBD is under-reported in the general population as many people with iRBD are unaware of their night-time behaviours, or their bed partner assumes that behaviours of mild intensity, such as jerking, are simply 'bad dreams' (Marras et al., 2023). The first step in trying to reduce the high risk of progression to αNDD is thus to identify who has iRBD.

The ideal 'gold standard' assessment to make an accurate diagnosis of iRBD requires a clinical history and video-polysomnography (vPSG) to capture evidence of motor events overnight (Cesari et al., 2022). The International RBD Study Group (IRBDSG) recently proposed that vPSG be made mandatory for the identification of iRBD, to confirm that either isolated REM sleep without atonia (RSWA; loss of muscle tone in REM sleep) or at least one motor event in REM sleep is detected (Cesari et al., 2022). However, due to limitations in accessibility, the current standard diagnostic criteria for RBD are set out in the International Classification of Sleep Disorders, Third Edition (Text Revision) 2023 and supported by the World Sleep Society (American Academy of Sleep Medicine, 2023; Schenck et al., 2023), which state that video identification of RBD behaviours are not required, only RSWA together with a convincing clinical history. Unfortunately, vPSGs and sleep specialists are often difficult to access, especially in regional or remote areas, and primary care physicians may take a pragmatic approach to treat the symptoms with benzodiazepines, thus delaying accurate and timely diagnosis.

Screening questionnaires for iRBD can be useful but they tend to overestimate the prevalence, as some symptoms of iRBD may be present in other conditions, such as obstructive sleep apnea, periodic limb movement disorder, or nightmare disorder. The features of limb movements and frequent awakenings seen in these other conditions show how initial suspicion of iRBD can be missed with screening questionnaires alone (Bramich et al., 2022). Additionally, the low specificity and positive predictive value of iRBD screening questionnaires, along with the need to develop other methods for appropriate screening of iRBD, have recently been highlighted (Stefani et al., 2023). These barriers mean that research into iRBD prevalence is limited, as performing vPSG for population-based studies is difficult to access and inefficient.

It is therefore valuable for an iRBD prevalence study to employ vPSG to validate the diagnosis, combined with screening questionnaire and clinical history interviews to identify who has 'probable' iRBD. Current research reflects a variety of iRBD prevalence rates in diverse populations and only five previous studies have reported the prevalence in large samples of older adults. The first included 1464 participants from Japan, with an average age of 76 years, and used a two-part screening method and vPSG assessment. For the screening questionnaire alone, a prevalence of 15.5% was found; however, after telephone interview follow-up, face-to-face interviews and then vPSG confirmation, the prevalence of iRBD in the elderly Japanese population was 1.23% (Sasai-Sakuma et al., 2020). Another study, undertaken in Spain, assessed 539 adults aged >60 years with screening questionnaires and vPSG (Pujol et al., 2017); they found an iRBD prevalence of 5.2% with screening questionnaires, but this dropped to 0.74% when vPSG was used. Haba-Rubio et al. (2018) studied 1997 adults in Switzerland, finding an 18.4% iRBD prevalence on questionnaire alone, dropping to 1.06% with home-based PSG confirmation (without video). Cicero et al. (2021) evaluated 1524 participants in Italy using the 'gold standard' vPSG protocol after screening. They identified a prevalence of 14.4% with questionnaires, then followed-up with telephone and in-person interviews to rule out other possible causes. Only 12 participants went on to have vPSG based on clinical findings, which resulted in an estimated iRBD prevalence of 1.18% in the Italian population (Cicero et al., 2021). Lastly, a Korean study by Kang et al. (2013) interviewed 696 adults aged >60 years, inviting 354 to vPSG for further sleep analyses, resulting in a calculated prevalence of 2.01%. These studies show that vPSG confirmed cases of iRBD are significantly lower than those with screening questionnaires alone (Cicero, Giuliano, Luna, et al., 2021) and demonstrate the need for vPSG confirmed iRBD prevalence estimates in further cross-cultural populations.

These initial findings also highlight the need for greater accessibility to vPSG. Home-based PSG studies *without* video recording are emerging as feasible and more accessible for common sleep disorders, such as obstructive sleep apnea (Bruyneel & Ninane, 2014). These have rarely been considered for iRBD as the basic home-based PSG cannot capture the specific increased tone on electromyography (EMG) during REM sleep and video evidence of dream enactment behaviour—both of which are recommended for a diagnosis (Cesari et al, 2022). However, by configuring a PSG system to include additional EMG leads and an ambulatory video system, there is a great potential to diagnose iRBD within the home, making it more easily accessible and comfortable for the patient, and easier to access for the clinician and researcher.

Increasing the understanding of differing phenotypes of iRBD will aid in stratifying risk of conversion to αNDD subtypes, as well as identify people in the prodromal phase of αNDD who are suitable for enrolment in prospective clinical trials of neuroprotective therapies. Careful assessment of associated features in iRBD may help predict the trajectory of conversion to αNDD; in particular, the association between iRBD and motor, cognitive, circadian, olfactory, and autonomic dysfunction. Previous research suggests that decreased cognitive and motor function in patients with iRBD, such as impaired short-term visual memory and slowing of gait, predicts conversion to PD (Del Din et al., 2020; Rolinski et al., 2016), whereas mild cognitive impairment and executive cognitive dysfunction seem to influence the risk of conversion to DLB (Bruscoli & Lovestone, 2004). Changes in 24-h sleep patterns (circadian rhythms) are seen in people with iRBD, and there is some evidence that dream content may change with progression to αNDD (Liguori et al., 2021; Uguccioni et al., 2013; Valli et al., 2015). Research also suggests that loss of smell, autonomic dysfunction, and mood changes are significant early symptoms in patients with iRBD, signifying these as key risk factors for the development of αNDD (Chiu et al., 2021; Elliott et al., 2023; Postuma et al., 2019). Further investigations are thus needed to better understand whether certain clustering of motor-cognitive-sleep-olfactory-autonomic features may predict iRBD progressing more rapidly, or specifically to one subtype of αNDD.

### 1.1 | Tasmania—an ideal setting for population research

Tasmania is an island state of Australia, and its population has the highest median age of all Australian states (Tasmania: 42 years; Australia: 37 years). Compared to other Australian states, Tasmania also has the highest rates of modifiable risk factors for dementia and other NDDs: the highest average cigarette consumption in men (14.5/day), one of the highest rates of adult obesity (70.9%), and the greatest percentage of adults with high blood pressure (27.2%) (Australian Bureau of Statistics, 2017–2018). These demographic profiles make Tasmania a valuable place to identify people at-risk of αNDD, to then recruit into clinical trials that aim to reduce their progression to overt αNDD. As such, this paper intends to outline the protocol for the Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study: a longitudinal research project investigating the prevalence and profiles of iRBD in Tasmania, Australia.

Tasmania provides an important opportunity to explore iRBD as it has an established large cohort of older adult research participants in the ISLAND Project; a public health initiative launched in June 2019 by the Wicking Dementia Research and Education Centre at the University of Tasmania, aiming to build dementia risk management self-efficacy and decrease dementia risk in Tasmanians aged ≥50 years (Bartlett et al., 2022). The project currently includes >6000 active participants who will be followed-up over the next 10 years. By inviting these study participants to take part in iRBD research, we have a rare opportunity to investigate the prevalence and profiles of iRBD. Through the planned 10-year follow-up of ISLAND participants, we will be able to track changes in iRBD profiles, quality of life, and overall dementia risk longitudinally, and establish the first vPSG-confirmed prevalence study of iRBD within Australia.

## 2 | AIMS

The primary aim of the ISLAND Sleep Study is to determine the population prevalence of iRBD in adults aged ≥50 years in Tasmania, Australia. This will be the first prevalence study of iRBD undertaken in Australia. The secondary aims are to: (a) stratify iRBD characteristics to determine profiles that are specific to people with iRBD; (b) track changes in these characteristics over time to investigate their contributions to αNDD phenoconversion; and (c) explore the association of biospecimens with biological markers and genotyping of iRBD. Based on previous epidemiological studies (Cicero, Giuliano, Luna, et al., 2021), we hypothesise that 2% of Tasmanians aged ≥50 years will have iRBD and that these participants will have differing profiles of sleep, olfaction, motor, cognitive, and autonomic characteristics, compared with healthy controls.

## 3 | METHODS

### 3.1 | Ethics

This study has been approved by University of Tasmania's Health and Medical Human Research Ethics Committee (HREC 26435 and HREC 18264) and will be conducted in accordance with the National Health and Medical Research Council's National Statement on Ethical Conduct in Human Research (NHaMR, 2018). Participants will be given up-to-date information and asked to provide consent at each stage of the research project.

### 3.2 | Study design

The ISLAND Sleep Study is a longitudinal, prospective observational study, supported by the Wicking Dementia Research and Education Centre at the University of Tasmania.

## 3.3 | Study population

Over 4000 participants were invited to take part in the ISLAND Sleep Study via email invitations or community advertisement between May and October 2022. Eligibility criteria included: (i) age ≥50 years; and (ii) resident in Tasmania (or did so at their entry into the study). Inclusion criteria were based on recruitment strategies in the ISLAND Project (Bartlett et al., 2022), as all participants were required to be a participant, or sign up to, the ISLAND Project. This was to allow for greater data collaboration between the two research projects, which will provide multiple datasets for future iRBD profiling analyses.

## 3.4 | Study procedures

### 3.4.1 | Stage1

Participants completed a battery of online validated questionnaires (Table 1), including the REM Sleep Behaviour Disorder Screening Questionnaire (RBDSQ) (Stiasny-Kolster et al., 2007) and the Single-Question Screen for REM Sleep Behaviour Disorder (RBD1Q) (Postuma et al., 2012). Baseline results for these questionnaires are outlined below (see *Preliminary Findings*). Participants had previously completed several assessments through their participation in the ISLAND Project in 2021, including the Dementia Risk Profile, Knowledge of Dementia Risk Reduction survey, Hospital Anxiety and Depression Scale, Assessment of Quality of Life, and 'TAS Test, a digital movement and cognitive test (Alty et al., 2022). Additional screening questions were also asked to identify participants with diagnosed NDDs, including dementia and PD, and these participants were excluded from the iRBD-positive group.

**TABLE 1** Validated online questionnaires.

| Questionnaire | Assessment domain |
|---|---|
| REM Sleep Behaviour Disorder Screening Questionnaire (RBDSQ) (Stiasny-Kolster et al., 2007) | RBD screening |
| The REM Sleep Behaviour Disorder Single Question Screen (RBD1Q) (Postuma et al., 2012) | RBD screening |
| Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) | Sleep quality |
| STOP-BANG Sleep Apnea Questionnaire (Chung et al., 2016) | Sleep apnea |
| The Composite Autonomic Symptom Score (COMPASS-31) (Sletten et al., 2012) | Autonomic dysfunction |
| Michael J Fox Parkinson's Screening Questionnaire (MJFF, 2023) | Parkinson's motor symptoms |
| COVID-19 Questionnaire | Infection acquired and vaccination status |
| Short Form-McGill Pain Questionnaire-2 (SF-MPQ-2) (Melzack, 1987) | Pain |
| The Mannheim Dream questionnaire (MADRE) (Shredl et al., 2014) | Dream history and content |

Abbreviations: RBD, REM sleep behaviour disorder; REM, rapid eye movement; STOP-BANG, snoring history, tired during the day, observed stop of breathing while sleeping, high blood pressure, BMI > 35 kg/m2 (or 30 kg/m2), age > 50 years, neck circumference > 40 cm and male gender.

### 3.4.2 | Stage 2

Participants who completed the RBD1Q in Stage 1 will be invited to participate in testing of olfactory function and sleep pattern monitoring using University of Pennsylvania Smell Identification Test (UPSIT) kits (U version) and GENEActiv accelerometer watch devices respectively. This will be a fully remote project, with all study materials being sent and returned via post. The UPSIT is a 40-item test that requires participants to select the correct odour from four options. It is well validated for research and age- and sex-specific normative data have been published (Brumm et al., 2023). These assessments will identify participants with olfactory dysfunction or reduced olfaction. Participants will also wear a GENEActiv accelerometer device on their wrist for 14 nights and complete a sleep diary. The GENEActiv device measures their level of activity and light exposure over 24-h periods. It will enable comparison of 24-h sleep/wake patterns between those participants with 'probable' RBD and those without.

### 3.4.3 | Stage 3

Participants who screen positive on the RBDSQ in Stage 1 (RBD+), will be invited to undertake a structured telephone screening interview (with their bed partner, if applicable) to ascertain further details about REM sleep behaviour symptoms (Supplemental material 1). This will be administered by a qualified sleep scientist, in consultation with a neurologist/sleep specialist. Answers from this interview will then be used to stratify participants most likely to have iRBD and these will be invited to have a home-based vPSG to assess their sleep and identify iRBD (Figure 1). This two-step approach to screening, using a validated questionnaire combined with a clinical interview, is based upon previous studies utilising a similar methodology (Pujol et al., 2017; Sasai-Sakuma et al., 2020).

All RBD+ participants, and an age/sex matched sample of participants who screen negative ($n = 50$), in this stage will undergo a vPSG (video recorded sleep study) in their usual home environment. This will provide a strong estimate of the population prevalence of iRBD with a margin of error calculated to be $d = 0.0053$. The vPSG equipment (Compumedics ONsight/Grael System with video) will be attached to each participant in their home prior to bedtime, to obtain data for 1 night of sleep. This will collect all physiological data required to determine the presence of iRBD in line with the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events (Iber, 2007), including video recordings, electroencephalogram and submentalis (chin), bilateral flexor digitorum superficialis (arm), and tibialis anterior (leg) EMG activity.

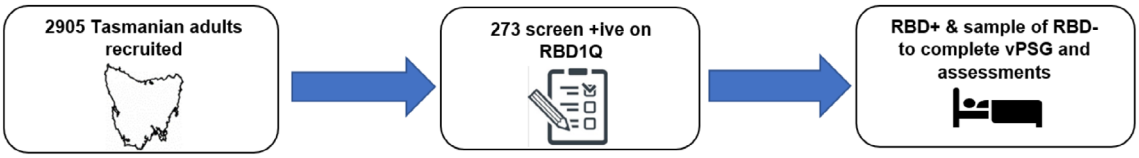


**FIGURE 1** Flow chart for Part 3 of the ISLAND Sleep Study. ISLAND, Island Study Linking Ageing and Neurodegenerative Disease; RBD(+)(–), rapid eye movement sleep behaviour disorder (positive) (negative); RBD1Q, Single-Question Screen for REM Sleep Behaviour Disorder; vPSG, video-polysomnography.

**TABLE 2** Objective assessments for Stage 3 of the Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study.

| Assessment name | Assessment domain |
|---|---|
| Montreal Cognitive Assessments (MOCA) | Global cognition |
| Trail-Making Test Part A and B | Executive function |
| MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) | Motor function |
| TAS Test (Alty et al., 2022) | Motor-cognitive function |
| Blood pressure sitting and standing | Autonomic dysfunction |
| Farnsworth-Munsell 100 Hue test | Colour discrimination |
| 2 Point Discrimination test | Tactile discrimination |
| Dynamometer assessment | Grip strength/ frailty |

At the time of the home-based vPSG, participants will also be invited to complete several objective assessments of cognitive and motor function as listed in Table 2. These assessments will gather additional information on cognition, movement, autonomic function, colour vision, and tactile function, which will assist in profiling participants with iRBD. All participants will also undergo a video-recorded Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) examination, rated by a certified neurologist, to identify those with a possible undiagnosed αNDD. Participants who have a home-based vPSG will later be invited to undergo a detailed neurological examination at the University of Tasmania ISLAND Assessment Clinic. All subjective and objective assessments will then be repeated every 2 years to better understand the progression and trajectory of iRBD to αNDD.

Additionally, participants will be invited to supply several non-invasive biospecimens that will be used for future DNA and genotyping analyses, in collaboration with national and international iRBD research groups. These will include sebum (skin oil), saliva, inner cheek (buccal) swab, and urine collection. Saliva samples will be studied for diagnostic value of oligomeric α-synuclein level in participants with high chance of developing PD. The oligomeric α-synuclein has shown diagnostic value in people with PD (Kang et al., 2016). Urine samples will be studied for the levels of biomolecules that have shown to be higher in the brain of people with PD (Huebecker et al., 2019; Rocha et al., 2015). In particular, the ratio of two lipids (sphingoid base lipids) to each other will be used to determine if there are signatures of changes in the way lipids are metabolised in the body in people with iRBD. The sebum collection will collect biomolecules (oils) covering the skin. These biomolecule levels will be compared with healthy participants to see if we can use them for diagnosing PD earlier and preventing the development of a range of symptoms that can occur as people age (Esfandiary et al., 2022). Changes in skin oils have previously been shown in PD cases (Sinclair et al., 2021) and the collection of non-invasive sebum samples allows for investigation into their applicability in early-stage PD and iRBD.

Buccal swabs will be used for extraction of DNA for future genotyping analyses. These may include a targeted approach of examining known risk genes associated with PD, such as leucine-rich repeat kinase 2 (*LRRK2*) and glucocerebrosidase (*GBA*) (Marras et al., 2023). DNA may also be used in combination with samples from collaborators for screening programmes (such as the Global Parkinson's Genetics Program [GP2]—https://gp2.org/) to identify new risk loci or rare variants in participants with iRBD. There is still much to learn about genetic risk factors and the path to further understanding requires working collaboratively and openly sharing data, processes, and results.

## 3.5 | Ethical approval and informed consent procedures

All participants will be made fully aware of the potential findings that may result from their participation in this study. Only participants who consent will be included in the study; they will be required to consent to: (a) being informed of any sleep disorder or cognitive/motor deficits found, and (b) to the sharing of this information with their general practitioner (GP). This is in line with recent research indicating that the majority of patients with iRBD prefer to be informed of their diagnosis and the prognosis of αNDD development (Gossard et al., 2023). However, participants will be informed that any results found during this study are research findings only and not indicative of a clinical diagnosis. They will be encouraged to seek further clinical investigations through their GP. Genetic tests will be run on a research basis and not be undertaken as diagnostic tests. As such, the results would not be revealed to the study participants but will instead inform the current and future risk algorithm.

**TABLE 3** Demographic variables of the Island Study Linking Ageing and Neurodegenerative Disease (ISLAND) Sleep Study cohort (not available for all participants).

| Variable, *n* (%) | Female *n* = 1975 (73.9%) | Male *n* = 715 (26.1%) | Total *n* = 2690 |
|---|---|---|---|
| Age, years | | | |
| 50–59 | 685 (34.7) | 151 (21.1) | 836 (31.1) |
| 60–69 | 893 (45.2) | 303 (42.4) | 1196 (44.5) |
| 70–79 | 363 (18.4) | 223 (31.2) | 586 (21.8) |
| 80–89 | 34 (1.7) | 37 (5.2) | 71 (2.6) |
| ≥90 | 0 (0) | 1 (0.1) | 1 (0.0) |
| Marital status | | | |
| Defacto | 202 (10.2) | 72 (10.1) | 274 (10.2) |
| Married | 1099 (55.6) | 499 (69.8) | 1598 (59.4) |
| Other | 15 (0.8) | 2 (0.3) | 17 (0.6) |
| Prefer not to say | 4 (0.2) | 0 (0) | 4 (0.1) |
| Separated or divorced | 304 (15.4) | 52 (7.3) | 356 (13.2) |
| Single | 156 (7.9) | 54 (7.6) | 210 (7.8) |
| Widowed | 150 (7.6) | 21 (2.9) | 171 (6.4) |
| Missing | 45 (2.3) | 15 (2.1) | 60 (2.2) |
| Highest level of education | | | |
| Primary school | 1 (0.1) | 0 (0) | 1 (0.0) |
| High school | 251 (12.7) | 92 (12.9) | 343 (12.8) |
| Certificate or apprenticeship (including certificate 2, 3 or 4) | 196 (9.9) | 82 (11.5) | 278 (10.3) |
| Diploma/associate degree | 368 (18.6) | 130 (18.2) | 498 (18.5) |
| Bachelor's degree | 424 (21.5) | 144 (20.1) | 568 (21.1) |
| Higher university degree (honours, graduate diploma, master's, or PhD) | 624 (31.6) | 244 (34.1) | 868 (32.3) |
| Other | 73 (3.7) | 14 (2.0) | 87 (3.2) |
| Missing | 38 (1.9) | 9 (1.3) | 47 (1.7) |
| Employed | | | |
| No | 1063 (53.8) | 463 (64.8) | 1526 (56.7) |
| Yes | 880 (44.6) | 246 (34.4) | 1126 (41.9) |
| Missing | 32 (1.6) | 6 (0.8) | 38 (1.4) |
| Retired | | | |
| No | 154 (7.8) | 46 (6.4) | 200 (7.4) |
| Yes | 927 (46.9) | 427 (59.7) | 1354 (50.3) |
| N/A | 0 (0) | 1 (0.1) | 1 (0.0) |
| Missing | 894 (45.3) | 241 (33.7) | 1135 (42.2) |
| Ancestry | | | |
| English | 972 (54.8) | 298 (49.7) | 1303 (53.3) |
| Irish | 438 (24.7) | 105 (17.5) | 561 (23.0) |
| Other | 565 (20.5) | 312 (32.8) | 826 (23.7) |

Abbreviations: N/A, not available.

## 3.6 | Data management

Survey, cognitive, motor, olfactory, autonomic, sleep pattern, and biomarker data will be de-identified and stored on secure databases in accordance with institutional ethics and privacy policies. Survey data are collated using the secure web-based ISLAND portal. Survey, cognitive/motor assessment, biomarker, and intervention data are linked by a unique identifier, forming a comprehensive database of participant demographics, functioning, and potential confounders at participant level.

### 3.7 | Data analysis

There are three main outcomes of interest for this project: (i) confirmation of iRBD through telephone screening and on home-based vPSG; (ii) cognitive and motor scores in those with confirmed iRBD, as well as a clinical profile of iRBD in terms of further tests such as visual and tactile discrimination, autonomic dysfunction, olfaction, and circadian function; and (iii) identification of new non-invasive biomarkers such as sebum (skin oils), saliva, urine, and genotyping in iRBD and their association with progression to αNDD.

Positive iRBD findings from the home-based vPSG will be used to determine the false-positive rate in our cohort, conditioned on age and sex. Multilevel regression with post-stratification will be used to estimate the (uncorrected) population prevalence in Tasmania from the completed RBD1Q questionnaire, by 're-weighting' estimates according to population demographics (such as age, sex, and highest level of education) (Downes et al., 2018). The corrected population prevalence will then be calculated using the estimated false-positive rate from the home-based vPSG as an informative, beta-distributed prior; whereupon the (corrected) posterior prevalence can be computed using Bayesian approximation (Diggle, 2011). Results from the assessments performed at the time of the home-based vPSG will be used to stratify characteristics in those with confirmed iRBD compared to those without, to identify profiles specific to iRBD.

## 4 | RESULTS

A total of 2905 participants (mean [SD] age 64 [7.7] years; 26.1% male) were recruited from throughout Tasmania. The characteristics of the cohort compared with the Tasmanian population (aged ≥50 years) can be seen below (Table 3.). The average participant age for the ISLAND Sleep Study is 64 years, showing a similar spread of age categories compared to the Tasmanian population, apart from those aged ≥80 years. Female largely outweighs male participation (73.9%/26.1%) in this study, along with nearly three quarters completing a higher education degree (74%). This is likely due to the predominance of female and university educated participation in the original ISLAND project (Bartlett et al, 2022). There is also a higher proportion of participants living in southern Tasmania (around the State's capital city of Hobart, 57.3%) compared to any other region, and the majority are married (60.1%), retired (56.3%), and report English or Irish ancestry (76.3%).

### 4.1 | Preliminary findings

Results from the online questionnaires alone reveal that 273 participants (9.4%) have 'probable' iRBD (pRBD) based on the RBD1Q. Compared to those without pRBD, this group report poorer sleep quality (66% versus 57%; $p < 0.01$), greater autonomic dysfunction (median score 18 versus 13; $p < 0.05$), more pain symptoms (particularly stabbing, itching and heavy pain), higher risk of sleep apnea (30% versus 13%; $p < 0.001$), more intense dreams (21% versus 8%; $p < 0.001$), and more early PD symptoms, including shaky limbs (16% versus 6%; $p < 0.001$) balance problems (35% versus 26%; $p < 0.01$), and slurred speech (12% versus 6%; $p < 0.001$) (Figure 2).

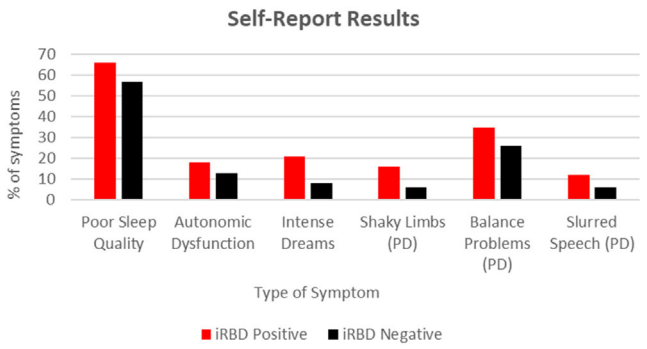


**FIGURE 2** Preliminary findings from the ISLAND Sleep Study self-report questionnaires ($n = 2887$). ISLAND, Island Study Linking Ageing and Neurodegenerative Disease; iRBD, isolated rapid eye movement sleep behaviour disorder; PD, Parkinson's disease.

## 5 | DISCUSSION

The ISLAND Sleep Study will be the first study to investigate the prevalence and profiles of iRBD in Australia. It is also one of few studies currently recruiting for iRBD within the community, alongside the North American prodromal Synucleinopathy (NAPS) consortium (Elliott et al., 2023) and the 'risk FActoRs PREdictive of phenoconversion in idiopathic REM sleep behavior disorder: the Italian STudy' (FARPRESTO) consortium (Pulighedu et al., 2022), which will greatly enhance the epidemiological knowledge of iRBD. iRBD prevalence studies show varied results throughout the world and evidence suggests that it may differ between ethnographic populations (Cicero, Giuliano, Luna, et al., 2021). Preliminary results of the ISLAND Sleep Study indicate that the probable prevalence of iRBD in Tasmania, as measured by screening questionnaire alone, is 9.4%. This appears to align with other international studies showing that prevalence estimates range from 5.2%–15.5% when using screening questionnaires, and we expect that the true prevalence will be closer to 2% as suggested by previous epidemiology research (Cicero et al., 2021; Haba-Rubio et al., 2018; Kang et al., 2013; Pujol et al., 2017; Sasai-Sakuma et al., 2020). Baseline characteristics from self-report questionnaires suggest that people with pRBD experience greater symptomology compared to healthy controls, particularly in terms of poor sleep quality and early PD-related symptoms. These findings suggest that people may notice subtle changes suggestive of a αNDD. However, this remains uncertain until the cohort have undergone vPSG to confirm iRBD.

The Tasmanian community presents a unique opportunity to study iRBD in a culturally uniform demographic over time, which has a relatively stable relocation rate. By including >2800 participants, estimating the population prevalence of iRBD and characterising its

profiles and changes over time, this study will contribute valuable knowledge to known and unknown features of iRBD that are associated with the development of αNDD. Over the course of the longitudinal follow-up, this study will help investigate whether certain iRBD characteristics are more likely to contribute to the onset of PD, DLB, MSA, or other NDDs, and whether these influence the speed and trajectory of αNDD development.

There are several strengths to our study. Firstly, we have access to a large population-based cohort of participants in the community who have an established record of long-term research participation. This indicates that participation for the planned longitudinal follow-up of assessments will be retained over the next 5–10 years. Second, the female predominance of our cohort will be most valuable to iRBD epidemiology, as little investigation had been made into females with iRBD. Third, much of this project will be conducted remotely, mitigating any future disruption to data collection due to COVID-19 or other unforeseeable events. Fourth, the development of a home-based vPSG system will make these studies more accessible for participants, and we hope that it may be used commercially or clinically in the future to allow for greater access to sleep investigations for people suspected of having iRBD. And finally, we have ongoing support from several national and international collaborators who are invested in iRBD research and supportive of collecting a wealth of data from our participants for several future projects (co-authors: A.J, N., S.L.N., S.J.G.L., K.J.B., L.C.B., L.P.C.).

The study also has limitations. Our sex and education spread are skewed compared to the Tasmanian population average, and therefore our sample will unlikely be fully representative of the Tasmanian (or broader Australian) population. We also acknowledge that this study is hindered by healthy cohort bias due to the self-selecting recruitment strategy originally used for ISLAND. To mitigate these, we will utilise multilevel regression with post-stratification to estimate the (uncorrected) population prevalence of iRBD in Tasmania, by 're-weighting' estimates according to population demographics (such as age, sex, and highest level of education).

## 6 | CONCLUSION

In conclusion, the ISLAND Sleep Study presents a unique opportunity to study iRBD prevalence and profiles in a large population of older adults. It will produce the first ever estimate of iRBD prevalence in Australia and will be one of the few studies worldwide to phenotype iRBD so widely. We are confident that the national and international collaborations made through this study will contribute to the body of iRBD knowledge and improve the lives of those living with iRBD through increased opportunities for enrolment in clinical and pharmaceutical trials.

### AUTHOR CONTRIBUTIONS

**Samantha Bramich:** Conceptualization; methodology; investigation; writing – original draft, review and editing; funding acquisition; formal analysis. **Alastair Noyce:** Conceptualization; methodology; writing – review and editing; investigation; supervision. **Anna King:** Conceptualization; writing – review and editing; methodology; supervision. **Sharon L. Naismith:** Writing – review and editing. **Maneesh Varghese Kuruvilla:** Writing – review and editing. **Simon J. G. Lewis:** Writing – review and editing. **Eddy Roccati:** Writing – review and editing. **Aidan Bindoff:** Formal analysis; writing – review and editing. **Kevin J. Barnham:** Writing – review and editing; resources. **Leah C. Beauchamp:** Writing – review and editing; resources. **James C. Vickers:** Writing – review and editing; funding acquisition. **Laura Pérez-Carbonell:** Methodology; writing – review and editing. **Jane Alty:** Conceptualization; methodology; investigation; writing – original draft, review and editing; funding acquisition; supervision.

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### CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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