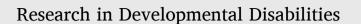
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Adaptive living skills, sleep problems, and mental health disorders in adults with 22q11.21 deletion syndrome

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ABSTRACT

Background: 22q11.21 deletion syndrome (22q11DS) is a neurodevelopmental syndrome caused by a microdeletion of genes at the 22q11.21 locus. It has a prevalence of 1:2000. This study investigated the prevalence of adaptive living skills, sleep problems, and mental health disorders in adults with 22q11DS and examined the relationship between these factors. *Methods:* Parents with an adult son or daughter with 22q11DS completed the following: A bespoke Demographic Information Questionnaire, Sleep Questionnaire (SQ-SP), Psychopathology in Autism Checklist (PAC), and Activities of Daily Living (ADL) scale. Descriptive statistics, correlations, and one-way between groups analysis of variance (ANOVA) were conducted.

Results: Mental health difficulties, sleep problems, and low levels of adaptive living skills are prevalent in adults with 22q11DS. Strong positive correlations were identified between sleep problems, depression, and anxiety subscale scores and moderate negative correlations between depression, psychosis, and activities of daily living skills.

Conclusion: Adults with 22q11DS need screening and treatment for mental health and sleep problems.

What this paper adds?

This paper examines parental reports of adaptive living skills, sleep, and mood disorders in adults with 22q11 deletion syndrome. It builds upon a small body of previous research concerning adults with this rare neurodevelopmental syndrome. The study reveals that sleep problems and mental health difficulties are prevalent in this population and that mood disorders may be underdiagnosed. Previous research has identified high rates of anxiety. To our knowledge, this is the first time that such high rates of depression have been identified. The study also revealed strong relationships between anxiety, depression, and sleep problems and moderate correlations between depression, psychosis, and skill levels for the activities of daily living. The knowledge revealed by the study has implications for clinicians and it highlights future directions for research.

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1. Introduction

22q11.2 deletion syndrome (22q11DS) is the most common multiple anomaly neurodevelopmental syndrome in humans with a prevalence of one in every 850-992 established pregnancies among low-risk populations (Grati et al., 2015). 22q11DS is also known as: Velo-cardio-facial syndrome (VCFS), DiGeorge syndrome (DGS), Sedlačková syndrome, and Conotruncal anomaly face syndrome (CAFS). This syndrome is caused by a microdeletion of genes from one copy of a chromosome at the 22q11.2 locus. Some of the more common physical manifestations include congenital heart defects, abnormalities of the palate and pharynx, immune disorders, hypocalcaemia, hypotonia, vascular anomalies, and structural differences in brain anatomy and function (Robin & Shprintzen, 2005; Shprintzen & Golding-Kushner, 2008). The neuropsychiatric manifestations of 22q11DS include cognitive, psychiatric, and psychological disorders such as intellectual disability (ID), learning difficulties, mood disorders, anxiety disorders, psychotic disorders, and catatonia (Shprintzen, 2000; Faedda et al., 2015). Tang et al. (2014) conducted a cross-sectional study on the presence of cognitive, behavioural, and psychiatric disorders among individuals (n = 112; aged 8–45 years) with 22q11DS. They found that 79% of the sample had at least one diagnosed disorder, and 16% experienced at least three disorders. In particular, a diagnosis of schizophrenia and the intelligence quotient levels have been found to significantly predict the adaptive functioning skills of adult males (n = 46) with 22q11DS. Schneider et al. (2014), found that anxiety disorders (40%-76%) were more prevalent than mood disorders (9-35%) when they investigated individuals with 22q11DS (n = 1402; aged six to 68 years). There is an association between anxiety and mood disorders and the risk of developing psychosis and a major depressive disorder increases with age when moving into adulthood (Tang et al., 2014; Schneider et al., 2014). Stress can act as a trigger for the onset of symptoms of psychosis, which can impact 30% of adolescents and adults (Jonas et al., 2014). Stress and psychopathology are likely to be exacerbated by sleep problems because they are a predictor of behaviour problems in children and adolescents (n = 149; aged 3–18 years) with 22q11DS (Leader et al., 2020). Sleep problems are experienced by 60% of individuals aged 6–17 years (n = 140) with insomnia and restless sleep being the most common problem (Moulding et al., 2019). Kennedy et al. (2014) identified that 10% of children and adolescents with 22q11DS met the criteria for obstructive sleep apnea. Sleep problems have a significant impact on the lives of individuals, affecting daytime functionality and the physical and mental well-being of those affected (Walia et al., 2016).

People with 22q11DS can display moderate impairment in communication and daily living skills (Butcher et al., 2012; Schneider et al., 2014) and they can have poorer social and emotional functioning compared to people with other medical conditions, despite having similarly rated levels of physical health (Looman et al., 2010). Therefore, it is likely that the presence of sleep problems and psychopathology negatively impact individuals' adaptive behaviour, real-world daily functioning, and their ability to cope with stressors and challenges (Angkustsiri et al., 2012).

1.1. The Current Study

Limited research to date has focused on adults with 22q11DS regarding their sleep problems, mental health disorders, and adaptive living skills. Therefore, it is unknown how the clinical manifestations that arise in 22q11DS are related to the likelihood that individuals will engage in successful adaptive behaviours. To our knowledge, this is the first study to investigate these issues in adults with 22q11DS. This study aimed to identify the sleep problems and the mental health disorders experienced by adults with 22q11DS and to determine the level of their adaptive living skills. It also examined the relationships between sleep problems, mental health disorders, and adaptive living skills.

2. Method

2.1. Participants

This study included n = 101 participants who were adults (aged 18 – 60 years; M = 25; SD = 7.92) with a diagnosis of 22q11DS. There were n = 48 (47.5%) males. ID was reported by parents to be present in n = 86 (85.1%) of the participants. Participants were residents in several countries, including Ireland (n = 17; 16.8%), United Kingdom (n = 19; 18.8%), USA.

(n = 51; 50.5%) and Other (n = 14; 13.9%).

2.2. Informants

Informants for this study were parents who had an adult son or daughter with 22q11DS. Parents completed the rating scales independently following the instructions written at the top of each questionnaire.

2.3. Procedure

Participants were recruited using a poster that explained the study's aims and objectives. This was posted online in 22q11DS support groups and relevant parent support groups, and websites. If parents expressed interest in participating, they were sent a participant information letter and a consent form. When consent had been obtained, the informants were provided with a battery of questionnaires to complete independently in their own time. If informants had any questions whilst completing the questionnaires, they were able to ask researchers for assistance. No informants requested this support.

2.4. Measures

2.4.1. Demographic information

A bespoke questionnaire was used to obtain demographic data. This included age, gender, country of residence, age of diagnosis, and type of professional who made the diagnosis. Informants were also asked about the presence of ID, the level of ID, the presence of any other current clinical features, the treatments being received for the syndrome, whether their adult son or daughter with 22q11DS had any children of their own, and if these children also had the 22q11DS syndrome. In addition, informants were asked about the presence of psychiatric diagnoses and current living status.

2.4.2. Psychopathology in Autism Checklist (PAC)

The PAC (Helverschou et al., 2009), was developed in 2010 by the National Autism Unit in Norway in collaboration with Ulleva University Hospital. It contains 42 items, based on ICD-10 and DSM-IV criteria. The PAC aims to differentiate between the symptoms related to autism and the symptoms of psychiatric conditions, to identify psychiatric disorders in individuals with autism. Thirty items represent symptoms specific to psychosis, depression, anxiety, and obsessive-compulsive disorder (OCD), and 12 items are indicators of general adjustment problems (Helverschou et al., 2009). Using the PAC, participants are asked to rate the extent to which each item is a problem for their adult son or daughter. Ratings include 0 = "not a problem", 1 = "mild", 2 = "moderate" and 3 = "severe". The reliability and validity of PAC were assessed in a study that found it was able to discriminate between autistic adults who had ID and who had psychiatric disorders (n = 35), and those who did not have psychiatric disorders (n = 9). This study found significant differences between the scores obtained for the autism only and the psychiatric disorders group, in regard to the psychosis subgroup ($\alpha = 7.36$, p < 0.01); the depression subgroup ($\alpha = 3.00$, p < 0.025); the anxiety subgroup ($\alpha = 3.00$, p < 0.025) and the OCD subgroup ($\alpha = 3.0$,

p < 0.025). They concluded the PAC had acceptable psychometric properties (Helverschou et al., 2008, 2009). The PAC has been previously used to assess the prevalence of psychiatric disorders in autistic individuals (n = 62) and individuals with intellectual disabilities (n = 132) (Bakken et al., 2010). While the PAC was developed for individuals with autism rather than those with 22q11DS, the checklist was selected as the most appropriate for this study. In addition, several studies have noted that 40–50% of individuals with 22q11DS also receive a diagnosis of autism (Niklasson et al., 2001; Roubertie et al., 2001), thus allowing for comparisons to be made.

2.4.3. The Sleep Questionnaire (Simonds and Parraga (SQ-SP: 1982)

Section 4 of the SQ-SP was used to identify and explore the sleep problems in adults with.

22q11DS. This questionnaire was developed by Simonds and Parraga (1982) and modified by Wiggs and Stores (1996, 2004). Section 4 focuses on the frequency of sleep behaviours. A seven-point Likert scale was used for the informant to answer ranging from "never" to "daily". This scale has not previously been used during published studies involving a 22q11DS population, but Section 4 of the SQ-SP has successfully identified the main sleep problems of individuals with Cri du Chat Syndrome (Maas et al., 2009). In addition, the psychometric properties of the Sleep Questionnaire had been investigated with individuals with ID (n = 345) (Maas et al., 2011). This study concluded that the SQ-SP: 1982 is a reliable and valid tool for assessing sleep. It was reported to have good internal consistency (Cronbach's α = .80), good test-retest reliability (Spearman's rank correlation =.83, p < .01) for the total SQ-SP score, adequate convergent validity (r = .79, p < .001), and satisfactory concurrent validity (r = .52, p < .001). Cut-off values were not obtained for this measure, as only Section 4 was used in this study. The method for obtaining the frequency of other behaviours which were not measured in this study.

2.4.4. Waisman – Activities of Daily Living Scale (ADL scale)

The ADL Scale is a scale modified by Maenner et al. (2013) according to quality criteria for measurement properties of health status questionnaires proposed by Terwee et al. (2007). The ADL Scale was used to assess the activity of daily living skills in people with developmental disabilities and it contains 17 items. Informants are asked to rate the level of independence in which their adult son or daughter can complete each activity. The ability to perform a task is rated as 0 = "does not do at all", 1 = "does with help", 2 = "independent or does on own". Participants who score higher on this scale are more independent and better at engaging in adaptive living skills. Maenner et al. (2013) administered the ADL Scale among four longitudinally studied groups of adolescents and adults with developmental disabilities including autism, Fragile-X syndrome, Down syndrome, and ID. It was determined to be an efficient measure of activities of daily living for people with developmental disabilities and shown to be reliable over time, with weighted kappas between 0.92 and 0.93. Criterion and construct validity were also supported (Maenner et al., 2013).

2.5. Analysis

The demographic data and prevalence rates of medical illness, psychiatric disorders, and the measures used in the study were examined for frequencies, percentages, means, and standard deviations. Pearson's correlations and Chi-square tests were then used to investigate the correlations between the following variables: total sleep score, PAC subscales, and ADL total scores. Results were corrected for multiple comparisons. Hierarchical multiple regression was conducted to examine whether subscale scores on the Sleep Questionnaire predicted total ADL score while controlling for presence of a psychiatric disorder.

2.6. Ethical approval

The study was conducted in accordance with guidelines outlined in the Declaration of Helsinki. All informants gave written informed consent before their inclusion in the study, and data were anonymised. Ethical approval for the study was granted from the School of Psychology Research Ethics Committee, at the University of Galway.

3. Results

3.1. Presence of behavioural and psychiatric disorder in adults with 22q11DS

As presented in Table 1, 46 (45.5%) participants presented with a diagnosis of a psychiatric disorder, with the most common psychiatric disorder being a parentally reported diagnosis of any anxiety disorders, reported among 13 (12.9%) participants. The prevalence of other psychiatric diagnoses, including depression, schizophrenia, and psychosis, ranged from 3.9% to 0.9%. Participants reported a variety of treatment approaches for their psychiatric disorder(s), including medication (n = 36, 78.36%), while counselling and a combination of medication and counselling were reported also. Informants also completed the PAC based on their adult son or daughter with 22q11DS. Scores for each sub-scale were compared to a cutoff score indicated by the PAC. Any score that equals or is above the cut-off score indicates that the participant is showing symptoms of that specific DSM classification. Cut-off values were determined from the results of a PAC validation study (Helverschou et al., 2009) and were as follows: severe general adjustment problems ($M \ge 2.0$), psychosis ($M \ge 2.3$), depression ($M \ge 2.0$), anxiety ($M \ge 1.8$) and OCD ($M \ge 2.4$).

Table 2 shows the percentage of participants that were above the cut-off scores on the PAC and its subscales, as well as the mean, range, and standard deviation of the overall sample. Out of the total group, 64 (63.67%) participants presented with symptoms of general adjustment problems (GAP), and 62 (61.39%) participants presented with symptoms of depression. This was followed by

Table 1

Demographic characteristics and frequency and percentage of participants with parent reported diagnosis of a psychiatric disorder.

	Range M		SD	
Age	18-60 25.20		7.91	
-	Frequency		Percentage	
Gender			c c	
Male	48		47.5%	
Female	53		52.5%	
Presence of Intellectual Disability				
Yes		86		85.1%
No		15		14.9%
Level of Intellectual Disability				
Mild		45		44.6%
Moderate		37		36.6%
Severe		4		4.0%
Country of Origin				
Ireland		17		16.8%
United Kingdom		19		18.8%
USA		51		50.5%
Australia		7		6.9%
Other		7		6.9%
Psychiatric disorder				
Diagnosis of a psychiatric disorder		46		45.5%
Any anxiety disorder		13		12.9%
Depression		4		3.9%
Psychosis		4		3.9%
Bi-polar disorder		3		2.9%
Schizophrenia		1		0.9%
More than one disorder		18	39.13%	
Clinician who made diagnosis				
Psychiatrist		25		24.8%
Psychologist	7		6.9%	
General practitioner (GP)	7		6.9%	
Multi-disciplinary team (MDT)	4		3.9%	
Counsellor	1		0.9.%	
Treatment of psychiatric disorder	-			
Medication	36		78.26%	
Counselling	5		10.87	
Medication and counselling	2		4.35%	
Current living status	-		1.0070	
Living independently	21		20.8%	
Living with parents/guardians	73		72.3%	
Sheltered/residential living	6		5.9%	
Other	1		1%	

Table 2

Range, mean, and standard deviation of PAC subscale scores, SQ-SP total sleep score and factor scores, and ADL total score for participants.

PAC subscale	n	Cut off	%	Range	Μ	SD
GAP	64	≥ 2.0	63.4	1–14	2.10	1.44
Psychosis	15	≥ 2.3	14.9	1-4	1.42	0.69
OCD	4	≥ 2.4	3.9	1-4	1.32	0.58
Depression	62	≥ 2.0	61.2	1-4	1.95	0.93
Anxiety	29	≥ 1.8	28.7	1-3.5	1.52	0.66
Total sleep and factors						
Total sleep score				44–44	96.42	38.29
Factor 1: Snoring				5–35	17.76	10.62
Factor 2: Daytime sleepiness				4–28	11.37	6.19
Factor 3: Complaints related to sleep				6-42	15.08	9.12
Factor 4: Sleep apnea				3–21	5.34	4.90
Factor 5: Anxiety related to sleep				3–18	5.99	3.99
ADL Scale Score	101			8–34	23.81	6.65

*Percentage of participants equal to or above the cut-off score for showing symptoms of the DSM classification.

51.4% (n = 52) of participants scoring more than one subscale. This indicates that 52 participants showed symptoms of more than one mental health condition. In addition, n = 62 (61.4%) participants had a diagnosis of a comorbid medical condition, and n = 26 (25.75%) were currently receiving treatment for medical condition(s).

3.2. Sleep problems in adults with 22q11DS

A total sleep score was determined for each participant using Section 4 of the SQ-SP. The highest possible score is 294, which may indicate the presence of one or more sleep problems in participants. Sub-scores of five different factors were also identified for each participant.

As shown in Table 2, snoring was the highest reported sleep problem (M = 17.76, SD = 10.62), followed by complaints related to sleep (M= 15.08, SD = 9.12), and daytime sleepiness (M = 11.37, SD = 6.19).

3.3. Sleep problems, behavioural, and psychiatric disorders

A moderate positive correlation was found between the total sleep score and the general adjustments problem subscale from the PAC (r = .42, n = 101, p < .001). A strong positive correlation was found between total sleep score and psychosis subscale from the PAC (r = .57, n = 101, p < .001). A weak positive correlation was found between total sleep scores, and the obsessive-compulsive disorder (OCS) subscale (r = .124, n = 101, p = .02). Furthermore, a strong positive correlation was found between total sleep scores and between total sleep scores and depression subscale scores (r = .63, n = 101, p < .001). Lastly, a strong positive correlation was found between total sleep scores and anxiety subscale scores (r = .61, n = 101, p = .001).

3.3.1. ADL and sleep problems

Table 2 presents the scores obtained on the ADL-Scale. Out of a total possible score of 34 on this measure, the mean ADL score in this sample was 23.81 (SD = 6.65), indicating a mild level of impairment in terms of daily living skills. A small negative correlation was found between total sleep score and total adaptive daily living score (r = -.25, n = 101, p = .01). To examine whether subscale scores on the Sleep Questionnaire predicted total ADL score while controlling for presence of a psychiatric disorder, a hierarchical multiple regression was conducted. The dichotomous predictor variable of presence of a psychiatric disorder was entered into the first step of the model, and the Sleep Questionnaire subscale scores were all entered into the second block. Multicollinearity was not present in the data, as Pearson's correlation coefficients for predictor variables were all less than.7 (range: r = -.03 to r = .38). VIF scores were all less than 10 (range: 1.19 - 1.64) and tolerance scores were all greater than.1 (range:.60 - .84). The results indicated that the overall regression model was not significant ($F_{(6, 100)} = 1.65$, $R^2 = .10$, Adj, $R^2 = .04$, p = .141).

3.3.2. ADL and the Presence of Behavioural and Psychiatric disorder

There was a weak negative correlation between ADL and GAP scores (r = -.23, n = 101, p = ..02) and moderate negative correlations identified between: ADL and Psychosis (r = -.38, n = .101, p < .001); ADL and depression scores (r = -.32, n = 101, p < .001) and ADL scores and. Anxiety subscale scores (r = -.35, n = 101, p < .001).

4. Discussion

This study's findings provide insights into the life of adults with 22q11DS. Among a large sample of adults with 22q11DS there were substantial differences (12.27%) between the number of people who reported the presence of a psychiatric diagnosis (39.13%), and the results from the PAC that indicated 51.4% of participants showed symptoms of more than one disorder. Such a disparity is a cause for

concern, as it implies there may be undiagnosed psychiatric disorders in the 22q11DS population. This possibility concurs with the findings of Tang et al. (2014) who found psychiatric disorder diagnoses were as high as 58%. It is also possible for the prevalence rates to be higher if parents do not recognise and report subtle symptoms of psychiatric disorders. These results suggest that rigorous mental health screening processes are required to detect the presence of psychiatric disorders in 22q11DS at the earliest opportunity.

In this study, 28.7% of participants had symptoms of a potential anxiety disorder, while 61.4% had symptoms of depression. These results highlight the prevalence of both anxiety and depression in 22q11DS. They are consistent with the results of Schneider et al. (2014), who found a prevalence of 30% and identified that anxiety and mood disorders are likely to occur in tandem. This highlights the wide prevalence of both anxiety and depression in 22q11DS, meaning they should be a prominent feature of any treatment plan.

The PAC scores indicated that 14.9% of participants showed symptoms of psychosis. This finding is in line with Tang et al. (2014), who found that 11% of their participants met the criteria for psychotic disorders. However, both findings are in contrast with much higher reports of 25–35% within the literature, as found by a review of longitudinal data by Tang and Gur (2018). There are several potential reasons for this discrepancy. For example, this study used parental report data, but many similar studies rely on observational data. Furthermore, the prevalence rate of OCD in this sample was 3.9%, considerably lower than other estimates. In general, reported rates of OCD in this population vary considerably, from 32.6% by Gothelf et al. (2004), who used a structured interview assessment method, to 2.3% by Apter et al. (1996), who used a brief screening instrument. Such large variance suggests there is a need for the development of tailored assessment measures to gauge the true prevalence of psychiatric disorders in adults with 22q11DS. These assessment measures would facilitate a more concerted approach to assessment and treatment.

Sleep problems correlated with the psychopathology of adults with 22q11DS. Depression, anxiety, and psychosis showed the strongest associations with sleep problems in adults with 22q11DS. Moulding et al. (2019) also found that insomnia and restless sleep were associated with elevated symptoms of anxiety disorder. Whilst to our knowledge there is no prior data available concerning sleep problems and depression in 22q11DS, Moulding et al. (2019) also found that insomnia and restless sleep were associated with elevated conduct disorder and with impaired executive functioning respectively. These findings suggest that affective and behaviour problems are related to sleep problems in this population. However, it is not possible to specify the direction of causality in these relationships due to the correlational nature of the analysis.

The correlation identified between ADL and sleep anxiety stresses the relationship between sleep and real-world outcomes, engagement by the individual with their environment, for example, starting and maintaining employment. Sleep problems are a predictor of generalised anxiety disorders (Shanahan et al., 2014). Therefore, clinicians should be aware that sleep problems may exacerbate psychiatric disorders such as generalized anxiety disorder. Indeed, regular screening of those with 22q11DS to identify and monitor sleep problems using validated questionnaires would help to detect and monitor for sleep problems before they cause substantial harm (Arganbright et al., 2020). Furthermore, any treatment programme for psychiatric disorders that involve individuals with 22q11DS should consider the management of sleep problems, including the potential use of continuous positive airway pressure (CPAP) in the treatment of obstructive sleep apnea.

The results of the analysis indicated that ADL shared negative correlations with sleep problems, GAP, and psychosis. These findings concur with previous research that individuals with 22q11DS and psychotic symptoms had lower adaptive socialisation skills than those with 22q11DS alone (Debbané et al., 2006). This suggests that the clinical manifestations of psychiatric disorders including anxiety in 22q11DS have severe consequences for an individual's ability to function in their everyday lives (Angkustsiri et al., 2012). Therefore, adequate treatment of psychiatric illnesses is paramount to the development of adaptive living skills, as is the provision of services such as behavioural and occupational therapists.

Though the results of this study provide valuable and novel knowledge regarding adults with 22q11DS, the study has limitations. This study did not include a control group and it relied on the parental report for the presence of intellectual disability, and psychiatric symptoms including anxiety, which may have underreported these subjective symptoms. The PAC was developed to assess psychopathology in individuals with autism and it was used as no other scale measures psychopathology in individuals with an ID. This study also only used Section 4 of the SQ-SP as these questions focused on the frequency of sleep behaviours. Future studies should include more than one subscale to provide a more detailed view of the individual's sleep behaviors. Furthermore, the SQ-SP included the subscale of snoring and it can be noted that snoring is a common medical issue in 22q11DS, rather than a behavioural issue as such. Finally, while the use of parent report has been widely used to assess the behavioral phenotype of individuals with 22q11DS, some findings suggest a lack of agreement between parent report and other observers. For instance, Klaassen et al. (2015) found that teachers' ratings of behavioral profiles of children with 22q11DS were significantly lower than parental ratings. As such, the findings of this study should be interpreted with caution.

Future research should aim to develop dedicated scales for use with an adult population with ID in the areas of both psychopathology and sleep, as this will serve to increase the validity of findings in these areas. The current study also included participants with a broad age range. Doing so the study provided valuable knowledge about this relatively rare condition, however, future research should focus on how sleep problems, psychiatric problems, and adaptive living skills are related in different age groups of adults with 22q11DS. Future longitudinal and prospective studies are also needed to identify causal relationships between psychiatric diagnosis, sleep problems, and adaptive living skills in adults with 22q11DS, and the extent to which these factors impact one another. Furthermore, to account more accurately for the differences between adults with 22q11DS and typically developing adults, future research should include a typically developing control group. It is also evident that mental health problems have a major presence in this population, but there is little empirical evidence regarding the efficacy of treatments.

The current research study examined the relationships between sleep problems, psychopathology, and levels of adaptive living skills in adults with 22q11DS. Findings suggest that psychiatric disorders and sleep problems are widespread in this population, and adaptive living skills are an area requiring further research. It also suggests there is a need for thorough screening of mental health and

sleep problems in adults who have 22q11DS. The findings of these assessments should inform the plans for treatment and support. With further research, knowledge, and support from families and relevant professionals, adults with 22q11DS can potentially lead more fulfilled and independent lives.

CRediT authorship contribution statement

Geraldine Leader: Conceptualization, Supervision, Methodology Andrea Curtin: Conceptualization, Methodology, Investigation, Writing – original draft. Robert J. Shprintzen: Supervision, Conceptualization. Sally Whelan: Writing – review & editing. Rory Coyne: Data analysis, Writing – review & editing. Arlene Mannion: Supervision, Conceptualization, Methodology, Writing – review & editing.

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

The authors do not have permission to share data.

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