ANXIETY IN AUTISM AND RARE GENETIC SYNDROMES ASSOCIATED WITH INTELLECTUAL DISABILITY

Volume 1

GEORGINA THERESA EDWARDS

Doctor of Philosophy

ASTON UNIVERSITY

June 2022

Aston University

ANXIETY IN AUTISM AND RARE GENETIC SYNDROMES ASSOCIATED WITH INTELLECTUAL DISABILITY

Georgina Theresa Edwards
Doctor of Philosophy
2022

Thesis Abstract

Many individuals with intellectual disability (ID), particularly those with moderate to profound ID, have co-occurring autism and/or a diagnosis of a genetic syndrome. Autism and/or a genetic syndrome diagnosis can confer risk for anxiety. However, most anxiety research focuses on autistic individuals without ID, or individuals with mild ID, resulting in an unrepresentative evidence base. Research is needed to explore anxiety in these under-researched groups who are at risk of anxiety. This thesis aims to address this gap using a variety of methodological approaches. Chapter one presents a critical synthesis of literature to inform the thesis aims. Chapter two presents a systematic review and meta-analysis detailing the prevalence of anxiety symptomatology and diagnosis in genetic syndromes associated with ID. The chapter highlights varying anxiety risk across groups and considers factors that may give rise to varying prevalence estimates. Chapter three utilises questionnaire methodology to identify correlates of anxiety in individuals with moderate to profound ID, identifying potential causal mechanisms that cut-across groups. Intolerance of uncertainty was consistently associated with anxiety. Chapter four utilises semi-structured interviews with parents/carers and clinicians to delineate anxiety presentation in a group at high risk of anxiety, autistic individuals with ID. The chapter also explores current anxiety assessment in practice and the development of new assessments. Behaviours indicating potential anxiety included increased vocalisation, avoidance, and behaviours that challenge. Changes to routine trigger anxiety. Clinicians emphasised identifying an individual's baseline behaviour, knowing an individual well and ruling out other forms of distress. Chapter five documents a direct assessment and fine-grained analysis, identifying behavioural markers of anxiety in autistic individuals. During anxiety-provoking situations, social gaze, rigidity, negative and positive affect were observed. Negative affect was accompanied by engagement in repetitive behaviour. Chapter six discusses implications and directions for further research. The thesis will inform early identification and intervention.

Key words/phrases: anxiety, autism, intellectual disability, genetic syndromes, speak few or no words, prevalence, assessment

Personal Acknowledgements

Thank you to my supervisors, Dr Jane Waite, Dr Jo Tarver, and Professor Chris Oliver. Thank you for supporting me through the highs and lows of the journey and always being a source of support and encouragement. Thank you for giving me the opportunity to work with you and for believing in me. Your passion for the work has been infectious and I will be taking that with me on my future career journey.

Thank you to Dr Christopher Jones, Professor Amanda Wood and Dr Gemma Mansell for your guidance and support. Thank you to members of the research team for your support, I really appreciate you all - Lauren Shelley, Dr Effie Pearson, Dr Rachel Royston, Megan Bird, Liana Potter, and Priya Malhi.

To Mike and Luca. Mike, thank you for being understanding and supportive when I was writing this thesis, during days, nights, weekends, and holidays. Thank you for listening to me moan when things felt overwhelming – I bet you're glad to see me submit this! Luca, for your cheeky personality that always makes me laugh at times when stress was high, and it felt there was a big hill to climb. Thank you for loving running after your ball so much that it meant I HAD to step away from my laptop long enough to get some fresh air.

To my family and friends, thank you for your encouragement and reminding me I could do this, providing me with motivation when I most needed it. Thank you for giving me things to look forward to. I hope I have made you all proud.

This research would not have been possible without the time and effort given by individuals and their families to participate in the studies. Thank you for supporting the work, it would not be here without you. I have learnt so much from you all.

Thank you to the Baily Thomas Charitable Fund for funding this research, none of this would have been possible without your support. Thank you for shaping me personally and professionally, I feel privileged to have been given the opportunity to conduct this research. I will certainly miss our annual meetings.

List of contents

List of Tables

Chapter two

Chapter three

Chapter four

Chapter five

Chapter six

List of Figures

Chapter two

Chapter five

Chapter 1: An introduction to anxiety in autism and intellectual disability

1.1 Preface

The first chapter of this thesis introduces the population of interest; individuals with moderate-profound intellectual disability (ID), including those with an autism diagnosis and/or a genetic syndrome diagnosis. First, this chapter defines autism and ID and their associated characteristics, highlighting the value of including individuals with rare genetic syndromes in autism and ID research. A common comorbidity across all diagnoses is anxiety. In this chapter, the current evidence base for the identification and assessment of anxiety in autistic and ID populations is reviewed. Existing literature mostly focuses on autistic individuals without ID or individuals with mild ID, demonstrating that the population of interest for this thesis is currently neglected in the evidence base. Key gaps in the literature regarding the identification and assessment of anxiety are then identified, informing the aims of the thesis.

1.2 Autism

Autism, also known as, Autism Spectrum Condition (ASC) or Autism Spectrum Disorder (ASD) is a neurodevelopmental condition that is behaviourally defined by differences in social communication and interaction, and the presence of restricted, repetitive interests, activities and/or patterns of behaviour as well as sensory processing differences (American Psychiatric Association [APA], 2013). These characteristics are categorised into sections A and B respectively by the Diagnostic and Statistical Manual, 5th edition (DSM-5; APA, 2013). Section A of the diagnostic criteria includes differences in social communication and interaction which may include limited social reciprocity for example, in terms of maintaining back-and-forth conversation, and a reduced rate of nonverbal communicative behaviours such as eye contact and facial expressions (APA, 2013). Section B of the diagnostic criteria includes restricted, repetitive interests, activities and/or patterns of behaviour and sensory processing differences (APA, 2013). This may include stereotyped or repetitive motor movements such as lining up objects or insistence on sameness behaviours, which may mean changes to routine and transitions are difficult. Whilst sensory processing differences may include hyperreactivity, hyporeactivity or sensory seeking behaviours (Miller et al., 2007).

Hyperreactivity can be defined as showing heightened and/or intense responses to sensory stimuli, for example, experiencing high levels of distress in the presence of hand dryers or vacuum cleaners may indicate potential auditory hyperreactivity (Miller et al., 2007; Stiegler & Davis, 2010). Hyporeactivity can be defined as reduced response to sensory stimuli, for example, an individual may need to be prompted to notice visual stimuli in their surroundings which may indicate visual hyporeactivity (Coulter, 2009; Miller et al., 2007). Sensory seeking behaviours are observed when an individual appears fascinated by objects or uses objects for prolonged periods of time for their sensory properties, for example, repeatedly feeling the texture of an object or for a prolonged period of time may indicate tactile sensory seeking behaviour (Kirby et al., 2017; Miller et al., 2007).

This introduction provides a focus on sensory processing because differences are highly common in autistic individuals with prevalence estimates ranging from 65-96% (Kadwa et al., 2019; Marco et al., 2011; Tavassoli et al., 2016). Furthermore, differences are known to impact the quality of life of autistic individuals (Lin & Huang, 2019). This includes experiencing less enjoyment when participating in social and recreational activities and the preference to engage in activities in the home (Hochhauser & Engel-Yeger, 2010). The severity of sensory processing difference is related to the diversity and intensity of participation in leisure activities; where the more severe the difficulty is, the less diverse and intense engagement in leisure activities (Hochhauser & Engel-Yeger, 2010). Furthermore,

sensory differences also have a negative impact on school participation and can increase distress, distraction and most importantly for the focus of this thesis, anxiety (Jones et al., 2020). Due to the identified link between sensory processing differences and anxiety in autism, sensory processing will be an important factor that is considered in subsequent chapters of this thesis.

1.2.1 Prevalence

The median global prevalence estimate of autism is 61/10,000 (Elsabbagh et al., 2012). Prevalence rates vary between countries with particularly high prevalence estimates identified in Japan at 93/1000 with the lowest reported prevalence of 0.8/1000 in Bangladesh (Chiarotti & Venerosi, 2020). The most recent known UK prevalence estimate indicates a prevalence rate of 3.90/1000 although previous studies have reported much higher rates at 15.7/1000 (Baron-Cohen et al., 2009; Taylor et al., 2013). The variation in prevalence estimates is likely due to differences in data sources, age of sample, case definition, socio-cultural/socio-economic factors associated with geographical area and exposure to potential risk factors linked to the aetiology of autism, for example, birth complications (Chiarotti & Venerosi, 2020; Modabbernia et al., 2017). Over time, there has been evidence to suggest increasing rates of prevalence, however, the extent to which this is reflective of a true increase is questioned by other factors that may account for a large proportion of the increase (Baio et al., 2018; Idring et al., 2015). Factors include increased professional and public awareness of autism, changes to diagnostic criteria and reporting practices, increased research focus and output and access to appropriate health care services (Elsabbagh et al., 2012; Hansen et al., 2015; Zablotsky et al., 2019).

1.2.2 Causes

Despite decades of research focused on identifying aetiological mechanisms of autism, there is currently no identified single cause (Hodges et al., 2020). Evidence suggests that a number of causes are likely to contribute, and a number of theories have been explored (Amaral, 2017).

Twin studies have demonstrated evidence of substantial genetic influence, with recent concordance rates of 62-75% and 5-40% for identical and fraternal twins, respectively (Colvert et al., 2015). As a result of this, attention has been focused on identifying potential genetic causes. Evidence of a genetic contribution is highlighted in the high rates of autism and autistic traits reported in rare genetic syndromes associated with ID. For example, Fragile X syndrome (FXS), a mutation in the FMR1 gene, leads to 22-30% of individuals receiving a comorbid autism diagnosis and Down syndrome caused by trisomy of chromosome 21, leads to 16% of individuals receiving a comorbid autism diagnosis (Bagni et al., 2012; Gardiner, 2010; Richards et al., 2015). Whilst no one genetic difference (e.g.,

FXS) accounts for more than 1% of autistic individuals, when considered together, identified specific genetic causes account for an estimated 10-20% of autism diagnoses (Rylaarsdam & Guemez-Gamboa, 2019; Yoo, 2015). Genetic differences in the remaining 80-90% of individuals remain unclear, however, in recent years with advances in genetic technology, research has explored candidate genes, with the gamma-aminobutyric acid (GABA) A receptor beta 3 (GABEB3), oxytocin receptor (OXTR) and reelin (RELN) among the most consistently implicated (Yoo, 2015).

Neuroimaging studies have also highlighted differences in the brains of autistic individuals (Hashem et al., 2020). Identified differences have included lower grey matter, white matter and amygdala volume but increased cerebellar volume (Amaral et al., 2008). Additionally, studies have found both decreased and increased cortical thickness, indicating that findings are not conclusive across studies (Hashem et al., 2020).

Furthermore, research has shown the importance of environmental factors in the aetiology of autism. Bacterial or viral infections in the mother during pregnancy, presence of gestational diabetes, increasing paternal age and preterm and post term pregnancy are all environmental factors that have been documented in the literature (Karimi et al., 2017; Modabbernia et al., 2017). However, it is important to note that as with genetic causes, there is not one environmental factor that has been deemed a definite cause of autism (Karimi et al., 2017). Whilst it is widely accepted that both genetic and environmental factors are important and therefore the exploration of gene × environment interactions, research is not conclusive in confirming the proportional contributions of these factors nor the understanding of mechanisms underpinning risk factors in the aetiology of autism (Amaral, 2017; Bölte et al., 2019).

1.2.3 Diagnosis

Professional guidelines for the process of assessment and diagnosis of autism have been documented and published. In the UK, the National Institute for Health and Clinical Excellence (NICE, 2011, 2012) published guidance stating a multi-disciplinary consensus approach to diagnosis is best practice. Professionals involved may include Clinical Psychologists, Educational Psychologists, Assistant Psychologists, Psychiatrists, Paediatricians, Occupational and Speech and Language Therapists (NICE, 2011, 2012; Rogers et al., 2016).

There are gold-standard assessments for autism diagnosis including the Autism Diagnostic Observation Schedule (ADOS, Lord et al., 1989; ADOS-2, Lord et al., 2012) and the Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003a). The ADOS-2 (Lord et al., 2012) is an observational, clinician-led assessment with five modules whereby one is chosen based on the age and speech ability of the individual undergoing assessment. The

ADOS-2 assessment involves a number of presses designed to elicit behaviours that are congruent with the diagnostic criteria for autism (Lord et al., 1989). The ADI-R is an in-depth, informant-based interview that explores behaviours and characteristics of autism in the individual undergoing assessment (Rutter et al., 2003a). There are also self and informant report screening measures commonly used within research studies to explore autism characteristics. The Social Communication Questionnaire (SCQ; Rutter et al., 2003b) is an informant measure which was derived from the ADI-R. Other measures include the informant report, Social Responsiveness Scale (SRS; Constantino & Gruber, 2005) and the self-report, Autism Spectrum Quotient (Baron-Cohen et al., 2001).

As part of an assessment, it is crucial to gather information regarding an individual's developmental and medical history, developmental ability and strengths, skills, difficulties and needs across different settings such as home, school/college and in the community which may involve gathering information from multiple informants in an individual's life (NICE, 2011, 2012). Additionally, it is also important to gather any information regarding any mental health difficulties or additional comorbid diagnoses such as epilepsy that may be having an impact on an individual's functioning and/or quality of life (NICE, 2011, 2012).

1.2.4 Characteristics

Parents/carers tend to identify concerns in terms of their child's speech development, social differences, or repetitive behaviour prior to obtaining an autism diagnosis (Herlihy et al., 2015). The most commonly reported early concern is speech development, followed by differences in social interaction and lastly repetitive behaviour as these behaviours may be present in neurotypical individuals (Chawarska et al., 2007; Hess & Landa, 2012; Werner et al., 2005). These concerns often prompt parents/carers to visit a healthcare professional (Crane et al., 2016). In the UK, the median age at diagnosis is 55 months/4.6 years old (Brett et al., 2016).

Historically, there have been gender differences whereby males have been more likely to receive an autism diagnosis than females, with an initial suggested gender ratio of ~4:1, which in more recent years has been suggested to be ~3:1 (Fombonne, 2009; Loomes et al., 2017; Zeestraten et al., 2017). These differences have been extensively explored, from biological theories of the extreme male brain and foetal testosterone (fT) theory to differences in brain connectivity, to gender biased diagnostic criteria leading to undiagnosed or misdiagnosed females (Baron-Cohen et al., 2011; Loomes et al., 2017; Zeestraten et al., 2017). Currently, there is no consensus within the literature for the mechanism underlying the gender difference although research is continuing to explore the different theories proposed (Zhang et al., 2020).

1.2.5 Comorbidity of intellectual disability

Autism is associated with a number of co-occurring conditions including intellectual disability (ID; Carlsson et al., 2013; Matson & Shoemaker, 2009). ID can be defined as "a disorder with onset during the developmental period that includes both intellectual and adaptive behaviour deficits in conceptual, social, and practical domains" (APA, 2013, p. 33). Deficits in intellectual functioning are measured using standardised tests that yield an intelligence quotient (IQ) where a score of 70 or below indicates an ID (Sansone et al., 2014). Historically, in DSM-IV, severity of ID was categorised based on IQ scores whereby an IQ range of 50-69 indicated mild ID, 35-49 for moderate ID, 20-34 for severe ID and <20 for profound ID (APA, 1994; Charman et al., 2011). However, in DSM-5, severity of diagnosis does not rely on obtaining a particular IQ score but is based on complete clinical presentation with a focus on adaptive function ability (APA, 2013). Whilst DSM-5 has moved away from grouping IQ scores to determine level of ID, ICD-11 continues to use this information alongside adaptive function ability to classify severity (Girimaji & Pradeep, 2018). Estimates suggest 50-55% of autistic individuals have a comorbid intellectual disability, with one study finding 39.4% of individuals with mild ID, 8.4% with moderate ID, 1.9% with severe ID and 5.5% with profound ID (Charman et al., 2011; Loomes et al., 2017).

1.3 Intellectual disability

1.3.1 Prevalence

In terms of ID alone, prevalence has been estimated at approximately 10.37/1000 (Maulik et al., 2011; McKenzie et al., 2016). As with the prevalence of autism, ID estimates vary depending on country with findings suggesting that prevalence is higher in low to middle-income countries such as Zambia and Pakistan, in comparison to high income countries such as the US and Spain (Durkin, 2002; Maulik et al., 2011; Salvador-Carulla et al., 2011). This difference in prevalence rates may be due to more illness, infection and poorer health care in low resource countries or methodological differences across studies such as the use of psychological scales vs. standardised diagnostic assessments (Maulik et al., 2011).

1.3.2 Causes

As is true for identifying causes of autism, there are also a multitude of causes for ID. Genetic factors account for a substantial number of cases with identified cause, estimated at 25-50% (Kaufman et al., 2010; Ellison et al., 2013), however, for up to 60% of cases, there is no identified specific cause (Rauch et al., 2006). In recent years with advances in genetic technology, rates of identified genetic causes of ID have increased. Evidence suggests that for more than 75% of individuals with severe ID, an underlying biologic cause is likely to be identified compared to less than 50% of those with mild ID (Patel et al., 2018). Factors

include chromosomal abnormalities such as Down syndrome and single-gene causes such as FXS (Ilyas et al., 2020; McKechanie et al., 2019). Environmental factors such as problems during pregnancy have also been documented as causes of ID such as fetal alcohol syndrome or iodine deficiency in the mother (Bath et al., 2013; Kodituwakku, 2007). Furthermore, illness and injury in childhood such as measles, meningitis and head injury have also been linked to ID (Shree & Shukla, 2016; Winnepenninckx et al., 2003).

1.3.3 Assessment and diagnosis

As mentioned above, the assessment and diagnosis of ID is based on the following criteria: significant difficulties related to intellectual functioning e.g., reasoning, learning, problem solving, and limitations in adaptive ability with onset during childhood (APA, 2013). Difficulties with adaptive ability are difficulties successfully carrying out age-appropriate daily life activities that include conceptual, social, and practical skills such as dressing oneself, engaging in interpersonal interactions and gross and fine motor skills that may allow engagement in activities such as walking, running, brushing teeth or drawing (Boat & Wu, 2015). Assessment for ID includes the administration of psychometric measures, for example, standardised IQ assessments such as the Wechsler Intelligence Scales for Children, Fifth Edition (WISC-V; Wechsler, 2014) or the Wechsler Abbreviated Scale of Intelligence-II (WASI-II; Wechsler, 2011) and the Adaptive Behavior Assessment System-Third Edition (ABAS-3; Harrison & Oakland, 2015) and the Vineland Adaptive Behavior Scales-Third Edition (VABS-3; Sparrow et al., 2016) are commonly used to assess adaptive behaviour. Such assessments are used to gather information about an individual's level of functioning and interpretation is based on clinical judgment (Papazoglou et al., 2014).

1.3.4 Characteristics

Identification of ID will vary widely across individuals, depending on the severity of difficulties and the potential cause. A new-born with ID may have feeding or breathing difficulties, micro or macro-cephaly, dysmorphic facial features or gross motor skill differences. It may be that parents/carers notice that developmental milestones are not reached, or interaction and engagement with the environment is different to what is to be expected, which may prompt parents/carers to visit a medical professional (Patel et al., 2018). When an individual is older, it may be that a delay in language acquisition or specific language difficulties are present, or differences noted in social behaviours with others. Additionally, deficits in the development of fine motor skills or attention and engagement when individuals enter an educational setting may also be noted. Most studies have found a higher prevalence of ID in males compared to females, with a suggested male to female ratio of 2:1 (McKenzie et al., 2016; Patel et al., 2018).

1.3.5 Genetic syndromes associated with ID and autism

As noted above, there is a substantial proportion of ID cases that are caused by genetic factors, including genetic syndromes. Individuals with a genetic syndrome diagnosis are more likely to display autism phenomenology when compared to the general population (Richards et al., 2015). FXS, Rett syndrome and Tuberous Sclerosis Complex are examples of genetic syndromes associated with ID that demonstrate high levels of comorbidity with autism diagnoses (Marlborough et al., 2021; Richards et al., 2015; Roberts et al., 2020). There is variability in the presence of autism phenomenology, highlighting groups at higher risk than others, for example, Rett syndrome and Tuberous Sclerosis Complex have high rates of autism phenomenology whilst individuals with 22q11.2 deletion and Down syndromes have lower rates of autism phenomenology (Richards et al., 2015). There is evidence that genetic syndrome groups have atypical autism profiles that differ from idiopathic autism. For example, individuals with Down Syndrome may show fewer social interaction differences to those with idiopathic autism (Warner et al., 2017). Those with FXS show a reduced level of autism characteristics across domains compared to idiopathic autism (i.e., communication, reciprocal social interaction, and repetitive behaviour and restricted interests in Moss et al., 2013) whilst those with Cornelia de Lange syndrome (CdLS) show a reduced level of autism characteristics but specifically in the repetitive behaviour domain compared to idiopathic autism (Moss et al., 2013). Delineating the profile of autism characteristics within and across genetic syndromes is important to reduce diagnostic overshadowing, where characteristics may be attributed to the syndrome diagnosis. It is crucial to ensure needs are explored and autism-associated comorbidities (i.e., mental health difficulties; see section 1.4.3) are considered to allow early intervention and appropriate support.

1.4 Anxiety

1.4.1 Conceptualisation, presentation, and prevalence of anxiety in the general population

The experience of fear can be an adaptive response to a life-threatening situation whereby the flight or fight response is activated via the sympathetic nervous system. However, anxiety can be defined as “requiring treatment when it arises in the absence of any threat, or in disproportionate relation to a threat, and keeps the affected individual from leading a normal life” (Kozlowska et al., 2015; Ströhle et al., 2018). Anxiety disorders are the most commonly reported mental health difficulty in the general population, with lifetime prevalence rates estimated at 33.7% (Bandelow & Michaelis, 2015). Evidence suggests that anxiety is more common and disabling in women compared to men, with recent studies suggesting a potential link between gonadal hormones and fear mechanisms, which may help to explain sex differences in anxiety (Li & Graham, 2017; Maeng & Milad, 2015;

McLean et al., 2011). Anxiety disorders tend to have an onset during childhood, adolescence, or early adulthood, with risk decreasing with further aging (Bandelow & Michaelis, 2015; Solmi et al., 2021). Different types of anxiety include specific phobia, panic disorder and generalised anxiety disorder, leading to differential diagnosis using standardised diagnostic criteria such as the DSM-5 (APA, 2013; Vallance & Fernandez, 2016).

1.4.2 Theories of anxiety

There have been a number of theories proposed to explain the presentation of anxiety in the general population, some of which are described below:

1.4.2.1 Dugas' Intolerance of Uncertainty Model

Dugas' Intolerance of Uncertainty model was developed in response to a lack of research conducted on Generalised Anxiety Disorder (GAD). GAD is described as "ongoing anxiety and worry about many events or thoughts that the patient generally recognises as excessive and inappropriate" (Gale & Davidson, 2007). The model comprises of four different components: the central one being the concept of intolerance of uncertainty. Intolerance of uncertainty can be defined as "a cognitive bias that affects how a person perceives, interprets, and responds to uncertain situations on a cognitive, emotional, and behavioural level" (Dugas et al., 2005). Importantly, intolerance of uncertainty leads to individuals finding uncertain situations stressful and difficult to manage, uncertain events (i.e., unexpected, unpredictable) are perceived as negative and should be avoided. The model argues that intolerance of uncertainty exacerbates questions such as "What if…?" that an individual may experience which trigger anxious thoughts (Dugas et al., 1998). Also contributing to the model includes beliefs about worry, for example, believing that worrying may stop bad events from happening. Thirdly, the model describes difficulty with problem orientation which includes having an awareness and being able to appraise problems in everyday life. Finally, cognitive avoidance is described as avoidance of threatening mental images which has implications for emotional processing that is needed to reduce worry. Research indicates that Dugas' model is relevant within the autism population, with evidence to suggest its utility and need for anxiety interventions to develop tolerance of uncertainty (Boulter et al., 2014; Rodgers et al., 2018). Intolerance of uncertainty, as a core factor in Dugas' model is further discussed in section 3.2.2.7.

1.4.2.2 Wells' Metacognitive Model

Wells' Metacognitive model differentiated two types of worry. Type 1 includes the life events that cause worry such as health and social factors, whilst Type 2 is described as meta-worry which includes judgements about how uncontrollable and significant thoughts are (Wells, 1995). It is the latter type that leads to worry that has a significant impact on day-

to-day functioning (Wells, 1995). Similarly, to Dugas' model described above, the model includes reference to positive beliefs about worry in the context of GAD. Positive beliefs may include worry is an appropriate way to manage perceived threat or worry about events prepares an individual for if and when the event occurs (Wells, 1995). Wells' model has also been explored within the autism population, with evidence to support the relationship between metacognitive processes and anxiety (Campbell et al., 2018). However, there is recognition that the applicability of models that focus on cognitive elements of anxiety are understudied in the autism population (Campbell et al., 2018). Furthermore, the very limited evidence base that does exist does not include individuals with a co-occurring ID and/or those who speak few or no words (Campbell et al., 2018).

1.4.2.3 Mennin model of Emotion Dysregulation

Mennin et al. (2004) argued that GAD can be best described as differences in the expression and/or modulation of emotional experience. For example, the combination of being emotionally sensitive, having difficulty understanding emotional experience and modulating emotions and responses may lead to situations being aversive and consequently individuals may feel a need to control emotional experience. Individuals with GAD utilise the cognitive strategy of worry and other strategies such as avoidance to control the experience, that in the long run perpetuates the experience of anxiety. Mennin's model has less so, been explicitly focused on in autism research, however relationships between emotion regulation and anxiety have been highlighted, as well as the potential value of interventions focusing on developing adaptive emotion regulation strategies (Cai et al., 2018; Weiss, 2014). Research is scarce focusing on the applicability of these models in ID and genetic syndrome populations. These models will be re-visited in section 6.4.2 in light of the current thesis findings.

1.4.3 Anxiety in autism

Anxiety is common in autistic populations, with estimated lifetime prevalence rates at ~40%, with ranges documented from 20% in autistic adults to 67% in autistic children (Hollocks et al., 2019; Kent & Simonoff, 2017; Lai et al., 2019; Nimmo-Smith et al., 2020; van Steensel et al., 2011). Studies have found that anxiety is more common in autistic populations compared to the general population (Lai et al., 2019; Nimmo-Smith et al., 2020; Vasa & Mazurek, 2015). Rates vary across studies due to methodological differences such as criteria used for anxiety, focus on any anxiety disorder vs. specific anxiety diagnoses (e.g., specific phobia), lifetime vs. current prevalence rates and sample differences. Because of the high prevalence documented in recent years, there has been an increase in research studies exploring anxiety in the autistic population (Vasa & Mazurek, 2015). This has included a drive towards participatory research documenting the voices of autistic people, their families, and professionals. For example, in 2016, the James Lind Alliance identified the

top ten priorities for autism research, there was an emphasis on improving the assessment and treatment of mental health difficulties, particularly anxiety, evidencing the importance of research focus on anxiety (Cusack & Sterry, 2016).

Studies have documented the challenges of assessing anxiety in this population, including 'atypical' presentations of anxiety which do not map onto traditional diagnostic criteria for anxiety (Adams et al., 2019; Kerns et al., 2014). This is concerning considering the elevated prevalence of anxiety, which suggests that individuals may not be receiving timely and appropriate assessment and support; hence, research is needed to address this gap. Therefore, studies have aimed to improve the identification and assessment of anxiety as well as focusing on the development of interventions that are appropriate and effective for the autistic population (Adams et al., 2019; Lau et al., 2020; Parr et al., 2020; Rodgers et al., 2016; Rodgers & Ofield, 2018; Rodgers et al., 2019). In section 4.2, the challenges of anxiety assessment will be discussed further.

1.4.4 Characteristics/presentation of anxiety

Kerns et al. (2014) explored "traditional" and "atypical" presentations, either consistent or inconsistent respectively, with diagnostic criteria for anxiety using the DSM-IV (APA, 2014), in autistic young people. 63% individuals were categorised as experiencing impairing anxiety: 17% with "traditional", 15% with "atypical" and 31% with both presentations. Young people classified as presenting with "atypical" anxiety experienced worry around routine, novelty, and restricted interests. Unusual specific fears of babies crying, coughing, balloons, toilets and supermarkets were also documented. Noted fears may be related to sensory processing differences that autistic individuals experience. These findings are consistent with further research (Lau et al., 2020; Rodgers et al., 2016).

Behaviours that are associated with/attributed to anxiety in autistic individuals include avoidance/escape, increase in repetitive/stereotyped behaviour and behaviours that challenge such as aggression and self-injurious behaviour (Adams et al., 2019; Ozsivadjian et al., 2012). Some behavioural indicators overlap with what is reported in the general population for example avoidance, whilst others are more specific to the experience of anxiety in the autistic population, for example, behaviours that challenge (Hofmann & Hay, 2018).

1.4.5 Impact

The experience of anxiety can have a significant impact on autistic children and adults' lives, as well as the individuals who support them. For autistic children, research has indicated that those with elevated anxiety have poorer quality of life in physical, emotional, and school functioning areas, when compared to individuals who experience lower levels of anxiety (Adams et al., 2020). Examples within these areas of functioning include lower levels

of activity such as walking and running, feeling angry and poorer school attendance respectively (Adams et al., 2020). This finding was over and above the contribution of autism symptomatology, highlighting the specific impact of anxiety on quality of life. Parents of autistic children experience poorer quality of life in terms of their physical health and psychological functioning (Adams et al., 2020). Autistic children experiencing anxiety also participate less frequently in home (e.g., household chores, indoor play) and community-based activities (e.g., groups, clubs, volunteer activities) and when they do attend, they are less involved than non-anxious individuals (Ambrose et al., 2021). Autistic adults have shared that anxiety has an impact on their ability to socially interact with others, live a full, meaningful life, succeed in employment, enjoy pleasurable activities, and engage in community activities outside of the home (Robertson et al., 2018). Whilst prevalence rates are high, they indicate that not every autistic individual experiences anxiety that has a significant impact on day-to-day living, it is not an inevitable outcome. This highlights the importance of improving the evidence base for identification, assessment, and intervention for anxiety.

1.4.6 Anxiety in ID

In ID populations, anxiety is common with prevalence rates ranging from 3.8% in adults to 11-22% in children and adolescents (Dekker & Koot, 2003a; Emerson & Hatton, 2007; Reardon et al., 2015; Reid et al., 2011). Evidence has been inconsistent when comparing rates of anxiety in the general vs. the ID populations, with studies suggesting there is no difference between groups (Buckley et al., 2020), others noting ID groups have higher rates than the general population (Emerson & Hatton, 2007; Green et al., 2015) and vice versa (Mazza et al., 2020). These findings would suggest that autism is a risk factor for anxiety over and above ID, as it seems that autistic individuals are consistently at increased risk of anxiety compared to the general population (Hollocks et al., 2019; Kent & Simonoff, 2017; Nimmo-Smith et al., 2020). This would be congruent with the finding that genetic syndromes associated with autism also experience high rates of anxiety; for example, FXS (Ezell et al., 2019; Kaufmann et al., 2017).

However, increased risk of anxiety in genetic syndromes due to an autism diagnosis is unlikely to be the sole and complete explanation, as some genetic syndromes such as Williams Syndrome, have low rates of autism but high levels of anxiety (Richards et al., 2015; Royston et al., 2017; Tager-Flusberg et al., 2006). Therefore, specific underlying risk factors, for example, sensory processing differences in the absence of other autism characteristics, may contribute to increased anxiety risk (Royston et al., 2018, 2019, 2020; see section 3.2 for an extended introduction reviewing the literature).

Documenting the prevalence of anxiety in genetic syndromes associated with ID may highlight groups at greatest risk of anxiety. Knowledge of the groups most at risk for anxiety

could allude to group characteristics that may explain variation in prevalence rates and inform causal models about the pathways to anxiety within and across groups. Glasson et al. (2020) documented the prevalence of anxiety in genetic syndromes, ranging from 38% in 22q11.2 deletion to 46% in Williams Syndrome, demonstrating variability across groups and the potential for these groups to inform models of anxiety. In Chapter two a systematic review and meta-analysis will be presented that explores this further.

Similar to autistic populations, the inappropriate use of standardised diagnostic criteria developed for the general population is likely to lead to underestimated anxiety rates in ID populations (Cooray & Bakala, 2005; Reid et al., 2011). This may particularly be the case for those with severe-profound ID where assessment may be most difficult due to language and cognitive ability as well as idiosyncratic presentations (Mazza et al., 2020). Further discussion regarding the challenges of anxiety assessment in autistic and ID populations is provided in section 4.2.

1.5 Approaches to assessment of anxiety in autistic and ID populations

1.5.1 Diagnostic assessment

In the general population, gold standard assessment of mental health difficulties, including anxiety would include self-report diagnostic assessment (Hagopian & Jennett, 2008; Moss et al., 2015). There are no diagnostic self-report clinical assessments for anxiety validated for use in autistic populations (Rodgers et al., 2020). Due to identified limitations of using diagnostic criteria to assess anxiety in individuals with ID, specific measures have been developed for ID populations. Examples include the Psychiatric Assessment Schedule for Adults with a Developmental Disability (PAS-ADD; Moss et al., 1993) interview and the Psychopathology checklists for Adults with Intellectual Disability (P-AID; Hove & Havik, 2008) (Hermans et al., 2011). However, for individuals with severe-profound ID, subjective aspects of the diagnostic criteria are difficult, if not impossible to apply, highlighting the importance of utilising a combination of observational and informant report approaches (Cooray & Bakala, 2005). Additionally, the psychometric properties of ID-specific assessments require further validation and replication (Hermans et al., 2011).

1.5.2 Rating scales

Self and informant report rating scales for anxiety have been developed for autistic individuals and individuals with ID. Self-report measures include the Anxiety Scale for Children with Autism Spectrum Disorder (ASC-ASD; Rodgers et al., 2016) and the Anxiety Scale for Autism-Adults (ASA-A; Rodgers et al., 2020) for autistic individuals and the Glasgow Anxiety Scale for people with an Intellectual disability (GAS-ID; Mindham & Espie, 2003) and the Self-Rating Anxiety Scale for Intellectual Disabilities (SAS-ID; Lindsay & Michie, 1988) for individuals with ID (Adams et al., 2019; de Witte et al., 2021; Hermans et

al., 2011). Informant report tools include the parent version of the ASC-ASD (Rodgers et al., 2016) and the Parent-Rated Anxiety Scale for ASC (PRAS-ASD; Scahill et al., 2019) for autistic individuals and the Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003), the Psychiatric Assessment Schedule for Adults with a Developmental Disability Checklist (PAS-ADD Checklist; Moss et al., 1998) and the Diagnostic Assessment for the Severely Handicapped-II (DASH-II; Matson, 1995) for individuals with ID (Hermans et al., 2011). Studies have also used measures of mental health developed for the general population such as the Child Behaviour Checklist (CBCL; Achenbach & Rescorla, 2000, 2001) and the Spence Children's Anxiety Scale, child, and parent versions (SCAS-C/SCAS-P; Spence, 1997, 1998; Nauta et al., 2004) (Green et al., 2015; Magiati et al., 2017; Ozsivadjian et al., 2014).

Hermans et al. (2011) conducted a systematic review concluding that the GAS-ID and the ADAMS were the most promising self and informant-report measures respectively for adults with ID. However, Flynn et al. (2017) identified a lack of research replication for the psychometric properties of existing measures of mental health in individuals with severe-profound ID.

1.5.3 Observation

Observation is a viable method for assessing anxiety which does not rely on an individual's verbal ability and therefore may be a more appropriate option for autistic individuals with ID and/or those who speak few or no words (Moskowitz et al., 2017; Rosen et al., 2016). A challenge with observations is presenting behaviour may be due to a variety of different causes e.g., pain, agitation, communication of needs, needs not being met. It becomes difficult to rely purely on observation due to this reason, which would involve inferences made by observers (Hagopian & Jennett, 2008).

There are ethical considerations when using observational assessments that may expose individuals to anxiety-provoking situations/presses. This is a particularly important consideration when a participant may not have capacity to provide informed consent. When considering the use of existing observational assessments with individuals with moderate-profound ID, or when developing new observational assessments of anxiety, situations/presses designed to elicit anxiety need to be carefully considered and should not be dissimilar (in content or magnitude) to situations that individuals may encounter during their daily life. Ideally, autistic individuals, individuals with moderate-profound ID and their families should be involved in the development of new observational assessments (Palmer et al., 2021). Further discussion regarding observational assessments for use with autistic individuals is presented in section 5.2.

1.5.4 Psychophysiological measures

Another potentially helpful approach to the assessment of anxiety is the use of physiological measures such as salivary cortisol, heart rate and electrodermal activity (Kushki et al., 2013). These approaches have been utilised in recent studies with autistic individuals with ID (Hollocks et al., 2014, 2016; Kushki et al., 2013; Moskowitz et al., 2013). These studies have shown promise in using these measures when exploring anxiety provoking situations as well as evidencing relationships between altered physiological functioning and anxiety. Further research is needed to explore this further in autistic individuals and individuals with moderate-profound ID who speak few or no words, where this approach could be particularly useful (Hagopian & Jennett, 2008). A multi-method approach combining assessments is crucial for differential diagnosis (Hagopian & Jennett, 2008).

1.6 The neglected populations

Individuals with moderate-profound ID, who may also have an autism and/or a genetic syndrome diagnosis are rarely the focus of mental health research, highlighting a gap in the evidence base for autistic and ID populations. In autistic populations, the majority of research presented above focuses on individuals without comorbid ID and those who speak in sentences. Russell et al. (2019) demonstrated in a recent meta-analysis that 94% of autistic participants did not have ID and only 2% spoke few or no words (Russell et al., 2019). Furthermore, the majority of measures developed for autistic populations have focused on those without comorbid ID and/or those who speak in sentences (Rodgers et al., 2016; Rodgers et al., 2020; Wigham & McConachie, 2014). Therefore, whilst there has been an increase in research focusing on anxiety, the current evidence base does not accurately reflect the autistic population as a whole.

In ID populations, most existing research has focused on individuals with mild ID, where studies do include individuals with moderate-profound ID, they are normally in the minority compared to the proportion of the sample with mild ID (Green et al., 2015; Reid et al., 2011). There is an identified need for the development of anxiety assessments for individuals with moderate-profound ID that have been specifically and exclusively developed and validated for this population (Crawford et al., 2017; Flynn et al., 2017). With those with moderate-profound ID rarely being included in mental health research, (Flynn et al., 2017; Vereenooghe et al., 2018), there is clear justification for including those with a diagnosis of a genetic syndrome within autism and ID research. This is especially the case due to the heightened risk of anxiety that these groups face and the increasing number of identifiable genetic causes of autism and ID (Glasson et al., 2020).

Therefore, whilst often excluded from existing literature, individuals with moderate-profound ID who speak few or no words, who may also have an autism and/or a genetic syndrome diagnosis are at increased risk of anxiety. Research dedicated to these groups will therefore provide useful opportunities to explore the pathways to anxiety outcomes within and across groups.

1.7 Diagnostic groups – to lump or to split?

Whilst studying specific groups that are high risk for anxiety (e.g., specific genetic syndromes and autistic individuals) is important for generating hypotheses about risk markers for the development of anxiety, and it is crucial to consider the importance of individual diagnoses and the impact on anxiety presentation (see section 4.4.2.4), there may also be benefits of aggregating groups to study transdiagnostic risk markers of anxiety (Oliver, 2017, 2019; Totsika et al., 2022). Aggregating groups increases the overall sample size and allows for multiple risk factors in the development of anxiety to be examined. In this chapter, existing literature has highlighted autism as a potential risk marker for anxiety across groups associated with moderate-profound ID, where autistic characteristics and genetic diagnoses are prevalent. It is of interest to explore whether risk markers are unique to autism or are applicable more widely to multiple groups. The exploration of risk markers that are evident across diagnostic groups may allow the identification of shared pathways to anxiety. Research that allows us to draw conclusions across groups will be more efficient within clinical services if assessment procedures and interventions can be applied across groups.

1.8 Summary and aims

This thesis focuses on individuals with moderate-profound ID and considers groups of individuals at high risk of experiencing anxiety, including autistic individuals and individuals with genetic syndromes who speak few or no words. The overarching aim was to inform models of anxiety and improve identification of anxiety in these populations.

The existing literature has highlighted key gaps in the evidence base that need to be addressed:

i) With advances in genetic technology, there are increasing numbers of genetic causes of autism and ID. Individuals with moderate-profound ID including those with an autism diagnosis and/or genetic syndrome diagnosis are at high risk of experiencing anxiety. Whilst there have been recent studies documenting the prevalence of anxiety in autism, there is a lack of research doing so in the genetic syndrome population. Documenting anxiety prevalence across genetic syndrome groups will highlight those at risk and allude to potential mechanistic underpinnings of anxiety that may help to explain varying prevalence.

Therefore, to address this gap, Chapter two describes the prevalence of anxiety symptomatology and diagnosis in genetic syndromes associated with ID.

ii) Autism has been noted as a potential risk marker in the development of anxiety; autism characteristics and high rates of anxiety have been identified in individuals with moderate-profound ID, including those with a genetic syndrome diagnosis. Exploring the role of autism as well as further potential risk markers for anxiety may highlight factors that cut across diagnostic groups and highlight shared pathways to anxiety.

Therefore, to address this gap, Chapter three identifies correlates of anxiety in autistic individuals and individuals with moderate-profound ID, including those with a genetic syndrome diagnosis.

iii) Whilst there are existing measures for autistic and ID populations that assess anxiety, these disproportionately focus on autistic individuals who do not have ID and individuals with mild ID. Research has documented the challenges of anxiety assessment for autistic individuals with ID and those with moderate-profound ID, which may be one explanation for the current lack of validated measures developed specifically for this population. Similarly, there is a paucity of research documenting the presentation of anxiety in these populations, therefore it is unclear whether anxiety presentation is similar to those without ID or mild ID. Currently, this means that the existing evidence base does not accurately reflect the entirety of autistic and ID populations. Additionally, without research exclusively focusing on anxiety presentation in individuals with moderate-profound ID and appropriate assessment measures, it is likely individuals are not receiving timely and effective support for anxiety.

Therefore, to address this gap, Chapter four describes the presentation of anxiety in an understudied group that are high risk for anxiety: autistic individuals with ID who speak few or no words. Furthermore, the chapter explores considerations for the development of new assessment tools for anxiety in autistic individuals with ID who speak few or no words.

iv) Multimodal assessment of anxiety is recommended in autistic individuals with ID due to limitations of self and informant measures. There are a lack of observational assessments utilised in this population to pinpoint observable anxiety-related behaviours

and provide validation for studies identifying behavioural markers via questionnaire measures.

Therefore, to address this gap, Chapter five identifies fine-grained behaviours associated with or attributed to anxiety in autistic individuals with ID who speak few or no words, and the temporal sequences of these behaviours during anxiety or fear-provoking situations.

Chapter 2: Prevalence of anxiety symptomatology and diagnosis in syndromic intellectual disability: a systematic review and meta-analysis

The research reported on in the following chapter has now been published with minor differences. It has been reproduced with retained copyright:

Edwards, G., (GE) Jones, C., Pearson, E., Royston, R., Oliver, C., Tarver, J., Crawford, H., Shelley, L., & Waite, J. (2022). Prevalence of anxiety symptomatology and diagnosis in syndromic intellectual disability: a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, 104719.

GE designed the study, selected included studies, extracted data from included studies, quality rated included studies, completed statistical analysis, wrote drafts of the manuscript, completed revisions, and submitted the final version for publication.

2.1 Preface

The previous chapter introduced the population of interest for the thesis, highlighting key existing literature used to identify gaps in the evidence base and inform the thesis aims. The current chapter presents a systematic review and meta-analysis documenting the prevalence of anxiety symptomatology and diagnosis in individuals with genetic syndromes associated with intellectual disability. The chapter is the first known research study to explore anxiety prevalence whilst accounting for the methodological quality of the included studies. Specific anxiety profiles are also explored across genetic syndromes. Genetic syndrome anxiety prevalence rates are compared to estimates from individuals with intellectual disability of mixed aetiology and the general population. The study highlights groups at risk of anxiety and alludes to potential pathways to anxiety that may explain increased risk.

2.2 Introduction

Annual health checks for people with intellectual disability (ID) are a welcome initiative that begin to address inequalities in health care provision experienced by this group (Robertson et al., 2014; Slowie & Martin, 2014). One challenge to delivering effective health care for this population is the diagnosis of physical and mental health difficulties when self-report is compromised and the clinical presentation atypical (Doherty et al., 2020; Kripke, 2018; Whittle et al., 2018). These difficulties can be partially mitigated when there is a known and elevated risk of specific physical and mental health difficulties associated with an identified cause of ID. Awareness of this association enables clinicians and carers to be vigilant for future and unidentified existing difficulties. The substantial literature on the association between syndromic ID and the associated physical and mental health difficulties enables the identification of risk for these difficulties in syndromes and so can inform prevention, early intervention, and clinical management.

With regard to mental health difficulties and conditions that affect mental health, a number of conditions are more prevalent in specific syndromes. Examples include psychosis in 22q11.2 deletion syndrome (Chawner et al., 2019; Weisman et al., 2017), and Prader-Willi syndrome caused by uniparental disomy (Boer et al., 2002; Soni et al., 2007), dementia caused by Alzheimer's disease in Down syndrome (Hithersay et al., 2017; Rubenstein et al., 2020) and autism in Cohen's syndrome (Richards et al., 2015), and Tuberous Sclerosis Complex (Vignoli et al., 2015). Importantly, there are often critical differences in the clinical course and presentation of mental health difficulties and disorders that affect mental health between those with a specific syndrome and: 1) people of typical development, 2) people with non-syndromic ID or ID of mixed aetiology and 3) people with a different syndrome. First, the age of onset and developmental trajectory can differ. For example, anxiety is evident in children with fragile X syndrome as young as 18 months old (Roberts et al., 2019a, 2019b), dementia has a significantly earlier onset in people with Down syndrome (Holland et al., 1998; Lautarescu et al., 2017), and an atypical developmental trajectory of autism is evident in Cornelia de Lange syndrome (Cochran et al., 2019). Second, the broader domains that define diagnostic criteria can drive diagnosis differentially. For example, for attention deficit and hyperactivity disorder (ADHD) in Fragile X syndrome (FXS) the domain of overactivity is comparatively more prominent than impulsivity whilst the opposite is true for Smith-Magenis syndrome (Oliver et al., 2011), and in Cornelia de Lange syndrome (CdLS) two domains of depression; pervasive low mood, and loss of interest and pleasure, are dissociated (Groves et al., 2019). Third, even when the criteria for a specific diagnosis such as autism are fulfilled, the profile of characteristics within domains can differ significantly. For example, the presentation of atypical social behaviour and the presence of

restricted behaviour and interests differ between CdLS and FXS, and those syndromes and non-syndromic autism (Moss et al., 2013). Finally, for a mental health difficulty such as anxiety, different types of anxiety diagnosis might be more prevalent with different co-morbidities across anxiety diagnosis evident (Crawford et al., 2017). In combination, these differences in clinical course, presentation and trajectory indicate the importance for clinicians' awareness of the association between syndromic ID and the risk and presentation of mental health difficulties.

One strategy for collating syndrome sensitive information about common mental health difficulties is to identify and review robust research on prevalence, course, and presentation of these problems in different syndromes. As indicated in section 1.4.1, anxiety is one of the most common mental health problems in the general population with lifetime prevalence estimated at 33.7%, rising to 52.3% when studies include subthreshold diagnosis or symptomatology (Bandelow & Michaelis, 2015; Bryant et al., 2008). Anxiety is often disabling, persistent and associated with poor long-term outcomes, and a negative impact on quality-of-life, physical health, work, and social functioning (Asselmann et al., 2018; Copeland et al., 2014, 2015; Olatunji et al., 2007; Ormel et al., 2009; Senaratne et al., 2010). A number of studies indicate that individuals with ID are at substantially higher risk of anxiety than the general population, with an estimated prevalence rate of 22% in comparison to 4-5% in the general population (Bratek et al., 2017; Einfeld et al., 2011; Green et al., 2015; James et al., 2018; Mazza et al., 2020; Munir, 2016; Reardon et al., 2015). Whilst rates of anxiety can be inconsistent for individuals with ID when compared to rates in the general population, as noted in section 1.4.6, Glasson et al. (2020) highlights that syndromic groups are at particularly high risk of anxiety. Therefore, a review of the association between anxiety and syndromic ID is likely to yield important information for risk, clinical presentation and aid diagnosis and management.

In the general population, genetic risk and gene disorder-phenotype-environment interactions are implicated in the aetiology of anxiety and increased risk of an anxiety diagnosis (Meier & Deckert, 2019). Within the ID population, anxiety is associated with several syndromes. For example, individuals with Williams Syndrome are at heightened risk of experiencing anxiety (48%) when compared to the general population and individuals with ID of heterogeneous aetiology (4% and 5% respectively (James et al., 2018; Maïano et al., 2018; Mazza et al., 2020; Royston et al., 2017). There is also evidence of an association between anxiety and other syndromes, such as FXS, 22q11.2 deletion, 7q11.23 duplication and CHARGE syndromes (Cordeiro et al., 2011; Hartshorne et al., 2017; Stephenson et al., 2015; Velleman & Mervis, 2011). Additionally, the identification of specific types of anxiety diagnosis across syndromes is of interest and raises the question of differing underlying causes of anxiety across groups. For example, in FXS and 22q11.2 deletion syndromes, the

most prevalent anxiety diagnoses are social anxiety and specific phobias (Bertrán et al., 2018; Gabis et al., 2011; Jolin et al., 2012). Noise related phobias are common in Williams syndrome, whereas separation distress is often reported in individuals with 7q11.23 duplication syndrome (Abbas et al., 2016; Mervis et al., 2012; Royston et al., 2017). High rates of obsessive-compulsive disorder (OCD) have been reported in CHARGE and Prader-Willi syndromes (Blake et al., 2005; Dykens & Shah, 2003; La Spata, 2019), although there is debate as to whether the presentation of OCD is similar to that seen in the general population and standard diagnostic criteria. These different levels of specific anxiety diagnoses allude to a shared general risk but potentially different causal pathways to type of anxiety disorder.

The presence of anxiety in a large proportion of individuals with a specific syndrome, where predictive characteristics often have relative stability, affords the opportunity to determine causal pathways to anxiety (Oliver et al., 2020). The noise related phobias frequently reported in Williams syndrome (e.g., sounds such as sirens) for example, are associated with hyperacusis, indicating likely classical conditioning of fear responses (Gothelf et al., 2006; Royston et al., 2017). Conversely, current health difficulties have been found to be predictive of broader psychopathology in Williams syndrome. These psychological, biological mechanisms, and possible interactions, indicate the value of examining syndrome associated genetic factors and gene disorder-phenotype-environment interactions. Such an approach also has the potential to inform causal models of anxiety more generally and has implications for the general population by identifying candidate genetic risk markers for anxiety vulnerability. In Williams syndrome, lower social anxiety has been associated with the deletion of gene, GTF2I (Dykens, 2003; Klein et al., 1990; Procyshyn et al., 2017; Royston et al., 2017). This has broader relevance because in the general population, variations in GTF2I are associated with social anxiety (Jabbi et al., 2015; Procyshyn et al., 2017; Swartz et al., 2017).

It is clear therefore that anxiety is common and disabling in people with ID and that syndromic ID appears to be associated with the clinical course and presentation of anxiety. Collating and evaluating information on risk and profiles of anxiety across syndromes is likely to inform clinical practice and identify useful group contrasts for future research. To date, one meta-analysis has investigated mental health difficulties across syndromes, reporting anxiety prevalence of 38% in 22q11.2 deletion and 42% in FXS (Glasson et al., 2020). The remaining analyses focused on general psychiatric symptoms, without a focus on anxiety. To date, no study has investigated the prevalence of anxiety symptomatology and diagnosis, including specific anxiety profiles, across syndromes in children and adults, while accounting for methodological quality of studies explored.

There are significant challenges when assessing mental health within the ID population that can impinge on the quality of research. Individuals with ID may have significant communication difficulties, hindering self-report (Hagopian & Jennett, 2008). Other factors that complicate the assessment of mental health difficulties are diagnostic overshadowing, a lack of validated measures developed specifically for individuals across varying levels of ID and the heavy reliance on proxy report, which may lead to misattribution of behaviours (Emerson et al., 2013; Flynn et al., 2017; Hagopian & Jennett, 2008). These challenges mean the quality of the literature should be examined, to weight and then synthesise the findings.

Therefore, the aim of this study was to systematically review the prevalence of anxiety symptomatology and diagnosis, and types of anxiety across syndromes associated with ID. Due to identified challenges of mental health assessment in individuals with ID, studies were included that explored anxiety symptomatology, taking an over inclusive approach to the literature. A scoping search was used to select syndromes included in the review by combining search terms for ID, syndrome, and anxiety in a database search.
The specific study aims were to:

i) Synthesise data from the existing literature and calculate pooled prevalence estimates of anxiety symptomatology and diagnosis across syndromes, while accounting for the methodological quality of included studies
ii) Complete subgroup and meta-regression analyses to explore methodological factors and their potential influence on anxiety prevalence
iii) Compare pooled prevalence estimates across syndromes with previously reported prevalence estimates from the general population and individuals with ID of mixed aetiology

2.3 Methods

The current study is a systematic review and meta-analysis, completed according to PRISMA guidelines (Moher et al., 2009). Methodology and analysis details were documented in a PROSPERO protocol prior to completion of this review (CRD42019123561).

2.3.1 Scoping search

A scoping search was conducted to identify syndromes to be included in this review. The search was completed using search terms for ID, syndrome, and anxiety to provide a ‘snapshot’ of available literature (See Appendix 1). The search terms were generated based on previous reviews (Dagnan et al., 2018; Kaur et al., 2017; Royston et al., 2017). A syndrome was included in the review if there was at least one empirical study identified

reporting anxiety prevalence during the scoping search. The current review did not endeavour to explore all possible syndromes associated with ID and anxiety, and therefore the scoping search was used to systematically narrow the review focus and ensure a manageable synthesis of the literature was completed relating to a selection of specific syndromes.

The scoping search was completed on Web of Science (all years, all databases) on 5th December 2018 resulting in 1,632 papers. The full text of papers were screened to identify studies where prevalence of anxiety had been reported in a sample of individuals with a syndrome associated with ID. GeneReviews; an expert-written, peer-reviewed, international resource, was also consulted to identify any syndrome that may not have been identified in the scoping search. 31 syndromes were identified during the scoping search (see Appendix 1). Although identified in the scoping search with empirical studies reporting anxiety prevalence, Williams syndrome was not included due to the completion of a recent systematic review and meta-analysis at the time that the current review was conceptualised (Royston et al., 2017). GeneReviews identified Tuberous Sclerosis Complex (TSC) as a condition associated with ID and anxiety, no further syndromes were identified. Therefore, eight syndromes were deemed appropriate for inclusion in the current review; fragile X (FXS), Tuberous Sclerosis Complex (TSC), 22q11.2 deletion, Down (DS), Rett (RS), CHARGE, 7q11.23 duplication and 3q29 deletion syndromes.

2.3.2 Search strategy and selection criteria

Individual searches were completed with search terms for each syndrome and anxiety search terms used in the scoping search (see Appendix 1). Searches were completed on Web of Science, Ovid PsycINFO, Ovid Embase and CINAHL Plus with no restriction on year of publication, up to mid 2019. All syndromes involve gene disorders that were not discovered until fairly recently (1959-2005). Syndrome search terms were selected based on a previous meta-analysis (Richards et al., 2015). For syndromes identified in the scoping search not included in the previous review, search terms were selected from Genetics Home Reference, an expert-reviewed online resource and GeneReviews was also consulted to identify additional synonyms.

Returned papers were assessed for inclusion with an independent second rater (Dr Rachel Royston, PhD). A training phase of screening was completed with the first 50 abstracts screened and discrepancies discussed. A further 100 abstracts were screened, where consensus was obtained (Polanin et al., 2019). Following this, the study selection process was completed with the author screening 82% (24,914) and the second rater screening 38% (11,594) of total papers. For stage one screening, papers were screened by review of titles and abstracts using predefined criteria (see Table 2.1). In line with similar reviews, inter-rater reliability was established on 20% (6,091) of total papers, with substantial

agreement achieved between the author and the second rater (Kappa =.91) (Flynn et al., 2017; Tough et al., 2017). Where there were discrepancies regarding inclusion at stage one, an over inclusive approach was adopted, and studies included to ensure relevant studies were not missed.

The full texts of articles included at stage one were screened to assess inclusion at stage two where additional criteria were deployed (see Table 2.1). In line with previous reviews, studies were included if they reported a prevalence of anxiety symptomatology (e.g., cut off on the Child Behaviour Checklist; Achenbach & Rescorla, 2001) or anxiety diagnosis (e.g., DSM/ICD criteria) (Buckles et al., 2013; Buckley et al., 2020; Green et al., 2015). At stage two, substantial inter-rater reliability was established between the author and the second rater (Kappa =.73). To resolve discrepancies of inclusion at stage two, a third independent rater (Dr Jane Waite, PhD, ClinPsyD) was consulted, and a consensus reached.

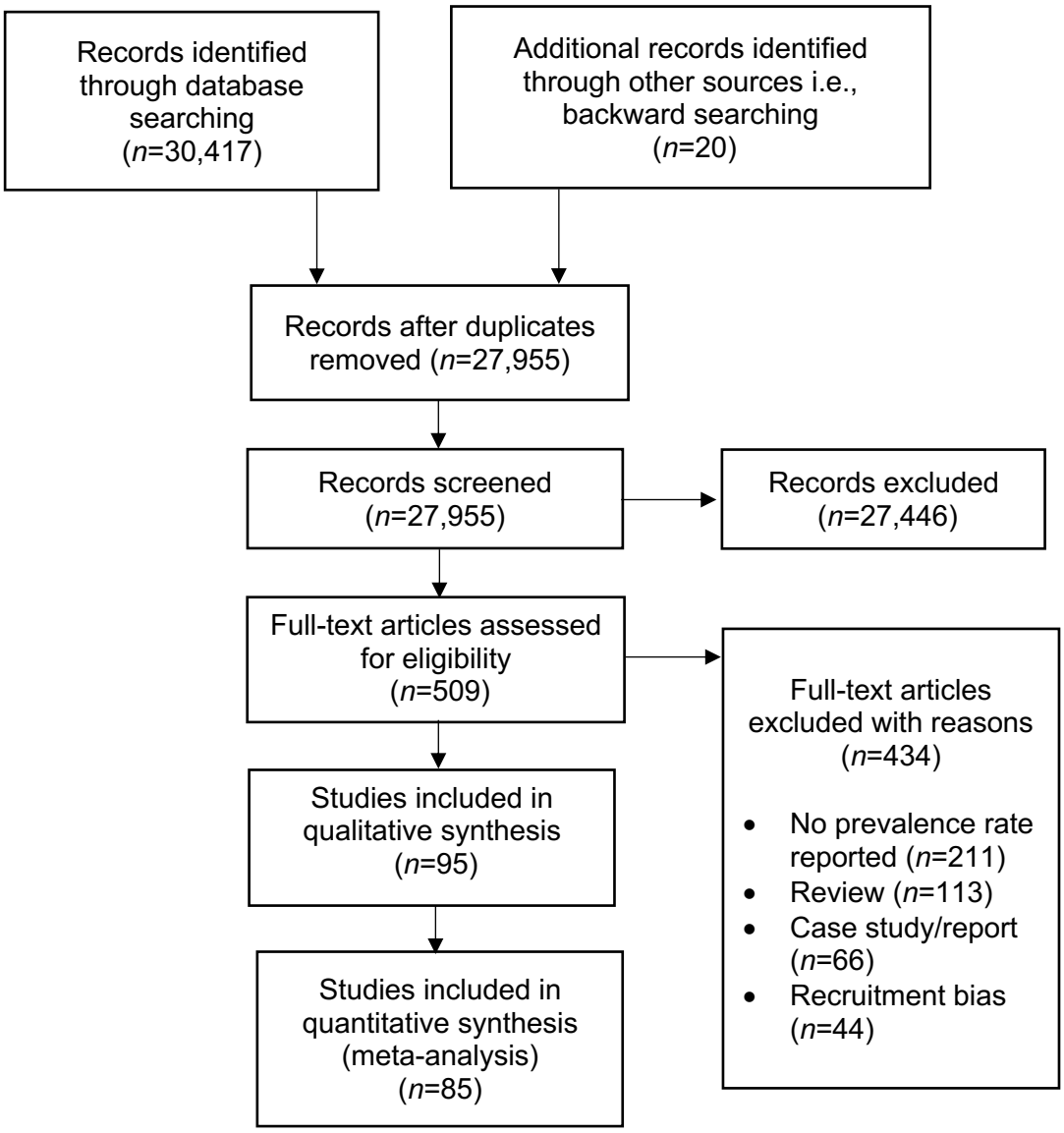
Table 2.1 Inclusion and exclusion criteria for stage 1 and stage 2 screening of papers

Stage one screening	
Inclusion criteria	**Exclusion criteria**
Studies including individuals with a given syndrome	Non-human studies
Studies that mention psychopathology/mental health/socio-emotional factors in abstract	Conference abstracts/papers, book chapters, patents, letters, editorial material, notes, brief reports
Studies published in English	Studies focusing on other genetic problems related to syndrome e.g., being a carrier of the syndrome/premutation in Fragile X syndrome
Studies published in peer reviewed journals	Studies focusing only on parental mental health
Stage two screening	
Inclusion criteria	**Exclusion criteria**
Studies reporting anxiety prevalence rates (e.g., any anxiety disorder, specific phobia, social anxiety disorder, panic disorder with/without agoraphobia, separation anxiety disorder, generalised anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder, selective mutism)	Reviews
	Case studies or series
	Studies with specific recruitment/eligibility bias (e.g., psychiatric clinic)
	Studies with identified identical samples[1]

[1]No studies had identified identical samples

Following screening, the author and a fourth independent rater (Dr Effie Pearson, PhD) completed backward searching of reference lists of included studies, identifying an additional 20 papers (see Figure 2.1).

Figure 2.1 PRISMA diagram detailing study selection. See Appendix 1 for further information.



2.3.3 Data extraction and quality assessment

All studies were then evaluated against quality rating criteria adapted from a previous meta-analysis (Royston et al., 2017; See Appendix 2). The quality rating tool was developed by Richards et al. (2015) specifically for exploring prevalence data across syndromes associated with ID. Literature reviews and consultation from active research experts

informed the development of the idiosyncratic quality criteria to highlight key areas of methodological concern; these evaluated sample identification, confirmation of syndrome diagnosis and method of anxiety assessment. Richards et al.'s (2015) criteria were deemed the most appropriate to assess quality of included studies due to the focus on methodological issues and key threats to validity that are specific to the genetic syndrome field. Training was received from the primary author who developed the rating tool (C, Richards; Richards et al., 2015) to ensure the quality criteria were used as developed and intended.

There was no minimum quality rating needed for inclusion in the current meta-analysis to prevent large samples with valuable data being excluded and to ensure that the analysis was a comprehensive review of available literature for each syndrome. To account for this, analyses were conducted to identify any potential influence of methodological quality on the overall effect and therefore, those of poorer quality rated studies. Furthermore, 59% (49) of studies obtained a 'good' rating for sample identification, suggesting the data were obtained from representative samples.

Each study was given a rating on a scale from poor to excellent (0-3) for the three areas of methodological concern: sample identification, confirmation of syndrome diagnosis and method of anxiety assessment. Scores of 0 were given to studies that did not specify, report or relied solely on parent report for the areas of interest in the quality criteria, while scores of 3 were given to studies that utilised random samples, completed genetic confirmation of syndrome diagnosis and obtained consensus from multiple assessments of anxiety. The quality weighting was calculated by dividing the total quality ratings for each study by the maximum score of nine. A traffic light colour coding system was used to visually present quality ratings (See Appendix 2). The author quality rated all studies while the fourth independent rater (Dr Effie Pearson, PhD) quality rated 26% (22) of studies, establishing substantial inter-rater reliability (Kappa=.74). The reported number and percentage of participants experiencing anxiety were extracted from each paper and checked independently.

2.3.4 Data analysis

Data analysis was conducted utilising the meta-analysis strategy of the Centre for Applied Psychology, University of Birmingham. Analysis was calculated using the 'Metafor' package for R, version 3.6.2. For each study, variables were extracted (e.g., age, sex, anxiety measure) with the reported anxiety prevalence, including specific anxiety profiles, to generate pooled prevalence estimates (See Appendix 3).

Decisions about inclusion of studies that reported an event rate of 0 were made on a case-by-case basis due to variation of study quality across syndromes. The study was either removed from further analysis due to the likelihood of the failure to detect an effect (i.e., in

small samples) or a continuity correction of 0.5 was added to the event rate to avoid division by zero errors (Cheng et al., 2016; Higgins et al., 2019). The continuity correction was applied only if the study sample size was considered to be sufficient to make a valid estimation of anxiety prevalence. Two papers reported an event rate of 0 with sample sizes of 14 and 371; the former was removed while the latter was retained with a continuity correction applied (Collacott et al., 1992; Way & Rojahn, 2012).

Pooled prevalence estimates were generated using a random-effects model, as opposed to the fixed-effects model, as the former considers variation between studies and does not assume a common effect size (Hedges & Vevea, 1998; Tufanaru et al., 2015). The quality-effects model was implemented to account for quality ratings for each study (Barendregt et al., 2013; Detsky et al., 1992; Doi and Thalib, 2008). The random and quality-effects estimates were plotted to allow comparison across syndromes (see Figure 2.2).

To identify influential studies impacting the overall meta-analytic effect, a Baujat chart was used (See Appendix 4) (Baujat et al., 2002). A Baujat chart is a graphical method used to identify studies that are heterogeneous, a 'leave-one-out' procedure is used to portray the change in the overall effect when each study is removed, one at a time, against the contribution of each study to the overall heterogeneity. This procedure allows us to explore how each individual study affects the overall prevalence estimate (Viechtbauer & Cheung, 2010). If omitting a study results in an effect outside the 95% CI for the meta-analytic synthesis with all studies included, then that study is deemed to have a disproportionate influence on the overall effect and is removed from subsequent analysis (Steenfeldt-Kristensen et al., 2020). Higgins I^2 was used as a measure of heterogeneity to explore inconsistency between study findings (Higgins et al., 2003).

To explore the impact of study level characteristics on anxiety prevalence, planned a priori subgroup analyses were conducted exploring quality ratings and outcome type (i.e., behavioural/psychiatric report of anxiety). Outcome type was chosen as a potential moderator as prevalence may differ when exploring behavioural vs. psychiatric report of mental health symptomatology in individuals with ID (Buckley et al., 2020). Reliance on psychiatric assessment and/or diagnosis may lead to the underestimation of anxiety due to the identified challenges when assessing individuals with ID, behavioural reports may ensure that anxiety is not missed due to individuals not meeting psychiatric criteria (Bertelli et al., 2015). Meta-regression analyses explored the impact of year of publication and sample size.

2.4 Results

30,417 papers were identified through database searching and 85 papers, across eight syndromes, were included in the meta-analysis (See Figure 2.1; see Appendix 1). From use of the Baujat chart, two studies were re-reviewed and subsequently excluded due to

identified bias, resulting in a final 83 papers, totalling 13,708 participants (See Appendices 3 and 4). Characteristics for each included study are presented in Appendix 3.

2.4.1 Prevalence of anxiety

The prevalence of anxiety ranged from 9% (95% CI 4-14) in individuals with DS to 73% (95% CI 70-77) in individuals with RS (See Table 2.2; Figure 2.2). See Figures 2.3, 2.4, 2.5 and 2.6 for a subset of forest plots documenting the prevalence of anxiety across FXS, 22q11.2 deletion, TSC and CHARGE syndromes respectively. The remaining forest plots are presented in Appendix 3.

Table 2.2 Quality ratings for each syndrome and pooled prevalence estimates for anxiety

	Studies[2]	Patients (n)	Mean quality weighting	Individual scores			Quality weighting score[3]			Prevalence of anxiety	
				Score of 3 for sample	Score of 3 for syndrome confirm-ation	Score of 3 for anxiety assess-ment	Poor	Adequate	Good	Random-effects pooled prevalence	Quality-effects pooled prevalence
Fragile X syndrome	19	3882	0·53 (0·12)	0	4 (21%)	0	9 (47%)	8 (42%)	2 (11%)	49% (39-60)	48% (38-59)
Fragile X syndrome (boys and men only)	7	1214	0·53 (0·11)	0	0	0	2 (29%)	5 (71%)	0	43% (23-62)	42% (22-62)
22q11.2 deletion syndrome	34	2272	0·63 (0·13)	0	10 (29%)	8 (24%)	7 (21%)	18 (53%)	9 (26%)	38% (32-45)	40% (33-46)
Down syndrome	11	2152	0·41 (0·17)	0	0	1 (9%)	8 (73%)	2 (18%)	1 (9%)	8% (4-13)	9% (4-14)
Tuberous sclerosis complex	8	6494[4]	0·37 (0·12)[5]	0	0	1 (13%)	10 (91%)	1 (9%)	0	16% (9-22)[6]	14% (7-21)
Rett syndrome	6	676	0·40 (0·06)	0	0	0	6 (100%)	0	0	74% (71-78)	73% (70-77)

[2] Based on 83 studies across syndromes due to the exclusion of 2 studies that were identified as highly discrepant and heterogeneous.
[3] Categories based on quality weighting score of poor (0.33-0.55), adequate (0.56-0.77) and good (0.78-1.0).
[4] Number of participants based on 8 studies with 3 studies reporting both a behavioural and psychiatric prevalence of anxiety. Therefore, the total number of participants is inflated due to overlap of participants within the 3 studies reporting multiple anxiety prevalence rates.
[5] Mean quality weighting and categories of quality weighting scores also based on 11 reported rates.
[6] Prevalence of anxiety based on 11 reported rates. Behavioural prevalence of anxiety based on 4 reports of 2525 participants; psychiatric prevalence of anxiety based on 7 reports of 3969 participants. Behavioural prevalence was significantly higher than psychiatric prevalence (25% and 10% respectively; p=0.0289).

CHARGE syndrome	2	140	0·17 (0·08)	0	0	0	2 (100%)	0	0	32% (7-57)	37% (10-64)
7q11.23 duplication syndrome	2	178[7]	0·44 (0·12)[8]	0	1 (50%)	0	2 (67%)	1 (33%)	0	72% (65-78)[9]	70% (63-77)
3q29 deletion syndrome	1	42	0·33	0	0	0	1 (100%)	0	0	19% (7-31)	19% (7-31)

[7] Number of participants based on 2 studies with 1 study reporting both a behavioural and psychiatric prevalence of anxiety. Therefore, the total number of participants is inflated due to overlap of participants in 1 study reporting multiple anxiety prevalence rates.
[8] Mean quality weighting and categories of quality weighting scores based on 3 reported prevalence rates.
[9] Prevalence of anxiety based on 3 reported rates. Behavioural prevalence of anxiety based on 1 report of 53 participants; psychiatric prevalence of anxiety based on 2 reports of 125 participants. Behavioural prevalence was not significantly different than psychiatric prevalence (72% and 71% respectively; p=0.9715).

Figure 2.2 Pooled prevalence estimates for anxiety across syndromes

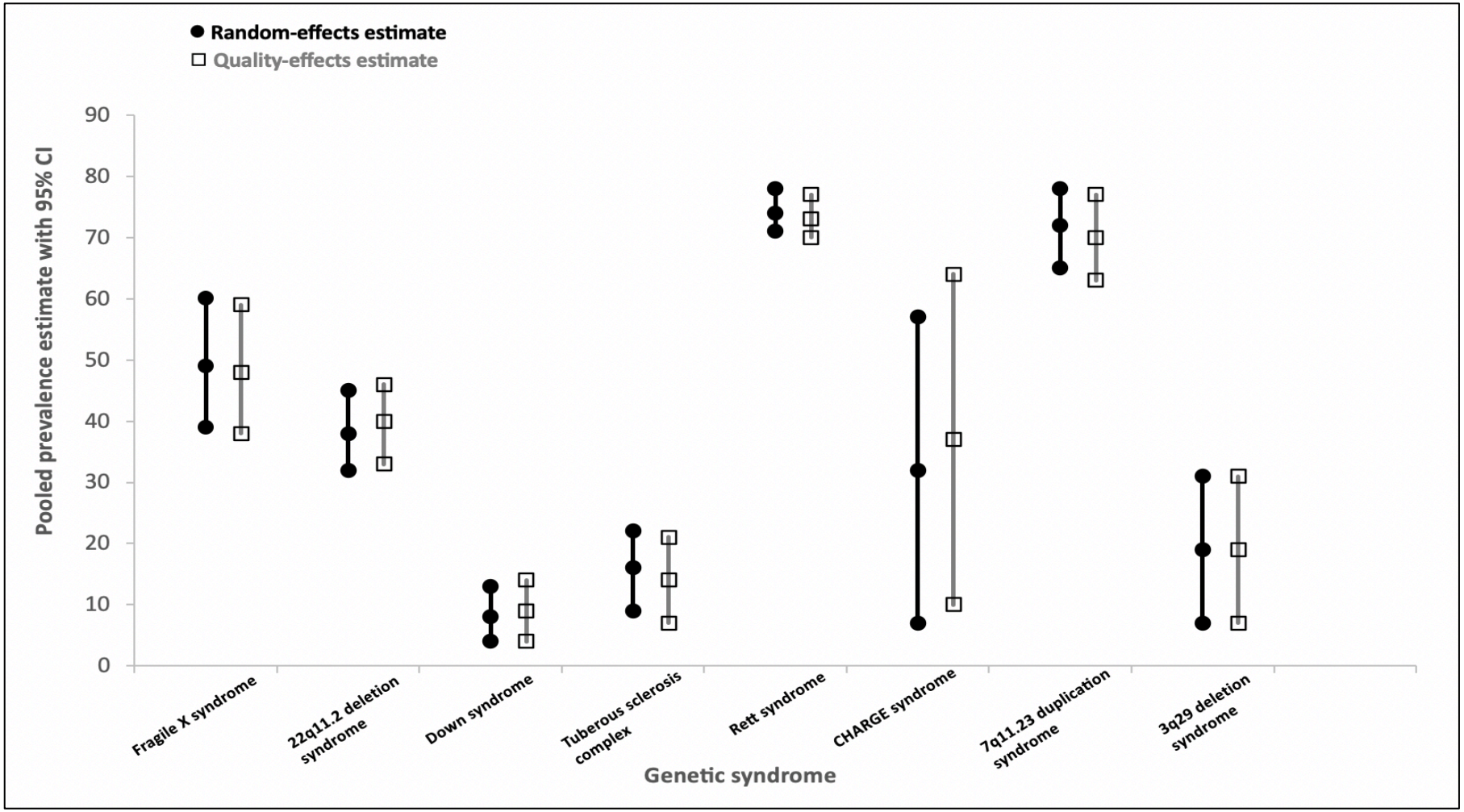


Figure 2.3 Forest plot for anxiety in Fragile X syndrome using a random-effects model.

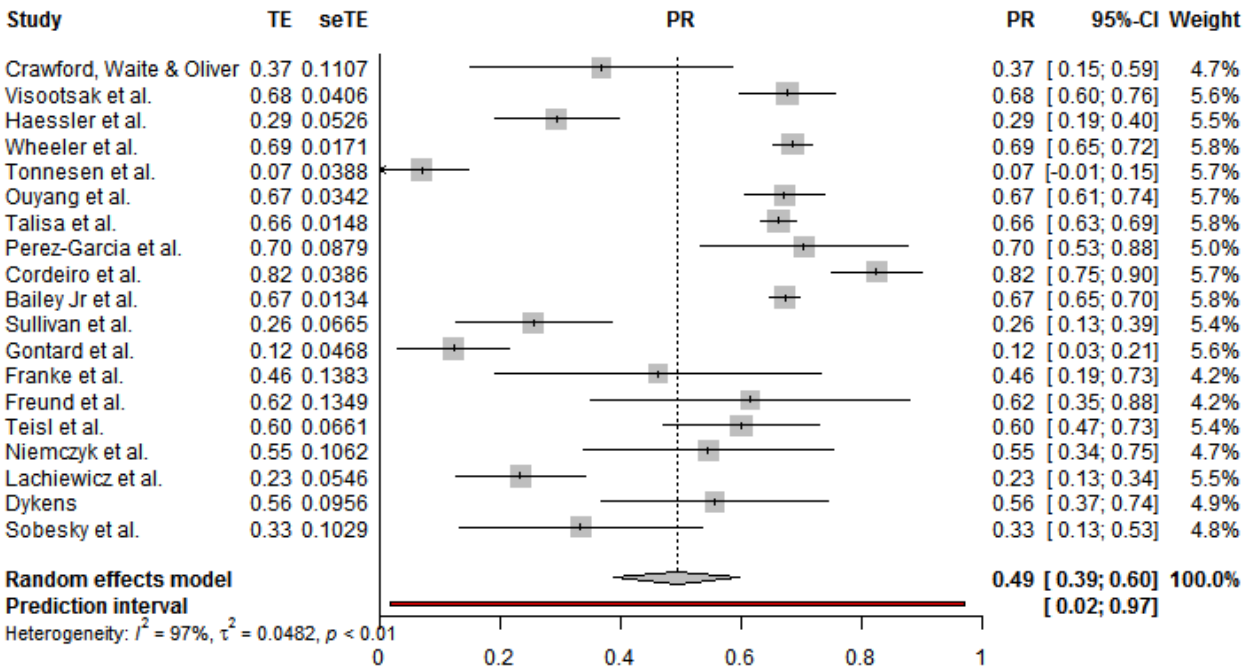


Figure 2.4 Forest plot for anxiety in 22q11.2 deletion syndrome using a random-effects model.

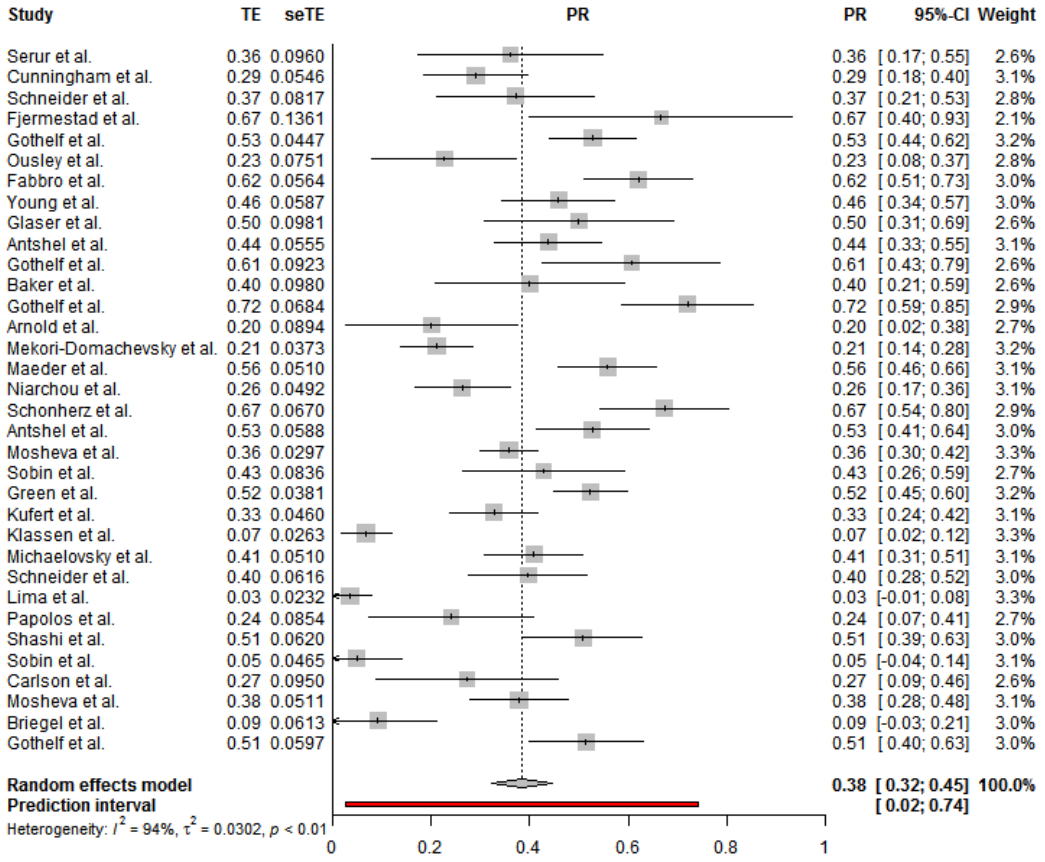


Figure 2.5 Forest plot for anxiety in Tuberous Sclerosis Complex using a random-effects model (final analysis with removal of Smalley).

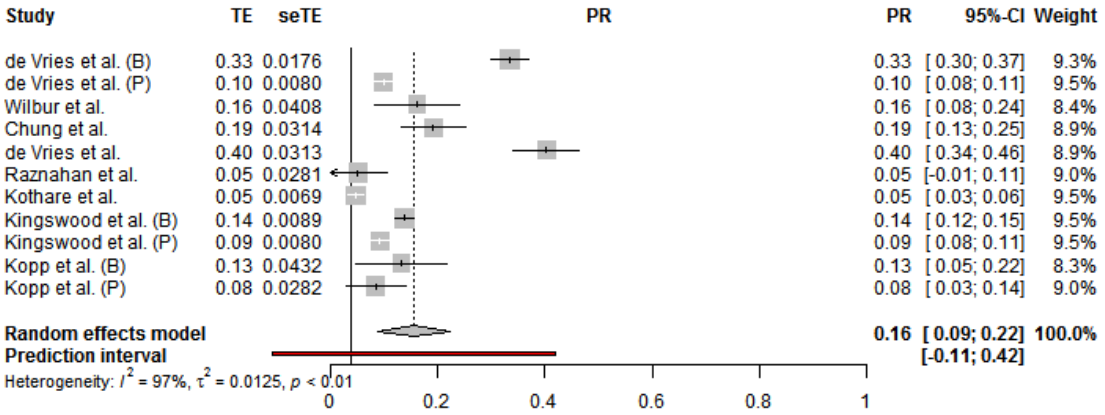
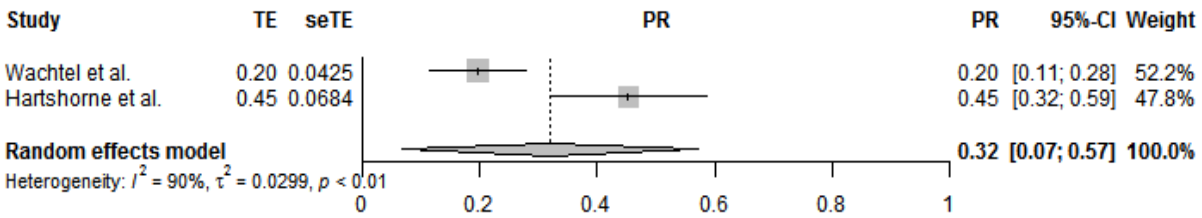


Figure 2.6 Forest plot for anxiety in CHARGE syndrome using a random-effects model.



No studies obtained the highest quality rating for sample identification. 15 (17.6%) studies obtained the highest quality rating for syndrome confirmation whilst ten (11.8%) obtained the highest quality rating for anxiety assessment. The 'leave-one-out' procedure indicated that across syndromes, no one study had a disproportionate effect on the pooled prevalence estimates of anxiety and so all studies were retained. A marked level of heterogeneity (Higgin's I^2=>75%) between reported prevalence rates was identified in five syndromes, suggesting that these analyses were biased by uncontrolled or confounding factors.

2.4.2 Subgroup analyses

Consistent with previous literature, subgroup analyses were conducted on three syndromes where there were ten studies or more (Richardson et al., 2019). Firstly, subgroup analyses were conducted on the quality ratings of studies (See Appendix 3). For 22q11.2 deletion syndrome, papers rated as 'poor' for anxiety assessment reported significantly lower anxiety prevalence than papers rated as 'good' (13% vs. 42% respectively; p<0.0001). For DS, papers rated as 'poor' on sample identification reported significantly higher anxiety prevalence than papers rated as 'good' (16% vs. 7% respectively; p=0.0532). Additionally, papers rated as 'poor' for anxiety assessment also reported significantly higher anxiety prevalence than papers rated as 'good' for DS (9% vs. 3% respectively; p=0.0235; See Appendix 3).

Secondly, subgroup analyses were conducted based on outcome type. For 22q11.2 deletion syndrome, behavioural reports of anxiety were significantly lower than psychiatric reports (5% vs. 42% respectively; p<0.0001). For DS, behavioural reports of anxiety were significantly higher than psychiatric reports of anxiety (25% vs. 7% respectively; p=0.0011; See Appendix 3).

2.4.3 Meta-regression analyses

Meta-regression analyses were conducted to explore the potential impact of year of publication and sample size on anxiety prevalence. Analyses found no significant differences in the estimated prevalence of anxiety, except for DS where, as the number of participants increased, the estimated prevalence of anxiety decreased (p=0.0004).

2.4.4 Specific anxiety symptomatology/diagnosis prevalence

Across syndromes, there were 42 studies that also reported specific anxiety profiles. There were eight additional studies that did not report 'any anxiety' prevalence but did report specific anxiety profiles, totalling 50 studies across the eight included syndromes (See Appendix 5). Pooled prevalence estimates ranged from 1% to 52% (See Appendix 5). High rates of specific phobia were evident for individuals with FXS, 22q11.2 deletion and 7q11.23 duplication syndromes (52%, 28%, 50% respectively). Social anxiety was common in FXS

and 7q11.23 duplication syndromes (28% and 51% respectively). Additionally, for FXS, physical injury fears and PTSD were noted (37% and 32% respectively). High rates of OCD were found in CHARGE syndrome (35%) and separation anxiety in 7q11.23 duplication syndrome (16%). Selective mutism was reported in 7q11.23 duplication and Down syndrome (29% and 6% respectively) whilst panic attacks were common in 3q29 deletion syndrome (29%). A high level of heterogeneity (Higgin's I^2=>75%) was identified in four syndromes suggesting that these analyses were biased by uncontrolled or confounding factors.

2.4.5 Subgroup analyses for specific anxiety symptomatology/diagnosis

Only 22q11.2 deletion syndrome had a sufficient number of studies to conduct subgroup analyses (Richardson et al., 2019). Analyses were conducted for specific phobia (SP), social anxiety (SA), generalised anxiety (GAD), separation anxiety (SAD) and OCD. For SP, papers rated as 'good' for sample identification had significantly higher anxiety prevalence than those rated as 'poor' (34% vs. 18% respectively; p=0.0045). Papers rated as 'good' for syndrome confirmation had significantly higher anxiety prevalence than papers rated as 'poor' (31% vs. 5% respectively; p<0.0001). For GAD, papers rated as 'good' for syndrome confirmation had significantly lower anxiety prevalence than papers rated as 'poor' (12% vs. 32% respectively; p=0.0372). For SAD, papers rated as 'good' for sample identification had significantly higher anxiety prevalence than papers rated as 'poor' (8% vs. 4% respectively; p=0.0187). All papers reported a psychiatric prevalence of anxiety, so analyses concerning outcome type were not conducted.

2.4.6 Meta-regression analyses for specific anxiety symptomatology/diagnosis

There were no significant differences for meta-regression analyses concerning year of publication and sample size on the prevalence of specific anxiety profiles in 22q11.2 deletion syndrome (See Appendix 5).

2.4.7 Comparison to general and ID population estimates

Finally, prevalence estimates for syndromes were compared to general and ID of mixed aetiology population estimates (See Table 2.3). These comparison estimates report psychiatric prevalence of anxiety while the current review includes studies that report the prevalence of anxiety symptomatology; therefore, it is important to apply caution when comparing prevalence rates across studies. Despite this, 80% (66) of studies in the current review reported a psychiatric prevalence of anxiety. Additionally, where subgroup analyses were completed comparing outcome type, the estimates for psychiatric prevalence of anxiety alone were still higher across syndromes than that reported for the general and ID of mixed aetiology populations.

In terms of specific anxiety profiles, meta-analytic studies, population-based studies, or the most recent study with the largest sample size known were used for comparison to the

estimates for specific anxiety diagnoses across syndromes. FXS, 22q11.2 deletion and 7q11.23 duplication syndromes had particularly high prevalence estimates compared to the general and ID of mixed aetiology populations (See Table 2.3 and Appendix 5).

Table 2.3 Prevalence rate estimates of anxiety for the general population and intellectual disability of mixed aetiology populations

	General population estimate for children/adolescents	General population estimate for adults	Intellectual disability estimate based on children and adolescents[10]	Intellectual disability estimate based on adults
Anxiety	3.2%[11]	3.86%[12]	5.4%	5.5%[13]
Specific phobia	0.8%[14]	7.4%[15]	11.5%	13.3%[16]
Social anxiety disorder	0.8%	4%[17]	2.7%	0.3%
Generalised anxiety disorder	1.5%	3.7%[18]	2.2%	1.7%
Separation anxiety disorder	0.7%	4.8%[19]	5%	N/A[20]
Obsessive-compulsive disorder	0.4%	2.3%[21]	2.4%	4%[22]
Post-traumatic stress disorder	0.6%	3.9%[23]	1.1%	0.3%

[10] Any anxiety disorder and specific anxiety disorder prevalence rates based on reports from Maïano et al., 2018
[11] Any anxiety disorder prevalence rate based on Erskine et al., 2017
[12] Any anxiety disorder prevalence rate based on James et al., 2018 (GBD 2017), based on all ages
[13] Any anxiety disorder prevalence rate based on Mazza et al., 2020. Specific anxiety disorder prevalence rates based on reports from Reid et al. (2011) except reported prevalence rates for OCD and specific phobia
[14] Remaining specific anxiety disorders based on Sadler et al., 2018 except for Panic disorder with and without agoraphobia
[15] Specific phobia prevalence rate from Wardenaar et al., 2017
[16] Specific phobia prevalence rate from Hove & Havik, 2008
[17] Social anxiety disorder prevalence rate from Stein et al., 2017
[18] Generalised anxiety disorder prevalence rate from Ruscio et al., 2017
[19] Separation anxiety disorder prevalence rate from Silove et al., 2015
[20] The removal of the age-of-onset criterion (before 18 years of age) for separation anxiety disorder in DSM-5, allows the diagnosis of separation anxiety experienced across the lifespan. Perhaps due to this recent change, there were no identified studies that explored the prevalence of separation anxiety disorder in adults with intellectual disability
[21] OCD prevalence rate from Ruscio, Stein, Chiu & Kessler, 2010
[22] OCD prevalence rate from Schützwohl et al., 2016
[23] PTSD prevalence rate from Koenen et al., 2017

Agoraphobia	0.5%	1.5%[24]	0.6%	0.7%
Panic disorder	1.1%	1.7%	0.3%	0.2%
Panic disorder with agoraphobia	0.8%[25]	0.3%	0.4%	0.2%
Panic disorder without agoraphobia	0.8%	1.2%	0.2%	0%
Selective mutism	0.18%[26]	N/A[27]	N/A[28]	N/A[29]

[24] Agoraphobia and panic disorder prevalence rates for general population estimate for adults from Roest et al., 2019
[25] Prevalence rate for panic disorder with and without agoraphobia based on Reed & Wittchen, 1998
[26] Reported prevalence rate from Sharkey & McNicholas, 2012
[27] No identified study reporting prevalence of selective mutism in a general population sample of adults as it is usually diagnosed during childhood (DSM-5; American Psychiatric Association, 2013).
[28] No identified study reporting prevalence of selective mutism in children with intellectual disability
[29] No identified study reporting prevalence of selective mutism in adults with intellectual disability as it is usually diagnosed during childhood (DSM-5; American Psychiatric Association, 2013).

2.5 Discussion

This is the first systematic review and meta-analytic study to document the prevalence of anxiety and types of anxiety diagnosis across syndromes associated with ID, whilst accounting for methodological quality of included studies. The prevalence of anxiety was notably high in Rett (73%), 7q11.23 duplication (70%) fragile X (48%), 22q11.2 deletion (40%), CHARGE (37%), 3q29 deletion (19%) syndromes and Tuberous Sclerosis Complex (14%), with the lowest prevalence in Down Syndrome (9%). It is striking that all syndrome prevalence estimates were higher than reports from general and ID of mixed aetiology populations (4% and 5% respectively; James et al., 2018; Maïano et al., 2018; Mazza et al., 2020). These estimates indicate the importance of clinicians knowing the cause of ID to inform risk of a specific, common, and treatable mental health problem.

There is concordance between the results of this review and meta-analysis and the results of reviews of single syndromes. Gold et al. (2018) reported that anxiety is notably common in RS, although there are very few research studies confirming anxiety prevalence. The high prevalence reported in 7q11.23 duplication syndrome is consistent with a previous review for that syndrome (Velleman & Mervis, 2011) and the prevalence estimates of 40% for 22q11.2 deletion syndrome and 48% for FXS are each consistent with previous meta-analyses for these syndromes (Glasson et al., 2020). Published estimates of prevalence rates for CHARGE syndrome are consistent with the 37% estimate from the current study but the comparatively large confidence intervals indicate the need for further research (Kennert et al., 2020; Souriau et al., 2005). Since the completion of the current study, two larger studies of 3q29 deletion syndrome have reported a higher anxiety prevalence rate of 28% compared to 19% in the current study based on a single estimate (Pollak et al., 2019, 2020). Anxiety is a known problem experienced by individuals with TSC, with variability depending on whether prevalence of anxiety symptomatology or diagnosis is considered (de Vries et al., 2018). Research investigating the prevalence of anxiety in DS is limited. However, individuals seem to be at lower risk of mental health difficulties and disorders (with the exception of dementia) than other ID groups, but at higher risk than the general population. This pattern was evident in the current review (Dykens, 2007; Glasson et al., 2020; Vicari et al., 2013). The concordance between the results of this study and published reviews supports the validity of the review methodology and meta-analytic strategy.

Similarly, for profiles of specific anxiety diagnoses, our findings are consistent with previous literature. For FXS, specific phobia and social anxiety were common (Cordeiro et al., 2011; Crawford et al., 2017; Ezell et al., 2019; Gabis et al., 2011; Groves et al., 2018). For 22q11.2 deletion syndrome, specific phobia had the highest prevalence rate and OCD was common in CHARGE syndrome (Bertrán et al., 2018; Blake et al., 2005; Jolin et al.,

2012; La Spata, 2019). Individuals with 7q11.23 duplication syndrome experience social anxiety, separation anxiety, specific phobia, and selective mutism (Abbas et al., 2016; Mervis et al., 2012). Panic attacks may be experienced in 3q29 deletion syndrome and selective mutism in Down syndrome (Pollak et al., 2019, 2020). It is striking to note the lack of research focusing on the presentation of trauma and post-traumatic-stress disorder (PTSD) in genetic syndrome populations. There is evidence of increased prevalence in ID populations more generally which may be explained by the risk of abuse and negative life events that ID populations are at risk of experiencing (Daveney et al., 2019; Dion et al., 2018). However, the current study indicated very low rates of PTSD in the ID population (1.1% for children and adolescents; 0.3% for adults, see Table 2.3). Changes to the conceptualisation of PTSD from within the anxiety disorder category (DSM-IV) to trauma and stressor-related disorders (DSM-5) may have impacted the studies identified in the current study. There is also evidence to suggest that ICD-11 identifies fewer individuals meeting criteria for PTSD compared to ICD-10 (Barbano et al., 2019). However, there is an identified need for further research focusing on the assessment and intervention within ID populations, including those with a genetic syndrome diagnosis (Daveney et al., 2019; Fjermestad et al., 2015; McNally et al., 2021). Increased risk of trauma and PTSD has implications for intervention delivery, such as ensuring services are trauma-aware and developing trauma-informed care pathways to intervention (Rich et al., 2021; Truesdale et al., 2019).

It is important to note that the specific anxiety profile findings should be interpreted with caution due to the majority of analyses (81%) including five studies or less, with studies less likely to explore specific anxiety profiles than anxiety more generally. This could preclude the identification of syndrome specific anxiety profiles and therefore may hinder effective intervention development.

However, the studies that did report specific anxiety profiles clearly indicate the presence of specific and divergent profiles of anxiety diagnosis that allude to syndrome associated causal pathways or gene disorder-phenotype-environment interactions that are syndrome related. This highlights the importance of exploring environmental, cognitive, emotional, and psychophysiological correlates of anxiety diagnoses that might indicate likely drivers of the development and maintenance of anxiety within syndromes. Previous studies of anxiety in Williams syndrome demonstrate this strategy, whereby high rates of generalised anxiety and specific phobia including noise stimuli, blood and injury are found (Gothelf et al., 2006; Royston et al., 2017). These specific diagnoses have been linked to phenotypic features of Williams syndrome such as hyperacusis and regular medical intervention due to complex physical health difficulties (Morris et al., 2020; Royston et al., 2017). For clinicians, there are implications for delivering preventative and responsive interventions that might target specific anxiety diagnoses differentially across syndromes.

For example, the treatment of phobias differs from that for generalised anxiety; the former focuses on gradual exposure techniques whilst the latter on cognitive-behavioural strategies (Maskey et al., 2014; McConachie et al., 2014).

Due to the varying levels of anxiety highlighted across syndromes in this review, it is important to consider the risk factors that could contribute to increased level of risk. Two syndromes with the highest prevalence rates, RS and 7q11.23 duplication syndrome have high levels of autism characteristics, noted sensory processing and physical health difficulties which could contribute to increased risk of anxiety (Cianfaglione et al., 2015; Klein-Tasman & Mervis, 2018; Lotan & Ben-Zeev, 2006; Morris et al., 2015; Richards et al., 2015; Velleman & Mervis, 2011). These characteristics are also noted in other syndromes included in the review such as FXS, 22q11.2 deletion and CHARGE syndromes (Giardino et al., 2014; Kidd et al., 2014; Rais et al., 2018; Richards et al., 2015; Slavin & Hartshorne, 2021). Section 3.2 reviews existing literature exploring risk markers of anxiety, highlighting the importance of considering risk markers that may impact anxiety prevalence across groups.

The subgroup analyses of individual syndromes revealed that for 22q11.2 deletion syndrome, anxiety symptomatology prevalence was significantly lower than psychiatric prevalence while the opposite was true for DS. One interpretation of this is that relying only on report of anxiety symptomatology for 22q11.2 deletion syndrome may underestimate anxiety prevalence. As 22q11.2 deletion syndrome is mostly associated with moderate to mild ID, the use of psychiatric assessment developed for the general population that relies on DSM/ICD criteria may be more appropriate for this group, as evidenced by the majority of included papers assessing anxiety using such criteria (94%) (De Smedt et al., 2007). For DS, report of anxiety symptomatology was higher compared to psychiatric anxiety prevalence, as might be expected from missed diagnoses due to an individual not meeting diagnostic criteria but still experiencing anxiety. However, across all DS papers, as sample size increased the prevalence of anxiety decreased, suggesting that when more representative samples are considered, estimates of anxiety prevalence are lower and hence more valid.

In terms of specific anxiety profiles, for specific phobia in 22q11.2 deletion syndrome, better quality rated papers for sample identification and syndrome confirmation reported significantly higher rates of anxiety prevalence than lower quality rated papers. This was also the case in terms of sample identification for separation anxiety. These findings indicate that studies that are more representative and have implemented more robust methods to obtain syndrome confirmation appear to show higher prevalence of anxiety, increasing confidence in the findings. For generalised anxiety, lower quality rated papers in terms of syndrome confirmation showed significantly higher reports of anxiety prevalence compared to higher

quality rated papers. In combination, these relationships between differences in estimates and quality indicate the need for more robust methods in research.

Meta-regression analyses indicated that year of publication and sample size did not have significant impact on anxiety prevalence across syndromes with the only exception being sample size in DS. It is important to note that in some cases there were a small number of papers included in the subgroup analyses and so future research would need to confirm these findings.

The current review utilised a broad search strategy and inclusive search criteria with the number of papers evaluated ranging from 70 in 7q11.23 duplication syndrome to 8,882 in CHARGE syndrome, with 83 studies included in the final analysis. The scale of the selection process enabled a comprehensive synthesis and evaluation of the quality of the literature. The results can inform both clinical practice and potential future research strategies. It is important to note that the current review did not endeavour to include all syndromes associated with ID and there were papers that reported anxiety prevalence that were not identified in the scoping search that subsequently came to light during the individual syndrome searches, for example, Crawford et al. (2017) reported anxiety prevalence in FXS, as well as CdLS and Rubinstein-Taybi syndrome. The decision not to conduct a scoping review according to defined guidelines e.g., PRISMA Extension for Scoping Reviews (PRISMA-ScR; Tricco et al., 2018) could be considered a limitation of the study (Peters et al., 2015). However, the systematic application of scoping criteria used was deemed appropriate within the timeframe of the study completion to limit the search as it was not possible to review all possible syndromes associated with ID. The study highlights variation across syndromes and the value of considering syndromic mechanisms that may drive anxiety presentation across groups. Future research should focus on characterising difference in presentation and profile of anxiety, and to explore the role of genetic factors and gene-disorder-phenotype-environment interactions within and across syndromes. This work will continue to inform clinicians as to the risk and type of anxiety diagnoses that might warrant proactive assessment and intervention.

A particular lack of research was highlighted in Rett, 7q11.23 duplication, CHARGE, 3q29 deletion and Down syndromes and TSC. Having a limited number of studies compromises accuracy of prevalence as this enhances the effect of heterogeneity of methods, decreasing confidence in conclusions and limiting ability to generalise findings. Striving to delineate the phenotypic characteristics of syndromes and identifying those groups most at risk of anxiety should be a high priority.

As noted in previous research, it was apparent in the current review that research groups publish multiple papers that appear to include similar but not identical samples (Richards et al., 2015). Consequently, it is not possible to avoid reporting on overlapping

samples, potentially reducing the representativeness of findings. Whilst data may be collected that address a number of manifestations within a particular syndrome, authors should strive to explicitly report overlap of participants across studies to increase transparency.

The current review documented and evaluated the methods used to assess anxiety across syndromes. Diagnostic criteria developed for the general population may not be appropriate for individuals with ID, particularly those with moderate-profound ID (Flynn et al., 2017). The use of criteria, such as the DSM or ICD, may underestimate anxiety in ID due to the reliance on items requiring verbal response and/or the description of emotions, and atypical presentations of anxiety such as self-injurious behaviour (Bailey & Andrews, 2003). Consequently, an individual may not meet diagnostic threshold and therefore be 'counted' within a prevalence rate but be experiencing anxiety that is impacting their quality of life. In the current review, 66% (55) of studies used DSM/ICD criteria, and therefore rates may underestimate anxiety prevalence.

While the quality rating applied favoured the use of a diagnostic instrument over proxy report, the latter may be important for exploring symptomatology not bound by diagnostic criteria, highlighting the importance of including studies reporting the prevalence of anxiety symptomatology (Bertelli et al., 2015). There was variation in methods of assessments across syndromes; in RS, studies relied exclusively on proxy reports of anxiety symptomatology, for 22q11.2 deletion syndrome, most studies used diagnostic interviews with the person, therefore comparing prevalence rates between syndromes is difficult. It is also crucial to note discrepancies in reports of anxiety when relying on self vs. proxy report, where studies have indicated that diagnoses of anxiety were more frequently derived from self-report rather than proxy report. Therefore, clinicians should be aware of this potential discrepancy and the impact of assessment method on anxiety prevalence (Stinton et al., 2010, 2012). If an individual is unable to self-report, relying solely on proxy report of anxiety may lead to individuals not receiving the support they require.

Currently, there are no consensus guidelines for assessing anxiety in individuals with ID (Flynn et al., 2017), stressing the need for the consideration of issues such as method of assessment (observation, diagnostic interview, rating scales), who completes the assessment (self, proxy), assessment outcome (symptoms/behaviours vs. diagnosis) and exploration of frequency, severity, and impact of anxiety to determine clinical significance. Clinicians need to be aware of these factors when assessing mental health in ID and use multi-method assessment to elucidate the clinical presentation. Researchers should strive to develop tools created and validated specifically for different groups to improve the validity of diagnosis and prevalence estimates.

The current study extends the existing evidence base highlighting the importance of identifying mental health difficulties in people with ID, as recognised as a key policy priority (National Institute for Health and Care Excellence [NICE], 2016). The findings indicate that individuals with syndromic ID are at increased risk of experiencing anxiety, in comparison to individuals in general and ID of mixed aetiology populations. Therefore, clinicians and professionals who support individuals with syndromes should promote early identification, assessment, and intervention. Studies investigating anxiety prevalence are sparse for the majority of the included syndromes and future studies should aim to extend the current study findings, enabling future reviews to include a larger number of studies, increasing the generalisability of the findings to the wider syndrome populations. Additionally, the unmet need in mental health care for individuals with ID more generally has been highlighted, stressing the need for future research and further service provision to support these vulnerable groups (Venville et al., 2015; Whittle et al., 2018).

Chapter 3: Identifying correlates of anxiety in children and adults with moderate-profound intellectual disability: A questionnaire study

3.1 Preface

The previous chapter provides a comprehensive systematic review and meta-analysis, highlighting groups at heightened risk of anxiety. The work identifies varying risk of anxiety for different genetic syndromes, arguing for an approach to explore gene-disorder-phenotype-environment interactions to inform causal models of anxiety to foster early identification and intervention. Following on from the chapter two findings, the current chapter reviews literature exploring risk factors associated with anxiety in moderate-profound ID. A study is then presented that explored whether environmental and individual characteristics influenced the development and maintenance of anxiety. Additionally, anxiety triggers were also explored; to consider whether characteristics and anxiety triggers cut across groups associated with ID. The chapter utilises a cross-sectional, large-scale questionnaire study design to explore associations between quantitative data and the drawing of statistical inferences about variables that allude to risk markers of anxiety. This work may help to inform explanations for differing prevalence rates across groups, whilst fostering an inclusive approach by including individuals with diagnoses associated with ID and autism, who may present to the same clinical services.

3.2 Introduction

3.2.1 Anxiety in intellectual disability (ID)

As noted in section 1.4.5, individuals with ID are at risk of experiencing anxiety, with prevalence estimates ranging from 11-22% compared to 3-13% for those without ID (Baxter et al., 2013; Cooray & Bakala, 2005; Dekker & Koot, 2003a; Emerson, 2003; Emerson & Hatton, 2007; Polanczyk et al., 2015; Steel et al., 2014). This increased risk has been demonstrated across individuals with ID of heterogeneous aetiology, including those with a known genetic cause of ID such as a diagnosis of a genetic syndrome (see Chapter two), and those without (Cordeiro et al., 2011; Reardon et al., 2015; Crawford et al., 2017; Wheeler et al., 2019).

Despite the identification of elevated risk for anxiety in people with ID, there is currently a lack of research exploring the presentation of anxiety across individuals with ID, or research examining factors associated with increased risk (Hsieh et al., 2020). Identifying the presentation of anxiety and the factors that may contribute to the development and maintenance of anxiety are key to promote early identification and intervention (Gobrial & Raghavan, 2012; Hsieh et al., 2020; Whitney et al., 2019).

A number of factors have been associated with anxiety in the ID literature such as sensory processing differences (Rais et al., 2018; Uljarević et al., 2018), repetitive behaviour (Joosten et al., 2012; Royston et al., 2021; Sullivan et al., 2007) and comorbid physical health issues (de Winter et al., 2015; Hsieh et al., 2020; Javaid et al., 2021). These factors may be relevant at different levels, from biological difference, to learnt responses and/or coping mechanisms. For example, sensory processing differences have been explored as a result of neurophysiological difference but also learned behaviour (Marco et al., 2011). Green et al. (2012) argues that sensory processing differences lead to increases in anxiety over time (see section 3.5 for further discussion). Furthermore, it has been argued that repetitive behaviour may be a learnt, coping mechanism in response to the experience of anxiety (Green et al., 2012; Sellick et al., 2021; see section 3.2.2.5). There has been suggestion that engaging in repetitive behaviour may alleviate anxiety in the short-term but in the long-term reduce an individual's ability to develop adaptive coping strategies, perpetuating anxiety over time (Sellick et al., 2021). Physical health issues may arise from biological difference, evidence suggests that health issues i.e., gastrointestinal problems, are related to anxiety, perhaps through dysregulation in the hypothalamic-pituitary-adrenal (HPA) axis (Mazurek et al., 2013) There is suggestion that anxiety leads to health difficulties, but it is also possible that health difficulties contribute to higher levels of anxiety (Ferguson et al., 2017; Mazurek et al., 2013; see section 3.2.2.6). Evidence implicating these factors and disentangling how these factors relate to anxiety is still sparse and often focuses on individuals with mild-moderate ID, despite 1-4% of the ID population having a severe-

profound ID diagnosis (Dekker & Koot, 2003b; Green et al., 2015; Bhate & Wilkinson, 2006). It is crucial to identify whether correlates identified in previous literature focusing on people with mild-moderate ID are comparable to individuals with moderate-profound ID, to be able to inform early targeted intervention.

The current chapter summarises existing literature exploring correlates of anxiety in individuals with ID and presents a study that focuses specifically on correlates of anxiety in those with moderate-profound ID as a population often neglected within the literature.

3.2.2 The influence of individual characteristics on anxiety in ID

3.2.2.1 Genetic diagnoses

In Chapter two it was demonstrated that there is variability in anxiety prevalence across individuals with a genetic syndrome diagnosis associated with ID, and high-risk groups were identified. There is research exploring the presentation of anxiety in genetic syndromes that may allude to potential risk markers for anxiety. For example, in Fragile X syndrome (FXS), the most prevalent anxiety diagnoses are social anxiety and specific phobias (Bertrán et al., 2018; Gabis et al., 2011; Jolin et al., 2012) and high rates of obsessive-compulsive disorder (OCD) have been reported in Prader-Willi syndrome (Dykens et al., 1996; Dykens & Shah, 2003; La Spata, 2019). High rates of autism in FXS may be linked to the presentation of social anxiety (Budimirovic & Kaufmann, 2011; Cordeiro et al., 2011; Richards et al., 2015), however, questions remain unanswered around the mechanisms underpinning social anxiety in FXS (Hong et al., 2019; Roberts et al., 2018). For Prader-Willi syndrome, presentations of OCD have been linked to resistance to change, difficulty with changes to routine and desire to increase predictability (Woodcock et al., 2009; Schwartz et al., 2021). These characteristics in PWS could be linked to intolerance of uncertainty, a transdiagnostic risk factor for poor mental health outcomes (Boswell et al., 2013). Intolerance of uncertainty is strongly associated with anxiety in autism and the general population (Boulter et al., 2014; Carleton, 2012; Jenkinson et al., 2020).

Describing syndrome specific anxiety presentations may help to identify risk markers for anxiety across groups; for example, by identifying exemplar syndromes where anxiety is common, researching pathways to anxiety within these exemplar syndromes, and then examining whether these pathways are relevant to other groups. However, as identified in chapter two, there is a lack of research exploring these pathways in depth and when they have been explored, the studies are often under-powered by small sample sizes, often due to the rarity of syndromes and subsequent impact on study recruitment (Hong et al., 2019; Roberts et al., 2018; Woodcock et al., 2009). Therefore, it would be of interest to study the risk factors that may cut across diagnostic groups, to identify intervention targets across ID groups more generally.

Specific presentations of anxiety have also been identified in individuals with ID of no known genetic cause (Maïano et al., 2018; Reid et al., 2011). For example, specific phobia, separation anxiety disorder, social phobia, obsessive-compulsive disorder (based on DSM-IV criteria), and generalised anxiety disorder are the most common anxiety subtypes (Maïano et al., 2018).

3.2.2.2 Gender, age, intellectual ability, verbal ability

In terms of demographic variables that might be risk factors for anxiety, research has been inconsistent when exploring the impact of age, gender, and level of intellectual/adaptive functioning on anxiety in individuals with ID. In line with research from the general population, some studies have shown that anxiety increases as individuals age (Emerson & Hatton, 2007; Green et al., 2015), however studies have also concluded that age has no impact on anxiety (Dekker & Koot, 2003b; Emerson, 2003).

Similarly for gender, some have argued that females are at heightened risk of anxiety (Chester et al., 2013; Hermans et al., 2013; McLean et al., 2011), however, there has also been evidence to suggest no gender differences in risk for anxiety in individuals with ID (Axmon et al., 2017; Dekker & Koot, 2003b; Emerson & Hatton, 2007; Green et al., 2015; Tsakanikos et al., 2006). When considering gender, it is also important to note that for some syndrome groups associated with ID there are gender differences in diagnosis. For example, Rett syndrome is diagnosed almost exclusively in females (Goh, 2017). Additionally, there are higher rates of males who receive a diagnosis of FXS, and they present with greater cognitive and behavioural differences so are often the focus of research, as opposed to females with a diagnosis (Bartholomay et al., 2019; Hunter et al., 2014). This has implications for the exploration of gender as a potential factor associated with anxiety when aggregating groups associated with ID. For example, the numbers of females, if all attributed to diagnosis of Rett syndrome may mean that this diagnosis is disproportionately contributing to the numbers of females in the sample. This in turn could mean that the diagnosis is a significant factor associated with anxiety, rather than specifically gender. Therefore, this needs to be taken into consideration when aggregating groups about how gender could impact interpretation.

Some evidence suggests that those with more mild ID are at heightened risk compared to those with severe ID (Bouras & Drummond, 1992; Hermans & Evenhuis, 2013; Mingins et al., 2021; Witwer & Lecavalier, 2008), whilst others have found the opposite (Cooper et al., 2007; Molteno et al., 2001). There have also been more recent studies concluding that there is no association between severity of ID and anxiety (Maïano et al., 2018; Whitney et al., 2019). In terms of adaptive ability, there is evidence of an association in specific genetic syndromes associated with ID, for example, in Prader-Willi syndrome (PWS), poorer adaptive ability has been found to predict generalised anxiety (Royston et al.,

2020). Therefore, intellectual, and adaptive ability may be important to consider as potential correlates of anxiety in individuals with moderate-profound ID.

There is likely to be overlap between intellectual ability and verbal ability (Bal et al., 2016), which may partially explain the similar pattern of conflicting findings when considering the impact of verbal ability on anxiety in individuals with ID. Molteno et al. (2001) found that individuals with ID who were non-verbal had higher levels of psychopathology, including anxiety, whilst Hoare et al. (1998) found greater verbal ability was associated with higher levels of emotional and behavioural disturbance, although the study did not specifically focus on anxiety. Due to the focus of this thesis on individuals who speak few or no words, the current study sought to explore the potential impact of verbal ability on anxiety in individuals with moderate-profound ID.

Overall, these findings preclude the generation of a conclusive hypothesis stating the direction of the association, if any, between these demographic variables and anxiety in individuals with ID.

3.2.2.3 Autism/Autistic characteristics

Studies have demonstrated that individuals with a comorbid diagnosis of autism or high levels of autism characteristics are at heightened risk of anxiety and display a differing presentation of anxiety when compared to individuals with ID alone (Appleton et al., 2019; Espie et al., 2003; Hsieh et al., 2020). As autism is highly comorbid with ID, with rates of 18-28% of individuals with ID receiving an autism diagnosis, it is crucial to explore how an autism diagnosis may impact on the presentation of anxiety (Arias et al., 2018; Bryson et al., 2008; Tonnsen et al., 2016). For example, autistic individuals with ID found transitions to be a particular trigger for anxiety and were more likely to engage in repetitive behaviours when anxious rather than for sensory seeking purposes, whilst the opposite was evident for individuals with ID alone (Appleton et al., 2019; Joosten et al., 2009, 2012; Joosten & Bundy, 2010). An autism diagnosis may be an important risk marker when intervening early and formulating how best to support an individual experiencing anxiety.

However, it is also important to consider that it may not be autism itself that is a risk marker for anxiety but the associated characteristics (e.g., communication difficulties, repetitive behaviour, intolerance of uncertainty) and these characteristics may present in individuals with varying diagnoses without necessarily the presence of an autism diagnosis. Within this chapter, whilst autism diagnosis is taken into consideration during analyses, associated characteristics of sensory processing differences, repetitive behaviour and intolerance of uncertainty are examined individually, to explore their association with anxiety in the ID population.

3.2.2.4 Sensory processing

More specifically, one element of the autism diagnostic criteria, sensory processing differences, are common in individuals with ID and individuals with a genetic syndrome diagnosis (Engel-Yeger et al., 2011; Heald et al., 2020). Furthermore, differences in sensory processing have been associated with anxiety in the autism population, warranting further exploration of this association and sensory processing difference as a standalone potential risk marker for anxiety (South & Rodgers, 2017). It has been found that anxiety is higher in autistic individuals the more severe sensory dysfunction an individual experiences (Gillott & Standen, 2007; Uljarević et al., 2016). More specifically, research has found strong links between sensory hyperreactivity and anxiety (Green & Ben-Sasson, 2010; Green et al., 2012; MacLennan et al., 2020; Wigham et al., 2015). Whilst more research is needed focusing on sensory processing in ID, there is still evidence indicating that sensory processing difficulties are common (Engel-Yeger et al., 2011).

Evidence of the association has also been demonstrated in genetic syndromes associated with ID. Sensory hyperreactivity is part of the FXS phenotype which may lead to anxiety and avoidance of noisy, busy environments (Rais et al., 2018). Similarly, for individuals with Williams syndrome (WS), sensory sensitivities have been identified as a trigger for anxiety (Royston et al., 2021).

There is a lack of research focusing specifically on the relationships between sensory domains within sensory subtypes (e.g., auditory hyperreactivity) and anxiety in the ID population. Within the autism population, there have been links made between auditory and tactile hyperreactivity and specific anxiety presentations; phobias to loud noises and worries of being touched (Lau et al., 2020; Muskett et al., 2019). Furthermore, increased input from tactile and auditory stimuli has been linked to OCD presentation in the general population (Ferrão et al., 2012). The current study will aim to fill the gap in existing literature by exploring sensory domains and their relationship with anxiety in the moderate-profound ID population. Delineating the profile of sensory processing difficulties may have important implications for understanding the heightened risk of anxiety in genetic syndromes and ID more generally (Crawford et al., 2017; Heald et al., 2020).

3.2.2.5 Repetitive behaviour

Repetitive behaviour is an observed characteristic in autistic individuals and individuals with ID (Joosten & Bundy, 2010). Research in Down syndrome identified links between repetitive behaviour and anxiety; with one hypothesis suggesting the function of repetitive behaviour as a coping strategy to reduce anxious feelings (Glenn, 2017). This finding has also been demonstrated in other genetic syndromes associated with ID such as FXS, Cornelia de Lange (CdLS) and Prader-Willi syndromes (Grados et al., 2017; Oakes et al., 2016; Woodcock et al., 2009). Glenn (2017) concluded that increased levels of repetitive

behaviour are evident across diagnoses associated with ID when compared to others of typical development, suggesting that repetitive behaviour may be a potential risk factor associated with anxiety.

3.2.2.6 Health difficulties

Research has indicated that physical health symptoms or pain may also be a correlate of anxiety in the ID population (Dekker & Koot, 2003b). Whitney et al. (2019) found for children with ID, experiencing pain such as headaches, back or body aches, were significantly associated with higher odds of anxiety and depression. Hsieh et al. (2020) provided support for this finding in their longitudinal study, demonstrating associations between chronic health conditions such as gastrointestinal pain/discomfort, constipation, epilepsy and joint pain and anxiety in individuals with ID.

Furthermore, evidence of a link between physical health difficulties/pain and anxiety has also been suggested in genetic syndrome research. In Cornelia de Lange syndrome, high rates of gastrointestinal difficulties are found (71%; Hall et al., 2008), which may cause anxiety (Kline et al., 2018).

As individuals with ID are at increased risk of experiencing a range of physical health difficulties (Liao et al., 2021), this link to anxiety is particularly concerning. It is crucial that physical health needs are met in the first instance to ensure effective identification of anxiety and appropriate intervention. However, it does need to be considered that across assessment measures of pain/physical discomfort and anxiety, there may be behavioural overlap on items that could explain the associations found. These issues are discussed further in sections 4.4.2.1 and 4.4.2.3.

3.2.2.7 Intolerance of uncertainty

In recent years, research within the general population has focused on intolerance of uncertainty and its relationship with anxiety (Carleton, 2012). These findings have also been replicated within the autism population (Boulter et al., 2014; Jenkinson et al., 2020). Research in children and adults has demonstrated the central role of intolerance of uncertainty in models that comprise of autism characteristics and anxiety. For example, intolerance of uncertainty is a significant mediator between sensory sensitivities and anxiety, as well as between anxiety and insistence on sameness behaviours in autistic adults (Hwang et al., 2020). Intolerance of uncertainty is also a significant mediator between autistic traits and anxiety in autistic children (Boulter et al., 2014; MacLennan et al., 2021).

Furthermore, there are anxiety intervention studies that have focused on improving tolerance of uncertainty with the aim to reduce anxiety in autistic individuals (Rodgers et al., 2019). Evidence of the acceptability and effectiveness of interventions is yet to be

established fully, although there is preliminary evidence to suggest acceptability in retention, focus of intervention and the usefulness of strategies included (Rodgers et al., 2018).

There is a paucity of research exploring intolerance of uncertainty in the ID population. However, consistent with research in the general and autism populations, CdLS and FXS (Perry, 2019). Therefore, it is possible that intolerance of uncertainty is a key factor across the entirety of the population that is involved in the development and maintenance of anxiety and could be an important target for intervention. This introduction has identified variables that are associated with anxiety; correlates, which may allude to risk markers; variables that increase the likelihood of anxiety in the moderate-profound ID population.

3.2.2.8 Anxiety triggers

Identifying correlates of anxiety is crucial to inform early identification of those most at risk and targeted intervention. Another way to improve the identification and assessment of anxiety is to pinpoint anxiety triggers; objects, situations or circumstances that may make anxiety more likely.

Academic expectations, social demands and uncertainty have been identified as anxiety triggers for autistic individuals (Simpson et al., 2020). Research has identified changes to routine and sensory processing difficulties (e.g., noise of hand dryer) as triggers for anxiety in autistic people with moderate-profound ID and/or those who speak few or no words (Tarver et al., 2021a). However, there is a lack of research exploring the triggers for anxiety specifically in the ID population (Simpson et al., 2020).

Evidence within genetic syndrome research has identified specific phobias (e.g., noise, blood, storms), new situations, sensory sensitivities, and negative emotions in others as anxiety triggers in WS (Royston et al., 2021). Although research specifically focusing on identifying anxiety triggers in other groups is scarce.

3.2.2.9 Causal pathways to anxiety

Identifying anxiety triggers and factors that may be implemented in the development and maintenance of anxiety in ID is crucial to improve identification of anxiety and targets for early intervention. Additionally, identifying potential risk factors allows us to hypothesise potential causal pathways to anxiety involving gene disorder-phenotype-environment interactions. As noted earlier, an example of where this has previously been achieved is in Williams syndrome (WS). WS is a genetic syndrome that has been associated with a heightened prevalence of anxiety (Royston et al., 2016). Work investigating the potential pathways to anxiety was based on existing literature in WS and the autism population due to the overlap in phenotypic characteristics such as sensory processing difficulties, high levels of anxiety and repetitive behaviours (Royston, 2018). Auditory sensory processing impairments, intolerance of uncertainty and health difficulties were associated with anxiety in

WS. Additionally, repetitive behaviour was found to be associated with intolerance of uncertainty. Furthermore, specific triggers of anxiety in individuals with WS (e.g., unpredictable people, new situations, loud noises) were associated with sensory processing impairments. Royston (2018) argued that these triggers include elements of unpredictability or uncertainty, stressing the need to assess intolerance of uncertainty as a potential cognitive process underlying the development of anxiety.

The potential pathways involved in the development of anxiety in WS described above are consistent with the constructs that will be explored within the current chapter. This further research is needed to identify whether these characteristics are relevant risk factors applicable to individuals with moderate-profound ID. This work will allow the development of a model of anxiety that may cut across diagnoses and allow the identification of transdiagnostic factors that are implemented in the development and maintenance of anxiety in the moderate-profound ID population.

3.2.3 The current study: Aims

There is no known study that focuses exclusively on identifying correlates of anxiety in individuals with moderate-profound ID. Existing literature highlights correlates of interest across the autism, ID, and genetic syndrome populations. There is an argument for taking an inclusive approach exploring relevant, common correlates across groups to identify intervention targets for individuals who present to clinical services. Therefore, the current study set out to address these gaps utilising an online, informant (i.e., parents/carers), large-scale questionnaire design. The aims of the study were to:

i) Explore relationships between existing anxiety measures developed for individuals with intellectual disability, this was due to the lack of a gold-standard measure for anxiety in this population

   It was hypothesised that significant, positive relationships would be found between existing anxiety measures (i.e., Anxiety, Depression and Mood Scale; **ADAMS**, Anxiety Triggers Questionnaire; **ATQ**, and the Diagnostic Assessment for the Severely Handicapped-II; **DASH-II**, further description of measures can be found in section 3.3.3).

ii) Explore how demographic variables such as age, gender, diagnosis, adaptive ability, verbal ability, and autism characteristics may contribute to or predict anxiety

   Due to the inconsistent findings in previous literature, no hypotheses were proposed on the potential direction or strength of the relationships between the explored demographic variables and anxiety

iii) Explore how sensory processing differences, repetitive behaviour, intolerance of uncertainty and health related difficulties may contribute to or predict anxiety, whilst adjusting for demographics and potential covariates in the analyses

Based on previous literature, it is hypothesised that sensory processing differences, repetitive behaviour, intolerance of uncertainty and health related difficulties will significantly predict increased anxiety

iv) Explore anxiety triggers that may have important implications for the development and maintenance of anxiety

Based on previous literature, it is hypothesised that anxiety triggers such as changes to routine and sensory sensitivities will be frequently endorsed, as demonstrated by descriptive statistics

v) Explore consistency of analyses noted in aims ii) and iii) across anxiety measures developed for individuals with intellectual disability

It is hypothesised and expected that across anxiety measures, sensory processing differences, repetitive behaviour, intolerance of uncertainty and health related difficulties will significantly predict increased anxiety

3.3 Methods

3.3.1 Recruitment: inclusion and exclusion criteria

This study was conducted as part of a broader project aiming to validate a new questionnaire measure to assess emotional well-being and distress in individuals with moderate-profound ID and/or those who speak few or no words. For the purposes of the current study, individuals who speak 'odd words only' or 'never a word' were included in the analysis regardless of ability categorisation on the Wessex Questionnaire (i.e., able, partly able, not able). Individuals who 'speak in sentences' were also included in the analysis **only** if they were categorised as 'partly able' or 'not able', as also assessed by the Wessex Questionnaire (full description below). These criteria were used to ensure that the study focused on individuals with moderate-profound ID and/or those who speak few or no words as these individuals are under-represented in existing literature.

An invitation letter including a link to access the online survey via survey software Qualtrics (Qualtrics, Provo, UT, 2018) was sent to parents/carers on the Cerebra Centre for Neurodevelopmental Disorders (CCND) participant database and a database held at Aston University, where parents/carers have consented to be contacted about future research studies (See Appendix 7). For the CCND database, letters were sent to all parents/carers of autistic individuals and individuals with a genetic syndrome associated with moderate-profound intellectual disability. These included Angelman, Cornelia de Lange, Cri du Chat and Fragile X syndromes (See Table 3.1). The Aston University database consists of contact

details for parents/carers of autistic individuals who speak few or no words, all were invited to take part in the current study. Parents/carers were also recruited via the Discover Network run by the charity Autistica, social media, word of mouth and three NHS Participant Identification Centres (PICs) who supported recruitment for the study (See Table 3.2).

The current study was approved by the NHS Wales REC 3 Committee (reference: 18/WA/0139; for approval letter, see Appendix 8).

3.3.2 Participants

There were 165 parents/carers who completed the online questionnaire survey. Overall, the mean age of autistic individuals or individuals with ID was 20.9 years old (*SD*=11.1, range=4-63 years) with 92 males (55.8% of sample). The mean age of parents/carers was 53.2 years old (SD=10.8, range=26-90) with 24 males (14.5% of sample). There were 132 mothers (80%), 21 fathers (12.7%), one adopted parent (0.6%), two foster parents (1.2%), one grandmother (0.6%), one brother (0.6%), one sister-in-law (0.6%), two carers (1.2%) and one care home manager (0.6%) who completed the study. Three parents/carers (1.8%) had missing data for the item relating to relationship to individual with ID. More specific diagnosis information for individuals with ID and demographic information for parents/carers are provided in Tables 3.1 and 3.2 respectively.

Table 3.1 Diagnosis information for individuals with ID

Diagnosis	Number of individuals (%)	Diagnosis	Number of individuals (%)
Autism	38 (23)	Potocki-Lupski syndrome	
Angelman syndrome		With autism	2 (1.2)
With autism	3 (1.8)	Without autism	2 (1.2)
Without autism	36 (21.8)	Pitt-Hopkins syndrome	
Cornelia de Lange syndrome		With autism	1 (0.6)
With autism	6 (3.6)	Without autism	1 (0.6)
Without autism	11 (6.7)	Syngap1	
Cri du chat syndrome		With autism	1 (0.6)
With autism	1 (0.6)	Without autism	1 (0.6)
Without autism	8 (4.8)	Intellectual disability	4 (2.4)
Fragile X syndrome		Pallister-Kilian syndrome	3 (1.8)
With autism	6 (3.6)	Phelan-McDermid syndrome	3 (1.8)
Without autism	4 (2.4)	Lowe syndrome and autism	1 (0.6)
Down syndrome		Rubinstein-Taybi syndrome and autism	1 (0.6)
With autism	3 (1.8)	Deletion on chromosome 5 and autism	1 (0.6)
Without autism	4 (2.4)	CHAMP1 and autism	1 (0.6)
Tuberous Sclerosis Complex		Lissencephaly and autism	1 (0.6)
With autism	1 (0.6)	Global developmental delay and learning difficulties	1 (0.6)
Without autism	3 (1.8)	Global developmental delay with atypical signs of autism	1 (0.6)
Kleefstra syndrome		Mef2c syndrome	1 (0.6)
With autism	2 (1.2)	Cerebral palsy	1 (0.6)
Without autism	3 (1.8)	Down syndrome, Eisenmenger's syndrome and autism	1 (0.6)
Prader-Willi syndrome		Cri du Chat syndrome and 8p+	1 (0.6)
With autism	2 (1.2)	Soto's syndrome	1 (0.6)
Without autism	2 (1.2)	CDLK5	1 (0.6)
		No reported diagnosis	1 (0.6)

Table 3.2 Demographic information for parents/carers

Parent/carer demographic information	*n* (%)
Highest level of parent/carer education, n (%)	
No formal educational qualifications	13 (7.9)
Fewer than 5 GCSE's or O Level's	13 (7.9)
Five or more GCSE's or O Level's	22 (13.3
Three or more A levels	24 (14.5)
University degree	60 (36.4)
Masters/Doctoral degree	32 (19.4)
Household income	
Less than £15,000	18 (10.9)
£15,001 to £25,000	17 (10.3)
£25,001 to £35,000	19 (11.5)
£35,001 to £45,000	21 (12.7)
£45,001 to £55,000	15 (9.1)
£55,001 to £65,000	11 (6.7)
£65,001 or more	43 (26.1)
Prefer not to say/no response	21 (12.7)
Recruitment source	
Received a letter from research team/database	121 (73.3)
Autistica Discover Network	17 (10.3)
NHS Trusts	11 (6.7)
Social media	10 (6.1)
Word of mouth	6 (3.6)

3.3.3 Measures

Parents/carers completed a range of questionnaires, described below, relating to their child's/person they care for's abilities, skills, behaviours, and mental health.

3.3.3.1 Background information questionnaire

A background questionnaire (Appendix 9) was included to collect demographic information from parents/carers regarding individuals with ID including age, gender, diagnoses, verbal ability, and mobility. The questionnaire also collects information about the family including parent/carer age, gender, relationship to the individual with ID, living circumstances for the individual with ID, education, and income.

3.3.3.2 Wessex Questionnaire

The Wessex Questionnaire (WX; Kushlick et al., 1973; See Appendix 10) assesses an individual's social and physical adaptive ability. The questionnaire has 16 items and covers vision, mobility, hearing, literacy, speech, continence, and self-help ability. The questionnaire can be used as a proxy measure of ability, with higher scores indicating greater ability. In the current study, the questionnaire was used as a proxy measure of moderate-profound ID. Scores also allow ability level to be categorised into 'able', 'partly able' and 'not able' groups. Inter-rater reliability is good, and it has been noted as an effective tool for large scale

questionnaire studies (Kushlick et al., 1973; Palmer & Jenkins, 1982). See Table 3.3 for ability data for individuals with ID included in the current study. In Table 3.3, the 12 participants who were categorised as 'able' spoke 'odd words only' or 'never a word', whilst the 20 participants who spoke 'sentences and normal' were categorised as 'partly able' or 'not able'. This was to adhere with the inclusion and exclusion criteria for the study detailed in section 3.3.2.

Table 3.3 Ability data for individuals with ID from Wessex Questionnaire

Ability data for individuals with ID	n (%)
Self-help score categorisation	
Not able	73 (44.2)
Partly able	80 (48.5)
Able	12 (7.3)
Verbal ability	
Never a word	57 (34.5)
Odd words only	88 (53.3)
Sentences and normal	20 (12.1)

3.3.3.3 Social Communication Questionnaire

The Social Communication Questionnaire (SCQ; Rutter et al., 2003b; See Appendix 11) is a screening tool for autism characteristics. It has 40 items rated dichotomously with response options of yes or no and scores are summed to provide a total score. The first item assesses an individual's verbal ability and is not included in the total score, if an individual is verbal, items 2-7 are answered, if an individual is non-verbal, items 2-7 are not answered therefore maximum total scores for verbal and non-verbal individuals are 39 and 33 respectively. A high score indicates more autism characteristics. The SCQ is suitable for individuals with ID (Berument et al., 1999) and good internal consistency has been demonstrated for verbal and non-verbal individuals (α=.94 and α=.89 respectively; Marvin et al., 2017). The good internal consistency was replicated in the present sample for verbal (*n*=56; α=.87) and nonverbal individuals (*n*=109; α=.87).

3.3.3.4 Anxiety, Depression and Mood Scale

The Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003; See Appendix 12) is an informant measure that explores behaviours/symptoms related to anxiety, depression, and mania. There are 28 items rated on a Likert scale of 0 'not a problem' to 3 'severe problem.' In the current study, the subscale of general anxiety was used as a dependent variable consisting of seven items. The questionnaire was validated with informants of individuals with mild to profound ID. The test-retest reliability of the general anxiety subscale was .78 and the internal consistency was .83 (Esbensen et al.,

2003). Good internal consistency for the general anxiety subscale was established in the current sample (α=.86).

3.3.3.5 Diagnostic Assessment for the Severely Handicapped-II (DASH-II)

The DASH-II (Matson et al., 1995; See Appendix 13) is an informant measure used to detect psychiatric and emotional difficulties in individuals with severe to profound ID. The measure includes 13 subscales including anxiety, depression, mania, and schizophrenia, however for the purpose of the current study only the anxiety subscale was used. The DASH-II anxiety subscale has been shown to have good internal consistency (α=.61; Vargas-Vargas et al., 2015) and excellent test-retest and inter-rater reliability (Matson et al., 1995; Flynn et al., 2017). Good internal consistency was replicated in the current sample (α=.81).

3.3.3.6 Sensory Profile

The Sensory Profile 2 (Dunn, 2014; See Appendix 14) is an informant measure used to evaluate an individual's sensory processing patterns. The measure consists of six sensory domain subscales: auditory, visual, tactile, movement, body position and oral. Items are rated on a five-point Likert scale, from 'almost never' to 'almost always'. For the purposes of this study, only the visual, auditory, and tactile subscales (26 items) were administered as the main areas of interest for this particular study, also reducing burden on parents/carers. The subscales have good internal consistency (.60-.86), test-retest reliability (.87-.94) and inter-rater reliability (.49-.80; Dunn, 2014). The current sample replicated good internal consistency for the visual (α=.69), auditory (α=.80) and tactile (α=.79) subscales with a mean of α=.76.

3.3.3.7 Repetitive behaviour questionnaire

The Repetitive Behaviour Questionnaire (RBQ-2; Leekam et al., 2007; See Appendix 15) is an informant questionnaire used to record repetitive behaviours known to occur in autistic individuals and children of typical development. There are 20 items rated on a three or four-point Likert scale. Scores on items were used to calculate two mean subscale scores: motor/sensory behaviours and rigidity/routines/preoccupation with restricted interests. Scores were also summed to produce a total repetitive behaviours score. The questionnaire has good internal consistency in studies with autistic individuals (Lidstone et al., 2014) for total score (α=.86) and subscales of motor/sensory behaviours (α=.79) and rigidity (α=.83). These findings were replicated in the current sample (α=.87, α=.79, α=.84 respectively).

3.3.3.8 Intolerance of uncertainty

The Responses to Uncertainty and Low Environmental Structure (RULES) questionnaire (Sanchez et al., 2017; See Appendix 16) examines an individual's response to uncertainty and low environmental structure. The measure has 17 items and is rated on a

five-point Likert scale with response options from ‘not at all’ to ‘very much’. The questionnaire has excellent internal consistency (α = .93; Sanchez et al., 2017). The current study adapted the questionnaire for appropriate use in the current sample; for parents/carers of autistic individuals and/or individuals with ID who speak few or no words. Therefore, an additional response option of ‘not applicable’ was added to question 3; “*my child says, ‘it is unfair’ when he/she cannot know what will happen*” to allow parents/carers to endorse this option if relevant for their child/the person they care for. If a parent/carer selected the ‘not applicable’ response option, the total score for this questionnaire was summed utilising scores from 16 complete items. If a parent/carer selected any other response (1-5) on this item, the total score was summed utilising 17 complete items. Cronbach’s alpha was α = .95 for 16 items (*n*=162) and α = .94 for 17 items (*n*=85) respectively in the current study.

3.3.3.9 Health Questionnaire

The Health Questionnaire (Hall, et al., 2008; See Appendix 17) examines the presence and severity of current health problems that have occurred in the last month. The questionnaire consists of 15 health problems scored on a scale of 0 = “No” to 3 = “Severe”. Scores are summed to provide a severity score; presence of health difficulties are summed to provide a frequency score. Item level reliability was .76 and internal consistency has been found to be good for the overall severity score at α=.77 (Hall et al., 2008; Watkins et al., 2019). Internal consistency was lower in the current study for severity scores (α=.55).

3.3.3.10 Anxiety triggers questionnaire

The Anxiety Triggers Questionnaire (ATQ; Royston, 2018; See Appendix 18) is an informant-based measure used to examine what situations/contexts are anxiety-provoking for an individual. The measure was developed as part of a PhD study assessing anxiety in Williams Syndrome. There are 33 items with the majority rated on a five-point Likert scale with response options ranging from ‘never’ to ‘always’. Spearman’s coefficients for the 28 frequency items ranged from .37 to .86 at item level with 61% of items above .60. As preparation for the current study, the ATQ was examined to consider the addition of items relevant for the current population, utilising data from chapter four, however, no additional anxiety triggers were mentioned in parent/carer and clinician interviews that were not already stated on the original ATQ, therefore, it was utilised in the current study as initially developed. A total score was obtained by summing scores for 24 items relating to specific anxiety triggers, with the total score being used in subsequent analysis.

3.3.4 Procedure

Parents/carers who received an invitation letter were given an online link to access the information sheets, consent forms and questionnaires via the survey platform, Qualtrics. See Appendix 19 for the information sheet. Parents/carers recruited through alternative strategies

were sent a link for the survey via email by a member of the research team when they expressed an interest in taking part in the study.

On invitations letters and email correspondence, parents/carers were made aware that they could request paper copies of the questionnaire if they preferred. Individuals with ID aged 16 or over, with the capacity to consent, also provided consent for participation using paper or online methods (See Appendix 20). Parents/carers of individuals aged 16 or over without capacity acted as personal or nominated consultee to their child/person they care for (See Appendix 21). An individual's capacity to consent was established by parents/carers, who were supported to make this decision if needed, for example, parents/carers could use a symbol information sheet to support the person they care for to provide informed consent. Parents/carers of individuals under 16 years of age provided consent for participation (See Appendix 22). Parents/carers were able to take breaks in the survey and continue from where they left off using the initial link provided within 72 hours. All parents/carers who took part in the study received a personalised feedback report. To enhance recruitment and to mitigate the impact of the Covid-19 pandemic on this study, each parent/carer was given a £5 online voucher for their participation.

3.3.5 Data analysis

Data were missing on the following variables: general anxiety subscale of the ADAMS (*n*=1, 0.6%), repetitive behaviour motor subscale items 3 and 5 (*n*=1, 0.6%, *n*=1, 0.6% respectively), repetitive behaviour mean total score item 20 (*n*=2, 1.2%), the auditory subscale on the sensory profile item 7 (*n*=1, 0.6%), the visual subscale on the sensory profile item 11 and 13 (*n*=1, 0.6%, *n*=1, 0.6% respectively), the health questionnaire items 11 and 16 (*n*=1, 0.6%, *n*=2, 1.2% respectively), the RULES questionnaire items 1, 2, 4, 6 (all *n*=1, 0.6%), the ATQ items 2, 3, 10, 12, 14 (all *n*=1, 0.6%) and item 2 on the DASH-II anxiety subscale (*n*=1, 0.6%). These missing data resulted in 0.072-0.081% of data values missing across analyses where data were incomplete for 8 parents/carers for the analyses utilising the general anxiety subscale of the ADAMS and the anxiety subscale of the DASH-II (4.9%) and 9 parents/carers when the ATQ total was used (5.4%). Missing data mechanisms were explored, and Little's Missing Completely at Random (MCAR) tests were not significant across analyses (*p*=.100-.185) suggesting data were missing randomly, this was further supported by the identification of no systematic pattern when analysing missing value patterns (Little, 1988).

Previous literature indicates that when data is assumed to be MCAR and there is a small amount of missing data (approximately 5%), complete case analysis does not bias the subsequent analysis (Blazek et al., 2021; Dziura et al., 2013; Jakobsen et al., 2017). In line with this finding, for the current study, parents/carers with missing data were not included and complete case analysis was utilised. Therefore, the final sample size for analyses was

156-159, retaining 94.5%-96.4% of the original sample. This is consistent with the required sample size based on power calculation for a medium expected effect (i.e., R^2=0.13; Cohen, 1988), as evidenced in previous studies exploring relationships between anxiety, sensory processing, repetitive behaviour, and intolerance of uncertainty in autistic individuals (Field, 2018; Lidstone et al., 2014; Syu & Lin, 2018; Wigham et al., 2015).

A series of multiple hierarchical regression analyses were conducted to explore relationships between anxiety and the predictors of sensory processing, repetitive behaviour, intolerance of uncertainty and health difficulties. These predictors were chosen based on previous literature demonstrating relationships between these predictors and anxiety in autistic individuals without ID/those who speak in sentences (Ferguson et al., 2019; Neil et al., 2016; Neuhaus et al., 2018; Wigham et al., 2015).

Given the evidence of varying anxiety prevalence in Chapter two, diagnosis was entered into the first step of the analysis. It was entered as a multinomial predictor using dummy coding, whereby each diagnosis with 10 or more individuals had its own group [i.e., Autism, Angelman (AS), Cornelia de Lange (CdLS) and Fragile X syndromes (FXS)] whilst any diagnosis with less than 10 individuals (e.g., Down syndrome) was categorised into a heterogenous diagnosis group. Individuals with genetic syndrome and autism diagnoses were categorised into their relevant genetic syndrome group, this was due to differences highlighted in presentation between syndromic and idiopathic autism, therefore it was deemed inappropriate to collate these groups (Cochran et al., 2019; Moss et al., 2013). In step 2, demographic variables and potential covariates were entered; age, gender, verbal ability (speaks in sentences/speaks few or no words), the self-help subscale score from the Wessex Questionnaire and the Social Communication Questionnaire total score. In step 3, sensory processing, repetitive behaviour, intolerance of uncertainty and health difficulties were entered to explore the potential additional contribution of these variables to the prediction of anxiety. Variables of sensory processing, repetitive behaviour and intolerance of uncertainty were of primary interest in the current study to align with existing literature exploring this model in autistic individuals without ID or those who speak in sentences (Neil et al., 2016; Wigham et al., 2015). Additional variables relating to health difficulties were explored during analyses to see how they may predict anxiety (Ferguson et al., 2019; Neuhaus et al., 2018). The dependent variable used in the primary analysis was the generalised anxiety subscale of the ADAMS. Additional analyses were conducted to explore consistency of findings across anxiety measures (described below in sections 3.4.4 and 3.4.5) where the total score of the ATQ and the anxiety subscale from the DASH-II were used as dependent variables.

Descriptive information from the Health Questionnaire highlighting the most commonly endorsed health difficulties is shown in Table 3.4. Descriptive statistics of the ATQ were also

summarised to identify factors that may contribute to the development and maintenance of anxiety and explore frequencies of specific anxiety triggers endorsed across diagnoses (See Table 3.5 and Appendix 23).

To address the issue of increasing R^2 with the addition of every predictor variable, the Akaike Information Criterion (AIC; Akaike, 1974) was used in the current study. The AIC penalises a model for having more variables and allows the comparison of models, whereby if the AIC is getting smaller, the fit of a model is improving (Field, 2018).

A significance *p*-value of 0.05 was chosen for the primary analysis utilising the ADAMS as an outcome variable of anxiety to address the study aims. Multiple comparison adjustments e.g., Bonferroni, were not applied in this analysis, this was considered justified to reduce risk of type II error as this is one of the first exploratory analyses of correlates of anxiety in this population. Further, secondary analyses using the ATQ and DASH-II were conducted to confirm findings of the primary analysis model, utilising the ADAMS (see sections 3.4.4 and 3.4.5 for further details).

Table 3.4 Descriptive statistics highlighting presence and severity of health difficulties in individuals with ID

Health questionnaire item	Mild, n (%)	Moderate, n (%)	Severe, n (%)	Presence of health difficulty, n (%)[30]
Eye problems	9 (5.5)	8 (4.8)	1 (0.6)	18 (10.9)
Ear problems	21 (12.7)	10 (6.1)	6 (3.6)	37 (22.4)
Dental problems	27 (16.4)	13 (7.9)	6 (3.6)	46 (27.9)
Cleft palate	2 (1.2)	3 (1.8)	0 (0)	5 (3.0)
Gastrointestinal difficulties	30 (18.2)	31 (18.8)	7 (4.2)	68 (41.2)
Bowel problems	37 (22.4)	20 (12.1)	7 (4.2)	64 (38.8)
Heart abnormalities or circulatory problems	4 (2.4)	1 (0.6)	1 (0.6)	6 (3.6)
Problems with genitalia	4 (2.4)	1 (0.6)	1 (0.6)	6 (3.6)
Hernia	0 (0)	0 (0)	2 (1.2)	2 (1.2)
Limb abnormalities	5 (3.0)	2 (1.2)	1 (0.6)	8 (4.8)
Epilepsy/seizures/neurological referrals	25 (15.2)	11 (6.7)	9 (5.5)	45 (27.4)
Lung or respiratory problems	14 (8.5)	4 (2.4)	3 (1.8)	21 (12.7)
Liver or kidney problems	3 (1.8)	3 (1.8)	0 (0)	6 (3.6)
Diabetes or thyroid function problems	5 (3.0)	1 (0.6)	2 (1.2)	8 (4.8)
Skin problems	47 (28.5)	18 (10.9)	3 (1.8)	68 (41.2)

[30] Based on a complete sample of *n*=165, except for item 11 which is based on a sample of *n*=164

Table 3.5 Descriptive statistics highlighting endorsement of anxiety triggers for individuals with ID (ordered total endorsement from high to low)

Item number	Anxiety Triggers Questionnaire item	About half of the time, n (%)	Most of the time, n (%)	Always, n (%)	Total, n (%)[31]
21	Crowds	29 (17.6)	29 (17.6)	30 (18.2)	88 (53.3)
5	Changes to routine	34 (20.6)	26 (15.8)	26 (15.8)	86 (52.1)
11	Loud/unexpected noises	29 (17.6)	14 (8.5)	37 (22.4)	80 (48.5)
22	Sensory sensitivities	20 (12.1)	24 (14.5)	34 (20.7)	78 (47.3)
10	Visiting the doctor/hospital	27 (16.5)	25 (15.2)	25 (15.2)	77 (47)
6	Being around people who are unpredictable (young children/babies)	30 (18.2)	25 (15.2)	22 (13.3)	77 (46.7)
3	When other people are upset or cross with someone else	35 (21.3)	21 (12.8)	19 (11.6)	75 (45.7)
14	Others being upset/cross with them	32 (19.5)	17 (10.4)	22 (13.4)	71 (43.3)
20	Injections, needles, blood	8 (4.8)	16 (9.7)	46 (27.9)	70 (42.4)
12	When injured/in pain	22 (13.4)	22 (13.4)	23 (14.0)	67 (40.9)
9	New situations	24 (14.5)	23 (13.9)	20 (12.1)	67 (40.6)
18	Being in unpredictable situations	13 (7.9)	20 (12.1)	25 (15.2)	58 (35.2)
19	Social situations	19 (11.5)	16 (9.7)	19 (11.5)	54 (32.7)
23	High demands	13 (7.9)	21 (12.7)	19 (11.5)	53 (32.1)
8	Anticipation about future events	22 (13.3)	13 (7.9)	14 (8.5)	49 (29.7)
2	Worries across multiple contexts and situations	26 (15.9)	14 (8.5)	7 (4.3)	47 (28.7)
16	Mechanical noises/noises in the environment	25 (15.2)	11 (6.7)	10 (6.1)	46 (27.9)
7	Animals	18 (10.9)	10 (6.1)	15 (9.1)	43 (26.1)
17	Using public transport	15 (9.1)	14 (8.5)	11 (6.7)	40 (24.2)
15	Thunder/lightening	18 (10.9)	8 (4.8)	7 (4.2)	33 (20)
1	Receiving criticism from others	15 (9.1)	12 (7.3)	2 (1.2)	29 (17.6)
13	Getting something wrong	16 (9.7)	6 (3.6)	4 (2.4)	26 (15.8)
4	Heights	14 (8.5)	7 (4.2)	5 (3.0)	26 (15.8)
24	Clowns	1 (0.6)	1 (0.6)	10 (6.1)	12 (7.3)

[31] Based on a complete sample of *n*=165, except for items 2, 3, 10, 12 and 14 which are based on a sample of *n*=164 due to missing data

3.4 Results

3.4.1 Assumptions

A number of assumptions were tested for the multiple hierarchical regression analyses. Variation inflation factors (VIF) ranged between 1.239-4.116, with all values well below 10 suggesting no evidence of multicollinearity between predictor variables. Assumptions of linearity and homoscedasticity were met, as assessed by visual inspection of plots of standardised predicted values against standardised residuals and partial regression plots. This was further confirmed during sensitivity analyses utilising bootstrapping and robust regression whereby model parameters and interpretations did not differ from the original models, suggesting that data were not affected by non-linearity and heteroscedasticity (Field, 2018). Normality of residuals was established utilising histograms and normal P-P plots. To identify potential outliers in the data, casewise diagnostics, leverage points and Cook's distance were explored. Data with large leverage values were retained in the analysis as it is suggested they do not have a large influence on the regression coefficients (Field, 2018). Standardised residuals were within expected ranges with 0.6-1.9% of cases ± 2.5 and 3.2%-5.1% of cases ± 2. In the analyses including the ATQ total score, one case had a residual greater than 3 and two cases had residuals greater than 3 in the DASH-II anxiety subscale analysis. The cases were revisited, and no reasons were identified for these outliers. Furthermore, Cook's distance across all analyses indicated that no case in the sample had an undue influence on the models with no cause for concern regarding outliers, therefore analyses included all cases with complete data (Cook & Weisberg, 1982; Stevens, 2002).

3.4.2 Relationships between anxiety measures

Due to non-normally distributed variables, Spearman's correlations were conducted to explore relationships between anxiety measures included in the current analyses. Moderate to strong correlations were found, ranging from, $r_s(161)=.588$, $p<.001$, between the ATQ total score and the DASH-II anxiety subscale and, $r_s(163)=.739$, $p<.001$ between the ADAMS generalised anxiety subscale and the ATQ total score. All correlations were statistically significant ($p<.001$).

3.4.3 Hierarchical regression analyses: Generalised anxiety subscale of the ADAMS

Diagnoses were entered in step 1, age, gender, verbal ability, the self-help subscale score from the WX and the SCQ total score were entered in step 2 and sensory processing, repetitive behaviour, intolerance of uncertainty and health difficulties in step 3. Step 1, 2 and 3 in the model accounted for 14%, 17.7% and 61.9% of the variance in anxiety scores respectively. The overall model predicted anxiety, with step 1 and 3 being statistically significant ($p<.001$) whilst step 2 was not ($p=.261$).

At step 1, autism was chosen as the baseline category whereby each other diagnostic category was compared (i.e., AS, CdLS, FXS, heterogenous). Overall, the model indicated that compared to autistic individuals, individuals with a diagnosis of AS or a heterogenous diagnosis have significantly lower anxiety scores (p<.001; p=.001 respectively), whilst those with a diagnosis of CdLS had similar anxiety scores to autistic individuals (p=.230). Individuals with FXS appeared to have similar anxiety scores to autistic individuals, however, analysis approached significant difference (p=.057). An individual's diagnosis explained 14% of the variance in anxiety scores and was significantly better at predicting anxiety than having no model.

In terms of individual predictors in step 2, age, gender, verbal ability, self-help subscale score on the WX and the SCQ total score did not significantly predict anxiety scores.

In terms of individual predictors in step 3, higher scores on frequency of health difficulties, auditory sensory processing difficulties and intolerance of uncertainty significantly predicted higher anxiety scores (p=.002; p=.012; p<.001 respectively). The diagnosis variables at step 1 were no longer significant in the overall model at step 3 for AS and heterogenous diagnostic groups (p=.056; p=.165 respectively). However, the finding that the AS group had significantly lower anxiety scores than autistic individuals in step 1 approached significant difference at step 3 (p=.056). Visual and tactile sensory processing difficulties did not significantly predict anxiety (p=.085, p=.222 respectively), nor did repetitive behaviour at a total score level (p=.689) or subscale level (motor/sensory behaviours: p=.261; rigidity/routines/preoccupation with restricted interests: p=.198). Furthermore, an additional model replacing the frequency of health difficulties with the severity of health difficulties indicated that severity was also a significant predictor of anxiety (p=.027). For the explored models, the AIC suggested a worse fit of the model with the addition of step 2 variables, however an improved fit from step 1 to 3 and step 2 to 3. The AIC was smallest for the model that included the frequency of health difficulties variable compared to the model including severity of health difficulties (AIC=383.282 and AIC=388.124 respectively).

3.4.4 Anxiety triggers as assessed by the ATQ

3.4.4.1 Descriptive statistics

The response options of at least "about half of the time" in response to a particular anxiety trigger were summed to represent endorsement of particular anxiety triggers (See Table 3.6). Overall, the most commonly endorsed anxiety triggers were crowds (n=88, 53.3%), changes to routine (n=86, 52.1%), loud or unexpected noises (n=80, 48.5%) and sensory sensitivities (n=78, 47.3%). Endorsement of anxiety triggers has also been considered across diagnoses and is presented in Appendix 23.

3.4.4.2 Hierarchical multiple regression analyses: ATQ

Principal component analysis (PCA) was conducted to explore the ATQ and identify clusters of items, with the aim to reduce items into a smaller set of components (Field, 2018; See Appendix 24). Due to findings from the scree plot and theoretical justification as described in the Appendix 24, the current study utilised a single total score from the ATQ as a dependent variable to be used in a subsequent hierarchical multiple regression analysis. The rest of the model was kept the same as described above.

Step 1, 2 and 3 in the model accounted for 10.3%, 18.9% and 72.7% of the variance in endorsement of anxiety triggers respectively. The overall model predicted the endorsement of anxiety triggers, all steps being statistically significant (step 1; p=.002, step 2; p<.001, step 3; p=.011).

At step 1, compared to autistic individuals, individuals with a diagnosis of AS or a heterogenous diagnosis had significantly lower scores for endorsement of anxiety triggers (p<.001; p=.01 respectively), whilst those with a diagnosis of CdLS or FXS had similar scores to autistic individuals (p=.103; p=.336 respectively). An individual's diagnosis explained 10.3% of the variance in anxiety trigger scores and was significantly better at predicting anxiety triggers than having no model.

In terms of individual predictors in step 2, age, gender, self-help subscale score on the WX and the SCQ total score did not significantly predict anxiety scores. Verbal ability did significantly predict endorsement of anxiety triggers (p=.003); for individuals who use more verbal language, a higher number of anxiety triggers were endorsed by parents/carers.

In terms of individual predictors in step 3, higher scores on auditory sensory processing difficulties and intolerance of uncertainty significantly predicted endorsement of a higher number of anxiety triggers (p=.003; p<.001 respectively). The diagnosis variables at step 1 (AS and heterogenous diagnosis) were no longer significant (p=.609; p=.861) at step 3. Verbal ability at step 2 was significant in the overall model at step 3 (p=.037), indicating that those with more verbal language endorsed a higher number of anxiety triggers. The remaining variables of visual and tactile sensory processing, repetitive behaviour and health were non-significant.

In contrast to the analysis including the ADAMS generalised anxiety subscale as the outcome variable, the current analysis showed a better fit of the model with the addition of step 2 variables, and a further improved fit from step 2 to 3. However, similarly to the previous analysis, the AIC was smallest for the model that included the frequency of health difficulties variable compared to the model including severity of health difficulties (AIC=773.139 and AIC=773.674 respectively).

3.4.5 Further analysis exploring consistency of findings across anxiety measures

Due to the lack of a gold standard measure for anxiety in individuals with moderate-profound ID (Flynn et al., 2017), the analyses utilised the generalised anxiety subscale of the ADAMS for the primary analysis and then used the total score from the ATQ to explore anxiety triggers. These analyses were compared to a further analysis utilising the anxiety subscale from the DASH-II. These analyses were completed to explore consistency of findings across anxiety measures that have been identified as appropriate to use in the moderate-profound ID population i.e., ADAMS and DASH-II (Flynn et al., 2017). The ATQ was chosen due to its specific focus on anxiety triggers and its use with individuals with genetic syndromes associated with ID (Royston, 2018). The rest of the model remained the same as previous analyses and was used to explore whether the same pattern of results were observed across existing measures for individuals with moderate-profound ID.

Consistent with analyses utilising the ADAMS and ATQ, higher scores on intolerance of uncertainty and auditory sensory processing difficulties predicted higher scores of anxiety on the DASH-II (p<.001-.011). More health difficulties and increased severity of health difficulties also predicted higher anxiety scores (p<.001-.003). Lastly, gender was a significant predictor of anxiety scores, whereby predicted anxiety for males was less than that predicted for females (p=.003-.005).

Similarly, to the analysis utilising the ATQ total score as the outcome variable, the current analysis showed a better fit of the model with the addition of step 2 variables, and a further improved fit from step 2 to 3. In contrast to the previous analyses, the AIC was smallest for the model that included the severity of health difficulties variable compared to the model including frequency of health difficulties (AIC=271.671 and AIC=275.169 respectively).

3.4.6 Sensory processing subtype analysis

Furthermore, due to analyses highlighting the possible importance of auditory sensory processing difficulties, items within the auditory domain of the Sensory Profile were summed to form hyperreactivity, hyporeactivity and sensory seeking subtype scores so that exploratory analysis could be conducted of fine-grained pathways to anxiety. As this is a deviation from how the Sensory Profile 2 is typically scored, two researchers examined and independently rated the items as measuring each of these sensory processing subtypes prior to them being included in analysis, to ensure there was consensus about what each item was measuring. These two researchers were the researcher leading this project and a Clinical Psychologist and Senior Lecturer with experience of sensory assessments (Kappa=.941). This allowed further exploration of how specific auditory sensory processing experiences predict anxiety.

Allocating items to sensory subtypes resulted in five items in the auditory hyperreactivity group, with demonstrated moderate item-level reliability (α=.775; *n*=157). Due to a limited number of items in the hyporeactivity (two) and sensory seeking groups (one), reliability was unable to be explored, therefore, these two groups were excluded from subsequent analysis. This decision was also in line with existing literature that has highlighted a link between auditory hyperreactivity and anxiety, with less evidence to suggest links with hyporeactivity and sensory seeking (Crawford et al., 2017; MacLennan et al., 2020; Royston et al., 2018). Auditory hyperreactivity was then entered into a hierarchical multiple regression analysis, instead of the original auditory sensory processing subscale. When utilising the ADAMS and the ATQ total score as the outcome variables, higher scores on auditory hyperreactivity predicted higher anxiety scores and a higher number of endorsement of anxiety triggers (*p*=.021-.029, *p*<.001 respectively). Findings were non-significant when utilising the DASH-II as an outcome variable (*p*=.230-.286). Regression analyses including R^2 and ANOVAs are found in tables 3.6, 3.7, 3.8 and 3.9.

Table 3.6 ANOVA models and R^2 for each outcome variable for model including frequency of health difficulties

		General anxiety subscale of ADAMS	Anxiety Triggers Questionnaire total score	Anxiety subscale of DASH
Step 1	F statistic	6.19 (p<.001)	4.33 (p=.002)	.47 (p=.759)
	df	(4,152)	(4,151)	(4,152)
	R^2	.14	.10	.01
Step 2	F statistic	3.51 (p=.001)	3.79 (p<.001)	2.75 (p=.005)
	df	(9,147)	(9,146)	(9,147)
	R^2	.18	.19	.14
Step 3	F statistic	15.24 (p<.001)	24.91 (p<.001)	8.89 (p<.001)
	df	(15,141)	(15,140)	(15,141)
	R^2	.62	.73	.49

Step 1: diagnosis, Step 2: age, gender, verbal ability, self-help subscale score on WX, SCQ total score, Step 3: auditory, visual, tactile sensory differences, repetitive behaviour, intolerance of uncertainty, frequency of health difficulties

Table 3.7 ANOVA models and R^2 for each outcome variable for model including severity of health difficulties

		General anxiety subscale of ADAMS	Anxiety Triggers Questionnaire total score	Anxiety subscale of DASH
Step 1	F statistic	6.3 (p<.001)	4.38 (p=.002)	.47 (p=.759)
	df	(4,154)	(4,153)	(4,154)
	R^2	.14	.10	.01
Step 2	F statistic	3.63 (p<.001)	3.87 (p<.001)	2.87 (p=.004)
	df	(9,149)	(9,148)	(9,149)
	R^2	.18	.19	.15
Step 3	F statistic	17.41 (p<.001)	29.43 (p<.001)	9.42 (p<.001)
	df	(13,145)	(13,144)	(13,145)
	R^2	.61	.73	.46

Step 1: diagnosis, Step 2: age, gender, verbal ability, self-help subscale score on WX, SCQ total score, Step 3: auditory, visual, tactile sensory differences, repetitive behaviour, intolerance of uncertainty, severity of health difficulties

Table 3.8 ANOVA models and R^2 for each outcome variable for model including auditory hyperreactivity and frequency of health difficulties

		General anxiety subscale of ADAMS	Anxiety Triggers Questionnaire total score	Anxiety subscale of DASH
Step 1	F statistic	6.19 (p<.001)	4.33 (p=.002)	.47 (p=.759)
	df	(4,152)	(4,151)	(4,152)
	R^2	.14	.10	.01
Step 2	F statistic	3.51 (p=.001)	3.79 (p<.001)	2.75 (p=.005)
	df	(9,147)	(9,146)	(9,147)
	R^2	.18	.19	.14
Step 3	F statistic	14.5 (p<.001)	24.79 (p<.001)	9.3 (p<.001)
	df	(15,141)	(15,140)	(15,141)
	R^2	.61	.73	.5

Step 1: diagnosis, Step 2: age, gender, verbal ability, self-help subscale score on WX, SCQ total score, Step 3: auditory hyperreactivity, repetitive behaviour, intolerance of uncertainty, frequency of health difficulties

Table 3.9 ANOVA models and R^2 for each outcome variable for model including auditory hyperreactivity and severity of health difficulties

		General anxiety subscale of ADAMS	Anxiety Triggers Questionnaire total score	Anxiety subscale of DASH
Step 1	F statistic	6.3 (p<.001)	4.38 (p=.002)	.47 (p=.759)
	df	(4,154)	(4,153)	(4,154)
	R^2	.14	.10	.01
Step 2	F statistic	3.63 (p<.001)	3.87 (p<.001)	2.87 (p=.004)
	df	(9,149)	(9,148)	(9,149)
	R^2	.18	.19	.15
Step 3	F statistic	16.53 (p<.001)	29.35 (p<.001)	9.95 (p<.001)
	df	(13,145)	(13,144)	(13,145)
	R^2	.60	.73	.47

Step 1: diagnosis, Step 2: age, gender, verbal ability, self-help subscale score on WX, SCQ total score, Step 3: auditory hyperreactivity, repetitive behaviour, intolerance of uncertainty, severity of health difficulties

3.5 Discussion

This is one of the first known studies to date to explore correlates of anxiety in individuals with moderate-profound ID. Due to the identified limitations of existing anxiety measures for this population, the current study conducted analyses including three different anxiety measures, to examine consistency and/or discrepancy of findings between measures (Flynn et al., 2017).

Findings demonstrated that individuals with Angelman syndrome or a heterogenous ID diagnosis experience less anxiety than autistic individuals. Whilst those with a diagnosis of Cornelia de Lange and Fragile X syndromes have similar anxiety scores to autistic individuals. However, diagnostic label no longer predicted anxiety when further variables were added into the model.

In terms of demographic variables, individuals who use more verbal language experienced a higher number of anxiety triggers and the female gender predicted higher anxiety scores. Both of these findings remained true when further factors were taken into consideration, suggesting that verbal ability and female gender may be important factors associated with anxiety in the moderate-profound ID population. Age, adaptive ability, and autism characteristics did not predict anxiety.

When focusing on the factors of interest, auditory sensory processing differences and intolerance of uncertainty were consistently associated with anxiety across all analyses, regardless of anxiety measure used. Frequency and severity of health difficulties were associated with anxiety, fairly consistently across analyses. Diagnosis no longer predicted anxiety, suggesting that, auditory sensory processing differences, intolerance of uncertainty and health difficulties may be factors associated with anxiety that cut across diagnoses. It

may be that these correlates are relevant to the moderate-profound ID population more generally. Verbal ability did significantly predict anxiety and therefore may be an important factor to consider above and beyond sensory processing differences, intolerance of uncertainty, health difficulties and diagnosis. When further exploring auditory sensory processing differences, auditory hyperreactivity was found to be associated with anxiety, fairly consistently across anxiety measures. Higher scores on auditory hyperreactivity predicted anxiety, using the ADAMS and ATQ, but not the DASH-II. The discrepancy is likely due to measurement difference across measures; one potential explanation could be due to the DASH-II utilising a frequency count of anxious behaviours (e.g., 1-10 times), whilst the ADAMS explores anxiety severity and the ATQ explores broad anxiety frequency (e.g., rarely, most of the time, always). Repetitive behaviour did not predict anxiety.

The current study findings are consistent with previous literature. Similarly high levels of anxiety are found in individuals with CdLS, FXS and autistic individuals (Crawford et al., 2017; Ezell et al., 2019; Ouyang et al., 2014). Research has indicated that individuals with AS do not demonstrate high levels of anxiety, although research is scarce in this area (Wink et al., 2015). It may be that levels of anxiety in AS are not comparable to individuals with CdLS, FXS or autism. More specifically, there is evidence to suggest that separation anxiety is observed in AS, therefore it is possible that the anxiety measures in the current study were not specific enough to demonstrate significance within the AS group. More research is needed to explore anxiety presentation in AS (Wheeler et al., 2019). The findings also suggested that the heterogenous group may have lower levels of anxiety compared to the autistic group. Due to the heterogenous group including small numbers of participants with varying diagnoses, it is important for further research to explore anxiety presentation in these groups. Furthermore, when dummy coding, individuals with a genetic syndrome and autism diagnosis were put into their relevant syndrome group rather than the autism group. It is important to consider the pros and cons of this approach. For example, grouping those with a genetic syndrome diagnosis with and without autism may have implications for factors associated with anxiety, which would be difficult to disentangle in the current analyses. However, the alternative of grouping all those with an autism diagnosis regardless of genetic syndrome diagnosis could be considered a limitation due to reported differences in presentation between idiopathic and syndromic autism. In the current study, coding individuals into the relevant syndrome group was considered the most appropriate option. Future research could strive to compare and contrast different diagnostic groups to explore the impact on factors associated with anxiety. That being said, the current study provides a starting point for correlates of anxiety that may cut across diagnostic groups to delineate shared pathways to anxiety, whereby individual diagnosis alone may not be a major factor in the development and maintenance of anxiety.

In terms of demographic variables, individuals with more verbal ability endorsed a higher number of anxiety triggers, which is consistent with previous literature (Hoare et al., 1998). This finding may suggest that those with more verbal ability are more likely to experience a higher number of anxiety triggers, or for individuals with less verbal ability, it may be that it is difficult for parents/carers to identify anxiety triggers as their child/the person they care for is less able to verbalise what triggers their anxiety (Hagopian & Jennett, 2008; Tarver et al., 2021a). The finding that being female predicted higher anxiety scores is consistent with previous literature in the general, autistic and ID populations (Chester et al., 2013; Hermans et al., 2013; McLean et al., 2011; Sedgewick et al., 2021). However, findings can be mixed in the autism literature where no gender differences in anxiety have been found (Magiati et al., 2016; Mayes et al., 2011), it is worth noting that these studies present predominantly male samples (81.7-85.6%) whilst the current study yields a relatively equal gender split (92 males, 55.8%; 73 females, 44.2%) which is a strength of the study and could be a more accurate representation of gender differences in anxiety. However, as discussed in section 3.2.2.2, potential gender differences in syndrome groups need to be considered when exploring gender as a potential factor associated with anxiety. In the current study, all individuals with FXS (*n*=10) were males. However, this sub-sample made up a small proportion of males in the overall sample (10.9%) so is unlikely to have disproportionately impacted the male group. It is important to note that the finding that those with FXS have similar anxiety scores to autistic individuals is restricted to males in the current study, and does not speak to anxiety scores in females diagnosed with FXS. Further studies should consider the split of gender and how these interact with diagnoses present, when deciding whether to aggregate or separate syndrome groups as well as when interpreting findings.

The finding that intolerance of uncertainty, auditory sensory processing difficulties and health difficulties were important predictors of anxiety in the current study is consistent with previous literature (Boulter et al., 2014; Hsieh et al., 2020; Lau et al., 2020; MacLennan et al., 2021; Muskett et al., 2019; Perry, 2019; Whitney et al., 2019). These findings suggest that these factors may have important implications for the development and maintenance of anxiety which may allow for early screening and intervention for individuals most at-risk. Determining relevant factors allows us to form hypotheses regarding potential pathways to anxiety in vulnerable groups. This study provides a starting point for future research to explore gender, auditory sensory processing difficulties, intolerance of uncertainty and health difficulties in more depth as predictors of anxiety in the moderate-profound ID population.

There are limitations of the current study that are worth noting. Firstly, utilising the Wessex Questionnaire as a proxy measure of moderate-profound ID could be considered a limitation of the current study as it is not an in-depth assessment of ability. Furthermore, it gives a self-help score that only includes elements of personal care, which does not consider

skills in different areas such as interpersonal and reasoning skills. However, for the purpose of the current study it was deemed appropriate to give an overall indication of ability due to the large-scale questionnaire design, it is also a measure that has been used with autism and genetic syndrome groups previously and it allows categorisation of ability level (Oliver et al., 2011; Palmer & Jenkins, 1982; Richards et al., 2016).

The study utilises a regression approach which is unable to determine causation between variables. Therefore, whilst an appropriate conclusion would be that intolerance of uncertainty is associated with anxiety, the study is unable to conclude whether intolerance of uncertainty leads to anxiety or vice versa. Additionally, there is difficulty in identifying and differentiating triggers of anxiety vs. consequences of anxiety vs. coping mechanisms. The current study only highlights key factors that may be important in the presentation and assessment of anxiety, it does not tell us **how** these factors relate to anxiety. For example, sensory sensitivities could be a trigger for anxiety, or a consequence of anxiety, if an individual is anxious, they may be more hypervigilant and sensitive to sensory stimuli (Green & Ben-Sasson, 2010). Green et al. (2012) has provided evidence that sensory over-responsivity increases the risk of developing anxiety over time, and therefore sensory sensitivities may be a trigger for anxiety. Additionally, whilst research has suggested that higher rates of intolerance of uncertainty may lead to anxiety, there is recognition it could be that anxiety leads to the consequence of higher levels of intolerance of uncertainty, resulting from exerting more control as a coping strategy (Boulter et al., 2014). Being able to differentiate these factors has clinical implications, for example, identification that a factor is a trigger for anxiety may allow preventative efforts and early intervention. This thesis provides a starting point for identifying relevant factors, future longitudinal research, utilising a range of methodologies (e.g., questionnaire, direct assessment) should focus on disentangling how different factors relate to anxiety and aim to build a theoretical model of anxiety for the moderate-profound ID population.

Whilst the current study has identified correlates of anxiety that cut across diagnostic groups, it is critical in clinical services to treat every person as an individual, not to make assumptions based on level of functioning and to continue to focus on the specificity of individual presentation. The considerations for anxiety assessment described in section 4.5 are paramount, however, this study provides evidence of potential risk markers that may be a starting point to identify individuals most at risk of experiencing anxiety.

The current study comprised of a large questionnaire battery, therefore, only specific subscales of interest from the Sensory Profile were used. When exploring the auditory hyperreactivity items, findings suggest that this is an important contributor to anxiety and there are a number of items (five) in the proposed scale allowing for the demonstration of item-level reliability. However, the Sensory Profile was used in a way that it was not

intended. Therefore, findings need to be interpreted with caution and future research would need to confirm these findings to explore sensory subtypes and how they might relate to anxiety in the moderate-profound ID population (MacLennan et al., 2021).

It is important to note the potential for circular relationships between measures used in the current study, for example, between the RULES (i.e., measure of intolerance of uncertainty) and the ATQ due to potential overlap between items that tap into uncertainty e.g., being in unpredictable situations. This was another reason why use of multiple measures of anxiety in the current study was crucial. Items on the ADAMS and DASH-II are more generic anxiety items, rather than specifically focusing on uncertain contexts, for example, trembles or shakes for no obvious reason. The analyses utilising the ADAMS and DASH-II evidenced significant relationships between anxiety and intolerance of uncertainty, and previous research has also reported this finding (MacLennan et al., 2021). Therefore, it is likely that these relationships do reflect true association, however, exploring these relationships utilising direct assessment methodology may help to overcome the limitations associated with potential item overlap and reliance on questionnaire measures.

Furthermore, due to the highlighted limitations of existing anxiety measures for the moderate-profound ID population, further research will need to confirm the current study findings when more appropriate measures are developed and validated for this population (Flynn et al., 2017).

The current study relies solely on parent/carer questionnaire measures to explore complex factors such as sensory processing, intolerance of uncertainty and anxiety. As is discussed further in sections 4.2 and 4.4.2, it may be that there is conceptual overlap between questionnaire items which conflate the relationships between these variables and anxiety, making it difficult to tease apart interrelationships. Parent/carer questionnaire measures also rely on a parents/carer's interpretation of an individual's behaviour, especially if those individuals are less able to verbalise about their experiences of anxiety (Tarver et al., 2021a). This is an important consideration as parents/carers do not always find it easy to identify what their child/the person they care for may be feeling (Tarver et al., 2021a). Future research would need to confirm these relationships in studies utilising direct assessment measures with individuals with moderate-profound ID. The initial plan for the final doctoral study (Chapter five) was to use direct assessment measures to further explore these relationships. However, due to the disruption from the Covid-19 pandemic, the focus of the final study had to be altered. To complete a study that was appropriate for a smaller predicted sample size, direct assessment measures were still used but to conduct fine-grained behavioural coding and analysis of behaviours associated with anxiety; this work is presented in Chapter five.

Despite these identified limitations, the current study is unique and has notable strengths; as it includes a large, heterogenous sample of individuals with moderate-profound ID with a range of diagnoses associated with ID, including individuals with rare genetic syndromes. Focusing on this population and the findings of this study have implications for clinical services providing support for the ID population. Whilst it is important to develop our understanding of phenotypic features of individuals with a specific diagnosis, it is also crucial to confirm whether similar factors are implicated in the development and maintenance of anxiety across groups. This study identified verbal ability, gender, auditory processing differences (namely hyperreactivity), intolerance of uncertainty and health difficulties as potentially important factors. Clinical services should aim to explore these factors when supporting individuals with ID, as much as possible prior to the presentation of anxiety to be able to prevent the development of anxiety or to intervene and disrupt the maintenance of anxiety.

Chapter 4: Utilising interview methodology to inform the development of new clinical assessment tools for anxiety in autistic individuals who speak or no words

The research reported on in the following chapter has now been published with minor differences. It has been reproduced with retained copyright:

Edwards, G., (GE) Tarver, J., Shelley, L., Bird, M., Hughes, J., Crawford, H., & Waite, J. (2022). Utilising Interview Methodology to Inform the Development of New Clinical Assessment Tools for Anxiety in Autistic Individuals Who Speak Few or no Words. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-022-05509-y

GE designed the study, recruited participants, collected data, completed analysis, wrote the drafts of the manuscript, completed revisions, and submitted the final version for publication.

4.1 Preface

The previous chapter presented a large-scale cross-sectional questionnaire study that identified shared correlates of anxiety in people with moderate to profound ID of varying aetiology. These correlates inform possible causal pathways to anxiety and may explain the heightened risk of anxiety experienced by individuals with moderate-profound ID more generally. A limitation noted in the previous chapter was the lack of measures validated for people with moderate-profound ID for the assessment of anxiety in this population and the need to replicate findings with measures that have been exclusively developed and validated for individuals with moderate-profound ID. The next chapter aims to provide a starting point for addressing this gap in the literature. The chapter presents an interview study completed with parents/carers and clinicians, delineating the presentation of anxiety in autistic individuals who speak few or no words. This autistic sample provided a relatively homogenous group where there is high risk for anxiety, which was a starting point for identifying behavioural markers of anxiety. Such anxiety markers may be important for detecting anxiety within and across groups. The chapter also explores the considerations needed for the development of new assessments of anxiety. Information regarding anxiety presentation and considerations needed for the development of new assessment measures has been taken forward to develop a new assessment measure that is currently under-going validation. Further information will be published elsewhere, outside of the current thesis.

4.2 Introduction

Autism is associated with reduced verbal language use and high rates of comorbidity with ID (Maljaars et al., 2012; Matson & Shoemaker, 2009; Mody & Belliveau, 2013). Approximately 50% of autistic individuals have an ID diagnosis (Charman et al., 2011; Loomes et al., 2017) and 25-30% speak few or no words (Anderson et al., 2007; Norrelgen et al., 2015), although rates of up to 50% have been reported (Magiati et al., 2011).

Autistic individuals and individuals with ID are at heightened risk of experiencing anxiety compared to the general population, as highlighted in sections 1.4.2 and 1.4.5 (Costello et al., 2005; Gotham et al., 2013; Green et al., 2015). In autistic individuals, prevalence rates are estimated at 20-42% and research has demonstrated the pervasive and significant impact that anxiety can have on the quality of life of individuals and their families (Adams & Emerson, 2021; Smith et al., 2019). This includes an impact on an individual's ability to engage in enjoyable activities both inside and outside of the home, classroom performance, social support, and self-esteem (Adams & Emerson, 2021; Smith et al., 2019). Anxiety also has an impact on the wider family, such as parental relationships, a caregiver's career, ability to attend events with and without the child and caregiver stress (Adams & Emerson, 2021). Autistic individuals and their families, as well as clinicians and professionals have highlighted that better understanding of anxiety is a key priority for autism research, to inform the development of appropriate and effective interventions to reduce anxiety (Cusack & Sterry, 2016).

Despite the increase in research focusing on anxiety in autism in recent years, studies have often focused disproportionately on autistic individuals without ID and/or those who speak in sentences (Jack & Pelphrey, 2017; Russell et al., 2019; Tager-Flusberg & Kasari, 2013). One explanation for the current under-representation of autistic people with ID in research may be the challenges of assessing anxiety in those who speak few or no words. These challenges may help to explain the historic lack of validated measures developed for this population. Assessment is complicated by atypical and complex presentations of mental health, difficulties utilising existing self-report measures, diagnostic overshadowing, and behavioural overlap (e.g., disentangling whether a behaviour is indicative of anxiety, autism, or pain) (Adams et al., 2019; Hagopian & Jennett, 2008; Lau et al., 2020; Vasa et al., 2016; White et al., 2015). As many as 40% of autistic individuals may meet criteria for impairing anxiety that does not map onto traditional definitions of anxiety using standard diagnostic criteria; anxiety associated with change to routine, novelty, losing access to special interests and unusual specific fears (e.g., balloons, fear of baby crying) have been reported (Hollocks et al., 2019; Kerns et al., 2014; van Steensel et al., 2011).

Several assessment tools have recently been developed to improve the identification of anxiety in autistic populations. Examples include the Anxiety Disorders Interview Schedule with Autism Spectrum Addendum (ADIS/ASA; Kerns et al., 2014), the Anxiety Scale for Autism Spectrum Disorder (ASC-ASD; Rodgers et al., 2016), the Anxiety Scale for Autism-Adults (Rodgers et al., 2020) and the Parent Rated Anxiety Scale for Youth with Autism Spectrum Disorder (PRAS-ASD; Scahill et al., 2019). Additionally, measures have been developed with the inclusion of individuals with ID (Bearss et al., 2016; Toscano et al., 2020). Whilst these measures explore presentations of anxiety that are more specific to autistic populations, individuals with ID only make up a small proportion of the study samples and several items may still require verbal expression of anxiety, making them less appropriate for individuals who speak few or no words. Another recent addition to the literature, the Assessment of Concerning Behavior Scale (ACB; Tarver et al., 2021b) is a screening measure designed to assess broad constructs of mental health in autistic individuals (internalizing and externalizing behaviours). A strength of the ACB is that it is validated in an autistic population with a broad range of abilities. However, the development of specific measures that focus on anxiety in autistic individuals with ID are needed, allowing for a nuanced and thorough understanding of anxiety when internalising difficulties are suspected; and so that the trajectory of anxiety symptomatology in this population can be examined over time.

While the availability of autism-specific assessment tools is improving gradually, there are very few studies focusing on identifying the presentation of anxiety in people with moderate-profound ID who speak few or no words. Flynn et al. (2017) reviewed existing mental health measures for this population, such as the Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003) and the Diagnostic Assessment for the Severely Handicapped Scale (DASH & DASH-II, Matson et al., 1991, 1995). An identified priority for future research was the confirmation of the validity and reliability of existing measures, as this information was reported for most measures based on a single research study. Additionally, measures were developed from diagnostic criteria for the general population, existing measures that used adapted diagnostic criteria for use with individuals with ID or clinical experience, whereas the authors argue a bottom-up descriptive approach to measure development may be more appropriate in this population. The inadequacy of existing measures may mean that those most at-risk of anxiety are not being identified, preventing early intervention (Costello & Bouras, 2006; Morgan et al., 2008).

Utilising bottom-up interview methodology to describe anxiety presentation can inform the development of the item pool for assessment measures, ensuring that the pool is not restricted to items derived from standard diagnostic criteria for the general population. In addition to examining anxiety presentation in autistic people with moderate-profound ID to

improve identification of anxiety, there is also a need to explore the features required in assessment tools to improve their overall utility for this population, e.g., items that aim to minimise diagnostic overshadowing and behavioural overlap.

Due to the identified limitations of existing measures, which may make their application inappropriate for this population, there is an identified gap in the literature and in clinical practice for validated anxiety measures specifically for autistic individuals with moderate-profound ID who speak few or no words (Flynn et al., 2017; Russell et al., 2019). Additionally, there is a paucity of research exploring anxiety presentation in this population and clinician experience of assessment, resulting in a lack of evidence to inform the development of new measures (Adams et al., 2019). There is a need for research to focus on this highlighted gap to document and justify measure development.

Here, the findings of a study that adopted a two-stage approach and combination of qualitative methods are presented. The study employed a bottom-up interview methodology with parents/carers and clinicians to address the following study aims: *i)* to explore the presentation of anxiety in autistic individuals who speak few or no words as described by parents/carers and clinicians.; *ii)* explore clinicians' experiences of identifying and assessing anxiety in individuals with ID who speak few or no words; *iii)* identify challenges faced by clinicians when assessing anxiety and the considerations needed to inform the development of assessment tools specifically for anxiety in individuals who speak few or no words. This study was conducted to inform the development of a comprehensive list of items for inclusion in a new assessment measure of anxiety; the validation of this measure against existing anxiety measures will be reported in detail elsewhere. However, sharing the detail of learning in the developmental stage of this project may help to stimulate the development of other new assessment tools for this population.

4.3 Methods

The current study used data collected from interviews conducted with parents/carers and clinicians from the first phase of a broader questionnaire development study. Parents/carers and clinicians were included to gain in-depth exploration and insight; they can provide unique perspectives and rich, detailed accounts of behaviour across contexts such as home, school, when out in the community and in clinical settings (Bearss et al., 2016; Cridland et al., 2015; Trembath et al., 2012). Clinician input was also crucial to ensure that information gathered was relevant within clinical practice. This study received a favourable ethical decision from the NHS Research Ethics Committee Wales REC 3 (ref: 18/WA/0139; See Appendix 8).

4.3.1 Participants

4.3.1.1 Parents/carers

Parents/carers were recruited via invitation letters distributed to parents of autistic individuals through an existing participant database held at the University of Birmingham, via social media and the Discover Network run by the charity Autistica (See Appendix 25). Individual clinical diagnosis of autism was confirmed via parent report, with the majority receiving a diagnosis from a paediatrician (*n*=13, 62%). All parents/carers included in the analyses reported that their child/the person they care for speaks odd words only or never a word, as assessed by the Wessex Questionnaire (Kushlick et al., 1973). Twenty-one interviews with parents/carers of autistic individuals (M_{age}=19.2, *SD*=11.3, range=7-52) were conducted. This included nine autistic individuals under 18 years of age (42.9%) and 12 who were 18 years or older (57.1%; see Table 4.1).

Table 4.1 Demographics for parent/carer interviews

Parent/carer and autistic individual demographics	
Autistic individual mean age in years (SD), *range*	19.2 (11.3), *7-52*
Autistic individual gender	
Male, n (%)	18 (85.7)
Female, n (%)	3 (14.3)
Diagnosis	
Autism, n (%)	21 (100)
Parent/carer gender	
Male, n (%)	1 (4.8)
Female, n (%)	20 (95.2)
Parent/carer mean age (SD), *range*	50.5 (7.2), *37-66*
Relationship to autistic individual	
Mother, n (%)	19 (90.5)
Father, n (%)	1 (4.8)
Sibling, n (%)	1 (4.8)
Household income	
Less than £15,000, n (%)	1 (4.8)
£15,001 to £25,000, n (%)	3 (14.3)
£25,001 to £35,000, n (%)	5 (23.8)
£35,001 to £45,000, n (%)	3 (14.3)
£45,001 to £55,000, n (%)	1 (4.8)
£55,001 to £65,000, n (%)	3 (14.3)
£65,000 or more, n (%)	4 (19)
Not provided, n (%)	1 (4.8)
Highest level of parent/carer education	
No formal qualifications, n (%)	1 (4.8)
Fewer than five GCSEs or O-levels, n (%)	0 (0)
Five or more GCSEs or O-levels, n (%)	2 (9.5)
Three or more A-levels, n (%)	2 (9.5)
University degree, n (%)	6 (28.6)
Masters or Doctoral degree, n (%)	6 (28.6)
Wessex	
Never a word, n (%)	6 (28.6)
Odd words only, n (%)	15 (71.4)
Mean self-help score (SD), *range*[32]	6.4 (1.1), *4-9*
SCQ mean score (SD), *range*[33]	23.9 (5.7), *13-31*
ADAMS[34] mean scores (SD), *range*	
General anxiety[35]	11.6 (4.1), *5-20*
Social avoidance	10.4 (4.4), *2-19*
Depressed	4.5 (2.6), *0-8*

[32] Scores of 3/4/5 are categorised as 'not able', scores of 6/7 are categorised as 'partly able', scores of 8/9 are categorised as 'able'
[33] SCQ=Social Communication Questionnaire; cut-off scores of 15 and 20 are suggestive of 'autism spectrum disorder' and 'autism' respectively
[34] ADAMS=Anxiety, Depression and Mood Scale
[35] Maximum subscale score of 21 for General anxiety, social avoidance and depressed subscales

Manic/hyperactive[36]	10.4 (3), *3-14*
Compulsive behaviour[37]	5.8 (2.6), *0-9*
Anxiety frequency[38]	
Never, n (%)	0 (0)
At least once a month, n (%)	4 (19)
At least once a week, n (%)	7 (33.3)
At least once a day, n (%)	8 (38.1)
At least once an hour, n (%)	1 (4.8)
Anxiety severity	
Mild, n (%)	1 (4.8)
Moderate, n (%)	7 (33.3)
Severe, n (%)	13 (61.9)

4.3.1.2 Clinicians

Clinicians were recruited from participating NHS learning disability clinics providing medical, psychology and nursing services in the West Midlands. Nine interviews were completed with clinicians with a range of roles (psychiatry, clinical psychology, nursing, paediatrics) and clinics. The average years of experience working in clinical services supporting individuals with autism and/or ID was 16 years (*SD*=10.48, range=5-36 years). Participant demographics are shown in Table 4.2.

Table 4.2 Demographics for clinician interviews

Clinician participant demographics	
Gender	
Female	6
Male	3
Clinician role	
Clinical Psychologist	2
Community Learning Disability Nurse	2
Clinical Nurse Specialist	2
Consultant Paediatric Neuropsychiatrist	1
Consultant Paediatric Liaison Psychiatrist	1
Consultant Community Paediatrician	1

[36] Maximum subscale score of 15
[37] Maximum subscale score of 9
[38] Anxiety frequency and severity based on parent/carer report in interview. One parent/carer felt unable to provide an accurate response to the question regarding anxiety frequency.

4.3.2 Procedure

4.3.2.1 Parents/carers

Parents/carers responding to study adverts and invitation letters were invited to complete study consent forms and questionnaires online (for sample characterisation, see section 4.3.3; See Appendix 26 for study information sheet and Appendix 27 for consent forms). Following this, a member of the research team arranged a date and time with parents/carers to complete the interview. Due to the national recruitment approach for parent/carer recruitment, interviews were completed over the telephone. Interviews were conducted by a member of the research team; interviewers were trained prior to data collection to ensure consistent interview style. With parental consent, parent interviews were audio-recorded and were transcribed verbatim. Two (9.5%) parents/carers did not consent to recording, so an interview coding document was used during these interviews to identify the presentation of anxiety for these individuals. Interview length varied from 25-149 minutes with a mean of 58 minutes (*SD*=30.4).

The main aim of the parent/carer interviews was to identify the presentation of anxiety in autistic individuals including behaviours associated with anxiety and triggers for anxiety to help inform the development of the item pool for a new measure. Parents/carers were also asked to discuss the frequency and severity of anxiety experienced by their child/the person they care for (See Table 4.1). The interview schedule was previously developed as part of a research project aiming to explore anxiety in ID utilising clinical formulation frameworks (Royston et al., 2021). Example interview questions are provided in Table 4.3. See Appendix 28 for full interview schedule.

Figure 4.3 Example interview questions (parents/carers)

Parent/carer interview question examples
• Can you describe a recent example or period of time when (X) showed this anxiety? • When (X) feels anxious, how do they behave during this time? • Does the onset of anxiety seem to be linked to any triggers or causes?
Example question prompts • Do you see any physical changes in their bodies? • Do you see changes in how the person moves? • Do you see any changes in their face? • Have you noticed any patterns when anxiety occurs?

4.3.2.2 Clinicians

Clinician interviews were designed to supplement parent/carer interviews regarding the presentation of anxiety. In addition, clinician interviews aimed to explore current methods and challenges of assessing anxiety in clinical services to highlight important considerations

for the development of assessment tools to assess mental health in individuals who speak few or no words. Clinician interviews were conducted face to face at the clinicians' usual place of work and were recorded and transcribed verbatim. The mean duration of these interviews was 55.89 minutes (*SD*=10.67, range= 33-70 minutes). The interview schedule was developed for the current study, mirroring questions on the parent/carer interview. Additional questions were asked to explore methods of assessing anxiety and associated challenges. Example questions are provided in Table 4.4. See Appendix 29 for full interview schedule.

Table 4.4 Example interview questions (clinicians)

Clinician interview question examples
• When you are assessing anxiety, are there specific things you look for in minimally verbal people? • When you are assessing anxiety in minimally verbal people, how do you differentiate this from other diagnoses, such as pain or autism spectrum disorder? • Do you ever think anxiety is diagnosed incorrectly, or overlooked? What leads to this?
Example question prompts • Do you see any physical changes in their bodies? • Do you see changes in how the person moves? • Are there particular behaviours that are shown that cause confusion?

4.3.3 Measures

Parents/carers completed the following questionnaire measures to characterise the sample of autistic individuals.

4.3.3.1 The Wessex Questionnaire

The Wessex Questionnaire (Kushlick et al., 1973; See Appendix 10) assesses an individual's social and physical adaptive ability (e.g., speech, self-help ability). The questionnaire has 16 items and can be used as a proxy measure of ability, with higher scores indicating greater ability. Inter-rater reliability is good at .62 (Kushlick et al., 1973; Palmer & Jenkins, 1982).

4.3.3.2 Social Communication Questionnaire

The Social Communication Questionnaire (SCQ; Rutter et al., 2003b; See Appendix 11) is a screening tool for autism characteristics. It has 40 items, and scores are summed to provide a total score with a high score indicating more autism characteristics. The SCQ is suitable for individuals with ID (Berument et al., 1999) with good internal consistency for verbal and non-verbal individuals (α=.94 and α=.89 respectively; Marvin et al., 2017).

4.3.3.3 Anxiety, Depression and Mood Scale

The Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003; See Appendix 12) explores behaviours related to anxiety, depression, and mania. There are 28 items rated on a Likert scale of 0 'not a problem' to 3 'severe problem.' The questionnaire is validated with informants of individuals with mild to profound ID. Test-retest reliability and internal consistency are excellent at .81 and .80 respectively (Esbensen et al., 2003).

4.3.4 Data analysis

The chapter presents the combination of content analysis for parent/carer and clinician responses to highlight and quantify the behaviours and triggers associated with anxiety. Further analysis was conducted for clinician responses, in the form of Interpretative phenomenological analysis (IPA) to explore clinician experience of assessing anxiety, associated challenges and considerations needed for the development of new assessment measures. The use of a combination of analysis techniques to make sense of qualitative data has been demonstrated in autism research previously (Brown et al., 2020). Each analysis approach is described below.

4.3.4.1 Content analysis to describe anxiety presentation

For all analyses, transcriptions were analysed using NVivo 12 (QSR International UK, 2018). To fulfil the first aim of the study, content analysis was used to identify codes in the parent/carer and clinician narratives to quantify behaviours associated with, or attributed to, anxiety. Information related to triggers for anxiety was also coded. A manifest analysis was chosen to ensure that findings remained true to the text and to code exact words used by participants, with limited interpretation from the researcher (Bengtsson, 2016). First, interview transcriptions were read several times to obtain familiarisation with the data. The text was then divided into meaning units, where the text relating to the presentation of anxiety was highlighted. The meaning units were then organised into codes and categories. A code is a descriptive label given to a meaning unit (e.g., hypervigilance). Codes that were related to each other were grouped together to form the categories of anxiety behaviours and triggers (Erlingsson & Brysiewicz, 2017). For example, proximity seeking was coded as an anxiety behaviour and busy environment was coded as an anxiety trigger (See Table 4.5 and 4.6 for further examples and endorsement across autistic children vs. adults).

4.3.4.2 Clinician assessment of anxiety and challenges of assessment

To fulfil the second and third aims of the study, further analysis was conducted on clinician interviews to gain understanding of clinicians' personal experience of the assessment of anxiety in ID clinical services and the challenges of assessment. IPA was chosen due to its ability to provide an in-depth exploration and sense-making of experiences, in a purposive and relatively homogeneous sample (Smith et al., 2009). Furthermore, it was

important in the current study that each clinician's experience was examined in detail, prior to making more general overarching claims across the sample, IPA can also be a particularly valuable approach when the topic is complex and ambiguous (Smith & Osborn, 2015).

For the IPA analysis, interview coding followed a step-by-step procedure as described by Smith and Osborn (2003). The first transcript was analysed using the following steps: *i.)* the transcript was read a number of times and initial comments of interest were made; *ii.)* initial comments were developed into theme titles; *iii.)* themes were collated and connections were made between themes, enabling more theoretical ordering where the aim was to make sense of theme connections; *iv.)* as themes and theme connections developed, the transcript was re-visited to ensure that the themes made sense for the words used by the clinician; *v.)* the themes were then ordered into a table, with the identification of overarching superordinate themes from the transcript. The table from the first transcript was used as a template for subsequent analysis of further transcripts, with careful consideration to ensure new experiences were acknowledged. Once each transcript had undergone this process, a final table of themes was created. To reduce bias and increase validity, a member of the research team reviewed a subset of the interview transcriptions and theme tables (*n*=3) to check agreement. Discussion with the team member led to consensus of the theme tables for the subset of interviews and facilitated the development of the final theme table for all interviews; the process taken was similar to previous IPA studies (MacMahon et al., 2015; Howard et al., 2021).

4.4 Results

4.4.1 Presentation of anxiety: content analysis

Across the parent/carer and clinician interviews, the overarching themes of behaviours associated with anxiety and anxiety triggers yielded 22 and 37 codes respectively (Table 4.5 and 4.6). For behaviours associated with or attributed to anxiety, the most frequently reported by parents/carers were increased vocalisation or communication (*n*=20; 95.2%), behaviours that challenge (*n*=19; 90.5%) and avoidance/refusal patterns (*n*=19; 90.5%). Behaviours that challenge included behaviours such as pushing, biting, or hitting others (*n*=13; 61.9%), self-injurious behaviour (e.g., hitting, biting, picking or pinching oneself; *n*=14; 66.7%) and damage to property (e.g., throwing, kicking or breaking objects; *n*=10; 47.6%). Behaviours were similar across autistic children and adults; for children, increased vocalisation (*n*=9, 100%) and behaviours that challenge (*n*=9, 100%) and for adults, increased vocalisation (*n*=11, 91.7%) and avoidance (*n*=11, 91.7%) were most frequently endorsed. Examples of the most frequently reported behaviours with their corresponding code are highlighted in quotes below, with further examples and child vs. adult break-down provided in Table 4.5. Presentations for each autistic individual are presented in Appendix 30.

"he might start making loud noises…a groaning" (Mother of 7-year-old male; quote coded as increased vocalisation/communication).

"what he does when he gets anxious, he tries to hit his head, he was kicking out and thumping, when he gets to a certain point, he starts to lash out…throwing chairs all the time" (Mother of 44-year-old male; quote coded as behaviours that challenge).

"not wanting to eat her dinner, or running out". (Mother of 26-year-old female; quote coded as avoidance/refusal patterns).

For the clinician interviews, the most frequently reported behaviours associated with or attributed to anxiety were behaviours that challenge (*n*=9; 100%), avoidance or refusal patterns (*n*=9; 100%) and increased vocalisation or communication (*n*=8; 88.8%). Behaviours that challenge included behaviours such as pushing, hitting, or pulling hair of others (*n*=9; 100%), self-injurious behaviour (*n*=9; 100%) such as hitting or biting oneself and damage to property (*n*=5; 55.6%) such as hitting or breaking objects.

"lots of anxiety that puts themselves and others at risk, the anxieties they're presenting cause them to lash out, extreme self-injurious behaviours" (Clinical Nurse Specialist/Lead, C008; quote coded as behaviours that challenge).

"avoidance of doing something they would normally do, a young person trying to refuse to do something, maybe refusing to go to school or refusing to go out" (Clinical Psychologist, C005; quote coded as avoidance/refusal patterns).

"they are increasingly distressed and making increased vocalisations" (Consultant Psychiatrist, C007; quote coded as increased vocalisation/communication).

The most common anxiety triggers reported by parents/carers were unpredictable/uncertain situations and changes to routine (*n*=16; 76.2%). Young children and animals were reported as triggers of anxiety due to unpredictability. Parents/carers also reported anxiety triggers such as loud noises/particular noises (*n*=14; 66.7%) and sensory overload (*n*=14; 66.7%). Identified triggers are similar to those endorsed in Table 3.5, including changes to routine, loud/unexpected noises, sensory sensitivities and unpredictable people and situations. In the current study, most parents/carers (*n*=14; 66.7%) also reported setting events (defined as broader, background antecedent conditions that are temporally distinct from stimuli that immediately proceed an event; Nosik & Carr, 2015). Examples of setting events were tiredness, hunger and pain/discomfort or physical illness. Triggers for anxiety were explored across autistic children and adults; for children, unmet needs (*n*=6, 66.7%) and setting events (*n*=6, 66.7%) were common triggers whilst for adults unpredictability/uncertainty (*n*=11, 91.7%) and changes to routine (*n*=11, 91.7%) were most frequently endorsed. Examples of the most commonly reported triggers with their

corresponding code are highlighted in quotes below, with further examples provided in Table 4.6 with the break-down across children vs. adults.

"it is all to do with things that are unknown, or it can be things that are familiar, but she is just uncertain about it…she doesn't like change, she likes to have a routine and if something is different then that would upset her" (Mother of 23-year-old female; quote coded as unpredictability/uncertainty and change to routine/expectation).

"if he is hungry, if he is thirsty, if he needs to go to the toilet, if he has maybe constipation and he cannot tell us about it, or the opposite, he has diarrhoea or has some stomach problem" (Father of 11-year-old male; quote coded as setting events).

Clinicians also commonly endorsed anxiety triggers related to changes to routine or expectations (*n*=9; 100%), followed by unpredictable or uncertain situations/feelings (*n*=7; 77.8%), setting events (*n*=7; 77.8%) and specific places, situations, or stimuli (e.g., hospitals, balloons; *n*=7; 77.8%).

"changes in the everyday routine structures, summer holidays, our referrals do not go up then but crisis calls come through in the summer holidays because I'm guessing the change in routine" (Clinical Psychologist, C005; quote coded as change to routine/expectation).

"Dogs, unpredictability probably, dogs bite. They can't control a dog; they don't know what that dog's going to do" (Community Learning Disability Nurse, C004; quote coded as unpredictability/uncertainty).

Table 4.5 Content analysis findings: behaviours associated with/attributed to anxiety reported by parents/carers (broken down to indicate endorsement by parents/carers for autistic children vs. adults) and clinicians

Behaviours associated with anxiety	*n* parent with code (%) [n/% child]	*n* of clinician with code (%)	Example codes	Quote example from parent	Quote example from clinician
Low order repetitive behaviour or stimming	**10 (47.6)** [3/30]	3 (33.3)	Hand flapping, rocking, bouncing	*"there's a rocking… it's not sort of calm rocking, it's distressed rocking"*	*"stereo-typical behaviours, rocking"*
Higher order repetitive behaviours or OCD-like behaviours	**10 (47.6)** [4/40]	4 (44.4)	Closing windows and doors, wanting thing straight	*"much more needing to control the environment around him"*	*"trying to exert control over the environment… insisting on having certain things a certain thing"*
Repetitive speech/asking	**12 (57.1)** [7/58.3]	1 (11.1)	"home, home, home", "no, no, no"	*"repetitive asking, requesting"*	*"even those with very low verbal skills might repeat whatever word they do know over and over again"*

Avoidance/refusal patterns	**19 (90.5)** [8/42.1]	9 (100)	Running away from something, not wanting to get out of car, hide behind arm, need to flee	*"he would perhaps try to run away"* *"his only way to express what he is feeling is to refuse to cooperate"*	*"tried to run away"*
Freezing/rooted to the spot	**4 (19)** [1/25]	0 (0)	Won't move from spot, physically getting stuck	*"he will plant himself… he will almost be quite rooted to the spot"*	*N/A*
Withdrawal/reduced vocalisation/shutting down	**12 (57.1)** [6/50]	7 (77.7)	Reduced ability to communicate, quiet, withdraws	*"he internalises when he's anxious about something… he doesn't say it, he will just kind of step back"*	*"they might just absolutely go in themselves and just not want to communicate with the world"*
Increased vocalisation/ communication	**20 (95.2)** [9/45]	8 (88.8)	Shouting, screaming, crying, groaning, moan, grumble, whimper	*"he will shout out or maybe scream… where you hear a groan noise, like a low rumble noise"*	*"an increase in cry-like sounds and a grunting or just any type of negative vocalisations"*

Facial expression/change	**17 (81)** [8/47.1]	6 (66.6)	Frown, grimace, blank, tense, worried, tighten lips	*"you can see it in her face, she looks anxious and agitated, sort of tense"*	*"you can see from their facial expression that they're concerned and they're not at ease"*
Body changes/movement	**18 (85.7)** [8/44.4]	6 (66.6)	Tense body, pacing, sweating, trembling, shaking, breathing changes, rigid	*"his heart is pounding, he's profusely sweating"* *"he'll start pacing up and down the room"*	*"increased sweating, increased heart rate, increased breathing"*
Behaviours that challenge	**19 (90.5)** [9/47.4]	9 (100)	Hitting, biting, pushing, kicking self or others, throwing or damaging things	*"bites his hand or he hits his head"* *"he will kick things… doors, walls, windows"*	*"an increase in self-injury or an increase in aggression or destruction"*
Proximity seeking	**9 (42.9)** [3/33.3]	2 (22.2)	Clinging, following, touching, holding onto others	*"he started to become a bit clingy… he would stick to somebody like glue"*	*"apparent increased need or wanting of attention from the main caregiver"*

Hypervigilance	**3 (14.3)** [0/0]	0 (0)	Looking around, watching, on edge	*"she's really honing in, you can see her… she's watching around… she can't focus on what to eat because she's too worried about the environment"*	*N/A*
Change in overall demeanour	**14 (66.7)** [7/50]	6 (66.6)	Agitated, frustrated, not so relaxed	*"I can pick up from her tension. You can just tell. She's not as relaxed"*	*"he becomes agitated", "just a general change in mood"*
Change in everyday behaviour/skills	**4 (19)** [1/25]	2 (22.2)	Regression in skills, defecating, wetting, vomiting	*"when his anxieties are high all that goes out the window, his communication goes back to where it was all those years ago"*	*"regression as well in skills, so maybe being less functionally able or appearing that way"*
Covers ears	**3 (14.3)** [2/66.7]	0 (0)	Puts hands/ sticking fingers in ears	*"he will put his hands over his ears, he wants to sort of*	*N/A*

				separate himself"	
Hyperactivity	**7 (33.3)** [4/57.1]	4 (44.4)	Unable to sit down/sit still, climbing, on the go	*"be unable to sit down, sit still, he'd be constantly climbing, constantly on the go"*	*"you can often see that they can't settle… they're circling the room"*
Changes in food habits	**8 (38.1)** [2/25]	5 (55.5)	Won't eat, regurgitation, eating too quickly	*"has an impact on how he eats, because he eats too quickly or too slowly"* *"he won't eat anything"*	*"you've got to consider appetite… either overeating maybe or not eating enough"*
Changes in sleep habits	**3 (14.3)** [0/0]	4 (44.4)	Couldn't sleep, scared to sleep	*"he was scared to go to sleep"*	*"somatic changes are indicators of anxiety… sleep disturbance"*
Covering self	**2 (9.5)** [0/0]	0 (0)	Wrap/ cover self in curtain, jumper, blanket	*"he then covers himself up with a jumper, or a blanket, or a cushion"*	*N/A*
Biting scarf	**1 (4.8)** [0/0]	0 (0)		*"she always wears a scarf so she can*	*N/A*

				bite into the scarf"	
Drawing	**1 (4.8)** [0/0]	0 (0)		*"he spends a lot of time drawing things and he will repeat he'll like create an exercise book out of sheets of paper and do about 40 drawings of a van"*	*N/A*
Non-epileptic seizure presentation	**1 (4.8)** [0/0]	0 (0)	Crawl around, lie down, shaking, trembling, can't walk, eyes flicker	*"her anxiety manifests itself as what we think are what are called non-epileptic seizures… she's physically incapacitated whilst that is going on"*	*N/A*

Table 4.6 Content analysis findings: anxiety triggers reported by parents/carers (broken down to indicate endorsement by parents/carers for autistic children vs. adults) and clinicians

Anxiety trigger	*n* parent with code (%) [n/% child]	*n* clinicians with code (%)	Examples	Quote example from parent	Quote example from clinician
Fear of what other's think/getting into trouble/upsetting others	**4 (19)** [2/50]	0 (0)	Very sensitive to being liked, thinks he's being told off	*"he thinks he's done something wrong, he thinks he's being told off"*	*N/A*
Communication frustration/difficulty	**7 (33.3)** [5/71.4]	2 (22.2)	Can't always communicate needs, she really wants to communicate	*"sometimes she really wants to communicate and she can't really communicate, I think she can probably understand more than she can voice"*	*"frustration around not being able to communicate his needs effectively"*
Unpredictability/uncertainty	**16 (76.2)** [5/31.3]	7 (77.8)	Not knowing what's happening, doesn't understand,	*"I think it's the unpredictability of the outside world that feeds his anxiety"*	*"not really knowing what's happening, what the plan is for them, in*

			dogs, young children, cats		*terms of the day and things"*
New/unfamiliar situations or people	**10 (47.6)** [4/40]	3 (33.3)	New teachers, students, unfamiliar children or adults, new staff, lack of trust	*"new experiences cause her huge anxiety"* *"anybody that is new that he doesn't know"*	*"new member of staff started working with this person…we started seeing an increase in behaviour"*
Needs not being met	**11 (52.4)** [6/54.5]	4 (44.4)	Not having enough support, not able to do something that he wants to do	*"he didn't feel supported, they didn't understand him"*	*"coming towards the end of primary when perhaps the child might have outgrown or the schools no longer meeting their needs"*
Demands/not meeting demands	**10 (47.6)** [5/50]	5 (55.6)	If he doesn't want to do something, social demand, questions, choices	*"whether it is demand of an interaction…a task…to do something that wasn't quite on his agenda at that moment"*	*"the expectations of them are massive because they're in college and just getting people to strip back*

					and work with them on a more functional level helps"
Absorbing tension in environment	**7 (33.3)** [3/42.9]	0 (0)	Other people upset around him, he doesn't like slight tension in the room, if voices are raised	*"if people sort of shout…she seems to pick up the vibe of the atmosphere"*	N/A
Changes to routine/expectation	**16 (76.2)** [5/31.3]	9 (100)	Lots of staff changes, Christmas because so many changes, changes from the norm, summer holidays	*"any change in routine seems to majorly unsettle him especially in his own environment"*	*"are there any changes going on at the moment, has anything been done differently in terms of change to teacher to cause anxiety, we're immediately kind of thinking"*
Too much structure/knowing plans too far in advance	**1 (4.8)** [0/0]	1 (11.1)	Her anxiety rises too far in advance, he's constantly asking questions	*"if she knows too far in advance, her levels of anxiety appear to rise"*	*"as soon as you start preparing him for something he's constantly*

					asking questions…st arts getting anxious"
Busy environments	**9 (42.9)** [3/33.3]	2 (22.2)	Crowds, lots of people, shopping centres, busy lobby, cafés, pubs	*"we can't take him on a normal school holiday… it's way too busy, he doesn't like crowds"*	*"does not like crowds or busy places"*
Loud environments/particular noises	**14 (66.7)** [5/35.7]	5 (55.6)	Places that are loud, people that are loud, too noisy, any kind of noise, very sensitive to noise	*"if people are loud or shouty around her"*	*"the noise, that was a real issue for him where hitting just went right up"*
Particular places, situations, stimuli or people	**12 (57.1)** [4/33.3]	7 (77.8)	Dentist, appointments, hospitals, balloons, pigeons	*"he's never liked going to appointments …I've always had his dentist going to him"*	*"birds is another one…balloons because they didn't like the movement of the balloon"*
Overwhelmed by sensory experiences/too many activities	**14 (66.7)** [5/35.7]	6 (66.7)	Sensory overload, sounds, lights, tactile defensive, lots of sensory stimuli	*"if that sensory mode gets too overloaded, that's where the coping mechanism goes"*	*"sensory overload is a massive thing"*

Under stimulated/bored/sensory seeking	**4 (19)** [2/50]	3 (33.3)	Under stimulation, linked to sensory needs, opportunity to express and release that	*"trying to not let him be bored or left unattended"*	*"under-stimulation can have a bearing upon, their levels of anxiety"*
Sensory difficulty (direction not stated)	**0 (0)** [0/0]	1 (11.1)		*N/A*	*"environmental type stuff, it could be linked to like sensory needs"*
Social interactions/meeting people	**4 (19)** [2/50]	0 (0)	She doesn't interact well with people, risk of social interaction	*"the risk of interaction, the fear of what might be expected"*	*N/A*
Transitions	**6 (28.6)** [3/50]	4 (44.4)	Transitioning between rooms, from home to school and home again, primary to secondary school	*"transitioning into school or from school back home or just moving into the dining area"*	*"we get spikes of referrals at key transition times…in October when schools have been back a month"*
Enclosed spaces	**2 (9.5)** [1/50]	0 (0)	Doesn't like small places, claustrophobic	*"he doesn't like being in enclosed spaces"*	*N/A*
Setting events	**14 (66.7)** [6/42.9]	7 (77.8)	Tired, pain, cold, hot, hunger, hormonal,	*"things like hunger or pain or tiredness*	*"could be pain or some physical*

			menstruation, physical health difficulty, epilepsy, medication change/effects	*may well influence that"*	*health syndrome but actually it is giving them anxiety because they can't understand what's happening in their body"*
Unable to fix issue	**2 (9.5)** [2/100]	0 (0)	Unable to fix problem, DVD stuck, iPad frozen	*"it's just 'fix this'…through desperation"*	*N/A*
Insistence on sameness	**5 (23.8)** [2/40]	1 (11.1)	Seat belt wasn't on right, deviation from rigidity, people in certain positions	*"he likes it a certain way…he's just decided that's his thing…it certainly causes anxiety"*	*"being very rigid about how you want things to be done and when that's deviated from they display anxiety"*
Removal of interests	**3 (14.3)** [2/66.7]	2 (22.2)	Worry that someone will take it, run out of bubbles, not being able to access special interest	*"I am anxious because I know my bubbles have nearly run out and I need to get some more"*	*"not being able to access their special interest or they have a particular restricted interest which means*

				they aren't able to access that particular interest as much"	
Worry after hurting others	**1 (4.8)** [1/100]	0 (0)	Trying to rub away blood from scratch	*"if it bleeds, you can see the anxiety, he tries to rub it out, 'go away, sore gone"*	*N/A*
Conscious of own limitations	**1 (4.8)** [1/100]	0 (0)	Feels different to others, aware of difficulties	*"he is more aware of his difficulties as in like his language and interaction skills"*	*N/A*
Missing out/not being part of activity	**1 (4.8)** [1/100]	0 (0)		*"he was feeling isolated that we were able to communicate in a way that he can't"*	*N/A*
The way others treat person	**4 (19)** [0/0]	0 (0)	They weren't very nice to him, some of the staff were getting bossy like 'do this, do that'	*"they might tell him off or they might shout at him…he doesn't feel safe if people do that"*	*N/A*

Weather	**2 (9.5)** [1/50]	0 (0)	Grey cloudy heavy day	*"if it's kind of a grey cloudy heavy day, I think she's more tense"*	*N/A*
Going out anywhere	**3 (14.3)** [2/66.7]	1 (11.1)	Being out of the house, not used to being in community, even just leaving the house	*"we want to try and get him out in the community but that does cause him a lot of anxiety"*	*"even just leaving the house for example, all that uncertainty"*
People coming into house to look after her/him	**2 (9.5)** [0/0]	0 (0)	He wouldn't accept people coming in, invading his territory	*"if there are new people coming in then that makes her anxious"*	*N/A*
Big people/big men	**1 (4.8)** [0/0]	0 (0)	Victim of attack	*"he was the victim of a sustained vicious attack so he has got…fear around big men"*	*N/A*
Separation anxiety	**2 (9.5)** [1/50]	0 (0)	If parents go out of sight when with them, following, clinging	*"going away from me, he feels separation anxiety"*	*N/A*
People talking about individual when they're present	**1 (4.8)** [0/0]	0 (0)	Having a conversation with the staff and he's sat there,	*"you're talking about the past…they are talking around*	*N/A*

			talking about the past	*him and he's listening"*	
People suddenly coming into home	**1 (4.8)** [0/0]	0 (0)	Classing that as his safe place, it's his home and he's got somebody from next door coming into it	*"he wouldn't accept people coming in here… I think its invading his territory"*	*N/A*
Significant life changes	**2 (9.5)** [0/0]	2 (22.2)	Bereavement, family member/friend moving away	*"she went off to university two years ago so obviously that has had an impact on him as well"*	*"significant loss for some of our youngsters"*
Waiting	**2 (9.5)** [2/100]	2 (22.2)	He won't wait for things, wait 3 hours before a procedure	*"he finds waiting really hard… if we have to queue or pause in traffic"*	*"he won't wait for things either"*
Anxious network	**0 (0)**	2 (22.2)	Parental anxiety, anxiety in the network around an individual	*N/A*	*"increase in anxiety in the network which then might translate to the poor person if they've got an anxious network around them"*

Attachment difficulties	**0 (0)**	3 (33.3)	Didn't form an attachment with anyone, breakage of primary attachment relationships, individuals going into care, looked after children	*N/A*	*"what we see clinically is the breakage of the primary attachment relationships with people in staff or sometimes parents or carers…that causes increased anxiety"*

4.4.2 Clinician experience of anxiety assessment: IPA analysis

The IPA analysis conducted on the clinician interviews yielded four themes: methods of assessment for anxiety; identification of behavioural change; differentiating anxiety from other forms of distress; and additional diagnoses (See Table 4.7 for the final theme table).

Table 4.7 IPA analysis: final theme table

Themes	Subthemes	Subthemes
1. Methods of assessment for anxiety	• Current anxiety assessment	
	• The importance of informant involvement and gathering information across contexts	
2. Identification of behavioural change	• Identification of an individual's baseline behaviour	
	• Importance of knowing an individual well, regular assessment and individualised approach	
3. Differentiating anxiety from other forms of distress	• Behavioural overlap and behavioural divergence	Importance of context and identification of anxiety trigger
	• The importance of ruling out other causes of distress	
	• Importance of working as part of a multidisciplinary team	
4. Additional diagnoses	• Consideration of diagnoses and impact on presentation	
	• Diagnostic overshadowing	

4.4.2.1 Theme 1: Methods of assessment for anxiety

This theme describes current assessment methods used by clinicians to assess anxiety. Data within this theme were further categorised into two subthemes: current anxiety assessment and the importance of informant involvement and gathering information/evidence across multiple contexts.

Clinicians described methods to assess anxiety including behavioural records, standardised questionnaires, observations, and Antecedent-Behaviour-Consequence (ABC) charts (record forms used to document events that occur before and after the behaviour of interest is observed; Delgado et al., 2017). However, clinicians noted the overlap between

items on measures of other forms of distress such as pain and anxiety questionnaire measures, as highlighted in the quote below.

"what we often find is most of our children score on pain measures… I often wonder whether the overlap is just still too great on these measures… often the child scores highly on everything and then you're left with that" (Clinical Psychologist; C001).

In keeping with the findings of the content analysis which identified unusual fears, anxiety associated with changes in routine and behaviours that challenge, clinicians also spoke of 'atypical' presentations of anxiety. Existing measures may miss these 'atypical' presentations, precluding a comprehensive assessment of anxiety.

"We've got flying things, pigeons was one… balloons, because they didn't like the movement of the balloon… didn't like the texture and the noise and it could pop".
(Community Learning Disability Nurse; C004).

Throughout the interviews, clinicians highlighted the importance of involving informants who know the person well during assessments of anxiety. Such input assisted clinicians in building a picture of how anxiety presents across settings and situations. An informant may be able to identify subtle differences in presentation when an individual is experiencing anxiety versus another form of distress and provide key information about the contexts most likely to induce anxiety related behaviours.

"observations… at home, at school, parent-reporting, school-reporting, reporting from wherever the child is or exists" (Community Learning Disability Nurse; C002).

4.4.2.2 Theme 2: Identification of behavioural change

Clinicians discussed assessment of behaviour change as a key area of importance in the assessment of anxiety. In the clinicians' opinion, understanding behaviour change is dependent on two factors: being able to identify an individual's baseline levels of behaviour; and a thorough and individualised approach to assessment leading to in-depth understanding of the individual.

Clinicians stressed the importance of having a working knowledge of an individual's baseline, including their presentation when they are comfortable, content, and relaxed, to be able to identify changes in behaviour that might indicate distress. This is particularly important as clinicians identified how behavioural markers of distress can overlap with autistic characteristics; for example, repetitive behaviours such as rocking or adherence to routine. Such behaviours may be characteristic of an individual when they are happy and content but may increase in duration or intensity when an individual is feeling anxious.

"What will make you think of anxiety is if there's been a behavioural change of some sort so that could be anything, it would be thinking about what a baseline of behaviour was

for that young person and thinking about clinically what's changed". (Clinical Psychologist; C001).

To aid this assessment of behaviour change, clinicians indicated the importance of knowing an individual well, having regular assessments and an individualised approach to assessing anxiety. This subtheme was crucial to helping clinicians identify a change from an individual's baseline. For example, similar to the importance of informant involvement in the assessment of anxiety, many clinicians commented on individual presentations that became apparent after they got to know an individual, including patterns of behaviour linked to key anxiety triggers. Clinicians commented that it is difficult to assess behaviour when they do not know an individual well; nuances and subtleties of behaviour can be missed. For example, one clinician mentioned that vocalisations can sound the same when an individual is not well-known to them. Several clinicians also highlighted that every individual is different, stressing the importance of an individualised approach to assessing anxiety. Clinicians commented on the importance of spending time with an individual, learning about them, and having regular appointments, including some in the community.

4.4.2.3 Theme 3: Differentiating anxiety from other forms of distress

Theme three includes three subthemes: behavioural overlap and behavioural divergence; the importance of ruling out other causes of distress; and the importance of working as part of a multidisciplinary team.

Speaking from their experience, clinicians reported that behaviours could be present for various reasons and behavioural overlap is common, making it difficult to discern why behaviours may be present. Further complicating this overlap, clinicians described links between factors such as anxiety and pain. For example, clinicians indicated that anxiety can be associated with the experience of physical symptoms (stomach-aches and feeling unwell), and vice versa; whereby pain can be associated with feelings of anxiety.

"it's really difficult in that sense to determine actually 'is he anxious?', 'is he in pain?' or is it 'he's anxious cause he's in pain?' or 'actually is he not in pain?". (Community Learning Disability Nurse; C004).

However, most clinicians were able to identify ways that helped them to differentiate the cause of behaviour, allowing behavioural divergence. For example, many mentioned that the presentation of self-injurious behaviour restricted to a particular part of the body (e.g., ear, teeth) was a key indicator of localised pain. Additionally, an acute presentation of a new behaviour, out of the blue and not linked to a known anxiety trigger was also noted as a sign of potential pain. A couple of clinicians explored this in more depth and identified behaviours highlighted in the quote below, with another clinician suggesting that they believed the presentation of aggressive behaviours was less associated with pain and an increase in

repetitive behaviour was more likely to be associated with anxiety than pain. Whilst clinicians were able to comment on behaviours that they use to differentiate anxiety from pain, they felt identifying behaviours that differentiate anxiety from low mood or depression was more difficult.

"there's subtle differences, you see more writhing behaviours in pain as opposed to (anxiety), you might have all the negative vocalisations, being uncooperative, cranky… but you might also see arching of the back, writhing, which for me are quite key related behaviours of pain as opposed to anxiety" (Clinical Psychologist; C001).

Context is also an important factor that clinicians described to help them differentiate anxiety from other forms of distress; this included identifying triggers for anxiety as part of the assessment. Clinicians highlighted how successful identification of an anxiety trigger can aid formulation and inform intervention, whilst the absence of an identified trigger provoked challenges in assessment and subsequent care planning.

"once you have a set of triggers for that person, it would become easily anxious and set off by, I think it would be more easy to pick up on that". (Clinical Nurse Specialist; C003).

Clinicians consistently stressed the importance of ruling out other causes of distress in individuals who speak few or no words to be more confident that anxiety is the presenting difficulty. For obvious reasons, clinicians particularly highlighted the importance of ruling out pain and physical health conditions during the first phase of assessment. Furthermore, one clinician described drastic, almost immediate changes in behaviour once health-related difficulties were addressed for a particular individual.

"We'd tend to try and rule out pain in the first instance, particularly if the presentation is self-injury… because we know health conditions are more likely in our children and often do get missed… also on ethical grounds… if the childs in pain, you could do something about it quite quickly". (Clinical Psychologist; C001).

However, clinicians highlighted that being able to rule out other causes of distress is not always straight-forward and there may be more than one factor contributing to presenting behaviour, which may include the interaction between health difficulties and anxiety.

"I think with a lot of children that we see it (pain) gets dismissed because it's too difficult to do the investigation on them". (Consultant Neuropsychiatrist; C006).

To properly assess physical health difficulties and the possibility of pain, clinicians highlighted the importance of working with physical health services/colleagues as part of a multidisciplinary team. There was a sense that this can take substantial time and effort but is essential to ensure the best health and behavioural outcomes for individuals who speak few or no words.

"for us I think that involves a lot of liaising, so say if they were under a paediatrician or school doctor, we'd be liaising with them, just to see what has been done, what could be done". (Community Learning Disability Nurse; C002).

4.4.2.4 Theme 4: Additional diagnoses

Theme four focuses on the importance of acknowledging additional neurodevelopmental, genetic, or neurological diagnoses and their impact on the identification and assessment of anxiety.

Specifically, clinicians mentioned diagnoses of autism, genetic syndromes, ADHD, and epilepsy. Clinicians stated that identification and diagnosis of conditions, such as autism, can aid understanding of phenotypic factors which inform assessment and formulation. For example, for autistic individuals, clinicians mentioned anxiety triggers such as transitions, routine changes, and sensory processing differences. However, for some rare genetic syndromes (e.g., Fragile X, Klinefelter's, Prader-Willi, Smith-Magenis and Kleefstra syndromes), a lack of awareness of phenotypic presentations can further complicate mental health assessments.

*"the genetic syndrome means they're more likely to have particular triggers to things and that often will get missed… people still don't know enough about them or they don't know to look for specific things". (*Clinical Psychologist; C001).

Many clinicians explored the issue of diagnostic overshadowing; whilst it is important to acknowledge an individual's comorbid diagnoses and the impact they may have on an individual's presentation; behaviour must not be assumed to just be part of an existing diagnosis. A thorough exploration of the potential role and impact of anxiety is needed when investigating presenting behaviour.

"…may not explore other things, so I think sometimes it's tricky because as a default what comes first in line in terms of behaviour, the child's got learning disability and ASD, could be attributed to that". (Consultant Psychiatrist; C007).

4.5 Discussion

The current study is one of the first known to focus exclusively on exploring anxiety in autistic individuals with moderate-profound ID who speak few or no words, addressing an identified gap in the literature (Adams & Oliver, 2011; Flynn et al., 2017; Simpson et al., 2020). The study utilised a bottom-up approach, free from the reliance on diagnostic criteria, and collated information from both parents/carers and clinicians, the latter a particular strength as research exploring clinician perspective is scarce (Brookman-Frazee et al., 2012). The clinician interviews provide an overview of the types of methods that can be

utilised in clinical practice for assessing anxiety, and the factors that may enhance health and behaviour outcomes. The interviews also gave rise to several considerations that may be important for the development of new assessment measures of anxiety in individuals who speak few or no words (See Table 4.8 for summary).

Table 4.8 Considerations for new assessment tools

Considerations for the development of new assessment measures
• Explore similar behaviours and triggers to existing measures but develop and validate new measures specifically for individuals who speak few or no words • Existing measures should be used to pinpoint key behavioural markers of anxiety, otherwise they should be used cautiously • Spend time getting to know an individual and collate information from several informants across contexts alongside use of questionnaire measures • Explore the potential role of physical discomfort/pain, form and maintain relationships with colleagues in physical health settings (e.g., MDT formulation)[39] to achieve this • Incorporate the assessment of baseline presentation to identify behavioural change and help tackle diagnostic overshadowing • Consider comorbid diagnoses and the impact they may have on an individual's presentation

The study used a two-stage approach to quantify behaviours that may be associated with anxiety and clinician experiences of anxiety assessment. Parents/carers and clinicians attributed similar behaviours to anxiety, including behaviours that challenge and increased vocalisation. This is consistent with studies using questionnaire and behavioural observation measures that indicate autistic individuals with ID and those with language difficulties may show these behaviours when anxious (Bitsika & Sharpley, 2016; Moskowitz et al., 2013). Avoidance/refusal behaviours were frequently endorsed by parents/carers and clinicians, a finding consistent with the typically developing anxiety literature (Dymond & Roche, 2009; Hofmann & Hay, 2018).

Parents/carers and clinicians reported similar triggers for anxiety, such as unpredictable situations/feelings and changes to routine. These findings concur with existing research identifying 'atypical' anxiety in autistic individuals without ID or mild ID, who speak in sentences (Bearss et al., 2016; den Houting et al., 2018; Kerns et al., 2016; Vasa et al., 2016). Existing research highlights associations between anxiety and intolerance of uncertainty in autistic individuals, which is consistent with unpredictable situations/feelings in the current study (Boulter et al., 2014; Jenkinson et al., 2020).

[39] MDT=Multidisciplinary team

Four key themes emerged from the interviews with clinicians about their experiences of assessing anxiety: 1) methods of assessment for anxiety, 2) identification of behavioural change, 3) differentiating anxiety from other forms of distress and 4) additional diagnoses.

First, clinicians commented on the limitations of existing methods of assessment. This mirrors limitations of existing tools reported in previous research: reliance on traditional diagnostic criteria and limited consideration of the overlap of anxiety with other forms of distress such as physical discomfort or pain (Flynn et al., 2017; South et al., 2017; Tarver et al., 2021a). As autistic individuals and individuals with ID are at increased risk of physical health difficulties and experiencing discomfort/pain, clinicians perceiving this limitation in existing measures is particularly concerning (Doody & Bailey, 2017; Whitney & Shapiro, 2019). As also indicated in previous research, clinicians in the current study highlighted the importance of informant involvement from someone who knows the individual well and collating information from different sources across contexts when assessing anxiety (Spain et al., 2017; Vasa et al., 2016; White et al., 2009). Linking to this is the importance of multi-method assessment of anxiety which may include use of psychophysiological measures, due to the identified limitations of other forms of assessment. There is evidence of reduced heart rate and cortisol responsiveness relating to anxiety in autistic individuals (Hollocks et al., 2014). Furthermore, Ferguson et al. (2019) has demonstrated the feasibility of psychophysiological methods, whereby increases in electrodermal activity preceded behaviours that challenge in autistic individuals with ID. Further research into the acceptability and feasibility of such measures in this population is crucial to complement other methods of anxiety assessment (Hollocks et al., 2014; Ferguson et al., 2019).

Second, clinicians commented on the importance of identifying an individual's baseline behaviour to help pinpoint behavioural change that may be associated with anxiety, a finding consistent with previous research (Ozsivadjian et al., 2012; Tarver et al., 2021a). Identifying an individual's baseline behaviour may help to discern which behaviours are 'typical' for that individual, helping to disentangle autism characteristics from anxiety (Kerns & Kendall, 2012; van Steensel & Heeman, 2017; Vasa et al., 2016; Vasa et al., 2018). Developing and validating assessments that address the overlap between autism characteristics and anxiety is a top priority to improve anxiety assessment in individuals who speak few or no words (Vasa et al., 2018).

In the third theme, clinicians explored behavioural overlap between anxiety and other forms of distress, such as pain. Investigating and ruling out other potential causes of distress, as part of a multidisciplinary team, was one way that clinicians aim to identify anxiety; an approach which is consistent with National Institute of Health and Care Excellence (NICE) guidelines (2013). Furthermore, clinicians discussed the importance of context for identifying anxiety triggers; once triggers were identified, clinicians felt able to

support individuals through to discharge from a service. Although less so than reference to the identification of anxiety vs. pain, there was comment about the difficulty of differentiating anxiety from other mental health difficulties, such as low mood. This finding aligns with existing literature identifying behavioural markers of depression such as behaviours that challenge and agitation, that overlaps with the presentation of anxiety described in this chapter (Eaton et al., 2021). This highlights the challenge of pinpointing the presenting difficulty, however there is indication that individuals with severe ID present with depressed affect and anhedonia, which would be consistent with the presentation of depression in the general population (Eaton et al., 2021). Studies could endeavour to control for potential confounds such as anxiety, however this may be a challenge due to high rates of comorbidity across mental health difficulties. Future research should focus on delineating the presentation of different mental health difficulties by utilising a bottom-up approach to inform the development of assessment tools for the moderate-profound ID population.

Finally, within theme four, clinicians emphasised the importance of considering additional diagnoses such as genetic syndromes, ADHD, and epilepsy, due to evidence of high rates of comorbidity with autism and ID (Karam et al., 2015; Neece et al., 2011; Robertson et al., 2015; Tonnsen et al., 2016). Gordon-Lipkin and colleagues (2018) found autistic individuals with ADHD are at greater risk of experiencing anxiety than autistic individuals without a diagnosis, therefore ADHD may be implicated in the development and presentation of anxiety. Furthermore, genetic syndromes are associated with specific presentations of anxiety. For example, as highlighted in section 2.2, in Williams Syndrome, phobias related to auditory stimuli are commonly reported and have been associated with hyperacusis, and the deletion of GTF2I is associated with low rates of social anxiety (Dykens, 2003; Klein et al., 1990; Procyshyn et al., 2017; Royston et al., 2017). Clinicians should explore how phenotypic characteristics may interact with and have an impact on the presentation of anxiety (Waite et al., 2014). Also, within the final theme, the ongoing challenge of diagnostic overshadowing was discussed, as evidenced in previous research (Kerns et al., 2015; Mason & Scior, 2004). Anxiety is distinguishable from other diagnoses and therefore assessment measures need to pinpoint the role and impact of anxiety on an individual, to allow targeted intervention to improve quality of life (Kerns et al., 2016; Renno & Wood, 2013).

More widely, the interviews provide a helpful summary to facilitate further learning for people who are new to the field of ID. The behaviour presentations obtained from parent/carer and clinician responses provide a starting point for identifying key patterns in behaviour when anxiety is considered a difficulty. These presentations could be disseminated through clinical training programmes to facilitate discussion around the

potential for overlap and confusion with signs of other difficulties (e.g., pain), as highlighted in this chapter.

It is important to note the limitations of this study. Firstly, whilst Smith & Osborn (2003) noted that there is "no single, definitive way to conduct IPA", the approach taken in the current analysis did not include an in-depth exploration and interpretation of clinicians' mental and emotional state, which could be considered a limitation. The analysis was interested in clinicians' perceptions of assessing anxiety in those with moderate-profound ID and did reflect on the difficult experience that clinicians have during this complex process. Further exploration of clinicians' mental and emotional state could have offered interesting personal narratives to add to the analysis. Ultimately, IPA was an appropriate qualitative method to use for the current study's research questions and the approach adopted was similar to previous IPA studies within the autism population, exploring clinician experience (Kildahl et al., 2020). Due to one of the analysis aims being to explore the considerations needed for the development of future anxiety assessments, the analysis did stay close to the clinicians' words, as these considerations would be taken forward to practically implement in the development of new assessments. However, it did still explore clinician's sense-making of the process, alongside their perspectives and experiences, as noted in an IPA approach (Smith & Osborn, 2003).

Whilst the clinician sample size was appropriate for the in-depth IPA analysis, the study explored views of clinicians in one geographic location. The current assessment methods and identified challenges of assessment may not be representative of clinicians working in other services. Therefore, while these findings may facilitate discussion and generate considerations for assessment design, service delivery or follow-up studies, it is not suggested that the findings should be implemented within clinical practice without reflection and further assessment, and substantial changes to practice based on these findings alone would be premature. Second, while the behaviours described may be useful for generating items for new anxiety measures, the behaviours are only based on parents/clinicians' attributions about anxiety. Further research will be needed to validate items included in new assessment measures to ensure these items are capturing anxiety. Thirdly, within qualitative research it is recommended that researchers obtain respondent validation (obtaining feedback from participants to ensure the analysis, interpretation and conclusions drawn align with their views; Busetto et al., 2020). This was beyond the scope of the current study as included participants were asked to provide feedback on the developed measure, currently undergoing validation. The decision not to obtain respondent validation could be considered a limitation of the study but was justified to avoid overburdening research participants. Finally, future research could adopt an approach whereby interviews are completed with parents/carers and clinicians about the same autistic individual, to allow triangulation of data

which may help to discern whether an individual's presentation is due to anxiety or another cause of behaviour.

4.5.1 Implications

The current study has key implications for researchers and clinicians. For researchers, when developing new assessment tools, teams may wish to take note of the considerations and challenges discussed by clinicians to ensure that assessment tools meet the needs of those likely to use them, and the populations they are designed to assess. Involving individuals, parents/carers, and clinicians in the development of such assessment tools is crucial to achieve this. For example, the current study highlighted change from baseline as a key factor to identify behavioural change, existing measures such as the ASC-ASD and the GAS-ID do not appear to explicitly assess this (Bearss et al., 2016; Mindham & Espie, 2003; Rodgers et al., 2016). It would be a recommendation that further iterations of existing measures or in the development of new measures for autistic individuals with ID that strategies are implemented to assess change from baseline.

Furthermore, the current study highlighted that similar behaviours and triggers associated with anxiety are identified across autistic children and adults. There was indication that unmet needs were more commonly endorsed for autistic children, this may be due to adults developing communication strategies over time to effectively communicate their needs. Setting events were endorsed at the same rate (66.7%) for both children and adults. Due to the qualitative nature of the study, it was beyond the scope to explore age differences statistically, therefore future research should explore the presentation of anxiety across age groups as well as gender (Adams et al., 2019). It may be that different behaviours and triggers are relevant to different groups, with the possibility of gender differences and/or age-related changes in presentation which will inform early identification and intervention. This would also have important implications for parents/carers responses to the person they care for's anxiety as this may vary by age and/or gender.

For clinicians, especially those working within mental health and behaviours that challenge pathways, working as part of a multi-disciplinary team is crucial due to behavioural overlap described in the current study. This collaborative, holistic approach should be adopted to rule out other possible causes of distress such as pain. The study also promotes reflection on the current methods of assessment of anxiety and associated challenges in individuals who speak few or no words. In-depth exploration of clinician experience is crucial to ensure that assessment tools are developed addressing the challenges faced within clinical practice. It may be that sharing clinician experience encourages conversation, new approaches to assessment and the formation of strategies to overcome highlighted challenges.

The study highlights the potential vulnerability of autistic individuals with ID who speak few or no words, where identification and assessment of anxiety is not straight-forward. Behaviours that challenge are observed in autistic individuals when appearing anxious, however it may not be considered that anxiety is a potential underlying factor. This has implications for professionals and sectors who individuals with ID may come into contact with (e.g., hospitality, law-enforcement, medical professionals). It is important that professionals have knowledge, ideally training, on how to best support autistic individuals who may be experiencing distress, including identification of a trusted adult who considers the individual's best interests.

In summary, the current study identified key behavioural markers associated with anxiety, triggers of anxiety and reflections on current anxiety assessment; all of which may be useful to inform the development of new clinical assessment tools for anxiety in individuals who speak few or no words. The feedback from clinicians across multiple themes within the IPA analysis highlighted the need for time and in-depth knowledge of clients to ensure the best health and behaviour outcomes for autistic individuals with ID. Improving the identification and assessment of anxiety will enable clinicians to provide targeted support early, improving quality of life for individuals and their families.

Chapter 5: Direct observation of anxiety-associated behaviours in anxiety and fear inducing situations: A remotely-conducted pilot study

5.1 Preface

The previous chapter provided a detailed examination of anxiety presentation in a group of individuals who are at high risk for anxiety: autistic individuals who speak few or no words. This high-risk group provided a relatively homogenous sample where it was anticipated that behaviours associated with anxiety would be observed. The chapter utilised bottom-up interview methodology to capture the anxiety behaviours parents/carers and clinicians observed when they perceived that individuals they support were experiencing anxiety. In addition, reported anxiety triggers and clinician experience of assessing anxiety in this population were examined. This work allowed for in-depth exploration of participants' experiences and highlighted key themes of interest when considering the profile of anxiety in autistic individuals with ID and/or those who speak few or no words. The chapter further highlighted that a multi-method assessment of anxiety is needed in this population. In the next chapter this work is extended by taking a fine-grained approach to describing relevant behaviours, utilising a direct assessment task to observe anxiety-related behaviour. In addition to the study specific aims described below, the study provided an indication of whether behaviours typically reported by parents/carers and clinicians (i.e., during the bottom-up interviews in Chapter four) occur during contrived situations that were anticipated to provoke mild anxiety.

5.2 Introduction

In recent years, there has been an expansion of studies exploring anxiety in autism and a drive towards the development of new assessment measures to address the identified limitations of existing measures such as reliance on verbal expression in self-report measures and attribution of behaviours associated with informant-report (Appleton et al., 2019; Hagopian & Jennett, 2008; Moskowitz et al., 2017; see section 4.2 for further discussion exploring limitations of existing anxiety measures). Recent questionnaire measures that have been developed specifically for the autistic population include the Anxiety Scale for Children with Autism Spectrum Disorder (ASC-ASD; Rodgers et al., 2016), the Anxiety Scale for Autism-Adults (ASA-A; Rodgers et al., 2020) and the Parent-Rated Anxiety Scale for ASD (PRAS-ASD; Scahill et a., 2019). However, as highlighted in section 4.2, there continues to be a paucity of research focusing on autistic individuals with ID and/or those who speak few or no words and there are few assessment measures developed and validated for this population (Rodgers et al., 2016; Rodgers et al., 2020; Scahill et al., 2019).

More specifically, there is a lack of behavioural observation assessments to explore anxiety in autistic individuals with comorbid ID and/or those who speak few or no words (Moskowitz & Braconnier, 2022). Most research to date relies on informant-report measures such as parent/carer/teacher report, that have identified limitations. For example, attribution of cause of behaviour, potential under-reporting of cognitive and physiological symptoms of anxiety and difficulty for informants to comment on an autistic individuals experience of life (Appleton et al., 2019; Keith et al., 2019). It is also important to consider that parents/carers may over-report on their child's anxiety due to their own experience of anxiety (Vasa et al., 2016).

The reliance on informant-measures of assessment is problematic due to the identified limitations and there is a recommendation that multi-method assessment is utilised (Moskowitz et al., 2013; Moskowitz & Braconnier, 2022; Vasa et al., 2016). However, it is rare for research studies to adhere to this recommendation, with a reliance on informant-based questionnaire measures (Appleton et al., 2019). Therefore, there is an identified gap in the evidence base and literature has highlighted the value of using more objective, observational measures to explore anxiety in this population (Moskowitz & Braconnier, 2022; Palmer et al., 2021). For example, more generally, direct assessment measures are invaluable for gathering data to examine mechanisms underlying behaviour and informing intervention planning (Aspland & Gardner, 2003). Furthermore, considering more observable behavioural patterns, how these may change over time and across contexts may provide a more reliable method of anxiety assessment in autistic individuals with ID (Appleton et al., 2019). Observational assessments are an important way to identify behavioural indicators of

anxiety and can overcome limitations of other methods of assessment. It is therefore crucial that appropriate and sensitive direct assessments are developed and validated for this population (Moskowitz & Braconnier, 2022). Observational assessments can be used in combination with informant report and physiological measures to ensure multimodal assessment (further discussed in section 4.5; Moskowitz et al., 2013; Moskowitz & Braconnier, 2022).

Moskowitz & Braconnier (2022) provide a summary of existing observational assessments for anxiety for use with autistic individuals. The Behavioral Avoidance Test (BAT; Dadds et al., 1994), the Anxiety Dimensional Observation Schedule (Anx-DOS; Mian et al., 2015) and the Observation Schedule for Children with Autism-Anxiety, Behaviour and Parenting (OSCA-ABP; Palmer et al., 2021) were noted. The BAT and Anx-DOS were developed for the typically developing population whilst the OSCA-ABP was developed to explore emotional and behavioural problems in autistic children as well as parenting behaviours (Dadds et al., 1994; Mian et al., 2015; Palmer et al., 2021). The BAT was described as useful when there is a known specific anxiety-provoking stimulus, so can be appropriate when assessing specific phobia or an obsessive-compulsive presentation (Moskowitz & Braconnier, 2022). The Anx-DOS and OSCA-ABP use presses designed to elicit mild anxiety and emotional/behavioural problems respectively (Mian et al., 2015; Moskowitz & Braconnier, 2022).

When selecting or developing observational assessments for anxiety in autism, key behavioural indicators and triggers for anxiety need to be considered. Existing literature highlights behaviours that challenge, increased vocalisation, and repetitive behaviour as behaviours associated with anxiety (see section 4.4; Baribeau et al., 2020; Edwards et al., 2022; Simpson et al., 2020; Tarver et al., 2021a). The latter has been described by autistic individuals and parents/carers as a potential self-regulation strategy to alleviate anxiety (Edwards et al., 2022; Goodwin et al., 2022; Joyce et al., 2017; Rodgers et al., 2012). Furthermore, repetitive behaviour can help to disentangle anxiety from autism as it can be observed when an individual is calm, but can increase in duration and/or intensity when anxious (see Table 4.5; Edwards et al., 2022; Goodwin et al., 2022).Triggers for anxiety have been noted, such as intolerance of uncertainty, novelty, threats in the environment and separation distress (see Table 4.6; Edwards et al., 2022; Goodwin et al., 2022; Kerns et al., 2014; Lau et al., 2020). In particular, a body of research has focused on the anxiety trigger of intolerance of uncertainty and its utility in explaining anxiety in autistic individuals. Intolerance of uncertainty and anxiety are heightened and positively associated in autistic individuals, with evidence suggesting intolerance of uncertainty mediates the relationship between autism and anxiety (Boulter et al., 2014; Jenkinson et al., 2020). This work demonstrates the theoretical importance of intolerance of uncertainty as an underlying

mechanism of anxiety in autism (Boulter et al., 2014; Goodwin et al., 2022; Jenkinson et al., 2020). In addition to this, floor effects have been reported in previous observational assessments for autistic individuals (Palmer et al., 2021). In order to tap into relevant mechanisms of anxiety and to avoid floor effects, it is therefore crucial for direct assessment measures to implement structured presses and/or coding schemes that tap into these noted behaviours, triggers and potential underlying mechanisms to pinpoint anxiety (Palmer et al., 2021). As with the development of assessment measures noted above and literature reviewed in section 3.2, most research exploring the mechanisms underlying anxiety in autistic individuals focuses on those without a comorbid ID and/or those who have phrase or sentence speech (Boulter et al., 2014; Goodwin et al., 2022; Russell et al., 2019).

Identifying the nature of behaviours observed during anxiety-provoking situations will inform assessment, highlight idiosyncratic behaviours for an individual, potential mechanisms underlying behaviour and demonstrate validity for observational assessments of anxiety. Considering the sequence of behaviours before, during and after anxiety-provoking situations will pinpoint potential pre-cursor behaviours which may allow identification of warning signs of anxiety. Identification of sequences of behaviour will therefore inform intervention and implementation of coping strategies to reduce further distress. Furthermore, this work may allude to potential observable behaviours that are used as self-regulation strategies when anxiety is experienced i.e., repetitive behaviour.

To summarise, most research to date on anxiety in autism utilises informant, questionnaire measures. There is a lack of research utilising direct observational assessments specifically for anxiety in autistic individuals with ID and/or those who speak few or no words, to highlight the nature and sequence of behaviours that may be observed.

Therefore, in order to address these gaps in the literature, the current study utilised the Anx-DOS (Mian et al., 2015) as an observational outcome measure; the Anx-DOS was the only observation measure to specifically assess anxiety known at the time of designing the study. Furthermore, the included presses align with the presentation of anxiety documented in the literature, tapping into novelty, uncertainty, present threat, and separation distress. The Anx-DOS (Mian et al., 2015) has highlighted observable anxiety-related behaviours in individuals with Fragile X; a genetic syndrome where rates of autism diagnoses are high (Crawford et al., in prep; Kaufmann et al., 2017). Furthermore, the Anx-DOS does not rely on an individual's verbal ability and therefore was appropriate to be used with autistic individuals who speak few or no words. It was used to observe anxiety-related behaviours in anxiety or fear-inducing situations. The study sought to evaluate its utility in highlighting anxiety-related behaviours as a potential method of assessment.

The fine-grained direct behavioural observation approach taken in the current study has been implemented in the ID population when focusing on delineating anxiety-related

behaviours in individuals with rare genetic syndromes. Richards et al. (2009) compared behavioural indicators of social anxiety in children with Cornelia de Lange (CdLS) and Cri du Chat (CdCS) syndromes during periods of social demand. Individuals with CdLS were significantly more likely to present with behaviours indicative of social anxiety such as increased hand movements and reduced eye contact to a researcher at times of social demand when compared to individuals with CdCS. These findings highlight the use of this approach to identify the nature and sequence of fine-grained behaviours associated with anxiety in individuals with reduced verbal language.

The current study extends this approach to observe anxiety-related behaviours in autistic individuals who speak few or no words. This is the first known study to report the findings of employing fine-grained observation of behaviour that may be indicative of anxiety in response to presses designed to elicit mild anxiety (Mian et al., 2015). Three presses taken from the Anx-DOS were utilised in the current study, tapping into responses to novelty/uncertainty, present threat, and separation distress because these presses aligned with the presentation of anxiety documented in existing literature (see section 5.3.2.2 below). The approach was adopted to address the following study aims: *i)* to document the presence and nature of anxiety behaviours observed during novel/uncertain/threatening/distressing situations, reporting percentage of time engaged in behaviours across participants *ii)* to describe the temporal sequence of behaviours in *any* novel/uncertain/threatening/distressing situation *iii)* to describe the temporal sequence of behaviours in *each* novel/uncertain/threatening/distressing situation *iv)* to describe the temporal sequence and potential co-occurrence of positive affect, negative affect and repetitive behaviour during novel/uncertain/threatening/distressing situations

5.3 Methods

This study received a favourable ethical decision from the NHS Research Ethics Committee West Midlands – Coventry & Warwickshire (ref: 19/WM/0154; See Appendix 31).

5.3.1 Participants

Families were recruited via an existing database at Aston University, consisting of parents/carers of autistic individuals and individuals with a diagnosis of a genetic syndrome associated with ID. Prior to the Covid-19 pandemic, this study aimed to focus on individuals with moderate-profound ID, including individuals with an autism diagnosis and those with a diagnosis of a genetic syndrome, who speak few or no words. However, when it was anticipated that the sample size for the study may not be as large as originally planned due to disruption caused by the Covid-19 pandemic, it was decided that the study would focus exclusively on autistic individuals who speak few or no words to ensure that the sample was as homogenous as possible and aligned with Chapter four.

Parents/carers who had consented to have their contact details stored on the research database at Aston University were invited to take part in the current study if their child/the person they care for met the following inclusion criteria:

- Autism diagnosis
- Spoke few or no words, as assessed by the Wessex Questionnaire (Kushlick et al., 1973; described in section 5.3.2.3 below)

Both criteria were assessed based on existing data from parents/carers due to their participation in previous research studies run by the research team. This resulted in thirteen participants and their families taking part in the current study. The mean age of participants was 14.77 years old (*SD*=6.51, range=4-28) with nine individuals under 18 years of age (69.2%) and four who were 18 years or older (30.8%). Participants included two females (15.4%) and eleven males (84.6%). All had a diagnosis of autism which was confirmed via receipt of medical documentation provided by parents/carers. Most of the sample received their diagnosis from a paediatrician (*n*=10, 76.9%). Eleven participants had a documented diagnosis of ID, confirmed by medical documentation (84.6%). Ten mothers (76.9%), two fathers (15.4%) and one teacher (7.7%) took part in the study. Further demographic information for participants is presented in Table 5.1. All families were reimbursed £15 for their participation in the study and received an individualised feedback report summarising the findings from the assessments completed.

Table 5.1 Participant demographics

Participant	Gender (M/F)	Age	Verbal ability	Wessex self-help score *(max=9)*	SCQ total score	ADAMS general anxiety subscale *(max=21)*
DA02	M	20	Odd words only	6	31	11
DA04	M	10	Odd words only	6	21	8
DA05	M	7	Odd words only	7	23	2
DA06	F	4	Odd words only	6	16	4
DA08	M	28	Odd words only	6	28	18
DA09	M	10	Odd words only	8	26	3
DA10	M	18	Never a word	4	28	5
DA12	M	17	Never a word	4	31	11
DA13	M	22	Odd words only	5	32	13
DA14	M	15	Odd words only	4	26	10
DA18	F	14	Never a word	6	25	4
DA19	M	11	Never a word	7	19	5
DA21	M	16	Odd words only	9	31	14
				Mean (*SD*): 6 (*1.5*)	Mean *(SD):* 25.9 (*5*)	*Mean (SD):* 8.3 *(4.9)*

5.3.2 Measures

5.3.2.1 Vineland Adaptive Behavior Scales-3

The Vineland Adaptive Behavior Scales-3 (VABS-3; Sparrow et al., 2016) is a semi-structured, informant interview assessing adaptive ability, including communication (subdomains: receptive, expressive, written), daily living skills (subdomains: personal, domestic, community), socialisation (subdomains: interpersonal relationships, play and leisure, coping skills), and motor skills (subdomains: gross, fine). The VABS-3 was completed via telephone with parents/carers prior to the remote direct assessment session. The interview provided a proxy measure of developmental and adaptive ability before conducting the remote assessment session. Chronological age and age equivalent scores for each sub-domain of the VABS are provided for each participant in Table 5.2. Based on a nationally representative sample, the four domains demonstrated reliability (Communication, Daily Living Skills, Socialization, Motor Skills) ranging from .93-.99 (Sparrow et al., 2016). The VABS-3 was included in the current study alongside the Wessex Questionnaire (described in section 5.3.2.3) to provide further in-depth information about an individual's

adaptive ability, including receptive and expressive language. This information was important to collect prior to conducting direct assessments to more accurately gauge an individual's ability based on several different areas of adaptive ability and to characterise the sample in more detail.

Table 5.2 Participant demographics: age equivalent scores (in years:months) for subdomains of the VABS

Participant	Age	Subdomain age equivalent scores										
Domain		Communication			Daily Living Skills			Socialisation			Motor Skills	
		R	**E**	**W**	**P**	**D**	**C**	**IR**	**PL**	**CS**	**G**	**F**
DA02	20	1:7	1:7	4:11	2:7	<3:0	3:1	0:11	0:2	<2:0	4:6	5:4
DA04	10	1:7	1:3	<3:0	2:7	<3:0	<3:0	0:10	0:8	<2:0	4:0	3:10
DA05	7	1:4	1:4	4:0	2:5	<3:0	<3:0	1:0	0:8	<2:0	3:3	3:10
DA06	4	2:5	0:7	5:1	2:4	<3:0	<3:0	0:10	0:9	<2:0	3:8	3:4
DA08	28	1:8	1:5	4:7	3:3	<3:0	<3:0	1:3	0:8	<2:0	8:10+	3:0
DA09	10	1:10	2:0	6:1	4:8	4:2	4:4	1:2	0:11	<2:0	8:10+	5:4
DA10	18	1:1	0:6	3:2	1:3	<3:0	<3:0	0:7	0:4	<2:0	3:6	1:9
DA12	17	1:2	0:9	<3:0	2:7	<3:0	<3:0	0:6	0:9	<2:0	3:0	2:9
DA13	22	1:8	1:3	3:6	2:6	<3:0	<3:0	0:5	0:8	<2:0	1:8	2:2
DA14	15	1:4	1:6	3:0	1:9	<3:0	<3:0	0:8	0:7	<2:0	2:3	1:9
DA18	14	1:8	0:8	5:1	2:0	<3:0	<3:0	0:4	0:9	<2:0	1:3	4:0
DA19	11	1:1	0:8	<3:0	1:10	<3:0	<3:0	0:9	0:8	<2:0	1:6	3:2
DA21	16	1:8	1:11	4:11	4:8	4:10	<3:0	0:6	0:8	<2:0	8:10+	4:6

R: receptive, E: expressive, W: written subdomains make up the communication domain. P: personal, D: domestic and C: community subdomains make up the daily living skills domain, IR: interpersonal relationships, PL: play and leisure and CS: coping skills subdomains make up the socialisation domain, G: gross and F: fine subdomains make up the motor skills domain. Whilst the Motor Skills domain is normed from birth – 9 years old. It can be useful to administer to individuals of any age to gain a complete picture of adaptive ability so was retained in the current study for all participants (Sparrow et al., 2016).

5.3.2.2 Anxiety Dimensional Observation Schedule

The Anxiety Dimensional Observation Schedule (Anx-DOS; Mian et al., 2015) is a direct assessment developed to elicit anxiety behaviours and responses. Three conditions of the Anx-DOS were included in the current study in the following order: the toy spider, mystery jar and parental separation conditions. The auditory startle condition was not included in the current study due to the difficulty of administering a standardised auditory stimulus across participants remotely and due to ethical considerations of using this press with a child who could not provide informed consent to this specific anxiety assessment and, due to sensory sensitivities, may find loud noises particularly aversive. For all other conditions the presses are not dissimilar to everyday situations that children encounter during play, and it is possible to monitor the child's response to the press and terminate the press if the child appeared distressed. See section 1.5.3 for a more detailed discussion regarding ethical considerations.

The *spider condition* involved the child being presented with a remote-controlled toy spider where they were verbally encouraged to touch the spider followed by the parent/carer moving the spider unexpectedly using the remote-control. This condition was pressing for novelty/present threat. The *mystery jar condition* involved the individual being presented with a black opaque jar and being asked to put their hand within the jar, parents/carers were asked to prevent the individual from peering inside the jar before placing their hand in as much as possible. This condition was pressing for novelty/uncertainty. The *parental separation condition* involved the parent/carer leaving the individual in a room with the remote presence of the researcher. This condition was pressing for separation distress. The Anx-DOS is developed to elicit very mild anxiety behaviours (e.g., hesitation) and the Anx-DOS was to be terminated if any individual experienced distress as determined by parents/carers, in response to any of the presses. The spider and jar in the study were made of a plastic material to allow for effective sanitisation.

Parents also completed the following questionnaire measures:

5.3.2.3 Wessex Questionnaire

The Wessex Questionnaire (Kushlick et al., 1973; See Appendix 10) assesses an individual's social and physical adaptive ability. There are 16 items covering five subscales: continence, mobility, self-help skills, speech, and literacy. The questionnaire can be used as a proxy measure of ability, with higher scores indicating greater ability. For the current study, the self-help skills and speech subscales were used to characterise the sample and confirm that individuals spoke few or no words. Inter-rater reliability is good with a mean Kappa value of 0.62 for overall classification (substantial agreement) and 0.54 for item-level reliability (moderate agreement) (Kushlick et al., 1973; Palmer & Jenkins, 1982). The Wessex

Questionnaire was included in the current study to stay consistent with the proxy measure of ability utilised in previous chapters, with a more in-depth assessment of ability completed using the VABS-3 (described in section 5.3.2.1).

5.3.2.4 Social Communication Questionnaire

The Social Communication Questionnaire (SCQ; Rutter et al., 2003b; See Appendix 11) is a screening tool for autism characteristics with 40 items, rating dichotomously with responses of yes/no. A high score indicates more autism characteristics, a total score of >15 indicates possible autism spectrum disorder, whilst a score of >22 indicates possible autism. The SCQ has good internal consistency and is suitable for individuals with ID (α = .90; Berument et al, 1999).

5.3.2.5 Anxiety, Depression and Mood Scale

The Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003; See Appendix 12) is an informant measure that explores behaviours/symptoms related to anxiety, depression, and mania. The general anxiety subscale data is presented as the focus in the current study. There are 28 items rated on a Likert scale of 0 'not a problem' to 3 'severe problem.' The questionnaire was validated with informants of individuals with mild to profound intellectual disability. Test-retest reliability and internal consistency are excellent at .81 and .80 respectively (Esbensen et al., 2003).

5.3.3 Procedure

Prior to the Covid-19 pandemic, it was planned for this to be a face-to-face direct assessment study that would take place at participants' homes or Aston University. There was a significant period where face-to-face research testing was not an option following the outbreak of Covid-19 and there was uncertainty surrounding when this may be a possible option in the future. Therefore, an ethics amendment was submitted to include options of face-to-face and remote assessment. However, as face-to-face testing was not feasible during the timeframe of this study, and to allow homogeneity across participants, it was decided that the current study would be a remote direct assessment study. Furthermore, the study was to include psychophysiological measures of anxiety including a heart rate wearable watch to allow for multi-method assessment of anxiety as recommended in previous literature (Moskowitz et al., 2013; Moskowitz et al., 2017). Due to the need for sanitisation of all materials sent to families, this was not a viable assessment method for this study at the time.

Families who met the inclusion criteria for the current study were called via telephone to invite them to take part. During this call, the study was described and any questions from families were answered. If families displayed an interest in taking part, an email was sent with an online link allowing them to access the study information sheet (See Appendix 32)

and consent forms via survey software Qualtrics (Qualtrics, Provo, UT, 2018). Parents/carers were made aware that they could request paper copies of the information sheet and consent forms if they preferred. After accessing the information sheet, parents were directed to the appropriate consent form based on their responses to questions exploring their child/the person they care for's age and ability to consent to take part. Parents/carers of autistic individuals aged 16 or under provided consent for participation. Autistic individuals aged 16 or over, with the capacity to consent, provided consent for participation using paper or online methods. Parents/carers of autistic individuals aged 16 or over without capacity to consent acted as personal or nominated consultee to their child/person they care for (See Appendix 33 for consent forms).

Once parents/carers had consented to take part in the study, they were telephoned to arrange the first measure to complete as part of the study, the VABS-3, described in section 5.3.2.1. Following completion of the VABS-3, a date was arranged with the family for the remote direct assessment session to take place. All assessments took place remotely, via the telecommunication platform of Zoom or Microsoft teams. Families were able to decide the most appropriate way for them to take part in the study to ensure engagement with the study during the difficult time of national lockdowns in the context of the Covid-19 pandemic, therefore two families (15.4%) took part via Zoom and eleven families (84.6%) took part via Microsoft teams. Prior to the assessment day, parents/carers were sent written instructions for the assessments electronically as well as images of the objects included in the assessments (See Appendix 34). All parents/carers were offered time to ask questions or talk through assessments before the remote session.

A risk assessment was completed prior to the session which asked parents/carers whether the person they care for engages in behaviours that challenge and what may cause this display of behaviour, parents/carers were also asked for any information that may be important before the assessment session (See Appendix 35). Questions concerning recent Covid-19 infection within the household were also asked due to potential contact when delivering assessment materials and cross-contamination with materials. All families reported that they had not experienced recent (within last week) Covid-19 infection, this also included being in personal contact with others. To take a cautious approach, there was a timeframe of at least 72 hours (as advised by Public Health England) for every participant between one family taking part in the study and using the assessment materials and the next family receiving the assessment materials. Approximately 48 hours prior to the arranged direct assessment session, parents/carers were emailed an individualised online link for them to access the assessment session on the arranged date and time.

Due to the remote nature of the study, parents/carers were either sent the assessment materials via a university approved courier service or the researcher conducting the study

delivered the assessment materials to the family's home address. Assessment materials were labelled and organised into plastic bags to allow sanitisation and to ensure the assessment session went as smoothly as possible. Laminated written instructions which included pictures of objects/toys were also sent with the assessment materials. Parents/carers were provided with a return label to attach to the parcel and a postal courier picked up the assessment materials or the researcher collected the materials following the remote assessment session. All materials and laminated instructions were sanitised whilst wearing personal protective equipment (PPE) after they were returned to the university following a remote assessment session.

With consent, assessments completed with participants and their families were recorded to be used in subsequent analysis. Video recordings of the assessments were downloaded and stored on Aston University's secure online cloud-based storage system. The mean duration of the online assessment was 11 minutes 34 seconds, with a range of 7 minutes 50 seconds to 16 minutes 32.5 seconds (*SD*=3 minutes 5 seconds). Due to the remote nature of the study, the researcher supported the parent/carer to administer the assessments with their child/the person they care for, by prompting parents/carers when to present new assessment materials.

Following the remote assessment session, parents/carers were asked to complete a battery of informant questionnaire measures to characterise the sample of autistic individuals further. Parents/carers were sent an online link to access the questionnaires via the survey platform, Qualtrics (Qualtrics, Provo, UT, 2018). Questionnaires completed are described in section 5.3.2 above.

Following participation in the study, documentation that was sent via email, e.g., personalised feedback report, to parents/carers which contained confidential information was password-protected with information that was specific to that individual i.e., date of birth.

5.3.3.1 Behaviour definitions and video coding

The original coding scheme developed for the Anx-DOS was not used in the current study due to not being appropriate for the study aims and the population. For example, the original scheme included coding the severity of facial fear (0-3) based on the number of facial regions where fear is observed. Autistic individuals may show different facial expressions, less frequently and as mentioned in section 1.4.3, 'atypical' presentations of anxiety may be common e.g., behaviours that challenge (Keating & Cook, 2020). The development of a specific, operationalised coding scheme was needed to fulfil the study aims, to include a range of possible anxiety-related behaviours and to align with the analysis of identifying anxiety-related behaviours in relation to presses and temporal sequences of behaviours. The behavioural coding scheme for the current study was developed based on existing literature including some behaviours noted in the Anx-DOS coding scheme e.g.,

negative vocalisations, previously developed anxiety coding schemes for individuals with genetic syndromes associated with intellectual disability (Royston et al., 2016) and preliminary screening of the video footage in the current study. Furthermore, a Clinical Psychologist (Dr Jane Waite, PhD, ClinPsyD) was consulted during the development of the coding scheme to ensure relevant behaviours were not missed.

The coding scheme was piloted on a subset of the videos (*n*=3, 23.1%) to assess the suitability of the codes to the assessment used in the current study; the Anx-DOS. Following this, the coding scheme was further refined, for example, changing an event variable to a duration variable. See finalised coding scheme in Table 5.3. Behaviours were coded as either event or duration variables, where the former codes the momentary presence of a variable and the latter codes the onset and offset of a variable. Each participant video was edited to obtain three separate videos for each participant of the three Anx-DOS conditions to allow observation of anxiety behaviours in relation to each anxiety press. Using these behavioural codes, footage was coded in real time using behavioural coding software, Obswin (Martin et al., 2000).

Table 5.3 Behaviour coding scheme

Variable	Event/ Duration	Code name	*Operationalised definition*
Body movements			
1. Body rocking	E	BodyRock	*Repeated rhythmic rocking movements of the upper body that involve two directions (i.e. backwards and forwards) and occur in close duration (e.g. rocking body back and forth). An individual rocking back-forward-back is the minimum movement needed to fulfil the code.*
2. Shaking/ fidgeting	D	ShakeFidget	*Repeated movements of mid to lower body parts that involve two directions and occur in close duration and rapidly (e.g. shaking of torso, leg shaking, moving in seat, shifting from one leg to another).*
3. Head shaking	E	HeadShake	*Repeated movement of the head from side to side (left to right or right to left), occurring in close duration.*
4. Hand flapping	E	HandFlap	*Flapping of the hands and/or arms in a repetitive manner (i.e. backwards and forwards), hands bending from the wrist.*
5. Clapping of hands	E	Clap	*Hitting palm of hands together. Hands must come together rapidly in the midline and then separate.*

6.	Tapping	E	Tap	*Repeated tapping movements with hands that involve two directions (i.e. up and down) and occur in close duration (e.g. tapping finger on desk/body/toy/object, tapping hand on leg). Contact must be made between hand/finger and object/body part.*
7.	Fiddling/ Twiddling	D	Fiddling	*Small and quick movements mostly of the hands to indicate restlessness, uneasiness, impatience or nervousness. Examples: fiddling hand or fingers movements, twiddling hand/fingers together, turning object in fingers.*
8.	Shrinking into self	D	Shrink	*Change in posture/positioning: Person may hunch over, put hands/feet together, wrapping arms around the body/self-hugging, etc. (If a person is showing this behaviour from the beginning of the footage, make a note of it and only code change).*
9.	Rigid/body tenseness	D	Rigid	*Noticeable change in torso becoming more rigid and tense. This may include straightening of the torso. Movement may also include slight arching of the back with chest protruding. When becoming rigid/tense, body may 'freeze'.*
10.	Avoidance	E	Avoid	*Coded as an increase in activity. The individual should be making an active attempt to distance themselves from an object. It should be clear that the individual is avoiding the object rather than moving away for some other reason (e.g., being curious about something else on the other side of room). For example, pushing objects away, backing away from objects, turning away.*
11.	Hesitation/ wariness	E	Hesit	*A slower or quicker reaction to the press than what is to be expected. For example, an individual may pause, slow down, resist, keep a distance from an object, or speed up an action to complete a task quickly.*
12.	Behaviours that challenge	E	BehChall	*Behaviour that could cause harm to the individual, others around them or damage to surrounding objects; e.g. hitting, kicking, grabbing, biting, hitting, scratching, picking, banging, pushing, throwing objects, hitting objects.*

13. Proximity seeking	E	Proxy	*Coded as an attempt to get closer to adult. The individual should be making an active attempt to get to adult or be in adult's presence. Only code if initiated by individual - do not code if initiated by adult, including if individual reciprocates. Examples of behaviour could include leaning towards an adult, touching an adult, putting head on adult.*
Variable	Event/ Duration	Code name	*Operationalised definition*
Facial movements and eye gaze			
14. Social Gaze	D	GazeSoc	*Gaze away from the task and directed towards researcher/caregiver for a fixed period. This includes looking in the direction of the adult, looking for the adult or obtaining eye contact with the adult. Therefore, obtaining eye contact with the adult is not needed to fulfil the code.*
15. Positive affect	D	PosAff	*The participant demonstrates laughing and/or smiling behaviour. Facial expression and vocalisation must clearly indicate expression of pleasure in activity or conversation. Facial expression may or may not be directed towards the examiner.*
16. Negative affect	E	NegAff	*Facial expression indicating upset, irritation, annoyance or confusion. This may include frowning such as the eyebrows being drawn down and together, screwing up the face, a strained expression, clenching of teeth, pressing lips tightly together, a scrunched up mouth or the mouth turned down at the corners. Behaviours may present alone.*
17. Lip licking	E	LipLick	*Movement of the tongue licking the upper or lower lip.*
18. Covering face/head	D	CoverFace	*Using hands, arms, objects, hair or clothing to physically cover any part of the face, including the covering of eyes, mouth, nose and ears, touching of cheeks or forehead. Do not code if appears to be related to comfort or posture.*
Vocalisations: *A sound produced by the voice - verbal or non-verbal.*			
19. Negative vocalisation	D	NegVoc	*Vocalisation indicating negativity, annoyance or nervousness to others or self. Examples: Grunting, panting, sighs, or nervous laughing.*

5.3.3.2 Interrater reliability

Video footage for four participants (30.8%) were independently coded by an independent second observer (Dr Effie Pearson, PhD). Participants were strategically chosen for reliability analysis due to the overall small sample size and the need to code as many behaviours present within the overall sample videos. Therefore, after preliminary screening of the video footage for all participants, the individual participant who displayed the highest number of behaviours on the coding scheme was used for the reliability analysis. Subsequent participants were chosen strategically based on behaviours that were not observed and coded in previous videos to ensure as many behaviours as possible were included in the reliability analysis. Based on this, 17 out of the total 19 (89.5%) coded behaviours were included in the reliability analysis. There were three rounds of reliability coding, each time, behaviours with low reliability were discussed and operationalisations refined if necessary. Following this, the participant videos were re-coded using the refined code independently by a second observer.

Two measures of inter-rater reliability were used in the current study; Kappa coefficients and prevalence-adjusted-bias-adjusted-kappa (PABAK; Byrt et al., 1993) analysis. This was due to the low prevalence of some behaviours coded in the current study and the documented impact of prevalence on Kappa coefficients as well as the impact of bias due to unequal marginal distributions (Byrt et al., 1993; Nurjannah & Siwi, 2017; Sim & Wright, 2005). PABAK analysis adjusts for the impact of prevalence and bias on Kappa values by relying solely on the observed proportion of agreement between observers (Sim & Wright, 2005).

Kappa values are organised into categories of no agreement (≤ 0), none to slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80) and almost perfect agreement (0.81-1.00; Landis & Koch, 1977; McHugh, 2012). The Kappa scores for behavioural codes ranged from 0-1 (mean of 0.39), indicating no to almost perfect agreement across behaviours. PABAK values are categorised as slight (0.00-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80) and excellent agreement (>0.81; Landis & Koch, 1977). PABAK values ranged from 0.499 to 1 (mean of 0.91), demonstrating moderate to excellent agreement. Kappa and PABAK values for each behaviour are presented together in Table 5.4 as suggested in previous literature (Nurjannah & Siwi, 2017).

Table 5.4 Inter-rater reliability indices

Behaviour categories and codes[40]	Final round of reliability coding	Kappa	PABAK
Body movements			
BodyRock	3	0.03	0.937
ShakeFidget	1	0.74	0.924
HeadShake	1	0.48	0.991
HandFlap	2	0.33	0.991
Clap	2	0.39	0.96
Tap	2	0	0.991
Fiddling	2	0.52	0.884
Rigid	2	0.21	0.982
Avoid	2	0.55	0.973
Hesit	2	0.16	0.982
BehChall	2	0.65	0.973
Proxy	2	0.22	0.893
Facial movements and eye gaze			
GazeSoc	2	0.34	0.499
PosAff	2	0.44	0.727
NegAff	2	0.25	0.915
CoverFace	1	1	1
Vocalisations			
NegVoc	2	0.35	0.857

5.3.4 Data Analysis

For the purpose of the current study, behaviours were aggregated to form classes of behaviour. The classes were repetitive behaviours, negative affect, and avoidance. Behaviours that did not fit into one of these three categories were explored as single behaviours in relation to the anxiety presses. The classes of behaviours were informed by the literature and findings from previous chapters in this thesis, for example, hand flapping was coded as a repetitive behaviour (Edwards et al., 2022; Kapp et al., 2019). The researcher leading the project, a Clinical Psychologist and Senior Lecturer and a Professor of Neurodevelopmental Disorders reviewed the proposed behaviour classes and reached consensus prior to analysis. Therefore, there were nine overall behavioural codes, including

[40] Behaviour codes of LipLick and Shrink were not included in the reliability analysis due to only occurring in one participant each and therefore they were not present in the participants coded for reliability

three classes of behaviour and six single behaviours (social gaze, behaviours that challenge, lip lick, positive affect, proximity seeking and rigid; see Table 5.5).

Table 5.5 Classes of behaviour

Classes of behaviour	
Repetitive behaviour	BodyRock, HandFlap, Fiddling, Tap, HeadShake, ShakeFidget, Clap
Negative affect	NegAff, NegVoc
Avoidance	Avoid, Hesit, Shrink, CoverFace
Single behaviours	
PosAff	
GazeSoc	
BehChall	
Proxy	
Rigid	
LipLick	

To address study aim one, descriptive statistics were generated across all participants to report the percentage of time intervals for which each anxiety-related behaviour was observed and coded. These statistics were used to identify behaviours most frequently observed in the current sample.

To address aims two and three of the study, sequential lag analyses were used to explore coded behaviours present during 15 one-second intervals before and 15 one-second intervals after the presence of the anxiety press. This lag length was chosen based on the number of participants displaying a behaviour at each lag interval; after the 15th interval, there were no occurrences of five behavioural codes (55.6%) therefore this cut-off was chosen. Analyses contrast the unconditional or simple probability of participants engaging in the target behaviour (e.g., behaviours that challenge) against the conditional probability of participants engaging in the target behaviour given the presence of a criterion behaviour (e.g., behaviours that challenge given anxiety press). In the current study, *Z* scores were used to determine whether the unconditional and conditional probabilities differed significantly. In previous research, a *Z* score of 1.96 (equating to $p < .01$) or above has been deemed significant (Moss et al., 2005), however, to avoid type 1 errors and in line with recent literature, this was increased to 3.10, $p < .001$ (Agar et al., 2020). Sequential analyses were completed to explore the relationship between behaviours and the anxiety presses. These analyses were completed based on any anxiety press (study aim two) as well as each anxiety press (study aim three) to determine if there were general sequences of behaviours related to any anxiety provoking situation or if there were specific relationships

between behaviours and presses tapping into specified areas of anxiety e.g., novelty/uncertainty.

To specifically address aim four of the study, further lag analyses were conducted to explore relationships and potential co-occurrence between negative and positive affect and repetitive behaviour, due to existing literature suggesting repetitive behaviour as an observable behaviour noted when an individual is calm, but it can increase in duration and/or intensity when anxious (Edwards et al., 2022; Goodwin et al., 2022).

5.4 Results

During the delivery of the Anx-DOS, termination of the assessment was not necessary for any participant, allowing completion of all three anxiety presses for all participants. To address the first aim of documenting the presence and nature of anxiety behaviours observed during the Anx-DOS, descriptive statistics were generated across participants. The most frequently observed and coded behaviours across Anx-DOS presses were social gaze (8.3% of intervals), positive affect (4.52% of intervals), repetitive behaviour (4.44% of intervals) and negative affect (3.06% of intervals). These behaviours were also the most frequently observed and coded in the individual presses (see table 5.6).

Table 5.6 Percentage of intervals where behaviours were observed across any Anx-DOS press and individual presses, with number of participants and percentage of sample where behaviour was observed (N/O=not observed). Con1=spider, Con2=mystery jar, Con3=parental separation

	Any press	Any press *n* (%)	Con1	Con1 *n* (%)	Con2	Con2 *n* (%)	Con3	Con3 *n* (%)
(Number of 1s intervals)	(9052)		(2485)		(1778)		(4789)	
Avoidance	1.59%	9 (69.2)	1.93%	6 (46.2)	1.97%	7 (53.8)	1.27%	3 (23.1)
Behaviours that challenge	0.11%	1 (7.7)	0.16%	1 (7.7)	0.11%	1 (7.7)	0.08%	1 (7.7)
Social gaze	8.3%	13 (100)	8.01%	13 (100)	11.3%	12 (92.3)	7.33%	13 (100)
LipLick	0.01%	1 (7.7)	N/O	0 (0)	0.06%	1 (7.7)	N/O	0 (0)
Negative affect	3.06%	6 (46.2)	3.42%	3 (23.1)	4.44%	5 (38.5)	2.36%	2 (15.4)
Positive affect	4.52%	11 (84.6)	6.64%	9 (69.2)	4.84%	5 (38.5)	3.3%	7 (53.8)
Repetitive behaviour	4.44%	12 (92.3)	4.43%	9 (69.2)	3.94%	5 (38.5)	4.64%	8 (61.5)
Rigid	0.21%	3 (23.1)	0.2%	1 (7.7)	N/O	0 (0)	0.29%	2 (15.4)
Proximity seeking	0.22%	7 (53.8)	0.24%	4 (30.8)	0.28%	4 (30.8)	0.19%	4 (30.8)

Statistically significant findings across the lag analyses are now presented in relation to each study aim. Behaviours that challenge and LipLick did demonstrate statistically significant findings across anxiety presses, however they were only coded in one participant across conditions, therefore graphs are presented in the Appendices and need to be interpreted with caution (see Appendix 36). Apart from the behaviours described below, no other anxiety-related behaviours demonstrated statistically significant differences between the unconditional and conditional probabilities during any press or individual press analyses and so graphs are presented in the Appendices (see Appendix 37).

To address the second aim of describing the temporal sequence of behaviours in *any* Anx-DOS press, analyses explored the unconditional probability of anxiety-related behaviours, and the conditional probability of individuals engaging in these behaviours *given* the occurrence of *any* anxiety press. Figure 5.1 demonstrates the levels and trend for the unconditional and conditional probabilities of negative and positive affect and rigid before, during and after the occurrence of any press. Given the presence of *any* anxiety press at lag 0, the conditional probability of negative affect at lag -1 is significantly greater than the

unconditional probability of negative affect (*Z*=3.62). Given the presence of *any* anxiety press at lag 0, the conditional probability of positive affect at lag -13 (*Z*=3.27), lag -12 (*Z*=3.16) and lag 0 (*Z*=3.27) are significantly greater than the unconditional probability of positive affect. Additionally, given the presence of *any* anxiety press at lag 0, the conditional probability of rigid at lag +1 is significantly greater than the unconditional probability of rigid (*Z*=3.22). So, negative affect is more likely to be observed just before an anxiety press, positive affect is more likely to be observed leading up to and during an anxiety press, whilst rigidity is more likely to be observed following an anxiety press.

To address the third aim of describing the sequence of behaviours in *each* Anx-DOS press, analyses explored the unconditional probability of autistic individuals engaging in anxiety-related behaviours, and the conditional probability of individuals engaging in these behaviours *given* the occurrence of a specific press. Figure 5.2 demonstrates the differences between the unconditional and conditional probabilities of social gaze before, during and after the occurrence of the spider press. Given the presence of the *spider press* at lag 0, the conditional probability of social gaze at lag -14 (*Z*=3.75), lag -12 (*Z*=3.66) and lag -11 (*Z*=3.61) is significantly greater than the unconditional probability of social gaze.

Figure 5.1 Mean unconditional probability (UP) of all participants displaying anxiety behaviours and conditional probability (CP) of participants displaying anxiety behaviours given **any anxiety press** at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z>3.10$, $p<.001$).

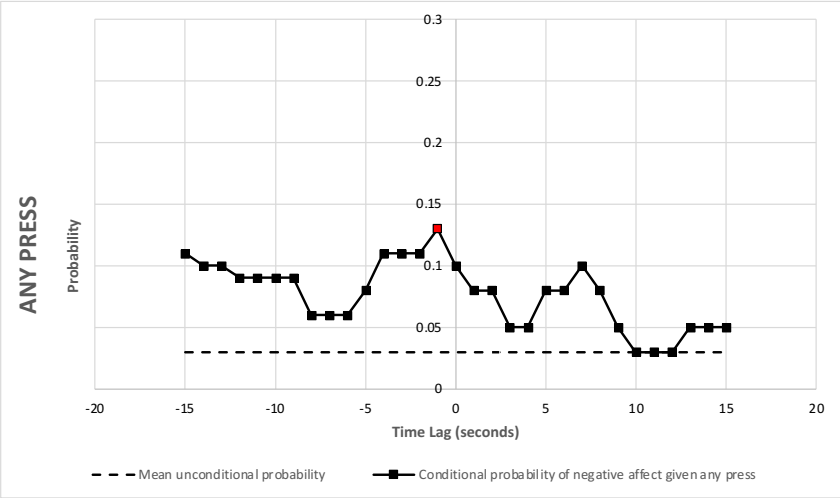


Figure 5.1a Mean UP of participants displaying negative affect and CP of participants displaying negative affect given any anxiety press at time zero.

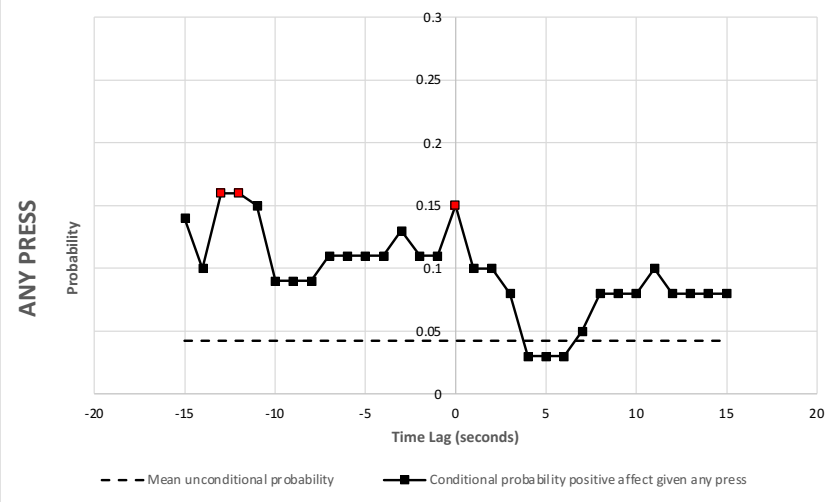


Figure 5.1b Mean UP of participants displaying positive affect and CP of participants displaying positive affect given any anxiety press at time zero.

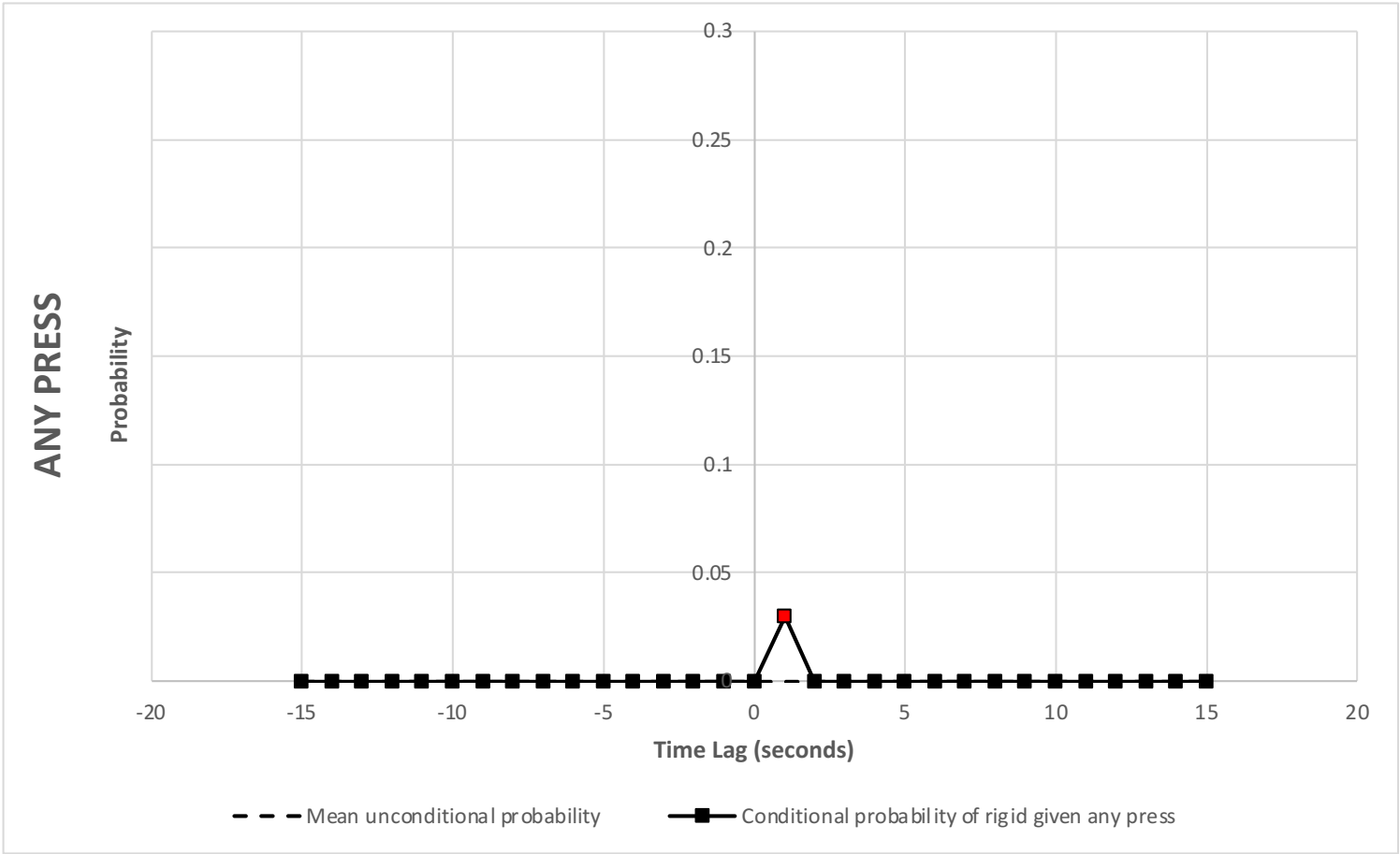
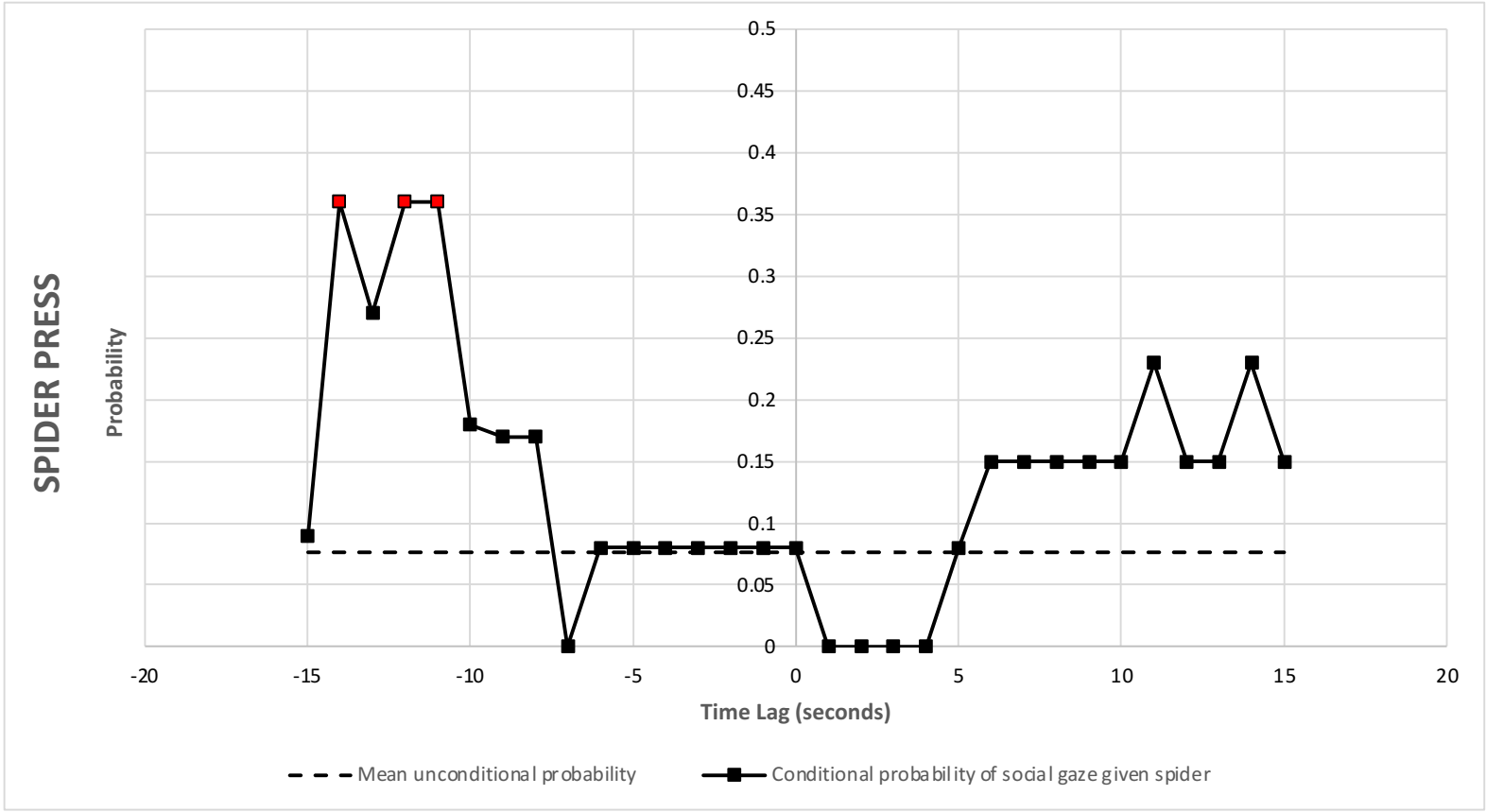


Figure 5.1c Mean UP of participants displaying rigid and CP of participants displaying rigid given any anxiety press at time zero.

Figure 5.2 Mean unconditional probability of all participants engaging in **social gaze** and conditional probability of participants engaging in **social gaze** given the **spider press** at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z>3.10$, $p<.001$).



In terms of the mystery jar press, analyses explored the unconditional probability of autistic individuals engaging in anxiety-related behaviours, and the conditional probability of individuals engaging in these behaviours *given* the occurrence of *the mystery jar press* at zero. Figure 5.3 demonstrates the differences between the unconditional and conditional probabilities of negative affect before, during and after the occurrence of the mystery jar press. Given the presence of the *mystery jar press* at lag 0, the conditional probability of negative affect at lag -1 is significantly greater than the unconditional probability of negative affect (Z=3.47).

In terms of the parental separation press, analyses explored the unconditional probability of autistic individuals engaging in anxiety-related behaviours, and the conditional probability of individuals engaging in these behaviours given the occurrence of *the parental separation press* at zero. Figure 5.4 demonstrates the differences between the unconditional and conditional probabilities of rigid before, during and after the occurrence of the parental separation press. Given the presence of the *parental separation press* at lag 0, the conditional probability of rigid at lag +1 is significantly greater than the unconditional probability of rigid (Z=4.95). Therefore, lag analyses demonstrated that social gaze was more likely to be observed *leading up to* the spider press, negative affect was more likely to be observed *just before* the mystery jar press and rigidity was more likely to be observed *following* the parental separation press.

Figure 5.3 Mean unconditional probability of all participants displaying **negative affect** and conditional probability of participants displaying **negative affect** given the **mystery jar press** at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z>3.10$, $p<.001$).

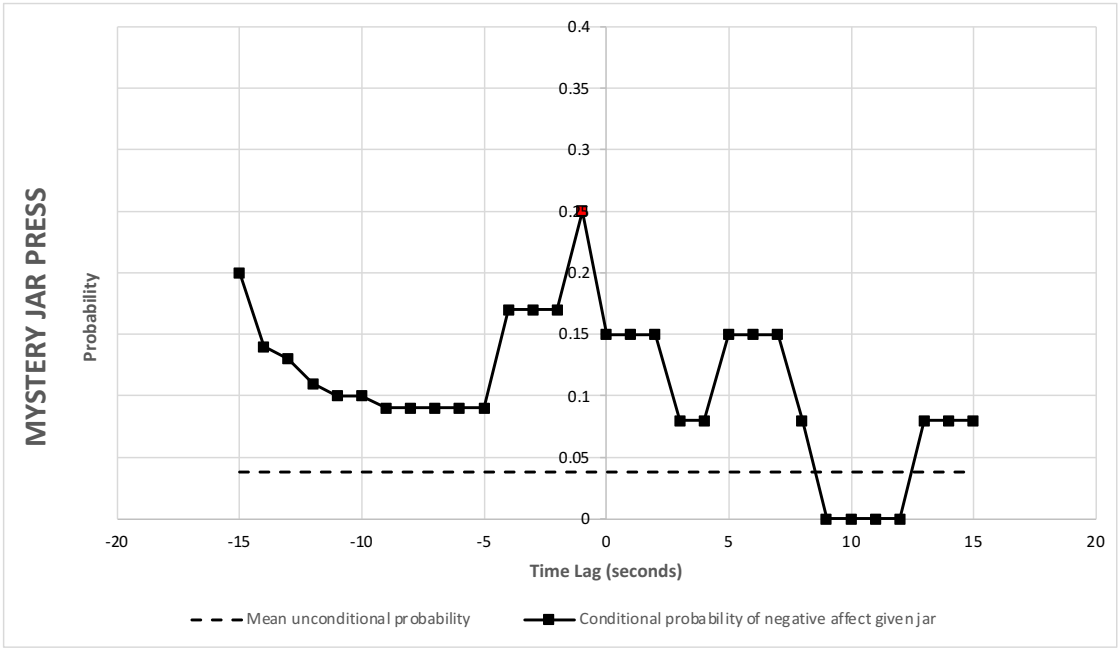
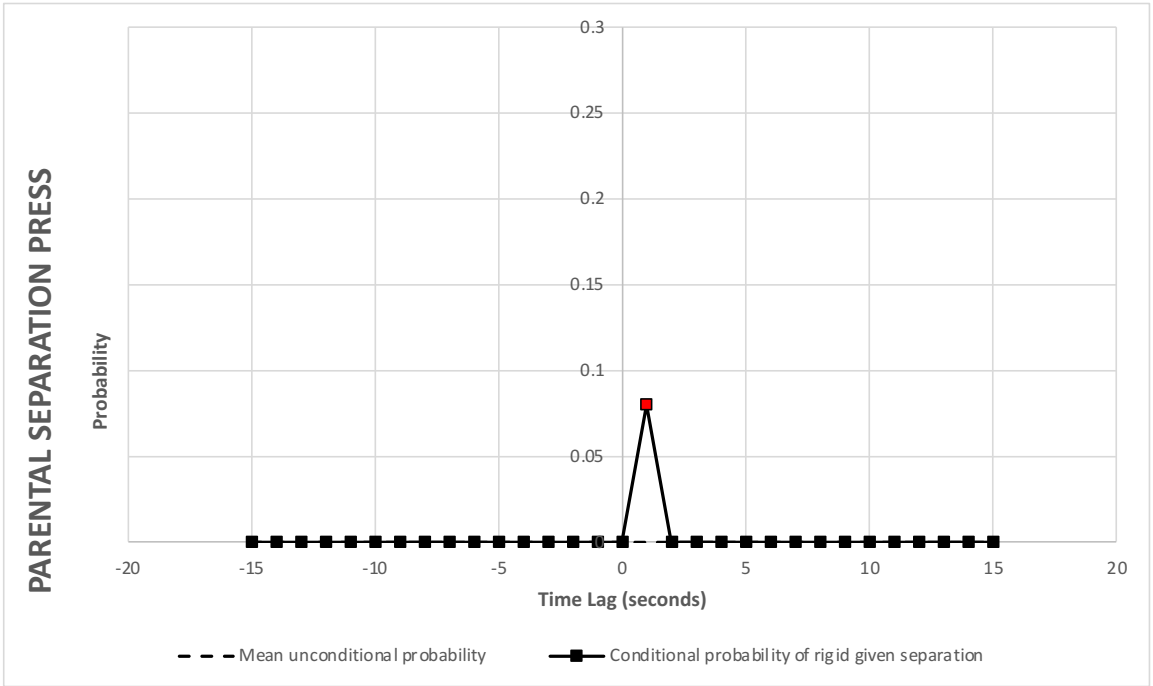


Figure 5.4 Mean unconditional probability of all participants displaying **rigid** and conditional probability of participants displaying **rigid** given the **parental separation press** at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability ($z>3.10$, $p<.001$).



To address the fourth study aim, analyses were conducted to explore the unconditional probability of autistic individuals engaging in negative and positive affect, and the conditional probability of individuals engaging in these behaviours *given* the occurrence of *repetitive behaviour* at lag 0. During any anxiety press and individual presses, analyses explored the unconditional and conditional probabilities of negative and positive affect occurring before, during and after engagement in repetitive behaviour (see Figure 5.5). During *any* anxiety press, given the presence of repetitive behaviour at lag 0, the conditional probability of negative affect is significantly greater than the unconditional probability of negative affect; **before, during** and **after** the engagement in repetitive behaviour (Z=15.84 to 21.94). Given the presence of repetitive behaviour at lag 0, the conditional probability of positive affect at lags -10 to 5 are significantly lower than the unconditional probability of positive affect (Z= -3.17 to -3.64).

During the *spider press*, given the presence of repetitive behaviour at lag 0, the conditional probability of negative affect is significantly greater than the unconditional probability of negative affect; **before** and **during** the engagement in repetitive behaviour (Z=3.43 to 7.4). During the *mystery jar* and *parental separation* presses, given the presence of repetitive behaviour at lag 0, the conditional probability of negative affect is significantly greater than the unconditional probability of negative affect; **before, during** and **after** the engagement in repetitive behaviour (Z= 9.98 to 22.58). To summarise, with regards to *any* anxiety press, negative affect is more likely to be observed before, during and after engagement in repetitive behaviour, whilst positive affect is less likely to be observed before repetitive behaviour. During the *spider press*, negative affect is more likely to be observed before and during repetitive behaviour. During the *mystery jar* and *parental separation* presses, negative affect is more likely to be observed before, during and after repetitive behaviour.

Figure 5.5 Mean unconditional probability (UP) of all participants displaying **negative affect/positive affect** and conditional probability of participants displaying **negative affect** given the display of **repetitive behaviour** at time zero. Red squares indicate a conditional probability which is significantly higher than the unconditional probability (z>3.10, p <.001). Blue squares indicate a conditional probability which is significantly lower than the unconditional probability (z>3.10, p <.001).

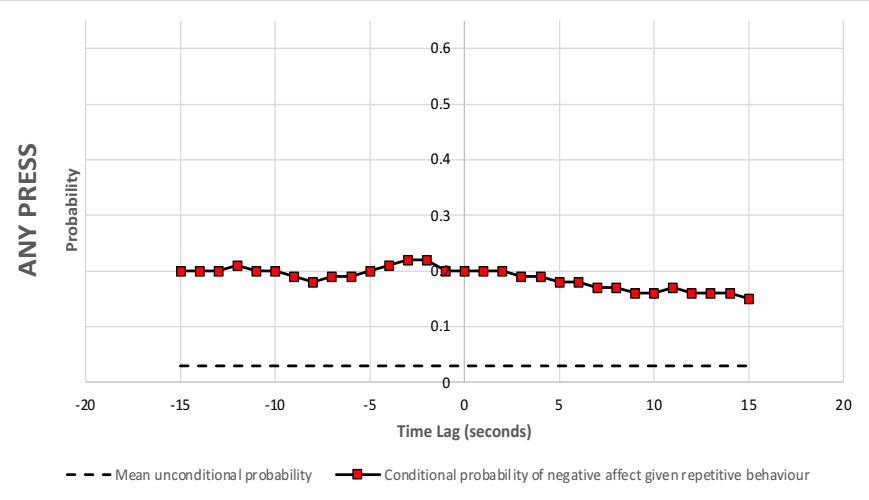


Figure 5.5a Mean UP of all participants displaying negative affect and CP of participants displaying negative affect given the display of repetitive behaviour at time zero, during any anxiety press.

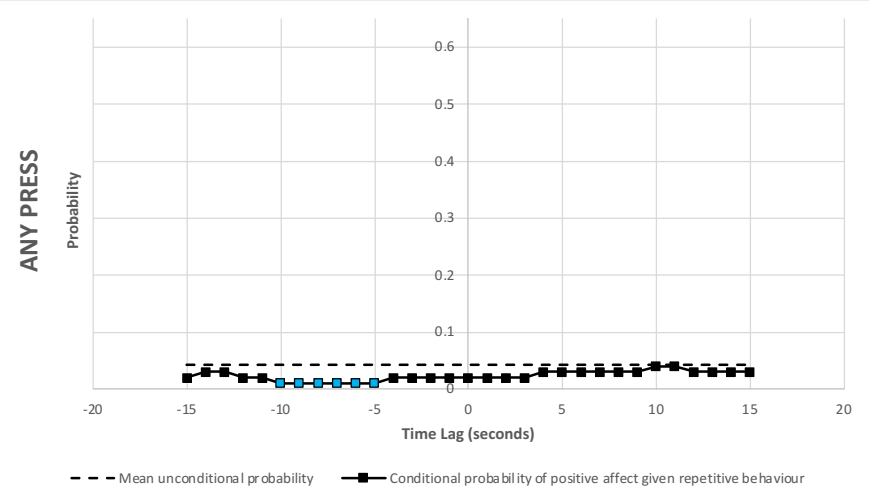


Figure 5.5b Mean UP of all participants displaying positive affect and CP of participants displaying positive affect given the display of repetitive behaviour at time zero, during any anxiety press.

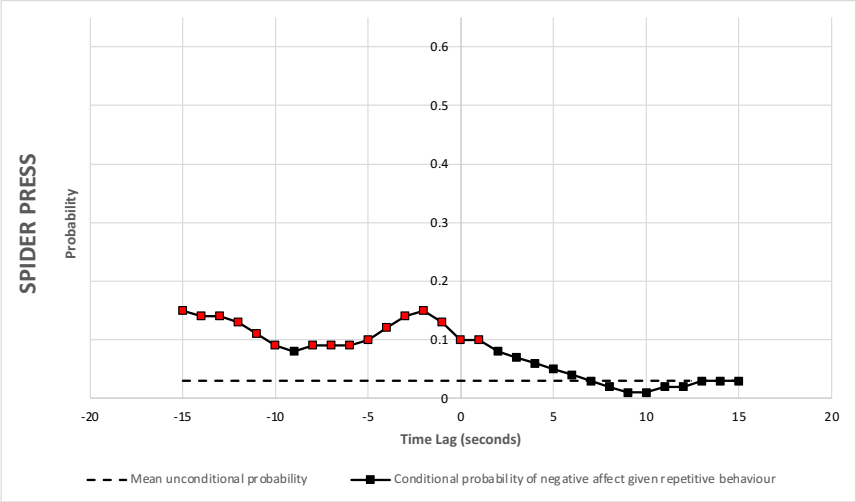


Figure 5.5c Mean UP of all participants displaying negative affect and CP of participants displaying negative affect given the display of repetitive behaviour at time zero, during the spider press.

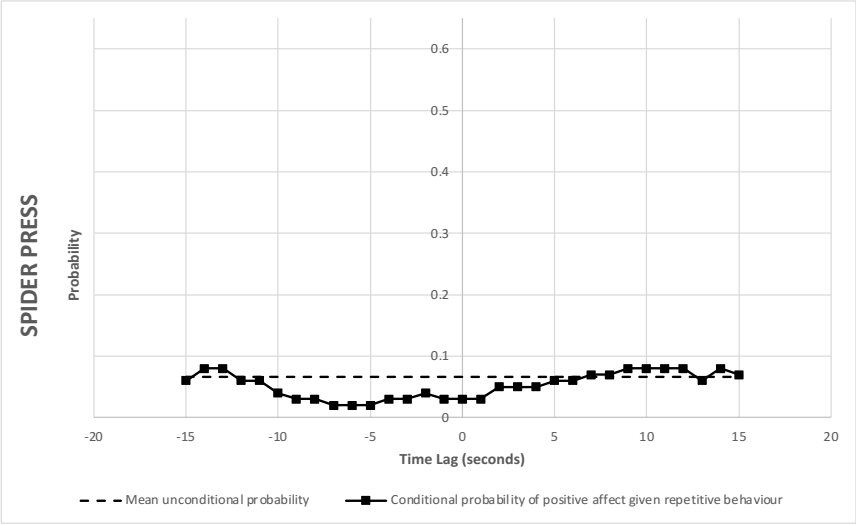


Figure 5.5d Mean UP of all participants displaying positive affect and CP of participants displaying positive affect given the display of repetitive behaviour at time zero, during spider press.

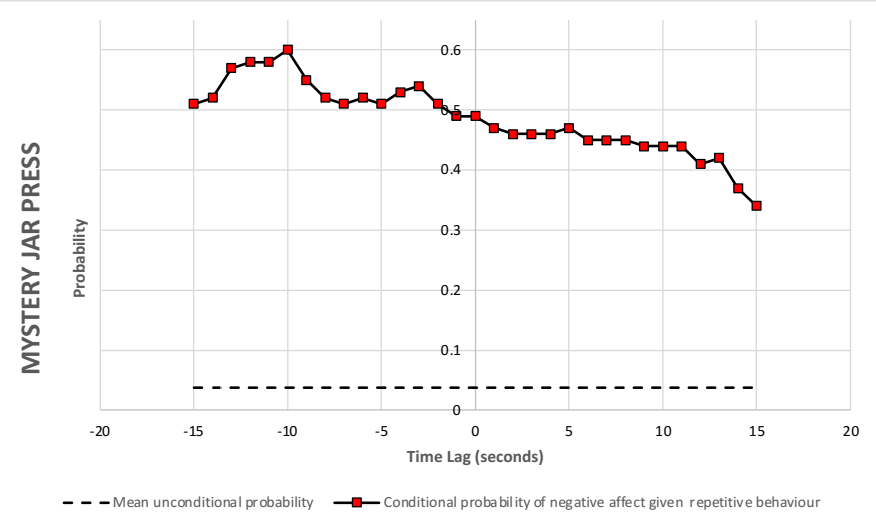


Figure 5.5e Mean UP of all participants displaying negative affect and CP of all participants displaying negative affect given the display of repetitive behaviour at time zero, during the mystery jar press.

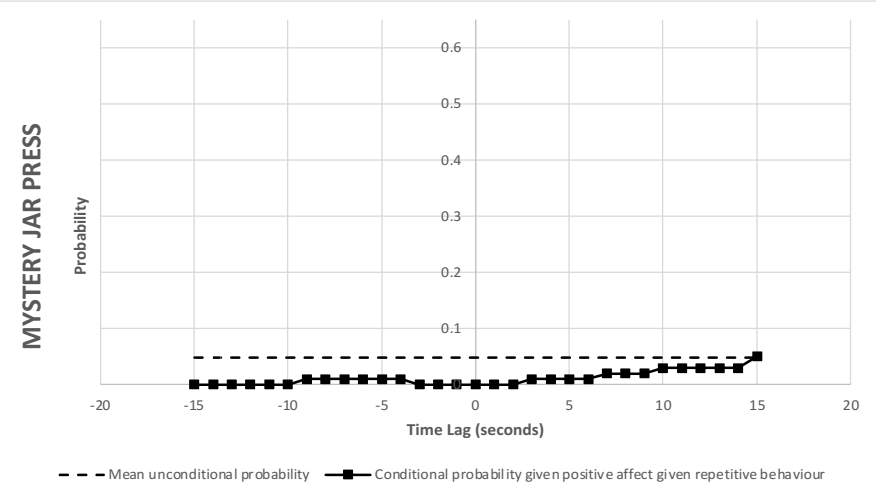


Figure 5.5f Mean UP of all participants displaying positive affect and CP of all participants displaying positive affect given the display of repetitive behaviour at time zero, during the mystery jar press.

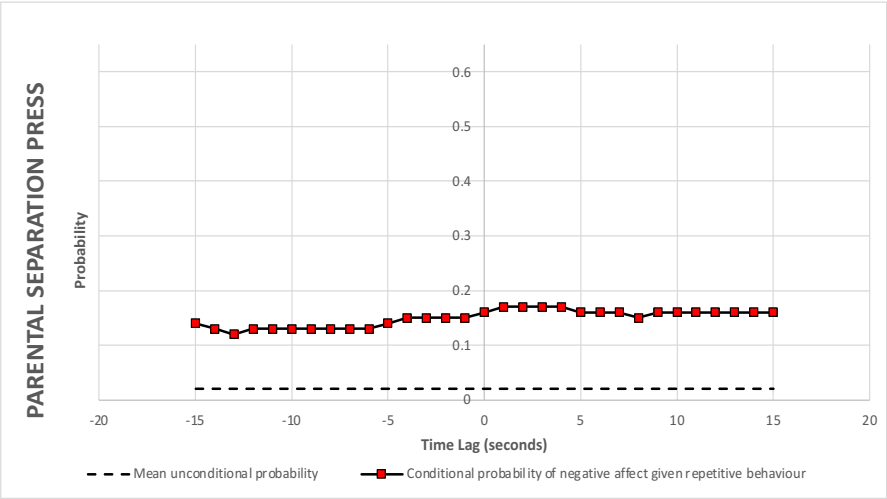


Figure 5.5g Mean UP of all participants displaying negative affect and CP of participants displaying negative affect given the display of repetitive behaviour at time zero, during the parental separation press.

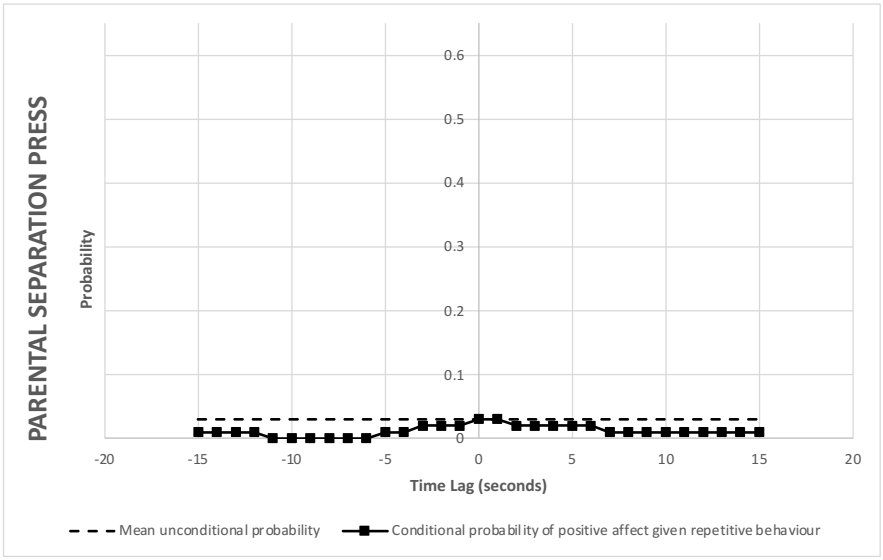


Figure 5.5h Mean UP of all participants displaying positive affect and CP of participants displaying positive affect given the display of repetitive behaviour at time zero, during the parental separation press.

5.5 Discussion

This is the first known study to utilise a fine-grained behavioural observation approach to examine the presence, sequence, and co-occurrence of anxiety-related behaviours in autistic individuals who speak few or no words. The focus of the study was exploring anxiety-related behaviours in the context of a direct assessment task designed to elicit mild anxiety responses.

The assessment presses were tapping into behavioural responses to novelty/uncertainty, present threat, and separation distress. When considering the first aim of the study, the most frequently observed behaviours across anxiety presses were social gaze, repetitive behaviour, positive and negative affect. This is consistent with previous literature including section 4.4, indicating that repetitive behaviour, negative affect, and social gaze are observable behaviours that could be anxiety-related (Edwards et al., 2022; Goodwin et al., 2022; Mian et al., 2015).

When addressing study aim two, the findings indicated that across situations that presented a potential threat, novelty, uncertainty, and separation distress, that positive and negative affect and rigidity were observed. The observation of positive affect may be unexpected given that the presses used were designed to elicit mild anxiety, however, this may be demonstrating the atypical presentation of anxiety reported in autistic individuals documented in previous literature where smiling/laughing behaviour has been noted (Adams et al., 2019). Furthermore, the observation of positive affect may be indicative of the documented association between anticipatory positive, thrilling emotions in fear-provoking situations in the typically developing literature (Dodd & Lester, 2021). While participants' reactions to the Anx-DOS stimuli were carefully monitored throughout to ensure the ethical application of this assessment, this finding provides further support that the Anx-DOS is an appropriate ethical measure to use to explore anxiety in this population as positive affect was commonly observed. Furthermore, termination of the assessment was not necessary for any participant, suggesting that the Anx-DOS presses did not appear to cause undue distress. Further exploration of negative affect and rigidity as relevant behaviours are discussed in the context of individual presses and study aim three below.

When considering the individual anxiety presses and addressing study aim three, the findings indicate that in novel situations or those that present a threat to an individual, social gaze towards an adult may be an anxious related behaviour leading up to an uncertain situation. Looking to a caregiver or glancing at the researcher was noted as an anxious-related behaviour in the development of the Anx-DOS (Mian et al., 2015). Social gaze could be a form of reassurance seeking including looking to an adult for signs about how to interpret a situation or emotions (Borelli et al., 2015). This finding has also been

demonstrated in individuals with Cornelia de Lange syndrome (CdLS) who are at heightened risk of anxiety, particularly social anxiety (Grados et al., 2017; Richards et al., 2009). Nelson et al. (2017) found that individuals looked for a significantly longer duration at a familiar adult in a social performance task, compared to those with Down Syndrome, who appear to be at lower risk of experiencing anxiety (Edwards et al., 2022b; van Gameren-Oosterom et al., 2011; see section 2.4.1). Individuals with CdLS have reduced verbal language use and so this finding is particularly pertinent to the current study's sample of autistic individuals who speak few or no words (Pearson et al., 2021). Social gaze may be a relevant anxiety-related behaviour for participants who speak few or no words and would perhaps have difficulty obtaining reassurance through verbal expression.

Additionally, the findings indicate that prior to a novel situation presenting uncertainty to an individual, negative affect is observed. This finding is consistent with previous literature in the general population highlighting a link between uncertainty and negative affect (Anderson et al., 2019). Negative affect is also a reported observable behaviour in autistic individuals who are experiencing anxiety (Vasa et al., 2016).

Furthermore, the findings indicate that rigidity was more likely to be observed around the press tapping into separation distress. However, this finding should be interpreted with caution due to the small number of participants who displayed rigidity in the current study (*n*=2). The finding warrants further investigation due to its consistency with previous research indicating that autistic individuals may show body tenseness when anxious (Adams et al., 2019; Edwards et al., 2022). However, there is a tentative suggestion that fewer participants displayed tense behaviour during this press compared to behaviours observed in the other presses (*n*=2, 15.4% of sample vs *n*=13, 100% of sample for social gaze in spider press and *n*=5, 38.5% of sample for negative affect in mystery jar press). This may be explained by research indicating that separation anxiety is more common in those with higher levels of IQ and therefore may be a less relevant trigger for anxiety in autistic individuals with ID (Mayes et al., 2022; van Steensel et al., 2011). Alternatively, due to the assessment taking place in the homes of participants, this press may not have truly reflected responses to separation distress, as a parent/carer being in another room in the house may be a daily reality for the participant.

Finally, when addressing study aim four, it was found that negative affect is more likely to be observed when individuals engage in repetitive behaviour compared to positive affect. There is evidence that repetitive behaviour can be observed when autistic individuals experience anxiety, as a proposed strategy to alleviate or regulate their emotions (Edwards et al., 2022; Goodwin et al., 2022). Repetitive behaviour may be observed when autistic individuals are calm and content (Edwards et al., 2022; Moskowitz & Braconnier, 2022; Vasa et al., 2016), however, in the current study the differential relationships between negative

affect and repetitive behaviour vs. positive affect suggests that repetitive behaviour may have been serving a self-regulatory purpose. These findings provide empirical, observational support for reports from autistic individuals and parents/carers that repetitive behaviour may be used as a self-regulation strategy (Edwards et al., 2022; Joyce et al., 2017). It also has implications for the sequence of behaviours, as repetitive behaviour may be observed when trying to reduce distress and therefore may precede behaviours associated with higher levels of distress where individuals may seek to sought support from caregivers around them i.e., increased vocalisation, proximity seeking, behaviours that challenge. Pinpointing behaviours reflecting self-regulation strategies may allow for early intervention. Further research implementing psychophysiological measures may provide further insight into self-regulation strategies and linking behaviour to internal experience.

It is important to note limitations of the current study. Findings from the study highlight behaviours observed during the Anx-DOS and the lag analyses demonstrate the association and sequence between the behaviour and the press. However, the current study did not have a control condition, therefore the findings do not confirm that these behaviours are observed exclusively in anxiety or fear-inducing situations. Further studies could strive to have a control condition, aiming to establish a baseline of behaviour for individuals, however careful consideration would be needed due to the difficulty of identifying an accurate baseline when individuals are subject to an experience that is outside of daily routine i.e., having a researcher physically or remotely present.

This study was conducted remotely, this may be seen as a limitation due to lack of researcher control. It is important to consider that the approach of the current study allowed participants to be comfortable and calm as it took place in their homes, without a researcher being physically present. Whilst engagement in the assessment may still have been a deviation from an individual's daily routine (e.g., being asked to sit in front of a device), the presses are not dissimilar to everyday situations that individuals may encounter during play. Additionally, if a researcher was present, it is important to consider that individuals may have experienced significantly heightened anxiety before taking part in the direct assessment which may have had an impact on the responses during the observation. It may be that conducting the assessment remotely allowed this confounding factor to be controlled, obtaining a more representative picture of participants' responses to the anxiety presses. This remote delivery of observational, anxiety assessment may be a viable method option which more closely reflects daily life for individuals compared to a clinical setting, when considering ecological validity.

The study included a small sample due to the disruption caused by the Covid-19 pandemic; further research needs to utilise this approach with a larger sample with more power to detect temporal sequences of behaviour. It is important to explore whether similar

patterns of behaviours are observed or new behavioural patterns come to light during anxiety-provoking situations. Despite the small sample, this study utilises a conservative approach in terms of determining significance and still highlights significant findings that note key anxiety-related behaviours during fine-grained observation of behaviour.

It could be considered a limitation of the current study that an independent researcher analysed the direct observation, as this is discrepant with the recommendation in section 4.4.2.2 that someone who knows an individual well should be involved in the assessment of anxiety. Whilst the coding scheme was comprehensive and utilised information from several different sources including existing literature, idiosyncratic behaviours and/or triggers may have been missed, which are common in autistic individuals (Bearss et al., 2016; Palmer et al., 2021). For example, Edwards et al. (2022) noted hypervigilance and hyperactivity as anxiety-related behaviours reported by parents/carers and clinicians which were not in the coding scheme for the current study. Despite this, the approach could be seen as a strength as a researcher may be more objective about the identification of observable behaviours. Ideally, future studies should strive to combine the expertise of individuals, parents/carers and researchers/clinicians. One way to do this could be autistic individuals and parents/carers providing input in the development of specific coding schemes or watching direct assessment videos back and pinpointing instances of anxiety-related behaviours.

It is important to consider the potential contamination of anxiety-related behaviours across presses, it is possible that participants may have been experiencing residual anxiety, for example, in the mystery jar press due to previous exposure to the spider press. In the current study, each participant video was edited to obtain three separate videos for each participant for each press. Videos were edited half-way between the previous press and the next press to optimise the time included in the behavioural coding for each press. Future studies should consider strategies to reduce the contamination across observational assessments as much as possible.

The Anx-DOS used in the current study was developed for the typically developing population, this was the only known direct assessment known to the researcher which allows observation of anxiety-related behaviour, without the reliance on verbal expression of anxiety. The Anx-DOS includes presses that tap into novelty and uncertain situations, which have been documented as triggers for anxiety in autistic individuals and so was deemed appropriate for the current study (Edwards et al., 2022; Mian et al., 2015). Whilst the original coding scheme for the Anx-DOS was not utilised in the current study, it was deemed a strength that the coding was adapted to better suit the population, study, and analysis design, with the reporting of comprehensive reliability analyses. The study has implications for future research, highlighting a need to develop and validate direct assessments of anxiety that are appropriate for use in autistic populations who speak few or no words

(Moskowitz & Braconnier, 2022). Whilst the Anx-DOS did include presses tapping into potential underlying mechanisms of anxiety in autism i.e., intolerance of uncertainty, and significant findings were demonstrated, it was developed for the typically developing population and the percentage of intervals where behaviours were observed could be considered small (*range*=0-8.3%). Developing autism-specific assessments tapping into mechanisms of anxiety is an important direction for future research, with this work more anxiety-related behaviours may be observed as measures are more appropriate and sensitive to the population. The OSCA-ABP (Palmer et al., 2021) was developed specifically for the autistic population focusing on presses that autistic individuals may be more likely to find difficult, however it explores emotional and behavioural problems more generally yielding an overall behaviours that challenge score and therefore, does not identify behaviours that are specific to the experience of anxiety alone (Palmer et al., 2021).

Despite the identified limitations, the current study demonstrates key behavioural markers of anxiety that can be identified utilising fine-grained observation that may inform early identification and intervention. During novel, uncertain situations, social gaze and negative affect may be observed in autistic individuals as anxiety-related behaviours. During separation from a caregiver, rigidity may be observed. Positive affect may also be observed during anxiety-provoking situations. The display of negative affect may be accompanied by engagement in repetitive behaviour, potentially as an emotion-regulation strategy to alleviate anxious feelings (Rodgers et al., 2012). Identification of fine-grained behaviours may inform care plan strategies and risk assessments to pinpoint warning signs of anxiety, to enable early intervention and subsequent reduction in the experience of distress.

Chapter 6: General discussion

6.1 Preface

The previous chapter utilised a direct assessment task to observe behaviours in anxiety-inducing situations with autistic individuals who speak few or no words; a group at high risk of experiencing anxiety. The chapter took a fine-grained behaviour observational approach to highlight the presence, sequence, and co-occurrence of anxiety-related behaviours. The findings indicated the potential value of utilising remote direct assessment tasks to explore anxiety-related behaviours in autistic individuals who speak few or no words. The current chapter provides a general discussion, bringing together the findings across all chapters of the thesis, discussing implications for further research, clinical practice, and theory. Strengths and weaknesses of the thesis are presented as well as exploration of research questions that remain unanswered.

6.2 Introduction

In the introduction of this thesis, Chapter one, it was highlighted that individuals with moderate-profound ID including those with an autism diagnosis and/or a genetic syndrome diagnosis, are at-risk of experiencing anxiety. In Chapter one, existing literature was discussed, which documents challenges of anxiety assessment in these groups and a subsequent bias in existing literature towards autistic individuals without comorbid ID and individuals with mild ID (Russell et al., 2019). It was argued that due to this bias, existing literature is not a representative evidence-base for autistic and ID populations.

Therefore, further research is needed to fill this gap. The overarching aim of the thesis was to improve the identification and assessment of anxiety in individuals with moderate-profound ID. Table 6.1 presents the identified gaps in the literature, the aims of each chapter to address these gaps, the methodological approach used and a brief summary of chapter findings.

In this general discussion, the findings for each chapter are noted, wider implications of the thesis are presented in relation to existing literature, strengths and limitations of the thesis are highlighted and the directions for future research.

Table 6.1 Overview of literature gaps, chapter aims, methods and findings of thesis

Identified gap in literature	Chapter	Chapter aims	Methodological approach	Summary of findings
Individuals with moderate-profound ID are at high risk of experiencing anxiety. Whilst there have been recent studies documenting the prevalence of anxiety in autism, there is a lack of research doing so in the genetic syndrome population. Documenting anxiety prevalence across genetic syndrome groups will highlight those at risk and allude to potential mechanistic underpinnings of anxiety that may help to explain varying prevalence	Two	• Calculate pooled prevalence estimates of anxiety symptomatology and diagnosis across syndromes, while accounting for the methodological quality of included studies • Complete subgroup and meta-regression analyses to explore methodological factors and their potential influence on anxiety prevalence • Compare estimates across syndromes with previously reported prevalence estimates from the general population and individuals with ID of mixed aetiology	Systematic review and meta-analysis	Anxiety prevalence ranged from 9-73%. Prevalence across syndromic ID was higher than for ID of mixed aetiology and general population estimates. Substantial variability between syndromes identified groups at higher risk than others.

Autism is a potential risk marker in the development of anxiety; autism characteristics and high rates of anxiety have been identified in individuals with moderate-profound ID. Exploring the role of autism as well as further potential risk markers for anxiety may highlight factors that cut across diagnostic groups and highlight shared pathways to anxiety	Three	• Explore relationships between existing anxiety measures developed for individuals with ID • Explore how demographic variables such as age, gender, diagnosis, intellectual ability, verbal ability, and autism characteristics may contribute to or predict anxiety • Explore how sensory processing differences, repetitive behaviour, intolerance of uncertainty and health related difficulties may contribute to or predict anxiety, whilst adjusting for demographics and potential covariates in the analyses • Explore anxiety triggers that may have important implications for the development and maintenance of anxiety • Explore consistency of analyses noted in aims 2 and 3 across anxiety measures developed for individuals with ID	Large scale cross-sectional questionnaire battery	Diagnosis was not significant in final model. Verbal ability and female gender predicted higher anxiety scores, age, adaptive ability, and autism characteristics did not. Intolerance of uncertainty and auditory sensory processing differences were consistently associated with anxiety. Frequency and severity of health difficulties were associated with anxiety, fairly consistently.

Research has documented the challenges of anxiety assessment for autistic individuals with ID and those with moderate-profound ID, which may be one explanation for the current lack of validated measures developed specifically for this population. Similarly, there is a paucity of research documenting the presentation of anxiety in these populations, therefore it is unclear whether anxiety presentation is similar to those without ID or mild ID. Currently, this means that the existing evidence base does not accurately reflect the entirety of autistic and ID populations.	Four	• Explore anxiety presentation in autistic individuals who speak few or no words as described by parents/carers and clinicians • Explore clinicians' experiences of identifying and assessing anxiety in individuals with ID who speak few or no words • Identify challenges faced by clinicians when assessing anxiety and the considerations needed to inform the development of assessment tools specifically for anxiety in individuals who speak few or no words.	Semi-structured interviews with parents/carers and clinicians	Anxiety behaviours included increased vocalisation, avoidance, and behaviours that challenge. Changes to routine were highlighted as triggering anxiety. Clinicians discussed the importance of identifying an individual's baseline of behaviour, knowing an individual well and ruling out other forms of distress.

Multimodal assessment of anxiety is recommended in autistic individuals with ID due to limitations of self and informant measures. There is a lack of observational assessments utilised in this population, to pinpoint observable anxiety-related behaviours and provide validation for studies identifying behavioural markers via questionnaire measures	Five	• Document the presence and nature of anxiety behaviours observed during anxiety-provoking situations • Describe the temporal sequence of behaviours in *any* anxiety-provoking situation • Describe the temporal sequence of behaviours in *each* anxiety-provoking situation • Describe the temporal sequence and potential co-occurrence of positive affect, negative affect and repetitive behaviour during anxiety-provoking situations	Remote direct assessment pilot study	Social gaze, repetitive behaviour, positive and negative affect were the most frequently observed behaviours. Across situations, social gaze, positive and negative affect, and rigidity were observed. Negative affect is more likely to be observed when individuals engage in repetitive behaviour compared to positive affect.

6.3 Main findings from the thesis

Chapter two documented a systematic review and meta-analysis of the prevalence of anxiety symptomatology and diagnosis in individuals with a diagnosis of a genetic syndrome associated with ID. It was highlighted that some groups are at higher risk of anxiety than others with prevalence rates as follows; Rett (73%), 7q11.23 duplication (70%) fragile X (48%), 22q11.2 deletion (40%), CHARGE (37%), 3q29 deletion (19%) syndromes and Tuberous Sclerosis Complex (14%) and Down Syndrome (9%). These rates were all higher than rates documented in the typically developing and intellectual disability of mixed aetiology populations (4% and 5% respectively).

Specific anxiety profiles were highlighted across syndromes. Specific phobia was common in fragile X (FXS) and 22q11.2 deletion syndromes, social anxiety was also prevalent in FXS. Obsessive-compulsive disorder (OCD) was noted as common in individuals with CHARGE syndrome. Social, separation anxiety, specific phobia and selective mutism were common in 7q11.23 duplication syndrome. Panic attacks were reported in 3q29 deletion syndrome and selective mutism in DS.

Subgroup analyses indicated that the use of diagnostic criteria (e.g., DSM-5) for individuals with a diagnosis of a genetic syndrome associated with mild-moderate ID may be an appropriate method of anxiety assessment. For example, for 22q11.2 deletion syndrome, it was found that relying only on report of anxiety symptomatology may underestimate anxiety prevalence. The use of psychiatric assessment that relies on DSM/ICD criteria may be more appropriate for this group, with the majority of papers assessing anxiety using such criteria. Alternatively, for other groups, relying solely on diagnostic criteria may under-estimate anxiety prevalence due to not endorsing all criteria but experiencing significant anxiety that is impacting day-to-day life. Papers obtaining a higher quality-rated syndrome confirmation and sample identification produced higher rates of specific phobia and separation anxiety prevalence in 22q11.2 deletion syndrome. For generalised anxiety, papers rated as low quality for syndrome confirmation had higher anxiety prevalence rates. Finally, as sample size increased in DS, prevalence of anxiety decreased. These findings highlight key methodological factors that have an impact on anxiety prevalence which should be considered within further studies documenting anxiety prevalence in genetic syndrome groups. Additionally, these relationships between differences in estimates and quality indicate the need for more robust methods in research. Due to these findings indicating that groups associated with ID are at heightened risk of anxiety, this warrants further exploration of factors that may contribute to the development and maintenance of anxiety as well as anxiety assessment.

Chapter three presents a large-scale cross-sectional questionnaire study, identifying correlates of anxiety in individuals with ID arising from various causes. Verbal ability and female gender were significant predictors of anxiety along with intolerance of uncertainty, auditory sensory processing differences and health difficulties. These factors were significant, cutting across diagnoses, autism characteristics did not predict anxiety across groups. When considering specific auditory sensory subtypes, there was a tentative suggestion that auditory hyperreactivity may be an important correlate of anxiety, but further research is needed to confirm this finding. Identifying correlates of anxiety alludes to risk factors that may be implemented in the development and maintenance of anxiety in ID. Additionally, identifying potential risk factors across diagnostic groups allows us to hypothesise potential shared causal pathways to anxiety, improving the identification of anxiety and targets for early intervention. These findings have implications for clinical practice and future research. For example, clinicians could take into consideration correlates of anxiety to inform early identification of individuals at risk, and further research should strive to explore identified correlates in more depth utilising direct assessment measures. This chapter also identified the limitations of existing anxiety assessments for individuals with moderate-profound ID, highlighting a significant gap in the literature.

Chapter four presents a semi-structured, interview study conducted with parents/carers and clinicians to explore anxiety presentation in autistic individuals and considerations needed for the development of new anxiety measures. The presentation of anxiety included behaviours of increased vocalisation, behaviours that challenge and avoidance. Changes to routine and unpredictability/uncertainty were triggers of anxiety. These findings are consistent with section 3.4 which identified intolerance of uncertainty as a consistent predictor of anxiety. Additionally, parents/carers and clinicians noted loud noises, sensory overload and setting events of pain and physical illness as anxiety triggers; factors which section 3.4 highlighted are predictors of anxiety. Qualitative analysis highlighted key themes associated with anxiety assessment in clinical practice. These included the importance of identifying an individual's baseline behaviour, ruling out other forms of distress and adopting an individualised and holistic approach, taking into consideration additional diagnoses an individual may present with. This chapter highlighted the need of multi-method assessment for anxiety in this group.

Finally, Chapter five builds on the theme of Chapter four, focusing on improving assessment of anxiety. A remote direct assessment is presented that involved anxiety-provoking presses to elicit responses to novelty/uncertainty and separation distress in autistic individuals. Social gaze was observed in novel situations or those that present a threat to an individual. Negative affect was observed in a situation presenting uncertainty to individuals. Negative affect was also found to be associated with repetitive behaviour. These

findings indicate the value of observational assessments as anxiety-related behaviours were observed during novel and uncertain situations, which aligns with the findings from sections 3.4 and 4.4.1 that uncertain situations are an anxiety trigger. Furthermore, potential precursor behaviours were identified e.g., social gaze, repetitive behaviour, that may be forms of reassurance seeking and self-regulation respectively. These fine-grained precursor behaviours may precede the more noticeable behaviours documented in section 4.4.1 of increased vocalisation, avoidance and behaviours that challenge as reported by parents/carers and clinicians. This highlights the importance of triangulation of findings and taking a multi-method approach.

6.4 Implications

6.4.1 Methodological implications for future research

In Chapter two, it was highlighted that research studies that had higher quality ratings for syndrome confirmation and sample identification had higher anxiety rates. It is therefore important to consider how methodological differences between studies impact prevalence rates. Future studies should strive to confirm genetic syndrome diagnosis utilising genetic testing and to recruit samples that are as representative as possible by utilising random sampling.

In Chapter three, the approach was taken to include individuals with moderate-profound ID, including those with an autism diagnosis and individuals with rare genetic syndromes in one sample. Whilst it is important to explore individual diagnoses and gene-disorder-phenotype interactions, as argued in section 2.5 there is also value and justification for aggregating groups. The chapter demonstrated that predictors of anxiety cut across diagnostic groups and may be more relevant to the moderate-profound ID population more generally. This has important implications for future research, for example, studies may be able to attain larger sample sizes due to a larger recruitment pool, which may overcome the small sample sizes associated with rare genetic syndrome research. Consequently, if groups have identified shared pathways to anxiety and common risk markers are relevant across groups, identification of those most at risk and the development of targeted, effective intervention is likely to happen sooner.

In Chapter four, the thesis highlighted implications for the development of new clinical assessment measures for anxiety. For researchers, important considerations such as behavioural overlap of anxiety ‘symptoms’ with other forms of distress such as pain or low mood and establishing an individual’s baseline of behaviour should be incorporated into newly developed measures of anxiety.

The thesis highlights implications for utilising fine-grained behavioural analysis to pinpoint behavioural markers of anxiety in autistic individuals who speak few or no words. Further research should aim to use this method with larger samples to explore temporal

sequences of behaviour which will allow early identification of anxiety and give caregivers the opportunity to intervene early and reduce distress.

6.4.2 Theoretical implications

As discussed in section 1.4.2, there are various models proposed to explain the presentation of anxiety in the general population. Dugas' Intolerance of Uncertainty model, Wells' Metacognitive model and Minnen's model of emotional dysregulation were introduced. These models have been explored in the autism population, with Dugas' Intolerance of uncertainty construct being the most focused on in recent years. In the context of the current thesis findings, intolerance of uncertainty is consistently highlighted as important in the identification and assessment of anxiety in the moderate-profound ID population, aligning with Dugas' model and literature with autistic participants without ID (Boulter et al., 2014). Other elements of existing theories such as beliefs about worry, cognitive avoidance and meta-worry were not the focus of the current thesis due to a focus on those with moderate-profound ID and/or those who speak few or no words, and therefore the difficulty of assessing more abstract, cognitive experiences. Due to the increased research focus on intolerance of uncertainty in recent years, measures have been developed that focus on behaviours and emotion (i.e., RULES), rather than relying on cognition, allowing measures to be used for the moderate-profound ID population. Existing literature in the autism population that has explored more abstract mechanisms is in its infancy and has relied on self-report measures, further research is needed to develop assessment measures that do not rely on self-report (Campbell et al., 2018). Additionally, it is likely that a combination of approaches will optimise outcomes in anxiety intervention, such as targeting intolerance of uncertainty and emotion regulation, rather than relying on one theory of anxiety (Cai et al., 2018). Further research is needed to continue highlighting the mechanistic underpinnings of anxiety in this group and how existing theories of anxiety may help us to better understand anxiety in the autism and ID populations.

The systematic review and meta-analysis in Chapter two identifies groups at higher risk of anxiety than others which has implications for informing future research to focus on gene disorder-phenotype-environment interactions in the development and maintenance of anxiety. This will then inform the creation of models of anxiety risk that are syndrome specific, highlighting links between phenotypic characteristics and anxiety presentation. As has been indicated with the evidence base of Williams Syndrome and the link between anxiety and hyperacusis, mapping out these models will inform early identification and intervention as well as intervention development (Blomberg et al., 2006; Royston et al., 2017; Royston et al., 2021).

From findings in Chapter three, autism characteristics did not predict anxiety and diagnostic label did not predict anxiety once other variables of interest had been taken into

account in the analyses. There was evidence that correlates of anxiety cut across diagnoses, for example intolerance of uncertainty, demonstrating shared correlates associated with moderate-profound ID that underpin anxiety risk. These findings have theoretical implications for transdiagnostic factors and interventions that are relevant beyond group level. This may allow for the development of models of anxiety risk that cut across groups and are relevant to moderate-profound ID more generally. This finding has implications for existing literature aiming to develop interventions for autistic individuals with mild-moderate ID focusing on intolerance of uncertainty, there is an argument to develop these interventions in a broader sense for a wider population rather than a targeted, population intervention (Rodgers et al., 2020). So, for individuals with moderate-profound ID, with varying comorbid diagnoses i.e., autism, genetic syndrome, a transdiagnostic approach to anxiety intervention may be more appropriate. This approach would be efficient within clinical services where individuals with different diagnoses would present. The transdiagnostic approach of core factors that cut across groups i.e., intolerance of uncertainty, could then be supplemented with syndrome-specific adaptations as we become more aware of gene-disorder-phenotype-environment interactions, for example, Williams Syndrome as described in the above paragraph.

6.4.3 Clinical implications

As highlighted in section 3.4, health difficulties are a predictor of anxiety. This relationship needs further exploration within future studies, to identify specific health difficulties and how they may relate to anxiety. It also may be that the relationship found in section 3.4 is reflective of a relationship between pain more generally and anxiety.

Those with more or severe health difficulties may access healthcare settings more frequently or for more significant medical intervention, exposing them to potentially anxiety-provoking environments. There is an evidence base for strategies that may be helpful in alleviating anxiety for individuals with ID in healthcare settings. Individuals can have hospital passports that let healthcare professionals know about their needs and preferences, the use of social stories may allow preparation and communication regarding medical procedures and adjustments to the environment to consider sensory needs should be implemented (Ong et al., 2022). Furthermore, screening measures for correlates could be utilised during annual health reviews for individuals with ID, before they present to mental health pathways or specialist mental health services. One potential example could be developing a brief screening tool to support identifying individuals at high risk of experiencing anxiety. Individuals deemed at risk could receive a low-level intervention (e.g., psychoeducation materials, individual/parent/carer workshops, group support) before anxiety develops or escalates to having a significant impact on day-to-day life. Effectiveness of such early

intervention strategies could be evaluated to assess impact and the implications of rolling out strategies.

As highlighted in section 4.4.2.3, for clinicians, the importance of multi-disciplinary working is highlighted to rule out physical causes of distress such as pain or discomfort due to physical ill-health, which is common in autistic individuals and individuals with ID (Liao et al., 2021; Perera et al., 2020; Sala et al., 2020). Physical health checks should be the priority when an individual presents to clinical services with any behavioural change, as pain or discomfort could be a difficulty that is easily resolved. Furthermore, if there is underlying pain or discomfort, further delay whilst undertaking a psychological or behavioural intervention raises ethical concerns, especially as they may be ineffective due to not targeting the underlying cause of behavioural change.

6.5 Strengths of the thesis

6.5.1 Population of interest and multi-method approach

There are a number of strengths of this thesis that should be highlighted. Firstly, the focus on individuals with moderate-profound ID, including those with an autism diagnosis and/or a genetic syndrome diagnosis, who speak few or no words is a strength of the thesis, as an under-represented group in the literature and evidence base (Russell et al., 2019). The thesis presents a range of methodological approaches taken to explore anxiety in this under-researched group. This highlights a multi-method approach to assessing anxiety which is recommended as best practice when working with autistic individuals (Vasa et al., 2016). The thesis includes qualitative and quantitative approaches, from a large-scale questionnaire study design to fine-grained behavioural analysis, informed by existing literature with involvement from parents/carers, clinicians working in clinical practice and autistic individuals. Furthermore, the thesis focused on a broad age range and was able to present research focusing on males and females. All studies included samples with broad age ranges (chapter three: 4-63 years, chapter four: 7-52 years, chapter five: 4-28 years), with consideration given to anxiety presentation in children and adults in Chapter four. In Chapters three, four and five there were more male autistic participants than females which is consistent with previous research highlighting gender bias in autism research (Kirkovski et al., 2013). However, Chapter three included the largest sample size of individuals with moderate-profound ID in the thesis and achieved a relatively equal gender-split overall (92 males, 55.8%; 73 females, 44.2%). This is a notable strength considering the reported higher prevalence of ID in males, compared to females (McKenzie et al., 2016; Patrick et al., 2021; Werling & Geschwind, 2013).

6.5.2 Utility of remote direct assessments with individuals who speak few or no words

Chapter five provides an illustration of how a direct assessment task exploring anxiety developed for the typically developing population, conducted remotely, can be used for autistic individuals who speak few or no words. This novel approach of remote testing may allow for larger sample sizes in future research studies, when often recruitment approaches are national in scope due to the rarity of some included genetic syndromes and autistic individuals with moderate-profound ID. Furthermore, within clinical practice, remote testing has implications for remote consultation and the growth in telepsychiatry, especially in the context of the Covid-19 pandemic (Bhardwaj et al., 2021). There are important considerations when utilising this approach with individuals with complex needs. For example, implementing communication aids such as Makaton interpreters, ease of use of technology equipment and the potential need for having someone to support with this access. It is also crucial to consider the drawbacks of remote assessment where subtleties in presentation may be missed or utilising remote equipment makes it difficult to develop a full picture of an individual's presentation (Krysta et al., 2021; Madhavan, 2019). However, it is also important to note that this approach could be preferable for some individuals due to reduced direct social demand, the uncertainty of new environments and having the comfort of a home environment rather than a healthcare setting as well as having a familiar adult conducting the assessment, which may promote better engagement (Madhavan, 2019). Having a familiar adult, in this case parent or carer, conduct the assessment may give a more accurate picture of participant's responses to specific presses due to potentially reduced anxiety, which could be heightened if an unfamiliar adult was conducting the assessment (Spain et al., 2020; Vaughan Van Hecke et al., 2009). Alternatively, participants may show reduced responses to presses due to the presence of a parent/carer being a safety cue. Future studies could include both familiar and unfamiliar adults to explore potential differences in response to anxiety presses.

Therefore, Chapter five highlights the value in research and clinical practice of exploring assessment tasks that are appropriate for remote delivery. Individuals may be more comfortable in their home environments, resulting in a more accurate presentation of anxiety in response to anxiety presses/tasks.

6.5.3 Statistically conservative approach

Finally, particularly Chapter five takes a conservative approach to statistical analysis. This takes into consideration the small sample size and is a strength as it indicates that findings may be less likely due to chance and reflecting true difference between the unconditional and conditional probabilities of observed behaviour.

6.6 Limitations of the thesis

6.6.1 Hearing the voices of individuals with moderate-profound ID

It is important to consider the limitations of this thesis in light of the research findings and to inform future research in the area. The majority of existing research as well as a significant proportion of this thesis focuses on informant report of anxiety. It is crucial to focus on involving individuals in the conceptualisation, delivery, and dissemination of research studies, by developing creative strategies for individuals with ID and/or those who speak few or no words to ensure that their voices are heard (e.g., augmentative, and alternative communication; AAC). For example, Talking Mats has been found to be useful and there is emerging research exploring the acceptability of accessible communication strategies (Bradshaw et al., 2018; Bunning et al., 2016; Dee-Price et al., 2021; Murphy & Cameron, 2008; Rowe & Nevin, 2013; Stewart et al., 2018; Tomlins & Cawley, 2016; Tyrrell & Woods, 2020). Future research should prioritise assessing the acceptability and feasibility of such methods to explore mental health with individuals with moderate-profound ID as an identified gap in the literature (Tarver et al., 2021a). However, it is important to note a strength of Chapter five utilising observational assessments of anxiety that overcome some pitfalls of relying on informant report. This method fostered a more objective approach that did not rely on an individual's verbal ability or existing measures that have not been developed and validated for individuals with moderate-profound ID who speak few or no words.

6.6.2 Limitations of existing anxiety measures

Furthermore, the informant measures that have been used in the current thesis, despite being validated and developed for ID populations, the Anxiety, Depression and Mood Scale (ADAMS; Esbensen et al., 2003), the Diagnostic Assessment for the Severely Handicapped-II (DASH-II; Matson et al., 1995) and the Anxiety Triggers Questionnaire (ATQ; Royston, 2018) have limitations that are worth noting. Firstly, the ADAMS includes subscales that explore general anxiety and social avoidance. Therefore, this may miss anxiety presentations due to subscales not exploring experiences of panic, separation, and specific phobia. Furthermore, as highlighted in sections 4.2 and 4.4.2.1, questionnaire items could overlap with other difficulties, for example, item 'does not relax or settle down' could also be attributed to Attention-Deficit-Hyperactivity Disorder (ADHD). The DASH-II uses an anxiety subscale that includes items that explore separation anxiety and phobia, but these items make up a general anxiety subscale, preventing exploration of specific types of anxiety. The ATQ was developed for individuals with Williams Syndrome who have mild to moderate ID, therefore it was unclear whether it would include all anxiety triggers that are relevant for individuals with moderate-profound ID, however, this was considered before use in the current thesis and no further triggers were identified to be added. Despite these limitations,

the measures were deemed the most appropriate to use given the existing literature and measures available. Furthermore, the overall psychometric properties are sound (Esbensen et al., 2003; Flynn et al., 2017; Royston, 2018). The thesis highlights the current lack of appropriate assessment tools for this population. It is important for future research to replicate the findings of this thesis using newly developed and validated measures specifically for this population (Flynn et al., 2017; Royston, 2018). For example, Chapters four and five highlight anxiety markers to be considered in the development of new anxiety measures, as reported by parents/carers and clinicians, and as observed via direct assessments. However, next stages of a broader project are currently in progress where these markers have been implemented into a new anxiety measure that is currently undergoing validation (Waite et al., in prep). The project is registered with the ResearchRegistry and the unique identifying number is researchregistry5086. Further studies are crucial to pinpoint anxiety as the difficulty, rather than other causes of behaviour. These findings highlight the inherent difficulty of assessing internal experiences and developing new assessment measures that are appropriate and effective for the moderate-profound ID population.

6.6.3 Representativeness of participants

Lastly, due to the recruitment strategies used in the thesis, there is potential that highly educated and knowledgeable parents/carers were recruited, and clinicians were recruited who work in the same geographical location. Additionally, no data were gathered regarding ethnicity of participants. Therefore, it is uncertain whether the studies include individuals that are highlighted as under-researched in the literature, for example, individuals from ethnic minority groups (Steinbrenner et al., 2022). Finally, the approach taken in Chapter five means that individuals may not have been able to take part due to limited access to technological equipment or not feeling confident utilising equipment. However, participants were supported with the latter if required which included being provided with step-by-step instructions of how to access the remote meeting (Appendix 38). Yet, it is important to consider that the findings may not be representative of all individuals, parents/carers and clinician's experiences. Research should strive to utilise recruitment strategies that are more accessible and widely targeted. One way to do this could be strengthening the research-practice links by having researchers present in clinics. There has been conversation about the integration of clinical psychology within primary care, there should be consideration of the benefits of also having clinical researchers present (Cubic et al., 2012; James, 2006; Nash et al., 2012). Additionally, we know that autistic individuals and individuals with ID can fall through the gaps in clinical services (Doherty et al., 2020; Sharpe et al., 2019; Sohl et al., 2017) and so researchers should endeavour to build and strengthen links with community settings, for example, partnering with agencies such as youth and faith services. This

approach has been shown to foster further commitment to participating in autism research, providing findings that are more representative of the populations we work with (Shaia et al., 2020; Zamora et al., 2016).

6.7 Future directions

The current thesis has provided a detailed, starting point for exploring anxiety in autistic individuals and individuals with moderate-profound ID who speak few or no words. Taking into consideration the findings, strengths, and limitations, the current chapter has highlighted unanswered questions that should be the focus of future research studies.

Firstly, there is a lack of research focusing on genetic syndromes associated with ID and anxiety, especially specific anxiety profiles. This is despite these groups being at higher risk of anxiety than the general population. Future research needs to focus on characterising the presentation and profile of anxiety across groups as well as exploring the role of genetic factors and gene-disorder-phenotype-environment interactions within and across syndromes. This will allow further understanding of specific anxiety presentation within groups, including the identification of divergent and/or convergent profiles across groups, which will allude to potential pathways to anxiety. Developing knowledge of specific profiles will help to ensure that individuals at high risk of anxiety are identified early whilst further understanding of pathways to anxiety will inform intervention development and delivery, to ensure individuals receive effective support.

The thesis highlighted correlates of anxiety that may allude to potential risk markers for anxiety, that may inform efforts towards early identification and intervention. Future research needs to explore correlates of anxiety such as verbal ability, gender, auditory sensory processing differences, health difficulties and intolerance of uncertainty. Health difficulties and pain are commonly under-recognised in individuals with ID, which is concerning considering individuals are at increased risk of difficulties including chronic health problems such as gastrointestinal problems (Barney et al., 2020; Oliver et al., 2020; Whitney et al., 2019). Health difficulties could be a potential risk marker of anxiety due to uncertainty about experience of medical interventions and hospital/clinic environments that can be difficult for individuals with ID due to high rates of change and sensory-rich environments (Grier et al., 2018). Further research exploring the link between health difficulties and anxiety within the moderate-profound ID population should pinpoint how best to support individuals within health settings. See section 6.4.3 where a few suggestions are made that could be the focus of further research.

Future research should endeavour to explore correlates utilising methodologies that do not rely on informant report alone, especially as there are direct assessment tasks exploring anxiety (Anxiety Dimensional Observation Schedule, Anx-DOS; Mian et al., 2015) and

sensory processing differences (Sensory Assessment for Neurodevelopmental Disorders, SAND; Siper et al., 2017) that are appropriate for use with autistic individuals who speak few or no words. More specifically, future research needs to extend the findings from this thesis and the work of MacLennan et al. (2021) to explore sensory subtypes and their relation to anxiety in the moderate-profound ID population. Continued focus on these correlates within research and clinical practice may aid early intervention by identifying risk markers for anxiety.

As highlighted in previous research, to support multi-method assessment of anxiety, studies exploring the acceptability and feasibility of using psychophysiological measures of anxiety with autistic individuals with ID are needed to complement other methods of anxiety assessment (Hollocks et al., 2014; Ferguson et al., 2019). This is a crucial assessment method option that does not rely on verbal or cognitive ability, however, research focusing on the feasibility and tolerability of utilising such methods is important moving forward.

This thesis highlighted key considerations for the development of future anxiety assessment measures for this population; a measure aiming to disentangling autism characteristics from anxiety is crucial, incorporating establishing a baseline of an individual's behaviour may be one way to do this. Whilst developing new measures, researchers and/or clinicians should also consider collaborating as part of a multi-disciplinary team to rule out other causes of distress such as pain or physical discomfort. Finally, a holistic approach where other diagnoses are taken into consideration during assessment of anxiety is crucial. Comorbid diagnoses may inform the anxiety assessment and have implications for the intervention approach, accelerating appropriate care.

Future studies need to expand the current thesis findings by involving more clinicians in future research studies to explore their experience of assessing anxiety in autistic individuals and individuals with moderate-profound ID who speak few or no words. Triangulation approaches whereby parents/carers and clinicians discuss the same individual's experience of anxiety may be a fruitful way to disentangle anxiety from other forms of distress. Furthermore, teachers may be useful as additional informants who could offer insight and perspective into an individual's experience of anxiety, this approach has been adopted previously in the development of assessment measures to explore anxiety in autistic individuals (Rodgers et al., 2016; Tarver et al., 2021b). Section 4.4.2.1 highlighted the recommendation to gather information from each context in which an individual exists to foster an assessment informed by multiple informants.

Future studies need to extend the thesis findings relating to fine-grained observation of anxiety-related behaviour. Due to the small sample size achieved in Chapter five, further research needs to corroborate these findings, exploring temporal sequences of behaviour in anxiety-provoking situations. It could be of interest to compare behaviour when conducting

direct assessments face-to-face and remotely to explore potential differences across modes of assessment delivery.

This chapter also highlights the lack of direct assessment measures to explore anxiety-related behaviours in autistic individuals and individuals with moderate-profound ID who speak few or no words (Moskowitz & Braconnier, 2022). Whilst there has been recent research aiming to fill this gap (e.g., OSCA-ABP; Palmer et al., 2021), there are no direct assessment measures known that specifically focus on anxiety, that have been developed and validated for this population. This identifies a gap in the literature that needs to be addressed, input from autistic individuals and parents/carers would be crucial in taking this work forward (Palmer et al., 2021).

More generally, whilst the broad age range and representation from males and females in the thesis is a strength, future research should consider the experience of anxiety and how that relates to age and gender as this may have implications for identification and intervention if differences are highlighted (Adams et al., 2019).

There is a paucity of research documenting research and practice links and the reciprocal benefits for both academic professionals and clinicians when working with autistic individuals and individuals with ID who speak few or no words (Brookman-Frazee et al., 2012). This is needed to develop and promote the best intervention strategies that are formed from evidence-based practice but also practice-based evidence. These professional links are crucial to ensure that research studies and findings are practical and realistic enough to be implemented within clinical practice, and that research priorities are relevant to challenges faced within clinical practice. Developing these links could be one way to bridge the gap between research and practice, aiming to improve quality of life for autistic individuals and individuals with ID (Brookman-Frazee et al., 2012; Dingfelder & Mandell, 2011; Maddox et al., 2021; Wong et al., 2015).

A continuation of research dedicated to improving the identification and assessment of anxiety in individuals previously under-represented in the literature will inform the development of targeted interventions, exclusively for this population. There are currently no validated anxiety interventions for this group. Cusack & Sterry's (2016) ten priorities for autism research highlight improved intervention for anxiety and other mental health difficulties as a top priority. This highlights that the current thesis and future related research is of key priority and importance to autistic individuals, their families, researchers, and clinicians.

6.8 Conclusions

This thesis highlights studies aiming to delineate the identification and assessment of anxiety, a common mental health difficulty, in individuals with moderate-profound ID

including those with an autism diagnosis and/or a genetic syndrome diagnosis, who speak few or no words. These groups are currently neglected and under-represented in the existing literature. The thesis has noted groups at higher risk of anxiety than others, correlates of anxiety that allude to potential risk markers for anxiety, the presentation of anxiety and considerations needed for the development of future assessment tools and fine-grained behaviours associated with the experience of anxiety. The work is likely to inform future research and practice, with the hope to support early identification and intervention to improve quality of lives for individuals and their families.

References

Abbas, E., Cox, D, M., Smith, T., & Butler, M. G. (2016). The 7q11.23 Microduplication Syndrome: A Clinical Report with Review of Literature. *J Pediatr Genet*, *5*(3), 129-140. https://doi.org/10.1055/s-0036-1584361

Achenbach, T, M., & Rescorla, L, A. (2000). *Manual for the ASEBA preschool forms & profiles: an integrated system of multi-informant assessment.* Research Center for Children, Youth & Families.

Achenbach, T, M., & Rescorla, L, A. (2001). *Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment.* Research Center for Children, Youth & Families.

Adams, D., & Oliver, C. (2011). The expression and assessment of emotions and internal states in individuals with severe or profound intellectual disabilities. *Clinical Psychology Review*, *31*(3), 293–306. https://doi.org/10.1016/j.cpr.2011.01.003

Adams, D., Young, K., Simpson, K., & Keen, D. (2019). Parent descriptions of the presentation and management of anxiousness in children on the autism spectrum. *Autism: The International Journal of Research and Practice*, *23*(4), 980–992. https://doi.org/10.1177/1362361318794031

Adams, D., Clark, M., & Simpson, K. (2020). The Relationship Between Child Anxiety and the Quality of Life of Children, and Parents of Children, on the Autism Spectrum. *Journal of Autism and Developmental Disorders*, *50*(5), 1756–1769. https://doi.org/10.1007/s10803-019-03932-2

Adams, D., & Emerson, L, M. (2021). The Impact of Anxiety in Children on the Autism Spectrum. *J Autism Dev Disord, 51,* 1909–1920. https://doi.org/10.1007/s10803-020-04673-3

Agar, G., Oliver, C., Trickett, J., Licence, L., & Richards, C. (2020). Sleep disorders in children with Angelman and Smith-Magenis syndromes: The assessment of potential causes of disrupted settling and night time waking. *Research in Developmental Disabilities*, *97*, 103555. https://doi.org/10.1016/j.ridd.2019.103555

Akaike, H. (1974). A new look at the statistical model identification. *IEEE Transactions on Automatic Control, 19*(6), 716-723. doi: 10.1109/TAC.1974.1100705.

Amaral, D. G., Schumann, C. M., & Nordahl, C. W. (2008). Neuroanatomy of autism. *Trends in Neurosciences*, *31*(3), 137–145. https://doi.org/10.1016/j.tins.2007.12.005

Amaral D. G. (2017). Examining the Causes of Autism. *Cerebrum: The Dana Forum on Brain Science*, cer-01-17.

Ambrose, K., Simpson, K. & Adams, D. (2021). The Impact of Anxiety on the Participation of Children on the Autism Spectrum. *J Autism Dev Disord*. https://doi.org/10.1007/s10803-021-05162-x

American Psychiatric Association (APA). (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.).

American Psychiatric Association (APA). (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425596

Anderson, D. K., Lord, C., Risi, S., DiLavore, P. S., Shulman, C., Thurm, A., Welch, K., & Pickles, A. (2007). Patterns of growth in verbal abilities among children with autism spectrum disorder. *Journal of Consulting and Clinical Psychology*, *75*(4), 594–604. https://doi.org/10.1037/0022-006X.75.4.594

Anderson, E. C., Carleton, R. N., Diefenbach, M., & Han, P. (2019). The Relationship Between Uncertainty and Affect. *Frontiers in Psychology*, *10*, 2504. https://doi.org/10.3389/fpsyg.2019.02504

Appleton, H., Roberts, J., & Simpson, K. (2019). How is Anxiety Identified and Diagnosed in Individuals with Autism Spectrum Disorder and Intellectual Disability? A Scoping Review, *Journal of Mental Health Research in Intellectual Disabilities, 12*(3-4), 152-175, DOI: 10.1080/19315864.2019.1679299

Arias, V. B., Gómez, L. E., Morán, M. L., Alcedo, M. Á., Monsalve, A., & Fontanil, Y. (2018). Does Quality of Life Differ for Children With Autism Spectrum Disorder and Intellectual Disability Compared to Peers Without Autism?. *Journal of Autism and Developmental Disorders*, *48*(1), 123–136. https://doi.org/10.1007/s10803-017-3289-8

Aspland, H., & Gardner, F. (2003). Observational Measures of Parent-Child Interaction: An Introductory Review. *Child and Adolescent Mental Health*, *8*(3), 136–143. https://doi.org/10.1111/1475-3588.00061

Asselmann, E., Wittchen, H-U., Lieb, R., & Beesdo-Baum, K. (2018). Sociodemographic, clinical, and functional long-term outcomes in adolescents and young adults with mental disorders. *Acta Psychiatr Scand*, *137*(1), 6-17. https://doi.org/10.1111/acps.12792

Axmon, A., Sandberg, M., & Ahlström, G. (2017). Gender differences in psychiatric diagnoses in older people with intellectual disability: a register study. *BMC psychiatry*, *17*(1), 192. https://doi.org/10.1186/s12888-017-1353-8

Bagni, C., Tassone, F., Neri, G., & Hagerman, R. (2012). Fragile X syndrome: causes, diagnosis, mechanisms, and therapeutics. *The Journal of Clinical Investigation*, *122*(12), 4314–4322. https://doi.org/10.1172/JCI63141

Bailey, N. M., & Andrews, T. M. (2003). Diagnostic Criteria for Psychiatric Disorders for Use with Adults with Learning Disabilities/Mental Retardation (DC-LD) and the diagnosis of anxiety disorders: a review. *Journal of Intellectual Disability Research: JIDR*, *47 Suppl 1*, 50–61. https://doi.org/10.1046/j.1365

Baio, J., Wiggins, L., Christensen, D. L., Maenner, M. J., Daniels, J., Warren, Z., Kurzius-Spencer, M., Zahorodny, W., Robinson Rosenberg, C., White, T., Durkin, M. S., Imm, P., Nikolaou, L., Yeargin-Allsopp, M., Lee, L. C., Harrington, R., Lopez, M., Fitzgerald, R. T., Hewitt, A., Pettygrove, S., … Dowling, N. F. (2018). Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014. *Morbidity and Mortality Weekly Report. Surveillance Summaries (Washington, D.C.: 2002)*, *67*(6), 1–23. https://doi.org/10.15585/mmwr.ss6706a1

Bal, V. H., Katz, T., Bishop, S. L., & Krasileva, K. (2016). Understanding definitions of minimally verbal across instruments: evidence for subgroups within minimally verbal children and adolescents with autism spectrum disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *57*(12), 1424–1433. https://doi.org/10.1111/jcpp.12609

Bandelow, B., & Michaelis, S. (2015). Epidemiology of anxiety disorders in the 21st century. *Dialogues in Clinical Neuroscience*, *17*(3), 327–335. https://doi.org/10.31887/DCNS.2015.17.3/bbandelow

Barbano, A. C., van der Mei, W. F., Bryant, R. A., Delahanty, D. L., deRoon-Cassini, T. A., Matsuoka, Y. J., Olff, M., Qi, W., Ratanatharathorn, A., Schnyder, U., Seedat, S., Kessler, R. C., Koenen, K. C., & Shalev, A. Y. (2019). Clinical implications of the proposed ICD-11 PTSD diagnostic criteria. *Psychological Medicine*, *49*(3), 483–490. https://doi.org/10.1017/S0033291718001101

Barendregt, J, J., Doi, S, A., Lee, Y, Y., Norman, R, E., & Vos, T. (2013). Meta-analysis of prevalence. *J Epidemiol Community Health*, *67*(11), 974-978. https://dx.doi.org/10.1136/jech-2013-203104

Baribeau, D. A., Vigod, S., Pullenayegum, E., Kerns, C. M., Mirenda, P., Smith, I. M., Vaillancourt, T., Volden, J., Waddell, C., Zwaigenbaum, L., Bennett, T., Duku, E., Elsabbagh, M., Georgiades, S., Ungar, W. J., Zaidman-Zait, A., & Szatmari, P. (2020). Repetitive Behavior Severity as an Early Indicator of Risk for Elevated Anxiety Symptoms in Autism Spectrum Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *59*(7), 890–899.e3. https://doi.org/10.1016/j.jaac.2019.08.478

Barney, C. C., Andersen, R. D., Defrin, R., Genik, L. M., McGuire, B. E., & Symons, F. J. (2020). Challenges in pain assessment and management among individuals with intellectual and developmental disabilities. *Pain Reports*, *5*(4), e821. https://doi.org/10.1097/PR9.0000000000000822

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism,

males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders*, *31*(1), 5–17. https://doi.org/10.1023/a:1005653411471

Baron-Cohen, S., Scott, F. J., Allison, C., Williams, J., Bolton, P., Matthews, F. E., & Brayne, C. (2009). Prevalence of autism-spectrum conditions: UK school-based population study. *The British Journal of Psychiatry: The Journal of Mental Science*, *194*(6), 500–509. https://doi.org/10.1192/bjp.bp.108.059345

Baron-Cohen, S., Lombardo, M. V., Auyeung, B., Ashwin, E., Chakrabarti, B., & Knickmeyer, R. (2011). Why are autism spectrum conditions more prevalent in males?. *PLoS Biology*, *9*(6), e1001081. https://doi.org/10.1371/journal.pbio.1001081

Bartholomay, K. L., Lee, C. H., Bruno, J. L., Lightbody, A. A., & Reiss, A. L. (2019). Closing the Gender Gap in Fragile X Syndrome: Review on Females with FXS and Preliminary Research Findings. *Brain Sciences*, *9*(1), 11. https://doi.org/10.3390/brainsci9010011

Bath, S. C., Steer, C. D., Golding, J., Emmett, P., & Rayman, M. P. (2013). Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Lancet (London, England)*, *382*(9889), 331–337. https://doi.org/10.1016/S0140-6736(13)60436-5

Baxter, A. J., Scott, K. M., Vos, T., & Whiteford, H. A. (2013). Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychological Medicine*, *43*(5), 897–910. https://doi.org/10.1017/S003329171200147X

Baujat, B., Mahé, C., Pignon, J-P., & Hill, C. (2002). A graphical method for exploring heterogeneity in meta-analyses: application to a meta-analysis of 65 trails. *Stat Med*, *21*(18), 2641-2652. https://doi.org/10.1002/sim.1221

Bearss, K., Taylor, C. A., Aman, M. G., Whittemore, R., Lecavalier, L., Miller, J., Pritchett, J., Green, B., & Scahill, L. (2016). Using qualitative methods to guide scale development for anxiety in youth with autism spectrum disorder. *Autism: The International Journal of Research and Practice*, *20*(6), 663–672. https://doi.org/10.1177/1362361315601012

Bengtsson, M. (2016). How to plan and perform a qualitative study using content analysis. *NursingPlus Open, 2*, 8-14. https://doi.org/10.1016/j.npls.2016.01.001

Bertrán, M., Tagle, F, P., & Irarrázaval, M. (2018). Psychiatric manifestations of 22q11.2 deletion syndrome: a literature review. *Neurologia*, *33*(2), 121-128. https://doi.org/10.1016/j.nrl.2015.07.007

Bertelli, M, O., Rossi, M., Scuticchio, D., & Bianco, A. (2015). Diagnosing psychiatric disorders in people with intellectual disabilities: issues and achievements. *Adv Ment Health Intellect Disabil*, *9*(5), 230-242. https://doi.org/10.1108/AMHID-05-2015-0023

Berument, S. K., Rutter, M., Lord, C., Pickles, A., & Bailey, A. (1999). Autism screening questionnaire: diagnostic validity. *The British Journal of Psychiatry: The Journal of Mental Science*, *175*, 444–451. https://doi.org/10.1192/bjp.175.5.444

Bhardwaj, A., Moore, A., Cardinal, R. N., Bradley, C., Cross, L., & Ford, T. J. (2021). Survey of CAMHS clinicians about their experience of remote consultation: brief report. *BJPsych Open*, *7*(1), e34. https://doi.org/10.1192/bjo.2020.160

Bhate, S., & Wilkinson, S. (2006). Aetiology of learning disability. *Psychiatry, 5*(9), 298-301. https://doi.org/10.1053/j.mppsy.2006.08.001

Bitsika, V., & Sharpley, C, F. (2016). Which Aspects of Challenging Behaviour Are Associated with Anxiety across two Age Groups of Young Males with an Autism Spectrum Disorder? *Journal of Developmental and Physical Disabilities, 28*, 685-701. https://doi.org/10.1007/s10882-016-9502-4

Blake, K, D., Salem-Hartshorne, N., Daoud, M, A., & Gradstein, J. (2005). Adolescent and adult issues in CHARGE syndrome. *Clin Pediatr (Phila)*, *44*(2), 151-159. https://doi.org/10.1177/000992280504400207

Blazek, K., van Zwieten, A., Saglimbene, V., & Teixeira-Pinto, A. (2021). A practical guide to multiple imputation of missing data in nephrology. *Kidney International*, *99*(1), 68–74. https://doi.org/10.1016/j.kint.2020.07.035

Blomberg, S., Rosander, M., & Andersson, G. (2006). Fears, hyperacusis and musicality in Williams syndrome. *Research in Developmental Disabilities*, *27*(6), 668–680. https://doi.org/10.1016/j.ridd.2005.09.002

Boat, T. F., Wu, J. T. (Eds.). (2015). Committee to Evaluate the Supplemental Security Income Disability Program for Children with Mental Disorders, Board on the Health of Select Populations, Board on Children, Youth, and Families, Institute of Medicine, Division of Behavioral and Social Sciences and Education, & The National Academies of Sciences, Engineering, and Medicine. *Mental Disorders and Disabilities Among Low-Income Children*. National Academies Press (US).

Boer, H., Holland, A., Whittington, J., Butler, J., Webb, T., & Clarke, D. (2002). Psychotic illness in people with Prader Willi syndrome due to chromosome 15 maternal uniparental disomy. *Lancet, 359*(9301), 135–136. https://doi.org/10.1016/S0140-6736(02)07340-3

Bölte, S., Girdler, S., & Marschik, P. B. (2019). The contribution of environmental exposure to the etiology of autism spectrum disorder. *Cellular and Molecular Life Sciences: CMLS*, *76*(7), 1275–1297. https://doi.org/10.1007/s00018-018-2988-4

Borelli, J.L., Rasmussen, H.F., John, H.K.S., West, J. L., & Piacentini, J. C. (2015). Parental Reactivity and the Link Between Parent and Child Anxiety Symptoms. *J Child Fam Stud*, *24,* 3130–3144. https://doi.org/10.1007/s10826-015-0117-7

Boswell, J. F., Thompson-Hollands, J., Farchione, T. J., & Barlow, D. H. (2013). Intolerance of uncertainty: a common factor in the treatment of emotional disorders. *Journal of Clinical Psychology*, *69*(6), 630–645. https://doi.org/10.1002/jclp.21965

Boulter, C., Freeston, M., South, M., & Rodgers, J. (2014). Intolerance of uncertainty as a framework for understanding anxiety in children and adolescents with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *44*(6), 1391–1402. https://doi.org/10.1007/s10803-013-2001-x

Bouras, N., & Drummond, C. (1992). Behaviour and psychiatric disorders of people with mental handicaps living in the community. *Journal of Intellectual Disability Research: JIDR*, *36 (Pt 4)*, 349–357. https://doi.org/10.1111/j.1365-2788.1992.tb00533.x

Bradshaw, J., Gore, N., & Darvell, C. (2018). Supporting the direct involvement of students with disabilities in functional assessment through use of Talking Mats®. *Tizard Learning Disability Review, 23*(2), 111-116. https://doi.org/10.1108/TLDR-01-2018-0004

Bratek, A., Krysta, K., & Kucia, K. (2017). Psychiatric comorbidity in older adults with intellectual disability. *Psychiat Danub*, *29*(3), 590-593.

Brett, D., Warnell, F., McConachie, H., & Parr, J. R. (2016). Factors Affecting Age at ASD Diagnosis in UK: No Evidence that Diagnosis Age has Decreased Between 2004 and 2014. *Journal of Autism and Developmental Disorders*, *46*(6), 1974–1984. https://doi.org/10.1007/s10803-016-2716-6

Brookman-Frazee, L., Drahota, A., Stadnick, N., & Palinkas, L. A. (2012). Therapist perspectives on community mental health services for children with autism spectrum disorders. *Administration and Policy in Mental Health*, *39*(5), 365–373. https://doi.org/10.1007/s10488-011-0355-y

Brown, M., Whiting, J., Haque, A., & Kahumoku-Fessler, E. (2020). A Summative Content Analysis of Stress and Coping among Parents of Children with Autism. *The American Journal of Family Therapy.* https://doi.org/10.1080/01926187.2020.1791764

Bryant, C., Jackson, H., & Ames, D. (2008). The prevalence of anxiety in older adults: methodological issues and a review of the literature. *J Affect Disord*, *109*(3), 233-250. https://doi.org/10.1016/j.jad.2007.11.008

Bryson, S. E., Bradley, E. A., Thompson, A., & Wainwright, A. (2008). Prevalence of autism among adolescents with intellectual disabilities. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, *53*(7), 449–459. https://doi.org/10.1177/070674370805300710

Buckles, J., Luckasson, R., & Keefe, E. (2013). A Systematic Review of the Prevalence of Psychiatric Disorders in Adults with Intellectual Disability. *J Ment Health Res Intellect Disabil*, *6*(3), 181-207. https://doi.org/10.1080/19315864.2011.651682

Buckley, N., Glasson, E. J., Chen, W., Epstein, A., Leonard, H., Skoss, R., Jacoby, P., Blackmore, A. M., Srinivasjois, R., Bourke, J., Sanders, R. J., & Downs, J. (2020). Prevalence estimates of mental health problems in children and adolescents with intellectual disability: A systematic review and meta-analysis. *The Australian and New Zealand Journal of Psychiatry*, *54*(10), 970–984. https://doi.org/10.1177/0004867420924101

Budimirovic, D. B., & Kaufmann, W. E. (2011). What can we learn about autism from studying fragile X syndrome?. *Developmental Neuroscience*, *33*(5), 379–394. https://doi.org/10.1159/000330213

Bunning, K., Alder, R., Proudman, L., & Wyborn, H. (2016). Co-production and pilot of a structured interview using Talking Mats® to survey the television viewing habits and preferences of adults and young people with learning disabilities. *British Journal of Learning Disabilities, 45*(1), 1-11. https://doi.org/10.1111/bld.12167

Busetto, L., Wick, W., & Gumbinger, C. (2020). How to use and assess qualitative research methods. Neurological Research and Practice, 2, 14. https://doi.org/10.1186/s42466-020-00059-z

Byrt, T., Bishop, J., & Carlin, J. B. (1993). Bias, prevalence and kappa. *Journal of Clinical Epidemiology*, *46*(5), 423–429. https://doi.org/10.1016/0895-4356(93)90018-v

Cai, R. Y., Richdale, A. L., Uljarević, M., Dissanayake, C., & Samson, A. C. (2018). Emotion regulation in autism spectrum disorder: Where we are and where we need to go. *Autism Research: Official Journal of the International Society for Autism Research*, *11*(7), 962–978. https://doi.org/10.1002/aur.1968

Campbell, B., Curran, M., Inkpen, R., Katsikitis, M., & Kannis-Dymand, L. (2018). A preliminary evaluation of metacognitive beliefs in high functioning children with autism spectrum disorder. *Advances in Autism*, 4 (2), 73-84. https://doi.org/10.1108/AIA-08-2017-0017

Carleton R. N. (2012). The intolerance of uncertainty construct in the context of anxiety disorders: theoretical and practical perspectives. *Expert Review of Neurotherapeutics*, *12*(8), 937–947. https://doi.org/10.1586/ern.12.82

Carlsson, L. H., Norrelgen, F., Kjellmer, L., Westerlund, J., Gillberg, C., & Fernell, E. (2013). Coexisting disorders and problems in preschool children with autism spectrum disorders. *The Scientific World Journal*, *2013*, 213979. https://doi.org/10.1155/2013/213979

Cattell, R. B. (1966). The Scree Test For The Number Of Factors. *Multivariate Behavioral Research, 1*(2), 245-276. https://doi.org/10.1207/s15327906mbr0102_10

Charman, T., Pickles, A., Simonoff, E., Chandler, S., Loucas, T., & Baird, G. (2011). IQ in children with autism spectrum disorders: data from the Special Needs and Autism Project (SNAP). *Psychological Medicine*, *41*(3), 619–627. https://doi.org/10.1017/S0033291710000991

Chawarska, K., Paul, R., Klin, A., Hannigen, S., Dichtel, L. E., & Volkmar, F. (2007). Parental recognition of developmental problems in toddlers with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *37*(1), 62–72. https://doi.org/10.1007/s10803-006-0330-8

Chawner, S, J, R, A., Niarchou, M., Doherty, J, L., Moss, H., Owen, M, J., & van den Bree, M, B, M. (2019). The emergence of psychotic experiences in the early adolescence of 22q11.2 deletion syndrome. *Journal of Psychiatric Research, 109*, 10-17. https://doi.org/10.1016/j.jpsychires.2018.11.002

Cheng, J., Pullenayegum, E., Marshall, J, K., Iorio, A., & Thabane, L. (2016). Impact of including or excluding both-armed zero-event studies on using standard meta-analysis methods for rare event outcome: a simulation study. *BMJ Open*, *6*(8): Article e010983. https://doi/org/10.1136/bmjopen-2015-010983

Chester, R., Chaplin, E., Tsakanikos, E., McCarthy, J., Bouras, N., & Craig, T. (2013). Gender differences in self-reported symptoms of depression and anxiety in adults with intellectual disabilities. *Advances in Mental Health and Intellectual Disabilities, 7*(4), 191-200. https://doi.org/10.1108/AMHID-03-2013-0025

Chiarotti, F., & Venerosi, A. (2020). Epidemiology of Autism Spectrum Disorders: A Review of Worldwide Prevalence Estimates Since 2014. *Brain Sciences*, *10*(5), 274. https://doi.org/10.3390/brainsci10050274

Cianfaglione, R., Clarke, A., Kerr, M., Hastings, R. P., Oliver, C., Moss, J., Heald, M., & Felce, D. (2015). A national survey of Rett syndrome: behavioural characteristics. *Journal of Neurodevelopmental Disorders*, *7*(1), 11. https://doi.org/10.1186/s11689-015-9104-y

Cochran, L., Welham, A., Oliver, C., Arshad, A., & Moss, J. F. (2019). Age-related Behavioural Change in Cornelia de Lange and Cri du Chat Syndromes: A Seven Year Follow-up Study. *Journal of Autism and Developmental Disorders*, *49*(6), 2476–2487. https://doi.org/10.1007/s10803-019-03966-6

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences (2nd ed.).* Erlbaum.

Collacott, R, A., Cooper, S, A., & McGrother, C. (1992). Differential Rates of Psychiatric Disorders in Adults With Down's Syndrome Compared With Other Mentally Handicapped Adults. *Br J Psychiatry*, *161*, 671-674. https://doi.org/10.1192/bjp.161.5.671

Colvert, E., Tick, B., McEwen, F., Stewart, C., Curran, S. R., Woodhouse, E., Gillan, N., Hallett, V., Lietz, S., Garnett, T., Ronald, A., Plomin, R., Rijsdijk, F., Happé, F., & Bolton, P. (2015). Heritability of Autism Spectrum Disorder in a UK Population-Based Twin Sample. *JAMA Psychiatry*, *72*(5), 415–423. https://doi.org/10.1001/jamapsychiatry.2014.3028

Constantino, J, N., & Gruber, C,P. (2005). *Social Responsiveness Scale: Manual.* Western Psychological Services.

Cook, D, R., & Weisberg, S. (1982). *Residuals and Influence in Regression.* Chapman and Hall.

Cooper, S. A., Smiley, E., Morrison, J., Williamson, A., & Allan, L. (2007). Mental ill-health in adults with intellectual disabilities: prevalence and associated factors. *The British Journal of Psychiatry: The Journal of Mental Science*, *190*, 27–35. https://doi.org/10.1192/bjp.bp.106.022483

Cooray, S., & Bakala, A. (2005). Anxiety disorders in people with learning disabilities. *Advances in Psychiatric Treatment, 11*(5), 355-361. doi:10.1192/apt.11.5.355

Copeland, W, E., Angold, A., Shanahan, L., & Costello, E, J. (2014). Longitudinal Patterns of Anxiety From Childhood to Adulthood: The Great Smoky Mountains Study. *J Am Acad Child Adolesc Psychiatry*, *53*(1), 21-33. https://doi.org/10.1016/j.jaac.2013.09.017

Copeland, W. E., Wolke, D., Shanahan, L., & Costello, E. J. (2015). Adult Functional Outcomes of Common Childhood Psychiatric Problems: A Prospective, Longitudinal Study. *JAMA Psychiatry*, *72*(9), 892–899. https://doi.org/10.1001/jamapsychiatry.2015.0730

Cordeiro, L., Ballinger, E., Hagerman, R., & Hessl, D. (2011). Clinical assessment of DSM-IV anxiety disorders in fragile X syndrome: prevalence and characterization. *J Neurodev Disord*, 3(1), 57-67. https://doi.org/10.1007/s11689-010-9067-y

Costello, E. J., Egger, H. L., & Angold, A. (2005). The developmental epidemiology of anxiety disorders: phenomenology, prevalence, and comorbidity. *Child and Adolescent Psychiatric Clinics of North America*, *14*(4), 631–48. https://doi.org/10.1016/j.chc.2005.06.003

Costello, H., & Bouras, N. (2006). Assessment of mental health problems in people with intellectual disabilities. *The Israel Journal of Psychiatry and Related Sciences*, *43*(4), 241–251.

Coulter, R. A. (2009). Understanding the visual symptoms of individuals with autism spectrum disorder (ASD). *Optometry and Vision Development, 40*(3), 164–175.

Crane, L., Chester, J. W., Goddard, L., Henry, L. A., & Hill, E. (2016). Experiences of autism diagnosis: A survey of over 1000 parents in the United Kingdom. *Autism: The International Journal of Research and Practice*, *20*(2), 153–162. https://doi.org/10.1177/1362361315573636

Crawford, H., Waite, J., & Oliver, C. (2017). Diverse Profiles of Anxiety Related Disorders in Fragile X, Cornelia de Lange and Rubinstein-Taybi Syndromes. *J Autism Dev Disord*, *47*(12), 3728-3740. https://doi.org/10.1007/s10803-016-3015-y

Crawford, H., Groves, L., Bradley, L., Roberts, J., Hogan, A., Smith, K., Oliver, C., Renshaw, D., & Waite, J. (in prep). A biobehavioural study of anxiety in fragile X syndrome.

Cridland, E, K., Jones, S, C., Caputi, P., & Magee, C, A. (2015). Qualitative research with families living with autism spectrum disorder: Recommendations for conducting semistructured interviews. *Journal of Intellectual & Developmental Disability, 40*, 78-91. https://doi.org/10.3109/13668250.2014.964191

Cubic, B., Mance, J., Turgesen, J. N., & Lamanna, J. D. (2012). Interprofessional education: preparing psychologists for success in integrated primary care. *Journal of Clinical Psychology in Medical Settings*, *19*(1), 84–92. https://doi.org/10.1007/s10880-011-9291-y

Cusack, J., & Sterry, R. (2016). *Your questions: shaping future autism research.* Autistica. https://www.autistica.org.uk/downloads/files/Autism-Top-10-Your-Priorities-for-Autism-Research.pdf

Dadds, M. R., Rapee, R. M., & Barrett, P. M. (1994). Behavioral observation. In T. H. Ollendick, N. J. King, & W. Yule (Eds.), *International handbook of phobic and anxiety disorders in children and adolescents* (pp. 349–364). Plenum Press. https://doi.org/10.1007/978-1-4899-1498-9_18

Dagnan, D., Jackson, I., & Eastlake, L. (2018). A systematic review of cognitive behavioural therapy for anxiety in adults with intellectual disabilities. *J Intell Disabil Res*, 62(11), 974-991. https://doi.org/10.1111/jir.12548

Daveney, J., Hassiotis, A., Katona, C., Matcham, F., & Sen, P. (2019). Ascertainment and Prevalence of Post-Traumatic Stress Disorder (PTSD) in People with Intellectual Disabilities, *Journal of Mental Health Research in Intellectual Disabilities, 12*(3-4), 211-233, DOI: 10.1080/19315864.2019.1637979

Dee-Price, B-J, M., Hallahan, L., Bryen, D. N., & Watson, J. M. (2021). Every voice counts: exploring communication accessible research methods. *Disability & Society, 36*(2), 240-264. https://doi.org/10.1080/09687599.2020.1715924

Dekker, M. C., & Koot, H. M. (2003a). DSM-IV disorders in children with borderline to moderate intellectual disability. I: prevalence and impact. *Journal of the American Academy of Child and Adolescent Psychiatry*, *42*(8), 915–922. https://doi.org/10.1097/01.CHI.0000046892.27264.1A

Dekker, M. C., & Koot, H. M. (2003b). DSM-IV disorders in children with borderline to moderate intellectual disability. II: child and family predictors. *Journal of the American Academy of Child and Adolescent Psychiatry*, *42*(8), 923–931. https://doi.org/10.1097/01.CHI.0000046891.27

Delgado, C., Gonzalez-Gordon, R. G., Aragón, E., & Navarro, J. I. (2017). Different Methods for Long-term Systematic Assessment of Challenging Behaviors in People with Severe Intellectual Disability. *Frontiers in Psychology*, *8*, 17. https://doi.org/10.3389/fpsyg.2017.00017

den Houting, J., Adams, D., Roberts, J., & Keen, D. (2018). Exploring anxiety symptomatology in school-aged children using an autism-specific assessment. *Research in Autism Spectrum Disorders, 50*, 73-82. https://doi.org/10.1016/j.rasd.2018.03.005

De Smedt, B., Devriendt, K., Fryns, J-P., Vogels, A., Gewillig, M., & Swillen, A. (2007). Intellectual abilities in a large sample of children with Velo-Cardio-Facial Syndrome: an update. *J Intellect Disabil Res, 51*(9), 666-670. https://doi.org/10.1111/j.1365-2788.2007.00955.x

Detsky, A. S., Naylor, C. D., O'Rourke, K., McGeer, A. J., & L'Abbé, K. A. (1992). Incorporating variations in the quality of individual randomized trials into meta-analysis. *Journal of Clinical Epidemiology*, *45*(3), 255–265. https://doi.org/10.1016/0895-4356(92)90085-2

de Vries, P, J., Wilde, L., de Vries, M, C., Moavero, R., Pearson, D, A., & Curatolo, P. (2018). A clinical update on tuberous sclerosis complex-associated neuropsychiatric disorders (TAND). *Am J Med Genet C Semin Med Genet*, *178*(3), 309-320. https://doi.org/10.1002/ajmg.c.31637

de Winter, C. F., Hermans, H., Evenhuis, H. M., & Echteld, M. A. (2015). Associations of symptoms of anxiety and depression with diabetes and cardiovascular risk factors in older

people with intellectual disability. *Journal of Intellectual Disability Research: JIDR*, *59*(2), 176–185. https://doi.org/10.1111/jir.12049

de Witte, M., Kooijmans, R., Hermanns, M., van Hooren, S., Biesmans, K., Hermsen, M., Stams, G. J., & Moonen, X. (2021). Self-Report Stress Measures to Assess Stress in Adults With Mild Intellectual Disabilities-A Scoping Review. *Frontiers in Psychology*, *12*, 742566. https://doi.org/10.3389/fpsyg.2021.742566

Dingfelder, H. E., & Mandell, D. S. (2011). Bridging the research-to-practice gap in autism intervention: an application of diffusion of innovation theory. *Journal of Autism and Developmental Disorders*, *41*(5), 597–609. https://doi.org/10.1007/s10803-010-1081-0

Dion, J., Paquette, G., Tremblay, K. N., Collin-Vézina, D., & Chabot, M. (2018). Child Maltreatment Among Children With Intellectual Disability in the Canadian Incidence Study. *American Journal on Intellectual and Developmental Disabilities*, *123*(2), 176–188. https://doi.org/10.1352/1944-7558-123.2.176

Dodd, H. F., & Lester, K. J. (2021). Adventurous Play as a Mechanism for Reducing Risk for Childhood Anxiety: A Conceptual Model. *Clinical Child and Family Psychology Review*, *24*(1), 164–181. https://doi.org/10.1007/s10567-020-00338-w

Doherty, A, J., Atherton, H., Boland, P., Hastings, R., Hives, L., Hood, K., James-Jenkinson, L., Leavey, R., Randell, E., Reed, J., Taggart, L., Wilson, N., & Chauhan, U. (2020). Barriers and facilitators to primary health care for people with intellectual disabilities and/or autism: an integrative review. *BJGP Open, 4*(3). https://doi.org/10.3399/bjgpopen20X101030

Doody, O., & Bailey, M, E. (2017). Pain and pain assessment in people with intellectual disability: Issues and challenges in practice. *British Journal of Learning Disabilities, 45*(3), 157-165. https://doi.org/10.1111/bld.12189

Doi, S. A., & Thalib, L. (2008). A quality-effects model for meta- analysis. *Epidemiology (Cambridge, Mass.)*, *19*(1), 94–100. https://doi.org/10.1097/EDE.0b013e31815c24e7

Dugas, M. J., Gagnon, F., Ladouceur, R., & Freeston, M. H. (1998). Generalized anxiety disorder: a preliminary test of a conceptual model. *Behaviour Research and Therapy*, *36*(2), 215–226. https://doi.org/10.1016/s0005-7967(97)00070-3

Dugas, M. J., & Koerner, N. (2005). Cognitive-Behavioral Treatment for Generalized Anxiety Disorder: Current Status and Future Directions. *Journal of Cognitive Psychotherapy, 19*(1), 61–81. https://doi.org/10.1891/jcop.19.1.61.66326

Dunn, W. (2014). *The Sensory Profile 2 Manual.* Pearson.

Durkin, M. (2002). The epidemiology of developmental disabilities in low-income countries. *Mental Retardation and Developmental Disabilities Research Reviews*, *8*(3), 206–211. https://doi.org/10.1002/mrdd.10039

Dykens, E. M., Leckman, J. F., & Cassidy, S. B. (1996). Obsessions and compulsions in Prader-Willi syndrome. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *37*(8), 995–1002. https://doi.org/10.1111/j.1469-7610.1996.tb01496.x

Dykens, E, M. (2003). Anxiety, fears, and phobias in persons with Williams syndrome. *Dev Neuropsychol*, *23*(1-2), 291-316. https://doi.org/10.1080/87565641.2003.9651896

Dykens, E., & Shah, B. (2003). Psychiatric Disorders in Prader-Willi Syndrome: Epidemiology and Management. *CNS Drugs, 17*, 167-178. https://doi.org/10.2165/00023210-200317030-00003

Dykens, E, M. (2007). Psychiatric and behavioral disorders in persons with Down syndrome. *Ment Retard Dev Disabil Res Rev*, *13*(3), 272-278. https://doi.org/10.1002/mrdd.20159

Dymond, S., & Roche, B. (2009). A contemporary behavior analysis of anxiety and avoidance. The Behavior Analyst, 32(1), 7–27. https://doi.org/10.1007/BF03392173

Dziura, J. D., Post, L. A., Zhao, Q., Fu, Z., & Peduzzi, P. (2013). Strategies for dealing with missing data in clinical trials: from design to analysis. *The Yale Journal of Biology and Medicine*, *86*(3), 343–358.

Eaton, C., Tarver, J., Shirazi, A., Pearson, E., Walker, L., Bird, M., Oliver, C., & Waite, J. (2021). A systematic review of the behaviours associated with depression in people with

severe-profound intellectual disability. *Journal of Intellectual Disability Research: JIDR*, *65*(3), 211–229. https://doi.org/10.1111/jir.12807

Edwards, G., Tarver, J., Shelley, L., Bird, M., Hughes, J., Crawford, H., & Waite, J. (2022). Utilising Interview Methodology to Inform the Development of New Clinical Assessment Tools for Anxiety in Autistic Individuals Who Speak Few or no Words. *Journal of Autism and Developmental Disorders*, 10.1007/s10803-022-05509-y. Advance online publication. https://doi.org/10.1007/s10803-022-05509-y

Einfeld, S, L., Ellis, L, A., & Emerson, E. (2011). Comorbidity of intellectual disability and mental disorder in children and adolescents: a systematic review. *J Intellect Dev Disabil*, 36(2), 137-143. https://doi.org/10.1080/13668250.2011.572548

Ellison, J. W., Rosenfeld, J. A., & Shaffer, L. G. (2013). Genetic basis of intellectual disability. *Annual Review of Medicine*, *64*, 441–450. https://doi.org/10.1146/annurev-med-042711-140053

Elsabbagh, M., Divan, G., Koh, Y. J., Kim, Y. S., Kauchali, S., Marcín, C., Montiel-Nava, C., Patel, V., Paula, C. S., Wang, C., Yasamy, M. T., & Fombonne, E. (2012). Global prevalence of autism and other pervasive developmental disorders. *Autism Research: Official Journal of the International Society for Autism Research*, *5*(3), 160–179. https://doi.org/10.1002/aur.239

Emerson E. (2003). Prevalence of psychiatric disorders in children and adolescents with and without intellectual disability. *Journal of Intellectual Disability Research: JIDR*, *47*(Pt 1), 51–58. https://doi.org/10.1046/j.1365-2788.2003.00464.x

Emerson, E., & Hatton, C. (2007). Mental health of children and adolescents with intellectual disabilities in Britain. *The British Journal of Psychiatry: The Journal of Mental Science*, *191*, 493–499. https://doi.org/10.1192/bjp.bp.107.038729

Emerson, E., Felce, D., & Stancliffe, R, J. (2013). Issues concerning self-report data and population-based data sets involving people with intellectual disabilities. *Intellect Dev Disabil*, *51*(5), 333-348. https://doi.org/10.1352/1934-9556-51.5.333

Erlingsson, C., & Brysiewicz, P. (2017). A hands-on guide to doing content analysis. *African Journal of Emergency Medicine, 7*(3), 93-99. https://doi.org/10.1016/j.afjem.2017.08.001

Engel-Yeger, B., Hardal-Nasser, R., & Gal, E. (2011). Sensory processing dysfunctions as expressed among children with different severities of intellectual developmental disabilities. *Research in Developmental Disabilities*, *32*(5), 1770–1775. https://doi.org/10.1016/j.ridd.2011.03.005

Erskine, H, E., Baxter, A, J., Patton, G., Moffitt, T, E., Patel, V., Whiteford, H, A., & Scott, J, G. (2017). The global coverage of prevalence data for mental disorders in children and adolescents. *Epidemiol Psychiatr Sci, 26*(4), 395-402. https://doi.org/10.1017/S2045796015001158

Esbensen, A. J., Rojahn, J., Aman, M. G., & Ruedrich, S. (2003). Reliability and validity of an assessment instrument for anxiety, depression, and mood among individuals with mental retardation. *J Autism Dev Disord, 33*(6), 617-629. https://doi.org/10.1023/b:jadd.0000005999.27178.55

Espie, C. A., Watkins, J., Curtice, L., Espie, A., Duncan, R., Ryan, J. A., Brodie, M. J., Mantala, K., & Sterrick, M. (2003). Psychopathology in people with epilepsy and intellectual disability; an investigation of potential explanatory variables. *Journal of Neurology, Neurosurgery, and Psychiatry*, *74*(11), 1485–1492. https://doi.org/10.1136/jnnp.74.11.1485

Ezell, J., Hogan, A., Fairchild, A., Hills, K., Klusek, J., Abbeduto, L., & Roberts, J. (2019). Prevalence and Predictors of Anxiety Disorders in Adolescent and Adult Males with Autism Spectrum Disorder and Fragile X Syndrome. *J Autism Dev Disord*, *49*(3), 1131-1141. https://doi.org/10.1007/s10803-018-3804-6

Ferguson, B. J., Marler, S., Altstein, L. L., Lee, E. B., Akers, J., Sohl, K., McLaughlin, A., Hartnett, K., Kille, B., Mazurek, M., Macklin, E. A., McDonnell, E., Barstow, M., Bauman, M. L., Margolis, K. G., Veenstra-VanderWeele, J., & Beversdorf, D. Q. (2017). Psychophysiological Associations with Gastrointestinal Symptomatology in Autism Spectrum

Disorder. *Autism Research: Official Journal of the International Society for Autism Research*, *10*(2), 276–288. https://doi.org/10.1002/aur.1646

Ferguson, B. J., Hamlin, T., Lantz, J. F., Villavicencio, T., Coles, J., & Beversdorf, D. Q. (2019). Examining the Association Between Electrodermal Activity and Problem Behavior in Severe Autism Spectrum Disorder: A Feasibility Study. *Frontiers in Psychiatry*, *10*, 654. https://doi.org/10.3389/fpsyt.2019.00654

Ferrão, Y. A., Shavitt, R. G., Prado, H., Fontenelle, L. F., Malavazzi, D. M., de Mathis, M. A., Hounie, A. G., Miguel, E. C., & do Rosário, M. C. (2012). Sensory phenomena associated with repetitive behaviors in obsessive-compulsive disorder: an exploratory study of 1001 patients. *Psychiatry Research*, *197*(3), 253–258. https://doi.org/10.1016/j.psychres.2011.09.017

Field, A, P. (2018). *Discovering statistics using IBM SPSS statistics (5th ed.).* SAGE.

Fjermestad, K, W., Vatne, T, M., & Gjone, H. (2015). Cognitive behavioral therapy for adolescents with 22q11.2 deletion syndrome. *Adv Ment Health Intellect Disabil*, *9*(1), 30-39. https://doi.org/10.1108/AMHID-05-2014-0017

Flynn, S., Vereenooghe, L., Hastings, R. P., Adams, D., Cooper, S. A., Gore, N., Hatton, C., Hood, K., Jahoda, A., Langdon, P. E., McNamara, R., Oliver, C., Roy, A., Totsika, V., & Waite, J. (2017). Measurement tools for mental health problems and mental well-being in people with severe or profound intellectual disabilities: A systematic review. *Clinical Psychology Review*, *57*, 32–44. https://doi.org/10.1016/j.cpr.2017.08.006

Fombonne E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric Research*, *65*(6), 591–598. https://doi.org/10.1203/PDR.0b013e31819e7203

Gabis, L, V., Baruch, Y, K., Jokel, A., & Raz, R. (2011). Psychiatric and autistic comorbidity in fragile X syndrome across ages. *J Child Neurol*, *26*(8), 940-948. https://doi.org/10.1177/0883073810395937

Gale, C., & Davidson, O. (2007). Generalised anxiety disorder. *BMJ (Clinical Research Ed.)*, *334*(7593), 579–581. https://doi.org/10.1136/bmj.39133.559282.BE

Gardiner K. J. (2010). Molecular basis of pharmacotherapies for cognition in Down syndrome. *Trends in Pharmacological Sciences*, *31*(2), 66–73. https://doi.org/10.1016/j.tips.2009.10.010

Giardino, G., Cirillo, E., Maio, F., Gallo, V., Esposito, T., Naddei, R., Grasso, F., & Pignata, C. (2014). Gastrointestinal involvement in patients affected with 22q11.2 deletion syndrome. *Scandinavian Journal of Gastroenterology*, *49*(3), 274–279. https://doi.org/10.3109/00365521.2013.855814

Gillott, A., & Standen, P. J. (2007). Levels of anxiety and sources of stress in adults with autism. *Journal of Intellectual Disabilities*, *11*(4), 359-370. https://doi.org/10.1177/1744629507083585

Girimaji, S. C., & Pradeep, A. J. (2018). Intellectual disability in International Classification of Diseases-11: A developmental perspective. *Indian Journal of Social Psychiatry, 34*(5), 68-74. https://doi.org/10.4103/ijsp.ijsp_35_18

Glasson, E. J., Buckley, N., Chen, W., Leonard, H., Epstein, A., Skoss, R., Jacoby, P., Blackmore, A. M., Bourke, J., & Downs, J. (2020). Systematic Review and Meta-analysis: Mental Health in Children With Neurogenetic Disorders Associated With Intellectual Disability. *Journal of the American Academy of Child and Adolescent Psychiatry*, *59*(9), 1036–1048. https://doi.org/10.1016/j.jaac.2020.01.006

Glenn S. (2017). Repetitive Behaviours and Restricted Interests in Individuals with Down Syndrome-One Way of Managing Their World?. *Brain Sciences*, *7*(6), 66. https://doi.org/10.3390/brainsci7060066

Gobrial, E., & Raghavan, R. (2012). Prevalence of anxiety disorder in children and young people with intellectual disabilities and autism. *Advances in Mental Health and Intellectual Disabilities, 6*(3), 130-140. https://doi.org/10.1108/20441281211227193

Goh, E. (2017). Rett syndrome: a sex-biased neurodevelopmental disorder. *Biochem (Lond)*, *39*(1), 30–33. doi: https://doi.org/10.1042/BIO03901030

Gold, W, A., Krishnarajy, R., Ellaway, C., & Christodoulou, J. (2018). Rett Syndrome: A Genetic Update and Clinical Review Focusing on Comorbidities. *ACS Chem Neurosci*, *9*(2), 167-176. https://doi.org/10.1021/acschemneuro.7b00346

Goodwin, J., Rob, P., Freeston, M., Garland, D., Grahame, V., Kernohan, A., Labus, M., Osborne, M., Parr, J. R., Wright, C., & Rodgers, J. (2022). Caregiver perspectives on the impact of uncertainty on the everyday lives of autistic children and their families. *Autism: The International Journal of Research and Practice*, *26*(4), 827–838. https://doi.org/10.1177/13623613211033757

Gordon-Lipkin, E., Marvin, A, R., Law, J, K., & Lipkin, P, H. (2018). Anxiety and Mood Disorder in Children with Autism Spectrum Disorder and ADHD. *Pediatrics, 141*(4), e20171377. https://doi.org/10.1542/peds.2017-1377

Gotham, K., Bishop, S. L., Hus, V., Huerta, M., Lund, S., Buja, A., Krieger, A., & Lord, C. (2013). Exploring the relationship between anxiety and insistence on sameness in autism spectrum disorders. *Autism Research: Official Journal of the International Society for Autism Research*, *6*(1), 33–41. https://doi.org/10.1002/aur.1263

Gothelf, D., Farber, N., Raveh, E., Apter, A., & Attias, J. (2006). Hyperacusis in Williams syndrome: characteristics and associated neuroaudiologic abnormalities. *Neurology*, *66*(3), 390–395. https://doi.org/10.1212/01.wnl.0000196643.35395.5f

Grados, M. A., Alvi, M. H., & Srivastava, S. (2017). Behavioral and psychiatric manifestations in Cornelia de Lange syndrome. *Current Opinion in Psychiatry*, *30*(2), 92–96. https://doi.org/10.1097/YCO.0000000000000311

Green, S. A., & Ben-Sasson, A. (2010). Anxiety disorders and sensory over-responsivity in children with autism spectrum disorders: is there a causal relationship? *Journal of Autism and Developmental Disorders*, *40*(12), 1495–1504. https://doi.org/10.1007/s10803-010-1007-x

Green, S. A., Ben-Sasson, A., Soto, T. W., & Carter, A. S. (2012). Anxiety and sensory over-responsivity in toddlers with autism spectrum disorders: bidirectional effects across time. *Journal of Autism and Developmental Disorders*, *42*(6), 1112–1119. https://doi.org/10.1007/s10803-011-1361-3

Green, S, A., Berkovits, L, D., & Baker, B, L. (2015). Symptoms and development of anxiety in children with or without intellectual disability. *J Clin Child Adolesc Psychol, 44*(1), 137-144. https://doi.org/10.1080/15374416.2013.873979

Grier, E., Abells, D., Casson, I., Gemmill, M., Ladouceur, J., Lepp, A., Niel, U., Sacks, S., & Sue, K. (2018). Managing complexity in care of patients with intellectual and developmental disabilities: Natural fit for the family physician as an expert generalist. *Canadian Family Physician Medecin de Famille Canadien*, *64*(Suppl 2), S15–S22.

Groves, L., Crawford, H., Moss, J., Royston, R., Waite, J., Bradley, L., Thomas, A., Moss, K., & Oliver, C. (2018). The prevalence and profile of anxiety disorders in Cornelia de Lange and Fragile X syndromes. *J Intellect Disabil Res*, *62*(8), 667. https://doi.org/10.1111/jir.12511

Groves, L., Moss, J., Crawford, H., Nelson, L., Stinton, C., Singla, G., & Oliver, C. (2019). Lifespan trajectory of affect in Cornelia de Lange syndrome: towards a neurobiological hypothesis. *Journal of Neurodevelopmental Disorders, 11*, 6. https://doi.org/10.1186/s11689-019-9269-x

Hagopian, L, P., & Jennett, H, K. (2008). Behavioral Assessment and Treatment of Anxiety in Individuals with Intellectual Disabilities and Autism. *J Dev Phys Disabil, 20,* 467–483. https://doi.org/10.1007/s10882-008-9114-8

Hall, S. S., Arron, K., Sloneem, J., & Oliver, C. (2008). Health and sleep problems in Cornelia de Lange Syndrome: a case control study. *Journal of Intellectual Disability Research: JIDR*, *52*(Pt 5), 458–468. https://doi.org/10.1111/j.1365-2788.2008.01047.x

Hansen, S. N., Schendel, D. E., & Parner, E. T. (2015). Explaining the increase in the prevalence of autism spectrum disorders: the proportion attributable to changes in reporting practices. *JAMA Pediatrics*, *169*(1), 56–62. https://doi.org/10.1001/jamapediatrics.2014.1893

Harrison, P., & Oakland, T. (2015). Adaptive Behavior Assessment System, Third edition (ABAS-3). Pearson.

Hartshorne, T, S., Stratton, K, K., Brown, D., Madhavan-Brown, S., Schmittel, M. C. (2017). Behavior in CHARGE syndrome. *Am J Med Genet C Semin Med Genet*, *175*(4), 431-438. https://doi.org/10.1002/ajmg.c.31588

Hashem, S., Nisar, S., Bhat, A.A., Yadav, S. K., Azeem, M. W., Bagga, P., Fakhro, K., Reddy, R., Frenneaux, M. P., & Haris, M. (2020). Genetics of structural and functional brain changes in autism spectrum disorder. *Transl Psychiatry, 10,* 229. https://doi.org/10.1038/s41398-020-00921-3

Heald, M., Adams, D., & Oliver, C. (2020). Profiles of atypical sensory processing in Angelman, Cornelia de Lange and Fragile X syndromes. *Journal of Intellectual Disability Research: JIDR*, *64*(2), 117–130. https://doi.org/10.1111/jir.12702

Herlihy, L., Knoch, K., Vibert, B., & Fein, D. (2015). Parents' first concerns about toddlers with autism spectrum disorder: effect of sibling status. *Autism: The International Journal of Research and Practice*, *19*(1), 20–28. https://doi.org/10.1177/1362361313509731

Hedges, L. V., & Vevea, J. L. (1998). Fixed- and Random-Effects Models in Meta-Analysis. *Psychological Methods*, *3*(4), 486-504. https://doi.org/10.1037/1082-989X.3.4.486

Hermans, H., van der Pas, F. H., & Evenhuis, H. M. (2011). Instruments assessing anxiety in adults with intellectual disabilities: a systematic review. *Research in Developmental Disabilities*, *32*(3), 861–870. https://doi.org/10.1016/j.ridd.2011.01.034

Hermans, H., Beekman, A. T., & Evenhuis, H. M. (2013). Prevalence of depression and anxiety in older users of formal Dutch intellectual disability services. *Journal of Affective Disorders*, *144*(1-2), 94–100. https://doi.org/10.1016/j.jad.2012.06.011

Hermans, H., & Evenhuis, H, M. (2013). Factors associated with depression and anxiety in older adults with intellectual disabilities: results of the healthy ageing and intellectual disabilities study. *International Journal of Geriatric Psychiatry, 28*(7), 691-699. https://doi.org/10.1002/gps.3872

Hess, C. R., & Landa, R. J. (2012). Predictive and concurrent validity of parent concern about young children at risk for autism. *Journal of Autism and Developmental Disorders*, *42*(4), 575–584. https://doi.org/10.1007/s10803-011-1282-1

Higgins, J, P, T., Thompson, S, G., Deeks, J, J., & Altman, D, G. (2003). Measuring inconsistency in meta-analyses. *BMJ, 327*(7414), 557-560. https://doi.org/10.1136/bmj.327.7414.557

Higgins, J, P, T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M, J., & Welch, V, A. (2019). *Cochrane Handbook for Systematic Reviews of Interventions* (2nd ed.). John Wiley & Sons. https://training.cochrane.org/cochrane-handbook-systematic-reviews-interventions#how-to-access

Hithersay, R., Hamburg, S., Knight, B., & Strydom, A. (2017). Cognitive decline and dementia in Down syndrome. *Current Opinion in Psychiatry*, *30*(2), 102–107. https://doi.org/10.1097/YCO.0000000000000307

Hoare, P., Harris, M., Jackson, P., & Kerley, S. (1998). A community survey of children with severe intellectual disability and their families: psychological adjustment, carer distress and the effect of respite care. *Journal of Intellectual Disability Research: JIDR*, *42 (Pt 3)*, 218–227. https://doi.org/10.1046/j.1365-2788.1998.00134.x

Hochhauser, M., & Engel-Yeger, B. (2010). Sensory processing abilities and their relation to participation in leisure activities among children with high-functioning autism spectrum disorder (HFASD). *Research in Autism Spectrum Disorders, 4*(4), 746-754. https://doi.org/10.1016/j.rasd.2010.01.015

Hodges, H., Fealko, C., & Soares, N. (2020). Autism spectrum disorder: definition, epidemiology, causes, and clinical evaluation. *Translational Pediatrics*, *9*(Suppl 1), S55–S65. https://doi.org/10.21037/tp.2019.09.09

Hofmann, S. G., & Hay, A. C. (2018). Rethinking avoidance: Toward a balanced approach to avoidance in treating anxiety disorders. *Journal of Anxiety Disorders*, *55*, 14–21. https://doi.org/10.1016/j.janxdis.2018.03.004

Holland, A. J., Hon, J., Huppert, F. A., Stevens, F., & Watson, P. (1998). Population-based study of the prevalence and presentation of dementia in adults with Down's syndrome. *The British Journal of Psychiatry: The Journal of Mental Science*, *172*, 493–498. https://doi.org/10.1192/bjp.172.6.493

Hollocks, M. J., Howlin, P., Papadopoulos, A. S., Khondoker, M., & Simonoff, E. (2014). Differences in HPA-axis and heart rate responsiveness to psychosocial stress in children with autism spectrum disorders with and without co-morbid anxiety. *Psychoneuroendocrinology*, *46*, 32–45. https://doi.org/10.1016/j.psyneuen.2014.04.004

Hollocks, M. J., Pickles, A., Howlin, P., & Simonoff, E. (2016). Dual Cognitive and Biological Correlates of Anxiety in Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *46*(10), 3295–3307. https://doi.org/10.1007/s10803-016-2878-2

Hollocks, M. J., Lerh, J. W., Magiati, I., Meiser-Stedman, R., & Brugha, T. S. (2019). Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. *Psychological Medicine*, *49*(4), 559–572. https://doi.org/10.1017/S0033291718002283

Hong, M. P., Eckert, E. M., Pedapati, E. V., Shaffer, R. C., Dominick, K. C., Wink, L. K., Sweeney, J. A., & Erickson, C. A. (2019). Differentiating social preference and social anxiety phenotypes in fragile X syndrome using an eye gaze analysis: a pilot study. *Journal of Neurodevelopmental Disorders*, *11*(1), 1. https://doi.org/10.1186/s11689-019-9262-4

Hove, O., & Havik, O, E. (2008). Mental Disorders and Problem Behavior in a Community Sample of Adults with Intellectual Disability: Three-month prevalence and comorbidity. *Journal of Mental Health Research in Intellectual Disabilities, 1*(4), 223-237. https://doi.org/10.1080/19315860802269198

Howard, K., Gibson, J., & Katsos, N. (2021). Parental Perceptions and Decisions Regarding Maintaining Bilingualism in Autism. *Journal of Autism and Developmental Disorders*, *51*(1), 179–192. https://doi.org/10.1007/s10803-020-04528-x

Hsieh, K., Scott, H. M., & Murthy, S. (2020). Associated Risk Factors for Depression and Anxiety in Adults With Intellectual and Developmental Disabilities: Five-Year Follow Up. *American Journal on Intellectual and Developmental Disabilities*, *125*(1), 49–63. https://doi.org/10.1352/1944-7558-125.1.49

Hunter, J., Rivero-Arias, O., Angelov, A., Kim, E., Fotheringham, I., & Leal, J. (2014). Epidemiology of fragile X syndrome: a systematic review and meta-analysis. *American Journal of Medical Genetics. Part A*, *164A*(7), 1648–1658. https://doi.org/10.1002/ajmg.a.36511

Hwang, Y., Arnold, S., Srasuebkul, P., & Trollor, J. (2020). Understanding anxiety in adults on the autism spectrum: An investigation of its relationship with intolerance of uncertainty, sensory sensitivities and repetitive behaviours. *Autism: The International Journal of Research and Practice*, *24*(2), 411–422. https://doi.org/10.1177/1362361319868907

Idring, S., Lundberg, M., Sturm, H., Dalman, C., Gumpert, C., Rai, D., Lee, B. K., & Magnusson, C. (2015). Changes in prevalence of autism spectrum disorders in 2001-2011: findings from the Stockholm youth cohort. *Journal of Autism and Developmental Disorders*, *45*(6), 1766–1773. https://doi.org/10.1007/s10803-014-2336-y

Ilyas, M., Mir, A., Efthymiou, S., & Houlden, H. (2020). The genetics of intellectual disability: advancing technology and gene editing. *F1000Research*, *9*, F1000 Faculty Rev-22. https://doi.org/10.12688/f1000research.16315.1

Jabbi, M., Chen, Q., Turner, N., Kohn, P., White, M., Kippenhan, J, S., Dickinson, D., Kolachana, B., Mattay, V., Weinberger, D, R., & Berman, K F. (2015). Variation in the Williams syndrome GTF2I gene and anxiety proneness interactively affect prefrontal cortical response to aversive stimuli. *Transl Psychiatry*, 5(8): Article e622. https://doi.org/10.1038/tp.2015.98

Jack, A., & A Pelphrey, K. (2017). Annual Research Review: Understudied populations within the autism spectrum - current trends and future directions in neuroimaging research. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *58*(4), 411–435. https://doi.org/10.1111/jcpp.12687

Jakobsen, J. C., Gluud, C., Wetterslev, J., & Winkel, P. (2017). When and how should multiple imputation be used for handling missing data in randomised clinical trials - a practical guide with flowcharts. *BMC Medical Research Methodology*, *17*(1), 162. https://doi.org/10.1186/s12874-017-0442-1

James, L. C. (2006). Integrating Clinical Psychology into Primary Care Settings. *Journal of Clinical Psychology, 62*(10), 1207-1212. https://doi.org/10.1002/jclp.20306

James, S, L., Abate, D., Abate, K, H., Abay, S, M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A., Abdollahpour, I., Abdulkader, R, S., Abebe, Z., Abera S, F., Abil, O, Z., Abraha, H, N., Abu-Raddad, L, J., Abu-Rmeileh, N, M, E., Accrombessi, M, M, K., et al. (2018). GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet, 392*(10159), 1789-1858. https://doi.org/10.1016/S0140-6736(18)32279-7

Javaid, A., Rushforth, E., Sajja, S., & Michael, D. (2021). Functional gastrointestinal disorders in patients with intellectual disability. *PROGRESS in Neurology and Psychiatry, 25*(2), 15-20. https://doi.org/10.1002/pnp.705

Jenkinson, R., Milne, E., & Thompson, A. (2020). The relationship between intolerance of uncertainty and anxiety in autism: A systematic literature review and meta-analysis. *Autism: The International Journal of Research and Practice*, *24*(8), 1933–1944. https://doi.org/10.1177/1362361320932437

Jolin, E, M., Weller, R, A., & Weller, E, B. (2012). Occurrence of affective disorders compared to other psychiatric disorders in children and adolescents with 22q11.2 deletion syndrome. *J Affect Disord*, *136*(3), 222-228. https://doi.org/10.1016/j.jad.2010.11.025

Jones, E. K., Hanley, M., & Riby, D. M. (2020). Distraction, distress and diversity: Exploring the impact of sensory processing differences on learning and school life for pupils with autism spectrum disorders. *Research in Autism Spectrum Disorders, 72*. https://doi.org/10.1016/j.rasd.2020.101515

Joosten, A. V., Bundy, A. C., & Einfeld, S. L. (2009). Intrinsic and extrinsic motivation for stereotypic and repetitive behavior. *Journal of Autism and Developmental Disorders*, *39*(3), 521–531. https://doi.org/10.1007/s10803-008-0654-7

Joosten, A. V., & Bundy, A. C. (2010). Sensory processing and stereotypical and repetitive behaviour in children with autism and intellectual disability. *Australian Occupational Therapy Journal*, *57*(6), 366–372. https://doi.org/10.1111/j.1440-1630.2009.00835.x

Joosten, A. V., Bundy, A. C., & Einfeld, S. L. (2012). Context influences the motivation for stereotypic and repetitive behaviour in children diagnosed with intellectual disability with and without autism. *Journal of Applied Research in Intellectual Disabilities: JARID*, *25*(3), 262–270. https://doi.org/10.1111/j.1468-3148.2011.00663.x

Joyce, C., Honey, E., Leekam, S. R., Barrett, S. L., & Rodgers, J. (2017). Anxiety, Intolerance of Uncertainty and Restricted and Repetitive Behaviour: Insights Directly from Young People with ASD. *Journal of Autism and Developmental Disorders*, *47*(12), 3789–3802. https://doi.org/10.1007/s10803-017-3027-2

Kadwa, R. A., Sahu, J. K., Singhi, P., Malhi, P., & Mittal, B. R. (2019). Prevalence and Characteristics of Sensory Processing Abnormalities and its Correlation with FDG-PET Findings in Children with Autism. *Indian Journal of Pediatrics*, *86*(11), 1036–1042. https://doi.org/10.1007/s12098-019-03061-9

Kaiser, H, F. (1960). The Application of Electronic Computers to Factor Analysis. *Educational and Psychological Measurement, 20(*1), 141-151. https://doi.org/10.1177/001316446002000116

Kaiser, H, F. (1974). An index of factorial simplicity. *Psychometrika, 39*(1), 31-36. https://doi.org/10.1007/BF02291575

Kapp, S. K., Steward, R., Crane, L., Elliott, D., Elphick, C., Pellicano, E., & Russell, G. (2019). 'People should be allowed to do what they like': Autistic adults' views and experiences of stimming. *Autism: The International Journal of Research and Practice*, *23*(7), 1782–1792. https://doi.org/10.1177/1362361319829628

Karam, S. M., Riegel, M., Segal, S. L., Félix, T. M., Barros, A. J., Santos, I. S., Matijasevich, A., Giugliani, R., & Black, M. (2015). Genetic causes of intellectual disability in a birth cohort: a population-based study. *American Journal of Medical Genetics. Part A*, *167*(6), 1204–1214. https://doi.org/10.1002/ajmg.a.37011

Karimi, P., Kamali, E., Mousavi, S. M., & Karahmadi, M. (2017). Environmental factors influencing the risk of autism. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences*, *22*, 27. https://doi.org/10.4103/1735-1995.200272

Kaufman, L., Ayub, M. & Vincent, J.B. (2010). The genetic basis of non-syndromic intellectual disability: a review. *J Neurodevelop Disord, 2,* 182–209. https://doi.org/10.1007/s11689-010-9055-2

Kaufmann, W. E., Kidd, S. A., Andrews, H. F., Budimirovic, D. B., Esler, A., Haas-Givler, B., Stackhouse, T., Riley, C., Peacock, G., Sherman, S. L., Brown, W. T., & Berry-Kravis, E. (2017). Autism Spectrum Disorder in Fragile X Syndrome: Cooccurring Conditions and Current Treatment. *Pediatrics*, *139*(Suppl 3), S194–S206. https://doi.org/10.1542/peds.2016-1159F

Kaur, Y., de Souza, R, J., Gibson, W, T., & Meyre, D. (2017). A Systematic Review of Genetic Syndromes with Obesity. *Obes Rev*, *18*(6) 603-634. https://doi.org/10.1111/obr.12531

Keating, C. T., & Cook, J. L. (2020). Facial Expression Production and Recognition in Autism Spectrum Disorders: A Shifting Landscape. *Child and Adolescent Psychiatric Clinics of North America*, *29*(3), 557–571. https://doi.org/10.1016/j.chc.2020.02.006

Keith, J. M., Jamieson, J. P., & Bennetto, L. (2019). The Importance of Adolescent Self-Report in Autism Spectrum Disorder: Integration of Questionnaire and Autonomic Measures. *Journal of Abnormal Child Psychology*, *47*(4), 741–754. https://doi.org/10.1007/s10802-018-0455-1

Kennert, B, A., Harshorne, T, S., Kanouse, S., & Johnson, C. (2020). Parent survey of sleep problems among children with CHARGE syndrome. *Res Dev Disabil*, *101.* https://doi.org/10.1016/j.ridd.2020.103614

Kent, R., & Simonoff, E. (2017). Prevalence of Anxiety in Autism Spectrum Disorders. In *Anxiety in Children and Adolescents with Autism Spectrum Disorder: Evidence-Based Assessment and Treatment* (pp. 5-32). Elsevier Inc.. https://doi.org/10.1016/B978-0-12-805122-1.00002-8

Kerns, C, M., & Kendall, P, C. (2012). The Presentation and Classification of Anxiety in Autism Spectrum Disorder. *Clinical Psychology Science and Practice, 19*(4), 323-347. https://doi.org/10.1111/cpsp.12009

Kerns, C. M., Kendall, P. C., Berry, L., Souders, M. C., Franklin, M. E., Schultz, R. T., Miller, J., & Herrington, J. (2014). Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *44*(11), 2851–2861. https://doi.org/10.1007/s10803-014-2141-7

Kerns, C. M., Kendall, P. C., Zickgraf, H., Franklin, M. E., Miller, J., & Herrington, J. (2015). Not to be overshadowed or overlooked: functional impairments associated with comorbid anxiety disorders in youth with ASD. *Behavior Therapy*, *46*(1), 29–39. https://doi.org/10.1016/j.beth.2014.03.005

Kerns, C. M., Rump, K., Worley, J., Kratz, H., McVey, A., Herrington, J., & Miller, J. (2016). The Differential Diagnosis of Anxiety Disorders in Cognitively-Able Youth with Autism. *Cognitive and Behavioral Practice, 23*(4), 530-547. https://doi.org/10.1016/j.cbpra.2015.11.004

Kidd, S. A., Lachiewicz, A., Barbouth, D., Blitz, R. K., Delahunty, C., McBrien, D., Visootsak, J., & Berry-Kravis, E. (2014). Fragile X syndrome: a review of associated medical problems. *Pediatrics*, *134*(5), 995–1005. https://doi.org/10.1542/peds.2013-4301

Kildahl, A. N., Helverschou, S. B., Bakken, T. L., & Oddli, H. W. (2020). "If we do not look for it, we do not see it": Clinicians' experiences and understanding of identifying post-traumatic stress disorder in adults with autism and intellectual disability. *Journal of Applied Research in Intellectual Disabilities: JARID*, *33*(5), 1119–1132. https://doi.org/10.1111/jar.12734

Kirby, A. V., Boyd, B. A., Williams, K. L., Faldowski, R. A., & Baranek, G. T. (2017). Sensory and repetitive behaviors among children with autism spectrum disorder at home. *Autism: The International Journal of Research and Practice*, *21*(2), 142–154. https://doi.org/10.1177/1362361316632710

Kirkovski, M., Enticott, P. G., & Fitzgerald, P. B. (2013). A review of the role of female gender in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *43*(11), 2584–2603. https://doi.org/10.1007/s10803-013-1811-1

Klein, A, J., Armstrong, B, L., Greer, M, K., & Brown, F, R. (1990). Hyperacusis and Otitis Media in Individuals with Williams Syndrome. *J Speech Hear Res*, *55*(2), 339-344. https://doi.org/10.1044/jshd.5502.339

Klein-Tasman, B. P., & Mervis, C. B. (2018). Autism Spectrum Symptomatology Among Children with Duplication 7q11.23 Syndrome. *Journal of Autism and Developmental Disorders*, *48*(6), 1982–1994. https://doi.org/10.1007/s10803-017-3439-z

Kline, A. D., Moss, J. F., Selicorni, A., Bisgaard, A. M., Deardorff, M. A., Gillett, P. M., Ishman, S. L., Kerr, L. M., Levin, A. V., Mulder, P. A., Ramos, F. J., Wierzba, J., Ajmone, P. F., Axtell, D., Blagowidow, N., Cereda, A., Costantino, A., Cormier-Daire, V., FitzPatrick, D., Grados, M., … Hennekam, R. C. (2018). Diagnosis and management of Cornelia de Lange syndrome: first international consensus statement. *Nature Reviews. Genetics*, *19*(10), 649–666. https://doi.org/10.1038/s41576-018-0031-0

Kodituwakku P. W. (2007). Defining the behavioral phenotype in children with fetal alcohol spectrum disorders: a review. *Neuroscience and Biobehavioral Reviews*, *31*(2), 192–201. https://doi.org/10.1016/j.neubiorev.2006.06.020

Koenen, K, C., Ratanatharathorn, A., Ng, L., McLaughlin, K, A., Bromet, E, J., Stein, D, J., Karam, E, G., Ruscio, A, M., Benjet, C., Scott, K., Atwoli, L., Petukhova, M., Lim, C, C, W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonson, J., Bunting, B., Ciutan, M., de Girolamo, G.,… Kessler, R. C. (2017). Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med, 47*(13), 2260-2274. https://doi.org/10.1017/S0033291717000708

Kozlowska, K., Walker, P., McLean, L., & Carrive, P. (2015). Fear and the Defense Cascade: Clinical Implications and Management. *Harvard Review of Psychiatry*, *23*(4), 263–287. https://doi.org/10.1097/HRP.0000000000000065

Kripke, C. (2018). Adults with Developmental Disabilities: A Comprehensive Approach to Medical Care. *American Family Physician, 97*(10), 649-656.

Krysta, K., Romańczyk, M., Diefenbacher, A., & Krzystanek, M. (2021). Telemedicine Treatment and Care for Patients with Intellectual Disability. *International Journal of Environmental Research and Public Health*, *18*(4), 1746. https://doi.org/10.3390/ijerph18041746

Kushki, A., Drumm, E., Pla Mobarak, M., Tanel, N., Dupuis, A., Chau, T., & Anagnostou, E. (2013). Investigating the autonomic nervous system response to anxiety in children with autism spectrum disorders. *PloS One*, *8*(4), e59730. https://doi.org/10.1371/journal.pone.0059730

Kushlick, A., Blunden, R., & Cox, G. (1973). A method of rating behaviour characteristics for use in large scale surveys of mental handicap. *Psychological Medicine*, *3*(4), 466–478. https://doi.org/10.1017/s0033291700054271

Lai, M. C., Kassee, C., Besney, R., Bonato, S., Hull, L., Mandy, W., Szatmari, P., & Ameis, S. H. (2019). Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. *The Lancet. Psychiatry*, *6*(10), 819–829. https://doi.org/10.1016/S2215-0366(19)30289-5

Landis, J. R., & Koch, G. G. (1977). The Measurement of Observer Agreement for Categorical Data. *Biometrics*, *33*(1), 159–174. https://doi.org/10.2307/2529310

La Spata, M, G. (2019). Assessment and Intervention for Individuals with CHARGE Syndrome. *J Health Serv Psychol*, *45*(2), 58-64.

Lau, B. Y., Leong, R., Uljarevic, M., Lerh, J. W., Rodgers, J., Hollocks, M. J., South, M., McConachie, H., Ozsivadjian, A., Van Hecke, A., Libove, R., Hardan, A., Leekam, S., Simonoff, E., & Magiati, I. (2020). Anxiety in young people with autism spectrum disorder: Common and autism-related anxiety experiences and their associations with individual

characteristics. *Autism: The International Journal of Research and Practice*, *24*(5), 1111–1126. https://doi.org/10.1177/1362361319886246

Lautarescu, B. A., Holland, A. J., & Zaman, S. H. (2017). The Early Presentation of Dementia in People with Down Syndrome: A Systematic Review of Longitudinal Studies. *Neuropsychology Review*, *27*(1), 31–45. https://doi.org/10.1007/s11065-017-9341-9

Leekam, S., Tandos, J., McConachie, H., Meins, E., Parkinson, K., Wright, C., Turner, M., Arnott, B., Vittorini, L., & Le Couteur, A. (2007). Repetitive behaviours in typically developing 2-year-olds. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *48*(11), 1131–1138. https://doi.org/10.1111/j.1469-7610.2007.01778.x

Li, S. H., & Graham, B. M. (2017). Why are women so vulnerable to anxiety, trauma-related and stress-related disorders? The potential role of sex hormones. *The Lancet. Psychiatry*, *4*(1), 73–82. https://doi.org/10.1016/S2215-0366(16)30358-3

Liao, P., Vajdic, C., Trollor, J., & Reppermund, S. (2021). Prevalence and incidence of physical health conditions in people with intellectual disability - a systematic review. *PloS One*, *16*(8), e0256294. https://doi.org/10.1371/journal.pone.0256294

Lidstone, J., Uljarevic, M., Sullivan, J., Rodgers, J., McConachie, H., Freeston, M…Leekam, S. (2014). Relations among restricted and repetitive behaviors, anxiety and sensory features in children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 8*(2), 82-92.

Lin, L. Y., & Huang, P. C. (2019). Quality of life and its related factors for adults with autism spectrum disorder. *Disability and Rehabilitation*, *41*(8), 896–903. https://doi.org/10.1080/09638288.2017.1414887

Lindsay, W. R., & Michie, A. M. (1988). Adaptation of the Zung self-rating anxiety scale for people with a mental handicap. *Journal of Mental Deficiency Research*, *32 (Pt 6)*, 485–490. https://doi.org/10.1111/j.1365-2788.1988.tb01440.x

Little, R, J, A. (1988). A Test of Missing Completely at Random for Multivariate Data with Missing Values. *Journal of the American Statistical Association, 83*(404), 1198-1202. https://doi.org/10.1080/01621459.1988.10478722

Loomes, R., Hull, L., & Mandy, W. (2017). What Is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis. *Journal of the American Academy of Child and Adolescent Psychiatry, 56*(6), 466–474. https://doi.org/10.1016/j.jaac.2017.03.013

Lord, C., Rutter, M., Goode, S., Heemsbergen, J., Jordan, H., Mawhood, L., & Schopler, E. (1989). Autism diagnostic observation schedule: a standardized observation of communicative and social behavior. *Journal of Autism and Developmental Disorders*, *19*(2), 185–212. https://doi.org/10.1007/BF02211841

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Jr, Leventhal, B. L., DiLavore, P. C., Pickles, A., & Rutter, M. (2000). The autism diagnostic observation schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders*, *30*(3), 205–223.

Lord, C., Rutter, M., DiLavore, P, C., Risi, S., Gotham, K., & Bishop, S. (2012). *Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Manual (Part I): Modules 1–4.* Western Psychological Services.

Lotan, M., & Ben-Zeev, B. (2006). Rett syndrome. A review with emphasis on clinical characteristics and intervention. *The Scientific World Journal*, *6*, 1517–1541. https://doi.org/10.1100/tsw.2006.249

MacLennan, K., Roach, L., & Tavassoli, T. (2020). The Relationship between Sensory Reactivity Differences and Anxiety Subtypes in Autistic Children. *Autism Research, 13*(5), 785-795. https://doi.org/10.1002/aur.2259

MacLennan, K., Rossow, T., & Tavassoli, T. (2021). The relationship between sensory reactivity, intolerance of uncertainty and anxiety subtypes in preschool-age autistic children. *Autism: The International Journal of Research and Practice*, *25*(8), 2305–2316. https://doi.org/10.1177/13623613211016110

MacMahon, P., Stenfert Kroese, B., Jahoda, A., Stimpson, A., Rose, N., Rose, J., Townson, J., Hood, K., & Willner, P. (2015). 'It's made all of us bond since that course…' - a

qualitative study of service users' experiences of a CBT anger management group intervention. *Journal of Intellectual Disability Research: JIDR*, *59*(4), 342–352. https://doi.org/10.1111/jir.12144

Maddox, B. B., Dickson, K. S., Stadnick, N. A., Mandell, D. S., & Brookman-Frazee, L. (2021). Mental Health Services for Autistic Individuals Across the Lifespan: Recent Advances and Current Gaps. *Current Psychiatry Reports*, *23*(10), 66. https://doi.org/10.1007/s11920-021-01278-0

Madhavan G. (2019). Telepsychiatry in intellectual disability psychiatry: literature review. *BJPsych Bulletin*, *43*(4), 167–173. https://doi.org/10.1192/bjb.2019.5

Maeng, L. Y., & Milad, M. R. (2015). Sex differences in anxiety disorders: Interactions between fear, stress, and gonadal hormones. *Hormones and Behavior*, *76*, 106–117. https://doi.org/10.1016/j.yhbeh.2015.04.002

Magiati, I., Moss, J., Charman, T., & Howlin, P. (2011). Patterns of change in children with autism spectrum disorders who received community based comprehensive interventions in their pre-school years: a seven-year follow-up study. *Research in Autism Spectrum Disorders, 5*(3), 1016-1027. https://doi.org/10.1016/j.rasd.2010.11.007

Magiati, I., Ong, C., Lim, X. Y., Tan, J. W., Ong, A. Y., Patrycia, F., Fung, D. S., Sung, M., Poon, K. K., & Howlin, P. (2016). Anxiety symptoms in young people with autism spectrum disorder attending special schools: Associations with gender, adaptive functioning and autism symptomatology. *Autism: The International Journal of Research and Practice*, *20*(3), 306–320. https://doi.org/10.1177/1362361315577519

Magiati, I., Lerh, J. W., Hollocks, M. J., Uljarevic, M., Rodgers, J., McConachie, H., Ozsivadjian, A., South, M., Van Hecke, A., Hardan, A., Libove, R., Leekam, S., & Simonoff, E. (2017). The measurement properties of the spence children's anxiety scale-parent version in a large international pooled sample of young people with autism spectrum disorder. *Autism Research: Official Journal of the International Society for Autism Research*, *10*(10), 1629–1652. https://doi.org/10.1002/aur.1809

Maïano, C., Coutu, S., Tracey, D., Bouchard, S., Lepage, G., Morin, A, J, S., & Moullec, G. (2018). Prevalence of anxiety and depressive disorders among youth with intellectual disabilities: A systematic review and meta-analysis. *J Affect Disord, 236*, 230-242. https://doi.org/10.1016/j.jad.2018.04.029

Maljaars, J., Noens, I., Scholte, E., & van Berckelaer-Onnes, I. (2012). Language in Low-Functioning Children with Autistic Disorder: Differences Between Receptive and Expressive Skills and Concurrent Predictors of Language. *Journal of Autism and Developmental Disorders, 42*, 2181-2191. https://doi.org/10.1007/s10803-012-1476-1

Marco, E. J., Hinkley, L. B., Hill, S. S., & Nagarajan, S. S. (2011). Sensory processing in autism: a review of neurophysiologic findings. *Pediatric Research*, *69*(5 Pt 2), 48R–54R. https://doi.org/10.1203/PDR.0b013e3182130c54

Marlborough, M., Welham, A., Jones, C., Reckless, S., & Moss, J. (2021). Autism spectrum disorder in females with fragile X syndrome: a systematic review and meta-analysis of prevalence. *Journal of Neurodevelopmental Disorders*, *13*(1), 28. https://doi.org/10.1186/s11689-021-09362-5

Martin, N., Oliver, C., & Hall, S. (2000). Obswin, Version 3.0. Birmingham: University of Birmingham.

Marvin, A. R., Marvin, D. J.,x Lipkin, P. H., & Law, J. K. (2017). Analysis of Social Communication Questionnaire (SCQ) Screening for Children Less Than Age 4. *Current Developmental Disorders Reports, 4*(4), 137–144. https://doi.org/10.1007/s40474-017-0122-1

Maskey, M., Lowry, J., Rodgers, J., McConachie, H., & Parr, J. R. (2014). Reducing specific phobia/fear in young people with autism spectrum disorders (ASDs) through a virtual reality environment intervention. *PloS One*, *9*(7), e100374. https://doi.org/10.1371/journal.pone.0100374

Mason, J., & Scior, K. (2004). 'Diagnostic Overshadowing' Amongst Clinicians working with People with Intellectual Disabilities in the UK. *Journal of Applied Research in Intellectual Disabilities, 17*(2), 85-90. https://doi.org/10.1111/j.1360-2322.2004.00184.x

Matson, J. L., Gardner, W. I., Coe, D. A., & Sovner, R. (1991). A scale for evaluating emotional disorders in severely and profoundly mentally retarded persons. Development of the Diagnostic Assessment for the Severely Handicapped (DASH) scale. *The British Journal of Psychiatry: The Journal of Mental Science*, *159*, 404–409. https://doi.org/10.1192/bjp.159.3.404

Matson, J. L. (1995). *The Diagnostic Assessment for the Severely Handicapped, Revised* (DASH-II). Disability Consultants, LLC.

Matson, J. L., & Shoemaker, M. (2009). Intellectual disability and its relationship to autism spectrum disorders. *Research in Developmental Disabilities*, *30*(6), 1107–1114. https://doi.org/10.1016/j.ridd.2009.06.003

Maulik, P. K., Mascarenhas, M. N., Mathers, C. D., Dua, T., & Saxena, S. (2011). Prevalence of intellectual disability: a meta-analysis of population-based studies. *Research in Developmental Disabilities, 32*(2), 419–436. https://doi.org/10.1016/j.ridd.2010.12.018

Mayes, S. D., Calhoun, S. L., Murray, M. J., & Zahid, J. (2011). Variables Associated with Anxiety and Depression in Children with Autism. *Journal of Developmental and Physical Disabilities, 23*, 325-337. https://doi.org/10.1007/s10882-011-9231-7

Mayes, S. D., Baweja, R., Waschbusch, D. A., & Calhoun, S. L. (2022). Relationship between IQ and Internalizing and Externalizing Symptoms in Children with Autism and Children with ADHD. *Journal of Mental Health Research in Intellectual Disabilities, 15*(2), 95-110, DOI: 10.1080/19315864.2022.2029643

Mazurek, M. O., Vasa, R. A., Kalb, L. G., Kanne, S. M., Rosenberg, D., Keefer, A., Murray, D. S., Freedman, B., & Lowery, L. A. (2013). Anxiety, sensory over-responsivity, and gastrointestinal problems in children with autism spectrum disorders. *Journal of Abnormal Child Psychology*, *41*(1), 165–176. https://doi.org/10.1007/s10802-012-9668-x

Mazza, M. G., Rossetti, A., Crespi, G., & Clerici, M. (2020). Prevalence of co-occurring psychiatric disorders in adults and adolescents with intellectual disability: A systematic review and meta-analysis. *Journal of Applied Research in Intellectual Disabilities: JARID*, *33*(2), 126–138. https://doi.org/10.1111/jar.12654

McConachie, H., McLaughlin, E., Grahame, V., Taylor, H., Honey, E., Tavernor, L., Rodgers, J., Freeston, M., Hemm, C., Steen, N., & Le Couteur, A. (2014). Group therapy for anxiety in children with autism spectrum disorder. *Autism: The International Journal of Research and Practice*, *18*(6), 723–732. https://doi.org/10.1177/1362361313488839

McHugh M. L. (2012). Interrater reliability: the kappa statistic. *Biochemia Medica, 22*(3), 276–282.

McKechanie, A. G., Barnicoat, A., Trender-Gerhard, I., Allison, M., & Stanfield, A. C. (2019). Fragile X-associated conditions: implications for the whole family. *The British Journal of General Practice: The Journal of the Royal College of General Practitioners, 69*(686), 460–461. https://doi.org/10.3399/bjgp19X705425

McKenzie, K., Milton, M., Smith, G., Ouellette-Kuntz, H. (2016). Systematic Review of the Prevalence and Incidence of Intellectual Disabilities: Current Trends and Issues. *Curr Dev Disord Rep, 3,* 104–115. https://doi.org/10.1007/s40474-016-0085-7

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research*, *45*(8), 1027–1035. https://doi.org/10.1016/j.jpsychires.2011.03.006

McNally, P., Taggart, L., & Shevlin, M. (2021). Trauma experiences of people with an intellectual disability and their implications: A scoping review. *Journal of Applied Research in Intellectual Disabilities, 34*(4), 927-949. https://doi.org/10.1111/jar.12872

Meier, S, M., & Deckert, J. (2019). Genetics of Anxiety Disorders. *Curr Psychiatry Rep*, *21*. https://doi.org/10.1007/s11920-019-1002-7

Mennin, D. S. (2004). Emotion regulation therapy for generalized anxiety disorder. *Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice*, *11*(1), 17-29. https://doi.org/10.1002/cpp.389

Mervis, C, B., Dida, J., Lam, E., Crawford-Zelli, N, A., Young, E, J., Henderson, D, R., Onay, T., Morris, C, A., Woodruff-Borden, J., Yeomans, J., & Osborne, L, R. (2012).

Duplication of GTF2I Results in Separation Anxiety in Mice and Humans. *Am J Hum Genet, 90*(6), 1064-1670. https://doi.org/10.1016/j.ajhg.2012.04.012

Mian, N. D., Carter, A. S., Pine, D. S., Wakschlag, L. S., & Briggs-Gowan, M. J. (2015). Development of a novel observational measure for anxiety in young children: The Anxiety Dimensional Observation Scale. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *56*(9), 1017–1025. https://doi.org/10.1111/jcpp.12407

Miller, L. J., Anzalone, M. E., Lane, S. J., Cermak, S. A., & Osten, E. T. (2007). Concept evolution in sensory integration: a proposed nosology for diagnosis. *The American Journal of Occupational Therapy: Official Publication of the American Occupational Therapy Association*, *61*(2), 135–140. https://doi.org/10.5014/ajot.61.2.135

Mindham, J., & Espie, C. A. (2003). Glasgow Anxiety Scale for people with an Intellectual Disability (GAS-ID): development and psychometric properties of a new measure for use with people with mild intellectual disability. *Journal of Intellectual Disability Research*, *47*(1), 22-30. https://doi.org/10.1046/j.1365-2788.2003.00457.x

Mingins, J. E., Tarver, J., Waite, J., Jones, C., & Surtees, A. D. (2021). Anxiety and intellectual functioning in autistic children: A systematic review and meta-analysis. *Autism: The International Journal of Research and Practice*, *25*(1), 18–32. https://doi.org/10.1177/1362361320953253

Modabbernia, A., Velthorst, E., & Reichenberg, A. (2017). Environmental risk factors for autism: an evidence-based review of systematic reviews and meta-analyses. *Molecular Autism*, *8*, 13. https://doi.org/10.1186/s13229-017-0121-4

Mody, M., & Belliveau, J. W. (2013). Speech and Language Impairments in Autism: Insights from Behavior and Neuroimaging. *North American Journal of Medicine & Science, 5*(3), 157–161. https://doi.org/10.7156/v5i3p157

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Molteno, G., Molteno, C. D., Finchilescu, G., & Dawes, A. R. (2001). Behavioural and emotional problems in children with intellectual disability attending special schools in Cape Town, South Africa. *Journal of Intellectual Disability Research: JIDR*, *45*(Pt 6), 515–520. https://doi.org/10.1046/j.1365-2788.2001.00368.x

Morgan, V. A., Leonard, H., Bourke, J., & Jablensky, A. (2008). Intellectual disability co-occurring with schizophrenia and other psychiatric illness: population-based study. *The British Journal of Psychiatry: The Journal of Mental Science*, *193*(5), 364–372. https://doi.org/10.1192/bjp.bp.107.044461

Morris, C. A., Mervis, C. B., Paciorkowski, A. P., Abdul-Rahman, O., Dugan, S. L., Rope, A. F., Bader, P., Hendon, L. G., Velleman, S. L., Klein-Tasman, B. P., & Osborne, L. R. (2015). 7q11.23 Duplication syndrome: Physical characteristics and natural history. *American Journal of Medical Genetics. Part A*, *167A*(12), 2916–2935. https://doi.org/10.1002/ajmg.a.37340

Morris, C. A., Braddock, S. R., & COUNCIL ON GENETICS (2020). Health Care Supervision for Children With Williams Syndrome. *Pediatrics*, *145*(2), e20193761. https://doi.org/10.1542/peds.2019-3761

Moskowitz, L. J., Mulder, E., Walsh, C. E., McLaughlin, D. M., Zarcone, J. R., Proudfit, G. H., & Carr, E. G. (2013). A multimethod assessment of anxiety and problem behavior in children with autism spectrum disorders and intellectual disability. *American Journal on Intellectual and Developmental Disabilities*, *118*(6), 419–434. https://doi.org/10.1352/1944.7558.118.6.419

Moskowitz, L. J., Rosen, T., Lerner, M. D., & Levine, K. (2017). Chapter 5 - Assessment of Anxiety in Youth With Autism Spectrum Disorder. In Kerns, C., M., Renno, P., Storch, E. A., Kendall, P. C., & Wood, J, J. (Eds.), *Anxiety in Children and Adolescents with Autism Spectrum Disorder: Evidence-based Assessment and Treatment* (pp. 79-104). Academic Press. https://doi.org/10.1016/B978-0-12-805122-1.00005-3

Moskowitz, L. J., & Braconnier, M. (2022). Assessing anxiety in youth with autism spectrum disorder. *Psychology in the Schools*. https://doi.org/10.1002/pits.22669

Moss, S., Patel, P., Prosser, H., Goldberg, D., Simpson, N., Rowe, S., & Lucchino, R. (1993). Psychiatric morbidity in older people with moderate and severe learning disability. I: Development and reliability of the patient interview (PAS-ADD). *The British Journal of Psychiatry: The Journal of Mental Science*, *163*, 471–480. https://doi.org/10.1192/bjp.163.4.471

Moss, S., Prosser, H., Costello, H., Simpson, N., Patel, P., Rowe, S., Turner, S., & Hatton, C. (1998). Reliability and validity of the PAS-ADD Checklist for detecting psychiatric disorders in adults with intellectual disability. *Journal of Intellectual Disability Research: JIDR*, *42 (Pt 2)*, 173–183. https://doi.org/10.1046/j.1365-2788.1998.00116.x

Moss, J., Oliver, C., Hall, S., Arron, K., Sloneem, J., & Petty, J. (2005). The association between environmental events and self-injurious behaviour in Cornelia de Lange syndrome. *Journal of Intellectual Disability Research: JIDR*, *49*(Pt 4), 269–277. https://doi.org/10.1111/j.1365-2788.2005.00649.x

Moss, J., Oliver, C., Nelson, L., Richards, C., & Hall, S. (2013). Delineating the profile of autism spectrum disorder characteristics in Cornelia de Lange and Fragile X syndromes. *American Journal on Intellectual and Developmental Disabilities*, *118*(1), 55–73. https://doi.org/10.1352/1944-7558-118.1.55

Moss, P., Howlin, P., Savage, S., Bolton, P., & Rutter, M. (2015). Self and informant reports of mental health difficulties among adults with autism findings from a long-term follow-up study. *Autism: The International Journal of Research and Practice*, *19*(7), 832–841. https://doi.org/10.1177/1362361315585916

Munir, K, M. (2016). The co-occurrence of mental disorders in children and adolescents with intellectual disability/intellectual developmental disorder. *Curr Opin Psychiatry*, *29*(2), 95-102. https://doi.org/10.1097/YCO.0000000000000236

Murphy, J., & Cameron, L. (2008). The effectiveness of Talking Mats® with people with intellectual disability. *British Journal of Learning Disabilities, 36*(4), 232-241. https://doi.org/10.1111/j.1468-3156.2008.00490.x

Muskett, A., Radtke, S., White, S., & Ollendick, T. (2019). Autism Spectrum Disorder and Specific Phobia: the Role of Sensory Sensitivity: Brief Review. *Rev J Autism Dev Disord, 6*, 289–293. https://doi.org/10.1007/s40489-019-00159-w

Nash, J. M., McKay, K. M., Vogel, M. E., & Masters, K. S. (2012). Functional roles and foundational characteristics of psychologists in integrated primary care. *Journal of Clinical Psychology in Medical Settings*, *19*(1), 93–104. https://doi.org/10.1007/s10880-011-9290-z

National Institute for Health and Care Excellence. [NICE] (2011). *Autism spectrum disorder in under 19s: recognition, referral and diagnosis* [NICE Clinical Guideline No. 128]. https://www.nice.org.uk/guidance/cg128

National Institute for Health and Care Excellence. [NICE] (2012). *Autism spectrum disorder in adults: diagnosis and management* [NICE Clinical Guideline No. 142]. https://www.nice.org.uk/guidance/cg142

National Institute for Health and Care Excellence. [NICE] (2013). *Autism spectrum disorder in under 19s: support and management.* https://www.nice.org.uk/guidance/cg170/chapter/1-recommendations

National Institute for Health and Care Excellence [NICE]. (2016). *Mental health problems in people with learning disabilities: prevention, assessment, and management* [NICE Guideline No. 54]. https://www.nice.org.uk/guidance/ng54

Nauta, M. H., Scholing, A., Rapee, R. M., Abbott, M., Spence, S. H., & Waters, A. (2004). A parent-report measure of children's anxiety: psychometric properties and comparison with child-report in a clinic and normal sample. *Behaviour Research and Therapy*, *42*(7), 813–839. https://doi.org/10.1016/S0005-7967(03)00200-6

Neece, C. L., Baker, B. L., Blacher, J., & Crnic, K. A. (2011). Attention-deficit/hyperactivity disorder among children with and without intellectual disability: an examination across time. *Journal of Intellectual Disability Research: JIDR*, *55*(7), 623–635. https://doi.org/10.1111/j.1365-2788.2011.01416.x

Neil, L., Olsson, N. C., & Pellicano, E. (2016). The Relationship Between Intolerance of Uncertainty, Sensory Sensitivities, and Anxiety in Autistic and Typically Developing Children.

Journal of Autism and Developmental Disorders, 46(6), 1962–1973. https://doi.org/10.1007/s10803-016-2721-9

Nelson, L., Crawford, H., Reid, D., Moss, J., & Oliver, C. (2017). An experimental study of executive function and social impairment in Cornelia de Lange syndrome. *Journal of Neurodevelopmental Disorders*, *9*(1), 33. https://doi.org/10.1186/s11689-017-9213-x

Neuhaus, E., Bernier, R. A., Tham, S. W., & Webb, S. J. (2018). Gastrointestinal and Psychiatric Symptoms Among Children and Adolescents With Autism Spectrum Disorder. *Frontiers in Psychiatry*, *9*, 515. https://doi.org/10.3389/fpsyt.2018.00515

Nimmo-Smith, V., Heuvelman, H., Dalman, C., Lundberg, M., Idring, S., Carpenter, P., Magnusson, C., & Rai, D. (2020). Anxiety Disorders in Adults with Autism Spectrum Disorder: A Population-Based Study. *Journal of Autism and Developmental Disorders*, *50*(1), 308–318. https://doi.org/10.1007/s10803-019-04234-3

Norrelgen, F., Fernell, E., Eriksson, M., Hedvall, Å., Persson, C., Sjölin, M., Gillberg, C., & Kjellmer, L. (2015). Children with autism spectrum disorders who do not develop phrase speech in the preschool years. *Autism: The International Journal of Research and Practice*, *19*(8), 934–943. https://doi.org/10.1177/1362361314556782

Nosik, M. R., & Carr, J. E. (2015). On the Distinction Between the Motivating Operation and Setting Event Concepts. *The Behavior Analyst*, *38*(2), 219–223. https://doi.org/10.1007/s40614-015-0042-5

Nurjannah, I., & Siwi, S. (2017). Guidelines for analysis on measuring interrater reliability of nursing outcome classification. *International Journal of Research in Medical Sciences, 5*(4), 1169-1175. doi:http://dx.doi.org/10.18203/2320-6012.ijrms20171220

Oakes, A., Thurman, A. J., McDuffie, A., Bullard, L. M., Hagerman, R. J., & Abbeduto, L. (2016). Characterising repetitive behaviours in young boys with fragile X syndrome. *Journal of Intellectual Disability Research: JIDR*, *60*(1), 54–67. https://doi.org/10.1111/jir.12234

Olatunji, B, O., Cisler, J, M., & Tolin, D, F. (2007). Quality of life in the anxiety disorders: a meta-analytic review. *Clin Psychol Rev*, *27*(5), 572-581. https://doi.org/10.1016/j.cpr.2007.01.015

Oliver, C., Berg, K., Moss, J., Arron, K., & Burbidge, C. (2011). Delineation of behavioral phenotypes in genetic syndromes: characteristics of autism spectrum disorder, affect and hyperactivity. *Journal of Autism and Developmental Disorders*, *41*(8), 1019–1032. https://doi.org/10.1007/s10803-010-1125-5

Oliver, C. (2017). The importance of knowing when to be precise. *Journal of Intellectual Disability Research, 61*(12), 1079-1082. https://doi.org/10.1111/jir.12446

Oliver, C. (2019). The importance of knowing when to be precise: there is both a lumper and a splitter in all of us. *Journal of Intellectual Disability Research, 63*(9), 1075-1077. https://doi.org/10.1111/jir.12677

Oliver, C., Adams, D., Allen, D., Crawford, H., Heald, M., Moss, J., Richards, C., Waite, J., Welham, A., Wilde, L., & Woodcock, K. (2020). The behaviour and wellbeing of children and adults with severe intellectual disability and complex needs: the Be-Well checklist for carers and professionals. *Pediatrics and Child Health, 30*(12), 416-424. https://doi.org/10.1016/j.paed.2020.09.003

Ong, N., Long, J. C., Weise, J., & Walton, M. (2022). Responding to safe care: Healthcare staff experiences caring for a child with intellectual disability in hospital. Implications for practice and training. *Journal of Applied Research in Intellectual Disabilities: JARID*, *35*(3), 675–690. https://doi.org/10.1111/jar.12978

Ormel, J., Petukhova, M., & Chatterji, S., Aguilar-Gaxiola, S., Alonson, J., Angermeyer, M, C., Bromet, E, J., Burger, H., Demyttenaere, K., de Girolamo, G., Haro, J, M., Hwang, I., Karam, E., Kawakami, N., Lepine, J, P., Medina-Mora, M, E., Posada-Villa, J., Sampson, N., Scott, K.,…Kessler, R. C. (2009). Disability and treatment of specific mental and physical disorders across the world: Results from the WHO Word Mental Health Surveys. *Br J Psychiatry, 192*(5), 368-375. https://doi.org/10.1192/bjp.bp.107.039107

Ouyang, L., Grosse, S. D., Riley, C., Bolen, J., Bishop, E., Raspa, M., & Bailey, D. B., Jr (2014). A comparison of family financial and employment impacts of fragile X syndrome,

autism spectrum disorders, and intellectual disability. *Research in Developmental Disabilities*, *35*(7), 1518–1527. https://doi.org/10.1016/j.ridd.2014.04.009

Ozsivadjian, A., Knott, F., & Magiati, I. (2012). Parent and child perspectives on the nature of anxiety in children and young people with autism spectrum disorders: a focus group study. *Autism: The International Journal of Research and Practice*, *16*(2), 107–121. https://doi.org/10.1177/1362361311431703

Ozsivadjian, A., Hibberd, C., & Hollocks, M. J. (2014). Brief report: The use of self-report measures in young people with autism spectrum disorder to access symptoms of anxiety, depression and negative thoughts. *Journal of Autism and Developmental Disorders*, *44*(4), 969–974. https://doi.org/10.1007/s10803-013-1937-1

Palmer, J., & Jenkins, J. (1982). The 'Wessex' Behaviour Rating System For Mentally Handicapped People: Reliability Study. *The British Journal of Mental Subnormality, 28*(55), 88-96. DOI: 10.1179/bjms.1982.011

Palmer, M., Paris Perez, J., Tarver, J., Cawthorne, T., Frayne, M., Webb, S., Baker, E., Yorke, I., Hay, D., Slonims, V., Pickles, A., Simonoff, E., Scott, S., & Charman, T. (2021). Development of the Observation Schedule for Children with Autism-Anxiety, Behaviour and Parenting (OSCA-ABP): A New Measure of Child and Parenting Behavior for Use with Young Autistic Children. *Journal of Autism and Developmental Disorders*, *51*(1), 1–14. https://doi.org/10.1007/s10803-020-04506-3

Papazoglou, A., Jacobson, L. A., McCabe, M., Kaufmann, W., & Zabel, T. A. (2014). To ID or not to ID? Changes in classification rates of intellectual disability using DSM-5. *Intellectual and Developmental Disabilities*, *52*(3), 165–174. https://doi.org/10.1352/1934-9556-52.3.165

Parr, J. R., Brice, S., Welsh, P., Ingham, B., Le Couteur, A., Evans, G., Monaco, A., Freeston, M., & Rodgers, J. (2020). Treating anxiety in autistic adults: study protocol for the Personalised Anxiety Treatment-Autism (PAT-A©) pilot randomised controlled feasibility trial. *Trials*, *21*(1), 265. https://doi.org/10.1186/s13063-020-4161-2

Patel, D. R., Apple, R., Kanungo, S., & Akkal, A. (2018). Intellectual disabilitiy: definitions, evaluation and principles of treatment. *Pediatric Medicine, 1*. doi:10.21037/pm.2018.12.02

Patrick, M. E., Shaw, K. A., Dietz, P. M., Baio, J., Yeargin-Allsopp, M., Bilder, D. A., Kirby, R. S., Hall-Lande, J. A., Harrington, R. A., Lee, L. C., Lopez, M., Daniels, J., & Maenner, M. J. (2021). Prevalence of intellectual disability among eight-year-old children from selected communities in the United States, 2014. *Disability and Health Journal*, *14*(2), 101023. https://doi.org/10.1016/j.dhjo.2020.101023

Pearson, E., Nielsen, E., Kita, S., Groves, L., Nelson, L., Moss, J., & Oliver, C. (2021). Low speech rate but high gesture rate during conversational interaction in people with Cornelia de Lange syndrome. *Journal of Intellectual Disability Research: JIDR*, *65*(6), 601–607. https://doi.org/10.1111/jir.12829

Perera, B., Audi, S., Solomou, S., Courtenay, K., & Ramsay, H. (2020). Mental and physical health conditions in people with intellectual disabilities: Comparing local and national data. *British Journal of Learning Disabilities, 48*(1), 19-27. https://doi.org/10.1111/bld.12304

Perry, V. (2019). Predicting anxiety within atypical development [Doctoral thesis, University of Warwick]. British Library. https://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.821143

Peters, M. D., Godfrey, C. M., Khalil, H., McInerney, P., Parker, D., & Soares, C. B. (2015). Guidance for conducting systematic scoping reviews. *International Journal of Evidence-Based Healthcare*, *13*(3), 141–146. https://doi.org/10.1097/XEB.0000000000000050

Polanczyk, G. V., Salum, G. A., Sugaya, L. S., Caye, A., & Rohde, L. A. (2015). Annual research review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *56*(3), 345–365. https://doi.org/10.1111/jcpp.12381

Polanin, J, R., Pigott, T, D., Espelage, D, L., & Grotpeter, J, K. (2019). Best practice guidelines for abstract screening large-evidence systematic reviews and meta-analyses. *Res Synth Methods*, *10*(3), 330-342. https://doi.org/10.1002/jrsm.1354

Pollak, R, M., Murphy, M, M., Epstein, M, P., Zwick, M, E., Klaiman, C., Saulnier, C, A., Emory 3q29 Project., & Mulle, J, G. (2019). Neuropsychiatric phenotypes and a distinct constellation of ASD features in 3q29 deletion syndrome: results from the 3q29 registry. *Mol Autism, 10,* 30. https://doi.org/10.1186/s13229-019-0281-5

Pollak, R, M., Zinsmeister, M, C., Murphy, M, M., Zwick, M, E., Emory 3q29 Project., & Mulle, J, G. (2020). New phenotypes associated with 3q29 duplication syndrome: Results from the 3q29 registry. *Am J Med Genet A*, *182*(5), 1152-1166. https://doi.org/10.1002/ajmg.a.61540

Procyshyn, T, L., Spence, J., Read, S., Watson, N, V., & Crespi, B, J. (2017). The Williams syndrome prosociality gene GTF2I mediates oxytocin reactivity and social anxiety in a healthy population. *Biol Lett*, *13*(4). https://doi.org/10.1098/rsbl.2017.0051

Rais, M., Binder, D. K., Razak, K. A., & Ethell, I. M. (2018). Sensory Processing Phenotypes in Fragile X Syndrome. *ASN Neuro*, *10*, 1759091418801092. https://doi.org/10.1177/1759091418801092

Rauch, A., Hoyer, J., Guth, S., Zweier, C., Kraus, C., Becker, C., Zenker, M., Hüffmeier, U., Thiel, C., Rüschendorf, F., Nürnberg, P., Reis, A., & Trautmann, U. (2006). Diagnostic yield of various genetic approaches in patients with unexplained developmental delay or mental retardation. *American Journal of Medical Genetics. Part A*, *140*(19), 2063–2074. https://doi.org/10.1002/ajmg.a.31416

Reardon, T. C., Gray, K. M., & Melvin, G. A. (2015). Anxiety disorders in children and adolescents with intellectual disability: Prevalence and assessment. *Research in Developmental Disabilities*, *36C*, 175–190. https://doi.org/10.1016/j.ridd.2014.10.007

Reed, V., & Witthcen, H, U. (1998). DSM-IV panic attacks and panic disorder in a community sample of adolescents and young adults: how specific are panic attacks? *J Psychiatr Res, 32*(6), 335-345. https://doi.org/10.1016/s0022-3956(98)00014-4

Reid, K. A., Smiley, E., & Cooper, S. A. (2011). Prevalence and associations of anxiety disorders in adults with intellectual disabilities. *Journal of Intellectual Disability Research: JIDR*, *55*(2), 172–181. https://doi.org/10.1111/j.1365-2788.2010.01360.x

Renno, P., & Wood, J. J. (2013). Discriminant and convergent validity of the anxiety construct in children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *43*(9), 2135–2146. https://doi.org/10.1007/s10803-013-1767-1

Rice, L. J., Woodcock, K., & Einfeld, S. L. (2018). The characteristics of temper outbursts in Prader-Willi syndrome. *American Journal of Medical Genetics. Part A, 176*(11), 2292–2300. https://doi.org/10.1002/ajmg.a.40480

Rich, A. J., DiGregorio, N., & Strassle, C. (2021). Trauma-informed care in the context of intellectual and developmental disability services: Perceptions of service providers. *Journal Of Intellectual Disabilities: JOID*, *25*(4), 603–618. https://doi.org/10.1177/1744629520918086

Richards, C., Moss, J., O'Farrell, L., Kaur, G., & Oliver, C. (2009). Social anxiety in Cornelia de Lange syndrome. *Journal of Autism and Developmental Disorders*, *39*(8), 1155–1162. https://doi.org/10.1007/s10803-009-0730-7

Richards, C., Jones, C., Groves, L., Moss, J., & Oliver, C. (2015). Prevalence of autism spectrum disorder phenomenology in genetic disorders: a systematic review and meta-analysis. *The Lancet. Psychiatry*, *2*(10), 909–916. https://doi.org/10.1016/S2215-0366(15)00376-4

Richards, C., Moss, J., Nelson, L., & Oliver, C. (2016). Persistence of self-injurious behaviour in autism spectrum disorder over 3 years: a prospective cohort study of risk markers. *J Neurodevelop Disord,* 8, 21. https://doi.org/10.1186/s11689-016-9153-x

Richardson, M., Garner, P., & Donegan, S. (2019). Interpretation of subgroup analyses in systematic reviews: A tutorial. *Clin Epidemiology Glob Health*, *7*(2), 192-198. https://doi.org/10.1016/j.cegh.2018.05.005

Roberts, J. E., Ezell, J. E., Fairchild, A. J., Klusek, J., Thurman, A. J., McDuffie, A., & Abbeduto, L. (2018). Biobehavioral composite of social aspects of anxiety in young adults with fragile X syndrome contrasted to autism spectrum disorder. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics: The Official Publication of the International Society of Psychiatric Genetics*, *177*(7), 665–675. https://doi.org/10.1002/ajmg.b.32674

Roberts, J. E., Crawford, H., Will, E. A., Hogan, A. L., McQuillin, S., Tonnsen, B. L., O'Connor, S., Roberts, D. A., & Brewe, A. M. (2019a). Infant Social Avoidance Predicts Autism but Not Anxiety in Fragile X Syndrome. *Frontiers in Psychiatry*, *10*, 199. https://doi.org/10.3389/fpsyt.2019.00199

Roberts, J., Crawford, H., Hogan, A. L., Fairchild, A., Tonnsen, B., Brewe, A., O'Connor, S., Roberts, D. A., & Abbeduto, L. (2019b). Social Avoidance Emerges in Infancy and Persists into Adulthood in Fragile X Syndrome. *Journal of Autism and Developmental Disorders*, *49*(9), 3753–3766. https://doi.org/10.1007/s10803-019-04051-8

Roberts, J., Bradshaw, J., Will, E., Hogan, A., McQuillin, S., & Hills, K. (2020). Emergence and rate of autism in fragile X syndrome across the first years of life. *Development and Psychopathology, 32*(4), 1335-1352. doi:10.1017/S0954579420000942

Robertson, J., Hatton, C., Emerson, E., & Baines, S. (2014). The impact of health checks for people with intellectual disabilities: An updated systematic review of evidence. *Research in Developmental Disabilities, 35*(10), 2450-2462. https://doi.org/10.1016/j.ridd.2014.06.007

Robertson, J., Hatton, C., Emerson, E., & Baines, S. (2015). Prevalence of epilepsy among people with intellectual disabilities: A systematic review. *Seizure*, *29*, 46–62. https://doi.org/10.1016/j.seizure.2015.03.016

Robertson, A. E., Stanfield, A. C., Watt, J., Barry, F., Day, M., Cormack, M., & Melville, C. (2018). The experience and impact of anxiety in autistic adults: A thematic analysis. *Research in Autism Spectrum Disorders, 46,* 8-18, https://doi.org/10.1016/j.rasd.2017.11.006

Rodgers, J., Glod, M., Connolly, B., & McConachie, H. (2012). The relationship between anxiety and repetitive behaviours in autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *42*(11), 2404–2409. https://doi.org/10.1007/s10803-012-1531-y

Rodgers, J., Wigham, S., McConachie, H., Freeston, M., Honey, E., & Parr, J. R. (2016). Development of the anxiety scale for children with autism spectrum disorder (ASC-ASD). *Autism research: Official Journal of the International Society for Autism Research*, *9*(11), 1205–1215. https://doi.org/10.1002/aur.1603

Rodgers, J., & Ofield, A. (2018). Understanding, Recognising and Treating Co-occurring Anxiety in Autism. *Current Developmental Disorders Reports*, *5*(1), 58–64. https://doi.org/10.1007/s40474-018-0132-7

Rodgers, J., Goodwin, J., Parr, J. R., Grahame, V., Wright, C., Padget, J., Garland, D., Osborne, M., Labus, M., Kernohan, A., & Freeston, M. (2019). Coping with Uncertainty in Everyday Situations (CUES©) to address intolerance of uncertainty in autistic children: study protocol for an intervention feasibility trial. *Trials*, *20*(1), 385. https://doi.org/10.1186/s13063-019-3479-0

Rodgers, J., Farquhar, K., Mason, D., Brice, S., Wigham, S., Ingham, B., Freeston, M., & Parr, J. R. (2020). Development and Initial Evaluation of the Anxiety Scale for Autism-Adults. *Autism in Adulthood, 2*(1), 24-33. http://doi.org/10.1089/aut.2019.0044

Roest, A, M., de Vries, Y, A., Lim, C, C, W., Wittchen, H-U., Stein, D, J., Adamowski, T., Al-Hamzawi, A., Bromet, E, J., Viana, M, C., de Girolamo, G., Demyttenaere, K., Florescu, S., Gureje, O., Haro, J, M., Hu, C., Karama, E, G., Caldas-de-Almeida, J, M., Kawakami, N., Lépine, J, P.,… de Jonge, P. (2019). A comparison of DSM-5 and DSM-IV agoraphobia in the World Mental Health Surveys. *Depress Anxiety, 36*(6), 499-510. https://doi.org/10.1002/da.22885

Rogers, C. L., Goddard, L., Hill, E. L., Henry, L. A., & Crane, L. (2016). Experiences of diagnosing autism spectrum disorder: A survey of professionals in the United Kingdom. *Autism: The International Journal of Research and Practice*, *20*(7), 820–831. https://doi.org/10.1177/1362361315611109

Rosen, T. E., Connell, J. E., & Kerns, C. M. (2016). A review of behavioral interventions for anxiety-related behaviors in lower-functioning individuals with autism. *Behavioral Interventions, 31*(2), 120–143. https://doi.org/10.1002/bin.1442

Rowe, G., & Nevin, H. (2013). Bringing 'patient voice' into psychological formulations of in-patients with intellectual disabilities, autism spectrum disorder and severe challenging behaviours: report of a service improvement project. *British Journal of Learning Disabilities, 42*(3), 177-184. https://doi.org/10.1111/bld.12026

Royston, R., Howlin, P., Waite, J., & Oliver, C. (2017). Anxiety Disorders in Williams Syndrome Contrasted with Intellectual Disability and the General Population: A Systematic Review and Meta-Analysis. *J Autism Dev Disord*, *47*(12), 3765-3777. https://doi.org/10.1007/s10803-016-2909-z

Royston, R. (2018). Anxiety in Adolescents and Adults with Williams Syndrome [Unpublished doctoral thesis]. University of Birmingham.

Royston, R., Waite, J., & Howlin, P. (2019). Williams syndrome: recent advances in our understanding of cognitive, social and psychological functioning. *Current Opinion in Psychiatry*, *32*(2), 60–66. https://doi.org/10.1097/YCO.0000000000000477

Royston, R., Oliver, C., Howlin, P., Dosse, A., Armitage, P., Moss, J., & Waite, J. (2020). The Profiles and Correlates of Psychopathology in Adolescents and Adults with Williams, Fragile X and Prader-Willi Syndromes. *Journal of Autism and Developmental Disorders*, *50*(3), 893–903. https://doi.org/10.1007/s10803-019-04317-1

Royston, R., Oliver, C., Howlin, P., & Waite, J. (2021). Anxiety characteristics in individuals with Williams syndrome. *Journal of Applied Research in Intellectual Disabilities.* https://doi.org/10.1111/jar.12864

Rubenstein, E., Hartley, S., & Bishop, L. (2020). Epidemiology of Dementia and Alzheimer Disease in Individuals with Down Syndrome. *JAMA Neurol, 77*(2), 262-264. https://doi.org/10.1001/jamaneurol.2019.3666

Ruscio, A, M., Stein, D, J., Chiu, W, T., & Kessler, R, C. (2010). The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. *Mol Psychiatry, 15*(1), 53-63. https://doi.org/10.1038/mp.2008.94

Ruscio, A, M., Hallion, L, S., Lim, C, C, W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonson, J., Andrade, L, H., Borges, G., Bromet, E, J., Bunting, B., Caldas de Almeida, J, M., Demyttenaere, K., Florescu, S., de Girolamo, G., Gureje, O., Haro, J, M., He, Y., Hinkov, H., Hu, C.,…Scott, K. M. (2017). Cross-sectional comparison of the epidemiology of DSM-5 Generalised Anxiety Disorder across the globe. *JAMA Psychiatry, 74*(5), 465-475. https://doi.org/10.1001/jamapsychiatry.2017.0056

Russell, G., Mandy, W., Elliott, D., White, R., Pittwood, T., & Ford, T. (2019). Selection bias on intellectual ability in autism research: a cross-sectional review and meta-analysis. *Molecular Autism*, *10*, 9. https://doi.org/10.1186/s13229-019-0260-x

Rutter, M., Le Couteur, A., & Lord, C. (2003a). *Autism Diagnostic Interview-Revised.* Western Psychological Services.

Rutter, M., Bailey, A., Lord, C., & Berument, S. K. (2003b). *Social Communication Questionnaire*. Western Psychological Services.

Rylaarsdam, L., & Guemez-Gamboa, A. (2019). Genetic Causes and Modifiers of Autism Spectrum Disorder. *Frontiers in Cellular Neuroscience*, *13*, 385. https://doi.org/10.3389/fncel.2019.00385

Sadler, K., Vizard, T., Ford, T., Goodman, A., & Goodman, R. (2018). Mental health of children and young people in England, 2017. NHS Digital. https://digital.nhs.uk/data-and-information/publications/statistical/mental-health-of-children-and-young-people-in-england/2017/2017

Sala, R., Amet, L., Blagojevic-Stokic, N., Shattock, P., & Whiteley, P. (2020). Bridging the Gap Between Physical Health and Autism Spectrum Disorder. *Neuropsychiatric Disease and Treatment*, *16*, 1605–1618. https://doi.org/10.2147/NDT.S251394

Salvador-Carulla, L., Reed, G. M., Vaez-Azizi, L. M., Cooper, S. A., Martinez-Leal, R., Bertelli, M., Adnams, C., Cooray, S., Deb, S., Akoury-Dirani, L., Girimaji, S. C., Katz, G., Kwok, H., Luckasson, R., Simeonsson, R., Walsh, C., Munir, K., & Saxena, S. (2011). Intellectual developmental disorders: towards a new name, definition and framework for "mental retardation/intellectual disability" in ICD-11. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, *10*(3), 175–180. https://doi.org/10.1002/j.2051-5545.2011.tb00045.x

Sanchez, A. L., Cornacchio, D., Chou, T., Leyfer, O., Coxe, S., Pincus, D., & Comer, J. S. (2017). Development of a scale to evaluate young children's responses to uncertainty and low environmental structure. *Journal of Anxiety Disorders*, *45*, 17–23. https://doi.org/10.1016/j.janxdis.2016.11.006

Sansone, S.M., Schneider, A., Bickel, E., Berry-Kravis, E., Prescott, C., & Hessl, D. (2014). Improving IQ measurement in intellectual disabilities using true deviation from population norms. *J Neurodevelop Disord, 6,* 16. https://doi.org/10.1186/1866-1955-6-16

Scahill, L., Lecavalier, L., Schultz, R. T., Evans, A. N., Maddox, B., Pritchett, J., Herrington, J., Gillespie, S., Miller, J., Amoss, R. T., Aman, M. G., Bearss, K., Gadow, K., & Edwards, M. C. (2019). Development of the Parent-Rated Anxiety Scale for Youth With Autism Spectrum Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *58*(9), 887–896.e2. https://doi.org/10.1016/j.jaac.2018.10.016

Schützwohl, M., Koch, A., Koslowski, N., Puschner, B., Voss, E., Salize, H, J., Pfennig, A., & Vogel, A. (2016). Mental illness, problem behaviour, needs and service use in adults with intellectual disability. *Soc Psychiatry Psychiatr Epidemiol, 51*(5), 767-776. https://doi.org/10.1007/s00127-016-1197-4

Schwartz, L., Caixàs, A., Dimitropoulos, A., Dykens, E., Duis, J., Einfeld, S., Gallagher, L., Holland, A., Rice, L., Roof, E., Salehi, P., Strong, T., Taylor, B., & Woodcock, K. (2021). Behavioral features in Prader-Willi syndrome (PWS): consensus paper from the International PWS Clinical Trial Consortium. *Journal of Neurodevelopmental Disorders*, *13*(1), 25. https://doi.org/10.1186/s11689-021-09373-2

Sedgewick, F., Leppanen, J., & Tchanturia, K. (2021). Gender differences in mental health prevalence in autism. *Advances in Autism, 7*(3), 208-224. https://doi.org/10.1108/AIA-01-2020-0007

Sellick, T., Ure, A. & Williams, K. (2021). Repetitive and restricted behaviours and anxiety in autism spectrum disorder: protocol for a systematic review and meta-analysis. *Syst Rev, 10*(303). https://doi.org/10.1186/s13643-021-01830-2

Senaratne, R., Van Ameringen, M., Mancini, C., & Patterson, B. (2010). The Burden of Anxiety Disorders on the Family. *J Nerv Ment Dis*, *198*(12), 876-880. https://doi.org/10.1097/NMD.0b013e3181fe7450

Shaia, W. E., Nichols, H. M., Dababnah, S., Campion, K., & Garbarino, N. (2020). Brief Report: Participation of Black and African-American Families in Autism Research. *Journal of Autism and Developmental Disorders*, *50*(5), 1841–1846. https://doi.org/10.1007/s10803-019-03926-0

Sharkey, L., & McNicholas, F. (2012). Selective Mutism: A prevalence study of primary school children in the Republic of Ireland. *Ir J Psychol Med, 29*(1), 36-40. https://doi.org/10.1017/S0790966700017596

Sharpe, R. A., Curry, W., Brown, R., & Shankar, R. (2019). A public health approach to reducing health inequalities among adults with autism. *The British Journal of General Practice: The Journal of the Royal College of General Practitioners*, *69*(688), 534–535. https://doi.org/10.3399/bjgp19X706133

Shree, A., & Shukla, P. C. (2016). Intellectual Disability: definition, classification, causes and characteristics. *Learning Community, 7*(1), 9-20. https://doi.org/10.5958/2231-458X.2016.00002.6

Silove, D., Alonso, J., Bromet, E., Gruber, M., Sampson, N., Scott, K., Andrade, L., Benjet, C., Caldas de Almeida, J, M., de Girolamo, G., de Jonge, P., Demyttenaere, K., Fieastas, F., Florescu, S., Gureje, O., He, Y., Karam, E., Lepine, J-P, Murphy, S.,…Kessler, R. C. (2015). Pediatric-onset and adult-onset Separation Anxiety Disorder across countries in the World Mental Health Survey. *Am J Psychiatry, 172*(7), 647-656. https://doi.org/10.1176/appi.ajp.2015.14091185

Siper, P. M., Kolevzon, A., Wang, A. T., Buxbaum, J. D., & Tavassoli, T. (2017). A clinician-administered observation and corresponding caregiver interview capturing DSM-5 sensory reactivity symptoms in children with ASD. *Autism Research: Official Journal of the International Society for Autism Research*, *10*(6), 1133–1140. https://doi.org/10.1002/aur.1750

Sim, J., & Wright, C. C. (2005). The kappa statistic in reliability studies: use, interpretation, and sample size requirements. *Physical Therapy*, *85*(3), 257–268. https://doi.org/10.1093/ptj/85.3.257

Simpson, K., Adams, D., Wheeley, E., & Keen, D. (2020). Parent Perspectives on the Presentation, Triggers, Impact, and Support of Anxiety in Young Children on the Autism Spectrum. *J Child Fam Stud, 29*, 572–582. https://doi.org/10.1007/s10826-019-01576-5

Slavin, L. J., & Hartshorne, T. S. (2021). The development of an educational checklist for individuals with CHARGE syndrome. *International Journal of Developmental Disabilities*, *67*(4), 256–262. https://doi.org/10.1080/20473869.2019.1642639

Slowie, D., & Martin, G. (2014). Narrowing the health inequality gap by annual health checks for patients with intellectual disability. *British Journal of General Practice, 64*(619), 101-102. https://doi.org/10.3399/bjgp14X677293

Smiley, E. (2005). Epidemiology of mental health problems in adults with learning disability: an update. *Advances in Psychiatric Treatment, 11*(3), 214-222. https://doi.org/10.1192/apt.11.3.214

Smith, J. & Osborn, M. (2003). Interpretive phenomenological analysis. In *Qualitative Psychology: A Practical Guide to Research Methods* (pp.51-80). Sage.

Smith, J, A., Flowers, P., & Larkin, M. (2009). *Interpretative Phenomenological Analysis: Theory, Method and Research.* Sage.

Smith, J, A., & Osborn, M. (2015). Interpretative phenomenological analysis as a useful methodology for research on the lived experience of pain. *British Journal of Pain*, *9*(1), 41–42. https://doi.org/10.1177/2049463714541642

Smith, I. C., Ollendick, T. H., & White, S, W. (2019). Anxiety moderates the influence of ASD severity on quality of life in adults with ASD. *Research in Autism Spectrum Disorders, 62,* 39-47. https://doi.org/10.1016/j.rasd.2019.03.001

Sohl, K., Mazurek, M. O., & Brown, R. (2017). ECHO Autism: Using Technology and Mentorship to Bridge Gaps, Increase Access to Care, and Bring Best Practice Autism Care to Primary Care. *Clinical Pediatrics*, *56*(6), 509–511. https://doi.org/10.1177/0009922817691825

Solmi, M., Radua, J., Olivola, M. Croce, E., Soardo, L., Salazar de Pablo, G., Shin, J. I., Kirkbride, J. B., Jones, P., Han Kim, J., Yeob Kim, J., Carvalho, A, F., Seeman, M. V., Correll, C. U., & Fusar-Poli, P. (2021). Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry*, https://doi.org/10.1038/s41380-021-01161-7

Soni, S., Whittington, J., Holland, A. J., Webb, T., Maina, E., Boer, H., & Clarke, D. (2007). The course and outcome of psychiatric illness in people with Prader-Willi syndrome: implications for management and treatment. *Journal of Intellectual Disability Research: JIDR*, *51*(Pt 1), 32–42. https://doi.org/10.1111/j.1365-2788.2006.00895.x

Souriau, J., Gimenes, M., Blouin, C., Benbrik, I., Benbrik, E., Churakowskyi, A., & Churakowskyi, B. (2005). CHARGE syndrome: Developmental and behavioural data. *Am J Med Genet A*, *133A*(3), 278-281. https://doi.org/10.1002/ajmg.a.30549

South, M., Carr, A. W., Stephenson, K. G., Maisel, M. E., & Cox, J. C. (2017). Symptom overlap on the SRS-2 adult self-report between adults with ASD and adults with

high anxiety. *Autism Research: Official Journal of the International Society for Autism Research*, *10*(7), 1215–1220. https://doi.org/10.1002/aur.1764

South, M., & Rodgers, J. (2017). Sensory, Emotional and Cognitive Contributions to Anxiety in Autism Spectrum Disorders. *Frontiers in Human Neuroscience*, *11*, 20. https://doi.org/10.3389/fnhum.2017.00020

Spain, D., Rumball, F., O'Neill, L., Sin, J., Prunty, J., & Happé, F. (2017). Conceptualising and treating Social Anxiety in Autism Spectrum Disorder: A Focus Group Study with Multidisciplinary Professionals. *Journal of Applied Research in Intellectual Disabilities, 30*(S1), 10-21. https://doi.org/10.1111/jar.12320

Spain, D., Zıvralı Yarar, E., & Happé, F. (2020). Social anxiety in adults with autism: a qualitative study. *International Journal of Qualitative Studies on Health and Well-Being*, *15*(1), 1803669. https://doi.org/10.1080/17482631.2020.1803669

Sparrow, S. S., Cicchetti, D. V., & Saulnier, C. A. (2016). Vineland Adaptive Behavior Scales, Third Edition (Vineland-3). Pearson.

Spence, S. H. (1997). Structure of anxiety symptoms among children: a confirmatory factor-analytic study. *Journal of Abnormal Psychology, 106*(2), 280-297. https://doi.org/10.1037/0021-843X.106.2.280

Spence, S. H. (1998). A measure of anxiety symptoms among children. *Behaviour Research and Therapy, 36*(5), 545-566. https://doi.org/10.1016/S0005-7967(98)00034-5

Steel, Z., Marnane, C., Iranpour, C., Chey, T., Jackson, J. W., Patel, V., & Silove, D. (2014). The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. *International Journal of Epidemiology*, *43*(2), 476–493. https://doi.org/10.1093/ije/dyu038

Steenfeldt-Kristensen, C., Jones, C. A., & Richards, C. (2020). The Prevalence of Self-injurious Behaviour in Autism: A Meta-analytic Study. *Journal of Autism and Developmental Disorders*, *50*(11), 3857–3873. https://doi.org/10.1007/s10803-020-04443-1

Stein, D, J., Lim, C, C, W., Roest, A, M., de Jonge, R., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonson, J., Benjet, C., Bromet, E, J., Bruffaerts, R., de Girolamo, G., Florescu, S., Gureje, O., Haro, J, M., Harris, M, G., He, Y., Hinkov, H., Horiguchi, I., Hu, c., Karam, A.,…Scott, K. M. (2017). The cross-national epidemiology of social anxiety disorder: Data from the World Mental Health Survey Initative. *BMC Med, 15*, Article number: 143. https://doi.org/10.1186/s12916-017-0889-2

Steinbrenner, J. R., McIntyre, N., Rentschler, L. F., Pearson, J. N., Luelmo, P., Jaramillo, M. E., Boyd, B. A., Wong, C., Nowell, S. W., Odom, S. L., & Hume, K. A. (2022). Patterns in reporting and participant inclusion related to race and ethnicity in autism intervention literature: Data from a large-scale systematic review of evidence-based practices. *Autism: The International Journal of Research and Practice*, 13623613211072593. Advance online publication. https://doi.org/10.1177/13623613211072593

Stephenson, D, D., Beaton, E, A., Weems, C, F., Angkustsiri, K., & Simon, T, J. (2015). Identifying patterns of anxiety and depression in children with chromosome 22q11.2 deletion syndrome: Comorbidity predicts behavioural difficulties and impaired functional communications. *Behav Brain Res*, *276*, 190-198. https://doi.org/10.1016/j.bbr.2014.05.056

Stevens, J. (2002). *Applied multivariate statistics for the social sciences (4th ed.).* Erlbaum.

Stewart, K., Bradshaw, J., & Beadle-Brown, J. (2018). Evaluating service users' experiences using Talking Mats®. *Tizard Learning Disability Review, 23*(2), 78-86. https://doi.org/10.1108/TLDR-05-2017-0023

Stiegler, L. N., & Davis, R. (2010). Understanding Sound Sensitivity in Individuals with Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities*, *25*(2), 67–75. https://doi.org/10.1177/1088357610364530

Stinton, C., Elison, S., & Howlin, P. (2010). Mental health problems in adults with Williams syndrome. *American Journal on Intellectual and Developmental Disabilities*, *115*(1), 3–18. https://doi.org/10.1352/1944-7558-115.1.3

Stinton, C., Tomlinson, K., & Estes, Z. (2012). Examining reports of mental health in adults with Williams syndrome. *Research in Developmental Disabilities*, *33*(1), 144–152. https://doi.org/10.1016/j.ridd.2011.09.002

Ströhle, A., Gensichen, J., & Domschke, K. (2018). The Diagnosis and Treatment of Anxiety Disorders. *Deutsches Arzteblatt International*, *155*(37), 611–620. https://doi.org/10.3238/arztebl.2018.0611

Sullivan, K., Hooper, S., & Hatton, D. (2007). Behavioural equivalents of anxiety in children with fragile X syndrome: parent and teacher report. *Journal of Intellectual Disability Research: JIDR*, *51*(Pt 1), 54–65. https://doi.org/10.1111/j.1365-2788.2006.00899.x

Swartz, J, R., Waller, R., Bogdan, R., Knodt, A, R., Sabhlok, A., Hyde, L, W., & Hariri, A, R. (2017). A common polymorphism in a Williams syndrome gene predicts amygdala reactivity and extraversion in healthy adults. *Biol Psychiatry*, *81*(3), 203-210. https://doi.org/10.1016/j.biopsych.2015.12.007

Syu, Y-C., & Lin, L-Y. (2018). Sensory overresponsivity, loneliness, and anxiety in Taiwanese adults with Autism Spectrum Disorder. *Occupational Therapy International*, 9165978. doi: 10.1155/2018/9165978. eCollection 2018.

Tager-Flusberg, H., Skwerer, D. P., & Joseph, R. M. (2006). Model syndromes for investigating social cognitive and affective neuroscience: a comparison of Autism and Williams syndrome. *Social Cognitive and Affective Neuroscience*, *1*(3), 175–182. https://doi.org/10.1093/scan/nsl035

Tager-Flusberg, H., & Kasari, C. (2013). Minimally verbal school-aged children with autism spectrum disorder: the neglected end of the spectrum. *Autism research: official journal of the International Society for Autism Research*, *6*(6), 468–478. https://doi.org/10.1002/aur.1329

Tarver, J., Pearson, E., Edwards, G., Shirazi, A., Potter, L., Malhi, P., & Waite, J. (2021a). Anxiety in autistic individuals who speak few or no words: A qualitative study of parental experience and anxiety management. *Autism*, *25*(2), 429–439. https://doi.org/10.1177/1362361320962366

Tarver, J., Vitoratou, S., Mastroianni, M., Heaney, N., Bennett, E., Gibbons, F., Fiori, F., Absoud, M., Ramasubramanian, L., Simonoff, E., & Santosh, P. (2021b). Development and Psychometric Properties of a New Questionnaire to Assess Mental Health and Concerning Behaviors in Children and Young People with Autism Spectrum Disorder (ASD): The Assessment of Concerning Behavior (ACB) Scale. *Journal of Autism and Developmental Disorders*, *51*(8), 2812–2828. https://doi.org/10.1007/s10803-020-04748-1

Tavassoli, T., Bellesheim, K., Siper, P. M., Wang, A. T., Halpern, D., Gorenstein, M., ... Buxbaum, J. D. (2016). Measuring sensory reactivity in autism spectrum disorder: Application and simpli- fication of a clinician-administered Sensory Observation Scale. *Journal of Autism and Developmental Disorders, 46*(1), 287–293. https://doi.org/10.1007/s10803-015-2578-3

Taylor, B., Jick, H., & Maclaughlin, D. (2013). Prevalence and incidence rates of autism in the UK: time trend from 2004-2010 in children aged 8 years. *BMJ Open*, *3*(10), e003219. https://doi.org/10.1136/bmjopen-2013-003219

Tomlins, R., & Cawley, J. (2016). 'I didn't know other people existed who hear voices…' – qualitative perceptions of a hearing voices group for people with learning disabilities. *British Journal of Learning Disabilities, 44*(3), 204-212. https://doi.org/10.1111/bld.12138

Tonnsen, B. L., Boan, A. D., Bradley, C. C., Charles, J., Cohen, A., & Carpenter, L. A. (2016). Prevalence of Autism Spectrum Disorders Among Children With Intellectual Disability. *American Journal on Intellectual and Developmental Disabilities*, *121*(6), 487–500. https://doi.org/10.1352/1944-7558-121.6.487

Toscano, R., Hudson, J. L., Baillie, A. J., Lyneham, H. J., & McLellan, L. F. (2020). Development of the Macquarie Anxiety Behavioural Scale (MABS): A parent measure to assess anxiety in children and adolescents including young people with autism spectrum disorder. *Journal of Affective Disorders, 276*, 678-685. https://doi.org/10.1016/j.jad.2020.06.076

Totsika, V., Liew, A., Absoud, M., Adnams, C., & Emerson, E. (2022). Mental health problems in children with intellectual disability. *The Lancet. Child & Adolescent Health*, *6*(6), 432–444. https://doi.org/10.1016/S2352-4642(22)00067-0

Tough, H., Siegrist, J., & Fekete, C. (2017). Social relationships, mental health and wellbeing in physical disabilitiy: a systematic review. *BMC Public Health*, *17*(1), 414. https://doi.org/10.1186/s12889-017-4308-6

Trembath, D., Germano, C., Johanson, G., & Dissanayake, C. (2012). The Experience of Anxiety in Young Adults with Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities, 27*(4), 213-224. https://doi.org/10.1177%2F1088357612454916

Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., Moher, D., Peters, M., Horsley, T., Weeks, L., Hempel, S., Akl, E. A., Chang, C., McGowan, J., Stewart, L., Hartling, L., Aldcroft, A., Wilson, M. G., Garritty, C., Lewin, S., … Straus, S. E. (2018). PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Annals of Internal Medicine*, *169*(7), 467–473. https://doi.org/10.7326/M18-0850

Truesdale, M., Brown, M., Taggart, L., Bradley, A., Paterson, D., Sirisena, C., Walley, R., & Karatzias, T. (2019). Trauma-informed care: A qualitative study exploring the views and experiences of professionals in specialist health services for adults with intellectual disabilities. *Journal of Applied Research in Intellectual Disabilities: JARID*, *32*(6), 1437–1445. https://doi.org/10.1111/jar.12634

Tsakanikos, E., Bouras, N., Sturmey, P., & Holt, G. (2006). Psychiatric co-morbidity and gender differences in intellectual disability. *Journal of Intellectual Disability Research: JIDR*, *50*(Pt 8), 582–587. https://doi.org/10.1111/j.1365-2788.2006.00832.x

Tufanaru, C., Munn, Z., Stephenson, M., & Aromataris, E. (2015). Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *Int J Evid Based Healthc*, *13*(3), 196-207. https://doi.org/10.1097/XEB.0000000000000065

Tyrrell, B., & Woods, K. (2020). Gathering the views of children and young people with ASD: a systematic literature review. *British Journal of Special Education, 47*(3), 376-398. https://doi.org/10.1111/1467-8578.12311

Uljarević, M., Lane, A., Kelly, A., & Leekam, S. (2016). Sensory subtypes and anxiety in older children and adolescents with autism spectrum disorder. *Autism Research: Official Journal of the International Society for Autism Research*, *9*(10), 1073–1078. https://doi.org/10.1002/aur.1602

Uljarević, M., Labuschagne, I., Bobin, R., Atkinson, A., & Hocking, D. R. (2018). Brief Report: The Impact of Sensory Hypersensitivity and Intolerance of Uncertainty on Anxiety in Williams Syndrome. *Journal of Autism and Developmental Disorders*, *48*(11), 3958–3964. https://doi.org/10.1007/s10803-018-3631-9

Vallance, A., & Fernandez, V. (2016). Anxiety disorders in children and adolescents: Aetiology, diagnosis and treatment. *BJPsych Advances, 22*(5), 335-344. doi:10.1192/apt.bp.114.014183

van Gameren-Oosterom, H. B., Fekkes, M., Buitendijk, S. E., Mohangoo, A. D., Bruil, J., & Van Wouwe, J. P. (2011). Development, problem behavior, and quality of life in a population based sample of eight-year-old children with Down syndrome. *PloS One*, *6*(7), e21879. https://doi.org/10.1371/journal.pone.0021879

van Steensel, F. J., Bögels, S. M., & Perrin, S. (2011). Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. *Clinical Child and Family Psychology Review*, *14*(3), 302–317. https://doi.org/10.1007/s10567-011-0097-0

van Steensel, F., & Heeman, E. J. (2017). Anxiety Levels in Children with Autism Spectrum Disorder: A Meta-Analysis. *Journal of Child and Family Studies*, *26*(7), 1753–1767. https://doi.org/10.1007/s10826-017-0687-7

Vargas-Vargas, C., Rafanell, A., Montalvo, D., Estarlich, M., Pomarol-Clotet, E., & Sarró, S. (2015). Validity and reliability of the Spanish version of the diagnostic assessment for the severely handicapped (DASH-II). *Research in Developmental Disabilities*, *36C*, 537–542. https://doi.org/10.1016/j.ridd.2014.10.034

Vasa, R. A., & Mazurek, M. O. (2015). An update on anxiety in youth with autism spectrum disorders. *Current Opinion in Psychiatry*, *28*(2), 83–90. https://doi.org/10.1097/YCO.0000000000000133

Vasa, R. A., Mazurek, M. O., Mahajan, R., Bennett, A. E., Bernal, M. P., Nozzolillo, A. A., Arnold, L. E., & Coury, D. L. (2016). Assessment and Treatment of Anxiety in Youth With Autism Spectrum Disorders. *Pediatrics*, *137 Suppl 2*, S115–S123. https://doi.org/10.1542/peds.2015-2851J

Vasa, R. A., Keefer, A., Reaven, J., South, M., & White, S. W. (2018). Priorities for Advancing Research on Youth with Autism Spectrum Disorder and Co-occurring Anxiety. *Journal of Autism and Developmental Disorders*, *48*(3), 925–934. https://doi.org/10.1007/s10803-017-3320-0

Vaughan Van Hecke, A., Lebow, J., Bal, E., Lamb, D., Harden, E., Kramer, A., Denver, J., Bazhenova, O., & Porges, S. W. (2009). Electroencephalogram and heart rate regulation to familiar and unfamiliar people in children with autism spectrum disorders. *Child Development*, *80*(4), 1118–1133. https://doi.org/10.1111/j.1467-8624.2009.01320.x

Velleman, S, L., & Mervis, C, B. (2011). Children with 7q11.23 Duplication Syndrome: Speech, Language, Cognitive, and Behavioral Characteristics and their Implications for Intervention. *Perspect Lang Learn Educ*, *18*(3), 108-116. https://doi.org/10.1044/lle18.3.108

Venville, A., Sawyer, A-M., Long, M., Edwards, N., & Hair, S. (2015). Supporting People with an Intellectual Disability and Mental Health Problems: A Scoping Review of What They Say About Service Provision. *J Ment Health Res Intellect Disabil*, *8*(3-4), 186-212. https://doi.org/10.1080/19315864.2015.1069912

Vereenooghe, L., Flynn, S., Hastings, R. P., Adams, D., Chauhan, U., Cooper, S. A., Gore, N., Hatton, C., Hood, K., Jahoda, A., Langdon, P. E., McNamara, R., Oliver, C., Roy, A., Totsika, V., & Waite, J. (2018). Interventions for mental health problems in children and adults with severe intellectual disabilities: a systematic review. *BMJ Open*, *8*(6), e021911. https://doi.org/10.1136/bmjopen-2018-021911

Vicari, S., Pontillo, M., & Armando, M. (2013). Neurodevelopmental and psychiatric issues in Down's syndrome: assessment and intervention. *Psychiatr Genet*, *23*(3), 95-107. https://doi.org/10.1097/YPG.0b013e32835fe426

Viechtbauer, W., & Cheung, M. W. (2010). Outlier and influence diagnostics for meta-analysis. *Research Synthesis Methods*, *1*(2), 112–125. https://doi.org/10.1002/jrsm.11

Vignoli, A., La Briola, F., Peron, A., Turner, K., Vannicola, C., Saccani, M., Magnaghi, E., Scornavacca, G. F., & Canevini, M. P. (2015). Autism spectrum disorder in tuberous sclerosis complex: searching for risk markers. *Orphanet Journal of Rare Diseases*, *10*, 154. https://doi.org/10.1186/s13023-015-0371-1

Waite, J., Heald, M., Wilde, L., Woodcock, K., Welham, A., Adams, D., & Oliver, C. (2014). The importance of understanding the behavioural phenotypes of genetic syndromes associated with intellectual disability. *Paediatrics and Child Health, 24*(10), 468-472. https://doi.org/10.1016/j.paed.2014.05.002

Waite, J., Rose, J., Wilde, L., Eden, K., Stinton, C., Moss, J., & Oliver, C. (2017). Associations between behaviours that challenge in adults with intellectual disability, parental perceptions and parental mental health. *The British Journal of Clinical Psychology, 56*(4), 408–430. https://doi.org/10.1111/bjc.12146

Wardenaar, K, J., Lim, C, C, W., Al-Hamzawi, A, O., Alonson, J., Andrade, L, H., Benjet, C., Bunting, B., de Girolamo, G., Demyttenaere, K., Florescu, S, E., Gureje, O., Hisateru, T., Hu, C., Huang, Y., Karam, E., Kiejna, A., Lepine, J, P., Navarro-Mateu, F., Oakley Browne, M.,…de Jonge, P. (2017). The cross-national epidemiology of specific phobia in the World Mental Health Surveys. *Psychol Med, 47*(10), 1744-1760. https://doi.org/10.1017/S0033291717000174

Warner, G., Howlin, P., Salomone, E., Moss, J., & Charman, T. (2017). Profiles of children with Down syndrome who meet screening criteria for autism spectrum disorder (ASD): a comparison with children diagnosed with ASD attending specialist schools. *Journal of Intellectual Disability Research: JIDR*, *61*(1), 75–82. https://doi.org/10.1111/jir.12344

Watkins, A., Bissell, S., Moss, J., Oliver, C., Clayton-Smith, J., Haye, L., Heald, M., & Welham, A. (2019). Behavioural and psychological characteristics in Pitt-Hopkins syndrome: a comparison with Angelman and Cornelia de Lange syndromes. *Journal of Neurodevelopmental Disorders*, *11*(1), 24. https://doi.org/10.1186/s11689-019-9282-0

Way, E, L., & Rojahn, J. (2012). Psycho-social Characteristics of Children with Prenatal Alcohol Exposure, Compared to Children with Down Syndrome and Typical Children. *J Dev Phys Disabil*, *24*, 247-268. https://doi.org/10.1007/s10882-012-9269-1

Wechsler, D. (2011). Wechsler Abbreviated Scale of Intelligence, Second Edition (WASI-II). NCS Pearson.

Wechsler, D. (2014). Wechsler intelligence scale for children (5th ed.). NCS Pearson.

Weisman, O., Guri, Y., Gur, R. E., McDonald-McGinn, D. M., Calkins, M. E., Tang, S. X., Emanuel, B., Zackai, E. H., Eliez, S., Schneider, M., Schaer, M., Kates, W. R., Antshel, K. M., Fremont, W., Shashi, V., Hooper, S. R., Armando, M., Vicari, S., Pontillo, M., Kushan, L., … International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome (2017). Subthreshold Psychosis in 22q11.2 Deletion Syndrome: Multisite Naturalistic Study. *Schizophrenia Bulletin*, *43*(5), 1079–1089. https://doi.org/10.1093/schbul/sbx005

Weiss J. A. (2014). Transdiagnostic Case Conceptualization of Emotional Problems in Youth with ASD: An Emotion Regulation Approach. *Clinical Psychology: A Publication of the Division of Clinical Psychology of the American Psychological Association*, *21*(4), 331–350. https://doi.org/10.1111/cpsp.12084

Wells, A. (1995). Meta-cognition and worry: A cognitive model of generalized anxiety disorder. *Behavioural and Cognitive Psychotherapy, 23*(3), 301–320. https://doi.org/10.1017/S1352465800015897

Werling, D. M., & Geschwind, D. H. (2013). Sex differences in autism spectrum disorders. *Current Opinion in Neurology*, *26*(2), 146–153. https://doi.org/10.1097/WCO.0b013e32835ee548

Werner, E., Dawson, G., Munson, J., & Osterling, J. (2005). Variation in early developmental course in autism and its relation with behavioral outcome at 3-4 years of age. *Journal of Autism and Developmental Disorders*, *35*(3), 337–350. https://doi.org/10.1007/s10803-005-3301-6

Wheeler, A. C., Okoniewski, K. C., Wylie, A., DeRamus, M., Hiruma, L. S., Toth, D., & Christian, R. B. (2019). Anxiety-associated and separation distress-associated behaviours in Angelman syndrome. *Journal of Intellectual Disability Research: JIDR*, *63*(10), 1234–1247. https://doi.org/10.1111/jir.12635

White, S. W., Oswald, D., Ollendick, T., & Scahill, L. (2009). Anxiety in children and adolescents with autism spectrum disorders. *Clinical Psychology Review*, *29*(3), 216–229. https://doi.org/10.1016/j.cpr.2009.01.003

White, S. W., Lerner, M. D., McLeod, B. D., Wood, J. J., Ginsburg, G. S., Kerns, C., Ollendick, T., Kendall, P. C., Piacentini, J., Walkup, J., & Compton, S. (2015). Anxiety in youth with and without autism spectrum disorder: examination of factorial equivalence. *Behavior Therapy*, *46*(1), 40–53. https://doi.org/10.1016/j.beth.2014.05.005

Whitney, D. G., & Shapiro, D. N. (2019). National Prevalence of Pain Among Children and Adolescents With Autism Spectrum Disorders. *JAMA Pediatrics*, *173*(12), 1203–1205. Advance online publication. https://doi.org/10.1001/jamapediatrics.2019.3826

Whitney, D. G., Shapiro, D. N., Peterson, M. D., & Warschausky, S. A. (2019). Factors associated with depression and anxiety in children with intellectual disabilities. *Journal of Intellectual Disability Research: JIDR*, *63*(5), 408–417. https://doi.org/10.1111/jir.12583

Whittle, E, L., Fisher, K, R., Reppermund, S., Lenroot, R., & Trollor, J. (2018). Barriers and Enablers to Accessing Mental Health Services for People with Intellectual Disability: A Scoping Review. *J Ment Health Res Intellect Disabil*, *11*(1), 69-102. https://doi.org/10.1080/19315864.2017.1408724

Wigham, S., & McConachie, H. (2014). Systematic review of the properties of tools used to measure outcomes in anxiety intervention studies for children with autism spectrum disorders. *PloS One*, *9*(1), e85268. https://doi.org/10.1371/journal.pone.0085268

Wigham, S., Rodgers, J., South, M., McConachie, H., & Freeston, M. (2015). The interplay between sensory processing abnormalities, intolerance of uncertainty, anxiety and restricted and repetitive behaviours in autism spectrum disorder. *Journal of Autism and Developmental Disorders, 45*(4), 943–952. https://doi.org/10.1007/s10803-014-2248-x

Wink, L. K., Fitzpatrick, S., Shaffer, R., Melnyk, S., Begtrup, A. H., Fox, E., Schaefer, T. L., Mathieu-Frasier, L., Ray, B., Lahiri, D., Horn, P. A., & Erickson, C. A. (2015). The neurobehavioral and molecular phenotype of Angelman Syndrome. *American Journal of Medical Genetics. Part A*, *167A*(11), 2623–2628. https://doi.org/10.1002/ajmg.a.37254

Winnepenninckx, B., Rooms, L., Kooy, R. F. (2003). Mental Retardation: A Review of the Genetic Causes. *The British Journal of Development Disabilities, 49*(96), 29-44. https://doi.org/10.1179/096979503799104138

Witwer, A. N., & Lecavalier, L. (2008). Psychopathology in Children with Intellectual Disability: Risk Markers and Correlates. *Journal of Mental Health Research in Intellectual Disabilities, 1*(2), 75-96. https://doi.org/10.1080/19315860801988327

Wong, C., Odom, S. L., Hume, K. A., Cox, A. W., Fettig, A., Kucharczyk, S., Brock, M. E., Plavnick, J. B., Fleury, V. P., & Schultz, T. R. (2015). Evidence-Based Practices for Children, Youth, and Young Adults with Autism Spectrum Disorder: A Comprehensive Review. *Journal of Autism and Developmental Disorders*, *45*(7), 1951–1966. https://doi.org/10.1007/s10803-014-2351-z

Woodcock, K., Oliver, C., & Humphreys, G. (2009). Associations between repetitive questioning, resistance to change, temper outbursts and anxiety in Prader-Willi and Fragile-X syndromes. *Journal of Intellectual Disability Research: JIDR*, *53*(3), 265–278. https://doi.org/10.1111/j.1365-2788.2008.01122.x

Yoo H. (2015). Genetics of Autism Spectrum Disorder: Current Status and Possible Clinical Applications. *Experimental Neurobiology*, *24*(4), 257–272. https://doi.org/10.5607/en.2015.24.4.257

Zablotsky, B., Black, L. I., Maenner, M. J., Schieve, L. A., Danielson, M. L., Bitsko, R. H., Blumberg, S. J., Kogan, M. D., & Boyle, C. A. (2019). Prevalence and Trends of Developmental Disabilities among Children in the United States: 2009-2017. *Pediatrics*, *144*(4), e20190811. https://doi.org/10.1542/peds.2019-0811

Zamora, I., Williams, M. E., Higareda, M., Wheeler, B. Y., & Levitt, P. (2016). Brief Report: Recruitment and Retention of Minority Children for Autism Research. *Journal of Autism and Developmental Disorders*, *46*(2), 698–703. https://doi.org/10.1007/s10803-015-2603-6

Zeestraten, E., Gudbrandsen, M., Daly, E., de Schotten, M. T., Catani, M., Dell'Acqua, F., Lai, M-C., Ruigrok, A. N. V., Lombardo, M. V., Chakrabarti, B., Baron-Cohen, S., Ecker, C., Consortium, MRC AIMS., Murphy, D. G. M., & Craig, M. C. (2017). Sex differences in frontal lobe connectivity in adults with autism spectrum conditions. *Transl Psychiatry, 7,* e1090. https://doi.org/10.1038/tp.2017.9

Zhang, Y., Li, N., Li, C., Zhang, Z., Teng, H., Wang, Y., Zhao, T., Shi, L., Zhang, K., Xia, K., Li, J., & Sun, Z. (2020). Genetic evidence of gender difference in autism spectrum disorder supports the female-protective effect. *Transl Psychiatry, 10* (4). https://doi.org/10.1038/s41398-020-0699-8