Global Prevalence of Anxiety Comorbidities in Youth with Autism Spectrum Disorder: A Meta-Analysis

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CONTRIBUTOR ROLES

ROLE	ROLE DESCRIPTION	STUDENT	SUPERVISOR 1	SUPERVISOR 2
CONCEPTUALIZATION	Ideas; formulation or evolution of overarching research goals and aims.		X	
METHODOLOGY	Development or design of methodology; creation of models.	X	X	
PROJECT ADMINISTRATION	Management and coordination responsibility for the research activity planning and execution.	X		
SUPERVISION	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.		X	
RESOURCES	Provision of study materials, laboratory samples, instrumentation, computing resources, or other analysis tools.	X	X	
SOFTWARE	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code.	X	X	
INVESTIGATION	Conducting research - specifically performing experiments, or data/evidence collection.			
VALIDATION	Verification of the overall replication/reproducibility of results/experiments.	X	X	
DATA CURATION	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later re-use.	X		
FORMAL ANALYSIS	Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data.	X		
VISUALIZATION	Visualization/data presentation of the results.	X		
WRITING – ORIGINAL DRAFT	Specifically writing the initial draft.	X		
WRITING – REVIEW & EDITING	Critical review, commentary or revision of original draft		X	

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Abstract

Background: The prevalence of anxiety disorders and symptoms in young children and adolescents (≤18 years) diagnosed with Autism Spectrum Disorder (ASD) is obfuscated by a reliance on self-reported ASD traits and treatment samples. **Aim:** To update current prevalence estimates of anxiety prevalence among ASD youth and examine the role of methodological and sample moderators. **Methods:** The Embase, PubMed, and PsycINFO databases were searched (1970 – August 2023). Included studies were critically appraised using the Joanna Briggs Institute (JBI) tool and prevalence estimates meta-analysed with random-effects modelling. Moderator analyses focused on IQ, publication date, anxiety measurement, age, and gender. **Results:** Fifteen studies, comprising a pooled sample of 4,459 ASD youth, who were primarily male (84%), were included. The overall prevalence of anxiety disorders or symptoms was 30% (95% CI 24% to 37%). Estimates based on diagnostic tools (19%, CI: 7% to 40%) and self-reported symptoms (33%, CI: 25% to 40%) were equally high (Q_B (1) = 1.633, p = .20). Specific phobia (41%) was the most common anxiety disorder. IQ (R^2 = .39, p =.004) and male gender (Q_B (1) = 35.02, p < .01) were also identified as significant moderators. **Conclusion**: Anxiety comorbidities affect 1 in 3 youth living with ASD. This rate is notably lower than previous meta-analyses that have used less stringent inclusion criteria relating to the assessment of ASD or anxiety (range 39.6% to 42%). The findings highlight the importance of screening for anxiety in this population. Protocol registered on Open Science Framework (https://osf.io/7mtca/).

Keywords: children, ASD, anxiety disorders, prevalence

DECLARATION

This thesis contains no material which has been accepted for the award for any other degree or diploma in any University, and, to the best of my knowledge, this thesis contains no material previously published except where due reference is made. I give permission for the digital version of this thesis to be made available on the web, via the University of Adelaide's digital thesis repository, the Library Search and through web search engines, unless permission has been granted by the School to restrict access for a period of time.

CONTRIBUTION STATEMENT

In writing this thesis, my supervisor and I collaborated to generate the research questions of interest and to develop the study eligibility and screening criteria. With the assistance of a Research Librarian, I created the logic grids for each database. conducted the database searches and study screening, extracted data, completed the risk of bias assessment, and undertook all statistical analyses, under the guidance of my project supervisor. I was responsible for the thesis write up, with review by my supervisor.

Global Prevalence of Anxiety Comorbidities in Youth with Autism Spectrum Disorder A Meta-Analysis

Background

The challenges of living with a lifelong neurodevelopmental condition such as Autism Spectrum Disorder (ASD) are well established. Social interactions, intense sensory stimulation, and changes in established and expected routines can increase stress due to core ASD traits (i.e., impairments in language, troubled executive functioning, difficulty with social interactions, repetitive behaviours etc; American Psychiatric Association (APA), 2013). These core traits are, however, associated with widely differing degrees of impairment, hence the need for a spectrum approach to ASD symptomology (Matson et al., 2008). Indeed, a small but significant portion of people diagnosed with ASD [1] exhibit exceptional cognitive capabilities, including enhanced perceptual skills, leading to a unique ability to focus on detail (Baron-Cohen, 2017; Uddin, 2022).

Recommendations for practice and research suggest that early learning-based interventions can enhance functional and behavioural outcomes for ASD (e.g., Zwaigenbaum et al., 2015), although very few of these interventions are sufficiently robust (Towle et al., 2020). Early intervention is also reliant on accurate detection and screening. The revised Autism Diagnostic Observation Schedule (ADOS-2) and Autism Diagnostic Interview (ADI-R) are the leading diagnostic instruments for the identification and recruitment of ASD populations in research (Lebersfeld et al., 2021). Both measures are informed by a diagnostic algorithm including the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV/V) and the International Classification of Diseases (ICD-10). Both instruments have also demonstrated high sensitivity (ADOS: .77 to .90; ADI-R: .53 to .92), and specificity (ADOS: .62 to.90, ADI-R: .62 to .95; Lord et al., 2012; Rutter et al., 2003). This level of accuracy is far superior to self-report measures traditionally used to ascertain ASD caseness, such as the Autism Spectrum Quotient, which displays a low specificity (20%; Ashwood et al., 2016).

[1] Both person-first (e.g., person with autism) and neuroaffirming, or identity-first language (e.g., ‘autistic person) are recognised by APA (Dunn & Andrews, 2015).

Despite recommendations that validated, ASD-specific assessment tools be used by qualified providers to identify ASD cases (McPheeters et al., 2016; Zwaigenbaum et al., 2015), there remains extensive heterogeneity in the assessment of ASD (Feczko & Fair, 2020, Mottron & Bzdok, 2020). This heterogeneity may, in part, contribute to the rising rates of ASD seen among children and adolescents, or youth (aged 18 years and under) in the last decade: from 62 per 10,000 cases in 2012 to 100 per 10,000 cases in 2022 (Zeidan et al., 2022). This rise in prevalence includes an enhanced detection of ASD among females and non-western populations, both previously underrepresented groups (Zeidan et al., 2022).

ASD identification can also be complicated by overshadowing psychological comorbidities (Harmens et al., 2022; Gupta et al., 2023). One such comorbidity is anxiety. Children diagnosed with ASD have a 65% increased likelihood of experiencing an anxiety disorder compared to neurotypical peers (van Steensel & Heeman., 2017). Although anxiety symptoms, such as difficulty in social communication and difficulty adapting to changing plans, may be considered part of the broader ASD phenotype, their presence contributes to functional impairment beyond what is associated with ASD alone (Matson & Nebel-Schwalm, 2007). Understanding potential factors that escalate the risk of anxiety disorders and symptoms in ASD can therefore help clinicians profile vulnerable children and adolescents (hereafter referred to as youth) and target interventions accordingly. Similarly, a child presenting with anxiety to a clinician may aid early identification of ASD if the proper overlapping symptoms and risk factors are understood. Given the increasing size and heterogeneity of the young ASD population, it is essential to collate and quantify current research on the prevalence of anxiety, whether diagnosed or self-reported, in this population to improve our understanding for ASD case identification and assist in treatment.

How Anxiety Manifests in ASD

Anxiety responses, in general, encompass feelings of tension, catastropising, and physiological reactions (e.g., trembling or shaking, insomnia; Siegel & Dickstein, 2012). Anxiety becomes maladaptive when the intensity, duration, and frequency of these symptoms are disproportionate to the triggering threat or situation, potentially leading to the development of debilitating avoidance behaviours (Beesdo et al., 2009). It has long been observed that the characteristics of ASD can intensify symptoms of anxiety. For instance, individuals with ASD who

are overly sensitive to loud noises may develop a discomfort towards social interactions, exacerbating their social withdrawal and social anxiety (Spain et al., 2018). Anxiety symptoms can also make it difficult for a child with ASD to learn and manage everyday tasks (e.g., attend school, engage in extracurricular activities), and negatively impact support and intimacy in peer and parental relationships (Hunsche et al., 2022). The current DSM-5 classifies anxiety across seven different categories which share typical clinical features but also have distinct symptomology (APA, 2013). Epidemiological studies on ASD often focus on investigating six of these anxiety disorders: generalised anxiety disorder, panic disorder, agoraphobia, separation anxiety disorder, social anxiety disorder and specific phobia. However, some anxiety symptoms appear to uniquely manifest in the ASD population: up to 46% of these children display atypical anxiety symptoms that do not neatly align with DSM criteria (Kerns et al., 2014). These symptoms include social fear without fear of negative social evaluation, fear of change or novelty, and atypical specific phobias. The diagnosis of anxiety disorder in ASD is further complicated by inconsistent symptom presentations, with rates for individual disorders among youth ranging from 8% to a staggering 84% (Mutluer et al., 2022; Simonoff et al., 2008). A combination of methodological and sample characteristics likely explain this between-study variance.

Methodological Characteristics as Moderators of Anxiety in ASD

The results of previous meta-analyses in this area have been limited in their generalisability largely due to their reliance on participants recruited from treatment trials or intervention settings (e.g., van Steesel et al., 2011). Such samples of convenience may not only overestimate anxiety prevalence estimates but can result in spurious associations, given the increased likelihood of these groups presenting with pronounced anxiety symptoms compared to the general populous. Indeed, more recent meta-analyses examining psychiatric comorbidities among community-based samples of ASD participants have reported lower rates (e.g., ~ 20% Lai et al.; 2019, Mutluer et al., 2022). However, the broad scope of these reviews, which focused on multiple psychiatric comorbidities, did not stratify the point prevalence of anxiety across specific anxiety disorders or age groups.

The measurement of anxiety is a further consideration. For example, Minami & Horikawa (2021) administered a self-report measure, the Liebowitz Social Anxiety Scale (LSAS) to identify

44.3% of their sample of Japanese high schoolers as socially anxious. Whilst the LSAS is a validated child measure it should, ideally, be supplemented with parental reports given noted emotional and language impairments in the ASD population (Mazefsky et al., 2011). That said, parental reports carry their own unintended risks, with parents tending to overestimate the prevalence of internalising symptoms, such as child worry (Muris et al. 1999; Cosi et al., 2010). As an example, Niditch et al. (2012) utilising the parent form of the Behaviour Assessment Schedule for Children (2nd edition; BASC-2), identified 13.5% as meeting the criteria for clinical anxiety. In this context, the development of structured diagnostic interview tools, such as the Schedule for Affective Disorders for Children (K-SADS; Chambers et al., 1985), offers promise. These tools rely on trained clinicians to determine if participants meet the criteria for diagnosis of an anxiety disorder. Notably, tools such as the K-SADS rely on the updated DSM-V criteria for anxiety disorders - which includes the additional disorder of separation anxiety, broadening the potential number of participants qualifying for an anxiety disorder (APA, 2013). Indeed, Guerrera et al., (2022) identified almost 86% of their sample as having an anxiety disorder based on the K-SADS. Whether DSM-5 diagnostic changes have altered (i.e., increased) prevalence estimates among adolescents with ASD remains to be determined (Crome et al., 2015; Roest & de Vries, 2019).

Sample Characteristics as Moderators of Anxiety in ASD

Intelligence Quotient (IQ)

ASD research examining the role of Intelligence Quotient (IQ) assessment on anxiety symptoms has shown some consistency, at least in terms of theoretical explanations for this relationship. There has been considerable traction around the hypothesis that greater cognitive functioning may create a greater vulnerability in self-esteem through one's own awareness of social and mental defects (Edirisooriya et al., 2020; Mazurek & Kanne 2010; Sukhodolsky et al., 2008). That said, empirical support for this theory has been mixed, with individual ASD studies reporting strong positive associations (r = .51, Niditch et al., 2012) but also weak to no association (r = .05, Mazurek & Petroski, 2015). Another proposed mechanism is that those with a lower verbal IQ may struggle to communicate feelings and thoughts, making dismissing and deconstructing fears and concerns difficult for support networks (Edirisooriya et al., 2021). It follows that those with a high IQ will have greater general understanding and knowledge that may protect against

upset routines or unfamiliar situations through adaptability skills. The specific anxiety disorders explained by this body of research has, however, varied. Indeed, Hallett et al. (2013) observed social anxiety as positively correlated with IQ, whereas separation anxiety was negatively correlated with IQ. The relationship between IQ assessment and anxiety symptoms in individuals with ASD presents consistent theoretical explanations but mixed empirical support. Additionally, the specific anxiety disorders studied vary, highlighting the need for further research to clarify this complex interaction.

Age and Gender

Age-based differences in anxiety prevalence estimates have been inconsistent in ASD research. While Niditch et al. (2012) found that anxiety in ASD youth decreased from toddlerhood (20%) into childhood (9%), Guerrera et al. (2022) reported that anxiety disorders slightly increased with chronological age, observing this across two age groups (under 11 and over 11 years old). However, Strang et al.'s (2012) case-control investigation of youth diagnosed with ASD (6–11 and 12–18 years old) revealed that anxiety levels remained unaffected by age.

The presentation of anxiety symptoms may also differ by gender. Despite overall similarities in psychological symptoms (e.g., rigidity of thought, sensory responsivity), physiological arousal has been found to be more prevalent among girls with ASD (Ambrose et al., 2020). There is also evidence of girls having increased anxiety risk compared to boys (Lohr et al., 2017). However, other studies have demonstrated equally high rates in boys (Dubin et al., 2015) or negligible differences between both groups (Sukhodolsky et al., 2008). Notably, Sukhodolsky et al. (2008) sampled their group from a help-seeking population (e.g., randomised clinical trial of risperidone), which may confound the latter data. Due to the presence of confounding variables and the variability in available data, there is a pressing requirement to gather more reliable data on gender differences in anxiety through population-based samples, thus avoiding spurious relationships.

COVID-19 as a History-Graded Life Event

The role of the 2019 coronavirus pandemic (COVID-19) on mental health, globally, is a further consideration. The onset of COVID-19 brought the intermission of health services worldwide, resulting in significant delays in ASD assessment and disrupted treatment within already overstretched healthcare systems for many children (Shaw et al., 2023). To date, no meta-analysis has explored the role of COVID-19 on anxiety prevalence estimates in ASD. Rather, reviews have examined the broader consequences of COVID across life domains (e.g., behaviour, communication, autonomy, socialisation; Dal Pai et al., 2022), as well as increased vulnerability to mental health conditions (e.g., impact of quarantine, inaccessible healthcare services, parental separation; Singh et al., 2020). Nonetheless, individual ASD studies have commented on the expected (e.g., negative impact of school disruption and learning) but also the unexpected, positive impacts of COVID-19 for these children, including improvements in mood and confidence and decreased anxiety (Simpson et al., 2022). By examining changes in anxiety prevalence before, during and after the lockdown, it can be ascertained how to better support individuals with ASD during times of crisis and beyond as well as investigate any long-lasting effects from the COVID-19 pandemic.

The Current Meta-Analysis

Anxiety disorders are prevalent among youth with ASD, however the available research is characterised by methodological inconsistencies as well as sample heterogeneity. An up-to-date quantitative review, using strict eligibility criteria relating to both ASD and anxiety measurement as well as recruitment source, will help clarify the current state of evidence and, importantly, aid in targeted assessment and treatment. The current review provides an up-to-date quantitative synthesis of available observational studies to answer the following research questions: *What is the point prevalence of anxiety symptoms and disorders in the international literature on youth diagnosed with ASD?* and *what (if any) are the moderating effects of sample and methodological characteristics on prevalence estimates (i.e., IQ, mean sample age, gender, publication date)?*

Methods

Search Strategy and Data Sources

Following prospective registration on 21st March 2022 (see research proposal in Appendix A), a systematic search of computerised databases (Embase, PubMed and PsychINFO) was undertaken to obtain studies that reported the prevalence of anxiety disorders among ASD youth. Search alerts were activated and reviewed until August 1st, 2023 to ensure that recent studies were captured. Literature was identified using search terms relating to *ASD* (such as 'autistic disorder', 'asperger syndrome') and *anxiety* (such as 'anxiety disorder', 'generalised anxiety disorder' – see Appendix C for complete logic grids). Search terms were verified by a research librarian. Search results were imported as XML files from each database and then uploaded onto Covidence software for systematic reviews (Covidence systematic review software, Version 1.0, Veritas Health Innovation). Additionally, the reference list of past meta-analyses on ASD youth and anxiety (van Steensel & Heeman, 2017; van Steensel et al., 2011) were searched to compensate for any eligible studies that may have been inadvertently missed in the initial database searches. A protocol for this review is available on the Open Science Framework (https://osf.io/7mtca/).

Eligibility Criteria

Eligible studies needed to include a child or adolescent sample (that is, age ≤ 18 years old, consistent with the age bracket for childhood adopted by the World Health Organisation, 2019), that had received a diagnosis of ASD based on the DSM or ICD classification systems. Studies also needed to include a validated measure of anxiety, whether self-reported or clinician-administered. Consideration only applied to studies published in English from 1970. This timeframe corresponds with the publication of the DSM II in 1968, which marked the removal of the notion that mental disorders were solely attributed to personality-driven reactions (American Psychiatric Association, 1980). Only point-in-time prevalence of anxiety (i.e., number of participants currently with an anxiety disorder or reporting symptom severity consistent with a clinical cut-off score) was considered, given issues with potential recall bias associated with lifetime prevalence estimates (Merikangas et al., 2009).

Studies that relied on self-report measures to ascertain ASD caseness in their samples, such as the Autism Spectrum Quotient (Barson-Cohen et al., 2001) or Social Responsiveness Scale (Constantino et al, 2003), were excluded given the increased risk of producing false diagnoses due to a lack of self-insight and/or socially desirable responses (Althubaiti, 2016). Studies that exclusively recruited participants who were currently undergoing a treatment or trial program were also deemed ineligible, as these settings typically over-represent the frequency and severity of anxiety diagnoses among the ASD community (Mutluer et al., 2022). Additionally, studies that used purposely designed or single-item questionnaires which cannot capture the full-breadth of a complex construct such as anxiety (Allen et al., 2022), or measures that did not define anxiety (i.e., no reference to a cut-off score) were excluded. Studies with prevalence information and co-occurring anxiety disorders or symptoms with fewer than 20 participants with ASD were also excluded; this threshold was chosen to minimise sample bias and maximise power (Lai et al., 2019). Lastly, qualitative studies, literature reviews and grey literature (non-peer reviewed sources) were excluded as the focus of this review was on primary, quantitative data from the peer-reviewed literature.

Study Selection

The search process was undertaken by the student author. To ensure that all papers identified were relevant, a second reviewer (D.D) independently reviewed all 163 full-text articles. The inter-rater reliability ($\kappa = 0.60$) indicated substantial agreement on studies' eligibility (Cohen, 1960). The few discrepant articles were discussed, and a consensus agreement then made. To ensure the validity of this meta-analysis it was also important to source data from independent samples (Borenstein et al., 2009). Studies were therefore carefully examined to avoid any duplication of samples. No overlap was found.

Data Extraction

As per the reporting guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2021), key information were extracted by the author: study characteristics (lead author, publication year, recruitment source, sample size, country of study), sample demographics (child age, gender, IQ, years since receiving ASD

diagnosis) and measurement outcomes (anxiety measure and prevalence, diagnostic method to confirm ASD diagnosis). These data were checked by a second reviewer (D.D.).

Assessment of Study Quality

To gauge the reporting quality of each included study, the Joanna Briggs Institute (JBI) Critical Appraisal tool was employed. This tool, formulated by Munn and colleagues (2020), is distinguished by 10 items that are specifically designed to evaluate potential biases in prevalence studies. It encompasses an examination of both external validity (criteria 1-5, 9, addressing coverage bias, nonresponse bias, and adequacy in sample size) and internal validity (criteria 6-8, valid measures for identifying conditions and appropriate statistical analysis) (see Appendix C). All 10 items ask if a pre-defined criterion was met, with binary responses of ‘Yes’ or ‘No’ corresponding to low and high bias respectively. Additionally, when a study lacks sufficient information for a judgment, an 'Unclear' option can be selected. An overall appraisal of study bias (item 10) is used to decide whether the study should be included or excluded from the meta-analysis based on the responses to the preceding nine items.

Statistical Analyses

All statistical analyses were conducted using Comprehensive Meta-Analysis (CMA) Software (Version 4, Biostat Inc, Englewood, NJ, USA) and a random-effects model.

Prevalence estimates were first grouped by anxiety measurement and pooled. The process for calculating pooled mean prevalence rates involved assigning weights to individual effects based on their inverse variance or the invariance of a square standard error. This approach meant that studies with greater precision (as indicated by larger sample sizes and smaller sampling variances), are given more weight approximate to their reliability (Borenstein et al., 2009). In addition, 95% per cent confidence intervals (CIs) were calculated to detect any statistical significance in either individual or weighted effect sizes (that is, either from individual studies or a combination of studies). In this meta-analysis, the confidence intervals (CIs) served as the upper and lower limits within the range that one express 95% confidence about the true prevalence of anxiety symptoms and disorders among the ASD youth population. Forrest plots were created to illustrate the distribution of effect sizes.

Between-study heterogeneity was estimated with Tau (*T*), akin to the pooled effect SD, and I^2, the proportion of variance observed across studies due to inter-study heterogeneity opposed to sampling error (Higgins et al., 2003). The higher the I^2 value is, the lower the probability that there is consistency across each study's true effect size. Given that the I^2 statistic lacks discriminative power in prevalence studies, 95% prediction intervals (PI) were also generated to determine the range of effect estimates that could be expected in further research (Hout et al., 2016). Finally, a one-study-removed sensitivity analysis was conducted to identify statistical outliers.

Publication bias is the tendency for studies that report larger, significant results to be more readily published compared to those that report non-significant or smaller results (Borenstein et al., 2009). A Doi plot, a recent measure to assess publication bias in prevalence data that is considered more robust than the traditional funnel plot, was computed using MetaXL (Version 5.3) (Furuya-Kanamori & Barendregtt, 2018; Cheema et al., 2022). The Doi plot illustrates the normal quantile (Z-score) plotted against the effect size. Plot asymmetry was quantified with the LFK index: the closer the LFK index to zero, the more symmetrical the plot (Furuya-Kanamori & Barendregtt, 2018).

The impact of potential sample and methodological characteristics on anxiety prevalence was then examined. Continuous variables (IQ, mean sample age) were entered as covariates in separate univariate meta-regressions. Cochrane's Q_B test (equivalent to a one-way analysis of variance) was then used to examine normative history-graded influences (studies published pre- versus post-Covid) as well as categorical variables (gender). Initial plans to record and analyse subgroup differences between informants on anxiety measures (i.e., parent, child, or both) were planned but did not proceed due to insufficient data segregating child and parent informants, as well as the underrepresentation of sole child informants.

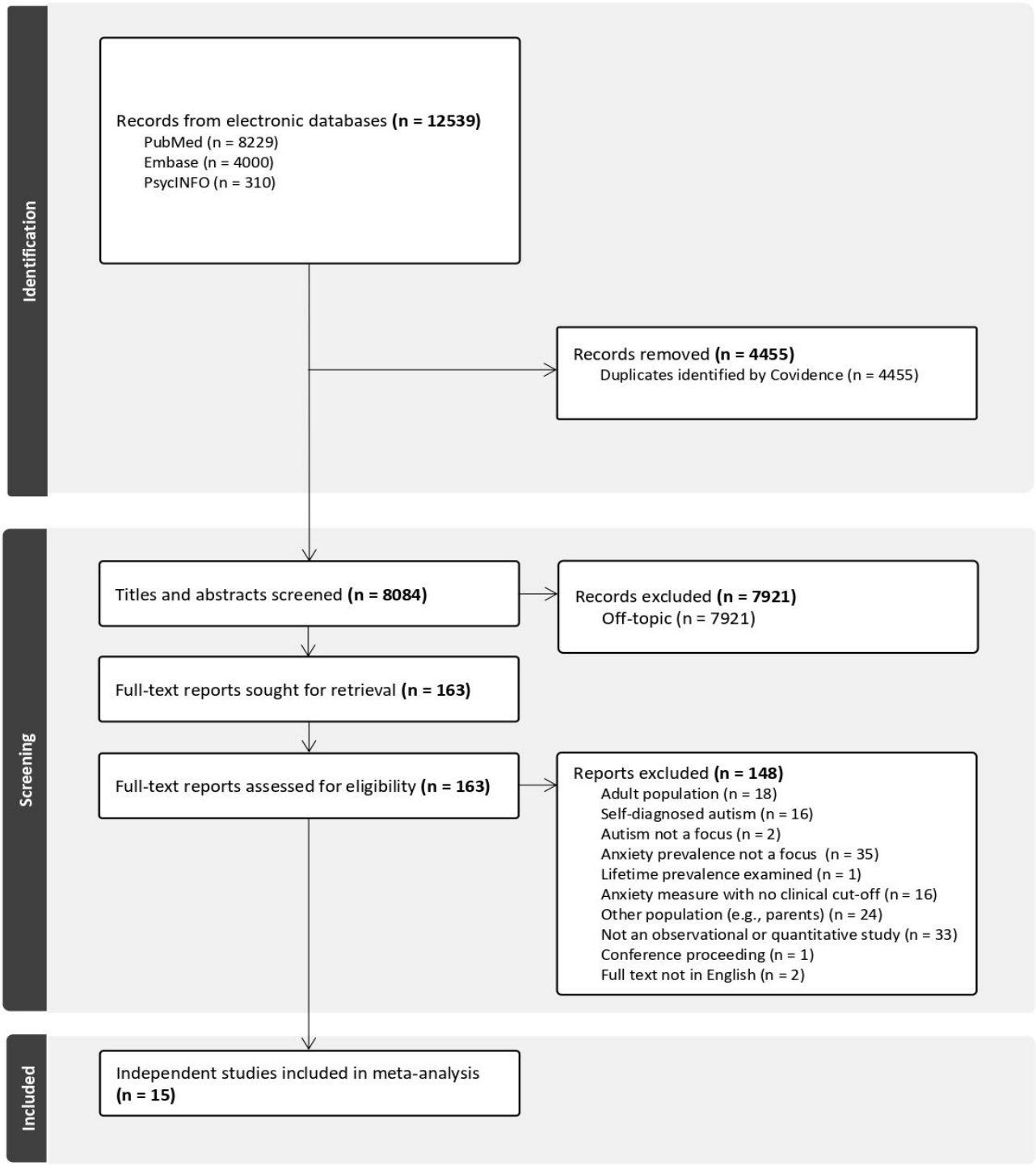
Results

Study Selection

A total of 8084 records were initially identified in the search process. After evaluating the titles and abstracts of each article based on the previously mentioned inclusion and exclusion criteria, a total of 163 reports were identified as potentially meeting the eligibility requirements. Following re-screening and citation searches in Scopus, a final sample of 15 independent studies was identified (see Figure 1 for study selection process).

Figure 1

Flow Diagram Illustrating Study Selection Process

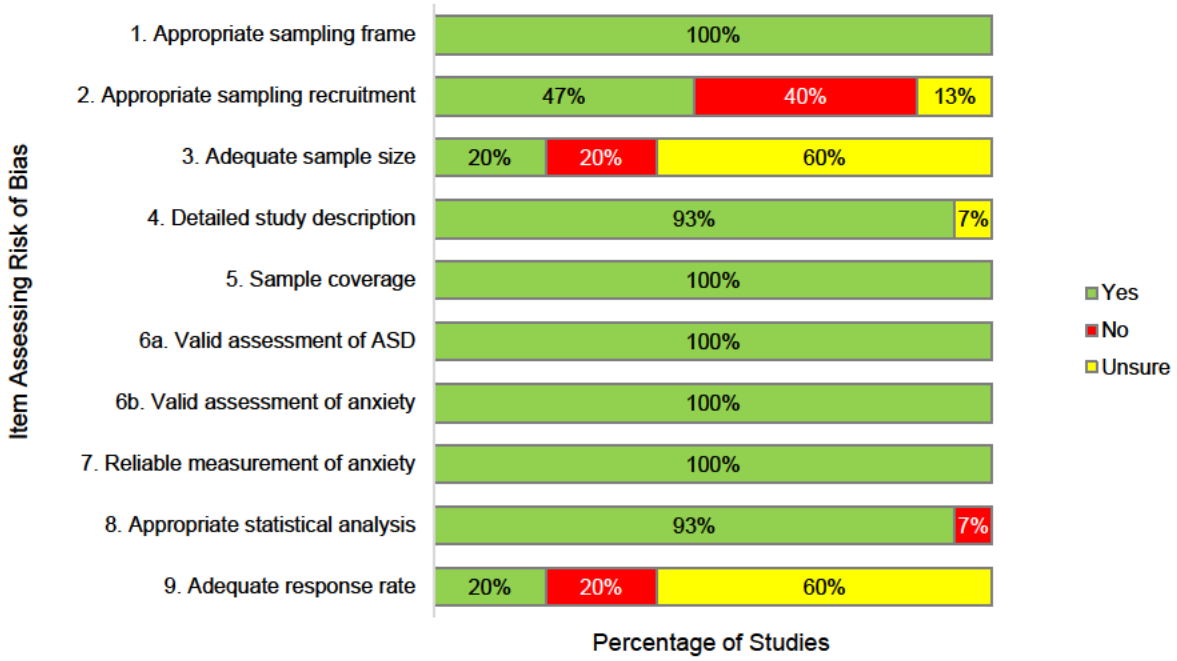


Reporting Quality of Included Studies

A summary of the JBI critical appraisal ratings for each included study is graphically illustrated below (Figure 2), with individual study ratings provided in Appendix B. None of the studies achieved the highest possible rating, although all attempted to recruit the majority of their target (ASD youth) population using community methods or registry data (criterion 1). The strict inclusion criteria also ensured that ASD and anxiety were based on reliable and valid assessments across all studies (criteria 6-7). Methodological weaknesses included limited details relating to sampling recruitment methods (criterion 2). In addition, few studies performed a priori or post-hoc power analysis to justify their sample size (criterion 3). Most studies also did not clarify or report reasons for study dropout or withdrawal, making external validity difficult to assess (criterion 9).

Figure 2

Critical Appraisal Rating for Included Studies Based on JB Prevalence Tool (Munn et al., 2020)



Study Characteristics

Included studies spanned the last 23 years (from 2000 till 2023; see Table 1). The pooled sample comprised of 4459 participants from 10 countries, primarily Western, but also Asian ($N_{studies}$ = 2) and Middle Eastern countries ($N_{studies}$ = 1). Most studies presented cross-sectional data, with four providing baseline prevalence derived from longitudinal datasets (Baribeau et al., 2020; Ben-

Itzchak et al., 2020; Kerns et al., 2021; van Steensel et al., 2012). Participants were typically recruited via community outreach methods (e.g., dissemination of posters and pamphlets; $N_{studies}$ = 6).

Sample Characteristics

The mean sample age was 10 years and eight months (SD = 2.27, range = 5 years to 14.22 years). Consistent with global patterns of autism, most participants were male (84%, *n* = 3774; Zablotsky et al., 2019). Of the 11 studies that reported baseline IQ (Mean sample IQ = 86.03; SD = 20.23), less than a quarter included participants with severe communication and behavioural deficits (that is, IQ < 75, $N_{studies}$ = 3), meaning a vast majority of youth had high-functioning autism (that is, IQ $\geq$ 75, $N_{studies}$ = 8). As per the eligibility criteria for this review, autism diagnoses were confirmed through established methods, namely the Autism Diagnostic Interview-Revised (ADI-R; $N_{studies}$ = 9) and Autism Diagnostic Observation Schedule (including two variants e.g., ADOS-2/G; $N_{studies}$ = 5). Medical records obtained from a research centre database were used in one study, that said, the use of the DSM classification system was confirmed (Bellini, 2004). However, autism severity was not consistently reported, both in construct and scale. For example, social ineptness was reported as a continuous variable by Cholemkery et al., (2014), using the Social Responsiveness Scale (Constantino et al., 2003), whereas Baribeau et al., (2020) used the Repetitive Behaviour Scale to capture ordinal frequencies of different behaviours (Barrett et al., 2018).

Overall Prevalence of Anxiety in ASD Youth

The pooled estimate of anxiety prevalence, whether defined as a disorder or clinically elevated symptoms, was 30% (see Figure 3). However, individual estimates varied substantially between studies (I^2 = 95.54; T = 0.37). This heterogeneity was confirmed by the wide prediction interval which indicated that the true population rate fell within the range of 10% to 63%. This pooled estimate was unlikely to be characterized by publication bias, as suggested by the symmetrical Doi plot and low LFK index (see Figure 4). A one-study removed sensitive analysis also revealed no statistical outliers.

Table 1. Study and Sample Characteristics

Lead author (date)	Study characteristics			Sample characteristics					
	Country	Design	Setting	*N*	Male: Female	Mean age (SD) in years	Mean years (SD) since diagnosis	Mean IQ (SD)	Diagnostic criteria/ method
Avni et al., 2018	Singapore	Cross-sectional	Archival data	260	228:32	7.5 (1.1)	2.7 (1.4)	83.93 (17.77)	ADI-R, ADOS
Baribeau et al., 2020	Canada	Longitudinal	Community	421	404:17	9.21 (2.6)			ADI-R
Bellini, 2004	India	Cross-sectional	Research Centre	41	35:6	14.22		99.94 (18.81)	Prior diagnosis
Ben-Itzchak et al., 2020	Israel	Longitudinal	Community	61	60:5	13.8 (1.9)	2.8 (-)	70.02 (24.98)	ADI-R
Boulter et al., 2014	United States & United Kingdom	Cross-sectional	Archival data	224	100:14	12.7 (2.9)	3.8 (1.7)	108.5 (13.8)	ADOS, UK National Autism Plan for Children
Cholemkery et al., 2014	Germany	Cross-sectional	Community	57	43:17	12.28 (3.03)		*102.15 (16.23)*	ADI-R
Dubin et al., 2015	North America	Cross-sectional	Archival data	2662	2302:360	8.82 (3.39)	3.3 (1.2)	80.61 (27.78)	ADOS
Factor et al., 2017	United States	Cross-sectional	Community	57	47:10	7.25 (3.85)	2.7 (2.3)	90.76 (17.87)	ADI-R
Guerrera et al., 2022	Italy	Cross-sectional	Hospital	21	10:11	11.8 (2.3)		96.7 (15.0)	ADOS-2
Kerns et al., 2021	Canada	Longitudinal	Community	75	55:20	11.5 (1)		77.4 (30.8)	ADI-R
Kim et al., 2000	Canada	Cross-sectional	Preschool	68	61:7	12 (1.2)			ADI
Kuusikko et al., 2008	Finland	Cross-sectional	Community	54	37:17	11.2 (1.7)			ADOS
Niditch et al., 2012	United States	Cross-sectional	Archival data	231	194:37	5 (2)		64.2 (17.9)	ADI-R
Simonoff et al., 2008	United Kingdom	Cross-sectional	Research Centre	112	98:14	11.5		72.7 (21.6)	ADOS-G, ADI-R
van Steensel et al., 2012	Netherlands	Longitudinal	Community	115	90:25	11.37 (2.63)			ADI-R

Abbreviations: *N* = total sample size, IQ = Intelligence quotient, SD = standard deviation, ADS = Autism Diagnostic Interview (includes ADS-Revised), ADOS = Autism Diagnostic Interview Schedule (includes 2nd edition and generic schedule).

Figure 3

Forest Plot of Overall Anxiety Symptoms and Disorders Prevalence by Study

Author, reference number	N	Proportion	95% CI		Forest Plot Proportion ± 95% CI	Weight (random)
			Lower	Upper		
Anvi et al., 2018	260	0.44	0.39	0.51		7.17
Baribeau et al., 2020	421	0.25	0.21	0.30		7.23
Benllini., 2004	41	0.48	0.34	0.64		5.92
Ben-Itzchak et al., 2020	61	0.25	0.20	0.32		7.00
Boulter et al., 2014	224	0.60	0.54	0.66		7.12
Cholemkery et al., 2014	57	0.05	0.02	0.10		4.93
Dubin et al., 2015	2662	0.38	0.36	0.40		7.44
Factor et al., 2017	57	0.54	0.41	0.67		6.28
Guerrera et al., 2022	21	0.42	0.31	0.55		6.29
Kerns et al., 2021	75	0.22	0.18	0.29		6.97
Kim et al., 2000	68	0.09	0.05	0.16		6.04
Kuuiskko et al., 2008	54	0.36	0.28	0.46		6.74
Niditch et al, 2012	231	0.07	0.05	0.12		6.39
Simonoff et al., 2008	112	0.22	0.18	0.27		7.20
van Steensel et al., 2012	115	0.50	0.45	0.55		7.28
Total random effects		**0.30**	**0.24**	**0.37**		
Prediction interval			**0.10**	**0.63**		

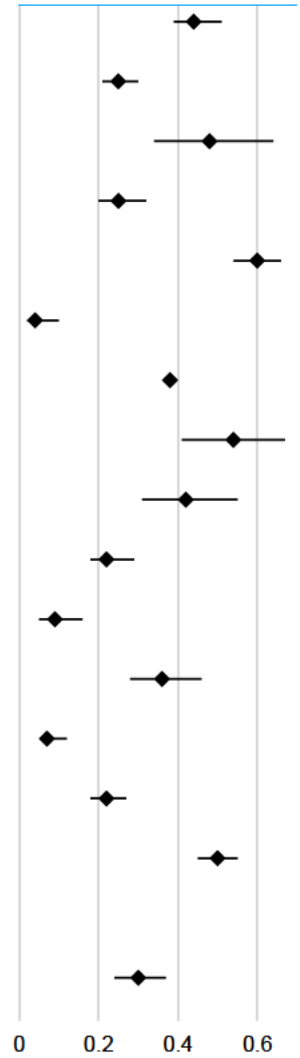
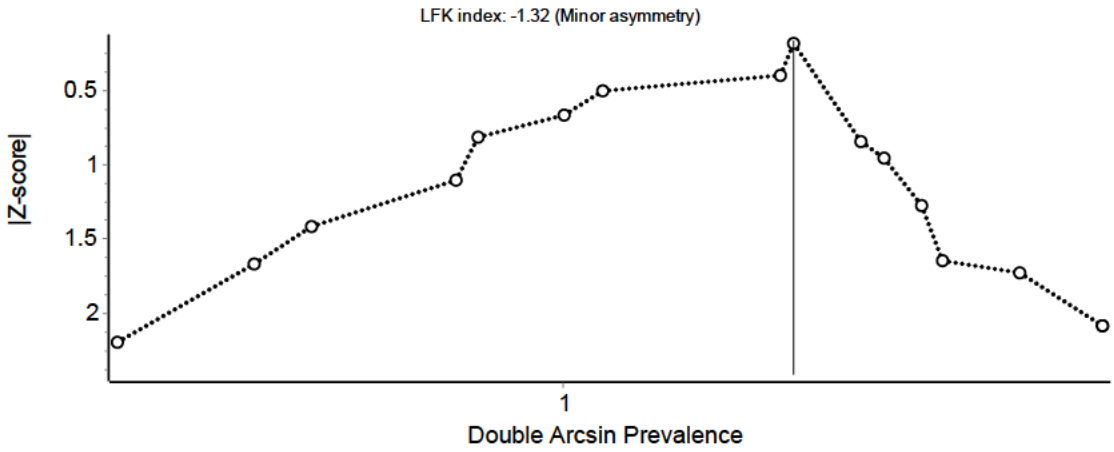


Figure 4

Doi Plot of Normal Quantile (Z-score) against the Effect Size



Prevalence by Anxiety Measure

Fifteen different anxiety measures were used across the included studies (see Table 2). The highest estimate (60%) was based on the parent version of the Spence Child Anxiety Scale (SCAS-P; Boulter et al., 2014), with the child version (SCAS-C) associated with a lower (albeit still high) estimate of 37% (Kuuiskko et al., 2008). The lowest estimate was reported by Cholemkery et al., (2014) using the Kinder-DIPS Diagnostic Interview for Mental Disorders in Children and Adolescents. Whilst pooled estimates based on clinician-administered tools (19%, CI: 7% to 40%) were lower than those based on self-reported symptoms (33%, CI: 25% to 40%), this group difference did not reach significance (Q_B (1) = 1.633, p = .20).

Table 2

Assessment of Anxiety across Included Studies

Anxiety measurement		$N_{studies}$	$N_{participants}$	Proportion (95% CI)	Lead author (date)
Diagnostic tool	Cut-off/criteria				
Kinder-DIPS	ICD-10/ DSM-IV-TR	1	57	0.04 (0.01, 0.13)	Cholemkery et al., 2014
K-SADS-PL	DSM-5	1	21	0.42 (0.22, 0.66)	Guerrera et al., 2022
CAPA	DSM-IV	1	112	0.22 (0.11, 0.40)	Simonoff et al., 2008
Symptom checklist					
ADIS C/P	>4	1	123	0.50 (0.30,0.70)	van Steensel et al., 2012
ADIS P	>4	1	75	0.22 (0.11, 0.42)	Kerns et al., 2021
BASC-2	>2	1	231	0.07 (0.05, 0.12)	Niditch et al., 2012
CBCL	>65	3	3140	0.37 (0.26, 0.50)	Baribeau et al., 2020, Dubin et al., 2015, Factor et al., 2017
CPRS-R-L	≥60	1	260	0.44 (0.25, 0.66)	Anvi el at., 2018
OCHS-R	> 69	1	68	0.09 (0.04, 0.22)	Kim et al., 2000
SASC-R	>48	1	54	0.33 (0.22, 0.47)	Kuuiskko et al., 2008
SCARED	>25	1	61	0.25 (0.13, 0.46)	Ben-Itzchak et al., 2020
SCAS-C	>48	1	168	0.37 (0.32, 0.42)	Kuuiskko et al., 2008
SCAS-P	>44	2	392	0.60 (0.39, 0.78)	Boulter et al., 2014
SPAI-C	≥18	1	54	0.39 (0.27, 0.52)	Kuuiskko et al., 2008
SAS-R	>50	1	41	0.48 (0.25, 0.73)	Bellini, 2004

Measure abbreviations: K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Parent Version, CAPA = The Child and Adolescent Psychiatric Assessment Parent Version, ADIS P/C = Anxiety Disorders Interview Schedule: Child and Parent Combination, ADIS P = Anxiety Disorders Interview Schedule:Parent Version, BASC-2 = Behavior Assessment System for Children – Second Edition, CBCL = The Conners' Rating Scales-Revised, CPRS-R-L = The Revised Conners' Parent Rating Scale, OCHS-R = Ontario Child Health Study, SASC-R = Social Anxiety Scale for Children-Revised, SCARED = Screen for Child Anxiety Related Disorders, SCAS-C = Spence Children's Anxiety Scale Child Version, SCAS-P = Spence Children's Anxiety Scale Parent Version, SPAI-C = Social Phobia and Anxiety Inventory for Children, SASR = Social Skills Rating System

Prevalence by Specific Anxiety Disorder

Prevalence estimates for each anxiety disorder, along with the associated heterogeneity statistics, are listed in Table 3. Of all types of anxiety disorder, specific phobia was the most common (41%), followed by social anxiety (28%), generalized anxiety disorder (27%) and separation anxiety (14%). Less common were panic attacks (0.6%) and agoraphobia (0.5%), although these latter estimates were based on considerably smaller samples. Notably, all estimates were characterized by substantial between-study heterogeneity, highlighting a need to explore additional study-level moderators.

Table 3

Prevalence of Anxiety Disorders in Children and Adolescents with ASD

Disorder	$N_{studies}$	$N_{participants}$	Proportion	Forest plot Proportion ± 95% CI	PI		Heterogeneity	
					L	U	I^2	T
Specific phobia	5	380	.41		.10	.81	95.29	.80
Social anxiety	6	425	.28		.06	.70	90.49	.80
GAD	6	431	.27		.06	.69	94.20	.80
Panic	2	176	.06		.0	.37	0.00	.80
Separation anxiety	7	509	.14		.02	.49	88.47	.80
Agoraphobia	2	169	.05		.0	.33	59.84	.80

Note. $N_{studies}$ = number of studies contributing to these data; $N_{participants}$ = number of participants contributing to these data; CI = 95% confidence interval; L/U = lower and upper limits of CI; PI: prediction interval; I^2 = proportional estimate of true effect variance; T = Tau, estimated standard deviation of underlying true effect across studies.

Moderator Analyses

A univariate meta-regression identified IQ as a key sample moderator (R^2 = 0.39, SE = 0.0133, p = .004): higher IQ explained 39% of the between-study variance in the reported effect sizes. In comparison, prevalence estimates were not significantly influenced by mean sample age (R^2 = -0.02, SE = 0.1030, p = 0.6867).

Subgroup analyses also revealed an association between gender and anxiety (Q_B (1) = 35.02, p < .01): anxiety symptoms and disorders had a higher prevalence in boys (0.391, CI = 0.275 to 0.522) compared to girls (0.056, CI = 0.032 to 0.097). This analysis was, however, limited to only three studies which stratified anxiety rates by gender (Dubin et al., 2015; Guerrera et al., 2022; Factor et al., 2017). Finally, prevalence estimates remained relatively consistent over time, with publication date not identified as a potential moderator (Q_B(1) = 1.133, p = 0.9627).

Discussion

Overview

This meta-analysis synthesised a body of ASD research that, to date, addressed the longstanding issue of varying rates on anxiety prevalence. Based on 15 global studies of 4459 ASD youth, anxiety prevalence estimates were computed and methodological and sample sources (that is, IQ, measure, gender, and publication date) of between-study heterogeneity were explored. The study findings confirm that 1 in 3 ASD youth will experience an anxiety disorder or clinically elevated anxiety symptoms. This prevalence estimate is notably lower than previous meta-analyses that have adopted less stringent inclusion criteria (e.g., 39.6%, van Steensel et al., 2011; 42%, White et al., 2009).

Summary of Findings

In the present study, specific phobia was the most frequent anxiety disorder with a prevalence of 41%, followed closely by social anxiety (28%), generalised anxiety disorder (27%), and separation anxiety (14%). However, these figures may be imprecise, given the wide confidence intervals and substantial heterogeneity associated with the pooled estimate for each disorder. That said, past meta-analyses with ASD groups have also reported substantial between-study variation (van Steensel et al., 2011). Moreover, prevalence studies based on population-based epidemiological research evaluating heterogeneous constructs such as mental health are typically characterised by high variability (Migliavaca et al., 2020).

The high prevalence of anxiety must be considered in the context of measurement error and diagnostic ambiguity that distort the rates currently reported in the literature. Indeed, there was both diversity and imprecision across assessment measures in the included studies. Notably, only the SCAS-C and Kinder-DIPS reported narrow confidence intervals (Cholemkery et al., 2014; Kuuiskko et al., 2008). In comparison, the SCARED reported a confidence interval as low as 0.13% to as high as 0.46% (Ben-Itzchak et al., 2020). The difficult process of diagnosing anxiety based on symptom checklists and interview schedules designed for the general populous is further complicated by the idiosyncratic symptom presentation found in ASD youth. For instance, it has long been noted that some children with ASD display unusual fears (e.g., toilets, swings, clouds) that would be tolerable for most neurotypical children (Mayes et al., 2013, Kerns et al., 2014).

Many social phobia questionnaires designed for neurotypical participants would miss this perspective, leading to undetected anxiety in ASD youth populations. Again, considering the SCARED questionnaire, the item *"I worry about other people liking me"* conceptualises social fear based on the fear of negative social evaluation; an aspect that tends not to be of concern in ASD populations (Kerns et al., 2014). Little consistency and consensus exist around how anxiety in children with ASD should be measured (White et al., 2009). To date, no anxiety questionnaire has been designed with sensitivities towards the ASD youth population. Such a measure would help detangle comorbidities and aid clinical formation in identifying and treating anxiety. Moreover, if a single measurement tool were available for a specific population like youth with ASD, it would probably gain widespread adoption. This, in turn, would offer essential standardisation in epidemiological anxiety studies, potentially reducing the broad confidence intervals observed in the current findings. Future research should also validate the effectiveness of proposed cut-off scores for anxiety caseness. Applying a specific threshold can be challenging since it may result in misdiagnosis, given that individuals above or below the threshold may not exhibit significant distinctions.

Methodological and Population Factors

Moderator analyses revealed strong associations between IQ and gender with ASD anxiety. Interestingly, the emergence of the coronavirus pandemic explained very little of the variance in effect estimates between studies - with anxiety rates remaining consistently high regardless of this disruptive and stressful historical milestone. Additionally, despite noted differences in estimates based on clinician-administered and self-rated measures, no significant between-group differences emerged. However, the accuracy of this finding can be contested considering that the clinician ratings were only based on three studies, resulting in an underpowered analysis (Cholemkery et al., 2014; Guerrera et al., 2022; Simonoff et al., 2008)

The finding that significant heterogeneity can be explained by IQ should be interpreted cautiously given that they pertain almost exclusively to children with high-functioning autism. Five of the 10 studies providing these data required participants to have an IQ above 70 (Bellini et al., 2004; Boulter et al., 2014; Guerrera et al., 2020; Kim et al., 2000; van Steensel et al., 2012). This is reflected in the high mean IQ of the total pooled sample. Such a recruitment bias may obfuscate

the true relationship IQ has with anxiety. A broader range of IQ could reveal a smaller or non-significant relationship. Nevertheless, it is possible that IQ has a non-linear relationship with anxiety prevalence. That is, there may be large differences in anxiety symptomatology between youth with the lowest IQs, those within the normal range, and those that are higher functioning. Possible mechanisms to explain this link between higher IQ and anxiety includes pre-emptive worries associated with anxiety, with greater abstract planning and higher executive functions possibly facilitating worries a child may have about the present, future, or their self-competency (Salazar et al., 2015). Whether the same pattern appears in neurotypical children with a high IQ remains to be seen (Penney et al., 2015). An environmental explanation has also been proposed - that is ASD youth with higher IQ are perceived as more capable and less in need of support, receiving higher expectations without the support to adapt to a neurotypical centric world (Mingins et al., 2021). Indeed, research has shown that people with high-functioning ASD may still display poor adaptive behaviours despite not having an intellectual disability (Alvares et al., 2020). Future ASD research should include group level data from varying IQ ranges to explore these issues further.

The relationship between male gender and anxiety identified in this review also needs to be interpreted in the context of the few studies that provided these data (Dubin et al., 2015; Guerrera et al., 2022; Factor et al., 2017). Additionally, it's worth noting that two of these studies included samples in the pre-pubescent phase (age range 8 to 12 years; Factor et al., 2017; Dubin et al., 2015). As important age-related developmental changes occur during adolescence (i.e., pubertal maturation), underrepresenting this older age group can conceal the impact of gender differences (Yoon et al., 2022). Indeed, research within the ASD youth population has shown that as females transition into later stages of childhood, their levels of anxiety tend to increase at a more accelerated pace than those of males - although girls' anxiety rates still do not surpass boys' (Varela et al., 2020). The gender disparity in anxiety noted in the present review may therefore be overestimate given that female anxiety rates become more pronounced with age.

Methodological Considerations

Several limitations arose during the study screening and data extraction processes that have repercussions for the interpretation of the current findings. First, the reliance on cross-sectional data precludes any inferences about changes in anxiety associated with child age. Studies employing longitudinal data are necessary to investigate relationships between sample moderators that are sensitive to temporal changes (e.g., age-related differences) and can establish causality (Caruana et al., 2015). An observational review across the lifespan can reveal such different developmental manifestations. This research might include, for example, comparisons of separation anxiety in ASD preschoolers to neurotypical children.

Another limitation encountered was the distribution of studies across geographical regions, with an overrepresentation (~60%) of western, educated, industrialised, rich and democratic nations. As such, the findings of this review may not be applicable to developing countries (McConkey et al., 2022) That said, while included studies were required to be published in the English language, no evidence suggests that this restriction has any impact on the quality or generalisability of meta-analyses (Morrison et al., 2012).

Furthermore, the reliance almost exclusively on parental reports posed some challenges. Research has consistently found low to moderate agreement of symptom ratings between parental and ASD children reports. Parent ratings of anxiety often exceed their child's (Cornish & Rinehart, 2015; Kalvin et al., 2019; Storch et al., 2012). The prevalence estimates presented in this review may therefore be inflated given that only two studies contained child reports (Bellini, 2004; Kuuiskko et al., 2008). That said, one sample characteristic known to attenuate the discrepancy between parental and self-reported anxiety is high child IQ (defined as ≥70; Kamp-Becker et al., 2011), an aspect that favours the current findings (Bitsika & Sharpley, 2015).

Additionally, a scarcity of studies using diagnostic tools hindered the current meta-analysis' ability to comprehensively evaluate how the evolution and impact of changes in the DSM criteria affect anxiety disorder prevalence. Only three studies incorporated clinician judgment based on DSM criteria (Cholemkery et al., 2014; Guerrera et al., 2022; Simonoff et al., 2008), and two of them used the same DSM edition (i.e., 4th). Without comparing anxiety prevalence across different

DSM editions, it is unclear whether the DSM-V's additions expanded the participant pool of anxiety caseness. If so, it would suggest that previous diagnostic tools may miss cases using outdated criteria and thus create an underestimation of the current point prevalence. To address such a limitation, future research should prioritise the utilisation of standardised diagnostic instruments based on the most current DSM criteria, allowing for a more rigorous examination of the diagnostic criteria's effectiveness and its implications for clinical practice.

This review exhibited notable strengths, primarily stemming from an extensive literature search, and the analyses not revealing any evidence of publication bias. This was the result of a stringent inclusion criteria that limited inclusion to high-quality studies that used validated assessment methods for anxiety and ASD caseness as well as recruitment methods that focused on population-based samples. Consequently, the studies featured in this review maintained a high level of internal and ecological validity.

Lastly, despite the noted significant heterogeneity in the analyses, which can be attributed to the intricate interaction of differing methodological and sample characteristics in the included studies, the computation of prediction intervals offered an alternative approach to addressing between-study heterogeneity allowing for more informative inferences in the current findings (Barker et al., 2021).

Clinical Implications & Future Research

This meta-analysis identified key issues pertaining to identifying and treating anxiety in ASD youth. Given the demonstrated high levels of anxiety across the young ASD population, it is essential to accurately assess and make available evidence-based treatment options to lessen the burden that many ASD children and adolescents live with. However, children with ASD experience elevated expenses and greater utilisation of healthcare services, yet encounter a disparity in high quality care delivery and adequate care access, compared to the general population (Bishop-Fitzpatrick & Kind, 2017). This may be in part due to treatment options that tend to work for the general population needing specific modifications to be effective for the ASD youth population. For instance, short-term trials of Cognitive Behavioural Therapy (CBT) has shown response rates from 38% to 71% with ASD youth clients, with most effect sizes exceeding 0.80 (Seligman & Ollendick, 2011). However, these benefits only appear when modifications are undertaken, such as CBT

programs being delivered in group settings to facilitate parental involvement and use of visual aids to develop emotional regulation strategies (Danial & Wood, 2013). The findings of this meta-analysis underscore the importance for policymakers to allocate increased funding to these programs, with the aim of enhancing their accessibility to an underserved population.

Additionally, a lack of standardisation in anxiety measures can make the assessment of anxiety challenging. Tools to measure ASD specific symptoms need to be developed and evaluated. Recently, the Anxiety Scale for Autism-Adults was created and proven to have robust psychometrics (Rodgers et al., 2020). This measure should be adapted for children in collaboration with parents, medical and health professionals, and ASD youth themselves. Additionally, low-functioning ASD individuals prove a notoriously difficult population to assess and, therefore, have gone understudied. The Autism Comorbidity Interview, Present and Lifetime Version, stands out as a diagnostic tool with established validity and reliability when assessing ASD youth across a wide IQ spectrum, spanning from 42 to 141. However, despite its effectiveness, this instrument has not gained widespread utilisation. (Mingins et al., 2021). Encouraging the use of such a measure in research and clinical settings can aid the inclusion of low-functioning ASD individuals in prevalence studies and reveal new depths of IQ as a mechanism for anxiety.

Estimating global prevalence rates faces a significant hurdle due to the absence of high-quality, nationally representative epidemiological studies in many parts of the world. This problem is especially prominent in developing nations, which are home to the majority of the world's adolescents (United Nations, 2022). Researching low-income countries can reveal a new and better understanding of anxiety mechanisms and sample characteristics that can help in creating culturally sensitive measures for both detecting ASD and anxiety in a currently understudied population. Additionally, developing culturally sensitive measures for identifying anxiety in ASD youth will facilitate cross-cultural research, encouraging research teams to collaborate across borders. Incentivising future studies to recruit ecological samples in both developed and developing countries will increase generalisability and ultimately accuracy in the prevalent estimate. Government policy initiatives, such as providing extra grant funding for cross-cultural research, can further support such research efforts in this crucial area.

To ensure precise and accurate data, future epidemiological studies should also adopt more stringent guidelines and reporting standards. For instance, a considerable number of included studies neglected to prove any justification for their sample sizes. Indeed, the use of a priori or post-hoc power analyses are essential in transparent to guarantee the replicability and validity of the study's findings. Consistent use of established reporting guidelines for observational studies, such as the CONSORT statement, can ensure that these standards are enshrined (Cuschieri, 2019).

Conclusions

The current meta-analysis synthesised an extensive body of ASD research that spanned the last 23 years. Community samples involving wide recruitment methods informed the prevalence estimate, thereby minimising the influence of recruitment bias found in clinical and treatment samples. These data were, however, reliant on clinician and parental reports and based on a sample that primarily included male youth with ASD from westernised countries. Nonetheless, the high estimate gives impetus to clinicians and researchers to develop tools that can detect ASD-specific symptoms of anxiety to ensure timely and accurate anxiety management for those most at risk.

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Appendix A: Psychology Honours Project 2023 - Research Plan

Student Name:
Student ID: [redacted]

Design Plan

Sampling Plan

Analysis Plan

Study Information

1. Title:

Anxiety Prevalence in Children and Adolescents with Autism Spectrum Disorder: A Meta-Analysis

2. Target Journal:

Journal of Autism and Developmental Disorders (SCIMAGO subject area and category: Psychology Developmental and Educational Psychology)

2.1. Research Aim/s:

The primary aim is to examine the point prevalence of anxiety symptoms and disorders in the international literature on children and adolescents diagnosed with autism spectrum disorder.

Depending on data availability, a secondary aim will be to examine the moderating effects of sample and methodological characteristics on prevalence estimates (e.g., mean sample age, IQ, autism severity, publication date – pre and post-COVID)

3. Research Question/s:

   What is the global prevalence of anxiety in autistic populations aged between 0-18 years? What (if any) methodological and ASD characteristics impact on prevalence estimates?

4. Use of Theory:

   Not applicable

Design Plan

5. Tradition (optional): Not applicable

   Frequentist (using random and mixed-effects models)

6. Study Design:

   Systematic review with meta-analysis

7. Study Measures (optional):

   The primary outcome is anxiety symptom severity (measured via child or parent-reported questionnaire) or diagnostic interview. Well-established anxiety measures for this subgroup include (but are not limited to): the Social Anxiety Scale for Children (SASC; La Greca et al., 1988), Child Behaviour Checklist Anxiety Problems Scale (CBCL; Mazefsky et al., 2011) and DSM-5 Anxiety Disorders (e.g. Generalised Anxiety Disorder, Panic Disorders, Specific Phobias, Social Phobia; American Psychological Association, 2013)

8. Study Materials (optional):
   - Covidence systematic review software (Veritas Health Innovation, Melbourne). Available at: www.covidence.org
   - Comprehensive Meta-analysis Software (Version 4, Biostat). Available at: https://www.meta-analysis.com/

9. Study Procedure:

The first step in this project involved formulating a research question. Following this, a list of terms was developed for each electronic database identified for this review. An expert research librarian was consulted during this process. Records were then located through database searching and uploaded into Covidence software. These records are currently being screened, based on pre-defined inclusion and exclusion criteria. Once a final group of studies has been identified, sample and effect size data for each study will be extracted and entered into CMA software for statistical analysis. The reporting quality of included studies will also be examined using a tool appropriate for observational data (see: https://www.equator-network.org). To transparently archive and share the data of the thesis, a protocol will be registered using Open Science Framework.

Sampling Plan

10. Existing Data/Partial Existing Data/Original Data (choose one)

    Existing data

11. Data Collection Procedures

    Peer-reviewed journal articles published in the English language will be the primary source of data for this meta-analysis. Included studies will use an observational (i.e., survey) design. Data will be extracted from each study (as per point 12, below) using a purposely designed data collection form. A second researcher (postgraduate student or project supervisor) will double check the screening and data extraction process, as a reliability check.

12. Type of Data Collected:

    Data collected from each study will include sample characteristics (e.g., sample size, demographics, method of ASD diagnosis and, if reported, autism symptom severity), and anxiety measurement (self vs. parent report vs clinical diagnosis). The primary effect size will likely involve proportions – calculated from the total sample size and the number of children/adolescents experiencing anxiety symptoms or diagnosed with an anxiety disorder. Attempts will be made to contact study authors where these data are not reported.

13. Sample Size:

    To ensure sufficient statistical power, at least 10 studies will be required for this meta-analysis (Higgins et al., 2022).

14. Stopping Rule:

    Not applicable.

Analysis Plan

15. Data Analyses:
    A pooled estimate will first be calculated using a random effects model. Publication bias will be checked using a funnel plot analysis and statistical outliers identified with a one-study-removed sensitivity analysis (Borenstein et al., 2021). Between-study heterogeneity will be estimated using two statistics: tau (i.e., the between-samples *SD)*, and I^2 (i.e., proportion of variation in observed effects due to true effect variance; Borenstein, 2021). The impact of demographic and ASD characteristics on anxiety will be examined with subgroup analysis and/or meta-regression depending on how these data are reported (i.e., whether categorical or continuous variables)

Other

16. Other (Optional):

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Appendix B: Research Plan Checklist

Students: This checklist must be completed and signed by your primary supervisor as a requirement of the research plan component of the thesis. Please append a signed copy of the completed checklist to your research plan document and submit them together (as a single PDF document) via the MyUni assignments tab no later than **9am 15th of May**. To ensure your supervisor has sufficient time to review your research plan and complete the checklist, we encourage you to provide them with a copy of the checklist and a draft of your research plan as early as possible — at least one week before the due date. We also encourage you to work with supervisors to develop your research plans from early on in the semester.

Supervisors: Research plans for honours projects should be well reasoned and well thought-out (sound), and also manageable within the scope of the timeline, available resources and the student's capabilities (feasibility). Please review the student's research plan (template provided on MyUni) and indicate if each step of their plan is sound and feasible by ticking the appropriate box. If the component is not applicable given the nature of the project please tick "Not Applicable". If any step of the plan is not yet sound or feasible please leave the box/s unticked.

Study Information	Not Applicable	Feasible	Sound
Title	☐	☐	☒
Target Audience	☐	☐	☒
Research Aim/s	☐	☐	☒
Research Question/s	☐	☐	☒
Use of Theory	☒	☐	☐

Design Plan	Not Applicable	Feasible	Sound
Tradition	☐	☐	☒
Study Design	☐	☐	☒
Study Measures	☐	☐	☒
Study Materials	☐	☐	☒
Study Procedure	☐	☐	☒

Sampling Plan	Not Applicable	Feasible	Sound
Data Collection Procedures	☐	☐	☒
Type of Data Collected	☐	☐	☒
Sample Size	☐	☐	☒
Stopping Rule	☒	☐	☐

Analysis Plan	Not Applicable	Feasible	Sound
Data Analyses	☐	☐	☒

Other	Not Applicable	Feasible	Sound
	☒	☐	☐

Student Name	Signature	Date
		11/05/2023

Primary Supervisor Name	Signature	Date

Risk of bias item	Criteria for answers	Additional notes
1. Was the sample frame appropriate to address the target population?	• **Yes (LOW RISK)**: A sample frame is appropriate when it includes close to all members of the target population • **No (HIGH RISK)**: A sample frame is not appropriate when specific population characteristics (e.g. age, gender, morbidities) overrepresents a diverse body of people	The term "target population" should not be taken to infer every individual from everywhere.
2. Were study participants recruited in an appropriate way?	• **Yes (LOW RISK)**: Studies that report random sampling from a population • **No (HIGH RISK)**: Studies that report convenience samples, that is street survey or interviewing lots of people at a public gathering may not be a representative sample of the population	Random probabilistic sampling is unnecessary when all individuals within the sampling frame will be included or analysed.
3. Was the sample size adequate?	• **Yes (LOW RISK)**: Evidence is provided that the authors used a sample size calculation to determine an adequate sample size. • **No (HIGH RISK)**: No sample size calculation is provided	As the sample size increases, the confidence interval around the prevalence estimate becomes narrower, enhancing the precision of the results.

4. Were the study subjects and setting described in detail?	• **Yes (LOW RISK)**: The study sample is described in such detail that other researchers should be able to determine if it comparable to the population of interest. • **NO (HIGH RISK)**: Insufficient information of the sample is provided (e.g. no info on gender ratio, age or state origin)	NA
5. Was data analysis conducted with sufficient coverage of the identified sample?	• **Yes (LOW RISK)**: All subgroups of the sample responded to participation in the study at the same rate • **No (HIGH RISK)**: All subgroups of the sample did not respond to participate in the study	Example: A survey is sent to a high school for students to fill out their attitudes towards healthy eating, all female students respond but only 20% of male students do **(HIGH RISK)**
6. Were valid methods uused d for the identification of the condition	• **Yes (LOW RISK)**: The measure used to identify the condition is psychometrically validated with the outcomes assessed being based on pre-existing definitions or diagnostic criteria. • **No (HIGH RISK)**: The measure used has no cut-off scores and used purposely designed or single-item questionnaires.	Studies using the revised Autism Diagnostic Observation Schedule (ADOS-2) and Autism Diagnostic Interview (ADI-R) can be considered low risk.
7. Was the condition measured in a	• **Yes (LOW RISK)**: Diagnostic instruments were carried out by professionals such as clinicians and any self-report administrated is done so to avoid confounding variables • **No (HIGH RISK)**: The	Were the results from multiple observers or collectors compared? Was the condition consistently measured for all participants?

standard, reliable way for all participants?	measure was administrated by someone with little training in it which lead to confusion from the participants	
8. Was there appropriate statistical analysis?	• **Yes (LOW RISK)**: The reporting provides clarity on both the numerator and denominator, while percentages are accompanied by confidence intervals. Additionally, the methods section offer sufficient detail for reviewers to discern the analytical approach employed and the measurement of specific variables. • **No (HIGH RISK)**: There is a lack of information on the statistical software and analysis used to reach the results.	NA
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	• **Yes (LOW RISK)**: If a high dropout rate is present, the author discusses any reasons for why and compares the participants in the study to those who were not. • **No (HIGH RISK)**: A high dropout rate is present yet no discussion as to why	A substantial occurrence of dropouts, refusals, or "not found" cases among selected subjects can undermine the validity of a study. However, the researchers may be able to justify a more modest response rate.

Appendix D: Logic Grids for Database Searches

Database	ASD	Anxiety
PubMed	Autistic*[mh] OR autism*[tiab] OR autistic disorder[tiab] OR asperger syndrome[tiab] OR child development disorders, pervasive*[tiab] OR asperger[tiab] OR asperger's[tiab] OR aspergers[tiab] OR pervasive development[tiab] OR pervasive developmental*[tiab] OR rett syndrome*[tiab] OR neurodevelopmental disorder*[tiab] OR developmental disorder*[tiab] OR developmental disabil*[mh] OR exp developmental disorder[tiab] OR neuro atypical people[tiab]	“anxiety disorders”[mh] OR anxiety disorder*[tiab] OR anxiety neurosis[tiab] OR phobias panic disorder*[tiab] OR panic disorder*[tiab] OR mental disorder*[tiab] OR mental illness of OR "Mental Health"[mh] OR depression[tiab] OR "stress, psychological"[tiab] OR "emotional impact"[tiab] OR psychologic*[mh] OR psychiatric[tiab] OR anxiety[tiab] OR anxiousness[tiab] OR "Stress Disorder”[mh]
PsycINFO	Autistic*.ti,ab OR autism*.ti,ab OR autistic disorder*.ti,ab OR asperger syndrome*.ti,ab OR child development disorders, pervasive*.ti,ab OR asperger*.ti,ab OR asperger's*.ti,ab OR aspergers*.ti,ab OR pervasive development*.ti,ab OR pervasive developmental*.ti,ab OR rett syndrome*.ti,ab OR neurodevelopmental disorder*.ti,ab OR developmental disorder*.ti,ab OR developmental disabil*.ti,ab OR exp developmental disorder*.ti,ab OR neuro atypical people*.ti,ab	anxiety disorder*.ti,ab OR anxiety neurosis*.ti,ab OR phobias panic disorder*.ti,ab OR panic disorder*.ti,ab OR mental disorder*.ti,ab OR mental ill*.ti,ab OR Mental Health*.ti,ab OR depression*.ti,ab OR "stress, psychological*.ti,ab OR emotional impact*.ti,ab OR psychologic*.ti,ab OR psychiatric*.ti,ab OR anxiety*.ti,ab OR anxiousness*.ti,ab OR "Stress Disorder*.ti,ab
Embase	Autistic*.ti,ab OR autism*.ti,ab OR autistic disorder*.ti,ab OR asperger syndrome*.ti,ab OR child development disorders, pervasive*.ti,ab OR asperger*.ti,ab OR asperger's*.ti,ab OR aspergers*.ti,ab OR pervasive development*.ti,ab OR pervasive developmental*.ti,ab OR rett syndrome*.ti,ab OR neurodevelopmental disorder*.ti,ab OR developmental disorder*.ti,ab OR developmental disabil*.ti,ab OR exp developmental disorder*.ti,ab OR neuro atypical people*.ti,ab	anxiety disorder*.ti,ab OR anxiety neurosis*.ti,ab OR phobias panic disorder*.ti,ab OR panic disorder*.ti,ab OR mental disorder*.ti,ab OR mental ill*.ti,ab OR Mental Health*.ti,ab OR depression*.ti,ab OR "stress, psychological*.ti,ab OR emotional impact*.ti,ab OR psychologic*.ti,ab OR psychiatric*.ti,ab OR anxiety*.ti,ab OR anxiousness*.ti,ab OR "Stress Disorder*.ti,ab

Appendix E: Risk of Bias Within Studies based on JBI Critical Appraisal Tool for Prevalence Studies (Munn et al., 2020)

Lead author (date)	1. Sample frame appropriate to address the target population	2. Study participants sampled in an appropriate way	3. Adequate sample size	4. Study subjects and setting described in detail	5. Data analysis conducted with sufficient coverage of the identified sample	6a. Valid methods used for the identification of ASD	6b. Valid methods used for the identification of anxiety	7. ASD measured in a standard, reliable way	8. 8. Appropriate statistical analysis	9. Adequate response rate – or low response rate managed appropriately
Anvi et al., 2018	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Baribeau et al., 2020	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Benllini, 2004	Yes	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No
Ben-Itzchak et al., 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Boulter et al., 2014	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Cholemkery et al., 2014	Yes	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Dubin et al., 2015	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Factor et al., 2017	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Guerrera et al., 2022	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Kerns et al., 2021	Yes	No	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Kim et al., 2000	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kuuiskko et al., 2008	Yes	Yes	No	Unclear	Yes	Yes	Yes	Yes	Yes	No
Niditch et al, 2012	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Simonoff et al., 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unclear
van Steensel et al., 2012	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear

Legend

Yes

No

Unclear