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REVIEW PAPER

Loneliness in Autism and Its Association with Anxiety and Depression: A Systematic Review with Meta-Analyses

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Abstract

Objectives This systematic review aimed to quantify differences in loneliness levels between autistic and neurotypical samples and investigate the association between loneliness and mental health in autistic individuals.

Methods Three meta-analyses were conducted. Studies were methodologically appraised using established tools.

Results Overall, 39 studies were included. The majority of these achieved moderate methodological quality ratings. The primary meta-analysis ($N = 23$) found autistic samples reported higher loneliness compared with neurotypical samples (Hedges' $g = .89$). The meta-analyses on the associations between loneliness and anxiety ($N = 14$) and depression ($N = 11$) in autistic samples found significant pooled correlations ($r = .29$ and $r = .48$, respectively).

Conclusions This review highlights numerous limitations within current autism and loneliness research. Nevertheless, loneliness in autism merits targeted clinical and research attention.

Keywords Autism · Loneliness · Anxiety · Depression

Introduction

Loneliness has been conceptualised as either a uni- or a multi-dimensional construct (Heinrich & Gullone, 2006), but can broadly be defined as 'A subjective unpleasant or distressing feeling of a lack of connection to other people, along with a desire for more, or more satisfying, social relationships.' (Badcock et al., 2022). Within a multidimensional approach, 'social loneliness' indicates the recognised shortage of desired social relationships with accompanying feelings of exclusion and boredom, whereas 'emotional loneliness' indicates the absence of emotional connection/attachment and a sense of sadness and emptiness (DiTommaso & Spinner, 1997; Weiss, 1973). Importantly, loneliness is distinct from — though may be related to — objective social isolation, i.e. those who have objectively small social networks may not feel lonely, and likewise, loneliness can be felt by those with a seemingly large social network (Hawkley & Cacioppo, 2010). The experience of loneliness is thought to drive the formation and maintenance of relationships necessary for the survival of the human species, therefore acting as a motivator of social connection (Cacioppo et al., 2006).

Occasional feelings of loneliness are commonplace, with reports of between 10 and 80% of people in the general population experiencing loneliness at least sometimes (Beutel et al., 2017). Rates of loneliness are unevenly distributed across the life-course with peaks in prevalence often found in both older and younger adults (Hawkley et al., 2020; Shovestul et al., 2020). Some research has delineated 'chronic loneliness' (i.e. feeling lonely for at least 2 years; Martín-María et al., 2020; Peplau & Perlman, 1982) and 'pathological loneliness' (i.e. increased distress resulting from loneliness; Tiwari, 2013). Research demonstrates between 2 and 38% of the general population in the UK may feel lonely 'most' or 'all of the time' and may feel moderately to severely distressed by loneliness (Victor & Yang, 2012).

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Loneliness and Mental Health

Loneliness is not a mental health condition; therefore, estimating the prevalence of — and threshold for — clinically relevant loneliness has been challenging in both research and clinical practice. Persistent and/or distressing feelings of loneliness can negatively impact on quality of life and wellbeing. A recent overview of 40 systematic reviews pertaining to the public health consequences of loneliness and social isolation found a consistent association with worse mental health outcomes, including depression and anxiety (Leigh-Hunt et al., 2017). Feelings of loneliness have also been found to be more prevalent among those with mental illnesses such as psychosis (Badcock et al., 2020). The association between loneliness and depressive symptoms has been shown to be moderate-large across the lifespan ($r = 0.50–0.63$; Erzen & Çikrikci, 2018; Matthews et al., 2016; Richardson et al., 2017). Similarly, the association between loneliness and anxiety has been found to be moderate-large in children and adult samples ($r = 0.41–0.67$; Beutel et al., 2017; Danneel et al., 2019; Richardson et al., 2017).

Loneliness in ASD

Individuals with autism spectrum disorder (ASD) may be at an increased risk of having fewer social relationships (Milton & Sims, 2016). This lifelong neurodevelopmental condition affects approximately 1% of the global population (Zeidan et al., 2022), and is characterised by difficulties in social communication and interaction, and engagement in restricted, repetitive behaviours or interests (American Psychiatric Association; APA, 2013). The characterisations of autism itself, as well as comparisons between autistic[1] and neurotypical (non-autistic) samples, may have maintained a narrative that autistic individuals are content in being alone; indeed, autistic individuals were historically considered to have 'a powerful desire for aloneness' (Kanner, 1943, p.249). Autism diagnostic criteria emphasise individuals' deficits in social skills and interaction, including the lack of social-emotional reciprocity and a failure to develop developmentally appropriate peer relationships (APA, 2013). In line with the social motivation theory of autism, some researchers have posited that autistic individuals have less desire for — and may derive less pleasure from — social interactions, which subsequently decreases the likelihood of successful relationship development and maintenance (Chevallier et al., 2012). Research suggests autistic people have fewer, or no friendships in comparison to neurotypical peers (Orsmond et al., 2004; Shattuck et al., 2011) and in both child and adult samples, friendships have been reported to be of lower quality, result in less enjoyment and be defined in terms of social proximity rather than emotional connectedness (Baron-Cohen et al., 2001; Bauminger et al., 2004; Whitehouse et al., 2009). Nevertheless, research demonstrates that autistic individuals not only desire social interaction but may experience loneliness to a greater degree without it, compared to neurotypical individuals. For example, Bauminger et al. (2003) found autistic adolescents reported increased feelings of both social and emotional loneliness compared to neurotypical peers. Much of the research on loneliness in autism pertains to children and adolescents, in line with broader autism research (Evans, 2013). However, studies within adult samples have also reported the occurrence of loneliness among autistic adults (Hickey et al., 2018; Mazurek, 2014) and suggest that this is higher than neurotypical adults (Sundberg, 2018). However, evidence for increased loneliness in autistic compared to neurotypical samples is not ubiquitous in the literature, e.g. Chamberlain et al. (2007) and Bottema-Beutel et al. (2019) did not find any significant differences in loneliness levels between autistic and neurotypical children. It is notable that these studies had small sample sizes (17–21 participants per group) which may have compromised statistical power (Cohen, 1992).

Loneliness may be understood, experienced and expressed differently in autistic individuals compared with neurotypical individuals (Bauminger & Kasari, 2001). Moreover, the current methods used for measuring loneliness may be unsuitable for autistic individuals. In a study of 7–12 year olds, an experimental approach-avoidance task demonstrated autistic children showed an implicit desire for social interaction which was not captured in explicit questionnaire responses (Deckers et al., 2014). In their study of loneliness in 8–14-year-old high-functioning autistic children, Bauminger and Kasari (2000) found neurotypical children defined and understood loneliness as being alone with accompanying feelings of sadness, whereas the majority of autistic children defined loneliness as being alone without attributing an affective component.

There are several important factors which may influence loneliness experiences in autistic individuals. Co-occurring intellectual disability (ID) is prevalent in those diagnosed with autism, with reported rates between 30 and 70% (Thurm et al., 2019). Those with higher intellectual functioning may have greater self-awareness and awareness of social isolation (Volkmar et al., 2005), increasing susceptibility to loneliness (Bauminger & Kasari, 2001). Additionally, gender and age may influence loneliness experiences in autistic samples. For example, research has suggested autistic adolescent males have lower social motivation and friendship quality compared to autistic females (Sedgewick et al., 2016). There is also evidence of changes in the number and quality of friendships in autistic samples across the lifespan, with fewer friends in

[1] The term 'autistic' is used following research by Kenny et al. (2016) who found this term is preferred by the majority of UK autistic community respondents.

adolescence and adulthood compared to childhood (Howlin et al., 2004), which may also impact on feelings of loneliness (Kasari & Sterling, 2013).

Loneliness and Mental Health in ASD

Autistic populations experience a disproportionately high incidence and prevalence of anxiety and depression, in comparison to neurotypical populations (Joshi et al., 2013). A recent systematic review and meta-analysis of 30 studies measuring anxiety and 29 studies measuring depression suggested a pooled estimate of current and lifetime prevalence of 27% and 42% for anxiety disorders, and 23% and 37% for depressive disorders in autistic adults, respectively (Hollocks et al., 2019). Similar rates of comorbid anxiety and depression are reported across child and adolescent autistic samples (Hudson et al., 2019; Vasa & Mazurek, 2015; Wigham et al., 2017), and higher rates are reported in females compared to males (Sedgewick et al., 2020).

Loneliness in autism may be especially important to investigate considering research has evidenced significant associations between loneliness and depression (Han et al., 2019; Hedley et al., 2018a, b) and anxiety (Schiltz et al., 2020) in autistic individuals. It is possible that risk, causal and maintaining mechanisms for both loneliness and mental health difficulties reflect the core socio-communicative differences inherent in ASD. Additionally, the bi-directional influence of loneliness and mental health difficulties is also important to consider (Nuyen et al., 2020), as negative feelings associated with loneliness, anxiety and/or depression may limit the opportunities to develop meaningful relationships with others, which in turn exacerbate such feelings, impede socio-communication and drive social withdrawal (Magnuson & Constantino, 2011).

Despite increasing recognition within the autism community that loneliness is experienced by autistic people (National Autistic Society, 2018), the occurrence and degree of loneliness in this population in comparison to neurotypical individuals have not been systematically reviewed or quantitatively synthesised. Understanding the prevalence of loneliness in autism could have important clinical implications, especially given the increasing provision of psychosocial interventions to reduce social isolation and enhance social functioning and integration of autistic individuals (Pallathra et al., 2019). The disproportionate prevalence of anxiety and depression in the autistic population, and the potential influencing role of loneliness, indicates synthesis of the current evidence is imperative in directing future research in this emerging field.

The primary aim of this review is therefore to examine differences in loneliness levels between autistic and neurotypical samples. The secondary aim is to explore the association between loneliness and anxiety and depression in autistic individuals. To address these aims, three meta-analyses were employed to evaluate the following questions: (1) Is there a difference in loneliness levels between autistic and neurotypical individuals? (2) What is the strength of association between loneliness and anxiety among autistic people? (3) What is the strength of association between loneliness and depression among autistic people?

Method

Search Strategy

As is recommended by the Centre for Reviews and Dissemination (CRD, 2009), this review was undertaken following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009). A protocol was published on the PROSPERO database prior to this review's formal commencement.[2] Four bibliographic electronic databases (Scopus, PsycINFO, MEDLINE and ProQuest Dissertations and Theses) were searched from their inception until 01st September 2021. Forward and backward citation searches were conducted, as well as manual searching of the reference lists of included articles and relevant reviews (see Table 1 for a search syntax example).

Eligibility Criteria

Table 2 lists the eligibility criteria specific to the primary review and meta-analysis. Inclusion and exclusion criteria for the second review were identical to those in the first review with the following exceptions: studies did not need to include a neurotypical comparison group or to report loneliness levels; however, they must have measured anxiety or depression via a symptom severity questionnaire.

Screening

The search yielded 906 articles following deduplication. Study titles and abstracts were screened for relevance and those considered likely to meet selection criteria were reviewed in full ($n = 83$). Some studies were deemed to include overlapping participant samples,[3] which resulted in three being excluded from inclusion in this review. Full-text

[2] This review was registered on PROSPERO on 09.09.2020: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020205493

[3] Where studies were thought to have overlapping samples, the first published study or those with most participants were selected (highlighted here in bold) for inclusion in summary tables e.g., (**Bauminger et al.,** 2003; Bauminger et al., 2004); (Bohnert et al., 2019; **Lieb & Bohnert,** 2017; Ward et al., 2017). Of note, two studies with overlapping participants (**Lin & Huang,** 2019; **Syu & Lin,** 2018) were included in separate meta-analyses and have been presented separately in tables.

Table 1 Search syntax example

Construct	Search terms
Autism	Autis* OR Asperger* OR "pervasive development* disorder*" OR "Autistic Disorder" OR "Child development* disorder*" OR ASD OR ASC OR PDD
Loneliness	"loneliness" OR Lonel* OR "Social* isolat*" OR "Social disconnect*" OR "alone*"
Anxiety or depression	Depress* OR "low mood" OR "negative affect" OR "depress* disorder*" OR "affective disorder*" OR "mood disorder" OR "dysthymi*" OR "major depress* disorder*" OR anxi* OR "anxi* disorder*"

Terms were searched as keywords and MeSH/thesauri terms in PsychINFO and Medline. The Boolean operator * was used to identify spelling variations and word-endings. Terms were combined using AND. Following the initial search, search terms for 'Anxiety' and 'Depression' were added to ensure articles pertaining to the secondary review question were not missed

Table 2 Inclusion and exclusion criteria for the primary review and meta-analysis

Inclusion criteria	Exclusion criteria
• Observational/cross-sectional designs or cross-sectional data from longitudinal designs • People with diagnosed or self-reported ASD (with or without comorbid ID diagnosis) • A neurotypical (NT) comparison group • Adults (aged ≥ 18 years) or children (aged ≤ 17 years). If study populations overlap, subgroups will be identified through sample age means • Utilised measures of subjective loneliness • Reported the percentage of participants meeting a pre-defined cut-off score or average score obtained in both ASD and NT samples. For inclusion in the meta-analysis, an appropriate effect size must be reported for mean differences between groups (or calculable from available statistics)	• Qualitative studies, case-study or case-series designs • Utilised an ASD screening tool in general populations in the absence of diagnosed or self-reported ASD • Studies measuring/reporting objective social isolation or social network size only • Prevalence or mean loneliness scores not reported separately for ASD and NT comparison group • Comparison groups whereby participants have intellectual disabilities, neurodevelopmental conditions or mental health diagnoses • For meta-analyses, relevant data for calculating effect sizes unavailable or not provided by corresponding authors upon request • Written in languages other than English, with no translated paper or abstract available

ASD, autism spectrum disorder; *NT*, neurotypical

review excluded 44 articles, resulting in 39 studies (38 unique cohorts) included in the final reviews. Figure 1 summarises the selection process. Note. *n*, number; *SR*, Systematic Review; *MA*, Meta-Analysis. *The corresponding author of this study (Pak, 2019) was unable to provide the necessary information for inclusion in the review. Several studies were included in more than one review.

Data Extraction

As is recommended for systematic reviews, a data extraction tool was developed a priori and amended following piloting on four randomly selected included studies (Boland et al., 2014). Data were extracted verbatim onto an excel spreadsheet to minimise transcription errors. This included information on study characteristics (i.e. authors, date, publication status, country, objectives and population), sample characteristics (i.e. sample size, age, gender, ethnicity and IQ) and study results (i.e. procedures for ascertaining autism diagnosis, loneliness and anxiety or depression measures, key findings and statistical data). Where relevant data were not reported, authors were contacted via email. Data extracted for the primary meta-analysis included differences between loneliness rates (%) or levels (means; including F, t or Z statistics) between autistic and neurotypical samples. If this was not reported, sample sizes, loneliness mean scores and standard deviations were extracted to allow an effect size to be calculated. For the secondary meta-analyses, correlation values (r) or t statistics were extracted from studies. Studies were synthesised narratively where appropriate statistical data were not reported for inclusion in the meta-analyses.

Quality Assessment

Study quality was appraised using the Effective Public Health Practice Project (EPHPP) Tool for Quantitative Studies (Thomas et al., 2004), which was adapted for use within this review. The EPHPP has established content and construct validity (Thomas et al., 2004), fair inter-rater agreement (Cohen's kappa = 0.60) for individual domains and excellent final rating agreement (Intra-class correlation coefficient = 0.77; Armijo-Olivo et al., 2012). This tool includes the essential criteria for methodological quality appraisal (CRD, 2009) and aligns with the recommended reporting of observational studies in epidemiology (Vandenbroucke

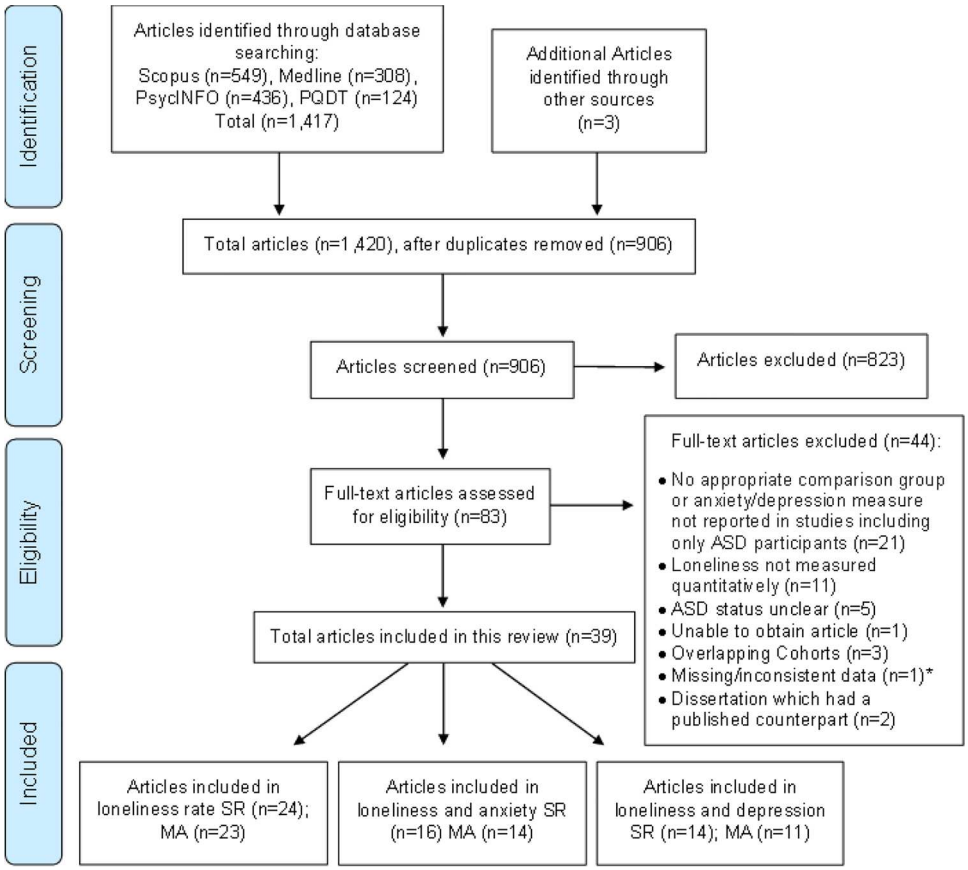

Fig. 1 PRISMA flow diagram

Note. n, number; SR, Systematic Review; MA, Meta-Analysis. *The corresponding author of this study (Pak, 2019) was unable to provide the necessary information for inclusion in the review. Several studies were included in more than one review.

et al., 2007). Additional criteria were included from the quality evaluation grid developed by Glod et al. (2015) which tailored methodological appraisal for studies including autistic samples. Criteria included as follows: how ASD diagnosis was confirmed for the study, whether cognitive functioning was assessed and reported and whether the measures used were validated for ASD populations.

Overall, studies were rated across seven domains: selection bias, study design, potential confounders (for studies including an NT comparison group), data collection (validity and reliability of measures used), management of participant drop-out/missing data, ASD diagnosis confirmation and cognitive functioning. In line with the EPHPP tool, criteria were rated as follows: Strong, Moderate or Weak. The overall quality of studies consisted of a rating of 'Strong' if no weak ratings were present, 'Moderate' if one weak rating was present and 'Weak' if two or more weak ratings were present. It was decided a priori that no studies would be excluded from the review or meta-analysis based on weak global ratings. Due to the nature of this review including studies pertaining to different research questions, an additional 'Not Applicable' option was added to criteria (see supplementary table 1 for details on how component ratings were assigned to studies).

All studies were quality appraised by the first author, with a subset (12 papers; 31%) appraised by an independent reviewer. Agreement in component and overall ratings was evaluated using weighted Cohen's Kappa[4] (Schuck, 2004), with any disagreements resolved following discussion. Inter-rater reliability before consensus ranged between 'fair' and 'very good' (see supplementary table 2 for agreement statistics).

Meta-analytic Strategy

Meta-analyses were conducted using Comprehensive Meta-Analysis (CMA-Version 3; Borenstein et al., 2013). Random

[4] The Byrt (1996) criteria were used to interpret the weighted kappa values as follows: none < 0.01, poor = 0.01–0.20; slight = 0.21–0.40; fair = 0.41–0.60; good = 0.61–0.80; very good = 0.81–0.92 and excellent = 0.93–1.00. The weighted kappa allows consideration of the closeness of agreement between raters (i.e. a disagreement of 'strong' vs 'moderate' is closer than 'strong' vs 'weak') and may not corresponded to the % of exact agreement.

effects models were employed to account for expected within-study and between-study variance in true effect size estimates (Borenstein et al., 2010). For the primary meta-analysis, Hedges *g* was selected as the effect size for standardised mean difference due to its increased (weighted) accuracy when used with small sample sizes ($n < 20$) compared to Cohen's *d* (Ellis, 2010). For the secondary meta-analyses, correlation coefficients (*r*) were selected as the effect size due to being easily interpretable and due to their inclusion in prior meta-analyses of associations between loneliness and mental health in neurotypical samples (Erzen & Çikrikci, 2018). Correlational statistics were transformed into Fisher's *Z* scores during meta-analytic computations to account for possible skewed data distributions (Cox, 2008). Effect size magnitudes were interpreted according to Cohen (1992), i.e. small, medium and large effect size estimates of 0.10, 0.30 and 0.50 for *r* and 0.2, 0.5 and 0.8 for Hedges' *g*, respectively.

Heterogeneity

Effect size variance between studies was assessed using the Cochran *Q* and I^2 statistics. A significant *Q* statistic indicates that statistical heterogeneity is present. An adjusted alpha level of 0.10 was used due to the low power of this statistical test when few studies are analysed (Israel & Richter, 2011). The I^2 statistic was used to quantify the proportion of variance across studies that was due to true heterogeneity rather than chance, whereby 25%, 50% and 75% indicate low, moderate and high heterogeneity respectively (Higgins et al., 2003).

Moderator Analysis

To investigate sources of heterogeneity, moderator analyses (including subgroup analysis for categorical variables and meta-regression for continuous variables) were planned (Borenstein et al., 2010). This included assessing the influence of age, gender, population (child or adult), presence of intellectual disability (ID), publication status (given the existence of larger effects being found in published as compared with unpublished studies; Boland et al., 2014) and the methodological quality of studies (Ioannidis, 2008). In line with previous systematic reviews and meta-analyses in autistic populations, the type of outcome measures used and the ASD diagnostic procedures reported (i.e. the diagnostic tools and procedures used to confirm autism) were also planned to be analysed as potential moderating variables[5] (Hollocks et al., 2019; Spain et al., 2018). For subgroup analyses, summary effects for each group were computed and compared through a random effects approach to allow the total variance to be investigated with respect to within- and between-subgroup means. Meta-regression allowed calculation of the relationship between continuous variables and variation in effect-sizes (Israel & Richter, 2011).

Where multiple outcome measures were reported, the most comprehensive construct and/or reliable measure was selected for meta-analytic computations, due to the reported invalidity of effect size estimates that may occur through averaging effect-sizes (Park & Beretvas, 2019). Where studies provided both self- and other-reported measures (e.g. child and parent), self-reported data were included in meta-analyses. Of note, gender could not be investigated via subgroup analyses due to fewer than three studies providing outcome data separately for males/females; Card, 2015). Subgroup analysis based on ID could not be conducted due to insufficient studies including participants with ID.

Publication Bias

Publication bias was mitigated through inclusion of unpublished studies and use of subgroup analyses based on publication status. Egger et al.'s (1997) regression test was also conducted, along with fail-safe analysis to quantify the number of missing studies that would be required to invalidate a significant result (the threshold of which was met if $N > 5k + 10$, where *k* is the number of included studies; Rosenthal, 1979). A funnel plot provided graphical representation of the assessment of each study's precision (i.e. standard error) plotted against its effect-size, whereby asymmetrical patterns of effect-sizes around the mean effect-size indicate publication bias (Sterne & Egger, 2005). Finally, trim and fill methods were employed to account for missing studies and provided an unbiased effect size estimate (Duval & Tweedie, 2000). The significance level of these publication tests was set to 10% due to their low power (Lin & Chu, 2018).

Results

Studies retrieved for the primary review (*differences in loneliness levels between ASD and NT samples*; $N = 24$) and secondary review (*associations between loneliness and anxiety*; $N = 16$, *associations between loneliness and depression*; $N = 14$) are described separately in the summary tables, narrative syntheses and meta-analyses.

Loneliness Levels Between ASD and NT Samples

Study and Participant Characteristics

As can be seen in Table 3, of the 24 studies with unique cohorts included in this review, 23 utilised a cross-sectional

[5] The following moderators were prespecified in the registered protocol: age, gender, population, presence of intellectual disability and the measures/procedures used to assess ASD and loneliness.

Table 3 Study and participant characteristics for studies measuring loneliness levels between ASD and NT samples

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study sample	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group (%)	IQ measure (M, SD, R)
Bauminger and Kasari (2000)	America	Explored children's understanding of the constructs of loneliness and friendship quality	Children	ASD: 22 NT: 19	ASD: M = 10.74, SD = 2.14, R = 7–14 NT: 10.89, SD = 2.10, R = 7–14	ASD: 95%; NT: 95%	ASD: 95% White NT: 95% White	WISC-R; ASD: M = 108.14, SD = 15.09, R = 84–138 NT M = 115.73, SD = 9.75, R = 92–129
Bauminger et al. (2003)*	Israel	Investigated children's spontaneous social interaction with peers in a naturalistic setting and their understanding and feelings of loneliness	Children	ASD: 18 NT: 17	ASD: M = 11.00, SD = 2.83; R = 8–17 NT M = 11.51, SD = 2.62, R = 8–16	ASD: 89%; NT: 88%	Rates NR. (states 'Caucasian families')	WISC-R; ASD: M = 93.61, SD = 13.61, R = 77–117 NT M = 98.35, SD = 7.19, R = 83–111
Bossaert et al. (2012)	Belgium	Examined whether perceived loneliness, number of friends, friendship quality and social self-concept differed among autistic, non-autistic and motor/sensory-impaired children	Children	ASD: 58 NT: 108	Age NR (states '7th Grade classrooms')	ASD: 90%; NT: 76%	NR	NR. States no participants had an intellectual disability (IQ < 70)
Bottema-Beutel et al. (2019)	America	Assessed children's endorsement of friendship expectations and associations with self-worth, friendship quality and loneliness in autistic and non-autistic samples	Children	ASD: 20 NT: 21	ASD M = 9.90, SD = 0.81, R = 8–11 NT M = 9.30, SD = 0.66, R = 8–11	ASD: 70%; NT: 42.9%	ASD: 57.9% Caucasian NT: 52.4% Caucasian	Mental Age derived from WASI-II. ASD: M = 10, SD = 1.77, R = 7.7–13.2 NT: M = 10.3, SD = 1.22, R = 7.5–12.2
Brooks (2014)	America	Explored gender differences in socio-emotional functioning among high functioning autistic and neurotypical samples [Dissertation]	Adults	ASD: 56 NT: 56	ASD: M = 26.3, SD = 6.0, R = 18–40 NT M = 26.4, SD = 4.6, R = NR	ASD: 50%; TD: 50%	ASD: 86% Caucasian NT: 80% Caucasian	WASI-II administered to ASD group only. FSIQ unreported. VCI female: M = 107, SD = 14.8 VCI male: M = 105, SD = 20.7

Table 3 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study sample	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group (%)	IQ measure (M, SD, R)
Chamberlain et al. (2007)	America	Used social network methods to explore friendship qualities, peer acceptance and loneliness in autistic and non-autistic children in mainstream classrooms	Children	ASD:17 NT: 17	NR (states '2nd through 5th grade classes')	ASD: 82%; NT: 44%	NR	IQ measured in ASD group only (unspecified assessment measure). M = FSIQ M = 107.3, R = 89–129
Chang et al. (2019)	Taiwan	Explored relationships between friendship quality and emotional well-being of autistic and neurotypical adolescents	Children	ASD: 101 NT:101	ASD: M = 16.6, R = 10–19 NT: M = 16.1, R = 10–19	ASD: 83%; NT: 52%	NR	NR. States no participants had an intellectual disability (IQ < 70)
Chiang (2003)	America	Examined the impact of a therapeutic intervention, within a technology-based physical activity context, on the social interaction of autistic and neurotypical peers [Dissertation]	Children	ASD: 6 NT: 6	ASD: M = 12.1, SD = 1.8 NT: M = 12.2, SD = 1.7	ASD: 100%; NT:100%	NR	NR. States 'All participants were intellectually average'
De Gennaro (2016)	America	Explored whether autistic adolescents experience higher rates of loneliness than peers and examined potential contributing factors [Dissertation]	Children	ASD: 17 NT: 25	ASD: M = 14.58, SD = 1.46 NT: M = 13.0, SD = 0	ASD: 82.4%; NT: 68.75%	NR	NR
Deckers et al. (2017)	Netherlands	Examined loneliness and social correlates, including social anxiety, in autistic and neurotypical children using a multi-informant approach (children, parents and teachers)	Children	ASD: aged 7–11 = 47, aged 12–18 = 26 NT: 54, 52, as above	ASD: M = 11.2, SD = 2.42 NT: M = 11.61, SD = 2.63	ASD: 85%; NT: 58%	NR. States 'predominantly Caucasian participants'	NR those with estimated IQ < 70 were excluded

Table 3 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study sample	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group (%)	IQ measure (M, SD, R)
Ee et al. (2019)	Australia	Compared levels and predictors of loneliness in autistic and neurotypical adults and thematically analysed data on autistic adults' socialisation experiences	Adults	ASD: 220 NT: 146	ASD: M = 41.9, SD = 12.24, R = 25–80 NT: M = 43.7, SD = 13.49, R = 25–80	ASD: 39% NT: 19.9%	NR	NR, Included those with formal diagnoses of 'intellectual disability'
Han et al. (2019)	America	Examined individual differences and associations in social and non-social pleasure, autism traits, loneliness and depressive symptoms across samples of autistic and non-autistic adults (with and without depression)	Adults	ASD: 49 NT: 28	ASD: M = 23.98, SD = 26.23 NT: M = 25.32, SD = 5.28, R = 18–35	ASD 61%; NT: 50%	NR	Unspecified IQ measure. ASD: verbal M = 103.63, SD = 12.75; non-verbal M = 103.04, SD = 19.11 NT: verbal M = 114.93, SD = 14; non-verbal M = 109.11, SD = 15.30
Hymas (2021)	UK	Explored social identity in autistic and neurotypical adults and its association with mental health, controlling for relevant confounders including loneliness levels [Dissertation]	Adults	ASD: 174 NT: 199	ASD: M = 35.85, SD = 13.23, R = 18–69 NT: M = 33, SD = 11.67, R = 18–69	ASD: 40% NT: 22%	ASD: 87% White NT: 86% White	NR. Learning disability diagnosis was an exclusion criterion
Kalyva (2010)	Greece	Examined social skills of children with Asperger's syndrome and matched peers via self-report as well as reports from their mothers, fathers and teachers	Children	ASD: 21 NT: 21	ASD: M = 12.56, SD = 2.34 NT: M = 12.53, SD = 2.39	ASD: 81%; NT: 81%	NR	WISC-III Verbal IQ. ASD: M = 93.95, SD = 12.70 NT: M = 101.38, SD = 12.05

Table 3 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study sample	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group (%)	IQ measure (M, SD, R)
Lasgaard et al. (2010)	Denmark	Compared the prevalence of loneliness in autistic and neurotypical boys and examined the value of multiple social support sources in relation to loneliness	Children	ASD: 39 NT: 199	ASD: M = 14.2, SD = 1.03, R = 13–17) NT: M = 14.1, SD = 0.43, R = 13–16	ASD: 100%; NT: 100%	NR	NR. Teachers rated participants' scholastic difficulties on a scale
Lin and Huang (2019)	Taiwan	Explored demographic and psychosocial factors associated with quality of life in autistic and neurotypical adults	Adults	ASD: 66 NT: 85	ASD: M = 27.8, R = 20–38, SD = 5.2 NT: M = 27.8, R = 20–38, SD = 4.3	ASD: 65%; NT: 61%	NR	NR. States no participants had an intellectual disability (IQ < 70)
Locke et al. (2010)	America	Examined the social–emotional relationships (loneliness, friendship quality and social networks) of autistic and non-autistic adolescents	Children	ASD: 7 NT: 13	ASD: M = 14.71, SD = 1.11 NT: M = 14.20, SD = 0.63	ASD: 57%; NT: NR	ASD: 72% Caucasian NT: NR	NR
Merkler (2007)	America	Developed a new measure of loneliness, incorporating dyadic and social group isolation and distress resulting from isolation and compared this between autistic and non-autistic samples [Dissertation]	Adults	ASD: 37 NT: 82	ASD: M = 29.65, SD = 10.19, R = 18–52 NT: M = 18, SD = 0.33, R = 17–19	ASD: 81%; NT: 32%	ASD: 89% Caucasian NT: 83% Caucasian	BETA III. ASD: M = 93.13, SD = 12.59, R = 69–118 NT: M = 107.45, SD = 11.41, R = 84–139
Nomura et al. (2012)	Japan	Explored the developmental differences in feelings of loneliness and its relationship to competence in children with high functioning PDD and neurotypical peers	Children	ASD: 45 (15 elementary, 16 higher elementary, 14 junior high) NT: 281 (89; 87; 105, as above)	ASD: elementary school M = 8.03, R = 6–9; higher elementary school M = 10.66, R = 9–12; junior high school M = 14.16, R = 12–15 NT: NR	NR	NR	NR. States verbal score above 70 on Japanese version of WISC-III

Table 3 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study sample	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group (%)	IQ measure (M, SD, R)
Russell (2020)	America	Examined and compared factors contributing to physical and mental health difficulties within and between autistic and neurotypical adults. [Dissertation]	Adults	ASD: 22; NT:21	ASD: M = 25.26, SD = 3.97 NT: M = 23.55, SD = 4.88	ASD: 72.7%; NT:38.1%	NR	NR
Schalbroeck et al. (2021)	Netherlands	Investigated the association between dopamine functioning and social defeat (as measured by unwanted loneliness) in autistic and neurotypical adults	Adults	ASD:44 NT:22	ASD: M = 23.74, SD = 2.64, R = 18–30 NT: M = 23.47, SD = 2.48, R = 18–30	ASD:64%; NT:64%	States participants are Dutch	States participants attained an IQ ≥ 85 on Dutch Adult Reading Test. ASD: M = 103.75 (5.19); NT: M = 105.05 (4.90)
Sundberg (2018)	Sweden	Investigated the associations between online gaming, loneliness and friendships in autistic and neurotypical adults	Adults	ASD: 85 NT: 66	ASD: M = 28.83, SD = 11.43, R = 14–60 NT: M = 28.5, SD = 9.78, R = 15–69	ASD:58%; NT: 52%	NR	NR
Whitehouse et al. (2009)	Australia	Explored the relationship between friendship, loneliness and depressive symptoms in adolescents with and without Asperger's syndrome	Children	ASD: 35 NT: 35	ASD: M = 14.17, SD = 0.67, R = 12–17 NT: M = 14.33, SD = 0.83, R = 13–16	ASD: 80%; NT: 83%	NR	NR
Yeung (2009)	America	Examined the quality of friendships and wellbeing (i.e. loneliness and depression) of sibling children with and without Asperger's syndrome. [Dissertation]	Children	ASD: 19 NT: 19	ASD: M = 10.05, SD = 1.38, R = 8–12 NT: M = 10.05 years, SD = 1.69, R = 8–12	ASD: 85.7%; NT: 57.9%	ASD: 86% Caucasian NT: 84% Caucasian	NR

Three studies (Chang et al., 2019; Merkler, 2007; Sundberg, 2018) had overlapping participant age ranges including both children and adults, so population categorisation was decided based on mean age. *M*, mean; *SD*, standard deviation; *R*, range; *NR*, not reported; *FSIQ*, Full Scale Intelligence Quotient; *VCI*, Verbal Comprehension Index; *BETA III*, Revised Beta Examination (Kellogg & Morton, 1999); *WASI*, Wechsler Adult Intelligence Scale (Wechsler, 2011); *WISC*, Wechsler Intelligence Scale for Children (Wechsler, 2008)

design and one (Chiang, 2003) employed a pre-post experimental design (the baseline cross-sectional data were used in this review). All studies apart from one (Schalbroeck et al., 2021) provided appropriate data for inclusion in the meta-analysis. Studies were published between 2000 and 2021 and were conducted across 11 different countries, with the majority conducted in America ($N = 11$). Most studies used child and/or adolescent populations ($N = 15$).

Collectively, studies included 2944 participants (ASD = 1251; NT = 1693); sample sizes varied from 12 to 373 and ages ranged from 7 to 80 years. Of those that reported the ethnicity of the included sample ($N = 10$), the most represented ethnicity was White/Caucasian. Males were disproportionately represented in the ASD samples in 15 studies and in the NT sample in one study; gender distributions were equal in six studies and unreported in two.

Outcomes

Quality appraisal of each study is reported in supplementary material 3. Eleven different self-report loneliness measures were used across the 24 studies, the most frequently used ($N = 5$) was the Children's Loneliness Scale (CLS; Asher et al., 1984). Of the 24 studies, 21 showed significantly higher average loneliness scores in the ASD sample compared to the NT sample. The remaining three reported no significant differences between groups, although all displayed a trend towards higher loneliness scores in the ASD group.

Four studies reported loneliness prevalence according to predetermined cut-off rates (Bauminger & Kasari, 2000; Bossaert et al., 2012; Chang et al., 2019; Lasgaard et al., 2010), of which three statistically compared rates between ASD and NT samples. Results showed ASD samples reported significantly higher levels of loneliness (i.e. reported feeling a higher magnitude of loneliness or felt lonely more often) (see Table 4 for an overview of study measures, outcomes and overall quality appraisal score).

Meta-Analysis

Figure 2 shows individual studies' mean effect sizes and the pooled mean effect size. As predicted, autistic samples reported significantly higher loneliness than NT samples, with a large weighted pooled effect (Hedges' $g = 0.89$; 95% CI [0.76, 1.02]; $Z = 13.66$, $p < 0.001$). Effect sizes ranged between $g = 0.18$ and 1.58. Two studies (Deckers et al., 2017; Nomura et al., 2012) included differing age groups. As the subgroups were all aged < 18, these were combined within each study for the purpose of meta-analytic computations at the study-level.

Heterogeneity

Significant heterogeneity was identified $Q(22) = 41.12$, $p = 0.008$. The I^2 statistic indicated low-moderate heterogeneity with 46.50% of the dispersion between studies estimated to be real differences in the study effects. Heterogeneity was explored through categorical moderator analyses and meta-regression and outlined in Table 5. Across studies, 11 unique loneliness measures were used, with only one (the CLS; Asher et al., 1984) being used in enough studies to warrant sub-group analyses; the moderator analysis, therefore, investigated CLS against the other measures used. An insufficient number of studies ($N = 3$) received 'strong' ratings of overall methodological quality to enable them to occupy a separate subgroup, based on a priori criteria (Card, 2015). Therefore, subgroup analyses were conducted on studies appraised as methodologically 'moderate-strong' ($N = 13$) or 'weak' ($N = 10$). Only one moderator was evidenced to significantly explain between-group heterogeneity; studies that reported using gold-standard methods (i.e. using ADOS and/or ADI) to confirm ASD diagnosis of included participants ($N = 5$) attained a significantly higher pooled effect size than studies that did not. In line with the moderator analysis that investigated whether loneliness prevalence differed according to population (i.e. child or adult), meta-regression analysis showed age was not a significant moderator of effect-size across the 21 studies that provided relevant statistical information on participant ages ($Q(1) = 0.00$, $b = 0.00$, $p = 0.98$, 95% CI [−0.02, 0.02], $Z = 0.03$).

Publication Bias

The funnel plot in Fig. 3 shows some asymmetry of study effect sizes around the effect size mean, with three studies falling outside of the 95% confidence limits. Trim and fill analysis corrected for asymmetry by imputing 6 studies to the left of the mean; however, this did not significantly alter the overall effect ($t(21) = 2.34$, $p = 0.03$). Moreover, fail-safe analysis indicated that 2116 missing studies with a mean effect of zero would be required to nullify the overall effect, exceeding the fail-safe threshold of $k = 125$. Taken together, these findings suggest no evidence of publication bias in this meta-analysis.

Loneliness and Mental Health in ASD

The results outlined below relate to the second review pertaining to studies reporting associations between loneliness and anxiety and/or depression within autistic samples.

Table 4 Measures and outcomes for studies measuring loneliness levels between ASD and NT samples

Authors (year)	Autism measure	Loneliness measure	ASD loneliness score (M, SD, R) and/or %	NT loneliness score (M, SD, R) and/or %	Key findings	Global quality rating
Bauminger and Kasari (2000)	• ADI-R	CLS	M = 43, SD = 14.21 R = 21–71; loneliness score[1] • Low = 27.3% • Low-mid = 36.3% • Mid-high = 27.3% • High = 9.1%	M = 27, SD = 6.42, R = 16–37; loneliness score • Low = 68.4% • Low-mid = 31.6% • Mid-high = 0 • High = 0	Autistic children reported greater feelings of loneliness than did neurotypical children $F(1, 39) = 19.4$, $p < .001$. Statistical analysis on % NR	Moderate
Bauminger et al. (2003)	• ADI-R	Adapted CLS	Global: M = 2.61, SD = .82; emotional: M = 2.44, SD = .87; social: M = 2.73, SD = .85	Global: M = 1.59, SD = .39; emotional: M = 1.53, SD = .47; social: M = 1.64, SD = .43	Autistic children presented higher feelings of global ($F(1,33) = 21.11$, $p < .001$), emotional ($F(1,33) = 14.35$, $p < .001$) and social ($F(1,33) = 22.17$, $p < .001$) loneliness	Moderate
Bossaert et al. (2012)	• Teacher report	LACA (peer-related subscale); scores higher than 1 SD from M = 'high loneliness'	ASD: M = 12.45, SD = 4.12, R = 6–23; high loneliness category: 31.03%	NT: M = 9.80, SD = 4.22, R = 6–24; high loneliness category: 13.89%	Autistic students reported higher loneliness than typically developing students ($p < .001$). Autistic students were twice as often lonely than typically developing students; $\times 2(1, N = 166) = 6.97$, $p < .05$	Weak
Bottema-Beutel et al. (2019)	• Teacher report • Parent/caregiver report • CARS-2 • SRS-2	CLSD	ASD M = 38.47, SD = 16.45, R = 16–80	NT M = 27.00, SD = 5.93, R = 16–38	No significant group differences in overall loneliness ($p = 0.10$, Hedges $g = -0.93$)	Strong
Brooks (2014)	• ADOS-G • Parent/caregiver report • ASSQ-REV • AQ	ULS-3	M = 50, SD = 10.4	M = 39.1, SD = 9	Autistic participants reported significantly higher levels of loneliness ($F(1, 110) = 35.23$, $p < .001$)	Moderate
Chamberlain et al. (2007)	• Parent report (including document check)	CLS	M = 30.12, SD = 10.8	M = 27.92, SD = 12.75	Autistic children did not report any greater loneliness than the matched peers group $F(1,32) = 0.28$	Moderate
Chang et al. (2019)	• Parent report • Document check • AQ (Chinese version)	ULS-8 (Chinese version); Loneliness ≥ 17 = high loneliness	M = 16.3, SD = 5.4 Loneliness ≥ 17: 47 (46.5%)	M = 12.0, SD = 2.6 Loneliness ≥ 17: 8 (7.9%)	Autistic participants reported significantly higher loneliness ($t = 7.11$, $p < .001$). Autistic participants report greater prevalence of 'high' loneliness (Statistics NR, calculated as follows: $\times 2(1, N = 202) = 38.00$, $p < .001$)	Moderate
Chiang (2003)	NR	CLS	M = 45.7, SD = 11.0;	M = 28.2, SD = 10.0	Autistic participants reported significantly higher levels of loneliness $Z = -2.17$ $p = .013$	Weak

Table 4 (continued)

Authors (year)	Autism measure	Loneliness measure	ASD loneliness score (M, SD, R) and/or %	NT loneliness score (M, SD, R) and/or %	Key findings	Global quality rating
De Gennaro (2016)	• Clinician report • CARS-2	ULS-3	Overall ASD: M = 41.71, SD = 9.43; Male ASD: 40.64, SD = 10.10; Female ASD: M = 46.67, SD = 2.31	Overall NT: M = 37.04, SD = 8.58; Male NT: M = 36.18, SD = 8.16; Female NT: M = 38.88, SD = 9.73	No statistical difference between groups as identified by diagnosis ($F(1, 38) = 3.17$, $p = .083$) or between groups as identified by gender ($F(1, 38) = 1.65$, $p = .213$	Moderate
Deckers et al. (2017)	• Multi-informant interviews, i.e. with the child, parents and teacher • Psychiatric examination, psychological assessment and clinical observations	LACA (peer-related subscale)	Child: M = 21.77, SD = 7.98 Adolescent: M = 23.50, SD = 7.04	Child: M = 20.32, SD = 6.14 Adolescent: M = 18.12, SD = 4.58	Autistic group had higher loneliness compared to NT group. In the child group, no group differences in loneliness were noted. In the adolescent group, the autistic group displayed higher loneliness. Children reported significantly higher levels of loneliness than adolescents in the NT group. In the autistic group, no significant difference in loneliness between age groups was found. Statistical data comparing ASD and NT groups directly were NR	Weak
Ee et al. (2019)	• Self-report diagnosis • Document check (not mandatory) • AQ	ULS-8	MDN = 24, IQR = 7	MDN = 14, IQR = 7	Significant difference between groups on loneliness score with the autistic group scoring higher ($p < .001$)	Moderate
Han et al. (2019)	• ADOS-2 • SRS-2 • AQ	LiCQ	M = 22.94, SD = 7.40	M = 13.70, SD = 4.27	Autistic group had significantly higher loneliness compared to control groups. Statistical data comparing ASD and NT groups directly were not reported	Moderate
Hymas (2021)	• RAADS-14 • Self-report diagnosis	UCLA	M = 6.65 SD = 2.03 R = 3–9	M = 5.31 SD = 1.83 R = 3–9	Autistic participants scored significantly higher compared with NT participants ($U = 100{,}017.5$, $z = -6.21$, $p < .001$, $d = .68$)	Moderate
Kalyva (2010)	• Medical record check	MESSY (Loneliness/Social Anxiety Subscale)	M = 21.57, SD = 3.94	M = 17.91, SD = 4.61	Autistic participants scored significantly higher on the loneliness measure ($F(1,40) = 13.12$, $p = .001$)	Strong

Table 4 (continued)

Authors (year)	Autism measure	Loneliness measure	ASD loneliness score (M, SD, R) and/or %	NT loneliness score (M, SD, R) and/or %	Key findings	Global quality rating
Lasgaard et al. (2010)	• Recruited from school supporting ASD children • Document check (unclear what/where from)	ULS-3 (Danish version) and single-item prevalence scale	M = 43.54, SD = 8.84; % of those feeling lonely often or always: 8 (21%)	M = 37.65, SD = 10.30; % of those feeling lonely often or always: 7 (4%)	Autistic boys reported significantly higher feelings of loneliness ($F(1,229) = 11.1$, $p < .01$) Feeling lonely often or always was associated with ASD (OR: 7.08 [95% CI: 2.40–20.91], $p < .001$)	Weak
Lin and Huang (2019)	• Document check • AQ (Chinese version)	ULS-8 (Chinese version)	M = 22.2, SD = 4.8	M = 18.3, SD = 3.9	Autistic adults had significantly higher loneliness scores ($t = 5.4$, $p < .001$)	Moderate
Locke et al. (2010)	• Recruited from a school programme which required ASD diagnosis	CLS	ASD: M = 37.71, SD = 10.93	NT: M = 26.25, SD = 7.02	Autistic participants had significantly higher loneliness scores ($F(1, 16) = 7.40$, $p < 0.05$)	Weak
Merkler (2007)	NR	Isolation and affect measure based on the PNDLS. Two subscales were included[2]	Social network distress: M = 9.91, SD = 3.90; dyadic distress: M = 10.69, SD = 3.17	Social network distress: M = 7.15, SD = 2.20; dyadic distress: NT = 9.42, SD = 1.49	No significant differences between autistic and NT groups on distress related to isolation	Weak
Nomura et al. (2012)[3]	• Children had been diagnosed according to established diagnostic criteria by psychiatrists, however confirmation NR	Adapted CLSD	Elementary: M = 16.94, SD = 3.95; higher elementary: M = 20.56, SD = 4.63; high school: M = 19.38, SD = 6.23	Elementary: M = 15.27, SD = 4.06; higher elementary: M = 14.31, SD = 3.27; high school: M = 15.52, SD = 4.08	Autistic participants had higher loneliness scores than NT participants (F (1, 302) = 36.32, $p < .01$). There was a significant interaction between group and school grade F (2, 302) = 3.488, $p < .05$) Further analyses showed significant differences between autistic and NT groups in higher elementary and junior high, but not lower elementary	Weak
Russell (2020)	• ADOS • AQ	ULS-3	M = 45.67, SD = 9.43	M = 34.84, SD = 9.58	Autistic group had higher perceived levels of loneliness	Weak
Schalbroeck et al. (2021)	• ADOS • Self-reported diagnosis	ULS-3	M = 44.66, SD = 8.65	M = 32.14, SD = 5.77	Autistic participants reported more loneliness than controls ($\beta = 0.60$; $p < 0.001$)	Strong
Sundberg (2018)	• Self-report	ULS-8	M = 20.13, SD = 4.20,	M = 16.61, SD = 3.58	Autistic participants were found to score significantly higher on loneliness measure than neurotypical participants ($t(149) = 5.45$, $p < 0.001$)	Weak

Table 4 (continued)

Authors (year)	Autism measure	Loneliness measure	ASD loneliness score (M, SD, R) and/or %	NT loneliness score (M, SD, R) and/or %	Key findings	Global quality rating
Whitehouse et al. (2009)	• Clinician report • CAST	LS	M = 18.29, SD = 8.49	M = 11.91, SD = 6.19	Autistic adolescents reported greater levels of loneliness than the non-autistic adolescents ($F(1,67) = 12.92$, $p < 0.001$)	Moderate
Yeung (2009)	NR	CLS	M = 44.21, SD = 13.87	M = 30.74, SD = 9.79	Autistic children reported significantly higher loneliness than their neurotypical siblings ($t(18) = 3.42$, $p = 0.002$)	Weak

M, mean; *SD*, standard deviation; *R*, range; *NR*, not reported; *MDN*, median; *IQR*, interquartile range; *ADI-R*, Autism Diagnostic Interview-Revised (Rutter et al., 2008); *ADOS*, Autism Diagnostic Observation Schedule (Gotham et al., 2006); *AQ*, Autism Quotient (Baron-Cohen et al., 2001); *ASSQ-REV*, Autism Spectrum Screening Questionnaire-Revised Extended Version (Kopp & Gillberg, 2011); *CARS-2*, Childhood Autism Rating Scale-2nd Edition (Schopler et al., 2010); *CAST*, Childhood Asperger Syndrome Test (Scott et al., 2002); *CLS*, Children's Loneliness Scale (Asher et al., 1984); *CLSD*, Children's Loneliness and Dissatisfaction Scale (Asher & Wheeler, 1985); *LACA*, Loneliness and Aloneness Scale for Children and Adolescents (Marcoen et al., 1987); *LiCQ*, Loneliness in Context Questionnaire (Asher & Weeks, 2013); *LS*, Loneliness Scale (de Jong-Gierveld & Kamphuls, 1985); *MESSY*, Matson Evaluation of Social Skills with Youngsters (Matson et al., 1983); *PNDLS*, Peer Network and Dyadic Loneliness Scale (Hoza et al., 2000); *RAADS-14*, Ritvo Autism and Asperger Diagnostic Scale-Revised (Eriksson et al., 2013); *SASA*, Social Anxiety Scale for Adolescents (La Greca & Lopez, 1998); *SELSA*, Social and Emotional Loneliness Scale for Adults (DiTommaso & Spinner, 1997); *SRS-2*, Social Responsiveness Scale (Constantino, 2012); UCLA (Hughes et al., 2004); *ULS-3*, UCLA Loneliness Scale-Version 3 (D. W. Russell, 1996); ULS-3 Danish Version (Mathias Lasgaard, 2007); *ULS-8*, UCLA Loneliness Scale-Version 8 (Hays & Dimatteo, 1987)

[1]These figures were obtained via Bauminger (1997)

[2]These subscales were amalgamated within comprehensive meta-analysis. Following sensitivity analyses, this study was kept in the meta-analysis due to its removal not having any significant influence on the pooled effect size

[3]Loneliness scores for this study were obtained via correspondence with the first author, due to this not being reported in the article

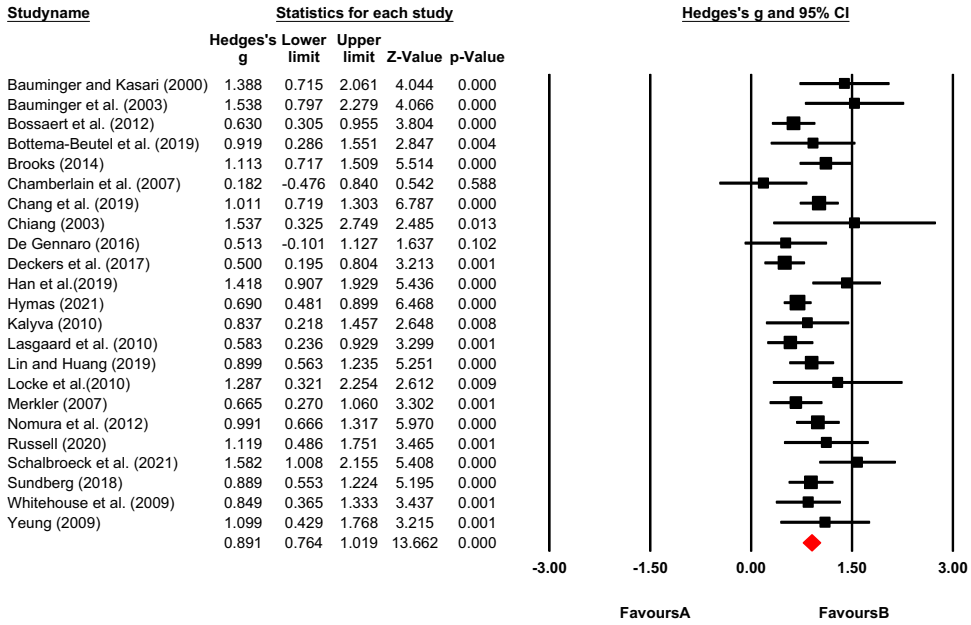

Fig. 2 Forest plot for meta-analysis on loneliness levels between ASD and NT samples

Study and Participant Characteristics

Table 6 outlines the characteristics of each study. Of the 21 studies with unique cohorts included in the second review, seven measured anxiety only, five depression only and nine measured both anxiety and depression. Overall, 14 utilised a cross-sectional design and seven employed a longitudinal or pre-post experimental design, for which baseline cross-sectional data were extracted. Of the 16 studies measuring anxiety, 14 provided appropriate data for inclusion in the meta-analysis ($N = 1224$) and 11 out of 14 studies were included in the loneliness and depression meta-analysis ($N = 980$).

Studies were published between 2009 and 2021 and were conducted across five different countries, with the majority conducted in America ($N = 13$). Most studies were conducted using child samples ($N = 11$). Collectively, studies included 1752 participants; sample sizes varied from 18 to 220 participants and ages ranged from 7 to 80 years. In the 14 studies that reported sample ethnicity, the most represented ethnicity was White/Caucasian.

Table 5 Categorical moderator analyses

Moderator	Subgroup	*k*	Effect size	95% CI	*p*-value	*Q* statistic and *p*-value
Population	Adult	8	.98	[.77–.1.19]	< .001	$Q(1) = 1.15, p = .28$
	Child	15	.83	[.67–1.00]	< .001	
	Overall	23	.89	[.76–1.02]	< .001	
Loneliness measure	CLS	5	1.03	[.52–1.55]	< .001	$Q(1) = .34, p = .56$
	Other loneliness measure	18	.88	[.75–1.01]	< .001	
	Overall	23	.89	[.76–1.01]	< .001	
ASD diagnosis confirmation	Gold-standard	7	1.19	[0.83–1.55]	< .001	$Q(1) = 4.38, p = .036$
	Not gold-standard	16	.79	[.69–.90]	< .001	
	Overall	23	.82	[.73–.92]	< .001	
Study quality	Moderate-high	13	.97	[.79–1.16]	< .001	$Q(1) = 2.45, p = .12$
	Low	10	.78	[.62–.94]	< .001	
	Overall	23	.86	[.74–.98]	< .001	
Publication status	Published	16	.91	[.75–1.03]	< .001	$Q(1) = .35, p = .56$
	Unpublished	7	.84	[.64–1.03]	< .001	
	Overall	23	.88	[.75–1.01]	< .001	

k, number of studies; *CI*, confidence interval

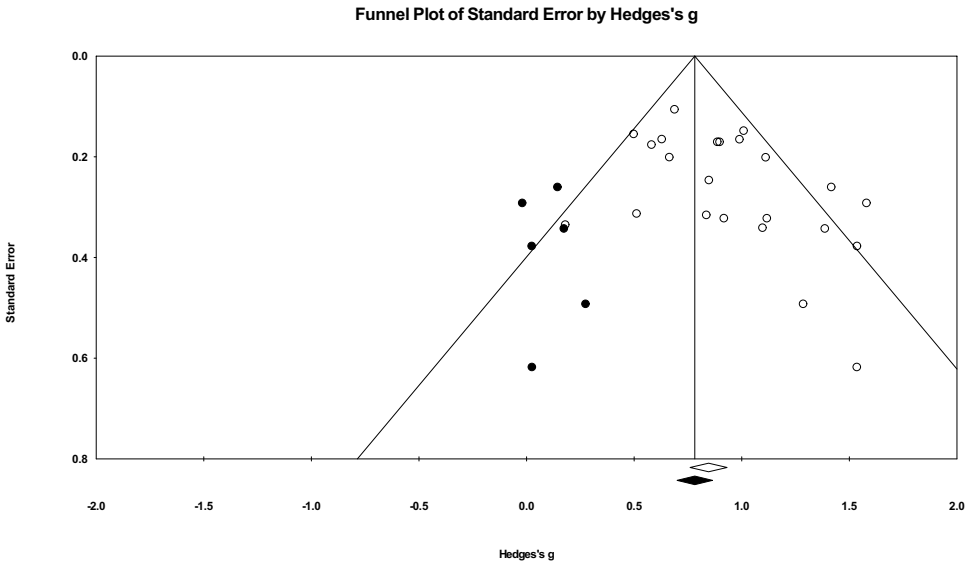

Fig. 3 Funnel plot of standard error against Hedges' *g* for meta-analysis on loneliness levels between ASD and NT samples, including imputed studies

Outcomes

Quality appraisal of each study is reported in supplementary material 4. Eight different self-report loneliness measures were used across the 21 studies, the most frequently used were the Children's Loneliness Scale (CLS; Asher et al., 1984) and the UCLA Loneliness Scale-8 (ULS-8; Hays & Dimatteo, 1987), both used in five studies. Thirteen different anxiety measures and 10 depression measures were used across studies; the most common were the Multidimensional Anxiety Scale for Children (MASC; March et al., 1997) and the Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001), used in three and four studies respectively. Two studies (Jackson et al., 2018; Wendler, 2019) did not report appropriate anxiety or depression subscale scores for inclusion in meta-analytic computations; however, they both reported at least one positive correlation between measures of emotional distress and loneliness. Two studies recruited participants from an overlapping source (Ee et al., 2019; Hedley et al., 2018a) resulting in only the latter being included in the depression meta-analysis (see Table 7 for an overview of study measures, outcomes and overall quality appraisal score. Where multiple measures and/or outcomes were reported, those in bold were used in the meta-analyses).

Meta-Analyses

Anxiety As can be seen in Fig. 4, and in line with expectations, there was a significant positive association between mean loneliness scores and mean anxiety scores across most studies, with a low-medium pooled effect size ($r = 0.29$; 95% CI [0.15, 0.41]; $Z = 4.09$, $p < 0.001$). Effect sizes ranged between $r = -0.17$ and $r = 0.59$. Of note, one study found a significant negative correlation between loneliness and anxiety (La Buissonniere Ariza et al., 2021). Significant heterogeneity was identified between studies $Q(13) = 57.86$, $p < 0.001$. The I^2 statistic indicated high heterogeneity, with 77.53% of the dispersion between studies suggested to be due to real differences in the study effects. The relatively small number of studies in the secondary meta-analyses (< 20) precluded the use of comprehensive moderator analyses to investigate this heterogeneity (Rubio-Aparicio et al., 2017).

Publication Bias

Some asymmetry of study effect sizes around the effect size mean were apparent in the funnel plot in Fig. 5, with five studies falling outside of the 95% confidence limits. Trim and fill analysis corrected for asymmetry by imputing 6 studies to the left of the mean; however, this did not significantly alter the overall effect ($t(12) = 1.13$, $p = 0.28$). Fail-safe analysis indicated that 229 missing studies with a mean effect of zero would necessitate nullifying the overall effect, exceeding the fail-safe threshold of $k = 80$. Therefore, there is no evidence of publication bias in this meta-analysis.

Depression Figure 6 outlines the significant positive relationship, with medium-large effect, between loneliness and depression ($r = 0.48$; 95% CI [0.40, 0.55]; $Z = 10.6$, $p < 0.001$). Effect sizes of studies ranged between $r = 0.27$ and $r = 0.81$, all in the expected direction. Again, there was evidence of significant heterogeneity identified between studies, ($Q(10) = 19.72$, $p = 0.03$). The I^2 statistic indicated low-moderate heterogeneity, with 49.29% of the dispersion

Table 6 Study and participant characteristics for studies measuring loneliness, anxiety and/or depression in ASD samples

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study population	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group(s) (%)	IQ measure (M, SD, R)
Capriola-Hall et al. (2021)	America	Investigated whether anxiety, depression and loneliness symptoms improved following a CBT intervention for autistic adults	Adults	32	M = 19.74, SD = 2.07, R = 16–25	75%	81% Caucasian	FSIQ ≥ 80 on WASI-II
Chang et al. (2019)	Taiwan	Explored relationships between friendship quality and emotional well-being of autistic and neurotypical adolescents	Children	101	M = 16.6, R = 10–19	83%	NR	NR. No participants had an intellectual disability (IQ < 70)
Deckers et al. (2017)	Netherlands	Examined loneliness and social correlates, including social anxiety, in autistic and neurotypical children using a multi-informant approach (children, parents and teachers)	Children	Aged 7–11 years = 47; aged 12–18 years = 26	M = 11.2, SD = 2.42	85%	NR 'The sample consisted predominantly of Caucasian participants'	NR. Those with estimated IQ < 70 were excluded
Ee et al. (2019)	Australia	Compared levels and predictors of loneliness in autistic and neurotypical adults and thematically analysed data on autistic adults' socialisation experiences	Adults	220	M = 41.9, SD = 12.24, R = 25–80	39%	NR	NR. Included those with formal diagnoses of 'intellectual disability'
Han et al. (2019)	America	Examined individual differences and associations in social and non-social pleasure, autism traits, loneliness and depressive symptoms across samples of autistic and non-autistic adults (with and without depression)	Adults	49	M = 23.98, SD = 26.23	61%	NR	Unknown IQ measure: verbal M = 103.63, SD = 12.75; non-verbal M = 103.04, SD = 19.11
Hedley et al. (2018a)	Australia	Examined loneliness, social support and autism trait severity as risk and protective factors associated with depression and suicidal ideation	Adults	185	M = 37.11, SD = 15.41, R = 14–80	45%	NR	NR

Table 6 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study population	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group(s) (%)	IQ measure (M, SD, R)
Hedley et al. (2018b)	Australia	Examined the associations between autistic traits, loneliness, depression and thoughts of self-harm, in autistic adults	Adults	71	M = 26.14, SD = 8.20, R = 17–56	89%	Non-Aboriginal Australian (84.5%)	NR
Hymas (2021)	UK	Explored social identity in autistic and neurotypical adults and its association with mental health, controlling for relevant confounders including loneliness levels [Dissertation]	Adults	174	M = 35.85, SD = 13.23, R = 18–69	40%	87% White	NR. Learning disability diagnosis was an exclusion criterion
Jackson et al. (2018)	America	Examined self-reported academic, social and mental health experiences in post-secondary autistic students	Adults	56	M = 22.98, SD = 6.01, R = 18–57	46.4%	80.4% White	NR, however all participants enrolled in post-secondary education
La Buissonniere Ariza et al. (2021)	America	Explored the risk factors associated with suicidal ideation in autistic children with comorbid anxiety disorders and assessed the unique contribution of externalizing behaviours	Children	166	Age M = 10, SD = 1.8, R = 7–13	81.3%	75.9% White, 81.3% non-Hispanic	WISC-IV: FSIQ: M = 100.6, SD = 16.3, R = 54–146. 19.9% presented with mild intellectual disability
Lieb and Bohnert (2017)	America	Explored associations between several executive functioning domains, social impairment and friendship quality on depressive symptoms and loneliness in autistic adolescents	Children	127	M = 13.95, SD = 1.60, R = 12–17	81%	Caucasian (86.6%)	Assumed WISC-IV: FSIQ M = 104.76, SD = 20.24 based on parent-report of prior IQ testing[1]
Maddox et al. (2017)	America	Evaluated impact of a CBT intervention on the social skills of autistic adolescents with anxiety, considering pre-treatment social anxiety and loneliness	Children	25	M = 14.42, SD = 1.55, R = 12–17	76%	84% Caucasian	WISC-IV: verbal IQ M = 98.32, SD = 15.18 R = 73–126

Table 6 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study population	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group(s) (%)	IQ measure (M, SD, R)
Mahjouri (2011)	America	Explored the social and emotional experiences (including loneliness, anxiety and depression) of autistic adolescents [Dissertation]	Children	18	M = 15.1, SD = 2.17, R = 12–18	86%	58.1% Caucasian	SB-5: M = 99.33, SD = 17.93, R = 67–139
Mazurek (2014)	America	Examined the associations among loneliness, friendship and emotional functioning in autistic adults	Adults	108	M = 32.4, SD = 12.5, R = 18–62	52.8%	Caucasian (88.0%)	NR
Schiltz et al. (2020)	America	Explored associations between loneliness, anxiety, depression, autism features and social contact among autistic adults	Adults	69	M = 20.24, SD = 2.77, R = 17–29	81%	85.5% White. 88.4% non-Hispanic	KBIT-2: M = 95.01, SD = 17.43
Syu and Lin (2018)	Taiwan	Investigated the relationships among sensory avoidance, anxiety and loneliness in autistic adults	Adults	70	M = 27.8, SD = 5.0, R = 20–39	66%	NR	NR. States no participants had IQ < 70
Wendler (2019)	America	Explored the impact of improv theatre classes on social-emotional functioning for autistic individuals, including impacts on depressive symptoms, anxiety symptoms and loneliness [Dissertation]	Children	21	M = 15, SD = 5.11	67%	90% European-heritage	NR
White and Roberson-Nay (2009)	America	Explored relationships between loneliness, social skill deficit and anxiety in autistic children	Children	20	M = 12.08, SD = 1.78, R = 7–14	90%	NR	Unknown IQ measure: M = 92.24, SD = 14.41
Wood (2014)	UK	Explored whether cognitive distortion in self-assessment of social performance occurred in autistic children with social anxiety [Dissertation]	Children	20	M = 17.5, SD = 2.134, R = 14–21	75%	NR	NR

Table 6 (continued)

Study characteristics				Participant characteristics				
Authors (year)	Country	Objectives/focus	Study population	Sample size	Age (M, SD, R)	Gender (% male)	Predominant ethnic group(s) (%)	IQ measure (M, SD, R)
Wright (2017)	America	Investigated the effect of parental mediation on the associations between cyber victimisation and depression, anxiety and loneliness in children	Children	128	R = 11–16	89%	White (86%)	NR
Yeung (2009)	America	Examined the quality of friendships and wellbeing (i.e. loneliness and depression) of sibling children with and without Asperger's syndrome [Dissertation]	Children	19	M = 10.05, SD = 1.38, R = 8–12	85.7%	85.7% Caucasian	NR

M, mean; *SD*, standard deviation; *R*, range; *NR*, not reported; *FSIQ*, Full Scale Intelligence Quotient; *KBIT-2*, Kaufman Brief Intelligence Test, Second Edition (Kaufman & Kaufman, 2004); *WASI-II*, Wechsler Abbreviated Scale of Intelligence-Second Edition (Wechsler, 2011); *WISC*, Wechsler Intelligence Scale for Children (Wechsler, 2008)

[1]Information ascertained through sister paper (Bohnert et al., 2019)

between studies suggested to be due to real study effect differences. This was not investigated further due to insufficient number of studies (Rubio-Aparicio et al., 2017).

Publication Bias

Some asymmetry of study effect sizes around the effect size mean was apparent in the funnel plot in Fig. 7, with three studies falling outside of the 95% confidence limits. However, no studies were imputed to correct for asymmetry based on trim and fill analysis and the regression test was non-significant ($t(9) = 1.33$, $p = 0.22$). Fail-safe analysis indicated that 660 missing studies with a mean effect of zero would necessitate nullifying the overall effect, exceeding the fail-safe threshold of $k = 65$. Overall, this demonstrated a lack of publication bias in this meta-analysis.

Discussion

Of the 23 studies included in the initial meta-analysis — investigating differences in loneliness levels between autistic and neurotypical samples, all found increased loneliness in autistic compared to neurotypical samples (this was a significant difference in 21 studies). The combined weighted effect size for this difference was large (Hedges' $g = 0.89$). Eight of the 14 studies included in the meta-analysis of loneliness and anxiety found a significant correlation between loneliness and anxiety (seven in the expected direction) with an overall low-medium effect size ($r = 0.29$). In the final meta-analysis, a pooled medium-large effect ($r = 0.48$) was found for the association between loneliness and depression, with all 11 studies finding a significant positive correlation.

This is the first review to quantify differences in loneliness ratings between autistic and neurotypical samples. The consistent finding that autistic individuals report increased loneliness compared to neurotypical individuals contradicts literature that implies autistic individuals are compromised in their desire to seek social connection (Chevallier et al., 2012). It may be that autistic individuals' 'atypical' social behaviour is *not* indicative of social disinterest (Jaswal & Akhtar, 2018), but manifests from reciprocal interactions within multiple ecological contexts (Bronfenbrenner, 1977). For example, autistic individuals are more susceptible to experiencing negative social interaction, e.g. through direct bullying and victimisation experiences and indirect broader societal stigmatisation (Schroeder et al., 2014). Such aversive experiences may lead to social withdrawal and fewer opportunities for social skill development and successful social experiences — yet the desire for more, or more meaningful, social connection remains.

The finding that loneliness was significantly positively correlated with both anxiety and depression is in line with

Table 7 Measures and outcomes for studies measuring loneliness and mental health

Authors (year)	Autism measure	Loneliness measure (M, SD, R)	Anxiety measure (M, SD, R)	Depression measure (M, SD, R)	Key findings	Global quality rating
Capriola-Hall et al., (2021)	• Self-reported ASD diagnosis • ADOS-2	UCLA (3-item); M = 5.86, SD = 1.90	ASR anxiety problems; M = 60, SD = 9.43	ASR depressive problems: M = 64.37, SD = 11.17	Significant positive association between loneliness and depression (r = .46*). Positive association between loneliness and anxiety (r = .23, NS)	Weak
Chang et al. (2019)	• Parent report • Document check • AQ (Chinese version)	ULS-8 (Chinese version); M = 16.3, SD = 5.4	BAI (Chinese version) M = 11.8, SD = 12.6	N/A	Significant association between anxiety and loneliness (r = 0.442***)	Moderate
Deckers et al. (2017)	• Multi-informant interviews, i.e. with the child, parents and teacher • Psychiatric examination, psychological assessment and clinical observations	LACA (peer-related subscale); child: M = 21.77, SD = 7.98 Adolescent: M = 23.50, SD = 7.04	Social anxiety subscale of the SCARED-71 (parent report) Child M = 8.50, SD = 5.20; adolescent M = 7.77, SD = 5.00	N/A	Loneliness was positively associated with parent ratings of social anxiety (r = 0.16, NS)	Weak
Ee et al. (2019)	• Self-report diagnosis • Document check (not mandatory) • AQ	ULS-8; MDN = 24, IQR = 7	Severity measure for GAD-adult; M = 14, SD = 8.4	PHQ-9; M = 10.4, SD = 7	Loneliness was positively correlated with both depression (r = 0.42***) and anxiety (r = 0.36***)	Moderate
Han et al. (2019)	• ADOS-2 • SRS-2 • AQ	LiCQ; M = 22.94, SD = 7.40	N/A	BDI-II; M = 11.83, SD = 9.89	Loneliness was the strongest predictor of depressive symptoms (t(41) = 3.41, p = 0.001, adjusted R^2 = 0.33)	Moderate
Hedley et al. (2018a)	• Self-report • AQ-Short	ULS-8; M = 22.80, SD = 4.87, R = 11–32	N/A	PHQ-9; M = 9.52, SD = 6.35, R = 0–24	Significant correlations between loneliness and depression for overall sample and when split by gender (**Overall = .437****; males = .502**; females = .409**) Loneliness emerged as a unique predictor of depression scores (t = 3.11, β = .24, p = .002)	Moderate
Hedley et al. (2018b)	• Self-report • AQ-Short	ULS-3; M = 51.35, SD = 11.45, R = 27–74	N/A	PHQ-9; M = 6.52, SD = 5.01, R = 0–19	UCLA loneliness was positively associated with PHQ depression (r = .392*)	Moderate
Hymas (2021)	• RAADS-14 • Self-report diagnosis	UCLA (3-item); M = 6.65 SD = 2.03, R = 3–9	DASS-21 anxiety M = 12.76, SD = 8.83, R = 0–36	DASS-21 depression M = 20.06, SD = 12.18, R = 0–42	Loneliness positively correlated with anxiety (r = .22***) and depression (r = .48***)	Moderate

Table 7 (continued)

Authors (year)	Autism measure	Loneliness measure (M, SD, R)	Anxiety measure (M, SD, R)	Depression measure (M, SD, R)	Key findings	Global quality rating
Jackson et al. (2018)	• Self-report • AQ-10	UCLA (3-item); M = 6.52, SD = 1.96	DASS-21; anxiety M = 10.82, SD = 7.73	DASS-21; depression M = 15.71, SD = 11.77	Overall loneliness emerged as a significant predictor of overall emotional distress in the study sample ($\beta = 0.417$, $p < .001$). Did not report depression or anxiety subscales separately	Moderate
La Buissonniere Ariza et al	• ADOS-2	CLS; M = 37.8, SD = 14.6, R = 16–80	PARS (parent report); M = 19.3, SD = 3.2, R = 12–28	N/A	Significant correlation between anxiety and loneliness ($r = -.17$, $p < .05$)	Moderate
Lieb and Bohnert (2017)	• Parent report • SRS	CLS (parent and child); parent: M = 31.63, SD = 9.14, R = 3–52. Child: M = 23.83, SD = 11.99, R = 0–51	N/A	CBCL-D (parent report); M = 0.71, SD = 0.39, R = 0–1.62 YSR-D (youth report); M = 0.70, SD = 0.39, R = 0–1.69	Significant correlation between depression and loneliness in both parent ($r = .48$**) and child (**$r = .60$****) report	Moderate
Maddox et al. (2017)	• ADI-R • ADOS	Adapted CLS M = 35.80, SD = 12.60, R = 15–61	The ADIS-C/P Social phobia module (joint clinician, parent and child report); M = 4.96, SD = 1.40, R = 3–7	N/A	Loneliness and social anxiety were not significantly correlated ($r = -.02$, $p = .95$)	Moderate
Mahjouri (2011)	• ADOS	CLS; M = 41.39, SD = 12.31, R = 21–71	SASA; M = 26.71, SD = 19.62, R = 7–65 MASC; M = 55.28, SD = 11.07, R = 32–71	CDI; M = 49.06, SD = 8.36, R = 39–68	Positive correlation between loneliness and SASA ($r = .503$ $p < .05$), **MASC ($r = .364$, NS)**; and CDI ($r = .683$ $p < 0.01$)	Strong
Mazurek (2014)	• AQ-Short	ULS-8; M = 20.9, SD = 4.7	PHQ 7-item Anxiety Scale M = 7.4, SD = 5.4	PHQ 9-item Depression Scale M = 8.4, SD = 6.2	Loneliness was positively correlated with (and predicted) anxiety ($r = .34$, $p = .001$; $\beta = .32$, $p = .002$) and depression ($r = .48$, $p < .001$; $\beta = .49$, $p < .001$)	Weak

Table 7 (continued)

Authors (year)	Autism measure	Loneliness measure (M, SD, R)	Anxiety measure (M, SD, R)	Depression measure (M, SD, R)	Key findings	Global quality rating
Schiltz et al. (2020)	• ADOS • AQ	SELSA; social loneliness (SOC): M = 47.26, SD = 21.13 Emotional family loneliness (EFAM): M = 25.35, SD = 12.81 Emotional romantic loneliness (EROM): M = 56.19, SD = 13.19	SPIN: M = 28.06, SD = 16.14 LSAS: M = 57.35, SD = 30.21	BDI-II M = 12.58, SD = 10.99	**SELSA SOC**: positive correlation with SPIN ($r = 0.52$**), **LSAS** (***r* = 0.59*****) and BDI-II ($r = 0.44$**) SELSA EFAM: positive correlation with SPIN ($r = 0.40$**), LSAS ($r = 0.47$**) and BDI-II ($r = 0.72$**) SELSA EROM: positive correlation with SPIN ($r = 0.22$, NS), LSAS ($r = 0.25$*) and BDI-II ($r = 0.31$*)	Moderate
Syu and Lin (2018)	• Document check • AQ (Chinese version)	ULS-8 (Chinese version); M = 21.9, SD = 4.9, R = 11–31	BAI (Chinese version); M = 21.2, SD = 11.9, R = 2–43	N/A	Positive correlation between loneliness and anxiety ($r = 0.501$***)	Moderate
Wendler (2019)	• Parental report • SRS-2	UCLA (3-item); M = 5.18, SD = 1.37	PHQ-4 (reported at overall and item-level only); Overall M = 7.38, SD = 2.65 Nervous item; M = 2.32, SD = 1.03 Worrying item; M = 1.85, SD = 0.95	Pleasure item; M = 1.35, SD = .79 Down item; M = 1.85, SD = .95	Positive correlation between loneliness and total PHQ-4 ($r = .62$) and between loneliness and nervous ($r = .44$) and worrying ($r = .63$) items. Negative correlation between loneliness and pleasure item ($r = -.08$) and positive correlation with down item ($r = .77$)	Moderate
White and Roberson-Nay (2009)	• ADOS	Adapted CLS; Global Score: M = 2.73, SD = 0.71; Social Score: M = 2.72, SD = 0.80; Emotional Score: M = 2.74, SD = 0.76	MASC; M = 56.65, SD = 15.19, R = 28–83 Social anxiety: M = 52.65, SD = 13.69, R = 32–74 High anxiety (i.e. MASC ≥ 61) $n = 5$	N/A	Positive correlation between total anxiety and global loneliness (***r* = .325**, NS). Social anxiety was significantly correlated with social ($r = .59$, $p = .01$) and global loneliness ($r = .50$, $p = .04$). The high-anxiety group self-reported more 'social' loneliness, compared to their less anxious peers ($t = 2.57$, $p < .05$)	Moderate
Wood (2014)	• Confirmed by professionals who worked with participants	CLS; M = 48.53, SD = 15.01, R = 22–73	SASA; M = 48.45, SD = 15.80, R = 18–74	N/A	A significant positive correlation was found between social anxiety and loneliness ($r = 0.482$, $p < 0.05$)	Weak

Table 7 (continued)

Authors (year)	Autism measure	Loneliness measure (M, SD, R)	Anxiety measure (M, SD, R)	Depression measure (M, SD, R)	Key findings	Global quality rating
Wright (2017)	• Clinician report	ULS-3; M = 2.16, SD = 1.00	MASC; M = 1.81, SD = .79	CES-D; M = 1.98, SD = .68	Significant positive correlation between loneliness and both anxiety ($r = .19$*) and depression ($r = .27$**)	Moderate
Yeung (2009)	• NR	CLS; M = 44.21, SD = 13.87	NR	CDI; M = 12.72, SD = 10.44	Significant positive correlation between depression and loneliness ($r = 0.81$, $p < .001$)	Weak

M, mean; *MDN*, median; *SD*, standard deviation; *R*, range; *IQR*, interquartile range; *NR*, not reported; *ADI-R*, Autism Diagnostic Interview-Revised (Rutter et al., 2008); *ADOS*, Autism Diagnostic Observation Schedule (Gotham et al., 2006); *ADIS-C/P*, Anxiety Disorders Interview Schedule for Children/Parents (Silverman & Albano, 1996); *AQ*, Autism Quotient (Baron-Cohen et al., 2001); *AQ Short*, Autism Quotient Short (Hoekstra et al., 2011); *ASR*, Adult Self Report Anxiety and Depressive Problems (Achenbach et al., 2003); *BAI*, Beck Anxiety Inventory (Chinese version; Che et al., 2006); *BDI-II*, Beck Depression Inventory (Beck et al., 1996); *CBCL-D*, Child Behaviour Checklist-Depression Scale (Clarke et al., 1992); *CDI*, Children's Depression Inventory (Kovacs, 1992); *CES-D*, Center for Epidemiological Studies Depression Scale (Radloff, 1977); *CLS*, Children's Loneliness Scale (Asher et al., 1984); *DASS-21*, Depression, Anxiety and Stress Scale 21-item version (Lovibond & Lovibond, 1995); *LACA*, Loneliness and Aloneness Scale for Children and Adolescents (Marcoen et al., 1987); *LiCQ*, Loneliness in Context Questionnaire (Asher & Weeks, 2013); *MASC*, Multidimensional Anxiety Scale for Children (March et al., 1997); *PARS*, Pediatric Anxiety Rating Scale (Pediatric Psychopharmacology Anxiety Study Group, 2002); *PHQ-4*, Public Health Questionnaire-4 (Kroenke et al., 2009); *PHQ-7*, Public Health Questionnaire-7 (Spitzer et al., 1999); *PHQ-9*, Public Health Questionnaire-9 (Kroenke et al., 2001); *SCARED-71*, Screen for Child Anxiety and Related Emotional Disorders (Bodden et al., 2009); Severity Measure for GAD-Adult (Craske et al., 2013); *SPIN*, Social Phobia Inventory (Connor et al., 2000); *SRS-2*, Social Responsiveness Scale (Constantino, 2012); *ULS-3*, UCLA Loneliness Scale-Version 3 (D. W. Russell, 1996); *ULS-8*, UCLA Loneliness Scale-Version 8 (Hays & Dimatteo, 1987); *LSAS*, Liebowitz Social Anxiety Scale (Heimberg et al., 1999); UCLA 3-Item Scale (Hughes et al., 2004); *YSR-D*, Youth Self Report-Depression Scale (Achenbach & Rescorla, 2001). Three studies (Mahjouri, 2011; Schiltz et al., 2020; White & Roberson-Nay, 2009) reported multiple anxiety measure/subscale outcomes and two studies (Schiltz et al., 2020; White & Roberson-Nay, 2009) reported outcomes for three or more loneliness measures/subscales; the most internally consistent measure was used for meta-analytic computations

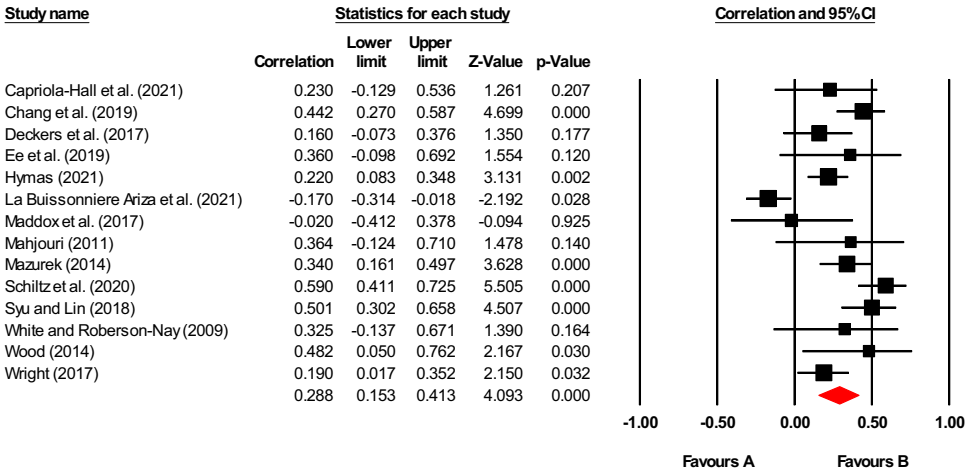

Fig. 4 Forest plot for meta-analysis on loneliness and anxiety

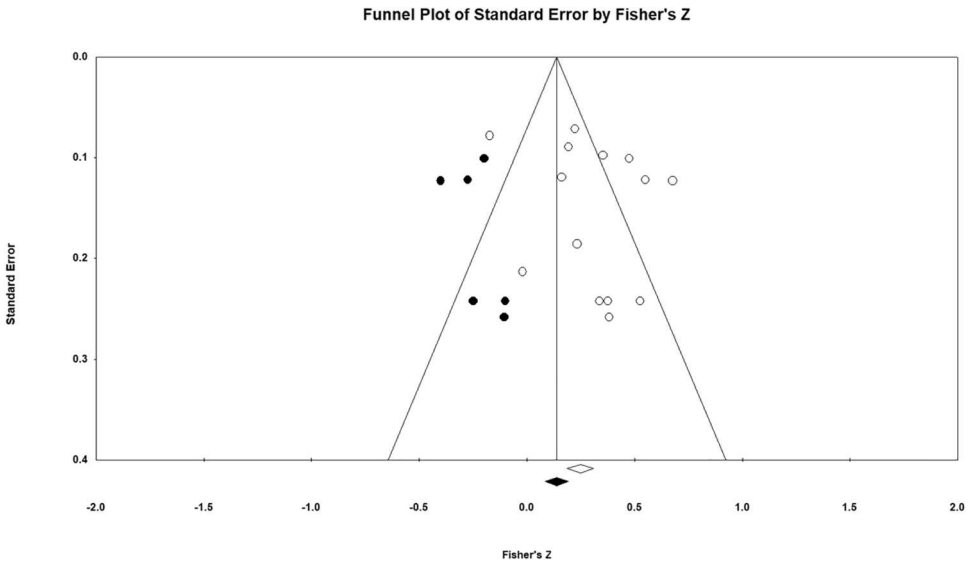

Fig. 5 Funnel plot of standard error against Fisher's *Z* for meta-analysis on loneliness and anxiety, including imputed studies

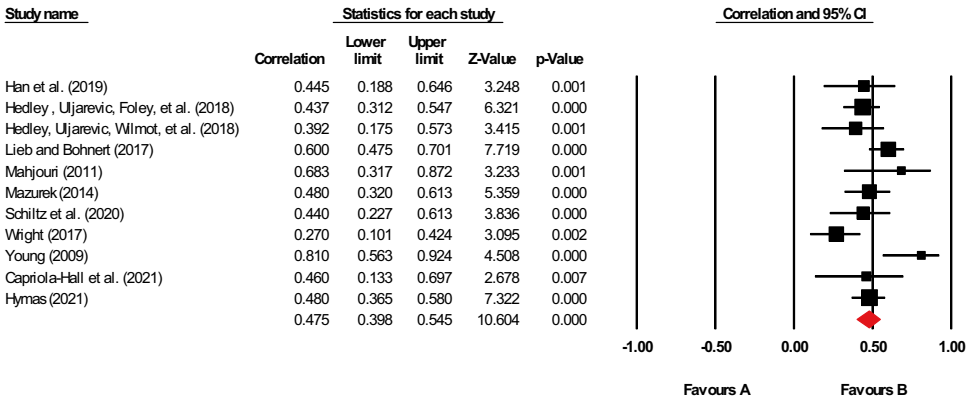

Fig. 6 Forest plot for meta-analysis on loneliness and depression

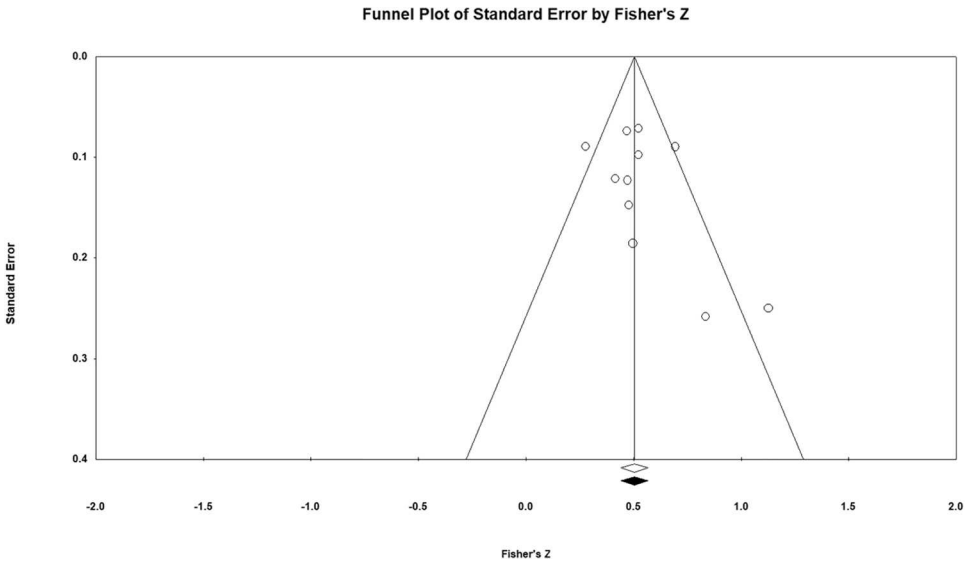

Fig. 7 Funnel plot of standard error against Fisher's *Z* for meta-analysis on loneliness and depression

previous research in neurotypical populations (Danneel et al., 2019; Erzen & Çikrikci, 2018; Leigh-Hunt et al., 2017). However, the cross-sectional nature of studies included in the meta-analyses precludes the interpretation of the direction of causality between loneliness, anxiety and depression. In the neurotypical population, the causal association between loneliness and mental health is considered to be bidirectional (Flett et al., 2016; Hawkley & Cacioppo, 2010), although evidence from longitudinal research has indicated loneliness being unidirectionally predictive of depressive symptoms over 1-year intervals (Cacioppo et al., 2010). Future research is required to establish whether loneliness shows a similar predictive effect in autistic individuals.

Significant between-study heterogeneity was found in all meta-analyses. Due to the number of studies included in meta-analytic computations, this could only be explored through moderator analysis in the first meta-analysis. In this analysis, only the use of gold standard diagnostic procedures, e.g. ADOS and ADI, for confirming autism diagnosis was found to significantly explain some between-study heterogeneity, suggesting that studies employing gold-standard procedures, with more accurate characterisation of autistic participants, had a greater effect size of mean differences in loneliness scores. The lack of significant findings for the other moderators is notable. For example, quality variance may not have significantly explained between-study heterogeneity due to the majority of included studies being considered as methodologically weak-moderate, with very few achieving strong ratings. Most studies utilised differing loneliness measures which were not validated in autistic samples which may explain why moderator analysis on loneliness measures did not explain significant heterogeneity. Likewise, most studies were conducted on younger samples (namely adolescents), potentially inflating the occurrence of type 2 errors for the moderator analyses on age and population type.

Strengths and Limitations of This Review

This review is strengthened by the employment of a comprehensive search strategy and the use of stringent eligibility criteria which fosters confidence that the included studies are representative of the current evidence base. The inclusion of unpublished literature reduces the likelihood of publication bias (Sterne & Egger, 2005); indeed, there was no evidence of publication bias within any of the meta-analyses. In addition, having independent ratings of methodological bias which resulted in 'fair' to 'very good' inter-rater agreement across all domains gives credibility to the reliability of the quality appraisal results.

Nevertheless, bias may have been inadvertently introduced during selection of studies due to this being conducted by only the first author, and a subsample was not cross-checked against the eligibility criteria by an independent reviewer (Boland et al., 2014). A further limitation is that due to the limited number of studies available for the meta-analyses on the association between loneliness and mental health, the influence of potential moderators in explaining the moderate-high between-study heterogeneity was not investigated. Additional data is therefore required to support further exploration of between-study heterogeneity.

Strengths and Limitations of Included Studies and Research Implications

There were numerous limitations in the literature included in this review. Measurement and reporting of participant

characteristics across studies was inconsistent. Some studies did not report ethnicity data; in those that did, there appeared to be an over-representation of Caucasian participants from western cultures. As the meaning, experience and presentation of loneliness may vary across cultures, the findings of this review may not be generalisable to non-Caucasian participants (Barreto et al., 2021). Most participants were male, and although this aligns with gender ratios in autism research (Loomes et al., 2017), the findings of the review may not accurately capture the experiences of autistic females. Furthermore, the lack of subgroup analysis by gender within studies and the non-inclusion of individuals diagnosed with ID or reporting of IQ scores across studies, prevents confidence that these were appropriately controlled for in studies and precluded investigation of these as potential sources of heterogeneity.

Most studies adequately reported their recruitment procedures; however, the reporting of participant selection and attrition was particularly weak across studies. The rate of participation in the studies out of those selected was unclear, and rates of non-completers or missing data were not reported which may have biased findings, e.g. participants who were particularly lonely may be more motivated to take part and complete the studies. It is important to note that the findings of this review may be more generalisable to autistic individuals in the community, as opposed to clinical samples, given most samples were recruited from non-treatment seeking populations. Consistent with other systematic reviews on autistic individuals across the lifespan, most studies recruited child or adolescent samples (Spain 2018), which reduces the generalisability of these findings to adult samples; nevertheless, findings were consistent across age groups in this review.

The varied assessment and outcome measures used across studies may have resulted in different operationalisations of constructs (Offord & Kraemer, 2000). For example, the lack of gold standard procedures in confirming ASD diagnoses decreases the assurance of the diagnostic characterisation of most participants included in this review. Moreover, few studies reported whether the measures used to assess anxiety and depression had been validated within an autistic population, and participants exceeding clinical cut-off in studies were rarely reported, limiting the generalisation of findings in this review to participants with sub-clinical anxiety and/or depression.

Studies may also have introduced bias by not considering diagnostic overshadowing, i.e. the overlapping symptomatology of anxiety, depression and ASD inflating estimates of association (Rosen et al., 2018). This is further confounded by the greater co-occurrence of alexithymia in autistic individuals, characterised by difficulties in identifying and/or describing ones emotional experiences (Poquérusse et al., 2018), which can lead to inaccurate self-reporting on measures that have only been validated in neurotypical samples. Only one study reported accounting for diagnostic overshadowing (Maddox et al., 2017) and they found no significant correlation between anxiety and loneliness. It is notable that no studies reported accounting for possible alexithymia in participants. Using gold-standard procedures for confirming autism diagnoses such as the ADOS (Gotham et al., 2006) and ADI-R (Rutter et al., 2008) would enable better generalisation of study findings to diagnosed autistic individuals. The lack of current valid and reliable measures of mental health in autism is a recognised research gap, especially within adult populations (Brugha et al., 2015), although recent research is addressing this (Rodgers et al., 2020). Future studies would benefit from including validated mental health and alexithymia measures.

Importantly, despite autistic individuals scoring higher on loneliness measures compared to neurotypical individuals across included studies, we cannot infer that the magnitude of loneliness is severe and/or *clinically* relevant. Only three studies reported loneliness prevalence according to predetermined cut-off rates, which all reported autistic individuals had increased prevalence of 'high' loneliness. However, all studies used different loneliness measures and cut-off criteria, and achieved weak or moderate quality ratings, making comparisons between studies difficult. Future studies would benefit from including a standardised measure of loneliness duration, intensity, distress and frequency, in line with recommendations for measuring loneliness in the general population (Office for National Statistics, 2018). This will aid understanding of the clinical magnitude of loneliness felt by autistic individuals.

Moreover, this review cannot confirm that autistic individuals define, experience or express loneliness in the same way that neurotypical individuals may. Only three studies utilised loneliness measures which encapsulated multiple loneliness dimensions, precluding this from being meta-analytically explored as a potential moderator. Future studies would benefit from exploring differing dimensions of loneliness through utilisation of multidimensional measures of loneliness, especially when comparing autistic and neurotypical samples, as it may be that autistic individuals score higher than neurotypical individuals on a certain dimension of loneliness, rather than loneliness as a global construct. Future studies should also implement outcome measures that have been validated in autistic populations. Given the absence of validated loneliness measures in autistic people, it is necessary to ascertain how loneliness can be measured in autistic individuals, and whether loneliness measures are comparable between autistic and neurotypical samples (e.g. conducting measurement invariance studies). This should be done in collaboration with autistic people to more accurately capture their understanding and experiences (Cassidy et al., 2018).

Finally, longitudinal research could advance understanding of the mechanisms, course and predictors of loneliness,

as well as factors which may mediate or moderate its association with anxiety and depression. This would help identify autistic individuals most vulnerable to experiencing loneliness and anxiety or depression, thus allowing early intervention to help mitigate the potential deleterious consequences.

Conclusions

Loneliness is an important yet overlooked construct in the socio-emotional experiences of autistic individuals. This is the first systematic review using meta-analytic procedures to compare loneliness levels between autistic and neurotypical samples. This is also the first review to quantify the associations between loneliness and anxiety and loneliness and depression in autistic individuals. Unexplained heterogeneity as well as the variance in study quality should be considered when interpreting these findings. Nevertheless, this review demonstrates consistently elevated loneliness scores reported by autistic individuals compared with neurotypical individuals, and significant correlations between loneliness scores and anxiety and depressive symptoms in autistic individuals, highlighting the importance of further research and awareness of loneliness in autism.

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Declarations

Conflict of Interest The authors declare no competing interests.

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