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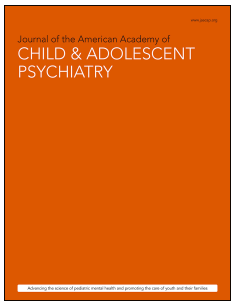

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Elna H. Suominen, DClinPsy, Calliope A. Chen, BSc, Andrew Dunlop, DClinPsy, Rob Saunders, PhD, William Mandy, PhD

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Sex/Gender Differences in Internalizing Problems of Autistic Children and Young People: A Systematic Review and Meta-Analysis

RH = Sex/Gender Differences in Internalizing of Autistic CYP

Elna H. Suominen, DClinPsy,[a] Calliope A. Chen, BSc,[a] Andrew Dunlop, DClinPsy,[a] Rob Saunders, PhD,[a] William Mandy, PhD[a,*]

Editorial
Supplemental Material

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[a] University College London, London, United Kingdom.

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This paper has not been published or presented elsewhere. The thesis that this work is based on has been uploaded to UCL Discovery.

Data Sharing: Data used in the meta-analysis will be available with publication upon request from the corresponding author.

Rob Saunders served as the statistical expert for this research.

Disclosure: Elna H. Suominen Calliope A. Chen Andrew Dunlop Rob Saunders, and William Mandy have reported no biomedical financial interests or potential conflicts of interest.

Correspondence to Prof William Mandy, PhD, 1-19 Torrington Place, London WC1E 6BT; e-mail: w.mandy@ucl.ac.uk

ABSTRACT

Objective: Findings on the presence and direction of a sex/gender difference in internalizing problems for autistic children and young people (CYP) are inconsistent. This systematic review investigated whether autistic boys and girls differ in internalizing problem severity.

Method: Studies comparing internalizing problems (including depression and anxiety) in autistic boys and girls using validated, continuous measures were included. We searched Medline, Embase, PsycINFO, ASSIA and Web of Science. The Joanna Briggs Institute appraisal checklist for cross-sectional studies was used to assess risk of bias. Random-effects meta-analyses estimated effect size differences for (1) overall internalizing, (2) anxiety symptoms and (3) depression symptoms between autistic boys and girls. Moderation effects of age, IQ, and study methodology were examined through meta-regression.

Results: We identified 56 studies from 4,093 non-duplicate records (N= 13,410 autistic CYP, girls n=3,657, boys n=9,753). Autistic girls experienced more anxiety symptoms than boys (*g*= 0.13 [0.03; 0.23], p=0.015). This effect was larger in community (versus clinic) samples (β=0.22, p=0.027), and in samples with higher average age (β= 0.037, p=0.014) and IQ (β=0.013, p=0.013). Autistic girls also showed higher overall internalizing (*g*=0.10[-0.04; 0.23], p= 0.148) and depression symptoms *(g*=0.12[-0.01; 0.25], p=0.067), but these differences did not reach significance. Heterogeneity for all pooled sex/gender differences was high.

Conclusion: In autistic CYP, girls show more anxiety symptoms than boys, and this is most pronounced in older girls and those with higher IQ. We did not find strong evidence for sex/gender differences in overall internalizing problems or depression symptoms. However, the high heterogeneity cautions against drawing conclusions with certainty.

Study registration information: Systematic review and meta-analysis of sex differences in internalising problems of autistic children and adolescents;

https://www.crd.york.ac.uk/PROSPERO/view/CRD42023466929

Key words: Autism; sex; gender; internalizing problems; depression; anxiety

INTRODUCTION

Autism Spectrum Disorder (ASD), henceforth 'autism, is a neurodevelopmental condition characterized by differences in social communication and sensory processing, intense focused interests, and a preference for certainty, routines, and sameness.[1,2] Reflecting community preferences, in this article, we use "autism" as a direct synonym for the diagnostic entity of ASD, encompassing those with DSM-5/ICD-11 clinical or research diagnoses of ASD as well as the DSM-IV/ICD-10 diagnoses of autism, pervasive developmental disorder not otherwise specified (PDD-NOS), atypical autism and Asperger's disorder. It is a lifelong condition with strong genetic influences[3], as well as sex and/or gender differences in autistic traits and co-occurring difficulties.[4,5] Biological sex refers to sex assigned at birth, which is based on physical characteristics, such as reproductive organs, chromosomes and hormones[6]. Gender identity, which includes the concepts of masculinity and femininity, is socially constructed, and may not always align with sex assigned at birth or with binary classifications. Most individuals' identities are informed by both sex and gender. Although distinct, the effect of these can be difficult to separate due to the impact of cultural socialization that takes place from birth[5]. Ideally, we could examine the influence of sex and gender separately, but most studies discussed in this paper, and in the autism literature more widely, are not able to tease apart their potentially distinct effects. Therefore, unless specified, 'sex/gender' will be used to reflect this[5].

Anxiety and depression are common co-occurring problems for autistic people, although it should be noted that prevalence estimates in systematic reviews are based on literature that shows substantial between-study heterogeneity[7]. A recent review estimated that 27% (95% CI 17-37%) of autistic adults meet criteria for a current anxiety disorder; and 23% (95% CI 17-29%) have depression[8].This is significantly higher than general population prevalence rates

for anxiety disorders (7.3%)[9] and depression (4.7%)[10]. This elevated level of risk for anxiety is present in childhood, as shown by one study of a population-derived cohort of autistic CYP (mean age=11.5 years), of whom 41.9% met criteria for an anxiety disorder[11]. In that same study, rates of depression were not notably elevated (1.4%). Nevertheless, there is some evidence that clinically meaningful depression symptoms are high in autistic CYP. For example, in one community-derived sample, 48% of autistic CYP scored in the at-risk range for depression, compared to 15% of an age-matched, non-autistic comparison group[12].

In the CYP literature, mental health symptoms are often described in terms of "internalizing" and "externalizing" symptoms. Internalizing symptoms refer to inwardly focused emotional problems, such as symptoms of depression and anxiety, in comparison to more outwards-oriented externalizing problems, which tend to refer to behavioral problems of the sort seen in oppositional defiant disorder and conduct disorder.[13] These groupings were established through factor analyses of difficulties identified in CYP referred to therapy clinics,[14] and offer a dimensional perspective on children's emotional and behavioral health, suggesting that an individual's challenges can be placed on a spectrum between impairment and functionality.[15] The groupings of internalizing and externalizing problems have been incorporated into well-established measures of child psychosocial wellbeing, such as the Strengths and Difficulties Questionnaire.[16]

Autistic CYP experience more internalizing problems than non-autistic CYP, in both clinical and community settings.[17,18] Several factors have been proposed to contribute to the higher levels of internalizing problems in autistic individuals. These include individual differences associated with autism, such as difficulties in social communication,[19] emotion regulation,[20] and in recognizing and describing emotions, and distinguishing them from bodily sensations,

also known as alexithymia.[21] Cognitive inflexibility, including difficulty tolerating uncertainty and preference for sameness,[22] are also linked to higher rates of internalizing problems in autistic CYP[23]. Social and environmental factors, such as peer-victimisation[24], parenting style[25], and negative life events are also associated with internalizing problems in autistic CYP[26].

Although robust sex/gender differences have been documented in the internalizing problems of non-autistic CYP[27], sex/gender differences in internalizing problems among the autistic population remain relatively poorly characterized, with existing studies providing conflicting conclusions. Some studies have reported higher level of internalizing problems in girls ,[28] others in boys,[29] and some studies report no significant sex/gender differences.[30-32]

Inconsistent sex/gender effects in the literature may stem from age and IQ differences in samples[8,28]. Developmental effects have been observed in non-autistic populations; girls tend to experience more growth in internalizing problems around adolescence than boys [33]. In autistic CYP, Oswald et al.[34] found a sex/gender difference in internalizing problems in early but not late adolescence, and Gotham et al.[35] reported similar trends, with adolescent girls showing more internalizing problems. IQ may moderate sex/gender differences, as higher IQ can predict internalizing problems in autistic youth[26,36], although some findings suggest otherwise.[37-38] Additionally, ADHD traits, which are more common in boys, could moderate the sex/gender difference in internalizing problems, given that ADHD traits are also associated with both autism and higher levels of internalizing symptoms[32,39].

Inconsistencies in the internalizing sex/gender differences found in literature on autistic CYP could also relate to methodological factors, such as type of sample or informant used. For

example, Ooi et al.[40] found that parent-child agreement on reporting anxiety symptoms ranged from low-to-moderate, where children rated themselves significantly higher on their anxiety symptoms compared to their parents. Methodological issues, such as sampling from predominantly male clinical populations, have also been proposed to contribute to the inconsistent findings[5,34]. A related issue concerns when a study was conducted. Definitions of autism and diagnostic practice have evolved, particularly in relation to girls[4], influencing the nature of autistic participants in research, which could in turn affect findings on sex/gender differences.

While there are previous meta-analyses investigating sex/gender differences in autistic traits[41-42] only a few reviews have summarized sex/gender differences in internalizing problems of autistic CYP. Hull and colleagues[41] provided a brief narrative review of studies investigating sex/gender differences in internalizing problems in autistic adults and CYP but did not complete a meta-analysis. Natoli et al.[43] pooled the effects from seven studies looking at sex/gender differences in internalizing problems in young autistic children, aged one to six years, as part of a wider systematic review on sex/gender differences in autistic traits and co-occurring conditions. They concluded that there were no significant sex/gender differences in internalizing problems for young autistic children but noted high heterogeneity.

Despite providing a helpful overview of sex/gender differences in internalizing problems found in autistic CYP, the number of studies included in Natoli and colleagues' [43] study was small and only focused on a narrow age range (one to six years). Internalizing behaviors change with age in autistic and non-autistic young people, and this change is likely different for boys and girls[33-35], so it will be useful to extend the age range of Natoli and colleagues' meta-analysis to encompass later childhood and adolescence.

Given the inconsistency in findings regarding the sex/gender difference in internalizing problems of autistic CYP and the potential for sex/gender differences to change during development, a comprehensive systematic review and meta-analysis is needed covering childhood and adolescence. The present study aims to address this gap.

The aim of the present study was to review and synthesize existing research to elucidate whether there is a sex/gender difference in the internalizing problems of autistic CYP. We chose to use continuous symptom scores of internalizing problems, rather than prevalence rates of internalizing-related mental health diagnoses. This was to reflect the dimensional nature of internalizing symptoms[15], allowing analyses to capture with more precision variability in symptom severity, compared to an approach using categorial diagnosis. Given the possible influences of individual characteristics and study methodology on the level of internalizing problems found in autistic CYP, we wished to ascertain whether clinical and sociodemographic factors or study characteristics would moderate this effect. Thus, we aimed to answer the following questions:

1. Are there sex/gender differences in internalizing problems (i.e., overall internalizing, anxiety symptoms, depression symptoms) of autistic CYP?
2. Are any sex/gender differences in internalizing problems moderated by clinical (age, IQ, ADHD diagnosis), sociodemographic (ethnicity) and study-related factors (setting, ratio of girls to boys, year of publication, referring to sex vs gender, risk of bias, and type of informant)?

METHOD

Search strategy

The systematic review was registered on PROSPERO before any searches were completed (PROSPERO: CRD42023466929). The PRISMA statement was used as guidance for the reporting of this systematic review.[44] See Tables S1 and S2, available online, for the PRISMA checklist. The searches were completed in the following databases: EMBASE, PsycInfo, Medline, Web of Science and ASSIA. The search terms included the condition (i.e., "autism"), the exposure (i.e., "sex" or "gender"), outcome (i.e., "internalizing"), and the population (i.e., "child" or "adolescent"). The search strategy and the full list of search terms used can be found in Supplement 1 and Table S3, respectively, available online. The initial search was completed on the 12th of October 2023, with an updated search completed on the 15th of October 2024 to identify studies published since the original search.

The results of the searches were reviewed against the inclusion and exclusion criteria, described in Table 1. The included studies were grouped according to the type of outcome reported in the study, e.g., anxiety, depression, or overall internalizing problems. The population of interest was autistic CYP. This included individuals with a research or clinical diagnosis of autism, or diagnoses of Asperger's or Pervasive Developmental Disorder Not otherwise specified (PDD-NOS; DSM-IV[2]), also referred to as atypical autism (ICD-10[45]).

[Table 1 here]

Data extraction

The search results were uploaded to EndNote, with duplicates removed. The primary author screened titles and abstracts based on inclusion and exclusion criteria, followed by review of full manuscripts of studies meeting or unclear on eligibility. A secondary reviewer (X.X.) independently screened 10% of the results: there was 96.8% agreement between raters at the title and abstract stage and 94.1% agreement at full text review. Any disagreements about inclusion or extraction were resolved in discussion with the second reviewer, or by consulting the wider research team, until a consensus was reached. Reasons for exclusion for each paper at the full manuscript stage are given in Table S5, available online. Data extraction was independently performed by the primary author and a secondary reviewer (X.X. and Y.Y.) and included country, sex/gender distribution, whether sex and/or gender was reported, mean age, ethnicity, IQ, study setting, unadjusted means and standard deviations for internalizing scores by sex/gender, percentage with ADHD, and how internalizing was measured. For longitudinal studies, data from the first time point were used. Where studies included multiple informants, parent-reports were preferred over child reports for consistency, since most studies relied on parent report. Authors were contacted for missing data, and if not provided, the studies were synthesized narratively where possible.

Risk of Bias and Certainty of Evidence

The Joanna Briggs Institute (JBI)[46] appraisal checklist for analytical cross-sectional studies was used to assess risk of bias within studies meeting eligibility criteria. It has been deemed suitable for systematic review of studies including an observational exposure[47] and found comparable to other risk of bias tools, such as the ROBINS-I (Risk Of Bias In Non-randomized Studies - of Interventions) and AHRQ (Agency for Healthcare Research and Quality) [48-49].

The selected studies were rated as “no”, “unclear”, or “yes”, in eight domains: (i) clarity of inclusion criteria, (ii) description of sample and setting, (iii) valid and reliable measure of exposure, (iv) objective, (v) standard measure of the condition, (vi) confounding factors identified, and appropriate strategies to account for them, (vii) a reliable and valid measure of outcome, and (viii) appropriate statistical analysis. In the present study, the exposure was sex and/or gender, the condition was autism, and the outcome was internalizing symptoms. For the exposure domain, studies were rated as “yes”, if they specified whether they are investigating sex or gender and provided a rationale for this. The identification and management of confounding variables was evaluated in view of the analysis of the sex/gender difference in outcome, even when this was not the main analysis of the study. The secondary reviewer independently evaluated 20% of the included studies.

Certainty of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method[50]. This approach rates the certainty of evidence in relation to risk of bias, inconsistency, indirectness, imprecision, and publication bias. The certainty of evidence varies from “high” to “very low”, where observational studies start at “low”.

Data Synthesis

A descriptive summary was compiled for all included studies based on the eligibility criteria, including the authors, participant characteristics, type of study, measure(s) used and the results. R and Rstudio software were used to complete the quantitative synthesis, utilizing the “metacont” and “metareg” functions within the [meta] package[51]. Separate analyses were completed for studies reporting (i) overall internalizing, (ii) anxiety, and (iii) depression scale scores. Higgins’ I^2, Cochran’s Q, and Tau^2 statistics were calculated to assess heterogeneity

and to determine whether the data gathered were suitable for pooling. A random-effects model was applied to calculate the pooled mean differences, using the inverse variance method and the Hartung Knapp adjustment for random effects. Pooled effect sizes were calculated using Hedge's g, based on the extracted mean internalizing scores, and standard deviations.

Meta-regression analyses were completed to investigate the impact of possible moderators driving effect size heterogeneity. These included the year of publication, mean age of the sample, mean IQ, the ratio of girls to boys, type of measure (parent-report, teacher-report, or self-report), type of sample (community, clinical, or mixed), referring to "sex" or "gender" (sex, gender or unclear) and risk of bias (the sum of ratings where no was rated as 0, unclear as 1, and yes as 2). Separate analyses were completed for each moderator variable to prevent loss of power due to listwise deletion. Ethnicity and the percentage of sample with ADHD were not included as moderators due to limited and inconsistent reporting of this within the selected studies.

RESULTS

After removal of duplicates, we screened the titles and abstracts of 4,093 citations against inclusion/exclusion criteria, of which 442 full-text articles were retrieved and reviewed, with 56 reports being identified as eligible for this systematic review. The search results are summarized in the PRISMA chart (Figure 1). The summary of the included studies can be found in Table 2.

[Figure 1 here]

[Table 2 here]

Study characteristics

The 56 included studies were conducted in the following countries: USA (k=24), UK (k=6), Netherlands (k=4), Canada (k=3), Australia (k=5), Italy (k=3), Taiwan, Japan, Poland, Greece, Finland, Indonesia, Belgium, Ireland, Singapore, Egypt, Saudi-Arabia, and Jordan (all k=1). Most of the included studies were cross-sectional (k=50), but baseline data were also included from six longitudinal (including cohort) studies. Study sample sizes ranged from 22 to 1,740. A total of 13,410 autistic CYP (girls n=3,657, boys n=9,753) were included in this review. Twenty-seven studies recruited samples from a clinical setting, 25 from a community setting, and four included data from community and clinical settings ("mixed"). Out of the selected studies, 19 studies just measured overall internalizing problems, 19 included just a measure of anxiety symptoms, and five studies only reported on depression symptoms. Eight studies reported on both anxiety and depression symptoms, and five studies included measures of anxiety, depression and overall internalizing symptoms.

The included studies incorporated 18 different measures in total. The most frequently used (k=17) measure was the Child Behavior Checklist (CBCL). The next most frequently used measures included the Spence Children's Anxiety Scale (k=8; SCAS) and the Behavior Assessment System for Children- Second Edition (k=6; BASC-2). The Strengths and Difficulties Questionnaire (SDQ) was used in five studies, and the Revised Child Anxiety and Depression scale (RCADS) was used in three studies. The Children's Depression Inventory 2 (CDI2), the Early Childhood Inventory-4 (ECI-4), Child and Adolescent Symptom Inventory (CASI), and the Anxiety Scale for Children- ASD (ASC-ASD) were included in two studies each. The rest of the measures were only included in one study each (See Table 2).

Twenty-two papers reported a cross-sectional effect of sex/gender on overall internalizing problems, anxiety and/or depression symptoms but did not report means and standard deviations. These tended to be studies where internalizing sex/gender differences were not the main focus of the research, which reported the relationship between sex/gender and internalizing as a correlation. These authors were contacted, and in seven instances authors were able to provide means and standard deviations for autistic boys and girls, to be included in the meta-analyses. Fifteen authors were unable or unavailable to provide the required data, and thus these studies were summarized narratively.

Participant characteristics

The mean age of participants in each study varied between 3.0 and 15.6 years, the median being 10.1 (IQR=2.7) years. The proportion of girls in the study populations ranged from 10% to 50%. The mean IQ of the samples ranged from 56.3 to 116.3.

Out of the 56 studies reviewed, 34 provided some information on race or ethnicity (See Table 2). Most studies reported a majority of white participants, with one study[75] reporting a majority of Chinese participants. The proportions of white participants ranged from 36.8% to over 90%. Sixteen studies contained over 70% white participants, indicating a lack of ethnic diversity in this corpus of literature. Black ethnicities were reported in 14 studies at rates between 1% and 28%. Hispanic/Latino/a/x participants were reported in 10 studies, ranging from 7-17% of samples. Asian ethnicities were included in 14 studies and, apart from the majority Asian sample in Magiati et al,[75] were present in samples at lower levels, typically around 0 to 8%. Other ethnic groups, such as Arab, “Indigenous/Native Hawaiian/Other Pacific Islander”, and Jewish people were represented in singular studies, at varying degrees

of prevalence (<1-6%). Multiracial or mixed individuals were represented in a few studies at 2.9-17.2%.

Risk of bias within studies

Agreement with the second reviewer for JBI Quality Appraisal Checklist ratings was above chance, at the moderate level (Cohen's Kappa= 0.51, 95% CI [-0.01,1.00]). The results are summarized in Table S5, available online. Only three studies were evaluated as having low risk of bias across all eight domains. However, 16 studies had low risk of bias across seven domains, with the only "unclear" domain being the definition or rationale regarding how they operationalized sex and/or gender. The risk of bias evaluation showed that 33 studies included unclear or missing information in two or more domains, with issues relating to the following domains being most commonly observed: (i) including a rationale or definition for the exposure (e.g. sex/gender) (n=49), (ii) information on the setting and sample (n=24), (iii) identifying (n = 14) or using appropriate strategies to deal with confounding factors (n = 20).

Certainty of Evidence

As all included studies were observational in nature due to looking at sex/gender differences, the GRADE approach indicates that they are rated mostly low in certainty of evidence. In addition, because many of the studies did not look at sex/gender differences as the primary outcome, the risk of bias and study limitations relating to identification and accounting for confounding variables and defining the exposure variable led to further reductions in certainty of evidence for some of the studies.

Moreover, the unexplained heterogeneity was high particularly for overall internalizing problems, suggesting that there was some inconsistency. For anxiety, the funnel plot showed that some studies, like Bagg et al.[53] and Di Vara et al.[62], found large opposite effects. These

outliers may represent distinct populations, or methodologies, that could contribute to these extreme values. In studies examining depression the inconsistency appeared lower. No issues relating to indirectness were identified for any of the outcomes. Publication bias will be discussed in the main results below.

Mean sex/gender difference in overall internalizing symptoms

Twenty studies investigating overall internalizing problems were suitable for inclusion in the meta-analysis. As illustrated by Figure 2a, the meta-analysis revealed a non-significant effect of sex/gender in overall internalizing symptoms (Hedges g=0.10, 95% CI [-0.04;0.23], t(19)=1.51, p=0.148). Higgins' I^2, Cochran's Q, and Tau^2 statistics indicated a high level of heterogeneity (I^2= 75.8%, 95% CI [62.7%;84.3%]; Q(17)=78.4, p<0.001; T^2= 0.06 95% CI [0.02;0.13]). A visual inspection of the funnel plot (Figure S1, available online), indicated that the overall literature might overrepresent findings favoring girls having higher internalizing problems, while findings that reported no effect, or higher rates in boys may be underrepresented. However, there was no significant evidence of publication bias, t(18)=1.97, p=0.065.

[Figure 2 here]

Mean sex/gender difference in anxiety symptoms

Twenty-six studies were eligible for inclusion in the meta-analysis of pooled sex/gender difference in anxiety symptoms. As illustrated in Figure 2b, the meta-analysis revealed a small, significant effect of sex/gender on anxiety symptoms (Hedges g=0.14[0.04;0.25], t(25)=2.78, p=0.010), whereby girls experienced slightly more anxiety symptoms than boys.

There was moderate heterogeneity within the pooled studies, as indicated by the Higgins' I^2, Cochran's Q, and Tau² statistics (I^2= 58.5%, 95% CI [36.0%;73.1%]; Q(26)=60.27, p<0.001; T^2=0.031, 95% CI [0.01; 0.09]). Egger's regression revealed significant evidence of publication bias towards reporting girls to experience more anxiety symptoms than boys, t(24)=4.23, p<0.001, as illustrated by the asymmetrical funnel plot, favoring an effect towards girls (Figure S2, available online). Rosenthal's fail-safe N analysis was conducted to assess the robustness of the meta-analytic findings against potential publication bias. Results indicated that 116 additional studies with null results would be required to reduce the overall effect to non-significance (p > .05), suggesting that the observed effect is relatively robust.

Mean sex/gender difference in depression symptoms

For depression symptoms, thirteen studies were eligible for being synthesized by meta-analysis (See Figure 2c). The meta-analysis revealed that there was a small tendency for autistic girls to show more depression symptoms than autistic boys, but this did not reach significance (Hedges *g*= 0.12, 95% CI [-0.01; 0.25], t(12)= 2.01, p=0.067). The Higgins' I^2, Cochran's Q, and Tau² statistics revealed moderate heterogeneity (I^2= 44.9%, 95% CI [0.0%; 71.2%]; Q(12)=21.80, p=0.040; T^2= 0.022, 95% CI [0.0; 0.08]). As illustrated by the symmetrical funnel plot (Figure S3, available online), there was no significant publication bias for depression symptoms, t(11)=0.58, p=0.577).

A narrative synthesis of the 15 studies not included in the meta-analysis[11,30,34-35,57,64,68,73-74,82,89,95] was completed based on results, such as correlations, p-values, and/or qualitative descriptions. This can be found in Supplement 2, available online.

Potential moderators of sex/gender differences in internalizing

Age. The mean age of the sample within the included studies varied from 3 to 15 years old, with median of 9.5 (IQR=4.12) for overall internalizing problems. When looking at anxiety and depression symptoms more specifically, the median age was 10.0 (IQR=4.93) for anxiety and 9.0 (IQR=5.48) for depression. Age was a significant moderator of the pooled sex/gender difference only for anxiety symptoms (k=26). It significantly explained 30.22% of the heterogeneity within the pooled mean difference (β=0.039, r^2= 30.22% F(1, 24) = 7.79, p= 0.010). The effect indicated that the tendency for girls to show higher anxiety was more pronounced in older samples. There were no significant moderation effects of age for overall internalizing problems (k=20) or depression (k=13; See Table 3).

IQ. For studies looking at overall internalizing problems, the mean IQ ranged from 60.93 to 103.97. For anxiety, the mean IQ ranged from 72.7 to 116.31 and was between 72.7 and 103.95 for depression. The meta-regression of 19 studies found IQ to significantly account for 84.2% of heterogeneity within the sex difference in anxiety problems, where a higher mean IQ of the sample suggested a slightly larger sex/gender difference (β=0.015, r^2= 84.2%, F(1,17)=14.7, p=0.001). There were no significant moderation effects of IQ for overall internalizing problems (k=12) or depression (k=10; See Table 3).

Sample Characteristics and Bias. The proportion of girls to boys, the type of informant used in the study, year of publication, setting, risk of bias ratings, and whether the study referred to "sex" or "gender" were tested as predictors of heterogeneity. As shown in Table 3, for studies looking at overall internalizing (k=20) and depression symptoms (k=13), none of these significantly impacted the sex difference found in internalizing problems.

For anxiety symptoms (k=26), the type of setting that the sample was recruited from explained 50.71% of the heterogeneity between studies. A community sample significantly predicted a greater sex/gender difference in anxiety symptoms, compared to a clinical sample ($\beta_{Community}$=0.22, p= 0.027, F(2, 23)=3.61, p=0.043). The rest of the study characteristics were not significant moderators of the sex difference, as shown in Table 3.

DISCUSSION

This systematic review and meta-analysis including 56 studies and 13,410 autistic participants found that autistic girls experienced more anxiety problems than autistic boys, and that this difference slightly increased with age and IQ. There were trends towards autistic girls, compared to autistic boys, also experiencing more overall internalizing problems and depression symptoms, but these effects did not reach significance. However, the high heterogeneity of pooled effects, particularly for overall internalizing problems, means that these results should be interpreted cautiously. Furthermore, the overall internalizing (k=20) and depression (k=13) meta-analyses included fewer studies than the anxiety meta-analysis (k=26), which would have impacted on power.

The higher level of anxiety problems in girls is consistent with literature on the general population.[99] Moreover, the effect of age increasing the magnitude of this sex/gender difference in autistic CYP coincides with the previous studies reporting an interaction between sex/gender and age, whereby autistic girls experienced higher levels of anxiety during adolescence.[34-35] The lack of such interaction between sex/gender and age for overall internalizing and depression symptoms could be due to lack of power, or the median age for anxiety studies being slightly higher for anxiety studies, thus possibly including more studies with older samples.

Nevertheless, the results suggest that autistic girls are more likely to experience anxiety than autistic boys, particularly in adolescence. Adolescence is typically a time of changes such as a heightened sensitivity to peer influence and rejection, as well as transitions to more demanding environments such as secondary school.[100] Although both autistic boys and girls are likely to encounter transitions and social changes in adolescence, research shows that autistic girls could be more motivated to engage socially than autistic boys,[101] and more susceptible to interpersonal stress.[102] Mandy et al[103] found that girls were more likely to experience increases in autistic social characteristics in adolescence than boys, which could also make adjusting to the social changes more difficult or contribute to painful social rejections. A related possibility is that this could also lead to increased pressures to camouflage, or 'use strategies to minimize autism in social situations'[104], which has been associated with internalizing problems in autistic CYP and adults.[104,86,54]

The increases in anxiety experienced by autistic girls, compared to autistic boys, in adolescence could also correspond with pubertal changes. One possibility is that pubertal surges in estradiol and progesterone in autistic girls could amplify hypothalamic-pituitary-adrenal (HPA) axis responses to stressful events, via their influence on amygdala reactivity[105-106]. These hormone-driven changes could increase the vulnerability of autistic girls to experiencing anxiety problems in the face of environmental challenges, such as interpersonal stress and sensory overload.[107-108] Furthermore, puberty might particularly increase anxiety symptoms in girls due to higher risk of sexual abuse and harassment.[109] It should be noted that the puberty-related effects we consider here would be expected to be relevant to depression as well as anxiety, yet we did not find a significant sex/gender difference for depression. Whilst we did observe higher levels of depression symptoms in autistic girls, compared to autistic boys, this narrowly missed the threshold for significance.

As stated above, given the high heterogeneity and lower power for the depression analyses, we are cautious about dismissing the possibility of a depression sex/gender difference, and highlight the need for longitudinal studies, sensitive to age and timing of puberty, to investigate trajectories of depression symptoms for autistic girls and boys.

The present findings may help explain the inconsistencies in sex differences found in previous research on autistic CYP. For example, the mean sample IQ explained some of the heterogeneity in the sex/gender difference in anxiety symptoms, which is in line with the hypothesis of previous authors that sex/gender differences in autistic samples may relate to cognitive ability heterogeneity across studies.[28,32,43] Additionally, some researchers argue that methodological biases, such as predominantly male samples and reliance on clinical settings, may contribute to the lack of sex/gender differences found.[5,34] The present findings support this, showing that anxiety sex/gender differences were larger in community versus clinical samples. This could be due to a ceiling effect, where children referred to clinics already show high levels of anxiety, thus obscuring any sex/gender differences.

Despite identifying some moderators for sex/gender differences, a significant amount of heterogeneity remained unexplained, particularly for overall internalizing problems. Variables such as ethnic composition and co-occurring ADHD symptoms were not included in the analysis due to inconsistent reporting across studies. Additionally, meta-regression analyses were conducted list-wise to preserve power, meaning potential interactions between covariates were not examined. As a result, it is unclear whether certain effects would hold once controlling for other moderators.

Although we tried to differentiate between sex and gender, these constructs were inconsistently defined in the included studies, likely making such analyses imprecise. This could have contributed to heterogeneity in sex/gender differences in internalizing problems,

particularly given that gender diversity rates are higher among autistic CYP compared to those who are not autistic.[110] Another feature of the literature reviewed is that a range of diagnostic ascertainment approaches were used when identifying autistic participants, and this likely further contributed to the high heterogeneity we observed when estimating sex/gender differences. This issue is especially relevant to community, as opposed to clinical, studies, where a range of diagnostic approaches would have been used. Moreover, this study focused on cross-sectional effects rather than on developmental trajectories of internalizing problems across childhood and adolescence. Research on such trajectories in autistic youth is currently limited.[35,70,98]

We may have missed some studies that reported on sex/gender differences, since our search strategy required the words 'sex' or 'gender' to appear in the title, abstract or keywords of a paper. Due to the limited number of studies reporting on multiple informants, we were unable to investigate in full the impact of using self-report compared to parent- and teacher informants. Primarily using parents as informants could present a biased view of the sex/gender difference in internalizing problems due to the potential discrepancies in reporting between parents and autistic young people[40] and contribute to the lack of power in regression analyses on the type of informant. Moreover, as most studies did not specifically exclude non-verbal participants, it is possible that non-verbal participants could have been included in the samples which may impact on the validity of internalizing problem ratings, particularly for self-report measures. A related issue is that we included outcome measures that have not been validated specifically for use with autistic people and those who are minimally verbal, which could potentially have undermined the validity of our findings. Currently, internalizing measures validated for autistic people (including those who are minimally verbal) are not widely used in the literature, and future research should address this, to increase

understanding of internalizing difficulties in this population, including sex/gender differences.

Finally, as we did not have two reviewers independently screen all articles, it is possible that some articles were excluded from consideration that would have otherwise been included, though our approach is consistent with AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews).[111] Readers may wish to read Table S5, available online, which lists articles that were excluded at the full-text stage.

Future studies should examine how sex and non-binary gender identities relate to internalizing problems in autistic children and adolescents, particularly as the included studies did not clearly define or operationalize gender, as distinct from sex. Distinguishing biological mechanisms, such as puberty and its timing, from environmental factors like sexism and stigma, could help explain sex/gender differences, and would point towards mechanisms for intervention. For instance, in non-autistic youth, early maturation and interpersonal stress are linked to increased internalizing problems, especially in girls.[106,112] In autistic youth, emerging evidence suggests sex differences in pubertal timing and tempo, which may explain some of the heterogeneity unaccounted for in this review.[113-114] Research comparing autistic and non-autistic boys and girls in terms of internalizing problem trajectories may help confirm whether the developmental effects of sex/gender differ between these groups.

Additionally, most included studies focused on white, Western samples, which limits the generalizability of the findings. More research is needed on ethnically and culturally diverse samples to better understand how sex/gender differences interact with cultural factors, such as societal views on autism and gender roles, differences in camouflaging behaviors, and

minority stress.[115] This would also allow for better generalization of the findings across populations.

There was evidence for sex/gender differences in anxiety symptoms but not in depression symptoms among autistic children and young people. A large portion of the heterogeneity observed may stem from methodological issues in the extant literature. Future research should include designs sensitive to age and IQ effects, focus on developmental trajectories, separately consider sex and gender, and include more ethnically and culturally diverse populations to further understand internalizing problems in autistic youth.

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TABLES

Table 1: Study Inclusion and Exclusion Criteria

Participants	Included	-	Children and adolescents, with mean sample age below 19
		-	Diagnosis of Autism, PDD-NOS/A-typical autism or Asperger's, using recognized diagnostic criteria at the time of the publication
	Excluded	-	Samples with mean age over 19
		-	Samples with only boys or only girls
		-	Samples with participants not meeting the criteria for ASD, PDD or Asperger's
Exposure	Included	-	Studies that included sex or gender as a variable
		-	Studies that segregated data based on sex and/or gender
	Excluded	-	Studies that did not include a sex or gender variable or provide results separated by sex or gender
Outcome	Included	-	Studies using continuous, quantitative measures of child or adolescent internalizing symptoms, anxiety, and/or depression, validated in general population samples.
		-	Studies reporting continuous scores
	Excluded	-	Studies using non-continuous, poorly validated, or qualitative measures
		-	Data not pertaining to scores on internalizing measures, such as frequencies
		-	Measures not assessing internalizing symptoms, anxiety, or depression
Type of study	Included	-	Studies that have been peer-reviewed
		-	Studies written in English or Finnish
		-	Cross-sectional or longitudinal studies
		-	Studies that investigate an intervention and provide baseline data
	Excluded	-	Studies only using qualitative data or analyses
		-	Case studies, review articles, book chapters or discussion papers
		-	Grey literature

Note: ASD = Autism Spectrum; PDD = Pervasive Developmental Disorder; PDD-NOS = Pervasive Developmental Disorder- Not Otherwise Specified

Table 2: Summary of Included Studies

	Study type	Country	Type of sample	Sample size	Percent of girls	Mean Age	Ethnicity and race (as reported in the study)	Mean IQ	Outcome	Measure	Variable (sex or gender)
Ambrose et al., 2020[52]	Cross-sectional	Australia	Community	48	50.0	10.1	n.r.	n.r.	Anxiety	Anxiety Scale for Children-ASD, parent report (ASC-ASD-P)	Sex
Amr et al., 2011[37]	Cross-sectional	Egypt, Saudi-Arabia and Jordan	Clinical	60	38.3	8.2	n.r.	60.93	Internalizing	Child Behavior Checklist internalizing subscale, parent-report (CBCL-P)	Sex
Bagg et al., 2024[53]	Cross-sectional	UK	Community	70	47.1	13.9	1.43% Black 2.85% Mixed race, 1.43% Other/Prefer not to say, 1.43% South Asian, 92.86% White	116.3	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	Sex
Bernardin et al., 2021[54]	Cross-sectional	USA	Mixed	78	29.5	15.0	n.r.	n.r.	Internalizing	The Depression, Anxiety and Stress Scale - 21 Items (DASS-21), self-report	Sex
Bitsika et al., 2024[55]	Cross-sectional	Australia	Community	64	50.0	10.2	n.r.	97.9	Anxiety	Child and Adolescent Symptom Inventory (CASI) Generalized Anxiety Disorder subscale, parent-report	Sex
Boonen et al., 2014[56]	Cross-sectional	Netherlands	Community	206	15.0	9.9	n.r.	n.r.	Internalizing	Strengths and Difficulties Questionnaire, internalizing subscale, parent report	gender
Brereton et al., 2006[30]	Cross-sectional	Australia	Clinical	367	15.0	7.4	n.r.	n.r.	Depression	Developmental Behaviour Checklist parent-report (DBC-P), depression subscale	sex
Butzer and Konstanta	Cross-sectional	Canada	n.r.	22	40.9	n.r.	n.r.	n.r.	Depression	n.r.	gender

reas., 2003[57]											
Cariveau et al., 2021[58]	Cross-sectional	USA	Clinical	682	14.2	7.4	5.6% Asian, 10.6% Black, 10.3% Hispanic, 69.1% White	n.r.	Anxiety	The Early Childhood Inventory-4 (ECI-4) parent-report, or Child and Adolescent Symptom Inventory (CASI) parent-report, anxiety subscale	gender
Chandler et al., 2016[59]	Cross-sectional	UK	Community	277	18.1	6.0	3% Asian, 14% Black African, 14% Black Caribbean , 10% Mixed, 8% other 51% White,	72.7	Anxiety, Depression	Developmental Behaviour Checklist (DBC-P) anxiety and depression subscales, parent report	sex
Chang et al., 2019[60]	Cross-sectional	Taiwan	Community	101	16.9	15.6	n.r.	n.r.	Anxiety	Beck Anxiety Inventory (BAI), self-report	gender
De Clercq et al., 2021[61]	Longitudinal	Belgium	Clinical	141	17.0	10.1	n.r.	n.r.	Internalizing	Child Behavior Checklist internalizing subscale, parent-report (CBCL-P)	gender
Di Vara et al., 2024[62]	Cross-sectional	Italy	Clinical	1740	17.4	6.98	n.r.	85.81	Internalizing, Anxiety, Depression	Child Behavior Checklist, parent-report (CBCL-P), internalizing, anxiety, and affective problem subscales	sex
Emerson et al., 2023[63]	Cross-sectional	Australia	Community	118	33.9	10.1	n.r.	n.r.	Anxiety	Anxiety Scale for Children - ASD-parent repot (ASC-ASD-P)	gender
Factor et al., 2017[64]	Cross-sectional	USA	Clinical	57	17.5	7.3	3.51% Asian, 5.26% Black, 3.51% Other 87.72% White	100.0	Anxiety	Child Behavior Checklist, parent report (CBCL-P), anxiety problems subscale	gender
Fombonne et al., 2022[65]	Cross-sectional	USA	Clinical	472	23.1	9.2	n.r.	n.r.	Internalizing	Strengths and Difficulties Questionnaire, emotional problems subscale, parent report	sex
Gadow et al., 2004[31]	Cross-sectional	USA	Clinical	172	20.9	4.2	1% Black, 3% Hispanic, 95% White	79.0	Anxiety, Depression,	The Early Childhood Inventory-4 (ECI-4) Generalized Anxiety Disorder and dysthymia subscales, parent-report	gender
Gotham et al., 2015[35]	Longitudinal	USA	Clinical	109	11.9	10.7	20% non-white	56.3	Anxiety, Depression	Child Behavior Checklist, parent-report (CBCL-P), anxiety subscale	gender

Guerrera et al., 2019[66]	Cross-sectional	Italy	Clinical	472	18.9	5.5	n.r.	92.99	Internalizing	Child Behavior Checklist, parent-report (CBCL-P), internalizing subscale	sex
Harrop et al., 2024[67]	Cross-sectional	USA	Community	146	18.5	9.4	4.2% Asian 15.3% Black, 70.8% White	86.6	Anxiety	Parent-Rated Anxiety Scale for Autism Spectrum Disorder (PRAS-ASD)	sex
Hartini et al., 2016[68]	Cross-sectional	Indonesia	Community	54	25.9	10.1	n.r.	n.r.	Internalizing	Child Behavior Checklist, parent report (CBCL-P), internalizing subscale	gender
Horiuchi et al., 2014[69]	Cross-sectional	Japan	Clinical	173	25.4	7.9	n.r.	88.3	Internalizing	Strengths and Difficulties Questionnaire emotional problems subscale, parent-report	sex
Horwitz et al., 2023[70]	Cohort	Netherlands	Clinical	152	27.0	11.0	n.r.	100.15	Internalizing	Child Behavior Checklist, self-report (CBCL-C), anxiety and affective subscales	sex
Hurtig et al., 2009[71]	Cross-sectional	Finland	Community	46	26.1	13.0	n.r.	n.r.	Internalizing	Child Behavior Checklist, parent-report (CBCL-P) Internalizing subscale	gender
Johnston and Iarocci 2017[12]	Cross-sectional	Canada	Community	67	15.0	9.8	n.r.	102.6	Anxiety, Depression	Behavior Assessment System for Children- Second edition (BASC-2), parent-report, generalized anxiety and depression symptoms subscales	gender
Kaat and Lecavalier 2015[72]	Cross-sectional	USA	Mixed	46	17.4	12.4	Caucasian 76 %	90.7	Anxiety, Internalizing, Depression	Revised Child Anxiety and Depression scale, parent report, anxiety and depression subscales	sex
Leader et al., 2022[73]	Cross-sectional	Ireland	Community	95	20.0	9.5	n.r.	n.r.	Depression	Child Behavior Checklist, parent report (CBCL-P), affective problems subscale	gender
Lohr et al., 2017[74]	Cross-sectional	USA	Clinical	100	12.0	12.9	86% of parents self-classified as Caucasian	n.r.	Anxiety	The Screen for Child Anxiety-Related Emotional Disorders (SCARED), self-report	gender
Magiati et al., 2016[75]	Cross-sectional	Singapore	Community	241	18.3	10.3	76.8% Chinese, 7.1% Indian, 9.5% Malay, 0.8% not reported/missing, 5.8% other	n.r.	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	gender

Mandy et al., 2012[28]	Cross-sectional	UK	Clinical	325	16.0	9.8	9% Afro-Caribbean, Asian, or mixed heritage) 91% White	92.6	Internalizing	Strengths and Difficulties Questionnaire emotional problems subscale, parent-report	sex
May et al., 2014[76]	Longitudinal	Australia	Clinical	56	50.0	9.9	2% Asian 91% Australian 7% European	96.2	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	gender
Mayes et al., 2011[36]	Cross-sectional	USA	Clinical	627	14.4	6.6	92.5% White	88	Anxiety, Depression	Pediatric Behavior Scale (PBS), parent-report anxiety and depression subscales	gender
Muratori et al., 2019[77]	Cross-sectional	Italy	Clinical	989	17.1	3.7	n.r.	79.2	Anxiety	Child Behavior Checklist, parent-report (CBCL-P), Affective- and anxiety problem subscales	gender
Nakai al., 2013[78]	Cross-sectional	Japan	Clinical	40	22.5	11.4	n.r.	95.7	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	sex
Nasca et al., 2020[79]	Cross-sectional	USA	Community	80	50.0	9.0	11% minority, 89% white	103.3	Internalizing, Anxiety, Depression	Behavior Assessment System for Children- Second edition (BASC-2) anxiety and depression scales, parent-report	sex
Neil et al., 2016[80]	Cross-sectional	UK	Community	69	14.5	10.4	n.r.	98.6	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	gender
Neuhaus et al., 2023[81]	Cross-sectional	USA	Clinical	142	43.0	12.8	14.3% of Hispanic/ Latino, 77.1% not Hispanic/Latino descent, 8.6% declined to answer. 4.3% Asian, 4.3% Black or African American, 0.4% Hawaiian or Pacific Islander,		Internalizing	Child Behavior Checklist, parent-report (CBCL-P), internalizing subscale	sex

							11.8% more than one race, 71.1% white, 8.2% declined to answer				
Nguyen et al., 2013[82]	Cross-sectional	UK	Community	54	50.0	13.7	n.r.	65.9	Internalizing	Strengths and Difficulties Questionnaire emotional problems scale, parent-report	sex
Nordahl et al., 2020[83]	Cross-sectional	USA	Community	300	30.3	3.0	15.2% POC, 67.1% white, 15% ≥2 Races reported, 2.85 not reported	n.r.	Internalizing, Anxiety, Depression,	Child Behavior Checklist, parent-report (CBCL-P), anxious and depressive scales	sex
Oswald et al., 2016[34]	Cross-sectional	USA	Community	32	43.8	14.9	n.r.	110.2	Anxiety, Depression	The Revised Child Anxiety and Depression Scale, parent-report, anxiety and depression subscales	sex
Penner et al., 2022[84]	Cross-sectional	Canada	Clinical	451	22.2	10.0	4% American/Hispanic, 1% Arab, 6% Black, 4% Chinese, <1% East Asian, 6% indigenous, <1% Japanese 4% Jewish <1% Korean, 2% South Asian, 1% South East Asian, 1% West Asian, 83% White	n.r.	Internalizing	Child Behavior Checklist, parent-report (CBCL-P), internalizing subscale	sex
Pisula et al., 2016[85]	Cross-sectional	Poland	Community	70	50.0	13.8	n.r.	103.2	Internalizing	Child Behavior Checklist, parent-report (CBCL-P) internalizing subscale	sex
Ross et al., 2023[86]	Cross-sectional	USA	Community	733	49.0	9.0	n.r.	82.0	Internalizing	Child Behavior Checklist, parent-report (CBCL-P)	sex and gender used interchangeably

Sanchez et al., 2024[87]	Cross-sectional	USA	Community	89	19.1	11.3	n.r.	97.5	Internalizing	Behavior Assessment System for Children- Second edition (BASC-2) internalizing subscale, parent-report.	gender
Schwartzman et al., 2022[88]	Longitudinal	USA	Mixed	212	32.1	11.4	8.8% African American, 0.4% Asian, 82.9% Caucasian, 7.0% Hispanic/Latino, and 7.5% Mixed race	101.2	Depression	Children's Depression Inventory 2 (CDI2), self-report	sex
Schwartzman et al., 2024[89]	Cross-sectional	USA	Clinical	100	39.0	13.7	1% American Indian/Alaska Native, 0% Asian 7% Black/African American, 4% biracial, 10% Hispanic/Latinx, 90% Not Hispanic/Latinx, 0% Native Hawaiian/Pacific Islander, 5% Multiracial, 80% White	n.r.	Anxiety, Depression	Revised Child Anxiety and Depression scale parent report (RCADS-P), anxiety and depression subscales	sex
Smith et al., 2024[90]	Cross-sectional	USA	Community/Clinical	128/1035	43.0/22.9	12.4/6.75	0.8/0% American Indian, 1.6/8.1% Asian, 4.7/17.8% Black, 0.8/0% Hawaiian or Pacific Islander, 17.2/7.6% Mixed, 0/17.9% Unknown	100.9/95.1	Anxiety, Depression	Child Behavior Checklist, parent report (CBCL-P), anxious and affective problem subscales	sex

							75.0/36.8% White, 17.19/11.7% Hispanic or Latino/a/x, na/82.8% Not Hispanic or Latino/a/x				
Solomon et al., 2011[91]	Cross-sectional	USA	Community	40	50.0	12.2	n.r.	103.95	Internalizing, Anxiety, Depression	Behavior Assessment System for Children- Second edition (BASC-2), parent-report	sex and gender used interchangeably
Storch et al., 2012[92]	Cross-sectional	USA	Clinical	72	19.4	10.8	2.8% Asian, 11.1% Hispanic, 4.2% other, 81.9% White	n.r.	Anxiety	Pediatric Anxiety Rating Scale (PARS)	gender
Syriopoulou-Delli et al., 2019[93]	Cross-sectional	Greece	Community	291	26.5	10	n.r.	91.3	Anxiety	School Anxiety Scale-Teacher Report (SAS- TR)	gender
Varela et al., 2020[94]	Cross-sectional	USA	Clinical	349	19.8	8.9	23.7% African American, 0.8% Asian, 5.1% Biracial 62.7% Caucasian, 4.5% Latino, 3.1% other	76.8	Anxiety	Behavior Assessment System for Children- Second edition (BASC-2), anxiety subscale, parent-report.	sex and gender used interchangeably
Wigham et al., 2015 [95]	Cross-sectional	UK and USA	Community	53	11.3	12.49	n.r.	106.2	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	gender
Wijnhoven et al., 2018[96]	Cross sectional	Netherlands	Clinical	172	22.1	11.3	90% Dutch	104.9	Anxiety	Spence Children's Anxiety Scale Parent Report (SCAS-P)	gender
Wijnhoven et al., 2019[97]	Cross sectional	Netherlands	Clinical	93	23.7	11.2	90.3% Dutch	102.16	Depression	Children's Depression Inventory 2 (CDI2), self-report	gender
Worley et al., 2011[98]	Cross-sectional	USA	Mixed	70	37.1	8.7	5.69% African American,	n.r.	Internalizing	Autism Spectrum Disorders-Comorbid for Children (ASD-CC), worry/depressed subscale, parent-report	gender

							55.69%, Caucasian, 4.27% Hispanic, 30.05% Non-specified, 4.24% Other.				
Wright et al., 2023[99]	Cohort	Canada	Clinical	365	15.6	3.4	n.r.	84.7	Internalizing	Child Behavior Checklist, parent-report (CBCL-P), Anxious depressed scale	sex

Note: n.r.=not reported.

Table 3: Moderator analyses investigating sources of heterogeneity

	Overall Internalizing problems	**Anxiety**	**Depression**
Age	β=-0.002, r^2=0.0%, F(1, 18) = 0.006, p= 0.941	**β=0.039, r^2= 30.22% F(1, 24) = 7.79, p= 0.010**	β=0.004, r^2=0%, F(1, 11)= 0.047, p=0.833
IQ	(β=0.009, r^2=0%, F(1, 10) = 1.66, p= 0.226	**(β=0.015, r^2= 84.2%, F(1,17)=14.7, p=0.001**	(β=0.007, r^2= 16.35%, F(1,8) = 0.94, p=0.362
Proportion of girls to boys	β= -0.09, r^2=0%, F(1, 18) = 0.16, p=0.691	β=0.31, r^2=35.05%, F(1, 24) = 3.24, p=0.085	β=0.23, r^2=21.08%, F(1,11)= 0.942, p=0.353
Type of informant (parent, child, teacher)	β_{child}= 0.07, r^2=0.0, F(1,18) = 0.996, p=0.789	β_{child}=0.24, p=0.170, $\beta_{teacher}$=-0.14, p=0.521, r^2=3.55%, F(2, 23)=1.29, p=0.293	β_{child} =-0.0125, r^2=0%, F(1,11)= 0.007, p=0.937
Year of publication	β= -0.021, r^2=10.34%, F(1,18) = 2.38, p=0.140	r^2=0, β= 0.001, F(1,24) = 0.01, p=0.921	β=0.001, r^2=0%, F(1,11)= 0.019, p=0.892
Participant setting (clinical, community or mixed)	$\beta_{Community}$= 0.09, p=0.58, β_{Mixed}=-0.005, p=0.983, r^2=0%, F(2,17)=0.173, p=0.843	**$\beta_{Community}$=0.22, p= 0.027, β_{Mixed}=0.32, p=0.095, r^2=50.71%, F(2, 23)=3.61, p=0.043.**	$\beta_{Community}$= 0.16, p=0.239, β_{Mixed}=0.064, p=0.735, r^2=16.53%, F(2,10)= 0.783, p=0.483
Risk of bias	β= 0.064, r^2=11.19%, F(1,18)=2.15, p=0.160	β=-0.016, r^2=0%, F(1, 24)=0.559, p=0.461	β=0.01, r^2=0%, F(1,11)= 0.045, p=836
Study referring to sex or gender (gender, sex, unclear)	$b_{sex=}$ -0.120, p=0.540, $b_{unclear}$=-0.137, p=0.623, r2=0, F(1,17)=0.21, p= 0.812	b_{sex} 0.074, p=0.505, $b_{unclear}$ =0.008, p=0.968, r2=0, F(2, 23)=0.24, p= 0.788	b_{sex} -0.032, p=0.846, $b_{unclear}$ -0.259, p=0.481, r2=0, F(2, 10)=0.27, p= 0.769

Note: Statistically significant results presented in bold. p<0.05

Figure 1: PRISMA Chart

(see attached files)

Figure 2: Meta-Analyses of Mean Differences in Internalizing Symptoms

Note: Meta-analyses of mean differences in internalizing symptoms among autistic boys and girls: (A) overall internalizing symptoms, (B) anxiety symptoms, and (C) depression symptoms. Forest plots were generated using RStudio.