Wigham S, Barton S, Parr JR, Rodgers J.

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Journal of Mental Health Research in Intellectual Disabilities 2017, 10(4), 267-287.

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This is an Accepted Manuscript of an article published by Taylor & Francis in *Journal of Mental Health in Intellectual Disabilities* on 22/03/2017, available online:

<https://doi.org/10.1080/19315864.2017.1299267>

DOI link to article:

<https://doi.org/10.1080/19315864.2017.1299267>

Date deposited:

21/03/2017

Embargo release date:

22 March 2018

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**A systematic review of the rates of depression in children and adults with high
functioning autism spectrum disorder**

Abstract

Accurate population rates of depression can inform allocation of health resources and service planning, to counter the impact of depression on quality of life and morbidity. A systematic review of the rates of depression in children and adults with ASD and without intellectual disability (HF ASD) was conducted. Nineteen studies met inclusion criteria. Reported rates of depression varied; the reasons for this are discussed including availability of psychometrically valid and reliable measures of depression for people with HF ASD, and heterogeneity of study design. Further examination of the phenomenology of depression in HF ASD linked to the development of psychometrically valid assessment measures would facilitate epidemiological studies, improve clinical case recognition and inform treatments and interventions.

Keywords: depression, autism, HF ASD, systematic review, children, adults, public health

Introduction

Depression is a potential co-existing condition in people with autism spectrum disorder (ASD). Some evidence suggests depression may be a secondary consequence of the social communication difficulties of people with HF ASD, who may experience increased risk of bullying, and pressures to conform to societal ‘norms’ (APA, 2013; Kelly, Garnett, Attwood & Peterson, 2008; Whitehouse, Durkin, Jaquet & Ziatas, 2009). Accurate population rates of depression are important for guiding resource allocation and service development, to minimize negative effects on quality of life and daily living activities, and reduce the risk of suicide (Johansson, Carlbring, Heedman, Paxling, & Andersson, 2013; Stewart, Barnard, Pearson, Hasan & O’Brien, 2006; Williams, O’Conner, Eder & Whitlock, 2009;). However, accurate epidemiological evidence of rates of depression in people with ASD relative to the general population is lacking, and to date there are no population wide studies of prevalence of depression in HF ASD (De la Iglesia & Olivar, 2015; Stewart et al., 2006).

In the United States, the general population prevalence of major depressive disorder during a 12 month period was 6.7% of adults ($n = 9282$), and 10.7% of children (Kessler, Chiu, Demler & Walters, 2005; US Department of Health, NSDUH, 2013). Current rates of depression in the UK were 3.7% of women and 2.5% of men ($n = 6815$) (Spiers et al., 2012). Comparable large scale surveys have not been undertaken with individuals with ASD.

Previous reviews have focused on depression occurrence, presentation, treatment, measurement, risk factors and psychiatric comorbidity in ASD (De la Iglesia & Olivar, 2015; Gillberg & Billstedt, 2000; Mannion & Leader, 2013; Tsai, 2014; Matson & Nebel-Schwalm, 2007; Mazzone, Ruta & Reale, 2012; Shtayermman, 2008; Skokauskas & Gallagher, 2009; Stewart et al., 2006). Previously reported rates of depression have been inconsistent and this may be due to a number of factors. For example, depression has been suggested to be higher in individuals with ASD without intellectual disability (HF ASD) (Mazurek & Kanne, 2010;

Sterling, Dawson, Estes & Greenson, 2008). However, this may be a methodological artefact or due to diagnostic overshadowing. For example, depression may manifest more behaviourally in people with intellectual disability (ID) (Hermans & Evenhuis, 2010; Magnuson & Constantino, 2011).

This review aimed to examine rates of depression in individuals with ASD without ID (HF ASD). IQ potentially confounds rates of depression, and may contribute to a different phenomenology in people with ID. Therefore a separate systematic review is needed to inform clinicians about depression in people with ASD and ID (Magnusen & Constantino, 2011). This review therefore included the following steps:

1. Identification of depression rates in previous studies including adults with HF ASD
2. Assessment of study quality
3. In the context of 1 and 2, make recommendations about future research directions.

Methods

The review was undertaken and results presented in accordance with Preferred Reporting Items for Systematic Reviews and Meta Analyses guidelines, and registered with PROSPERO (registration CRD 42014014340).

Inclusion and exclusion criteria

Published articles reporting empirical research and printed in English, were included if they met the inclusion criteria; resources did not permit translation of articles in other languages. The inclusion and exclusion criteria are presented in Table 1. Where studies included people with IQs > 70 and ≤ 70 , and the data was not presented separately, these were excluded unless at least 85% of participants had average range IQ. Studies reporting current rates of major depressive disorder (MDD) were included in the review. Studies reporting clinical or severe depression were included in the review if scaled scores used were specified as a numerical value. Studies on subclinical depression, dysthymia and lifetime

rates of MDD were not included, facilitating meaningful comparison with general population prevalence rates of depression. Studies were only included if they used a measure of depression, a generic measure with a depression subscale, or assessed depression according to DSM/ICD criteria. For example, studies were excluded if they used the Child Behaviour Checklist (CBCL), which has anxious/ depressed and withdrawn/ depressed subscales, plus has some limitations in specificity for case recognition (Gjevik, Sandstad, Andreassen, Myhre & Sponheim, 2015). No age restrictions were imposed.

Table 1 around here

Information sources

The following electronic databases were searched: MEDLINE, EMBASE, Cinahl, ERIC and PsycINFO. The reference lists of selected articles identified in the search were checked for further publications. Searches were carried out in September 2015, and limited to those published since 1992 when the term Asperger syndrome was defined by WHO; this review therefore covers the periods of DSM-IV and 5, ICD-9 and 10.

The search terms used in the titles field were: *autis**; *asperger**; *depress**; *comorbid**; *mood*; *psych**.

Study selection

Screening of articles identified in the electronic searches was titles and abstracts, then full text and completed by SW. Where inclusion was uncertain, the team discussed the article and reached consensus.

Data extraction

Data were recorded in an extraction form and included: author, country, population, number of participants, age, depression measure used, IQ, study outcomes and study findings.

Risk of bias

Within study bias was assessed using criteria adapted from validated tools (Hoy et al., 2012; Munn, Moola, Riitano & Lisy, 2014) (see Table 2), with the aim of highlighting characteristics with the potential to over or underestimate depression rates (Higgins & Green, 2011). Bias was assessed independently by a second reviewer on 20% of the papers to check coding reliability; agreement was 79%. Coding for the measurement of bias was discussed with the wider team, and consensus was reached.

Table 2 around here

Results

Nineteen studies met the inclusion criteria (Figure 1); data extracted on the characteristics of studies are shown in Table 3. No articles were excluded on grounds of bias. Given the considerable heterogeneity in study methodology, it was concluded that articles could not realistically be combined for a meta-analysis to show pooled rates of depression, therefore a narrative synthesis was used (The Joanna Briggs Institute, 2014).

Figure 1. Summary of the search selection process

Sample characteristics

Participants were predominately male. Thirteen studies included children and young adults (<21 years), and in six studies participants were adolescents and adults (age 16 years and above).

Geographical location

Six studies were from the United States (USA). The remainder were from: the United Kingdom (UK) (4), Australia (2), Sweden (2), Turkey (1), Finland (1), the Netherlands (1); one study included data from both France and the UK; and one from both the USA and Canada.

Design

All studies were cross-sectional or case control apart from four prospective studies (Cederlund et al 2010; Gillberg et al 2015; Mukkades & Fateh 2010; Mattila et al 2010) and two using retrospective design (Gadow et al, 2005; Russell et al, 2015). Participants were recruited from clinical settings (11 studies), ASD support or community groups (4 studies) and mixed community/ clinical settings (4).

Study topics of investigation

The focus of the studies included: examining psychiatric comorbidity (12 studies), psychosocial function (4), self and informant report (2) and profiles of depression (1).

Table 3 around here

Risk of bias within studies

The difference in design between studies that may have contributed to variations in reported rates of depression, are shown in Table 4 and include the following: the majority of studies recruited small numbers of participants (all fewer than 71), with the exception of Russell et al. (2015) ($n = 474$), Salazar et al. (2015) ($n = 101$), and Gadow et al. (2005) ($n = 284$). A diagnosis of HF ASD was confirmed during the majority of studies, and so risk of

bias relating to this was low. Twelve studies had some missing detail regarding participants' characteristics (e.g. ethnicity, use of medication), and four studies had missing detail on the recruitment setting (which could have been useful to support generalisability). In four studies IQ was not measured contemporaneously or was not reported (e.g. with participants described as 'high functioning').

Three studies (Bitsika & Sharpley, 2015; Gadow et al, 2005; Mazefsy et al, 2011) used measures that have some psychometric evidence for their use with people with ASD, including the Autism Comorbidity Interview-Present and Lifetime Version (ACI-PL: Leyfer et al., 2006), the Child and Adolescent Symptom Inventory (CASI: Gadow & Sprafkin, 2010), and the Child Symptom Inventory-4 (CSI-4: Gadow & Sprafkin, 2002). These are generic measures with a depression subscale. Otherwise, studies used measures of depression psychometrically validated in the general population, where evidence of psychometric properties in ASD populations was limited or missing.

Table 4 around here

Measures of depression used

In addition to diagnosis according to ICD-10 criteria the following measures of depression were used.

Informant report and diagnostic interview

Structured Clinical Interview for DSM-IV (SCID) and Structured Clinical Interview for DSM-IV Childhood Disorders (Kid-SCID). The SCID (Spitzer et al, 1992) and Kid-SCID (Hien et al, 1994) are established diagnostic interviews administered to an individual or child and their parent or carer. Based on DSM-IV criteria their purpose is to help clinicians make a psychiatric diagnosis across a range of conditions including depression.

Schedule for Affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version (KSADS-PL). The KSADS-PL (Kaufman et al., 1997) is a psychometrically established semi-structured clinical interview for children. Developed from DSM-IV, its purpose is diagnosis of current or lifetime psychiatric disorders, via child or parent report.

Isle of Wight semi structured interview (IOW). The IOW (Institute of Psychiatry) is a subject and informant psychiatric interview exploring functioning and behaviour.

Children's Interview for Psychiatric Symptoms (P-ChIPS). The P-ChIPS (Weller, Weller, Teare & Fristad, 1999) is a one-hour structured psychiatric interview for parents, and which has some psychometric evidence for children with ASD (Witwer, Lecavalier & Norris, 2012).

Child Symptom Inventory-4 (CSI-4). The CSI-4 (Gadow & Sprafkin, 2002) is a standardized screening measure which includes a MDD subscale. There are 97 items in the parent, and 77 in the teacher versions. Items are informant rated for frequency and severity of difficulties, and there is evidence of psychometric properties in ASD groups (Gadow, DeVincent & Schneider, 2008).

Preschool Age Psychiatric Assessment (PAPA). The PAPA (Egger and Angold, 2004) is a DSM-IV based semi-structured diagnostic interview for parents of toddlers. Interviews are conducted with parents who are asked about symptoms of disorders, including MDD during the last 3 months.

Autism Comorbidity Interview-present and Lifetime (ACI-PL). The ACI-PL (Lainhart et al., 2003) is a semi-structured psychiatric interview about symptoms in the last 3 months, or ever. It was developed from DSM-IV-TR with some evidence of psychometric properties in children with ASD demonstrated (Leyfer et al., 2006).

Mini International Neuropsychiatric Interview (MINI). The MINI (Sheehan et al. 1998) is a short structured psychiatric diagnostic interview for clinical and research purposes based on DSM 1V and ICD 10.

Self-report measures

Child and Adolescent Symptom Inventory-4 (CASI-4). The CASI-4 (Gadow & Sprafkin, 2010) is a standardised self-report measure corresponding to DSM, in which items are rated 0 (never) to 3 (very often). It has a 10 item MDD subscale. The psychometric properties of the CASI-4 have been explored in children with ASD and found to be good, and ASD norms been published.

Patient Health Questionnaire for Adolescents (PHQ-A). The PHQ-A (Johnson, Harris, Spitzer, & Williams, 2002) is a self-report screening measure with a 15 item MDD section.

Beck Depression Inventory (BDI). The BDI (Beck & Steer, 1996) is a 21 item self-report screening measure of depression symptoms during the previous week. The BDI is standardised, has been used in prevalence studies (Cederlund et al., 2010), and scoring thresholds are as follows: ≤ 10 no depression; 11–14 dysphoria; 15–19 dysphoria/depression; ≥ 20 –28 moderate depression; and ≥ 29 severe depression.

Child Depression Inventory (CDI). The CDI (Kovacs, 1992) is a standardised screening measure of depression symptoms, with 3 response options across 27 items scores of ≥ 19 suggest clinical depression.

Hospital Anxiety and Depression Scale (HADS). The HADS (Snaith & Zigmond, 1994) is a widely used 14 item self-report measure of mood symptoms for medical settings, with much accumulated psychometric evidence.

The measures of depression in the studies reviewed were appropriately used given the ages of study participants. However, the measures developed for the general population could

have introduced some bias, possibly affecting accuracy of reported rates of depression. For example, although the Beck and Child Depression Inventories (BDI and CDI), the SCID, the HADS and the KSADS, have an established evidence base for their psychometric properties in the general population, reliability and validity are not established for individuals with HF ASD. The CSI, the ACI-PL and the CASI-4, do have evidence of reliability and validity in individuals with ASD. However these measures are not depression specific, but rather have a depression subscale, limiting the amount of clinical detail that can be gathered on depression symptoms.

Study Findings: rates of depression

Informant report

Informant report current rates of MDD in children are shown in Table 5. Rates of MDD using generic mental health measures with a depression subscale were between 2.5% and 29%. Rates of MDD calculated using measures with psychometric evidence for ASD groups were lower: including 15.8% on the Autism Co-morbidity Interview (Mazefsky et al., 2011), and between 0% and 6.2% on the Child Symptom Inventory (Gadow et al., 2005).

Self-report

Self-reported rates of depression are shown in Table 6. MDD was 47.1% measured on the CASI, a generic child measure with a depression subscale (Bitsika & Sharpley, 2015). Rates were lower using depression specific screening measures. 29% of children scored above the suggested clinical cut off on the Child Depression Inventory (Vickerstaff et al, 2007), while 35% of adults self-reported rates of depression above the clinical cut point on the Beck Depression Inventory (Crane et al, 2011). However, only 1% of adults scored within the severe range (scoring ≥ 30 on the BDI) (Cederlund et al, 2010), and when the Beck Depression Inventory was used in conjunction with, (the Mini International Neuropsychiatric Interview) only 4% had MDD (Gillberg et al, 2015).

275 *Tables 5 and 6 around here*

276 **Discussion**

277 **Rates of depression identified**

278 Rates of depression in people with HF ASD varied widely across studies, from 1% to
 279 47.1%. Most rates for people with HF ASD were higher than the general population
 280 prevalence rates of 2.5% to 10.7% (NSDUH, 2013; Spiers et al, 2012). However, confidence
 281 in the validity of comparing these rates of MDD in people with HF ASD to general
 282 population prevalence rates, is compromised by a number of factors related to
 283 methodological aspects of the studies.

284 **Methodological aspects of the studies**

285 Only three studies in the review used measures with some psychometric validity for
 286 people with HF ASD (the ACI-PL, CSI and the CASI). There is therefore increased
 287 confidence in the validity of their reported rates of MDD from studies using these measures
 288 (between 15.8% and 47%) (Bitsika & Sharpley, 2015; Mazefsky et al., 2011). Nevertheless,
 289 these measures are not depression specific, but rather are generic with a depression subscale.
 290 This may influence reported rates for example, the generic Child Behaviour Checklist
 291 (CBCL) has some limitations in case recognition, and rates of depression do vary depending
 292 on the assessment measures used (Gjevik et al., 2015; Reijnders, Ehrt, Weber, Aarsland &
 293 Leentjens et al., 2008). The remaining studies measured depression using assessments and
 294 severity thresholds based on general population norms, which are not necessarily valid for
 295 people with HF ASD (Magnuson & Constantino, 2011). Measures of depression developed
 296 for the general population may not accurately capture the presentation of depression in HF
 297 ASD, and evidence of psychometric properties with people with ASD was often not available
 298 (Stewart et al., 2006).

The seemingly high rates of depression in some of the studies reviewed may also result from the relatively small number of participants and select samples used. This is in contrast to the large scale, and demographically representative epidemiological studies on which general population prevalence rates of depression are based. Where studies recruit participants from clinical services (as the studies reviewed predominately did), levels of co-existing conditions are expected to be higher compared to those from community settings (Reijnders et al., 2008). Similarly, medication and comorbidities including physical conditions are confounders with the potential to affect reported rates of depression, but were not always described in studies.

Clinical Implications

Knowledge of the rates of depression in people with HF ASD facilitates clinicians, managers and commissioners planning services and allocating resources appropriately. UK National Institute for Health and Care Excellence (NICE) (2009) guidance advocates the use of validated measures for assessment and evaluation of depression interventions. This is currently difficult to implement for people with HF ASD, given the lack of measures of depression psychometrically validated for this group. This may mean clinicians find case recognition and proving treatment effectiveness difficult (Geurts, Stek & Comijs, 2016; Rosbrook & Whittingham, 2010). Further work developing a conceptualisation of depression specifically in relation to people with ASD, would facilitate deeper understanding of specific difficulties and the tailoring of treatment interventions for best support.

Strengths and limitations of the review

We think this is the first systematic review to investigate rates of depression in people with HF ASD. The review adds to existing knowledge by highlighting issues which may influence the magnitude of reported rates in research and clinical settings.

ASD and ID often co-exist, and it is debated whether depression may be relatively high in people with ID, due to social circumstances and being less responsive to treatment (APA, 2013; Cooper, Smiley, Morrison, Williamson & Allan, 2007; Jahoda et al., 2015; Tsakanikos et al., 2006). Therefore one limitation of the review is that studies reporting rates of depression in people with ID were excluded, so the findings will not necessarily generalize to individuals with ASD and ID.

For this review the risk of bias was assessed using a measure that was adapted from validated tools. This adaptation may have compromised the reliability and validity of bias assessments.

Recommendations for Future Research

Prevalence studies of depression across national population samples of people with ASD are a future research priority. Systematic epidemiological surveys of individuals with ASD are rare, but feasible given a large and representative enough sample. For example, Brugha et al., (2011) examined the prevalence of ASD across a sample of 7461 community adults, though information about mental health conditions were not available, and it would be ideal to include a measure of depression in a such a future study. Autism research registry databases are more able to yield population estimates of depression than small clinical samples, or those derived from one geographical area (Baird et al., 2006; Brugha et al., 2011). Fewer adult studies were found reflecting the need for research beyond childhood (Magiati, Tay & Howlin, 2014). Consideration of the confounding effects of any medication would be important in future studies.

Consolidation of findings to date on phenomenology and correlates of depression in people with HF ASD, would inform development of reliable and valid depression diagnostic and screening measures. Studies have found particular items on the BDI endorsed in ASD groups e.g. guilt, though some general population indicators may be less useful, for example

asking about social withdrawal given the overlap with ASD characteristics (Gotham, Unruh & Lord, 2014; Stewart et al, 2006). Further exploration of the relationship between depression and cognitive style e.g. a bias towards internal attributions, or less positive appraisal would inform such developments (Barnhill & Myles, 2001; Happe & Frith, 2006). Further exploration of the interaction between depression, core ASD characteristics and IQ, would facilitate case recognition and treatment planning in people with ID and ASD.

In conclusion, rates of depression identified in studies reviewed varied widely. However, the rates should be interpreted cautiously given studies mainly recruited from clinical groups, had small numbers of participants and, given the limited choice of measures psychometrically validated for people with ASD, mainly used measures of depression developed for typically developing groups. Epidemiological studies of depression in ASD could inform service providers and influence decisions on resource allocation. Measures of depression psychometrically validated for people with ASD would be important for these studies, along with accurate case recognition and evaluation of treatment interventions.

The authors have no conflicts of interest to declare.

Acknowledgements

We are grateful to Northumberland Tyne and Wear NHS Foundation Trust for funding this systematic review. We are also grateful to the UK autism research charity Autistica for funding Sarah Wigham's current post.

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Table 1. Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Population	Individuals of all ages with HF ASD and without intellectual disability (FSIQ $\geq$ 70)	FSIQ < 70
Context	Clinical and community	None
Condition	Current major depressive disorder; severe or clinical depression with specified thresholds.	Non-specific affective disorder; subclinical depression/dysthymia. Lifetime depression. No actual thresholds described in the paper.
Design	Empirical group studies	Case studies, case series, reviews
Measure	Specific measures of depression; generic measures with a depression subscale; ICD or DSM	Studies measuring presence of depression with one question e.g. ‘has anyone ever told you that you have/ your child has depression?’

Table 2. Bias rating chart for studies selected for the review

1. Diagnosis of HF ASD

1. A diagnosis of HF ASD was made prior to the study – no details given on method; or a different test used to those listed below (see 3)
2. Individuals were recruited from an HF ASD research database. A diagnosis of HF ASD was made prior to the study using the methods below.
3. A diagnosis of HF ASD was confirmed at the time of the study by standardised test including; or by a psychologist or psychiatrist and DSM or ICD.

2. Assessment of depression

1. Non standardised
2. Depression subscale within a standardised generic measure
3. Standardised depression specific assessment or clinical interview; or diagnosis of depression according to DSM or ICD by psychiatrist or psychologist

3. Clear description of participants

1. Key demographic information missing.
2. Some descriptive characteristics included; or reference to where further details can be found is provided
3. Key characteristics described including: mean age, age range, gender, comorbidity, medication, ethnicity

4. Description of recruitment pool provided

1. Recruitment pool is not described.
2. Some detail provided
3. Recruitment pool described including: geographical area, method of referral (e.g. self, database), setting (e.g. clinic or school)

5. Reliability and validity of depression outcome measure in HF ASD populations

1. No psychometric properties reported for HF ASD
 2. Some evidence of reliability and validity
 3. The measure is standardised for HF ASD populations
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6. Measure of IQ

1. None give
 2. IQ given or e.g. described as all being >70 or having Asperger
 3. IQ measured during study (using e.g. Wechsler Adult Intelligence Scale (WAIS), Wechsler Intelligence Scale for Children (WISC), Stanford-Binet)
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Table 3. Characteristics of included studies

Author	Country	Population	ASD N (male)	Age (years) Mean (SD); range	Mean FSIQ (SD); range	Medication	Outcomes related to depression
Green, Gilchrist, Burton & Cox (2000)	UK	Clinical referrals	20 (20)	13.75 (11–19)	92.15 (17.7); 71-141	10%	Psychosocial functioning
Hill, Berthoz & Frith (2004)	France and UK	Support groups/ community centres	27 (15)	35.07 (12.26); 16-63	HF ASD	NR	Emotion processing
Gadow, DeVincent, Pomeroy & Azizian (2005)	USA	Developmental disability clinic	284 (242)	8.3 (1.8) 6-12	92(22.2)	38%	Psychiatric comorbidity
Vickerstaff, Heriot, Wong, Lopes & Dossetor (2007)	Australia	Social skills training	22 (19)	11.86 (1.65) 7-13	105.41 (15.34); 82–141	NR	Social skills
Shtayermman (2008)	USA	Autism Websites; previous research participants	10 (9)	19.7 (3)	Asperger	89%	Suicidal ideation; comorbidity
Cederlund, Hagberg & Gillberg (2010)	Sweden	Neuropsychiatric clinic	71 (71)	21.8 (4.6) 16–36	103.8 (15.2)	18%	Informant agreement
Mattila et al. (2010)	Finland	Community & clinical	50 (38)	12.7 (1.5); 9–16	>75	NR	Psychiatric comorbidity
Mukkades & Fateh (2010)	Turkey	Psychiatric clinic	37 (32)	10.9 (4.5) 6-20	116 (14) 90-139	NR	Psychiatric comorbidity
Witwer & Lecavalier (2010)	USA	University and psychiatry clinics; previous research participants, ASD groups	61 (50)	11.2 (3.8); 6–17	>70 (<i>n</i> = 22)	5% - 61%	Psychiatric comorbidity
Crane, Goddard & Pring (2011)	UK	National Autistic Society. Support groups / web pages	28 (14)	41.57 (16.49)	117.18 (13.47)	NR	Autobiographical memory
Mazefsy, Kao & Oswald (2011)	USA	Word of mouth /fliers in developmental disorder clinic	38 (31)	12(2) 10-17	105(17); 71-144	42%	Self-report measures

Joshi et al (2013)	USA	ASD clinic	63 (41)	29 (11); 18-63	104.4 (17.3); 97% > 70	60%	Psychiatric comorbidity
van Steensel, Bögels, & de Bruin (2013)	Netherlands	Outpatient mental health centre	40 (36)	11.10 (2.82); 8–18	88%>70	NR	Psychiatric comorbidity
Hepburn, Stern, Blakeley-Smith, Kimel & Reaven (2014)	USA	Participants in a CBT study	42 (34)	10.9 (1.8); 8-14	98.4 (15) 63-129	NR	Psychiatric comorbidity
Bitsika & Sharpley (2015)	Australia	Parent support group; schools	70 (70)	10.9 (3.4); 8-18	FSIQ: 96.21 (14.23)	No anti-depressants	Prevalence, severity and symptom profiles
Gillberg, Helles, Billstedt & Gillberg, (2015)	Sweden	Neuropsychiatric clinic	50 (50)	30.2 (5.0); 23–43	FSIQ: 107.6	NR	Psychiatric disorders 20 years after ASD diagnosis
Orinstein et al. (2015)	USA and Canada	Multiple hospital and university sites	42 (38)	13.9 (2.7); 8-20	VIQ: 105.5 (14.7); 81–142	NR	Psychiatric comorbidity
Russell et al. (2015)	UK	ASD clinic	474 (372)	30.59 (11.18)	Excluded those with suspected ID	NR	Psychiatric comorbidity
Salazar et al. (2015)	UK	Primary care and ASD support group	101 (57)	6.7 (1); 4-9	>70 (<i>n</i> =44)	NR	Psychiatric comorbidity

NR: not reported

Table 4. Bias within studies

Article	Diagnosis of ASD	Depression measure	Description of participants	Description of recruitment pool	Reliability/ validity of depression measure in ASD	Measure of IQ
Green et al. (2000)						
Hill et al. (2004)						
Gadow et al. (2005)						
Vickerstaff et al. (2007)						
Shtayermman (2008)						
Cederlund et al. (2010)						
Mattila et al. (2010)						
Mukkades et al. (2010)						
Witwer et al. (2010)						
Crane et al. (2011)						
Mazefsky et al. (2011)						
Joshi et al (2013)						
van Steensel et al. (2013)						
Hepburn et al. (2014)						
Bitsika & Sharpley (2015)						
Gillberg et al. (2015)						
Orinstein et al. (2015)						
Russell et al. (2015)						
Salazar et al. (2015)						

Low risk of bias	Medium risk of bias	High risk of bias	
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Table 5. Study findings: diagnostic interview or informant reported current rates of depression and measure used (parent reported unless stated otherwise)

Author	Age group Child/Adult (C/A)	Rates of major depressive disorder	Measure
Generic measures with a depression subscale			
Joshi et al (2013)	A	31% (self and parent/ guardian report)	Structured Clinical Interview for DSM-IV (SCID)
Van Steensel et al. (2013)	C	2.5%	Structured Clinical Interview for DSM-IV Childhood Disorders (KID SCID)
Mattilla et al. (2010)	C	6%	Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (KSADS-PL)
Mukkades et al. 2010	C	29%	
Hepburn et al. (2014)	C	14.3%	
Orinstein et al. (2015)	C	7%	
Green et al. (2000)	C	5%	Isle of Wight Semi structured Interview
Gadow et al. (2005)	C	Parent rated: males (6.2%) females (2.4%) Teacher rated: males (2.9%) females (0%)	Child Symptom Inventory-4 (CSI-4)
Witwer et al. (2010)	C	22.7%	Children's Interview for Psychiatric Symptoms (P-ChIPS)
Salazar et al. (2015)	C	18.8 %	Preschool Age Psychiatric Assessment (PAPA)
Measures of ASD Co-morbidity			
Mazefsky et al. (2011)	C	15.8%	Autism Comorbidity Interview-present and Lifetime (ACI-PL)

Table 6. Study findings: self-reported current rates of depression and measure used

Author	Age group Child/Adult (C/A)	Clinical depression	MDD	Measure
Generic measures with a depression subscale				
Bitsika & Sharpley (2015)	C		47.1%	Child and Adolescent Symptoms Inventory (CASI)
Russell et al (2015)	A	15.8% depressive episode		Hospital Anxiety and Depression Scale (and ICD 10)
Shtayermman (2008)	C		20%	Patient Health Questionnaire for Adolescents
Standardised depression specific measures				Beck Depression Inventory (BDI)
Hill et al. (2004)	A	22.2% (scored ≥ 20)		
Cederlund et al. (2010)	A	1% severe depression (scored ≥ 30)		
Crane et al. (2011)	A	35% (scored ≥ 20)		
Gillberg et al. (2015)	A		4%	BDI in combination with Mini International Neuropsychiatric Interview
Vickerstaff et al. (2007)	C	29% (scored ≥ 19)		Child Depression Inventory