Psychological interventions for depression in children and young people with an intellectual disability and/or autism: A systematic review

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Abstract

Background

Children and young people with intellectual disability and/or Autism Spectrum Disorder (autism) experience higher rates of mental health problems, including depression, than their typically developing peers. While international guidelines suggest psychological therapies as first line intervention for children and young people, there is limited research evidence for psychological therapy for depression in children and young people with intellectual disability and/or autism.

Aims

To evaluate the current evidence base for psychological interventions for depression in children and young people with an intellectual disability and/or autism, and examine the experiences of children and young people with intellectual disability and/or autism, their families, and therapists, in receiving and delivering psychological treatment for depression.

Method

Databases were searched up to 30 April 2020 using pre-defined search terms and criteria. Articles were independently screened and assessed for risk of bias. Data were synthesised and reported in a narrative review format.

Results

A total of 10 studies met inclusion criteria. Four identified studies were clinical case reports and six were quasi-experimental or experimental studies. All studies were assessed as being of moderate or high risk of bias. Participants with intellectual disability were included in four studies. There was limited data on the experiences of young people, their families, or therapists in receiving or delivering psychological treatment for depression.

Conclusion

Well-designed randomised controlled trials are critical to develop an evidence base for psychological treatment for young people with intellectual disability and/or autism with depression. Future research should evaluate young people, family, and therapist experience of treatment.

Introduction

Mental health disorders have been found to be three to five times more prevalent in children and adolescents with intellectual disability compared to their typically developing peers[1, 2]. Consistent with this general mental health inequity, adolescents with intellectual disability, Autism Spectrum Disorder (hereafter referred to as autism), or both conditions are at higher risk for depression than their same-age peers[1, 3-6]. Specifically, children and young people with intellectual disability are 1.7 times more likely to experience depression compared to other children[5]. Although young people with autism have demonstrated higher rates of depression than typically developing children and adolescents, reported rates vary considerably[6].

Treatment for mental health problems in people with intellectual disability has historically relied on pharmacological approaches[7, 8]. However, international guidelines and recommendations suggest that first line treatments for depression in children and young people should include psychological therapies[9, 10]. There is some support for the use of cognitive behavioural therapy for depression in adults with mild-moderate intellectual disability[7] but a lack of research focus on children and adolescents. Research evidence for the psychological treatment of depression in children and adolescents with autism is available but limited, with the evidence to-date focused on the treatment of anxiety or disruptive behaviours[11, 12]. The current study, therefore, had the following review questions: (1) What is the current evidence base for psychological interventions for depression in children and young people with an intellectual disability and/or autism?, (2) What are the experiences of children and young people with intellectual disability and/or autism and their family members of psychological intervention for depression?, and (3) What are the experiences of therapists delivering psychological intervention for depression to children and young people with intellectual disability and/or autism?

Method

The review protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO, registration number CRD42019145495) and can be accessed here: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019145495. The review was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13].

Search strategy

PsycINFO, MEDLINE, Embase via Elsevier, CINAHLPlus, Social Sciences Index and Sciences Index via Web of Science, and Scopus databases were searched by two authors (L.A.C and K.P.) on 1st May 2020 for articles published from inception to 30th April 2020. Searches were conducted using keywords identified for each domain (see Table 1 for an example search string) and limited to articles written in English. Hand searching of reference lists and citation searching of included studies were also conducted to identify potential additional articles.

[INSERT TABLE 1 ABOUT HERE]

Inclusion/exclusion criteria

Studies were included if they met the following criteria:

a) Study design: pre-post single group designs, case series, clinical case reports, single case experimental designs, and qualitative studies. Studies with a comparison group, control group, or no control group were all included. Observational and case-control studies involving no treatment were excluded.

b) Participants: children, adolescents, or young people up to age 21 years with an intellectual disability (including borderline intellectual disability) and/or autism. Studies were included if the entire sample included the relevant population, or if outcomes were reported separately for the relevant population. Studies that involved young people up to the age of 25 years were included if 75% of the sample was under 21 years.

c) Participant diagnosis: either (i) major depressive disorder as diagnosed by standardised criteria (e.g. the Diagnostic and Statistical Manual for Mental Disorders, International Classification of Diseases, Diagnostic Manual-Intellectual Disability), (ii) dysthymia or minor depression as diagnosed by standardised criteria, or (iii) depressive status, as defined by meeting cut-offs on a standardised depression screening questionnaire (e.g., Children's Depression Inventory[14], Beck Depression Inventory[15], Glasgow Depression Scale[16]).

d) Treatment or intervention: any psychological or psychosocial intervention (e.g. life skills training, lifestyle intervention) with the aim of treating depression or depressive symptoms. Pharmacological or medical treatments, transcranial magnetic stimulation, complementary, and alternative therapies and treatments were excluded.

Screening

First stage title and abstract screening was undertaken by two authors (L.A.C. and K.P.) to identify any articles that were clearly not relevant to the review, with a randomly selected 20% screened by both authors to determine interrater reliability. Agreement was 99.1% (kappa 0.940). Full text review was independently undertaken by the same two authors with any conflicts of inclusion/exclusion resolved through discussion, and consultation with additional authors (K.M.G. and G.A.M.) where necessary (n = 1).

Data extraction

Data were extracted from each article and coded for: (a) study information (type of study, country of publication, year of publication), (b) participant information (age, gender, intellectual disability/autism diagnosis), (c) assessment of depression, (d) treatment information (type of treatment/intervention, length of treatment, length of follow-up), and (e) study outcomes.

Risk of bias

Risk of bias assessments were conducted by a panel of four authors (L.A.C., K.P., G.A.M., and K.M.G.). Assessments of controlled and uncontrolled trials were conducted using pre-developed proformas based on the Cochrane risk of bias tool and the Newcastle Ottawa Scale[17, 18]. These proformas have been used previously in large international systematic reviews e.g. Blackmore *et al.* [19]. Single case studies and case series were appraised using criteria described by Horner *et al.* [20]. Each study was assessed overall as being of low, moderate, or high risk of bias.

Results

A total of 13,936 records were retrieved in the search. After removal of duplicates, 9,343 records remained for abstract and title screening. A further 9,231 records were excluded, leaving 114 for full text review. No additional articles were identified through reference lists of included studies or forward citation searching. A total of 10 studies met inclusion criteria (Figure 1).

Summary data for all included studies, including sample description, assessment of depression, description of treatment and treatment duration, outcome measures, and study results related to the impact of treatment on depression or depressive symptoms, can be viewed in Tables 2 and 3.

Research Question 1: What is the evidence base for psychological interventions for depression for children and young people with intellectual disability and/or autism?

Of the 10 included studies, four were clinical case reports[21-24], and the remaining six were experimental or quasi-experimental designs, including: one multiple baseline design study[25], two uncontrolled group design trials[26, 27], and three controlled group design trials[28-30].

Clinical case reports

Across the four clinical case reports, n = 5 participants were described (n = 3 male, ages ranging from 12 – 18 years). One clinical case report used a combination of psychotherapy and behavioural training to target depressive symptoms in a 17 year old female with a mild intellectual disability[21]. Three clinical case reports used adapted versions of cognitive behavioural therapy (CBT) with a 12 year old male[22], a 17 year old female[23], and two males aged 17 and 18 years old[24], all with Asperger Syndrome.

Three clinical case reports utilising CBT adapted their programme for young people with autism. Greig and MacKay [22] highlight that their CBT programme, *The Homunculi*, involves the creation of characters to help the individual to visualise various processes and behaviours. Loades [23] reported that the CBT programme was adapted for their participant with Asperger Syndrome, but did not describe what these adaptations involved. Selvapandiyan [24] implemented *pragmatic CBT* [31], described by the author as being designed to target the social communication difficulties evident in Asperger Syndrome. The duration of treatment varied across the clinical case reports, ranging from 15 individual sessions to eight months.

Behavioural training was more intensive, with sessions being undertaken almost daily, while CBT was undertaken weekly. Behavioural training in these instances involved behavioural modification of identified behaviours, including compliance, lack of interest, oppositional behaviours, and self-harm[21].

Three clinical case reports relied on questionnaires to assess change in depressive symptoms over the course of treatment[22-24]. One clinical case report used the depression scale of the Briere Trauma Scales (self-report)[32] pre- and post-treatment[22]. Another clinical case report used the Revised Children's Anxiety and Depression Scales (self-report)[33] at pre-treatment and throughout the course of treatment at sessions 6, 12 and 20 weeks[23]. The remaining clinical case report used the Hamilton Depression Rating Scale (HDRS)[34], rated by the clinician at the end of each treatment session. The study reported that progress was monitored over two months post treatment, however, the HDRS scores at follow-up were not reported[24].

All clinical case reports reported an improvement in depressive symptoms following the intervention, whether that was a decrease in problem behaviours[21], or a reduction in depressive scores on screening measures[22-24]. Maintenance of improvements were reported for the one clinical case report that included longer term follow-up[24]. Two of the clinical case reports reported the use of medication throughout the study period; one introduced medication (olanzapine and chlorpromazine) at the beginning of the treatment period[21], and the other reported that the client had been prescribed medication 10 weeks prior to the commencement of the CBT intervention, with a stable dose maintained throughout the intervention programme[23]. Neither study considered the potential impact of the medication when reporting treatment outcomes.

Experimental and quasi-experimental designs

Multiple-baseline design

One study employed an experimental multiple baseline across behaviours design with a 10 year old male with borderline intellectual disability (WISC-R IQ = 79)[25]. The intervention took place on an inpatient unit, using behavioural treatment to target behaviours deemed to be reflective of depression in the participant. This included "inappropriate body position", lack of eye contact, poor speech quality, and bland affect. Behavioural intervention involved specific skill training incorporating instruction, modelling, role-playing, and feedback of a more appropriate response in place of the inappropriate behaviour, over 20 minute sessions each day. Baseline was established over eight days for all behaviours, followed by introduction of the behavioural treatment for the first two behaviours simultaneously (six sessions), the third behaviour (five sessions), and the final behaviour (nine sessions). Frequency of target behaviours was recorded during each session, with reductions in each target behaviour observed following the introduction of the intervention, and maintenance improvements at a 12 week follow-up. While the study involved administration of a number of depression screening tools during their initial diagnostic process, these were not used to assess post-treatment outcomes.

Uncontrolled trials

Two studies were uncontrolled trials. One study was a case series with a pre-post design, reporting on existing patients seen in an inpatient setting[26]. This study identified patients (N = 31) with an intellectual disability aged three to 16 years, diagnosed with depression according to DSM-III[35]. Gender was not reported. Treatment was described as the standard treatment used in the clinical setting. Individual psychotherapy was the primary treatment utilised, although frequency and duration of therapy were not specified. An unspecified number of participants were prescribed medication when it was clear the psychotherapy alone was not effective. The timing of the introduction of medication was not reported, and the impact was not considered in the reporting of outcomes. Outcomes were reported after approximately six

months of treatment before discharge from the facility. Eighty-seven percent of patients (n=27) were considered to have shown a clear clinical improvement by the time of discharge. However, a definition of clinical improvement was not reported, nor was the effect of medication.

The second pre-post design was an uncontrolled trial involving participants with autism and no co-occurring intellectual disability (n = 39, 82% male, mean age 10 years) to receive a structured intervention[27]. Participants in this study undertook a 12-week group CBT programme targeting social competence skills. Depressive symptoms were measured at the beginning and at the end of the treatment programme using the depression subscale score of the Behavior Assessment System for Children (BASC-II)[36], a parent-report measure. No change was seen in depressive symptoms from the beginning to end of treatment, although improvements were seen in aggression, emotion control, and autism symptoms.

Controlled trials

Three studies were controlled trials. One trial evaluated the impact of a lifestyle intervention, a physical exercise programme, specifically Assisted Cycling Therapy (ACT), in a group of young people with Down Syndrome (n = 49. 59% male, mean age = 18.3 years (SD = 4.1 years))[29]. ACT involved the use of a mechanical motor attached to a stationary exercise bicycle to increase the individual's cycling rate above their preferred voluntary cycling rate. Participants were counterbalanced to one of two active treatment groups ACT or Voluntary Cycling (VC)), although how the counterbalancing was achieved was not described, nor was it clear whether participants were randomised to each group. A No Cycling (NC) control group was recruited through convenience sampling, recruited through advertising in local communities. There were no group differences at baseline in terms of gender, chronological age, receptive language ability, hours of sport per week, or BMI. However, the ACT group

scored significantly higher on a measure of cognitive planning compared to both the VC and NC groups. Depression symptomatology was measured both pre- and post-treatment using the Children's Depression Inventory (CDI)[14], with greater improvements on CDI scores seen in the ACT group when compared to both the VC and the NC control group at the end of the eight week therapy.

The second controlled trial reported on the impact of a group CBT programme for young people with Asperger Syndrome or autism without intellectual disability (n = 42, 72% male, mean age = 20.6 years (SD = 4.1))[28]. Participants were allocated to either treatment or waitlist control according to alternating order of study enrolment (i.e., pseudo-randomisations). The nine week CBT programme was developed with particular regard to the social difficulties often experienced by young people with autism. Depression was measured by the Depression subscale of the Depression, Anxiety and Stress Scales (DASS)[37] at pre-treatment, post-treatment, and again at three and nine month follow-ups. There was no significant difference between the groups post treatment. However, there was a significant decrease in DASS Depression scores for those participants with scores in the clinical range at pre-treatment. These improvements were maintained at both three and nine month follow-up.

The final controlled study also evaluated a group CBT programme for young people with autism with no intellectual disability (n = 23, 60% male, mean age = 15.75 years (SD = 1.37))[30]. Participants were randomly allocated to either waitlist or control via a computer-generated random sequence programme. The ten week group CBT programme was designed specifically for young people with autism[38]. Depression was measured using both the DASS Depression subscale and the Beck Depression Inventory (BDI-II)[15] at pre-treatment, post-treatment, and at four and 12 week follow-ups. The authors reported no significant change in BDI-II scores from pre- to post- treatment, although a significant decrease was seen in DASS Depression scores for the treatment group.

Research Questions 2 and 3: What are the experiences of young people and their families and treatments for depression? What are the experiences of professionals in delivering treatment for depression?

No studies were identified that had a focus on evaluating the experiences of young people with intellectual disability and/or autism and their families in receiving psychological treatment for depression. Only two of the included studies reporting on treatments for depression also reported on participant experience[22, 30]. Santomauro *et al.* [30] gathered feedback from 15 young people with autism during their final group booster session, as a group discussion. Fourteen out of 15 young people reported enjoying the programme, with the fifteenth participant still recommending the programme for its usefulness. Participants considered the group setting the most beneficial aspect of the CBT programme. Greig and MacKay [22] briefly noted that the participant in their single case study felt that the intervention had worked for him in real life situations.

No studies evaluated the professional or clinician experience of delivering treatment for depression to children and young people with intellectual disability and/or autism.

Risk of bias

Risk of bias was assessed for all studies. No studies were considered to have a low risk of bias. All of the clinical case reports (n = 4) were assessed as high risk of bias[21-24]. Clinical case reports are inherently biased; they have a high risk of publication bias, they are retrospective reports and subject to information bias in that they involve subjective interpretation by the author who is often the treating clinician, outcome assessment measures are often administered by the clinician, and causal relationships and generalisation are not

possible due to the nature of describing treatment outcome for one individual, often leading to overinterpretation of results and treatment effectiveness[39]. In addition to these overarching issues, the included clinical case reports had particular problems with outcome measures, including selecting inappropriate measures, not reporting how scores were calculated, and not reporting on all outcomes as stated.

Of the quasi-experimental and experimental studies, four studies were rated to have a moderate risk of bias, including the multiple baseline design[25, 28-30] and the remaining two rated as high risk of bias (both uncontrolled trials)[26, 27]. Reasons for ratings of moderate and high risk of bias included: no control group, no or poor randomisation when there was a control group, outcome measures administered by the clinician delivering treatment, use of outcome measures with unestablished psychometric properties in intellectual disability and/or autism, and not considering impact of confounding variables (e.g. medication).

[INSERT TABLES 2 AND 3 ABOUT HERE]

Discussion

This systematic search identified ten studies that evaluated psychological treatments for depression in children and young people with intellectual disability and/or autism. However, four of these were clinical case reports with a high risk of bias and thus are unable to directly inform a research evidence base to guide treatment[21-24]. The remaining six studies included four studies with either a single case experimental design[25], an uncontrolled group design[26, 27] or a controlled group design[28-30]. The six experimental/quasi-experimental studies each focused on different treatments, different population groups, used different outcome measures for depression, and were all rated with a moderate or high risk of bias. Therefore, no conclusions can be drawn with any confidence about the suitability or effectiveness of any particular psychological or psychosocial intervention for treating depression in children and

young people with intellectual disability and/or autism. There was also essentially a complete lack of information about the experiences of young people or their families who received psychological intervention for depression, or the therapists who delivered the intervention.

Study design

High quality randomised controlled trials are essential to improve the evidence-base for effectiveness of these interventions. Only one of the three controlled trials employed adequate randomisation strategies[30], with the others allocating participants based on order of enrolment[28], or through counterbalancing, which was not thoroughly described[29]. Future studies should focus on developing well-designed randomised controlled trials to address this important gap in the literature.

In addition to the need for well-designed trials, future research should evaluate existing evidence-based psychological and psychosocial treatments for depression adapted specifically to meet the needs of children and young people with intellectual disability and/or autism. While a range of psychological and psychosocial interventions were identified in this review, only two of the experimental studies reported that the intervention used had been adapted for young people with autism[28, 30]. Importantly, none of the interventions described had been adapted for young people with intellectual disability. Development of new interventions tailored specifically for this population is also important. New interventions should be developed and evaluated through pilot studies, and further trialled in randomised controlled trials. The role of a parent / caregiver as support or facilitator within psychological interventions should also be considered. This approach has been successfully demonstrated in interventions with adults with intellectual disability (for example, Jahoda *et al.* [40, 41]). Particularly important in any adaptation or development of interventions is collaboration with

the key stakeholders: young people with intellectual disability and/or autism, their parents and families, and the therapists delivering the interventions.

Exclusion of intellectual disability

Inclusion of children and young people with intellectual disability was extremely limited. Only four studies included participants with an intellectual disability[21, 25, 26, 29] and six studies included participants with a diagnosis of Asperger Syndrome or autism without co-occurring intellectual disability[22-24, 27, 28, 30]. No studies involved participants with both intellectual disability and autism, consistent with a recent meta-analysis demonstrating selection bias against participants with intellectual disability in autism research[42]. The exclusion of young people with intellectual disability was particularly evident in the controlled trials, with only the physical exercise intervention, involving no cognitive component, including participants with intellectual disability[29]. This is a significant gap in the literature in that we have limited evidence of effective interventions for depression in children with intellectual disability, despite knowledge that rates of mental health problems, in particular, depression, are prevalent in this population.

Outcome measures

Outcome measures of depression and depression symptomatology were inconsistent, and in some cases, not valid measures of depression. While a number of studies used validated measures and screening tools for depression, including the Revised Children's Anxiety and Depression Scale (RCADS) depression subscale[23], the Hamilton Depression Rating Scale[24], the DASS Depression scale[28, 30], the CDI-II[29], and the BDI-II[30], others relied on subjective measurement such as clinical judgement, or changes in behaviour not necessarily indicative of depression. None of the depression measures used were developed or adapted for people with intellectual disability and/or autism. Further, selection of outcome measures was not

suitable in all studies. For example, the DASS is a tool designed for use with a typically developing adult population yet was used with children and young people as young as 13 years in these studies. Use of suitable depression outcome measures is critical for future studies to ensure effectiveness in treating depression presenting in children and young people with intellectual disability and/or autism. Some caregiver-report measures of depressive symptoms in children and young people with intellectual disability already exist, such as the Developmental Behavior Checklist 2[43] and the Anxiety, Depression and Mood Scale[44], and could be used to assess change in depressive symptoms. Some research has used adapted versions of the Children's Depression Inventory[14] for young people with intellectual disability[45, 46]. In addition, adapting existing self-report measures of depression validated for use with adults with intellectual disability, such as the Glasgow Depression Scale[16], for use with children and young people, could be considered in future research.

Strengths and limitations

The current review was conducted with strong methodological rigour, in line with PRISMA guidelines and following a pre-registered protocol. Strengths of this review include the broad definition of psychological and psychosocial therapies used, ensuring all relevant treatments and interventions were identified, the inclusion of all publication types, including theses, and no restrictions on date of publication. Non-English publications were excluded, however two studies were identified from countries without English as a first language. A meta-analysis was not undertaken due to the small number of studies identified, their poor quality and moderate-high risk of bias.

Summary and future directions

This systematic review highlights a number of significant gaps in the literature for treatment of depression for children and young people with intellectual disability and/or autism, in

particular. The lack of well-designed randomised controlled trials was clear, as was the exclusion of young people with intellectual disability. The complete lack of research on psychological interventions for young people with intellectual disability was striking and concerning. Adaptation and development of specifically tailored psychological and psychosocial interventions for depression in children and young people with intellectual disability and/or autism, as well as measures of depression and depressive symptomatology, is an essential next step in the research. Future research should also ensure accurate records of medication are taken and considered when interpreting the effectiveness of a psychological intervention.

Further, evaluating experiences of both receiving treatment for depression (children and parents) and delivering treatment (therapists and professionals) is paramount in ensuring that interventions, both existing, adapted, and newly developed, meet the needs of the end user. Future research should ensure that families and professionals are consulted on the design of interventions and evaluations of their experiences are embedded within any study design.

It is important to note that these findings are not unique to the treatment of depression for children and young people with intellectual disability and/or autism. There is an absence of intervention research of any psychological treatments for any mental health disorder in this population[7]. Further, children and young people with severe intellectual disability are a particularly vulnerable group, and often neglected in research of mental health problems and intervention[47]. As highlighted in a recent systematic review, future research into psychological treatments for depression for children and young people with intellectual disability and/or autism should also be supported by the development of appropriate outcome measures of any mental health symptoms for this population[48].

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574 **Table 1** Search terms

Domain	Search terms
Age group	adolescen* OR teen* OR youth OR child* OR "young person" OR juvenile OR paediatric OR pediatric
Intellectual disability and/or autism spectrum disorder	(mental* AND (handicap* OR retard* OR disab* OR impair* OR defici*)) OR ((learning OR intellect* OR development*) AND (difficult* OR disab* OR impair* OR disorder* OR handicap*)) OR ((Down* OR "Smith-Magenis" OR Rett* OR "Lesch-Nyhan" OR "Prader Willi" OR Angelman OR "Fragile X" OR "Cri-du-chat" OR "Cornelia de Lange" OR "de Lange" OR "Rubenstein-Taybi" OR velocardiofacial) AND syndrome*) OR (moron OR imbecile OR feeble-minded) OR (autis* OR ASD OR Asperger*)
Depression	(depress* AND (symptom* OR disorder OR thought* OR behavi*)) OR ((affective OR mood* OR emotion*) AND (disorder OR symptom* OR disturb*)) OR (depression OR dysthymi* OR melancholy*)
Treatment or intervention	therap* OR treat* OR intervention OR management OR counsel* OR training OR case OR psychotherap*

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Table 2 Clinical Case Reports

Author, Year Country	Sample Size & Description	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
Fernandez *et al*., 2005[21] USA	N = 1 Female 17 years old Mild intellectual disability	Clinical intake interview: Major Depression (DSM-IV[49])	Psychotherapy (weekly) - relaxation exercises, responding empathetically, and assistance with reframing Therapeutic behavioural treatment (25-35 hours per week) - occurred both at school and group home Medication – olanzapine and chlorpromazine introduced at the beginning of treatment. Olanzapine continued throughout treatment, fluoxetine replaced chlorpromazine at 7 months	8 months	Observation of target behaviours: compliance, lack of interest, oppositional behaviours and self-harm. Number of times each behaviour occurred within the observational period was recorded monthly	Psychotherapy - improved coping skills, improvement in ability to express feelings, and improve capacity for self-advocacy Behavioural treatment - decrease in frequency of maladaptive (target) behaviours, recurrence of oppositional behaviours in last 2 months of treatment Improvement in GAF (DSM-IV[49]) score from 25 (beginning of treatment) to 40 (end of treatment)	High

Author, Year Country	Sample Size & Description	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
Greig & MacKay, 2005[22] USA	N = 1 Male 12 years old Asperger Syndrome WISC-III[50] FSIQ = 118	Clinically significant scores on self-report measure: Briere Trauma Scales, depression scale	CBT (The Homunculi) – a meta-cognitive visual aid using development of characters to support the use of tools to improve targeted behaviours, specifically developed by authors for people with autism	15 sessions	Measured post-intervention. Emotional state: anxiety, depression, anger and stress scales of the Briere Trauma Scales[32] Social competence and social skills: assessment by parent and self-report School adjustment: teacher feedback	Emotional state on all scales, including depression, reduced to lower than clinically significant levels and were at the mean for the participant's age group. Improvements in perceived social competence and social skills, although still at lower levels than same-aged peers. Reduction in concerns expressed by teacher about school adaptation.	High
Loades, 2015[23] USA	N = 1 Female 17 years old Asperger Syndrome	Clinically significant score on self-report measure: Revised Children's Anxiety and	CBT for low self-esteem with adaptations made for autism, although what adaptations were made was not	20 sessions	Progress assessments at Session 6, Session 12 and Session 20.	Clinically significant reduction in anxiety and depression at the end of treatment. Depression subscale score just below clinical range at end of treatment.	High

Author, Year Country	Sample Size & Description	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
		Depression Scale (RCADS)[33] (T score 85)	reported (weekly sessions) Medication – antidepressant medication prescribed 10 weeks prior to commencement of therapy and continued throughout		RCADS scores (T scores on depression, overall anxiety, and specific anxiety subscales)		
Selvapandiyan, 2019[24] India	N = 2 Male, 17 years old Male, 18 years old Asperger Syndrome	Clinical interview: Depressive Disorder (ICD-10-DCR[51])	Pragmatic CBT (specifically adapted for Asperger Syndrome to focus on difficulties with social communication [31]) with acceptance and mindfulness techniques (weekly, 60-minute sessions) Medication – both participants had been treated with psychotropic medication for some months	20 weeks	Measured at the end of each session. Additional follow-up period for 2 months post-intervention. Hamilton Depression Rating Scale[34] Social Functioning Questionnaire[52]	Both participants saw a reduction in scores on the Hamilton Depression Rating Scale to below clinically significant levels. Participants remained free from depressive symptoms over the follow-up period. Improvement in scores on Social Functioning Questionnaire at the end of treatment.	High

Author, Year Country	Sample Size & Description	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
			before commencing CBT				

Note: DSM = Diagnostic and Statistical Manual of Mental Disorders; GAF = Global Assessment of Functioning; WISC = Wechsler Intelligence Scale for Children; FSIQ = Full Scale Intelligence Quotient; CBT = cognitive behavioural therapy; ICD-10-DCR = The International Classification of Diseases-10 Classification of Mental and Behavioural Disorders, Diagnostic Criteria for Research

Table 3 Experimental and Quasi Experimental Designs

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
Frame *et al*., 1982[25] USA	N = 1 Male 10 years old Borderline intellectual disability WISC-R[53] FSIQ = 79	NA	NA	NA	Psychiatric interview: Major Depressive Episode (DSM-III[35]) Clinical cut off met on parent-report measures: Children's Depression Inventory[14], Child Behavior Problem Checklist[54], and Bellevue Index of Depression[55]	Behavioural training (20-minute sessions each weekday) - instructions, modelling, role-play, and performance feedback Multiple baseline across behaviours design - 8-day pre-treatment baseline for all behaviours, followed by implementation of behavioural training for each target behaviour (first two behaviours introduced simultaneously, followed by the third behaviour	28 sessions	12-week follow-up after completion of treatment Target behaviours: inappropriate body position, lack of eye contact, poor speech quality, bland affect Frequency of target behaviours recorded during each baseline and intervention session	Each behaviour improved (i.e. less frequent occurrence) from baseline to when the intervention was introduced. Improvements in behaviour continued to be evident at 12-week follow-up (i.e. frequency of behaviours were still below the baseline rate).	Moderate

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
						and finally the last behaviour)				
Dosen, 1984[26] The Netherlands	N = 31 Age 3 – 16 years Gender not reported Intellectual disability 32% IQ 30-50 48% IQ 50-80 20% IQ 80-90	NA	NA	NA	Evaluation of symptoms: Depression (DSM-III[35])	Individual psychotherapy based on relationship therapy (frequency not reported; not reported whether adapted for people with intellectual disability) Medication – tricyclic antidepressants prescribed for children who had little to no success with psychotherapy	Approximately 6 months	Clinical judgement on change in symptoms	87% showed clear clinical improvement on depressive symptoms, impact of medication not reported	High
Habayeb *et al*., 2017[27] USA	N = 39 82.1% male	NA	NA	NA	Depression subscale score of BASC-2[36]:	Resilience Builder Program. Manualised	12 weeks	Measured at the end of the treatment programme.	Significant improvement in self-reported	High

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
	M_{age} = 10 years (SD = 1.6 years) Autism without intellectual disability				overall sample mean clinically significant T-score	group CBT targeting social competence skills through a broader resilience framework (not an autism specific intervention). 12x one-hour sessions weekly, with 4-6 children in each group.		Internalising and externalising symptoms BASC-2[36], parent-report Autism related social and communication impairments (Social Responsiveness Scale[56], parent-report; Social Communication Questionnaire[57], parent-report) Positive and negative emotions and emotion control (How I Feel Questionnaire[58], self-report)	emotion control following treatment. No changes in depressive symptoms (measured by the BASC-2 Depression subscale).	

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
McGillivray & Evert, 2014[28] Australia	N = 42 72% male M_{age} = 20.6 years (SD = 4.1 years), range 15-25 years Asperger Syndrome (72%) and High Functioning Autism (28%)	N = 26 73.1% male M_{age} = 20.27 years (SD = 4.39 years)	Waitlist control: N = 16 81.3% male M_{age} = 20.50 years (SD = 3.40 years)	Allocation to group according to alternating order of enrolment	Scores above normal range on any of the following: DASS[37], ATQ[59], ASSQ[60]	Group CBT: "Think well, feel well and be well", developed to address the social difficulties experienced by young people with autism Weekly, 2-hour sessions	9 weeks	Measured post treatment, and at 3- and 9-month follow-ups. DASS[37] Total, Depression, Anxiety, and Stress subscales ATQ[59] ASSQ[60]	Significant decrease in DASS Total and Depression subscale scores from pre- to pos-treatment, regardless of allocation to treatment or control group For participants with DASS Depression scores above the normal range, a significant decrease on DASS Depression scores was found between pre- and post-treatment for	Moderate

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
									those in the treatment group No differences in DASS Depression scores at 3 or 9 month follow-up DASS Depression scores at 9 month follow-up were significantly lower than at pre-treatment	
Ringenbach *et al*., 2019[29] USA	N = 49 59% male M_{age} = 18.3 years (SD = 4.1 years) Down Syndrome	Assisted Cycling Therapy (ACT) group: N = 10 70% male	No cycling (NC) control: N = 11 45% male	Counterbalanced to ACT or VC groups NC group made of convenience sample	Depressive symptoms assessed by Children's Depression Inventory (CDI)[14]	Cycling intervention, 3 x 30-minute sessions per week	8 weeks	Measured pre- and post-treatment VABS[61] CDI[14]	Participants in the ACT group had greater improvements on CDI scores when compared to the VC and	Moderate

Author, Year Country	Sample Size & Description			Randomisation	Assessment of Depression	Treatment	Duration of Treatment	Outcome Measures	Results	Risk of Bias
	Total sample	Treatment group	Control group							
	Mean mental age (PPV) = 5.5 years	Voluntary Cycling (VC) group: N = 8 100% male						Physical Activity Self-Efficacy[62]	NC groups. The VC and NC groups did not differ.	
Santomauro *et al*., 2016[30] Australia	N = 23 60% male M_{age} = 15.75 years (SD = 1.37 years), range 13 – 18 years Autism Spectrum Disorder VIQ > 85	N = 11 M_{age} = 16 years (SD = 1.33 years)	Waitlist control: N = 12 M_{age} = 15.50 years (SD = 1.43 years)	Allocation via computer-generated random sequence program	Score 14 or higher on BDI-II[15]	Group CBT: "Exploring Depression: cognitive behavior therapy to understand and cope with depression" [38], designed for individuals with Asperger Syndrome 11 x 1-hour sessions 3-4 participants per group	10 weeks	Measured pre- and post-treatment, and 4 and 12 weeks post treatment BDI-II[15] DASS[37] Emotion Regulation Questionnaire[63]	No significant change in BDI score from pre- to post-intervention or across the treatment and control groups Significant decrease in DASS Depression scores for the treatment group when analysed independently of the waitlist control	Moderate

Note: BASC-2 = Behaviour Assessment System for Children, 2nd edition; DASS = Depression, Anxiety and Stress Scales; ATQ = Automatic Thoughts Questionnaire; ASSQ = Anxious Self-Statements Questionnaire; VABS = Vineland Adaptive Behavior Scales; CDI = Children's Depression Inventory; BDI = Beck Depression Inventory; VIQ = verbal IQ; PPV = Peabody Picture Vocabulary; DSM = Diagnostic and Statistical Manual of Mental Disorders

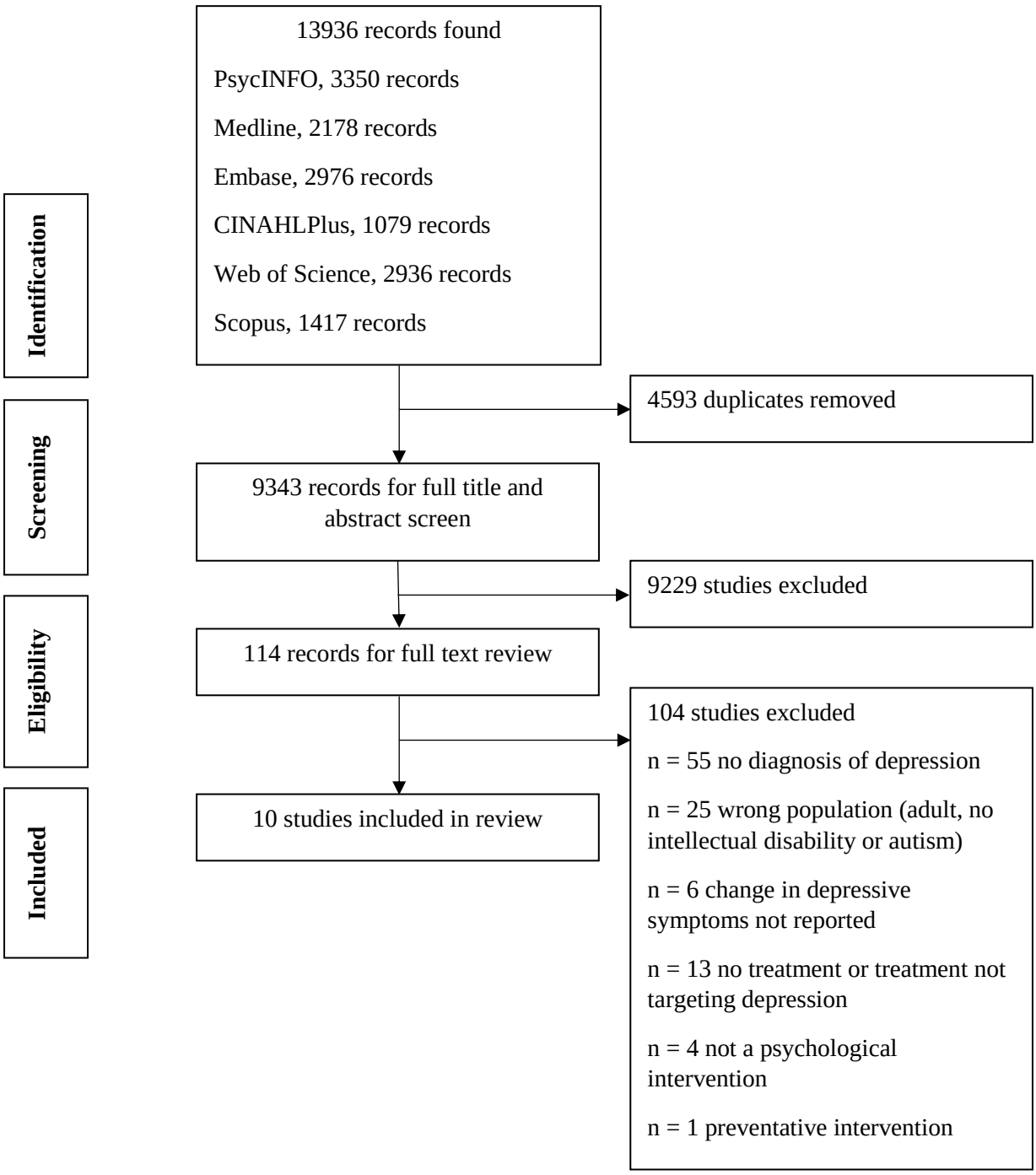

Fig. 1 Study flow diagram.