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Interventions for mental health problems in children and adults with severe intellectual disabilities: A systematic review.

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ABSTRACT

Objective: Mental health problems are more prevalent in people with than without intellectual disabilities, yet treatments options have received little attention. The aim of this study was to identify and evaluate the effectiveness of pharmacological and psychological interventions in the treatment of mental health problems in children and adults with severe and profound intellectual disabilities, given their difficulties in accessing standard mental health interventions, particularly talking-therapies, and difficulties reporting drug side-effects.

Design: A systematic review using electronic searches of PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, and CENTRAL was conducted to identify eligible intervention studies. Study selection, data extraction and quality appraisal were performed by two independent reviewers.

Participants: Study samples included at least 70 % children and/or adults with severe or profound intellectual disabilities or reported the outcomes of this subpopulation separate from participants with other levels of intellectual disabilities.

Interventions: Eligible intervention studies evaluated a psychological or pharmacological intervention using a control condition.

Outcomes: Symptom severity, frequency or other quantitative dimension (e.g., impact), as assessed with standardised measures of mental health problems.

Results: We retrieved 41,232 records, reviewed 573 full-text articles and identified 5 studies eligible for inclusion: 3 studies evaluating pharmacological interventions, and 2 studies evaluating psychological interventions. Study designs ranged from double-blind placebo-controlled crossover trials to single-case experimental reversal designs. Quality appraisals of this very limited literature base revealed good experimental control, poor reporting standards, and a lack of follow-up data.

Conclusions: Mental ill-health requires vigorous treatment, yet the current evidence base is too limited to identify with precision effective treatments specifically for children or adults with severe and profound intellectual disabilities. Clinicians therefore must work on the basis of general population evidence, whilst researchers work to generate more precise evidence for people with severe and profound intellectual disabilities.

PROSPERO registration number CRD 42015024469

Keywords: intellectual disability, mental health, systematic review, psychological therapies, pharmacotherapies

Strengths and limitations of this study

- To our knowledge this is the first systematic review focused on interventions to improve the mental health of both children and adults with severe and profound intellectual disabilities.
- Review eligibility was not restricted to randomised controlled trials which limits the strength of the review's findings.
- Treatment of mental health problems in people with severe or profound intellectual disabilities can be complex in light of the particular cognitive and biophysiological profile of this population, yet the body of evidence we identified was very slim.

INTRODUCTION

Intellectual disabilities affect approximately 1 percent of the population and are characterised by significantly impaired intellectual and adaptive skills with onset before adulthood. Their prevalence of mental health problems has been reported to be more than seven times higher than for the general population [1]. People with severe and profound intellectual disabilities, as indicated by an intelligence quotient of less than 40, have limitations in problem-solving skills, cognitive and communication skills which can affect their ability to cope with stressful life events. The life circumstances of people with an intellectual disability may increase their risk of developing mental health problems or experiencing mental distress. Factors that have been identified as protective in adults without intellectual disabilities, such as employment opportunities, meaningful day activities and socially supportive networks, may be less likely to be present for people with intellectual disabilities and with additional impact for those with severe and profound intellectual disabilities compared to those with mild or moderate intellectual disabilities [2–4]. Genetic factors may further increase the vulnerability of some people with intellectual disabilities for mental health problems, as evidenced by significant comorbidity rates of anxiety problems and psychosis in people with intellectual disabilities and certain genetic syndromes [5–9].

Mental health problems are as common in people with severe and profound intellectual disabilities as in people with mild or moderate intellectual disabilities, reported to have a point prevalence of 22.4% [10–14]. Their treatment of mental health problems requires particular attention for three main reasons. First, longitudinal research investigating the mental health of children and young people with intellectual disabilities over a 14 year period suggest recovery may be poorer for those with severe intellectual disabilities, and therefore standard treatments may be sub-optimal [10–12]. Second, given their limitations in communication skills and understanding, people with severe and profound intellectual disabilities cannot be assumed to find talking therapies such as CBT-based interventions as accessible as other people do; yet these therapies are considered first line treatments of choice for many types of mental health problems. Third, it is possible that people with intellectual disabilities are more sensitive to the side effects of pharmacotherapies, or have greater difficulties in reporting side-effects when these occur, so raising the potential of more serious consequences, and the

need for different dosing regimes compared with other people. The high prevalence and potentially persistent mental health problems experienced by people with severe and profound intellectual disabilities thus call for effective interventions to treat such problems and to promote well-being.

Existing systematic reviews have evaluated either the psychological or pharmacological treatment of mental health problems in people with intellectual disabilities. Cognitive behavioural therapies (CBT) were found to have moderate positive treatment effects for people with intellectual disabilities who experience anger problems, anxiety and depression [15–17], but these findings are limited to adults with mild to moderate intellectual disabilities, however, as children or individuals with severe and profound intellectual disabilities were not represented in the primary studies. Reviews of pharmacological interventions have largely focused on behaviour problems independent of their association with mental health problems. For example, potentially effective interventions for behaviour problems in adults with intellectual disabilities include risperidone, lithium and anti-epileptic mood stabilisers [18,19]. However, the methodological quality of the evidence and registered adverse effects indicate that the use of these pharmacological agents requires caution [18,19]. Whilst behaviour problems can be associated with mental health problems and take on a precipitating or perpetuating role, they are more indicative of emotional dysregulation than of psychiatric symptomatology, and have been demonstrated in robust studies to be distinct from other types of mental health problems [20]. We have not identified reviews on treatment response and side-effects to pharmacotherapies for other types of mental health problems experienced by people with severe and profound intellectual disabilities. The objective of the present systematic review was to evaluate the effectiveness of psychological and pharmacological treatments for mental health problems and their key symptoms in both children and adults with severe or profound intellectual disabilities.

METHODS

The review was conducted and written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [21]. The review protocol was registered with PROSPERO, Centre for Reviews and Dissemination, under the reference number CRD 42015024469.

Search strategy

The search strategy was developed for two conjoint systematic reviews focused on the evaluation of measures of mental health problems and interventions respectively in people with severe and profound intellectual disabilities. Although separate search terms were used for each systematic review, records identified through the respective searches were pooled together prior to the study eligibility screening to ensure that studies piloting an assessment as an intervention outcome measure would also be identified.

Initial systematic searches were conducted in the week of 13 to 17 July 2015 for the following databases: PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, Cochrane Central Register of Controlled Trials (CENTRAL). Searches used Boolean terms to combine search strings for intellectual disabilities, mental health, and psychological or pharmacological interventions, as shown in Table 1 for the PsycINFO, PsycTESTS and ASSIA searches. Full search strategies for each database can be requested from the authors.

Searches were updated in September 2017, to cover the time period from the original searches, and no new studies were identified from these searches. The updated searches followed the same search strategy and study screening protocol as the original searches.

Table 1

Search strategy for simultaneous database searches of PsycINFO, PsycTESTS and ASSIA using ProQuest database host.

	Search terms	Results
Intellectual disabilities		
1	SU.EXACT.EXPLODE("Intellectual Development Disorder")	37548
2	TI(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*)) OR AB(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*))	38279

3	TI(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder)) OR AB(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder))	36985
4	TI(moron OR imbecile OR feeble-minded OR subnormal OR retard) OR AB(moron OR imbecile OR feeble-minded OR subnormal OR retard)	4289
5	TI(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*)) OR AB(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*))	16059
6	TI((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*) OR AB((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*)	11067
7	OR/ 1-6	105392
Mental health		
8	SU.EXACT.EXPLODE("Depression (Emotion)")	22448
9	SU.EXACT.EXPLODE("Anxiety Disorders") OR SU.EXACT.EXPLODE("Generalized Anxiety Disorder") OR SU.EXACT.EXPLODE("Anxiety") OR SU.EXACT.EXPLODE("Social Anxiety")	124637
10	TI(anger NEAR/3 (problem* OR disorder*)) OR AB(anger NEAR/3 (problem* OR disorder*))	1212

11	TI(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*) OR AB(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*)	272855
12	TI(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*)) OR AB(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*))	226542
13	TI(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*) OR AB(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*)	273779
14	OR/ 8-13	655607
Mental well-being		
15	TI(psycho* NEAR/2 function*) OR AB(psycho* NEAR/2 function*)	23372
16	TI(well* OR health*)	207285
17	TI((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*)) OR AB((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*))	193401
18	TI(quality NEAR/2 life)	19555
19	OR/ 15-18	358684
Psychological interventions		
20	TI((psychological N/3 therap*) OR psychotherap* OR counsel*) OR AB((psychological N/3 therap*) OR psychotherap* OR counsel*)	196693

21	TI(psychoanaly* OR psychodynamic*) OR AB(psychoanaly* OR psychodynamic*)	90160
22	TI((behavior* OR behaviour* OR cognitive) N/2 therap*) OR AB((behavior* OR behaviour* OR cognitive) N/2 therap*)	39534
23	TI((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*) OR AB((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*)	25851
24	TI((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*) OR AB((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*)	1984
25	TI(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive") OR AB(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive")	10630
26	TI((group OR individual) N/2 therap*) OR AB((group OR individual) N/2 therap*)	25884
27	TI(anger N/2 (manag* OR train*)) OR AB(anger N/2 (manag* OR train*))	1612
28	TI((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*) OR AB((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*)	17343
29	OR/ 20-28	342375
Pharmacological interventions		
30	TI(pharmacotherapy* OR pharmacolog* OR pharmacological therap*) OR AB(pharmacotherapy* OR pharmacolog* OR pharmacological therap*)	49958

31	TI(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*) OR AB(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*)	41884
32	TI(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*)) OR AB(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*))	6622
33	TI(tricyclic antidepressant OR anti-depress* OR antidepress*) OR AB(tricyclic antidepressant OR anti-depress* OR antidepress*)	34457
34	TI(adrenergic blocking drugs OR monoamine oxidase inhibitors) OR AB(adrenergic blocking drugs OR monoamine oxidase inhibitors)	1905
35	TI(anxiolytic* OR antipanic* OR antianxiety) OR AB(anxiolytic* OR antipanic* OR antianxiety)	7153
36	TI(anticonvulsant*) OR AB(anticonvulsant*)	4142
37	TI(lithium*OR lithium carbonate OR SSRI* OR "selective serotonin reuptake inhibitor" OR serotonin reuptake inhibitor OR serotonin antagonist) OR AB(lithium*OR lithium carbonate OR SSRI* OR "selective serotonin reuptake inhibitor" OR serotonin reuptake inhibitor OR serotonin antagonist)	12261

38	TI(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine) OR AB(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine)	61771
39	OR/ 30-38	153952
Final search string		
40	7 AND (14 OR 19) AND (29 OR 39)	2607

Study eligibility criteria

The following inclusion criteria were applied to (1) publication type, (2) study design, (3) participants, (4) interventions, and (5) outcomes.

(1) Publication. Peer-reviewed publications written in English, French, German or Dutch were eligible for review.

(2) Study design. The following study designs were eligible for inclusion in the review: (a) randomised controlled trials, (b) controlled trials without randomisation, (c) single group pre-post designs, (d) case series with outcome measures reported as group mean data, (e) single-case experimental designs, and (f) case-control studies. Case studies without a control condition or a return to baseline were excluded.

(3) Participants. To ensure that the outcome data were representative for people with severe and profound intellectual disabilities it was required that either a minimum of 70% of participants were diagnosed or reported as having severe or profound intellectual disabilities, or that data for participants with severe or profound intellectual disabilities were reported separately in the study. Although this was an arbitrary criterion, this was to ensure that a majority of people with severe or profound intellectual disabilities were in the study samples. Studies that did not provide any usable information about the level of intellectual disabilities within samples were excluded. No exclusions were applied concerning participants' age or gender or any other characteristics except for degree of intellectual disability.

(4) Intervention. Eligible psychological interventions were delivered by a trained lay therapist or qualified professional who systematically applied interventions based on well-established psychological principles and techniques directly to the person with an intellectual disabilities, either individually or in a group. For pharmacological interventions, it was expected that the pharmaceutical agent was given with regular review by a qualified medical practitioner or health professional, and recognised at least in principle as a potential treatment for a mental health problem/symptom.

(5) Outcomes. Interventions had to target mental disorders or their key symptoms as assessed by a qualified clinician using standardised assessments and which have a significant impact on daily

functioning. However, we acknowledge that defining the mental and physical components of mental and physical disorders into mutually exclusive categories can be challenging, not in the least because certain components are symptomatic of multiple disorders and certain disorders have shown high rates of co-morbidity with one another. For the purpose of this systematic review, the inclusion criteria for mental disorders and their symptoms were derived from the DSM-IV [22], as this version was most likely to be used by the primary studies to be identified by the systematic review. Mental and behavioural disorders, and their key symptoms, eligible for review fell within the following classifications: (a) attention-deficit and disruptive behaviour disorders, (b) tic disorders, (c) other disorders of infancy, childhood, or adolescence, (d) schizophrenia and other psychotic disorders, (e) mood disorders, (f) anxiety disorders, (g) somatoform disorders, (h) factitious disorders, (i) dissociative disorders, (j) eating disorders, (k) adjustment disorders, and (l) personality disorders. Studies focused on key symptoms of mental disorders were included as not all treatment offers a holistic approach, and interventions may instead aim to alleviate one or more symptoms of a disorder. By contrast, challenging behaviours and behaviour problems may be associated with or indicative of underlying mental disorders [20,23] but are not recognised as a key diagnostic feature of the above listed mental disorders and are hence excluded from this review.

The broad scope of the systematic review in terms of study designs, type of interventions and range of participants was advised as initial scoping searches indicated that only few studies included individuals with severe and profound intellectual disabilities.

A single post-hoc exclusion criterion was applied to exclude records from the searches published prior to 1980 (n=106 records, but not fully checked for inclusion criteria), coinciding with the publication of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III); [24]. This assured a minimal level of consistency in the recognition and diagnosis of mental health problems from DSM-III through to DSM-IV. It is likely that there would have been a delay between the publication of the DSM-III and its first use in published research, but searches back to 1980 were essential to ensure that no potentially relevant studies were missed.

Study selection

Data collection and abstract screening were performed by the first author (LV). Twenty percent of records were also screened by the second author (SF), leading to an overall agreement rate of 99.8 % and a Kappa coefficient of 0.91 for studies to proceed to full text evaluation. Second screening a proportion of results is an accepted practice when a review is large and resources are limited [25]. The overall inclusion rate for the screening of titles and abstracts was 2.3 %. Full-text review of 573 articles was performed independently by the two reviewers (LV and SF), which resulted in a Kappa coefficient of 0.76 for inclusion in the review and the data extraction stage. Eleven disagreements between the two reviewers were resolved through joint discussion. All disagreements concerned the proporption of participants with severe and profound intellectual disabilities and were not related to study design, intervention or outcomes. The review of one full text article required consultation with the third author (RH) to determine whether this study met the review eligibility criteria regarding mental health outcomes. Upon discussion, the paper was excluded from the review.

Next, reference lists and citation records of all included studies were screened to identify additional papers that may not have fulfilled the search term criteria. No additional studies were identified in this way.

Data extraction and quality synthesis

Data extraction was conducted by the second author and reviewed by the first author for variables including: study design, study population, intervention, outcome measures, and follow-up data.

The certainty in the evidence for each outcome measure could not be assessed with the GRADE approach [26–28], as used by the Cochrane collaboration and national guideline organisations such as NICE in the UK, due to the incomparability of identified studies in terms of study design, interventions, and outcomes. Likewise, it was not possible to conduct a meta-analysis or provide other summary measures because no two studies addressed the same mental health problem using a similar intervention.

Both reviewers independently performed a quality appraisal of all included studies. No disagreements were recorded at either stage. Quality assessment followed the Critical Appraisal Skills

Programme [29,30] checklists or the quality indicators for within single-subjects research [31], dependent on the study design.

RESULTS

The search strategy for the conjoint systematic review identified 24,883 unique records, of which 573 were retained for full-text eligibility screening. The study selection process is illustrated in Figure 1. Excluded articles most commonly did not meet the eligibility criteria concerning the severity of intellectual disabilities of study participants (n = 242). Initial records were also excluded based on their study design (n = 113), a publication date prior to 1980 (n = 106), because the intervention or outcomes were not focused on recognised mental health problems (n = 59), due to their publication status (e.g. conference abstracts; n = 38), or because the full-text paper could either not be retrieved (n = 6) or was published in a non-eligible language (n = 4). In total, five studies were included in the review and are described in Table 2. Three studies included only adults with intellectual disabilities: a double-blind placebo-controlled crossover trial [32] and a single-case experimental reversal design of pharmacotherapy [33], as well as a single-case experimental reversal design of a psychological intervention [34]. Two studies included children and young people: a randomised trial of pharmacotherapy by White and Aman [35] and a single-case study of a psychological intervention for a 13-year old girl [36].

[Figure 1 about here]

Table 2

Characteristics of pharmacological and psychological interventions studies.

First author (Year)	Study Design[a]	Participants	Intervention	Outcomes	Follow-up
Psychopharmacological interventions					
Aman (1986)	Double-blind placebo-controlled crossover trial Within-group randomisation I1: Imipramine I2: placebo 1-week washout period between interventions	Adults with depressive and affective symptoms N = 5 (2M/3F) Age range: 18 – 23 years intellectual disabilities severity: Slosson IQ[b] range 10 -14	Imipramine (Dumex) or placebo Duration: 4W Dose: 3 mg/kg/day Setting: residential ward	Imipramine caused symptom deterioration for ABC[c] scores related to irritability, lethargy, and hyperactivity. No intervention effects were observed for: stereotypy and inappropriate speech. Statistical data only provided for analyses including a second intervention group, non-eligible for review.	No follow-up
Rosenquist (1997)	Single-case experimental reversal design (ABABA) A, Baseline B, Haloperidol Single blind, masked	Adult with Gilles de la Tourette syndrome N = 1, Female Age = 35 years Severe intellectual disabilities	Haloperidol Duration: 22W, A: 2W baseline B: 8W intervention A: 2W baseline B: 8W intervention A: 2W baseline	Weekly observations using Behavioral Observation and Tic Checklist[d] of 3 videotaped conditions: (1) table setting task, (2) mealtime, and (3) waiting. Pre-post % time (SD)	W6 of increased dosage % time (SD) engaged in tic behavior at W6 (dose 10 mg/day): Mealtime: SM-tic: 6.3 (6)

	assessment		Dose: -W1: 1 mg/day -W2: 2mg/day -W3-4: 5 mg/day -W5-6: 10 mg/day -W7-8: washout Setting: community group home	engaged in tic behavior at baseline and W1 (dose 1mg/day): Mealtime: SM-tic: 34.8 (20); 11.0 (12) CM-tic: 13.6 (10); 5.3 (8) SV-tic: 35.4 (28); 2.0 (4) CV-tic: 1.3 (3); 0.0 (0) Waiting: SM-tic: 46.8 (31); 20.8 (26) CM-tic: 41.2 (19); 25.3 (21) SV-tic: 65.3 (29); 69.6 (25) CV-tic: 42.5 (18); 23.0 (18)	CM-tic: 3.0 (3) SV-tic: 1.0 (3) CV-tic: 1.0 (2) Waiting: SM-tic: 24.7 (20) CM-tic: 41.5 (18) SV-tic: 48.4 (26) CV-tic: 34.8 (20) Dose-specfic improvements (10mg/day), reversible
White (1985)	Double-blind placebo-controlled crossover trial I1: Pimozide I2: Placebo Randomisation within participants	Inpatients with serious behaviour disturbances, including hyperactivity N = 8, 7M/1F Mean age 15.7 years (SD = 3.42) intellectual disabilities severity: moderate to profound; mean IQ =	Pimozide or placebo Baseline: 4W Intervention: 4W + 4W Dose: I1: 6 mg/day Setting: no info	ANCOVA for drug effects and baseline as covariate on ABC subscales Pimozide has an effect: Irritability: F = 11.78 Hyperactivity: F = 7.69 No significant effects	No follow-up

	1-week washout period between interventions	20.4 (SD = 12.11)		for: Lethargy: F = 0.84 Stereotypy: F = 3.48 Inappropriate speech: F = 1.31	
Psychological interventions					
Lindauer (1999)	Single-case experimental reversal design (ABAB) A, Baseline: empty room & quiet hands procedure B, Enriched Environment & quiet hands	Mood disorder, major depression N = 1, Female Age = 23 years Severe intellectual disabilities	Enriched environment: 12 items selected for inclusion by paired-choice assessment Duration: 57 sessions; A: 11 sessions B: 5 sessions A: 29 sessions B: 12 sessions Dose: 10 minute sessions Setting: Laboratory, padded room	Percentage of 10-s intervals of signs of negative and positive affect Pre: relatively high levels of negative affect (M = 27.4%) and low levels of positive affect (M = 2.3%) Post: negative affect decreased (M = 0.1%) and positive affect increased, especially during B2 (M = 11.5% across phases).	No follow-up
Zarkowska (1989)	2 Single-case experimental reversal designs (ABA) I1: Relaxation: A, Baseline: school activity, tics ignored B, relaxation A, Baseline: return to	Gilles de la Tourette syndrome N = 1, Female Age = 13 years Severe intellectual disabilities (Griffiths Mental Development Scale score ranged	I1: verbal instructions for relaxation exercises and praise when calm Duration: 10 minutes I2: verbal interruption following the occurrence of a verbal tic	I1 reduced tic frequency during relaxation but return to baseline after intervention I2 increased vocal tic frequency.	No follow-up

	school activity, tics ignored I2: interruption A, Baseline: school activity, tics ignored B, interruption A, Baseline: return to school activity, tics ignored	from 17 to 42 months)	Duration: 10 minutes	After I1 and I2: No generalised reduction in tic frequency

Note. I1, intervention 1; I2, intervention 2; G1, group 1; G2, group 2; Gender ratio expressed as Male/Female; W1, week 1; SD, standard deviation. Outcomes reported for primary outcome measure only, unless where mental health or mental well-being outcome measure were recorded as secondary outcome measures.

[a] AB designs with A: baseline and B: treatment.

[b] Slosson IQ scores correlate highly with Stanford Binet Intelligence Test scores and correlate with the Cattell Infant Intelligence Scale when used with children under the age of 2 (Slosson, 1975).

[c] ABC, Aberrant Behavior Checklist.

[d] SM-tic, simple motor tic; CM-tic, complex motor tic; SV-tic, simple vocal tic; CV-tic, complex vocal tic.

Psychological interventions

Two studies evaluated interventions based on psychological principles. Interventions were offered for symptoms of depressive disorder and to manage tic frequency in Gilles de la Tourette syndrome.

In a single-case experimental ABAB design, Lindauer and colleagues [34] offered an enriched environment for the management of major depressive disorder in a 23-year old woman with severe intellectual disabilities who also presented with self-injurious behaviour. Pre-existing treatment of the mood disorder with carbamazepine (5.3 mg/kg/day) was continued during the study. The enriched environment setting was a 3 metre by 3 metre padded room, in an inpatient unit, in which stimuli were present that were chosen following a paired-choice assessment to identify the woman's preferred stimuli and assess signs of positive and negative affect. Smiling, giggling and laughing were considered examples of positive 'affect', whereas frowning, whining, crying and verbal expressions such as "I am sad" were identified as signs of negative 'affect'. No other outcome measures relating to the mood disorder were employed. Behavioural observations, through a one-way mirror, showed that the enriched environment increased signs of positive affect and decreased signs of negative affect, in particular during the second intervention phase. The lack of follow-up measures and the delivery of interventions in a padded room in an inpatient setting reduce the ecological validity of this intervention. Likewise, the replicability of findings is impeded in terms of participant selection and intervention fidelity (see Table 3).

Zarkowska et al. [36] adopted a basic single-case experimental design to examine interventions for vocal and motor tics in a 13-year old girl with Gilles de la Tourette syndrome and severe intellectual disabilities. Two treatment probes, cued relaxation and interruption, were evaluated using an ABA return to baseline design for each intervention comprised of a five minute baseline recording, a five minute intervention, and a five minute post-baseline recording. Cued relaxation appeared to lead to better outcomes but neither intervention had lasting effects and interruption increased vocal tic frequency. The study design showed strong external and social validity and provided clear descriptions of dependent and independent variables (see Table 3). However, internal

validity was weak and the ABA design was not the most suitable for demonstrating experimental control. Following the evaluation of treatment probes, the study continued as an A-B case study implementing successive interventions of relaxation training, treatment with clonidine and treatment with pimozide. Due to the non-controlled nature of these interventions, their respective outcome data and follow-up data were not considered eligible for inclusion in this review.

The replicability of findings from both studies is hindered by a lack of information regarding participant selection, physical setting of the intervention, implementation fidelity, and the reliability of outcome measurements.

Table 3

Quality appraisal of single-subject studies using the Quality Indicators Within Single-Subject Research [31] .

Quality indicator	Lindauer et al. (1999)	Rosenquist et al. (1997)	Zarkowska (1989)
Participant description and setting			
Ability to select individuals with similar characteristics	yes	yes	yes
Replicability of participant selection process	no	no	no
Replicability of physical setting	yes	yes	partial
Dependent variable			
Described with operational precision	yes	yes	yes
Measured to generate a quantifiable index	yes	yes	yes
Measure is valid and replicable	yes	yes	yes
Measurements repeated over time	yes	yes	no
Measures assessed in terms of reliability or inter-	yes	yes	no

observer agreement			
Independent variable			
Described with replicable precision	yes	yes	yes
Systematically manipulated and under control of experimenter	yes	yes	yes
Overt measure of implementation fidelity	no	not applicable	no
Baseline			
Repeated measurements baseline	yes	yes	no
Described with replicable precision	yes	yes	yes
Experimental control / Internal validity			
Minimum of 3 demonstrations of experimental effect at 3 points in time	yes	yes	no
Controlling for threats to internal validity	unclear	yes	unclear
Document a pattern of experimental control	yes	yes	yes
External Validity			
Effects replicated across participants, settings, or materials	yes	yes	no
Social validity			
Dependent variable is socially important	yes	yes	yes

Magnitude of change is socially important	yes	yes	yes
Implementation of independent variable is practical and cost-effective	yes	yes	yes
Implementation of independent variable over extended period of time, by typical intervention agents and in typical contexts	yes	yes	yes

Pharmacological interventions

Two double-blind placebo-controlled crossover trials and one single-case experimental reversal design evaluated pharmacological interventions for use in people with severe intellectual disabilities and mental health problems.

Aman and colleagues [32] employed within-group randomisation of order of administration of 4 week treatment with imipramine, in a dosage of 3 mg/kg/day, and 4 weeks with placebo, with one week drug-free in between. Interventions were offered to five adults with severe intellectual disabilities and depressive symptoms, in addition to a group of five adults with acting-out behaviours. The latter were not eligible for inclusion in this review as these behaviours were not considered a mental health problem. Eligible depressive symptoms were based on evidence from prior research studies and required behavioural observation instead of information obtained from diagnostic interviews. Symptoms included 'seclusion and social withdrawal, sleep loss, weight loss, tearfulness or the appearance of sad affect, and a pervasive lack of overt behavior' [31, p. 265]. Intervention effects were assessed with the Aberrant Behavior Checklist [37] and indicated imipramine to have a detrimental effect on symptoms related to irritability, lethargy, and hyperactivity, and no effect on stereotypical behaviours and inappropriate speech. Adverse effects were recorded but not described separately for the five adults with severe intellectual disabilities and depressive symptoms. For one person with affective symptoms, imipramine was found to improve behaviour and relieve chronic constipation.

White and Aman [35] evaluated the use of pimozide on maladaptive behaviours and hyperactivity, in young people and adults with moderate to profound intellectual disabilities.

Following a four-week baseline, the eight participants received two four-week treatments with either pimozide, in a dosage of 0.12 mg/kg/day, or placebo, with a one-week washout period between intervention phases. Treatment effects were evaluated using assessments with the ABC for the last three weeks of each intervention. Hyperactivity scores on the ABC reduced following the intervention, as did irritability levels, based on nurses' behaviour ratings of participants. No intervention effects were observed for ABC lethargy, stereotypy, and inappropriate speech domains. Furthermore, behavioural observations also did not identify any treatment effects.

The methodological quality of these two studies was confirmed using the CASP quality appraisal checklist (see Table 4). However, follow-up measures were notably absent and sample sizes too small to provide sufficient power for the conducted statistical analyses. Additionally, the period of treatment was of too short duration, as imipramine can take up to 6 weeks to be effective in the general population, so that intervention was of poor design.

Table 4

Critical Appraisal Skills Programme (CASP Checklists; CASP, 2014) for studies with N > 1.

Quality indicator	Aman et al. (1986)[a]	White et al. (1985)[a]
Validity of the results		
Study addresses a clearly focused issue	yes	yes
Cohort recruited in an acceptable way	yes	yes
Exposure accurately measured to minimise bias	yes	yes
Outcome accurately measured to minimise bias	yes	yes
Identification of all important confounding factors	yes	yes
Design and/or analysis account for confounding factors	No: length of intervention too short to observe	No: length of intervention too short to observe

	treatment effects.	treatment effects.
Complete enough follow-up of participants	no	no
Long enough follow-up of participants	no	no
Scope of the results		
Description of study results	yes	yes
Precision of study results	No exact p-values, no effect sizes, no differentiation between depressive-like and acting-out group	No exact p-values, no effect sizes
Believability of study results	yes	yes
Impact of the results		
Results applicable to local population	Yes	Yes
Results in line with available evidence	no	Yes
Implications for practice	Length of intervention too short to draw conclusions regarding implictions	The study is now out-dated given improved knowledge on the risks of the long-term use of the drug

Note. [a] CASP Checklist for Randomised Controlled Trials.

The only fully experimental single subject experimental design study evaluated the effect of haloperidol on tic frequency in a 35-year old woman with Gilles de la Tourette syndrome and severe intellectual disabilities [33]. Using an ABABA design, the dose of haloperidol was gradually increased during the intervention phases and maximal effectiveness was reached with the highest dosage of 10 mg/day. Weekly behavioural observation at the community residential setting where the participant lived showed reduced tic frequencies during mealtimes, nearing zero-levels, and during waiting times. Intervention effects reversed when the dose was lowered. These findings are considered reliable due to masked assessment and reversal design, alongside the replicability of measures and intervention, see Table 3.

Overall quality appraisal of the evidence base

Methodological quality of the identified studies was poor, with concern in terms of small sample sizes, lack of masked assessment, and lack of follow-up measures. By contrast, reporting standards were generally high in terms of variable descriptions and the internal and external validity of the results. Implications of the quality appraisal are integrated in the study descriptions above, whereas a detailed overview of the quality review for each study is reported in Tables 3 and 4.

DISCUSSION

Despite their very high rates of mental health problems, there is a lack of research in interventions that explicitly target mental health problems in people with severe and profound intellectual disabilities. The scope of this review was wide. However, only five studies were eligible for inclusion and the findings are inconclusive at best. This is highly problematic for clinicians who have to manage these disorders. Whilst precision medicine is recognised to be of crucial importance, the evidence allows for no precision in management of the mental health problems so frequently experienced by people with severe intellectual disabilities. Clinicians can only rely upon the use of interventions designed for the general population, despite the likely limitations/inaccessibility of these for people with severe intellectual disabilities.

Haloperidol was demonstrated to improve tics, but in a single person. Pimozide was reported to reduce hyperactivity and other behaviour problems [35], but it is not a recognised treatment for hyperactivity in the general population; and NICE concludes that there is no evidence that

antipsychotics drugs are of use in this condition (NICE, 2016). Whilst it can calm disturbed patients in the short term through its sedative properties, it is not recommended for this use longer term in view of potential side-effects which includes death, with its use being reserved for schizophrenia only. Whilst meeting the inclusion criteria of the review, the study is therefore out-dated given subsequent advances in knowledge about this class of drugs. Imipramine caused deterioration of affective symptoms, but the study was poorly designed by today's standards, including the drug not being prescribed for long enough duration to be effective [32]. Additionally, the use of imipramine has declined in the whole population since the introduction of selective serotonin reuptake inhibitors in the 1980s and other newer antidepressant agents, on the basis of side-effect profile.

Evidence for the effectiveness of psychological interventions is also weak in the absence of controlled trials or high quality single case experimental designs (such as multiple baseline approaches). Across intervention types, two studies aimed to reduce tic frequency in people with severe intellectual disabilities and Gilles de la Tourette Syndrome yielding putative positive effects for relaxation techniques and treatment with haloperidol. Evidence relating to common mental health problems (e.g., anxiety, depression) was notably very limited. Studies including children with severe and profound intellectual disabilities involved different interventions than for studies with adults and while the geographic spread of the research was diverse, all included studies were conducted in English speaking countries. Overall, a quantitative synthesis of the evidence was not possible due to the heterogeneity of the identified studies as no two studies addressed the same mental health problem with a similar intervention or similar outcome measures. Furthermore, the total sample size across the five identified studies was only sixteen participants: nine children and seven adults, nine male and seven female. Finally, the review demonstrates that research in this area has stalled over the last decade. The most recent study we identified was published nearly two decades ago [34], whilst the methodologically stronger studies using controlled design employed outdated pharmacotherapies that are currently not recommended due to their potential side-effects [36, 39].

The rigour with which the systematic review was conducted is in stark contrast to the scientific quality of the identified studies. In line with PRISMA guidelines, the prior publication of the review protocol enhances its transparency and replicability, whilst double reviewing of full-length

articles and quality appraisal strengthens the findings. The current review improves upon previous reviews in this area by employing a broader scope to identify both psychological and pharmacological interventions for a range of mental health problems. Whilst the search strategy did not include terms for every specific possible disorder or potential treatment, it did identify a considerably large number of records compared to the eventual included studies. Meanwhile, requiring at least 70% people with severe and profound intellectual disabilities to be included in a sample where outcomes are not reported separately for this group was a pragmatic decision so people with severe and profound intellectual disabilities would be sufficiently represented in the review findings. However, reducing the required proportion of participants with severe and profound intellectual disabilities to 50% would not have added any eligible studies (a post-review check completed by the first author). A major challenge in mental health research for people with severe and profound intellectual disabilities, including this systematic review, lies with the selection of study outcomes. The appropriateness of measures such as the ABC [37] can be questioned when used to assess the wide spectrum of symptoms of mental health problems. However, the ABC was found to be one of the few reliable measures relating to mental health problems for individuals with severe and profound intellectual disabilities [38]. Indeed, behavioural outcomes can assess key symptoms of mental disorders according to ICD-10 criteria, but can equally be associated with distress and reduced quality of life. Whilst this diagnostic taxonomy was practical for conducting the systematic review, it may not be sufficient to evaluate all relevant interventions aimed at improving the general well-being of people with severe and profound intellectual disabilities.

The scarcity of trials addressing the mental health needs of people with severe and profound intellectual disabilities is worrisome in light of the fact that they do experience mental health problems. Yet, there is awareness of the mental health needs in this population amongst researchers and clinicians, as demonstrated by the wide range of descriptive case reports. These case reports did not employ an experimental design required to provide empirical evidence for the effectiveness of an intervention. On a positive note, the 101 studies identified as including at least some individuals with severe and profound intellectual disabilities show that this population is not routinely excluded from clinical practice evaluations. Although beyond the objectives of this systematic review, a scoping

overview of the range of interventions evaluated in these studies and those being offered in routine clinical practice could help set the direction to guide future research. Establishing evidence-based interventions to treat mental health problems in people with severe and profound intellectual disabilities requires more research with stronger methodological designs.

Challenging the status quo and developing an evidence base from which to treat people with severe and profound intellectual disabilities and mental health problems is a joint responsibility of practitioners and researchers. Bi-directional knowledge transfer is particularly important in this regard: research into severe and profound intellectual disabilities making its way into the training of practitioners, as well as practitioners highlighting difficulties in assessment and treatment that need addressing. Commissioning and exploring funding opportunities to conduct research into evidence-based pharmacological and psychological interventions, and an open discussion regarding the ethical considerations of research involving people who may lack the capacity to consent also require attention. A large inequality in evidence for effective treatments for mental health problems is experienced by children and adults with severe and profound intellectual disabilities. Until this inequality is adequately addressed, health services need to provide treatments found to be effective for people with mild to moderate intellectual disabilities where they exist- although the availability of interventions for this population is also poor in comparison to interventions for people without intellectual disabilities. Particular attention should be given to how these treatments might affect people with severe and profound intellectual disabilities differently regarding symptom presentation and outcome assessment, accessibility of a range of psychological therapies, and side effect reporting which may indicate a need for differences in dosing regimens. Keeping detailed accounts of how treatments were subsequently modified will benefit the development of a more solid evidence base.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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Authors' contributions

RH, DA, UC, S-A C, NG, CH, KH, AJ, PEL, RMN, CO, AR, VT, JW, Nigel Beail, Michael Kerr and Howard Ring conceived the study and acquired funding. LV and RH designed and registered the review protocol. LV and SF conducted the systematic searches, study selection and data collection. LV wrote the manuscript.

All authors provided methodological and clinical perspectives, commented on manuscript drafts and read and approved the final version of this manuscript.

Figure 1. PRISMA Flow Diagram

Data sharing statement

To obtain the full search strategies for each database please contact leen.vereenooghe@uni-bielefeld.de or s.flynn.1@warwick.ac.uk.

This systematic review presents previously published data. Please refer to the original articles and their authors for these research data.

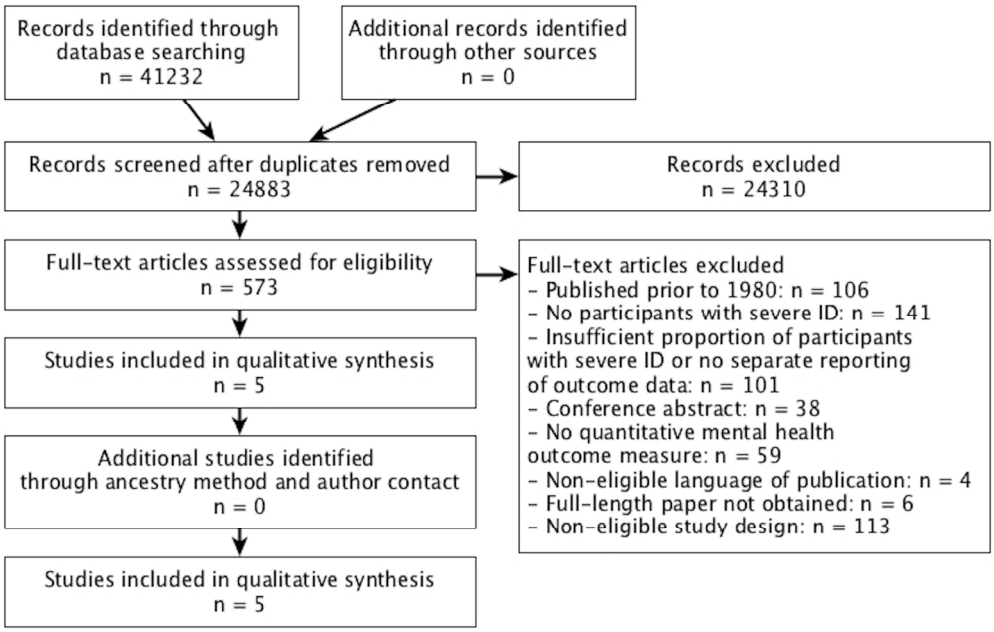

Figure 1. PRISMA Flow Diagram

244x155mm (300 x 300 DPI)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	13
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	15
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	15
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	13, 15
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	15
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n/a

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	16
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	17
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	27-28
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	29
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	30
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	31

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Interventions for mental health problems in children and adults with severe intellectual disabilities: A systematic review.

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ABSTRACT

Objective: Mental health problems are more prevalent in people with than without intellectual disabilities, yet treatments options have received little attention. The aim of this study was to identify and evaluate the effectiveness of pharmacological and psychological interventions in the treatment of mental health problems in children and adults with severe and profound intellectual disabilities, given their difficulties in accessing standard mental health interventions, particularly talking-therapies, and difficulties reporting drug side-effects.

Design: A systematic review using electronic searches of PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, and CENTRAL was conducted to identify eligible intervention studies. Study selection, data extraction and quality appraisal were performed by two independent reviewers.

Participants: Study samples included at least 70 % children and/or adults with severe or profound intellectual disabilities or reported the outcomes of this subpopulation separate from participants with other levels of intellectual disabilities.

Interventions: Eligible intervention studies evaluated a psychological or pharmacological intervention using a control condition.

Outcomes: Symptom severity, frequency or other quantitative dimension (e.g., impact), as assessed with standardised measures of mental health problems.

Results: We retrieved 41,232 records, reviewed 573 full-text articles and identified 5 studies eligible for inclusion: 3 studies evaluating pharmacological interventions, and 2 studies evaluating psychological interventions. Study designs ranged from double-blind placebo-controlled crossover trials to single-case experimental reversal designs. Quality appraisals of this very limited literature base revealed good experimental control, poor reporting standards, and a lack of follow-up data.

Conclusions: Mental ill-health requires vigorous treatment, yet the current evidence base is too limited to identify with precision effective treatments specifically for children or adults with severe and profound intellectual disabilities. Clinicians therefore must work on the basis of general population evidence, whilst researchers work to generate more precise evidence for people with severe and profound intellectual disabilities.

PROSPERO registration number CRD 42015024469

Keywords: intellectual disability, mental health, systematic review, psychological therapies, pharmacotherapies

Strengths and limitations of this study

- To our knowledge this is the first systematic review focused on interventions to improve the mental health of both children and adults with severe and profound intellectual disabilities.
- Review eligibility was not restricted to randomised controlled trials which limits the strength of the review's findings.
- The body of evidence we identified was very slim and does not allow for generalisation of findings for either psychological or pharmacological interventions.

INTRODUCTION

Intellectual disabilities affect approximately 1 percent of the population and are characterised by significantly impaired intellectual and adaptive skills with onset before adulthood. Their prevalence of mental health problems has been reported to be more than seven times higher than for the general population [1]. People with severe and profound intellectual disabilities, as indicated by an intelligence quotient of less than 40, have limitations in problem-solving skills, cognitive and communication skills which can affect their ability to cope with stressful life events. The life circumstances of people with an intellectual disability may increase their risk of developing mental health problems or experiencing mental distress. Factors that have been identified as protective in adults without intellectual disabilities, such as employment opportunities, meaningful day activities and socially supportive networks, may be less likely to be present for people with intellectual disabilities and with additional impact for those with severe and profound intellectual disabilities compared to those with mild or moderate intellectual disabilities [2–4]. Genetic factors may further increase the vulnerability of some people with intellectual disabilities for mental health problems, as evidenced by significant comorbidity rates of anxiety problems and psychosis in people with intellectual disabilities and certain genetic syndromes [5–9].

Mental health problems are as common in people with severe and profound intellectual disabilities as in people with mild or moderate intellectual disabilities, reported to have a point prevalence of 22.4% [10–14]. Their treatment of mental health problems requires particular attention for three main reasons. First, longitudinal research investigating the mental health of children and young people with intellectual disabilities over a 14 year period suggest recovery may be poorer for those with severe intellectual disabilities, and therefore standard treatments may be sub-optimal [10–12]. Second, given their limitations in communication skills and understanding, people with severe and profound intellectual disabilities cannot be assumed to find talking therapies such as CBT-based interventions as accessible as other people do; yet these therapies are considered first line treatments of choice for many types of mental health problems. Third, it is possible that people with intellectual disabilities are more sensitive to the side effects of pharmacotherapies, or have greater difficulties in reporting side-effects when these occur, so raising the potential of more serious consequences, and the

need for different dosing regimes compared with other people. The high prevalence and potentially persistent mental health problems experienced by people with severe and profound intellectual disabilities thus call for effective interventions to treat such problems and to promote well-being.

Existing systematic reviews have evaluated either the psychological or pharmacological treatment of mental health problems in people with intellectual disabilities. Cognitive behavioural therapies (CBT) were found to have moderate positive treatment effects for people with intellectual disabilities who experience anger problems, anxiety and depression [15–17], but these findings are limited to adults with mild to moderate intellectual disabilities, however, as children or individuals with severe and profound intellectual disabilities were not represented in the primary studies. Reviews of pharmacological interventions have largely focused on behaviour problems independent of their association with mental health problems. For example, potentially effective interventions for behaviour problems in adults with intellectual disabilities include risperidone, lithium and anti-epileptic mood stabilisers [18,19]. However, the methodological quality of the evidence and registered adverse effects indicate that the use of these pharmacological agents requires caution [18,19]. Whilst behaviour problems can be associated with mental health problems and take on a precipitating or perpetuating role, they are more indicative of emotional dysregulation than of psychiatric symptomatology, and have been demonstrated in robust studies to be distinct from other types of mental health problems [20]. We have not identified reviews on treatment response and side-effects to pharmacotherapies for other types of mental health problems experienced by people with severe and profound intellectual disabilities. The objective of the present systematic review was to evaluate the effectiveness of psychological and pharmacological treatments for mental health problems and their key symptoms in both children and adults with severe or profound intellectual disabilities.

METHODS

The review was conducted and written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [21]. The review protocol was registered with PROSPERO, Centre for Reviews and Dissemination, under the reference number CRD 42015024469.

Search strategy

The search strategy was developed for two conjoint systematic reviews focused on the evaluation of measures of mental health problems and interventions respectively in people with severe and profound intellectual disabilities. Although separate search terms were used for each systematic review, records identified through the respective searches were pooled together prior to the study eligibility screening to ensure that studies piloting an assessment as an intervention outcome measure would also be identified.

Initial systematic searches were conducted in the week of 13 to 17 July 2015 for the following databases: PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, Cochrane Central Register of Controlled Trials (CENTRAL). Searches used Boolean terms to combine search strings for intellectual disabilities, mental health, and psychological or pharmacological interventions. A sample search strategy for the PsycINFO, PsycTESTS and ASSIA searches is provided in the appendix. Full search strategies for each database can be requested from the authors.

Searches were updated in September 2017, to cover the time period from the original searches, and no new studies were identified from these searches. The updated searches followed the same search strategy and study screening protocol as the original searches.

Study eligibility criteria

The following inclusion criteria were applied to (1) publication type, (2) study design, (3) participants, (4) interventions, and (5) outcomes.

(1) Publication. Peer-reviewed publications written in English, French, German or Dutch were eligible for review.

(2) Study design. The following study designs were eligible for inclusion in the review: (a) randomised controlled trials, (b) controlled trials without randomisation, (c) single group pre-post designs, (d) case series with outcome measures reported as group mean data, (e) single-case experimental designs, and (f) case-control studies. Observational and retrospective cohort studies, as well as case studies without a control condition or a return to baseline were excluded.

(3) Participants. To ensure that the outcome data were representative for people with severe and profound intellectual disabilities it was required that either a minimum of 70% of participants were diagnosed or reported as having severe or profound intellectual disabilities, or that data for participants with severe or profound intellectual disabilities were reported separately in the study. Although this was an arbitrary criterion, this was to ensure that a majority of people with severe or profound intellectual disabilities were in the study samples. Studies that did not provide any usable information about the level of intellectual disabilities within samples were excluded. No exclusions were applied concerning participants' age or gender or any other characteristics except for degree of intellectual disability.

(4) Intervention. Eligible psychological interventions were delivered by a trained lay therapist or qualified professional who systematically applied interventions based on well-established psychological principles and techniques directly to the person with an intellectual disability, either individually or in a group. For pharmacological interventions, it was expected that the pharmaceutical agent was given with regular review by a qualified medical practitioner or health professional, and recognised at least in principle as a potential treatment for a mental health problem/symptom.

(5) Outcomes. Eligible outcomes were standardised assessments of mental disorders or their key symptoms which have a significant impact on daily functioning. However, we acknowledge that defining the mental and physical components of mental and physical disorders into mutually exclusive categories can be challenging, not in the least because certain components are symptomatic of multiple disorders and certain disorders have shown high rates of co-morbidity with one another. For the purpose of this systematic review, the inclusion criteria for mental disorders and their symptoms were derived from the DSM-IV [22], as this version was most likely to be used by the primary studies to be identified by the systematic review. Mental and behavioural disorders, and their key symptoms, eligible for review fell within the following classifications: (a) attention-deficit and disruptive behaviour disorders, (b) tic disorders, (c) other disorders of infancy, childhood, or adolescence, (d) schizophrenia and other psychotic disorders, (e) mood disorders, (f) anxiety disorders, (g) somatoform disorders, (h) factitious disorders, (i) dissociative disorders, (j) eating disorders, (k) adjustment disorders, and (l) personality disorders.

Studies focused on key symptoms of mental disorders were included as not all treatment offers a holistic approach, and interventions may instead aim to alleviate one or more symptoms of a disorder. By contrast, challenging behaviours and behaviour problems may be associated with or indicative of underlying mental disorders [20,23] but are not recognised as a key diagnostic feature of the above listed mental disorders and are hence excluded from this review.

The broad scope of the systematic review in terms of study designs, type of interventions and range of participants was advised as initial scoping searches indicated that only few studies included individuals with severe and profound intellectual disabilities.

A single post-hoc exclusion criterion was applied to exclude records from the searches published prior to 1980 (n=106 records, but not fully checked for inclusion criteria), coinciding with the publication of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III); [24]. This assured a minimal level of consistency in the recognition and diagnosis of mental health problems from DSM-III through to DSM-IV. It is likely that there would have been a delay between the publication of the DSM-III and its first use in published research, but searches back to 1980 were essential to ensure that no potentially relevant studies were missed.

Study selection

Data collection and abstract screening were performed by the first author (LV). Twenty percent of records were also screened by the second author (SF), leading to an overall agreement rate of 99.8 % and a Kappa coefficient of 0.91 for studies to proceed to full text evaluation. Second screening a proportion of results is an accepted practice when a review is large and resources are limited [25]. The overall inclusion rate for the screening of titles and abstracts was 2.3 %. Full-text review of 573 articles was performed independently by the two reviewers (LV and SF), which resulted in a Kappa coefficient of 0.76 for inclusion in the review and the data extraction stage. Eleven disagreements between the two reviewers were resolved through joint discussion. All disagreements concerned the proporption of participants with severe and profound intellectual disabilities and were not related to study design, intervention or outcomes. The review of one full text article required consultation with the third author (RH) to determine whether this study met the review eligibility criteria regarding mental health outcomes. Upon discussion, the paper was excluded from the review.

Next, reference lists and citation records of all included studies were screened to identify additional papers that may not have fulfilled the search term criteria. No additional studies were identified in this way.

Data extraction and quality synthesis

Data extraction was conducted by the second author and reviewed by the first author for variables including: study design, study population, intervention, outcome measures, and follow-up data.

The certainty in the evidence for each outcome measure could not be assessed with the GRADE approach [26–28], as used by the Cochrane collaboration and national guideline organisations such as NICE in the UK, due to the incomparability of identified studies in terms of study design, interventions, and outcomes. Likewise, it was not possible to conduct a meta-analysis or provide other summary measures because no two studies addressed the same mental health problem using a similar intervention.

Both reviewers independently performed a critical appraisal of all included studies. No disagreements were recorded at either stage. The assessment followed the Critical Appraisal Skills Programme [29,30] checklists or the quality indicators for within single-subjects research [31], dependent on the study design.

Patient and public involvement

Patients and public were not involved in the conception, development or implementation of this systematic review, nor in the selection of outcome measures and the interpretation of the study findings.

RESULTS

The search strategy for the conjoint systematic review identified 24,883 unique records, of which 573 were retained for full-text eligibility screening. The study selection process is illustrated in Figure 1. Excluded articles most commonly did not meet the eligibility criteria concerning the severity of intellectual disabilities of study participants (n = 242). Initial records were also excluded based on their study design (n = 113), a publication date prior to 1980 (n = 106), because the intervention or outcomes were not focused on recognised mental health problems (n = 59), due to their publication

status (e.g. conference abstracts; n = 38), or because the full-text paper could either not be retrieved (n = 6) or was published in a non-eligible language (n = 4). In total, five studies were included in the review and are described in Table 1. Three studies included only adults with intellectual disabilities: a double-blind placebo-controlled crossover trial [32] and a single-case experimental reversal design of pharmacotherapy [33], as well as a single-case experimental reversal design of a psychological intervention [34]. Two studies included children and young people: a randomised trial of pharmacotherapy by White and Aman [35] and a single-case study of a psychological intervention for a 13-year old girl [36].

[Figure 1 about here]

Table 1

Characteristics of pharmacological and psychological interventions studies.

First author (Year)	Study Design[a]	Participants	Intervention	Outcomes	Follow-up
Psychopharmacological interventions					
Aman (1986)	Double-blind placebo-controlled crossover trial Within-group randomisation I1: Imipramine I2: placebo 1-week washout period between interventions	Adults with depressive and affective symptoms N = 5 (2M/3F) Age range: 18 – 23 years intellectual disabilities severity: Slosson IQ[b] range 10 -14	Imipramine (Dumex) or placebo Duration: 4W Dose: 3 mg/kg/day Setting: residential ward	Imipramine caused symptom deterioration for ABC[c] scores related to irritability, lethargy, and hyperactivity. No intervention effects were observed for: stereotypy and inappropriate speech. Statistical data only provided for analyses including a second intervention group, non-eligible for review.	No follow-up
Rosenquist (1997)	Single-case experimental reversal design (ABABA) A, Baseline B, Haloperidol Single blind, masked	Adult with Gilles de la Tourette syndrome N = 1, Female Age = 35 years Severe intellectual disabilities	Haloperidol Duration: 22W, A: 2W baseline B: 8W intervention A: 2W baseline B: 8W intervention A: 2W baseline	Weekly observations using Behavioral Observation and Tic Checklist[d] of 3 videotaped conditions: (1) table setting task, (2) mealtime, and (3) waiting. Pre-post % time (SD)	W6 of increased dosage % time (SD) engaged in tic behavior at W6 (dose 10 mg/day): Mealtime: SM-tic: 6.3 (6)

	assessment		Dose: -W1: 1 mg/day -W2: 2mg/day -W3-4: 5 mg/day -W5-6: 10 mg/day -W7-8: washout Setting: community group home	engaged in tic behavior at baseline and W1 (dose 1mg/day): Mealtime: SM-tic: 34.8 (20); 11.0 (12) CM-tic: 13.6 (10); 5.3 (8) SV-tic: 35.4 (28); 2.0 (4) CV-tic: 1.3 (3); 0.0 (0) Waiting: SM-tic: 46.8 (31); 20.8 (26) CM-tic: 41.2 (19); 25.3 (21) SV-tic: 65.3 (29); 69.6 (25) CV-tic: 42.5 (18); 23.0 (18)	CM-tic: 3.0 (3) SV-tic: 1.0 (3) CV-tic: 1.0 (2) Waiting: SM-tic: 24.7 (20) CM-tic: 41.5 (18) SV-tic: 48.4 (26) CV-tic: 34.8 (20) Dose-specfic improvements (10mg/day), reversible
White (1985)	Double-blind placebo-controlled crossover trial I1: Pimozide I2: Placebo Randomisation within participants	Inpatients with serious behaviour disturbances, including hyperactivity N = 8, 7M/1F Mean age 15.7 years (SD = 3.42) intellectual disabilities severity: moderate to profound; mean IQ =	Pimozide or placebo Baseline: 4W Intervention: 4W + 4W Dose: I1: 6 mg/day Setting: no info	ANCOVA for drug effects and baseline as covariate on ABC subscales Pimozide has an effect: Irritability: F = 11.78 Hyperactivity: F = 7.69 No significant effects	No follow-up

	1-week washout period between interventions	20.4 (SD = 12.11)		for: Lethargy: F = 0.84 Stereotypy: F = 3.48 Inappropriate speech: F = 1.31	
Psychological interventions					
Lindauer (1999)	Single-case experimental reversal design (ABAB) A, Baseline: empty room & quiet hands procedure B, Enriched Environment & quiet hands	Mood disorder, major depression N = 1, Female Age = 23 years Severe intellectual disabilities	Enriched environment: 12 items selected for inclusion by paired-choice assessment Duration: 57 sessions; A: 11 sessions B: 5 sessions A: 29 sessions B: 12 sessions Dose: 10 minute sessions Setting: Laboratory, padded room	Percentage of 10-s intervals of signs of negative and positive affect Pre: relatively high levels of negative affect (M = 27.4%) and low levels of positive affect (M = 2.3%) Post: negative affect decreased (M = 0.1%) and positive affect increased, especially during B2 (M = 11.5% across phases).	No follow-up
Zarkowska (1989)	2 Single-case experimental reversal designs (ABA) I1: Relaxation: A, Baseline: school activity, tics ignored B, relaxation A, Baseline: return to	Gilles de la Tourette syndrome N = 1, Female Age = 13 years Severe intellectual disabilities (Griffiths Mental Development Scale score ranged	I1: verbal instructions for relaxation exercises and praise when calm Duration: 10 minutes I2: verbal interruption following the occurrence of a verbal tic	I1 reduced tic frequency during relaxation but return to baseline after intervention I2 increased vocal tic frequency.	No follow-up

	school activity, tics ignored I2: interruption A, Baseline: school activity, tics ignored B, interruption A, Baseline: return to school activity, tics ignored	from 17 to 42 months)	Duration: 10 minutes	After I1 and I2: No generalised reduction in tic frequency

Note. I1, intervention 1; I2, intervention 2; G1, group 1; G2, group 2; Gender ratio expressed as Male/Female; W1, week 1; SD, standard deviation. Outcomes reported for primary outcome measure only, unless where mental health or mental well-being outcome measure were recorded as secondary outcome measures.

[a] AB designs with A: baseline and B: treatment.

[b] Slosson IQ scores correlate highly with Stanford Binet Intelligence Test scores and correlate with the Cattell Infant Intelligence Scale when used with children under the age of 2 (Slosson, 1975).

[c] ABC, Aberrant Behavior Checklist.

[d] SM-tic, simple motor tic; CM-tic, complex motor tic; SV-tic, simple vocal tic; CV-tic, complex vocal tic.

Psychological interventions

Two studies evaluated interventions based on psychological principles. Interventions were offered for symptoms of depressive disorder and to manage tic frequency in Gilles de la Tourette syndrome.

In a single-case experimental ABAB design, Lindauer and colleagues [34] offered an enriched environment for the management of major depressive disorder in a 23-year old woman with severe intellectual disabilities who also presented with self-injurious behaviour. Pre-existing treatment of the mood disorder with carbamazepine (5.3 mg/kg/day) was continued during the study. The enriched environment setting was a 3 metre by 3 metre padded room, in an inpatient unit, in which stimuli were present that were chosen following a paired-choice assessment to identify the woman's preferred stimuli and assess signs of positive and negative affect. Smiling, giggling and laughing were considered examples of positive 'affect', whereas frowning, whining, crying and verbal expressions such as "I am sad" were identified as signs of negative 'affect'. No other outcome measures relating to the mood disorder were employed. Behavioural observations, through a one-way mirror, showed that the enriched environment increased signs of positive affect and decreased signs of negative affect, in particular during the second intervention phase. The lack of follow-up measures and the delivery of interventions in a padded room in an inpatient setting reduce the ecological validity of this intervention. Likewise, the replicability of findings is impeded in terms of participant selection and intervention fidelity (see Table 2).

Zarkowska et al. [36] adopted a basic single-case experimental design to examine interventions for vocal and motor tics in a 13-year old girl with Gilles de la Tourette syndrome and severe intellectual disabilities. Two treatment probes, cued relaxation and interruption, were evaluated using an ABA return to baseline design for each intervention comprised of a five minute baseline recording, a five minute intervention, and a five minute post-baseline recording. Cued relaxation appeared to lead to better outcomes but neither intervention had lasting effects and interruption increased vocal tic frequency. The study design showed strong external and social validity and provided clear descriptions of dependent and independent variables (see Table 2). However, internal

validity was weak and the ABA design was not the most suitable for demonstrating experimental control. Following the evaluation of treatment probes, the study continued as an A-B case study implementing successive interventions of relaxation training, treatment with clonidine and treatment with pimozide. Due to the non-controlled nature of these interventions, their respective outcome data and follow-up data were not considered eligible for inclusion in this review.

The replicability of findings from both studies is hindered by a lack of information regarding participant selection, physical setting of the intervention, implementation fidelity, and the reliability of outcome measurements.

Table 2

Quality appraisal of single-subject studies using the Quality Indicators Within Single-Subject Research [31] .

Quality indicator	Lindauer et al. (1999)	Rosenquist et al. (1997)	Zarkowska (1989)
Participant description and setting			
Ability to select individuals with similar characteristics	yes	yes	yes
Replicability of participant selection process	no	no	no
Replicability of physical setting	yes	yes	partial
Dependent variable			
Described with operational precision	yes	yes	yes
Measured to generate a quantifiable index	yes	yes	yes
Measure is valid and replicable	yes	yes	yes
Measurements repeated over time	yes	yes	no
Measures assessed in terms of reliability or inter-	yes	yes	no

observer agreement			
Independent variable			
Described with replicable precision	yes	yes	yes
Systematically manipulated and under control of experimenter	yes	yes	yes
Overt measure of implementation fidelity	no	not applicable	no
Baseline			
Repeated measurements baseline	yes	yes	no
Described with replicable precision	yes	yes	yes
Experimental control / Internal validity			
Minimum of 3 demonstrations of experimental effect at 3 points in time	yes	yes	no
Controlling for threats to internal validity	unclear	yes	unclear
Document a pattern of experimental control	yes	yes	yes
External Validity			
Effects replicated across participants, settings, or materials	yes	yes	no
Social validity			
Dependent variable is socially important	yes	yes	yes

Magnitude of change is socially important	yes	yes	yes
Implementation of independent variable is practical and cost-effective	yes	yes	yes
Implementation of independent variable over extended period of time, by typical intervention agents and in typical contexts	yes	yes	yes

Pharmacological interventions

Two double-blind placebo-controlled crossover trials and one single-case experimental reversal design evaluated pharmacological interventions for use in people with severe intellectual disabilities and mental health problems.

Aman and colleagues [32] employed within-group randomisation of order of administration of 4 week treatment with imipramine, in a dosage of 3 mg/kg/day, and 4 weeks with placebo, with one week drug-free in between. Interventions were offered to five adults with severe intellectual disabilities and depressive symptoms, in addition to a group of five adults with acting-out behaviours. The latter were not eligible for inclusion in this review as these behaviours were not considered a mental health problem. Eligible depressive symptoms were based on evidence from prior research studies and required behavioural observation instead of information obtained from diagnostic interviews. Symptoms included 'seclusion and social withdrawal, sleep loss, weight loss, tearfulness or the appearance of sad affect, and a pervasive lack of overt behavior' [31, p. 265]. Intervention effects were assessed with the Aberrant Behavior Checklist [37] and indicated imipramine to have a detrimental effect on symptoms related to irritability, lethargy, and hyperactivity, and no effect on stereotypical behaviours and inappropriate speech. Adverse effects were recorded but not described separately for the five adults with severe intellectual disabilities and depressive symptoms. For one person with affective symptoms, imipramine was found to improve behaviour and relieve chronic constipation.

White and Aman [35] evaluated the use of pimozide on maladaptive behaviours and hyperactivity, in young people and adults with moderate to profound intellectual disabilities.

Following a four-week baseline, the eight participants received two four-week treatments with either pimozide, in a dosage of 0.12 mg/kg/day, or placebo, with a one-week washout period between intervention phases. Treatment effects were evaluated using assessments with the ABC for the last three weeks of each intervention. Hyperactivity scores on the ABC reduced following the intervention, as did irritability levels, based on nurses' behaviour ratings of participants. No intervention effects were observed for ABC lethargy, stereotypy, and inappropriate speech domains. Furthermore, behavioural observations also did not identify any treatment effects.

The methodological quality of these two studies was confirmed using the CASP quality appraisal checklist (see Table 3). However, follow-up measures were notably absent and sample sizes too small to provide sufficient power for the conducted statistical analyses. Additionally, the period of treatment was of too short duration, as imipramine can take up to 6 weeks to be effective in the general population, so that intervention was of poor design.

Table 3

Critical Appraisal Skills Programme (CASP Checklists)[38] for studies with N > 1.

Quality indicator	Aman et al. (1986)[a]	White et al. (1985)[a]
Validity of the results		
Study addresses a clearly focused issue	yes	yes
Cohort recruited in an acceptable way	yes	yes
Exposure accurately measured to minimise bias	yes	yes
Outcome accurately measured to minimise bias	yes	yes
Identification of all important confounding factors	yes	yes
Design and/or analysis account for confounding factors	No: length of intervention too short to observe	No: length of intervention too short to observe

	treatment effects.	treatment effects.
Complete enough follow-up of participants	no	no
Long enough follow-up of participants	no	no
Scope of the results		
Description of study results	yes	yes
Precision of study results	No exact p-values, no effect sizes, no differentiation between depressive-like and acting-out group	No exact p-values, no effect sizes
Believability of study results	yes	yes
Impact of the results		
Results applicable to local population	Yes	Yes
Results in line with available evidence	no	Yes
Implications for practice	Length of intervention too short to draw conclusions regarding implications	The study is now out-dated given improved knowledge on the risks of the long-term use of the drug

Note. [a] CASP Checklist for Randomised Controlled Trials.

The only fully experimental single subject experimental design study evaluated the effect of haloperidol on tic frequency in a 35-year old woman with Gilles de la Tourette syndrome and severe intellectual disabilities [33]. Using an ABABA design, the dose of haloperidol was gradually increased during the intervention phases and maximal effectiveness was reached with the highest dosage of 10 mg/day. Weekly behavioural observation at the community residential setting where the participant lived showed reduced tic frequencies during mealtimes, nearing zero-levels, and during waiting times. Intervention effects reversed when the dose was lowered. These findings are considered reliable due to masked assessment and reversal design, alongside the replicability of measures and intervention, see Table 2.

Overall quality appraisal of the evidence base

Methodological quality of the identified studies was poor, with concern in terms of small sample sizes, lack of masked assessment, and lack of follow-up measures. By contrast, reporting standards were generally high in terms of variable descriptions and the internal and external validity of the results. Implications of the quality appraisal are integrated in the study descriptions above, whereas a detailed overview of the quality review for each study is reported in Tables 2 and 3.

DISCUSSION

Despite their very high rates of mental health problems, there is a lack of research in interventions that explicitly target mental health problems in people with severe and profound intellectual disabilities. The scope of this review was wide. However, only five studies were eligible for inclusion and the findings are inconclusive at best. This is highly problematic for clinicians who have to manage these disorders and can only rely upon the use of interventions designed for the general population, despite the likely limitations/inaccessibility of these for people with severe intellectual disabilities.

Haloperidol was demonstrated to improve tics, but in a single person. Pimozide was reported to reduce hyperactivity and other behaviour problems [35], but it is not a recognised treatment for hyperactivity in the general population; and NICE concludes that there is no evidence that antipsychotics drugs are of use in this condition (NICE, 2016). Whilst it can calm disturbed patients in the short term through its sedative properties, it is not recommended for this use longer term in view of

potential side-effects which includes death, with its use being reserved for schizophrenia only. Whilst meeting the inclusion criteria of the review, the study is therefore out-dated given subsequent advances in knowledge about this class of drugs. Imipramine caused deterioration of affective symptoms, but the study was poorly designed by today's standards, including the drug not being prescribed for long enough duration to be effective [32]. Additionally, the use of imipramine has declined in the whole population since the introduction of selective serotonin reuptake inhibitors in the 1980s and other newer antidepressant agents, on the basis of side-effect profile. Empirical evidence for current pharmacological interventions has not yet been published.

Evidence for the effectiveness of psychological interventions is also weak in the absence of controlled trials or high quality single case experimental designs (such as multiple baseline approaches). Across intervention types, two studies aimed to reduce tic frequency in people with severe intellectual disabilities and Gilles de la Tourette Syndrome yielding putative positive effects for relaxation techniques and treatment with haloperidol. Evidence relating to common mental health problems (e.g., anxiety, depression) was notably very limited. Studies including children with severe and profound intellectual disabilities involved different interventions than for studies with adults and while the geographic spread of the research was diverse, all included studies were conducted in English speaking countries. Overall, a quantitative synthesis of the evidence was not possible due to the heterogeneity of the identified studies as no two studies addressed the same mental health problem with a similar intervention or similar outcome measures. Furthermore, the total sample size across the five identified studies was only sixteen participants: nine children and seven adults, nine male and seven female. Finally, the review demonstrates that research in this area has stalled over the last decade. The most recent study we identified was published nearly two decades ago [34], whilst the methodologically stronger studies using controlled design employed outdated pharmacotherapies that are currently not recommended due to their potential side-effects [36, 39].

Strengths and limitations

Strengths of this systematic review are the rigour with which it was conducted. In line with PRISMA guidelines, the prior publication of the review protocol enhances its transparency and replicability, whilst double reviewing of full-length articles and quality appraisal strengthens the

findings. The current review improves upon previous reviews in this area by employing a broader scope to identify both psychological and pharmacological interventions for a range of mental health problems.

Limitations of the study relate to the search strategy. The systematic search did not include terms for every specific possible disorder or potential treatment, neither did it include a wide range of behavioural descriptions. In spite of this, we identified a considerably large number of potential records. Meanwhile, requiring at least 70% people with severe and profound intellectual disabilities to be included in a sample where outcomes are not reported separately for this group was a pragmatic decision so people with severe and profound intellectual disabilities would be sufficiently represented in the review findings. However, reducing the required proportion of participants with severe and profound intellectual disabilities to 50% would not have added any eligible studies (a post-review check completed by the first author).

Explanations and implications

A major challenge in mental health research for people with severe and profound intellectual disabilities, including this systematic review, lies with the selection of study outcomes. The appropriateness of measures such as the ABC [37] can be questioned when used to assess the wide spectrum of symptoms of mental health problems. However, the ABC was found to be one of the few reliable measures relating to mental health problems for individuals with severe and profound intellectual disabilities [38]. Indeed, behavioural outcomes can assess key symptoms of mental disorders according to ICD-10 criteria, but can equally be associated with distress and reduced quality of life. Whilst this diagnostic taxonomy was practical for conducting the systematic review, it may not be sufficient to evaluate all relevant interventions aimed at improving the general well-being of people with severe and profound intellectual disabilities.

The scarcity of trials addressing the mental health needs of people with severe and profound intellectual disabilities is worrisome in light of the fact that they do experience mental health problems. Yet, there is awareness of the mental health needs in this population amongst researchers and clinicians as is evident from the wide range of descriptive case reports, which did not provide empirical evidence for the effectiveness of an intervention. On a positive note, the 101 studies

identified as including at least some individuals with severe and profound intellectual disabilities show that this population is not routinely excluded from clinical practice evaluations. Although beyond the objectives of this systematic review, a scoping overview of the range of interventions evaluated in these studies and those being offered in routine clinical practice could help set the direction to guide future research. Establishing evidence-based interventions to treat mental health problems in people with severe and profound intellectual disabilities requires more research with stronger methodological designs.

Future directions

Challenging the status quo and developing an evidence base from which to treat people with severe and profound intellectual disabilities and mental health problems is a joint responsibility of practitioners and researchers. Bi-directional knowledge transfer is particularly important in this regard: research into severe and profound intellectual disabilities making its way into the training of practitioners, as well as practitioners highlighting difficulties in assessment and treatment that need addressing. Commissioning and exploring funding opportunities to conduct research into evidence-based pharmacological and psychological interventions, and an open discussion regarding the ethical considerations of research involving people who may lack the capacity to consent also require attention. A large inequality in evidence for effective treatments for mental health problems is experienced by children and adults with severe and profound intellectual disabilities. Until this inequality is adequately addressed, health services need to provide treatments found to be effective for people with mild to moderate intellectual disabilities where they exist- although the availability of interventions for this population is also poor in comparison to interventions for people without intellectual disabilities. Particular attention should be given to how these treatments might affect people with severe and profound intellectual disabilities differently regarding symptom presentation and outcome assessment, accessibility of a range of psychological therapies, and side effect reporting which may indicate a need for differences in dosing regimens. Keeping detailed accounts of how treatments were subsequently modified will benefit the development of a more solid evidence base.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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Authors' contributions

RH, DA, UC, S-A C, NG, CH, KH, AJ, PEL, RMN, CO, AR, VT, JW, Nigel Beail, Michael Kerr and Howard Ring conceived the study and acquired funding. LV and RH designed and registered the review protocol. LV and SF conducted the systematic searches, study selection and data collection. LV wrote the manuscript.

All authors provided methodological and clinical perspectives, commented on manuscript drafts and read and approved the final version of this manuscript.

Figure 1. PRISMA Flow Diagram

Data sharing statement

To obtain the full search strategies for each database please contact leen.vereenooghe@uni-bielefeld.de or s.flynn.1@warwick.ac.uk.

This systematic review presents previously published data. Please refer to the original articles and their authors for these research data.

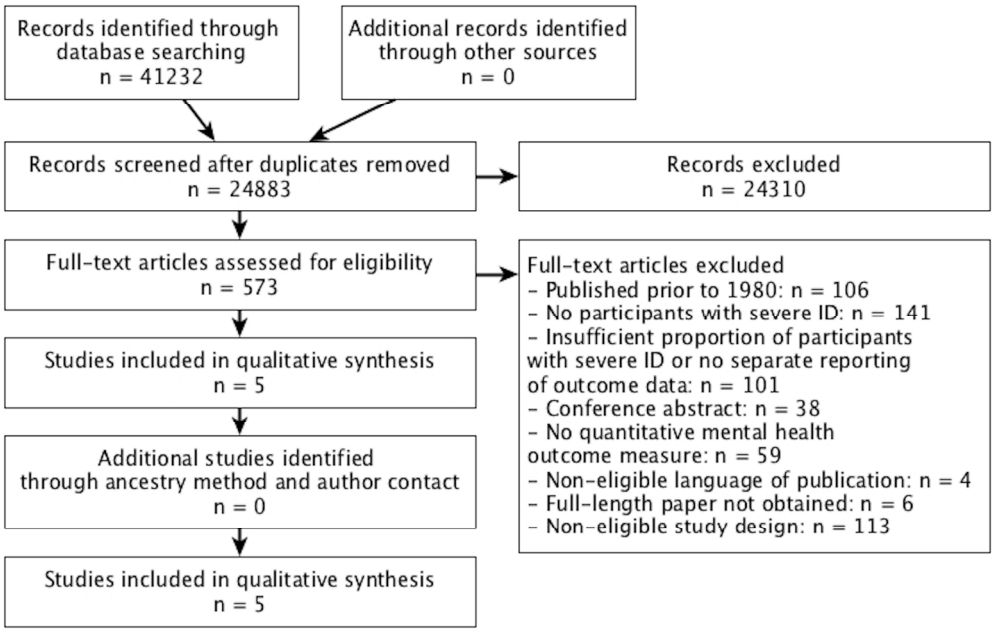

Figure 1. PRISMA Flow Diagram

244x155mm (300 x 300 DPI)

Appendix

Table 1

Search strategy for simultaneous database searches of PsycINFO, PsycTESTS and ASSIA using ProQuest database host.

	Search terms	Results
	Intellectual disabilities	
1	SU.EXACT.EXPLODE("Intellectual Development Disorder")	37548
2	TI(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*)) OR AB(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*))	38279
3	TI(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder)) OR AB(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder))	36985
4	TI(moron OR imbecile OR feeble-minded OR subnormal OR retard) OR AB(moron OR imbecile OR feeble-minded OR subnormal OR retard)	4289
5	TI(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*)) OR AB(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*))	16059
6	TI((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*) OR AB((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*)	11067
7	OR/ 1-6	105392
	Mental health	

8	SU.EXACT.EXPLODE("Depression (Emotion)")	22448
9	SU.EXACT.EXPLODE("Anxiety Disorders") OR SU.EXACT.EXPLODE("Generalized Anxiety Disorder") OR SU.EXACT.EXPLODE("Anxiety") OR SU.EXACT.EXPLODE("Social Anxiety")	124637
10	TI(anger NEAR/3 (problem* OR disorder*)) OR AB(anger NEAR/3 (problem* OR disorder*))	1212
11	TI(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*) OR AB(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*)	272855
12	TI(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*)) OR AB(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*))	226542
13	TI(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*) OR AB(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*)	273779
14	OR/ 8-13	655607
Mental well-being		
15	TI(psycho* NEAR/2 function*) OR AB(psycho* NEAR/2 function*)	23372
16	TI(well* OR health*)	207285

17	TI((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*)) OR AB((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*))	193401
18	TI(quality NEAR/2 life)	19555
19	OR/ 15-18	358684
Psychological interventions		
20	TI((psychological N/3 therap*) OR psychotherap* OR counsel*) OR AB((psychological N/3 therap*) OR psychotherap* OR counsel*)	196693
21	TI(psychoanaly* OR psychodynamic*) OR AB(psychoanaly* OR psychodynamic*)	90160
22	TI((behavior* OR behaviour* OR cognitive) N/2 therap*) OR AB((behavior* OR behaviour* OR cognitive) N/2 therap*)	39534
23	TI((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*) OR AB((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*)	25851
24	TI((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*) OR AB((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*)	1984
25	TI(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive") OR AB(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive")	10630
26	TI((group OR individual) N/2 therap*) OR AB((group OR individual) N/2 therap*)	25884
27	TI(anger N/2 (manag* OR train*)) OR AB(anger N/2 (manag* OR train*))	1612

28	TI((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*) OR AB((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*)	17343
29	OR/ 20-28	342375
Pharmacological interventions		
30	TI(pharmacotherapy* OR pharmacolog* OR pharmacological therap*) OR AB(pharmacotherapy* OR pharmacolog* OR pharmacological therap*)	49958
31	TI(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*) OR AB(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*)	41884
32	TI(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*)) OR AB(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*))	6622
33	TI(tricyclic antidepressant OR anti-depress* OR antidepress*) OR AB(tricyclic antidepressant OR anti-depress* OR antidepress*)	34457
34	TI(adrenergic blocking drugs OR monoamine oxidase inhibitors) OR AB(adrenergic blocking drugs OR monoamine oxidase inhibitors)	1905
35	TI(anxiolytic* OR antipanic* OR antianxiety) OR AB(anxiolytic* OR antipanic* OR antianxiety)	7153
36	TI(anticonvulsant*) OR AB(anticonvulsant*)	4142
37	TI(lithium*OR lithium carbonate OR SSRI* OR "selective serotonin reuptake inhibitor" OR serotonin reuptake inhibitor OR serotonin antagonist) OR AB(lithium*OR lithium carbonate OR SSRI* OR "selective serotonin reuptake inhibitor" OR serotonin reuptake inhibitor OR serotonin antagonist)	12261

38	TI(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine) OR AB(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine)	61771
39	OR/ 30-38	153952
Final search string		
40	7 AND (14 OR 19) AND (29 OR 39)	2607

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n/a

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	17, 20
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	16, 19, 20
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	24
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	25
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	27

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Interventions for mental health problems in children and adults with severe intellectual disabilities: A systematic review

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Primary Subject Heading:	Mental health
Secondary Subject Heading:	Pharmacology and therapeutics
Keywords:	MENTAL HEALTH, intellectual disabilities, systematic review, psychological therapies, pharmacotherapies

Interventions for mental health problems in children and adults with severe intellectual disabilities: A systematic review.

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Word count: 4483

ABSTRACT

Objective: Mental health problems are more prevalent in people with than without intellectual disabilities, yet treatments options have received little attention. The aim of this study was to identify and evaluate the effectiveness of pharmacological and psychological interventions in the treatment of mental health problems in children and adults with severe and profound intellectual disabilities, given their difficulties in accessing standard mental health interventions, particularly talking-therapies, and difficulties reporting drug side-effects.

Design: A systematic review using electronic searches of PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, and CENTRAL was conducted to identify eligible intervention studies. Study selection, data extraction and quality appraisal were performed by two independent reviewers.

Participants: Study samples included at least 70 % children and/or adults with severe or profound intellectual disabilities or reported the outcomes of this subpopulation separate from participants with other levels of intellectual disabilities.

Interventions: Eligible intervention studies evaluated a psychological or pharmacological intervention using a control condition.

Outcomes: Symptom severity, frequency or other quantitative dimension (e.g., impact), as assessed with standardised measures of mental health problems.

Results: We retrieved 41,232 records, reviewed 573 full-text articles and identified 5 studies eligible for inclusion: 3 studies evaluating pharmacological interventions, and 2 studies evaluating psychological interventions. Study designs ranged from double-blind placebo-controlled crossover trials to single-case experimental reversal designs. Quality appraisals of this very limited literature base revealed good experimental control, poor reporting standards, and a lack of follow-up data.

Conclusions: Mental ill-health requires vigorous treatment, yet the current evidence base is too limited to identify with precision effective treatments specifically for children or adults with severe and profound intellectual disabilities. Clinicians therefore must work on the basis of general population evidence, whilst researchers work to generate more precise evidence for people with severe and profound intellectual disabilities.

PROSPERO registration number CRD 42015024469

Keywords: intellectual disability, mental health, systematic review, psychological therapies, pharmacotherapies

Strengths and limitations of this study

- To our knowledge this is the first systematic review focused on interventions to improve the mental health of both children and adults with severe and profound intellectual disabilities.
- Review eligibility was not restricted to randomised controlled trials which limits the strength of the review's findings.
- The body of evidence we identified was very slim and does not allow for generalisation of findings for either psychological or pharmacological interventions.

INTRODUCTION

Intellectual disabilities affect approximately 1 percent of the population and are characterised by significantly impaired intellectual and adaptive skills with onset before adulthood. Their prevalence of mental health problems has been reported to be more than seven times higher than for the general population [1]. People with severe and profound intellectual disabilities, as indicated by an intelligence quotient of less than 40, have limitations in problem-solving skills, cognitive and communication skills which can affect their ability to cope with stressful life events. The life circumstances of people with an intellectual disability may increase their risk of developing mental health problems or experiencing mental distress. Factors that have been identified as protective in adults without intellectual disabilities, such as employment opportunities, meaningful day activities and socially supportive networks, may be less likely to be present for people with intellectual disabilities and with additional impact for those with severe and profound intellectual disabilities compared to those with mild or moderate intellectual disabilities [2–4]. Genetic factors may further increase the vulnerability of some people with intellectual disabilities for mental health problems, as evidenced by significant comorbidity rates of anxiety problems and psychosis in people with intellectual disabilities and certain genetic syndromes [5–9].

Mental health problems are as common in people with severe and profound intellectual disabilities as in people with mild or moderate intellectual disabilities, reported to have a point prevalence of 22.4% [10–14]. Their treatment of mental health problems requires particular attention for three main reasons. First, longitudinal research investigating the mental health of children and young people with intellectual disabilities over a 14 year period suggest recovery may be poorer for those with severe intellectual disabilities, and therefore standard treatments may be sub-optimal [10–12]. Second, given their limitations in communication skills and understanding, people with severe and profound intellectual disabilities cannot be assumed to find talking therapies such as CBT-based interventions as accessible as other people do; yet these therapies are considered first line treatments of choice for many types of mental health problems. Third, it is possible that people with intellectual disabilities are more sensitive to the side effects of pharmacotherapies, or have greater difficulties in reporting side-effects when these occur, so raising the potential of more serious consequences, and the

need for different dosing regimes compared with other people. The high prevalence and potentially persistent mental health problems experienced by people with severe and profound intellectual disabilities thus call for effective interventions to treat such problems and to promote well-being.

Existing systematic reviews have evaluated either the psychological or pharmacological treatment of mental health problems in people with intellectual disabilities. Cognitive behavioural therapies (CBT) were found to have moderate positive treatment effects for people with intellectual disabilities who experience anger problems, anxiety and depression [15–17], but these findings are limited to adults with mild to moderate intellectual disabilities, however, as children or individuals with severe and profound intellectual disabilities were not represented in the primary studies. Reviews of pharmacological interventions have largely focused on behaviour problems independent of their association with mental health problems. For example, potentially effective interventions for behaviour problems in adults with intellectual disabilities include risperidone, lithium and anti-epileptic mood stabilisers [18,19]. However, the methodological quality of the evidence and registered adverse effects indicate that the use of these pharmacological agents requires caution [18,19]. Whilst behaviour problems can be associated with mental health problems and take on a precipitating or perpetuating role, they are more indicative of emotional dysregulation than of psychiatric symptomatology, and have been demonstrated in robust studies to be distinct from other types of mental health problems [20]. We have not identified reviews on treatment response and side-effects to pharmacotherapies for other types of mental health problems experienced by people with severe and profound intellectual disabilities. The objective of the present systematic review was to evaluate the effectiveness of psychological and pharmacological treatments for mental health problems and their key symptoms in both children and adults with severe or profound intellectual disabilities.

METHODS

The review was conducted and written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [21]. The review protocol was registered with PROSPERO, Centre for Reviews and Dissemination, under the reference number CRD 42015024469.

Search strategy

The search strategy was developed for two conjoint systematic reviews focused on the evaluation of measures of mental health problems and interventions respectively in people with severe and profound intellectual disabilities. Although separate search terms were used for each systematic review, records identified through the respective searches were pooled together prior to the study eligibility screening to ensure that studies piloting an assessment as an intervention outcome measure would also be identified.

Initial systematic searches were conducted in the week of 13 to 17 July 2015 for the following databases: PsycINFO, PsycTESTS, EMBASE, MEDLINE, CINAHL, ERIC, ASSIA, Science Citation Index, Social Science Citation Index, Cochrane Central Register of Controlled Trials (CENTRAL). Searches used Boolean terms to combine search strings for intellectual disabilities, mental health, and psychological or pharmacological interventions. Instead of listing all potential diagnosis and treatments the search strategy included the most common diagnoses and treatments in conjunction with more general mental health descriptions. This approach could limit the initial records to be screened, whereas relavant studies could still be identified through the ancestry method which screens citing and cited articles of included studies and through contact with authors. A sample search strategy for the PsycINFO, PsycTESTS and ASSIA searches is provided in the appendix. Full search strategies for each database can be requested from the authors.

Searches were updated in September 2017, to cover the time period from the original searches, and no new studies were identified from these searches. The updated searches followed the same search strategy and study screening protocol as the original searches.

Study eligibility criteria

The following inclusion criteria were applied to (1) publication type, (2) study design, (3) participants, (4) interventions, and (5) outcomes.

(1) Publication. Peer-reviewed publications written in English, French, German or Dutch were eligible for review.

(2) Study design. The following study designs were eligible for inclusion in the review: (a) randomised controlled trials, (b) controlled trials without randomisation, (c) single group pre-post

designs, (d) case series with outcome measures reported as group mean data, (e) single-case experimental designs, and (f) case-control studies. Observational and retrospective cohort studies, as well as case studies without a control condition or a return to baseline were excluded.

(3) Participants. To ensure that the outcome data were representative for people with severe and profound intellectual disabilities it was required that either a minimum of 70% of participants were diagnosed or reported as having severe or profound intellectual disabilities, or that data for participants with severe or profound intellectual disabilities were reported separately in the study. Although this was an arbitrary criterion, this was to ensure that a majority of people with severe or profound intellectual disabilities were in the study samples. Studies that did not provide any usable information about the level of intellectual disabilities within samples were excluded. No exclusions were applied concerning participants' age or gender or any other characteristics except for degree of intellectual disability.

(4) Intervention. Eligible psychological interventions were delivered by a trained lay therapist or qualified professional who systematically applied interventions based on well-established psychological principles and techniques directly to the person with an intellectual disability, either individually or in a group. For pharmacological interventions, it was expected that the pharmaceutical agent was given with regular review by a qualified medical practitioner or health professional, and recognised at least in principle as a potential treatment for a mental health problem/symptom.

(5) Outcomes. Eligible outcomes were standardised assessments of mental disorders or their key symptoms which have a significant impact on daily functioning. However, we acknowledge that defining the mental and physical components of mental and physical disorders into mutually exclusive categories can be challenging, not in the least because certain components are symptomatic of multiple disorders and certain disorders have shown high rates of co-morbidity with one another. For the purpose of this systematic review, the inclusion criteria for mental disorders and their symptoms were derived from the DSM-IV [22], as this version was most likely to be used by the primary studies to be identified by the systematic review. Mental and behavioural disorders, and their key symptoms, eligible for review fell within the following classifications: (a) attention-deficit and disruptive behaviour disorders, (b) tic disorders, (c) other disorders of infancy, childhood, or adolescence, (d)

schizophrenia and other psychotic disorders, (e) mood disorders, (f) anxiety disorders, (g) somatoform disorders, (h) factitious disorders, (i) dissociative disorders, (j) eating disorders, (k) adjustment disorders, and (l) personality disorders.

Studies focused on key symptoms of mental disorders were included as not all treatment offers a holistic approach, and interventions may instead aim to alleviate one or more symptoms of a disorder. By contrast, challenging behaviours and behaviour problems may be associated with or indicative of underlying mental disorders [20,23] but are not recognised as a key diagnostic feature of the above listed mental disorders and are hence excluded from this review.

The broad scope of the systematic review in terms of study designs, type of interventions and range of participants was advised as initial scoping searches indicated that only few studies included individuals with severe and profound intellectual disabilities.

A single post-hoc exclusion criterion was applied to exclude records from the searches published prior to 1980 (n=106 records, but not fully checked for inclusion criteria), coinciding with the publication of the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III); [24]. This assured a minimal level of consistency in the recognition and diagnosis of mental health problems from DSM-III through to DSM-IV. It is likely that there would have been a delay between the publication of the DSM-III and its first use in published research, but searches back to 1980 were essential to ensure that no potentially relevant studies were missed.

Study selection

Data collection and abstract screening were performed by the first author (LV). Twenty percent of records were also screened by the second author (SF), leading to an overall agreement rate of 99.8 % and a Kappa coefficient of 0.91 for studies to proceed to full text evaluation. Second screening a proportion of results is an accepted practice when a review is large and resources are limited [25]. The overall inclusion rate for the screening of titles and abstracts was 2.3 %. Full-text review of 573 articles was performed independently by the two reviewers (LV and SF), which resulted in a Kappa coefficient of 0.76 for inclusion in the review and the data extraction stage. Eleven disagreements between the two reviewers were resolved through joint discussion. All disagreements concerned the proporption of participants with severe and profound intellectual disabilities and were

not related to study design, intervention or outcomes. The review of one full text article required consultation with the third author (RH) to determine whether this study met the review eligibility criteria regarding mental health outcomes. Upon discussion, the paper was excluded from the review.

Next, reference lists and citation records of all included studies were screened to identify additional papers that may not have fulfilled the search term criteria. No additional studies were identified in this way.

Data extraction and quality synthesis

Data extraction was conducted by the second author and reviewed by the first author for variables including: study design, study population, intervention, outcome measures, and follow-up data.

The certainty in the evidence for each outcome measure could not be assessed with the GRADE approach [26–28], as used by the Cochrane collaboration and national guideline organisations such as NICE in the UK, due to the incomparability of identified studies in terms of study design, interventions, and outcomes. Likewise, it was not possible to conduct a meta-analysis or provide other summary measures because no two studies addressed the same mental health problem using a similar intervention.

Both reviewers independently performed a critical appraisal of all included studies. No disagreements were recorded at either stage. The assessment followed the Critical Appraisal Skills Programme [29,30] checklists or the quality indicators for within single-subjects research [31], dependent on the study design.

Patient and public involvement

Patients and public were not involved in the conception, development or implementation of this systematic review, nor in the selection of outcome measures and the interpretation of the study findings.

RESULTS

The search strategy for the conjoint systematic review identified 24,883 unique records, of which 573 were retained for full-text eligibility screening. The study selection process is illustrated in Figure 1. Excluded articles most commonly did not meet the eligibility criteria concerning the severity

of intellectual disabilities of study participants (n = 242). Initial records were also excluded based on their study design (n = 113), a publication date prior to 1980 (n = 106), because the intervention or outcomes were not focused on recognised mental health problems (n = 59), due to their publication status (e.g. conference abstracts; n = 38), or because the full-text paper could either not be retrieved (n = 6) or was published in a non-eligible language (n = 4). In total, five studies were included in the review and are described in Table 1. Three studies included only adults with intellectual disabilities: a double-blind placebo-controlled crossover trial [32] and a single-case experimental reversal design of pharmacotherapy [33], as well as a single-case experimental reversal design of a psychological intervention [34]. Two studies included children and young people: a randomised trial of pharmacotherapy by White and Aman [35] and a single-case study of a psychological intervention for a 13-year old girl [36].

[Figure 1 about here]

Table 1

Characteristics of pharmacological and psychological interventions studies.

First author (Year)	Study Design[a]	Participants	Intervention	Outcomes	Follow-up
Psychopharmacological interventions					
Aman (1986)	Double-blind placebo-controlled crossover trial Within-group randomisation I1: Imipramine I2: placebo 1-week washout period between interventions	Adults with depressive and affective symptoms N = 5 (2M/3F) Age range: 18 – 23 years intellectual disabilities severity: Slosson IQ[b] range 10 -14	Imipramine (Dumex) or placebo Duration: 4W Dose: 3 mg/kg/day Setting: residential ward	Imipramine caused symptom deterioration for ABC[c] scores related to irritability, lethargy, and hyperactivity. No intervention effects were observed for: stereotypy and inappropriate speech. Statistical data only provided for analyses including a second intervention group, non-eligible for review.	No follow-up
Rosenquist (1997)	Single-case experimental reversal design (ABABA) A, Baseline B, Haloperidol Single blind, masked	Adult with Gilles de la Tourette syndrome N = 1, Female Age = 35 years Severe intellectual disabilities	Haloperidol Duration: 22W, A: 2W baseline B: 8W intervention A: 2W baseline B: 8W intervention A: 2W baseline	Weekly observations using Behavioral Observation and Tic Checklist[d] of 3 videotaped conditions: (1) table setting task, (2) mealtime, and (3) waiting. Pre-post % time (SD)	W6 of increased dosage % time (SD) engaged in tic behavior at W6 (dose 10 mg/day): Mealtime: SM-tic: 6.3 (6)

	assessment		Dose: -W1: 1 mg/day -W2: 2mg/day -W3-4: 5 mg/day -W5-6: 10 mg/day -W7-8: washout Setting: community group home	engaged in tic behavior at baseline and W1 (dose 1mg/day): Mealtime: SM-tic: 34.8 (20); 11.0 (12) CM-tic: 13.6 (10); 5.3 (8) SV-tic: 35.4 (28); 2.0 (4) CV-tic: 1.3 (3); 0.0 (0) Waiting: SM-tic: 46.8 (31); 20.8 (26) CM-tic: 41.2 (19); 25.3 (21) SV-tic: 65.3 (29); 69.6 (25) CV-tic: 42.5 (18); 23.0 (18)	CM-tic: 3.0 (3) SV-tic: 1.0 (3) CV-tic: 1.0 (2) Waiting: SM-tic: 24.7 (20) CM-tic: 41.5 (18) SV-tic: 48.4 (26) CV-tic: 34.8 (20) Dose-specfic improvements (10mg/day), reversible
White (1985)	Double-blind placebo-controlled crossover trial I1: Pimozide I2: Placebo Randomisation within participants	Inpatients with serious behaviour disturbances, including hyperactivity N = 8, 7M/1F Mean age 15.7 years (SD = 3.42) intellectual disabilities severity: moderate to profound; mean IQ =	Pimozide or placebo Baseline: 4W Intervention: 4W + 4W Dose: I1: 6 mg/day Setting: no info	ANCOVA for drug effects and baseline as covariate on ABC subscales Pimozide has an effect: Irritability: F = 11.78 Hyperactivity: F = 7.69 No significant effects	No follow-up

	1-week washout period between interventions	20.4 (SD = 12.11)		for: Lethargy: F = 0.84 Stereotypy: F = 3.48 Inappropriate speech: F = 1.31	
Psychological interventions					
Lindauer (1999)	Single-case experimental reversal design (ABAB) A, Baseline: empty room & quiet hands procedure B, Enriched Environment & quiet hands	Mood disorder, major depression N = 1, Female Age = 23 years Severe intellectual disabilities	Enriched environment: 12 items selected for inclusion by paired-choice assessment Duration: 57 sessions; A: 11 sessions B: 5 sessions A: 29 sessions B: 12 sessions Dose: 10 minute sessions Setting: Laboratory, padded room	Percentage of 10-s intervals of signs of negative and positive affect Pre: relatively high levels of negative affect (M = 27.4%) and low levels of positive affect (M = 2.3%) Post: negative affect decreased (M = 0.1%) and positive affect increased, especially during B2 (M = 11.5% across phases).	No follow-up
Zarkowska (1989)	2 Single-case experimental reversal designs (ABA) I1: Relaxation: A, Baseline: school activity, tics ignored B, relaxation A, Baseline: return to	Gilles de la Tourette syndrome N = 1, Female Age = 13 years Severe intellectual disabilities (Griffiths Mental Development Scale score ranged	I1: verbal instructions for relaxation exercises and praise when calm Duration: 10 minutes I2: verbal interruption following the occurrence of a verbal tic	I1 reduced tic frequency during relaxation but return to baseline after intervention I2 increased vocal tic frequency.	No follow-up

	school activity, tics ignored I2: interruption A, Baseline: school activity, tics ignored B, interruption A, Baseline: return to school activity, tics ignored	from 17 to 42 months)	Duration: 10 minutes	After I1 and I2: No generalised reduction in tic frequency

Note. I1, intervention 1; I2, intervention 2; G1, group 1; G2, group 2; Gender ratio expressed as Male/Female; W1, week 1; SD, standard deviation. Outcomes reported for primary outcome measure only, unless where mental health or mental well-being outcome measure were recorded as secondary outcome measures.

[a] AB designs with A: baseline and B: treatment.

[b] Slosson IQ scores correlate highly with Stanford Binet Intelligence Test scores and correlate with the Cattell Infant Intelligence Scale when used with children under the age of 2 (Slosson, 1975).

[c] ABC, Aberrant Behavior Checklist.

[d] SM-tic, simple motor tic; CM-tic, complex motor tic; SV-tic, simple vocal tic; CV-tic, complex vocal tic.

Psychological interventions

Two studies evaluated interventions based on psychological principles. Interventions were offered for symptoms of depressive disorder and to manage tic frequency in Gilles de la Tourette syndrome.

In a single-case experimental ABAB design, Lindauer and colleagues [34] offered an enriched environment for the management of major depressive disorder in a 23-year old woman with severe intellectual disabilities who also presented with self-injurious behaviour. Pre-existing treatment of the mood disorder with carbamazepine (5.3 mg/kg/day) was continued during the study. The enriched environment setting was a 3 metre by 3 metre padded room, in an inpatient unit, in which stimuli were present that were chosen following a paired-choice assessment to identify the woman's preferred stimuli and assess signs of positive and negative affect. Smiling, giggling and laughing were considered examples of positive 'affect', whereas frowning, whining, crying and verbal expressions such as "I am sad" were identified as signs of negative 'affect'. No other outcome measures relating to the mood disorder were employed. Behavioural observations, through a one-way mirror, showed that the enriched environment increased signs of positive affect and decreased signs of negative affect, in particular during the second intervention phase. The lack of follow-up measures and the delivery of interventions in a padded room in an inpatient setting reduce the ecological validity of this intervention. Likewise, the replicability of findings is impeded in terms of participant selection and intervention fidelity (see Table 2).

Zarkowska et al. [36] adopted a basic single-case experimental design to examine interventions for vocal and motor tics in a 13-year old girl with Gilles de la Tourette syndrome and severe intellectual disabilities. Two treatment probes, cued relaxation and interruption, were evaluated using an ABA return to baseline design for each intervention comprised of a five minute baseline recording, a five minute intervention, and a five minute post-baseline recording. Cued relaxation appeared to lead to better outcomes but neither intervention had lasting effects and interruption increased vocal tic frequency. The study design showed strong external and social validity and provided clear descriptions of dependent and independent variables (see Table 2). However, internal

validity was weak and the ABA design was not the most suitable for demonstrating experimental control. Following the evaluation of treatment probes, the study continued as an A-B case study implementing successive interventions of relaxation training, treatment with clonidine and treatment with pimozide. Due to the non-controlled nature of these interventions, their respective outcome data and follow-up data were not considered eligible for inclusion in this review.

The replicability of findings from both studies is hindered by a lack of information regarding participant selection, physical setting of the intervention, implementation fidelity, and the reliability of outcome measurements.

Table 2

Quality appraisal of single-subject studies using the Quality Indicators Within Single-Subject Research [31] .

Quality indicator	Lindauer et al. (1999)	Rosenquist et al. (1997)	Zarkowska (1989)
Participant description and setting			
Ability to select individuals with similar characteristics	yes	yes	yes
Replicability of participant selection process	no	no	no
Replicability of physical setting	yes	yes	partial
Dependent variable			
Described with operational precision	yes	yes	yes
Measured to generate a quantifiable index	yes	yes	yes
Measure is valid and replicable	yes	yes	yes
Measurements repeated over time	yes	yes	no
Measures assessed in terms of reliability or inter-	yes	yes	no

observer agreement			
Independent variable			
Described with replicable precision	yes	yes	yes
Systematically manipulated and under control of experimenter	yes	yes	yes
Overt measure of implementation fidelity	no	not applicable	no
Baseline			
Repeated measurements baseline	yes	yes	no
Described with replicable precision	yes	yes	yes
Experimental control / Internal validity			
Minimum of 3 demonstrations of experimental effect at 3 points in time	yes	yes	no
Controlling for threats to internal validity	unclear	yes	unclear
Document a pattern of experimental control	yes	yes	yes
External Validity			
Effects replicated across participants, settings, or materials	yes	yes	no
Social validity			
Dependent variable is socially important	yes	yes	yes

Magnitude of change is socially important	yes	yes	yes
Implementation of independent variable is practical and cost-effective	yes	yes	yes
Implementation of independent variable over extended period of time, by typical intervention agents and in typical contexts	yes	yes	yes

Pharmacological interventions

Two double-blind placebo-controlled crossover trials and one single-case experimental reversal design evaluated pharmacological interventions for use in people with severe intellectual disabilities and mental health problems.

Aman and colleagues [32] employed within-group randomisation of order of administration of 4 week treatment with imipramine, in a dosage of 3 mg/kg/day, and 4 weeks with placebo, with one week drug-free in between. Interventions were offered to five adults with severe intellectual disabilities and depressive symptoms, in addition to a group of five adults with acting-out behaviours. The latter were not eligible for inclusion in this review as these behaviours were not considered a mental health problem. Eligible depressive symptoms were based on evidence from prior research studies and required behavioural observation instead of information obtained from diagnostic interviews. Symptoms included 'seclusion and social withdrawal, sleep loss, weight loss, tearfulness or the appearance of sad affect, and a pervasive lack of overt behavior' [31, p. 265]. Intervention effects were assessed with the Aberrant Behavior Checklist [37] and indicated imipramine to have a detrimental effect on symptoms related to irritability, lethargy, and hyperactivity, and no effect on stereotypical behaviours and inappropriate speech. Adverse effects were recorded but not described separately for the five adults with severe intellectual disabilities and depressive symptoms. For one person with affective symptoms, imipramine was found to improve behaviour and relieve chronic constipation.

White and Aman [35] evaluated the use of pimozide on maladaptive behaviours and hyperactivity, in young people and adults with moderate to profound intellectual disabilities.

Following a four-week baseline, the eight participants received two four-week treatments with either pimozide, in a dosage of 0.12 mg/kg/day, or placebo, with a one-week washout period between intervention phases. Treatment effects were evaluated using assessments with the ABC for the last three weeks of each intervention. Hyperactivity scores on the ABC reduced following the intervention, as did irritability levels, based on nurses' behaviour ratings of participants. No intervention effects were observed for ABC lethargy, stereotypy, and inappropriate speech domains. Furthermore, behavioural observations also did not identify any treatment effects.

The methodological quality of these two studies was confirmed using the CASP quality appraisal checklist (see Table 3). However, follow-up measures were notably absent and sample sizes too small to provide sufficient power for the conducted statistical analyses. Additionally, the period of treatment was of too short duration, as imipramine can take up to 6 weeks to be effective in the general population, so that intervention was of poor design.

Table 3

Critical Appraisal Skills Programme (CASP Checklists)[38] for studies with N > 1.

Quality indicator	Aman et al. (1986)[a]	White et al. (1985)[a]
Validity of the results		
Study addresses a clearly focused issue	yes	yes
Cohort recruited in an acceptable way	yes	yes
Exposure accurately measured to minimise bias	yes	yes
Outcome accurately measured to minimise bias	yes	yes
Identification of all important confounding factors	yes	yes
Design and/or analysis account for confounding factors	No: length of intervention too short to observe	No: length of intervention too short to observe

	treatment effects.	treatment effects.
Complete enough follow-up of participants	no	no
Long enough follow-up of participants	no	no
Scope of the results		
Description of study results	yes	yes
Precision of study results	No exact p-values, no effect sizes, no differentiation between depressive-like and acting-out group	No exact p-values, no effect sizes
Believability of study results	yes	yes
Impact of the results		
Results applicable to local population	Yes	Yes
Results in line with available evidence	no	Yes
Implications for practice	Length of intervention too short to draw conclusions regarding implications	The study is now out-dated given improved knowledge on the risks of the long-term use of the drug

Note. [a] CASP Checklist for Randomised Controlled Trials.

The only fully experimental single subject experimental design study evaluated the effect of haloperidol on tic frequency in a 35-year old woman with Gilles de la Tourette syndrome and severe intellectual disabilities [33]. Using an ABABA design, the dose of haloperidol was gradually increased during the intervention phases and maximal effectiveness was reached with the highest dosage of 10 mg/day. Weekly behavioural observation at the community residential setting where the participant lived showed reduced tic frequencies during mealtimes, nearing zero-levels, and during waiting times. Intervention effects reversed when the dose was lowered. These findings are considered reliable due to masked assessment and reversal design, alongside the replicability of measures and intervention, see Table 2.

Overall quality appraisal of the evidence base

Methodological quality of the identified studies was poor, with concern in terms of small sample sizes, lack of masked assessment, and lack of follow-up measures. By contrast, reporting standards were generally high in terms of variable descriptions and the internal and external validity of the results. Implications of the quality appraisal are integrated in the study descriptions above, whereas a detailed overview of the quality review for each study is reported in Tables 2 and 3.

DISCUSSION

Despite their very high rates of mental health problems, there is a lack of research in interventions that explicitly target mental health problems in people with severe and profound intellectual disabilities. The scope of this review was wide. However, only five studies were eligible for inclusion and the findings are inconclusive at best. This is highly problematic for clinicians who have to manage these disorders and can only rely upon the use of interventions designed for the general population, despite the likely limitations/inaccessibility of these for people with severe intellectual disabilities.

Haloperidol was demonstrated to improve tics, but in a single person. Pimozide was reported to reduce hyperactivity and other behaviour problems [35], but it is not a recognised treatment for hyperactivity in the general population; and NICE concludes that there is no evidence that antipsychotics drugs are of use in this condition (NICE, 2016). Whilst it can calm disturbed patients in the short term through its sedative properties, it is not recommended for this use longer term in view of

potential side-effects which includes death, with its use being reserved for schizophrenia only. Whilst meeting the inclusion criteria of the review, the study is therefore out-dated given subsequent advances in knowledge about this class of drugs. Imipramine caused deterioration of affective symptoms, but the study was poorly designed by today's standards, including the drug not being prescribed for long enough duration to be effective [32]. Additionally, the use of imipramine has declined in the whole population since the introduction of selective serotonin reuptake inhibitors in the 1980s and other newer antidepressant agents, on the basis of side-effect profile. Empirical evidence for current pharmacological interventions has not yet been published.

Evidence for the effectiveness of psychological interventions is also weak in the absence of controlled trials or high quality single case experimental designs (such as multiple baseline approaches). Across intervention types, two studies aimed to reduce tic frequency in people with severe intellectual disabilities and Gilles de la Tourette Syndrome yielding putative positive effects for relaxation techniques and treatment with haloperidol. Evidence relating to common mental health problems (e.g., anxiety, depression) was notably very limited. Studies including children with severe and profound intellectual disabilities involved different interventions than for studies with adults and while the geographic spread of the research was diverse, all included studies were conducted in English speaking countries. Overall, a quantitative synthesis of the evidence was not possible due to the heterogeneity of the identified studies as no two studies addressed the same mental health problem with a similar intervention or similar outcome measures. Furthermore, the total sample size across the five identified studies was only sixteen participants: nine children and seven adults, nine male and seven female. Finally, the review demonstrates that research in this area has stalled over the last decade. The most recent study we identified was published nearly two decades ago [34], whilst the methodologically stronger studies using controlled design employed outdated pharmacotherapies that are currently not recommended due to their potential side-effects [36, 39].

Strengths and limitations

Strengths of this systematic review are the rigour with which it was conducted. In line with PRISMA guidelines, the prior publication of the review protocol enhances its transparency and replicability, whilst double reviewing of full-length articles and quality appraisal strengthens the

findings. The current review improves upon previous reviews in this area by employing a broader scope to identify both psychological and pharmacological interventions for a range of mental health problems. In spite of this, our findings show that this area of research has received very little attention over the years with no recent treatments studies being identified and pharmacological interventions having employed drugs that would no longer comply with today's medical standards.

Limitations of the study relate to the search strategy. The systematic search did not include terms for every specific possible disorder or potential treatment, neither did it include a wide range of behavioural descriptions. In spite of this, we identified a considerably large number of potential records. Meanwhile, requiring at least 70% people with severe and profound intellectual disabilities to be included in a sample where outcomes are not reported separately for this group was a pragmatic decision so people with severe and profound intellectual disabilities would be sufficiently represented in the review findings. However, reducing the required proportion of participants with severe and profound intellectual disabilities to 50% would not have added any eligible studies (a post-review check completed by the first author).

Explanations and implications

A major challenge in mental health research for people with severe and profound intellectual disabilities, including this systematic review, lies with the selection of study outcomes. The appropriateness of measures such as the ABC [37] can be questioned when used to assess the wide spectrum of symptoms of mental health problems. However, the ABC was found to be one of the few reliable measures relating to mental health problems for individuals with severe and profound intellectual disabilities [38]. Indeed, behavioural outcomes can assess key symptoms of mental disorders according to ICD-10 criteria, but can equally be associated with distress and reduced quality of life. Whilst this diagnostic taxonomy was practical for conducting the systematic review, it may not be sufficient to evaluate all relevant interventions aimed at improving the general well-being of people with severe and profound intellectual disabilities.

The scarcity of trials addressing the mental health needs of people with severe and profound intellectual disabilities is worrisome in light of the fact that they do experience mental health problems. Yet, there is awareness of the mental health needs in this population amongst researchers

and clinicians as is evident from the wide range of descriptive case reports, which did not provide empirical evidence for the effectiveness of an intervention. On a positive note, the 101 studies identified as including at least some individuals with severe and profound intellectual disabilities show that this population is not routinely excluded from clinical practice evaluations. Although beyond the objectives of this systematic review, a scoping overview of the range of interventions evaluated in these studies and those being offered in routine clinical practice could help set the direction to guide future research. Establishing evidence-based interventions to treat mental health problems in people with severe and profound intellectual disabilities requires more research with stronger methodological designs.

Future directions

Challenging the status quo and developing an evidence base from which to treat people with severe and profound intellectual disabilities and mental health problems is a joint responsibility of practitioners and researchers. Bi-directional knowledge transfer is particularly important in this regard: research into severe and profound intellectual disabilities making its way into the training of practitioners, as well as practitioners highlighting difficulties in assessment and treatment that need addressing. Commissioning and exploring funding opportunities to conduct research into evidence-based pharmacological and psychological interventions, and an open discussion regarding the ethical considerations of research involving people who may lack the capacity to consent also require attention. A large inequality in evidence for effective treatments for mental health problems is experienced by children and adults with severe and profound intellectual disabilities. Until this inequality is adequately addressed, health services need to provide treatments found to be effective for people with mild to moderate intellectual disabilities where they exist- although the availability of interventions for this population is also poor in comparison to interventions for people without intellectual disabilities. Particular attention should be given to how these treatments might affect people with severe and profound intellectual disabilities differently regarding symptom presentation and outcome assessment, accessibility of a range of psychological therapies, and side effect reporting which may indicate a need for differences in dosing regimens. Keeping detailed accounts of how treatments were subsequently modified will benefit the development of a more solid evidence base.

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Conflicts of interest

The authors have no conflicts of interest to disclose.

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Authors' contributions

RH, DA, UC, S-A C, NG, CH, KH, AJ, PEL, RMN, CO, AR, VT and JW conceived the study and acquired funding. LV and RH designed and registered the review protocol. LV and SF conducted the systematic searches, study selection and data collection. LV wrote the manuscript.

All authors provided methodological and clinical perspectives, commented on manuscript drafts and read and approved the final version of this manuscript.

Figure 1. PRISMA Flow Diagram

Data sharing statement

To obtain the full search strategies for each database please contact leen.vereenooghe@uni-bielefeld.de or s.flynn.1@warwick.ac.uk.

This systematic review presents previously published data. Please refer to the original articles and their authors for these research data.

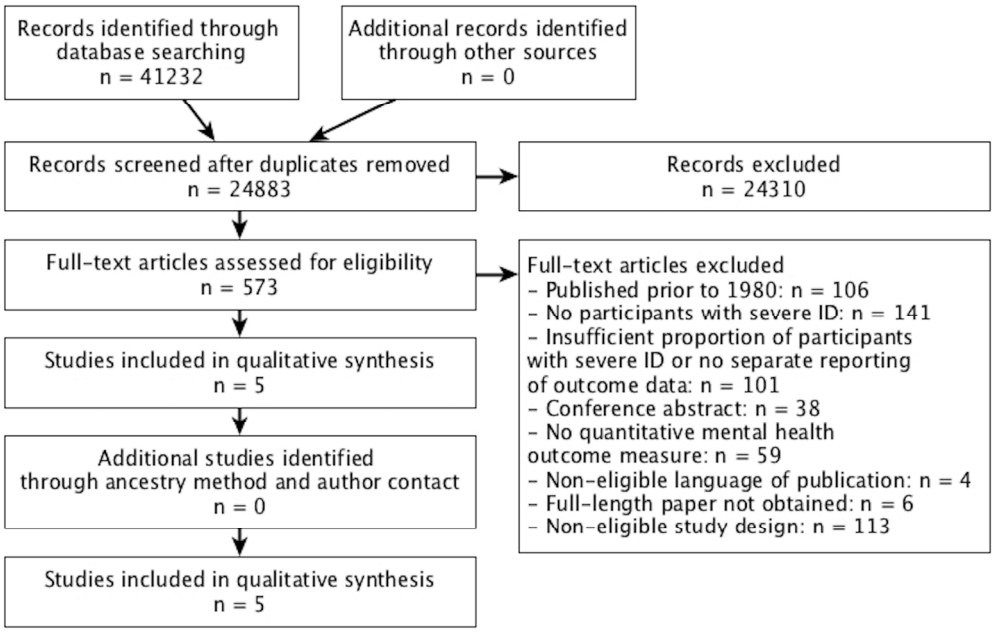

Figure 1. PRISMA Flow Diagram

244x155mm (300 x 300 DPI)

Appendix

Table 1

Search strategy for simultaneous database searches of PsycINFO, PsycTESTS and ASSIA using ProQuest database host.

	Search terms	Results
	Intellectual disabilities	
1	SU.EXACT.EXPLODE("Intellectual Development Disorder")	37548
2	TI(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*)) OR AB(mental* NEAR/3 (disab* OR impair* OR handicap* OR subnormal* OR deficien* OR retard*))	38279
3	TI(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder)) OR AB(learning NEAR/3 (disab* OR impair* OR difficult* OR disorder))	36985
4	TI(moron OR imbecile OR feeble-minded OR subnormal OR retard) OR AB(moron OR imbecile OR feeble-minded OR subnormal OR retard)	4289
5	TI(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*)) OR AB(intellect* NEAR/3 (disab* OR impair* OR handicap* OR disorder* OR subnormal* OR deficien*))	16059
6	TI((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*) OR AB((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 "Rubinstein-Taybi" OR velocardiofacial) NEAR/3 syndrome*)	11067
7	OR/ 1-6	105392
	Mental health	

8	SU.EXACT.EXPLODE("Depression (Emotion)")	22448
9	SU.EXACT.EXPLODE("Anxiety Disorders") OR SU.EXACT.EXPLODE("Generalized Anxiety Disorder") OR SU.EXACT.EXPLODE("Anxiety") OR SU.EXACT.EXPLODE("Social Anxiety")	124637
10	TI(anger NEAR/3 (problem* OR disorder*)) OR AB(anger NEAR/3 (problem* OR disorder*))	1212
11	TI(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*) OR AB(anxiet* OR anxious* OR gad* OR phobia* OR phobic* OR trauma* OR posttraum* OR ptsd OR psychotraum*)	272855
12	TI(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*)) OR AB(mental* NEAR/2 (ill* OR disorder* OR problem* OR health* OR well*))	226542
13	TI(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*) OR AB(depress* NEAR/2 (disorder* OR symptom* OR behavio* OR thought*) OR depression OR affective disorder* OR emotion* NEAR/2 (disorder* OR problem*) OR dysthymi* OR dysphori* OR melanchol*)	273779
14	OR/ 8-13	655607
Mental well-being		
15	TI(psycho* NEAR/2 function*) OR AB(psycho* NEAR/2 function*)	23372
16	TI(well* OR health*)	207285

17	TI((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*)) OR AB((mental* OR psycholog* OR psychosoc*) NEAR/2 (health* OR well*))	193401
18	TI(quality NEAR/2 life)	19555
19	OR/ 15-18	358684
Psychological interventions		
20	TI((psychological N/3 therap*) OR psychotherap* OR counsel*) OR AB((psychological N/3 therap*) OR psychotherap* OR counsel*)	196693
21	TI(psychoanaly* OR psychodynamic*) OR AB(psychoanaly* OR psychodynamic*)	90160
22	TI((behavior* OR behaviour* OR cognitive) N/2 therap*) OR AB((behavior* OR behaviour* OR cognitive) N/2 therap*)	39534
23	TI((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*) OR AB((family OR interpersonal OR systemic OR "client centered" OR "client centred" OR narrative OR relational) N/2 therap*)	25851
24	TI((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*) OR AB((supportive OR talking OR solution*focused OR emotion*focused OR non-pharmacological) N/2 therap*)	1984
25	TI(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive") OR AB(dialectical behavio*r therap* OR mindfulness* OR "acceptance and commitment" OR "rational emotive")	10630
26	TI((group OR individual) N/2 therap*) OR AB((group OR individual) N/2 therap*)	25884
27	TI(anger N/2 (manag* OR train*)) OR AB(anger N/2 (manag* OR train*))	1612

28	TI((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*) OR AB((play OR art OR relax* OR music OR dance OR creative OR drama OR activity) N/2 therap*)	17343
29	OR/ 20-28	342375
Pharmacological interventions		
30	TI(pharmacotherapy* OR pharmacolog* OR pharmacological therap*) OR AB(pharmacotherapy* OR pharmacolog* OR pharmacological therap*)	49958
31	TI(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*) OR AB(antipsychotic* OR anti-psychotic* OR psychotrop* OR psychopharmac*)	41884
32	TI(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*)) OR AB(atypical N/2 (antipsychotic* OR anti-psychotic* OR psychotrop*))	6622
33	TI(tricyclic antidepressant OR anti-depress* OR antidepress*) OR AB(tricyclic antidepressant OR anti-depress* OR antidepress*)	34457
34	TI(adrenergic blocking drugs OR monoamine oxidase inhibitors) OR AB(adrenergic blocking drugs OR monoamine oxidase inhibitors)	1905
35	TI(anxiolytic* OR antipanic* OR antianxiety) OR AB(anxiolytic* OR antipanic* OR antianxiety)	7153
36	TI(anticonvulsant*) OR AB(anticonvulsant*)	4142
37	TI(lithium*OR lithium carbonate OR SSRI* OR “selective serotonin reuptake inhibitor” OR serotonin reuptake inhibitor OR serotonin antagonist) OR AB(lithium*OR lithium carbonate OR SSRI* OR “selective serotonin reuptake inhibitor” OR serotonin reuptake inhibitor OR serotonin antagonist)	12261

38	TI(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine) OR AB(risperidone OR olanzapine OR clozapine* OR Leponex OR Denzapine OR Zaponex OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR trazodone OR clomipramine OR amoxapine OR isocarboxazid OR phenelzine OR tranylcypromine OR moclobemide OR amoxapine OR bupropion OR sulpiride OR maprotiline OR imipramine OR clomipramine OR desipramine OR opipramol OR doxepin OR amitriptyline OR lofepramine OR nortriptyline OR benzodiazepine* OR alprazolam OR clonazepam OR diazepam OR temazepam OR melatonin OR methylphenidate OR sodium valproate OR carbamazepine OR lamotrigine)	61771
39	OR/ 30-38	153952
Final search string		
40	7 AND (14 OR 19) AND (29 OR 39)	2607

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	10
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	n/a

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	17, 20
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	16, 19, 20
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	24
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	25
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	27

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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