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GRADE EVIDENCE PROFILES FOR CLINICAL EVIDENCE

1.1 PSYCHOSOCIAL INTERVENTIONS

1.1.1 Behavioural therapies aimed at communication

1.1.1.1 Natural language teaching compared with analog language teaching for communication in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Analog language teaching	With Natural language teaching		Risk with Analog language teaching	Risk difference with Natural language teaching (95% CI)
Communication (measured with: Language acquisition measured by number of nouns generalized; Better indicated by lower values)											
24 (1 study) 3 months	serious ¹	no serious inconsistency	no serious indirectness	very serious ^{2,3}	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, imprecision	11.5	11.5	-		The mean communication in the intervention groups was 0.71 standard deviations lower (1.55 lower to 0.13 higher)

¹ Non-randomised and non-blind so high risk of bias

² Study was designed to compare two alternative treatments and not to determine overall treatment efficacy

³ Small sample size

1.1.1.2 Observational studies of functional communication skills training in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Functional communication skills training		Risk with Control	Risk difference with Functional communication skills training (95% CI)
Communication (measured with: Vineland Adaptive Behaviour Scale (VABS) subscale of communication; Better indicated by lower values)											
18 (1 study) 18 months	very serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, imprecision	-	18	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational study and cannot extract efficacy data

² Small sample size

1.1.2 Facilitated communication

1.1.2.1 Observational studies of facilitated communication in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Observational studies of facilitated communication for adults with autism		Risk with Control	Risk difference with Observational studies of facilitated communication for adults with autism (95% CI)
Behavioural and social interaction responses (measured with: Behavioural observations; Better indicated by lower values)											
12 (1 study) 17 weeks	very serious ^{1,2}	no serious inconsistency	no serious indirectness	very serious ^{3,4}	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, imprecision	-	12	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group

² Efficacy data could not be extracted

³ Small sample size

⁴ Behavioural observations were non-blind

1.1.3 Behavioural therapies aimed at behaviour management

1.1.3.1 Independence training versus no-treatment control group in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With No treatment	With Behavioural therapies		Risk with No treatment	Risk difference with Behavioural therapies (95% CI)
Activities of daily living (showering) (measured with: Task-specific checklist for showering; Better indicated by lower values)											
72 (1 study) 7 months	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	36	36	-		The mean activities of daily living (showering) in the intervention groups was 8.40 higher (6.99 to 9.81 higher)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-blind so risk of performance and detection bias

² Extrapolating from adults with learning disabilities

³ The outcome measure was designed specifically for this study and lacks formal assessments of reliability and validity

1.1.3.2 Observational studies of adaptive skills training in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Behavioural therapies		Risk with Control	Risk difference with Behavioural therapies (95% CI)
Activities of daily living (measured with: Behaviour Maturity Checklist II-1978 toileting subscale; Better indicated by lower values)											
51 (1 study) 10 years	very serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	-	51	-	See comment	See comment

¹ Observational study with no control group and efficacy data cannot be extracted

² Extrapolating from adults with learning disabilities

1.1.3.3 Behavioural weight control versus no treatment control in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With No treatment	With Behavioural therapies		Risk with No treatment	Risk difference with Behavioural therapies (95% CI)
Self care (measured with: Weight loss; Better indicated by lower values)											
21 (1 study) 26 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	11	10	-		The mean self care in the intervention groups was 0.44 standard deviations higher (0.43 lower to 1.30 higher)

¹ Control group consisted of drop-outs from the experimental group so there was high risk for selection bias. The study was also non-randomised and non-blind increasing the risk of performance and detection bias

² Extrapolating from adults with learning disabilities

³ Small sample size

1.1.3.4 Observational studies of self-instructional pictorial child care manuals in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Behavioural therapies		Risk with Control	Risk difference with Behavioural therapies (95% CI)
Parenting skill (measured with: Target child-care behaviour checklist; Better indicated by lower values)											
10 (1 study) 3 years	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	10	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational study and efficacy data cannot be extracted

² Extrapolating from adults with learning disabilities

³ Small sample size

1.1.4 Cognitive behavioural therapies

1.1.4.1 Cognitive behavioural therapy versus treatment-as-usual for coexisting conditions in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Cognitive behavioural therapies		Risk with Treatment as usual	Risk difference with Cognitive behavioural therapies (95% CI)
Severity of coexisting condition (OCD) (measured with: Yale-Brown Obsessive Compulsive Scale (YBOCS) severity scale; Better indicated by lower values)											
24 (1 study) 16 months	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, imprecision	12	12	-		The mean severity of coexisting condition (ocd) in the intervention groups was 2.42 higher (3.6 lower to 8.44 higher)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-randomised and non-blind so risk of selection, performance and detection bias

² Small sample size

1.1.4.2 Cognitive behavioural therapy versus treatment-as-usual for anti-victimization skills in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Cognitive behavioural therapies		Risk with Treatment as usual	Risk difference with Cognitive behavioural therapies (95% CI)
Anti-victimization skills (measured with: Self Social Interpersonal Decision Making Scale & The Protective Behaviour Skills Evaluation; Better indicated by lower values)											
80 (3 studies ¹) 3-9 weeks	serious ²	no serious inconsistency	serious ³	serious ⁴	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3,4} due to risk of bias, indirectness, imprecision	40	40	-		The mean anti-victimization skills in the intervention groups was 1.07 standard deviations higher (0.58 to 1.56 higher)
Anti-victimization skills (assessed with: Bullying victimization rates)											
38 (1 study) 3 months	serious ²	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3} due to risk of bias, indirectness	7/18 (38.9%)	5/20 (25%)	RR 0.64 (0.25 to 1.67)	Study population	
										389 per 1000	140 fewer per 1000 (from 292 fewer to 261 more)
										Moderate	
									389 per 1000	140 fewer per 1000 (from 292 fewer to 261 more)	

¹ 2 RCTs (KHEMKA2000 & KHEMKA2005) and 1 QE (MAZZUCHELLI2001) combined

² No attention-placebo control group so participants did not receive same care apart from intervention, and non-blind so risk of performance and detection bias

³ Extrapolating from adults with learning disabilities

⁴ The precision of the outcome measures for KHEMKA2000 and KHEMKA2005 is unclear

1.1.4.3 Cognitive behavioural therapy versus waitlist control or treatment-as-usual for anger management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Waiting list or treatment as usual control	With Cognitive behavioural therapies		Risk with Waiting list or treatment as usual control	Risk difference with Cognitive behavioural therapies (95% CI)
Anger management (measured with: Dundee Provocation Inventory, Anger Inventory, & Provocation Inventory; Better indicated by lower values)											
169 (3 studies) 4-9 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	70	99	-		The mean anger management in the intervention groups was 0.59 standard deviations lower (0.9 to 0.27 lower)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-randomised and non-blind so risk of selection, performance and detection bias

² Extrapolating from adults with learning disabilities

1.1.4.4 Cognitive behavioural therapy for anger management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Cognitive behavioural therapies		Risk with Control	Risk difference with Cognitive behavioural therapies (95% CI)
Anger management (measured with: Aggressive gestures on the videotaped roleplay test & Anger Inventory for Mentally Retarded Adults; Better indicated by lower values)											
65 (2 studies) 19-27 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	65	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational studies and cannot extract efficacy data

² Extrapolating from adults with learning disabilities

³ The precision of the outcome measure in BENSON1996 is unclear

1.1.5 Leisure programmes

1.1.5.1 Leisure programmes versus waitlist control in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Leisure program versus waiting list control in adults with autism spectrum conditions		Risk with Control	Risk difference with Leisure program versus waiting list control in adults with autism spectrum conditions (95% CI)
Quality of life (measured with: Quality of Life Questionnaire-Spanish version (QOL); Better indicated by lower values)											
71 (1 study) 1 years	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊕⊕⊖ MODERATE ¹ due to risk of bias	34	37	-		The mean quality of life in the intervention groups was 8.33 higher (5.21 to 11.45 higher)
Emotion recognition (measured with: The Facial Discrimination Battery (FDB)-Spanish version - recognition of emotion subscale; Better indicated by lower values)											
40 (1 study) 1 years	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊕⊕⊖ LOW ^{1,2} due to risk of bias, imprecision	20	20	-		The mean emotion recognition in the intervention groups was 12.77 higher (2.12 to 23.42 higher)

¹ No attention-placebo control group which increases the risk of performance bias

² Small sample size

1.1.6 Social learning interventions

1.1.6.1 Emotion recognition training versus treatment-as-usual in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Emotion recognition training		Risk with Treatment as usual	Risk difference with Emotion recognition training (95% CI)
Emotion recognition (measured with: The Cambridge Mindreading (CAM) Face task; Better indicated by lower values)											
40 (1 study) 15 weeks	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊕⊕⊖ LOW ^{1,2} due to risk of bias, imprecision	22	18	-		The mean emotion recognition in the intervention groups was 2.70 higher (2.27 lower to 7.67 higher)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-blind so risk of performance and detection bias

² Small sample size

1.1.6.2 Observational studies of social skills group in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Social skills group		Risk with Control	Risk difference with Social skills group (95% CI)
Social interaction (measured with: Empathy quotient and role play 'party' scenario; Better indicated by lower values)											
23 (2 studies) 8-52 weeks	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, imprecision	-	23	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational study and cannot extrapolate efficacy data

² Small sample size

1.1.6.3 Social skills group versus waitlist control group in adolescents with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Waitlist control	With Social skills group		Risk with Waitlist control	Risk difference with Social skills group (95% CI)
Social interaction (measured with: Test of Adolescent Social Skills Knowledge; Better indicated by lower values)											
33 (1 study) 24 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	16	17	-		The mean social interaction in the intervention groups was 6.30 higher (4.32 to 8.28 higher)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-blind so risk of performance and detection bias

² Extrapolating from adolescents with autism spectrum conditions

³ Sample size is small

1.1.6.4 Observational studies of social skills groups for adolescents with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Social skills group		Risk with Control	Risk difference with Social skills group (95% CI)
Social interaction (measured with: Blind-expert video rating and social responsiveness/social skills rating scales; Better indicated by lower values)											
49 (3 studies) 2.5-11 months	serious ¹	serious ²	serious ³	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, inconsistency, indirectness, imprecision	-	49	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Challenging behaviour (measured with: Aberrant Behaviour Checklist Irritability subscale; Better indicated by lower values)											
30 (1 study) 12 weeks	serious ¹	no serious inconsistency	serious ³	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,3,4} due to risk of bias, indirectness, imprecision	-	30	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational studies and efficacy data cannot be extracted

² HERBRECHT2009 and WEBB2004 found no significant treatment effects, while TSE2007 found a significant treatment effect (effect size 0.39)

³ Extrapolating from adolescents with autism spectrum conditions

⁴ Sample size is small

1.1.6.5 Social skills group versus treatment-as-usual in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Social skills group		Risk with Treatment as usual	Risk difference with Social skills group (95% CI)
Challenging behaviour (measured with: Part 2 of the AAMD Adaptive Behavior Scale; Better indicated by lower values)											
44 (1 study) 10 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	24	20	-		The mean challenging behaviour in the intervention groups was 2.03 lower (11.79 lower to 7.73 higher)

¹ No attention-placebo control group so participants did not receive same care apart from intervention, and non-blind so risk of performance and detection bias

² Extrapolating from adults with learning disabilities

³ Sample size is small

1.1.7 Supported employment programmes

1.1.7.1 Supported employment versus sheltered workshop in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Sheltered workshop	With Supported work		Risk with Sheltered workshop	Risk difference with Supported work (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale (CARS); Better indicated by lower values)											
51 (1 study) 3 years	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, imprecision	26	25	-		The mean autistic behaviours in the intervention groups was 6.07 lower (10.09 to 2.05 lower)
Quality of life (measured with: Quality of Life Survey (QLS); Better indicated by lower values)											
51 (1 study) 3 years	serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, imprecision	26	25	-		The mean quality of life in the intervention groups was 5.20 higher (2.69 to 7.71 higher)

¹ Group allocation not randomised

² Sample size figures varied throughout the paper with no explanation as to the changing values. The sample sizes used for analysis were selected from the demographic table but not clear that this assumption valid or correct

1.1.7.2 Supported employment versus waitlist control in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Waiting list control	With Supported work		Risk with Waiting list control	Risk difference with Supported work (95% CI)
Executive function (measured with: Stockings of Cambridge (SOC) Planning task from CANTAB; Better indicated by lower values)											
44 (1 study) 30 months	serious ¹	no serious inconsistency	no serious indirectness	very serious ^{2,3}	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, imprecision	22	22	-		The mean executive function in the intervention groups was 2.75 lower (4.41 to 1.09 lower)

¹ Group allocation not randomised

² Sample size not reported for each group. Analysis based on assumption of equal numbers in each group but may be invalid.

³ Sample size is small

1.1.7.3 Supported employment versus treatment-as-usual control in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control group	With Supported work		Risk with Control group	Risk difference with Supported work (95% CI)
Job placements (assessed with: Number of participants in work)											
50 (1 study) 2 years	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ¹ due to risk of bias	5/20 (25%)	19/30 (63.3%)	RR 2.53 (1.13 to 5.67)	Study population	
										250 per 1000	382 more per 1000 (from 32 more to 1000 more)
										Moderate	
									250 per 1000	382 more per 1000 (from 32 more to 1000 more)	

¹ Group allocation not randomised

1.1.7.4 Observational studies of supported employment in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Supported work		Risk with Control	Risk difference with Supported work (95% CI)
Job placements (measured with: Number of participants in work; Better indicated by lower values)											
89 (1 study) 1 years	very serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ¹ due to risk of bias	-	89	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group and efficacy data cannot be extracted

1.1.8 Support for families and carers

1.1.8.1 Coping skills training programme versus treatment as usual for mothers of adolescents with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Coping skills training program		Risk with Treatment as usual	Risk difference with Coping skills training program (95% CI)
Social support (measured with: Coping Strategy Indicator; Better indicated by lower values)											
20 (1 study) 4 weeks	very serious ^{1,2,3}	no serious inconsistency	no serious indirectness	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, imprecision	10	10	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Hopelessness (measured with: Beck Hopeless Scale; Better indicated by lower values)											
20 (1 study) 4 weeks	very serious ^{1,2,3}	no serious inconsistency	no serious indirectness	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, imprecision	10	10	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Group allocation not randomised

² Efficacy data cannot be extracted

³ Short duration of follow-up

⁴ Small sample size

1.1.8.2 Psychoeducational group permanency planning intervention versus treatment as usual for mothers of adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Psychoeducation group permanency planning intervention		Risk with Treatment as usual	Risk difference with Psychoeducation group permanency planning intervention (95% CI)
Knowledge and awareness about planning (measured with: Cluster based on standardized and original scales; Better indicated by lower values)											
27 (1 study) 6 weeks	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	13	-		The mean knowledge and awareness about planning in the intervention groups was 0.99 standard deviations lower (1.79 to 0.19 lower)
Competence and confidence to plan (measured with: Cluster based on standardized and original scales; Better indicated by lower values)											
27 (1 study) 6 weeks	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	13	-		The mean competence and confidence to plan in the intervention groups was 1.36 standard deviations lower (2.20 to 0.53 lower)

Appraisals of the planning process (measured with: Cluster based on standardized and original scales; Better indicated by lower values)											
27 (1 study) 6 weeks	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	13	-		The mean appraisals of the planning process in the intervention groups was 0.61 standard deviations lower (1.39 lower to 0.1 higher)
Intermediate planning behaviours (measured with: Cluster based on standardized and original scales; Better indicated by lower values)											
27 (1 study) 6 weeks	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	13	-		The mean intermediate planning behaviours in the intervention groups was 0.49 standard deviations lower (1.25 lower to 0.28 higher)
Residential and legal planning (measured with: Cluster based on standardized and original scales; Better indicated by lower values)											
27 (1 study) 6 weeks	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	13	-		The mean residential and legal planning in the intervention groups was 1.02 standard deviations lower (1.82 to 0.21 lower)

¹ Non-blind allocation, administration and assessment. Randomisation methods are unclear. It is not clear that the control group received the same care apart from the intervention. There was also a relatively short duration of follow-up and concerns regarding the reliability and validity of outcome measures

² Extrapolating from adults with intellectual disability

³ Small sample size and group N not clear (assumed N=13 in experimental and N=14 in control but not clear that this assumption is correct)

1.2 BIOMEDICAL INTERVENTIONS

1.2.1 Antipsychotics: grade profiles

1.2.1.1 Risperidone versus placebo for behaviour management in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Risperidone		Risk with Placebo	Risk difference with Risperidone (95% CI)
Challenging behaviour (measured with: Aberrant Behaviour Checklist and SIB-Q (Aggression); Better indicated by lower values)											
66 (2 studies) 12-22 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	33	33	-		The mean challenging behaviour in the intervention groups was 0.79 standard deviations lower (1.29 to 0.28 lower)
Autistic behaviours (measured with: Ritvo-Freeman Real-life Rating Scale; Better indicated by lower values)											
31 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	16	15	-		The mean autistic behaviours in the intervention groups was 0.72 standard deviations lower (1.45 lower to 0.01 higher)
Core ASC symptom (repetitive behaviour) (measured with: Yale-Brown Obsessive Compulsion Scale; Better indicated by lower values)											
31 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	16	15	-		The mean core asc symptom (repetitive behaviour) in the intervention groups was 0.94 standard deviations lower (1.68 to 0.19 lower)

Symptom severity/improvement (measured with: Clinical Global Impression (CGI) scale; Better indicated by lower values)											
31 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	16	15	-		The mean symptom severity/improvement in the intervention groups was 1.40 standard deviations lower (2.18 to 0.61 lower)

¹ Sample size is small

1.2.1.2 Risperidone versus placebo for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Risperidone		Risk with Placebo	Risk difference with Risperidone (95% CI)
Challenging behaviour (measured with: Aberrant Behaviour Checklist score (challenging behaviour); Better indicated by lower values)											
58 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	29	-		The mean challenging behaviour in the intervention groups was 4.77 lower (18.38 lower to 8.84 higher)
Aggression (measured with: Modified Overt Aggression Scale (MOAS); Better indicated by lower values)											
58 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	29	-		The mean aggression in the intervention groups was 0.58 higher (4.90 lower to 6.06 higher)

Symptom severity/improvement (measured with: Clinical Global Impressions (CGI) Scale; Better indicated by lower values)											
132 (2 studies) 4-26 weeks	serious ¹	serious ³	very serious ^{2,4}	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3,4} due to risk of bias, inconsistency, indirectness	66	66	-		The mean symptom severity/improvement in the intervention groups was 0.30 standard deviations lower (0.64 lower to 0.04 higher)
Quality of life (measured with: Quality of life questionnaire; Better indicated by lower values)											
58 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ LOW ^{1,2} due to risk of bias, indirectness	29	29	-		The mean quality of life in the intervention groups was 2.88 higher (2.56 lower to 8.32 higher)
Challenging behaviour (narrative reporting) (measured with: Aberrant Behaviour Checklist total score; Better indicated by lower values)											
38 (1 study) 8 weeks	serious ⁵	no serious inconsistency	serious ²	serious ⁶	undetected	⊕⊕⊕⊕ VERY LOW ^{2,5,6} due to risk of bias, indirectness, imprecision	19	19	-	See comment	See comment
Symptom severity/improvement (narrative reporting) (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
38 (1 study) 8 weeks	serious ⁵	no serious inconsistency	serious ²	serious ⁶	undetected	⊕⊕⊕⊕ VERY LOW ^{2,5,6} due to risk of bias, indirectness, imprecision	19	19	-	See comment	See comment

¹ Data is skewed in TYRER2008

² Extrapolating from a learning disabilities population

³ GAGIANO2005 found significant differences whereas TYRER2008 did not

⁴ Participants in GAGIANO2005 had co-existing conditions including conduct disorder, disruptive behaviour disorder, intermittent explosive disorder, oppositional defiant disorder, and antisocial personality disorder

⁵ The data reported does not allow for a calculation of effect size

⁶ Small sample size

1.2.1.3 Open-label risperidone for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Open-label risperidone		Risk with Control	Risk difference with Open-label risperidone (95% CI)
Challenging behaviour (narrative reporting) (measured with: Aberrant Behaviour Checklist (ABC); Better indicated by lower values)											
24 (1 study) 76.4 days	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	24	-	See comment	See comment
Symptom severity/outcome (narrative reporting) (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
24 (1 study) 76.4 days	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	24	-	See comment	See comment
Quality of life (measured with: Composite Autonomic Symptom Scale (COMPASS) modified version; Better indicated by lower values)											
24 (1 study) 76.4 days	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	24	-	See comment	See comment

¹ Observational study with open-label treatment and data extracted did not allow for calculation of effect sizes

² Extrapolating from adults with learning disabilities

³ Learning disabilities population also have co-existing psychiatric conditions including epilepsy and organic behaviour disorder

⁴ Small sample size

1.2.1.4 Haloperidol versus placebo for behaviour management in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Haloperidol		Risk with Placebo	Risk difference with Haloperidol (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale ; Better indicated by lower values)											
33 (1 study) 21 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	16	17	-		The mean autistic behaviours in the intervention groups was 2.70 lower (7.19 lower to 1.79 higher)
Side effects (measured with: Dosage Treatment Emergent Symptom Scale; Better indicated by lower values)											
33 (1 study) 21 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	16	17	-		The mean side effects in the intervention groups was 1.50 higher (0.28 lower to 3.28 higher)

¹ High risk of attrition bias due to higher dropout as a consequence of side effects in the haloperidol group

² Sample is of adolescents with autism

³ Sample size is small

1.2.1.5 Haloperidol versus placebo for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Haloperidol		Risk with Placebo	Risk difference with Haloperidol (95% CI)
Challenging behaviour (measured with: Aberrant Behaviour Checklist (ABC); Better indicated by lower values)											
57 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	28	-		The mean challenging behaviour in the intervention groups was 4.30 lower (19.30 lower to 10.70 higher)
Aggression (measured with: Modified Overt Aggression Scale; Better indicated by lower values)											
57 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	28	-		The mean aggression in the intervention groups was 4.12 lower (8.53 lower to 0.29 higher)
Symptom severity/improvement (measured with: Clinical Global Impressions Scale (CGI) - Improvement; Better indicated by lower values)											
57 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	28	-		The mean symptom severity/improvement in the intervention groups was 0.88 lower (1.57 to 0.19 lower)
Quality of life (measured with: Quality of life questionnaire; Better indicated by lower values)											
57 (1 study) 26 weeks	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	29	28	-		The mean quality of life in the intervention groups was 1.87 lower (7.38 lower to 3.64 higher)

¹ Data is skewed in TYRER2008

² Extrapolating from adults with learning disabilities

1.2.1.6 Zuclopenthixol versus placebo for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Zuclopenthixol		Risk with Placebo	Risk difference with Zuclopenthixol (95% CI)
Challenging behaviour (aggression)											
39 (1 study) 18 weeks	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	1/20 (5%)	7/19 (36.8%)	RR 7.37 (1.2 to 16.85)	Study population	
										50 per 1000	319 more per 1000 (from 10 more to 793 more)
										Moderate	
50 per 1000	319 more per 1000 (from 10 more to 793 more)										
Challenging behaviour (irritability) change from baseline (measured with: Nurse's Observation Scale for In-patient Evaluation (NOISE-30); Better indicated by lower values)											
85 (1 study) 12 weeks	serious ³	no serious inconsistency	very serious ^{1,4}	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,3,4} due to risk of bias, indirectness	40	45	-		The mean challenging behaviour (irritability) change from baseline in the intervention groups was 2.20 lower (3.86 to 0.54 lower)

Symptom severity/improvement (endpoint data) (assessed with: Clinical Global Assessment (CGA) derived from the Clinical Global Impression (CGI) scale)										
43 (1 study) 18 weeks	serious ³	no serious inconsistency	very serious ^{1,4}	serious ²	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	1/19 5/24 (5.3 (20.8%))	RR 3.96 (0.51 to 13.47)	Study population	
									53 per 1000	156 more per 1000 (from 26 fewer to 656 more)
									Moderate	
									50 per 1000	148 more per 1000 (from 25 fewer to 624 more)
Symptom severity/improvement (change from baseline) (measured with: Clinical Global Impression (CGI) scale; Better indicated by lower values)										
85 (1 study) 12 weeks	serious ³	no serious inconsistency	very serious ^{1,4}	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,3,4} due to risk of bias, indirectness	40 45	-		The mean symptom severity/improvement (change from baseline) in the intervention groups was 0.70 higher (0.25 to 1.15 higher)

¹ Extrapolating from a learning disabilities population

² Sample size is small

³ Higher attrition rate in the placebo group

⁴ Study is very old

1.2.1.7 Prothipendyl versus placebo for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Prothipendyl		Risk with Placebo	Risk difference with Prothipendyl (95% CI)
Symptom severity/improvement (assessed with: Clinical observation rating scale)											
39 (1 study) 16 weeks	serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	9/19 (47.4%)	16/20 (80%)	RR 1.69 (1.04 to 1.99)	Study population	
										474 per 1000	327 more per 1000 (from 19 more to 469 more)
										Moderate	
										50 per 1000	35 more per 1000 (from 2 more to 49 more)

¹ Pre-trial differences between experimental and control groups in IQ
² Extrapolating from adults with learning disabilities
³ Study is very old
⁴ Sample size is small

1.2.1.8 Pipamperone versus placebo for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Pipamperone		Risk with Placebo	Risk difference with Pipamperone (95% CI)
Challenging behaviour (narrative reporting) (measured with: Experiment-specific behaviour checklist; Better indicated by lower values)											
20 (1 study) 4 months	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	10	10	-	See comment	See comment

¹ Data reported did not allow for calculation of effect size

² Extrapolating from a learning disabilities population

³ Small sample size

1.2.1.9 Cis(z)-clopenthixol versus haloperidol for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Haloperidol	With Cis(z)-clopenthixol		Risk with Haloperidol	Risk difference with Cis(z)-clopenthixol (95% CI)
Symptom severity/improvement (assessed with: Clinical Global Impression (CGI) scale)											
98 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	very serious ^{1,2}	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness	7/49 (14.3%)	24/49 (49%)	RR 3.43 (1.86 to 5.02)	Study population	
										143 per 1000	347 more per 1000 (from 123 more to 574 more)
										Moderate	
									143 per 1000	347 more per 1000 (from 123 more to 575 more)	
Side effects (assessed with: Clinical Global Impression (CGI) scale)											
98 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	very serious ^{1,2}	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness	39/49 (79.6%)	33/49 (67.3%)	RR 0.85 (0.57 to 1.05)	Study population	
										796 per 1000	119 fewer per 1000 (from 342 fewer to 40 more)
										Moderate	
									796 per 1000	119 fewer per 1000 (from 342 fewer to 40 more)	

¹ Extrapolating from a learning disabilities population

² Study is very old

1.2.1.10 Open-label olanzapine for behaviour management in adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Open-label olanzapine		Risk with Control	Risk difference with Open-label olanzapine (95% CI)
Challenging behaviour (narrative reporting) (measured with: Aberrant Behaviour Checklist (ABC); Better indicated by lower values)											
16 (1 study) 8 weeks	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	16	-	See comment	See comment
Symptom severity/outcome (narrative reporting) (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
16 (2 studies) 8-11 weeks	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	16	-	See comment	See comment

¹ Observational studies with open-label treatment and data extracted did not allow for calculation of effect sizes

² Extrapolating from adults with learning disabilities

³ Learning disabilities population also have co-existing psychiatric conditions including disruptive behaviour disorder, attention-deficit/hyperactivity disorder, oppositional defiant disorder, stereotypic movement disorder, conduct disorder, impulse control disorder, epilepsy, and organic behaviour disorder

⁴ Small sample size

1.2.2 Anticonvulsants

1.2.2.1 Valproate versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Valproate		Risk with Placebo	Risk difference with Valproate (95% CI)
Challenging behaviour (irritability) (measured with: ABC Irritability and CGI-Irritability; Better indicated by lower values)											
57 (2 studies) 8-12 weeks	no serious risk of bias	serious ¹	serious ²	serious ³	undetected	⊕⊕⊕⊖ VERY LOW ^{1,2,3} due to inconsistency, indirectness, imprecision	25	32	-		The mean challenging behaviour (irritability) in the intervention groups was 0.05 standard deviations lower (0.58 lower to 0.48 higher)
Challenging behaviour (irritability) (assessed with: CGI-Irritability)											
27 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊖ LOW ^{2,3} due to indirectness, imprecision	1/11 (9.1%)	10/16 (62.5%)	RR 6.87 (1.59 to 10.36)	Study population	
										91 per 1000	534 more per 1000 (from 54 more to 851 more)
										Moderate	
									91 per 1000	534 more per 1000 (from 54 more to 852 more)	

Challenging behaviour (aggression) (measured with: Parent Overt Aggression Scale; Better indicated by lower values)											
30 (1 study) 8 weeks	no serious risk of bias	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊖⊖ LOW ^{2,3} due to indirectness, imprecision	14	16	-		The mean challenging behaviour (aggression) in the intervention groups was 0.14 higher (2.93 lower to 3.21 higher)
Symptom severity/improvement (CGI-Improvement) (measured with: Clinical Global Impressions - Improvement scale; Better indicated by lower values)											
30 (1 study) 8 weeks	no serious risk of bias	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊖⊖ LOW ^{2,3} due to indirectness, imprecision	14	16	-		The mean symptom severity/improvement (cgi-improvement) in the intervention groups was 0.37 lower (0.97 lower to 0.23 higher)
Side effects (assessed with: Checklist derived from Physicians' Desk Reference)											
30 (1 study) 8 weeks	no serious risk of bias	no serious inconsistency	serious	serious ³	undetected	⊕⊕⊖⊖ LOW ³ due to indirectness, imprecision	11/14 (78.6%)	15/16 (93.8%)	RR 1.19 (0.73 to 1.26)	Study population	
										786 per 1000	149 more per 1000 (from 212 fewer to 204 more)
										Moderate	
										786 per 1000	149 more per 1000 (from 212 fewer to 204 more)

¹ HELTINGS2005 found a negative response and HOLANDER2010 found a positive response for valproate on ABC irritability scores

² Extrapolation from children with ASC

³ Small sample sizes

1.2.2.2 Lamotrigine versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Lamotrigine		Risk with Placebo	Risk difference with Lamotrigine (95% CI)
Autistic behaviours (narrative reporting) (measured with: Childhood Autism Rating Scale; Better indicated by lower values)											
28 (1 study) 18 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	14	-	See comment	See comment
Challenging behaviour (narrative reporting) (measured with: Aberrant Behaviour Checklist - Irritability; Better indicated by lower values)											
28 (1 study) 18 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	14	-	See comment	See comment

¹ Efficacy data could not be extracted
² Extrapolating from children with ASC
³ Small sample size

1.2.2.3 Open-label topiramate for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Open-label topiramate		Risk with Control	Risk difference with Open-label topiramate (95% CI)
Challenging behaviour (narrative reporting) (measured with: Conners Parent Scale - Conduct subscale; Better indicated by lower values)											
15 (1 study ¹) 25 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	15	-	See comment	See comment

¹ Observational case series and efficacy data could not be extracted

² Extrapolating from children with ASC

³ Small sample size

1.2.3 Drugs affecting cognition

1.2.3.1 Donepezil hydrochloride versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Donepezil hydrochloride		Risk with Placebo	Risk difference with Donepezil hydrochloride (95% CI)
Autistic behaviours (measured with: Modified parent-completed Childhood Autism Rating Scale (CARS); Better indicated by lower values)											
34 (1 study) 6 weeks	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	17	17	-		The mean autistic behaviours in the intervention groups was 0.40 higher (4.88 lower to 5.68 higher)

¹ Extrapolating from children with autism spectrum conditions

² Small sample size

1.2.3.2 Amantadine hydrochloride versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Amantadine hydrochloride		Risk with Placebo	Risk difference with Amantadine hydrochloride (95% CI)
Challenging behaviour (irritability) (assessed with: Aberrant Behaviour Checklist (ABC) parent-completed)											
38 (1 study) 5 weeks	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	7/19 (36.8%)	9/19 (47.4%)	RR 1.29 (0.60 to 2.74)	Study population	
										368 per 1000	107 more per 1000 (from 147 fewer to 641 more)
										Moderate	
									368 per 1000	107 more per 1000 (from 147 fewer to 640 more)	

¹ Extrapolating from children with autism spectrum conditions

² Small sample size

1.2.3.3 Open-label memantine for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Memantine		Risk with Control	Risk difference with Memantine (95% CI)
ASC core symptoms (communication) (measured with: Clinical Global Impression Improvement Scale (CGI-Language); Better indicated by lower values)											
151 (1 study) 9 months	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	151	-	See comment	See comment
Challenging behaviour (measured with: CGI-Improvement Behaviour Scale and Aberrant Behaviour Checklist (ABC) Irritability subscale; Better indicated by lower values)											
165 (2 studies) 6-8 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	165	-	See comment	See comment
Symptom severity/improvement (measured with: Clinical Global Impressions - Severity scale (CGI-S); Better indicated by lower values)											
32 (2 studies) 8-19 weeks	very serious ¹	serious ⁴	serious ²	serious ⁵	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,4,5} due to risk of bias, inconsistency, indirectness, imprecision	-	32	-	See comment	See comment

¹ No control group and efficacy data cannot be extracted

² Extrapolating from children with autism spectrum conditions

³ Clinical Global Impressions (CGI) scale usually used to rate symptom severity /improvement and not clear it is a precise enough scale to evaluate and differentiate language and behaviour scores as used in this study

⁴ ERICKSON2007 reports large treatment effect and OWLEY2006 reports non-significant treatment effect

⁵ Small sample size

1.2.3.4 Open-label galantamine for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Galantamine		Risk with Control	Risk difference with Galantamine (95% CI)
Challenging behaviour (measured with: Aberrant Behaviour Checklist (ABC) Irritability subscale; Better indicated by lower values)											
13 (1 study) 12 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	13	-	See comment	See comment
Autistic Behaviours (measured with: Children's Psychiatric Rating Scale Autism Factor; Better indicated by lower values)											
13 (1 study) 12 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	13	-	See comment	See comment
Symptom severity/improvement (measured with: Clinical Global Impressions - Severity scale (CGI-S); Better indicated by lower values)											
13 (1 study) 12 weeks	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	13	-	See comment	See comment

¹ No control group and efficacy data could not be extracted
² Extrapolating from children with autism spectrum conditions
³ Small sample size

1.2.4 Adrenocorticotrophic hormones

1.2.4.1 Adrenocorticotrophic hormone (ORG 2766) versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Adrenocorticotrophic hormone (ORG 2766)		Risk with Placebo	Risk difference with Adrenocorticotrophic hormone (ORG 2766) (95% CI)
Challenging behaviour (social withdrawal) (assessed with: Aberrant Behaviour Checklist)											
47 (1 study) 6 weeks	serious ¹	serious ²	serious ³	serious ⁴	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3,4} due to risk of bias, inconsistency, indirectness, imprecision	4/18 (22.2%)	10/29 (34.5%)	RR 1.55 (0.57 to 4.22)	Study population	
										222 per 1000	122 more per 1000 (from 96 fewer to 716 more)
										Moderate	
									222 per 1000	122 more per 1000 (from 95 fewer to 715 more)	
Challenging behaviour (social isolation) (measured with: General Assessment Parents Scale; Better indicated by lower values)											
20 (1 study) 36 weeks	no serious risk of bias	serious ²	serious ³	serious ⁴	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3,4} due to inconsistency, indirectness, imprecision	10	10	-		The mean challenging behaviour (social isolation) in the intervention groups was 0.92479 standard deviations lower (1.82 to 0.02 lower)

Symptom severity/improvement (measured with: Clinical Global Impression Scale; Better indicated by lower values)											
69 (2 studies) 6-36 weeks	serious ¹	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,3} due to risk of bias, indirectness	29	40	-		The mean symptom severity/improvement in the intervention groups was 0.97 standard deviations lower (1.48 to 0.45 lower)

¹ Randomisation methods were unclear in BUITELAAR1996 (authors state 'randomised in principle' and there was a trend for group differences in age and CARS score at baseline)

² BUITELAAR1992 found statistically significant treatment effects for challenging behaviour as measured by social isolation on the GAP, whereas BUITELAAR1996 found no significant differences for social withdrawal as measured by ABC

³ Extrapolating from children with autism spectrum conditions

⁴ Small sample size

1.2.5 Secretin

1.2.5.1 Secretin versus placebo for autistic behaviours in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Secretin		Risk with Placebo	Risk difference with Secretin (95% CI)
Core ASC symptom of communication (measured with: Communication and Symbolic Behaviour Scale and Preschool Language Scale-3; Better indicated by lower values)											
157 (2 studies) 3-8 weeks	serious ¹	serious ²	serious ³	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, inconsistency, indirectness	79	78	-		The mean core asc symptom of communication in the intervention groups was 0.29 standard deviations lower (0.77 lower to 0.2 higher)
Autistic behaviours (measured with: Childhood Autism Rating Scale & Real Life Ritvo Behaviour Scale; Better indicated by lower values)											
86 (2 studies) 3-8 weeks	serious ¹	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊖ LOW ^{1,3} due to risk of bias, indirectness	43	43	-		The mean autistic behaviours in the intervention groups was 0.24 standard deviations lower (0.67 lower to 0.18 higher)
Challenging behaviour (measured with: Parent-completed Global Behaviour Rating Scales; Better indicated by lower values)											
62 (1 study) 8 weeks	serious ¹	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊖ LOW ^{1,3} due to risk of bias, indirectness	31	31	-		The mean challenging behaviour in the intervention groups was 0.13678 standard deviations lower (0.64 lower to 0.36 higher)

¹ For LEVY2003 there was a significant difference between the groups in baseline CARS total score

² The studies found modest but non-significant effect sizes in different directions

³ Extrapolating from children with autism spectrum conditions

1.2.6 Melatonin

1.2.6.1 Open-label melatonin for insomnia in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Melatonin		Risk with Control	Risk difference with Melatonin (95% CI)
Sleep patterns (measured with: Actigraph; Better indicated by lower values)											
15 (1 study) 5 weeks	very serious ^{1,2}	no serious inconsistency	serious ³	serious ²	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	15	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Open-label study with no control group and efficacy data cannot be extracted

² Small sample size

³ Extrapolating from children with autism spectrum conditions

1.2.7 Stimulants

1.2.7.1 Methylphenidate versus placebo for coexisting hyperactivity in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Methylphenidate		Risk with Placebo	Risk difference with Methylphenidate (95% CI)
Hyperactivity (measured with: Aberrant Behaviour Checklist Hyperactivity subscale (parent-report); Better indicated by lower values)											
62 (1 study) 5 weeks	no serious risk of bias	no serious inconsistency	serious ¹	no serious imprecision	undetected	⊕⊕⊕⊖ MODERATE ¹ due to indirectness	30	32	-		The mean hyperactivity in the intervention groups was 8.80 lower (13.72 to 3.88 lower)
Social interaction (initiating joint attention) (measured with: Joint Attention Measure from the ESCs (Early Social Communication Scales) (JAMES); Better indicated by lower values)											
34 (1 study) 5 weeks	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊕⊖ LOW ^{1,2} due to indirectness, imprecision	17	17	-		The mean social interaction (initiating joint attention) in the intervention groups was 6.50 higher (2.85 lower to 15.85 higher)
Repetitive behaviour (measured with: Children's Yale-Brown Obsessive Compulsive Scales-PDD (CYBOCS-PDD); Better indicated by lower values)											
63 (1 study) 5 weeks	no serious risk of bias	no serious inconsistency	serious ¹	no serious imprecision	undetected	⊕⊕⊕⊖ MODERATE ¹ due to indirectness	31	32	-		The mean repetitive behaviour in the intervention groups was 0.92 lower (2.82 lower to 0.98 higher)

¹ Extrapolating from children with autism spectrum conditions

² Small sample size

1.2.8 Antidepressants

1.2.8.1 Clomipramine versus placebo for autistic behaviours in adolescents with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Clomipramine versus placebo for behaviour management in adults with autism		Risk with Control	Risk difference with Clomipramine versus placebo for behaviour management in adults with autism (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale (CARS); Better indicated by lower values)											
32 (1 study) 21 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	16	16	-		The mean autistic behaviours in the intervention groups was 1.60 lower (7.07 lower to 3.87 higher)
Side effects (global) (measured with: Dosage Treatment Emergent Symptom Scale (DOTES); Better indicated by lower values)											
32 (1 study) 21 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	16	16	-		The mean side effects (global) in the intervention groups was 1.20 higher (0.45 lower to 2.85 higher)

¹ Risk of attrition bias due to high drop out in the clomipramine group

² Sample includes children and adolescents with autism and mean age is 16 years

³ Small sample size

1.2.8.2 Fluvoxamine versus placebo for autistic behaviours in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Fluvoxamine versus placebo for behaviour management in adults with autism		Risk with Control	Risk difference with Fluvoxamine versus placebo for behaviour management in adults with autism (95% CI)
Core autistic symptom (repetitive behaviour) (measured with: Yale-Brown Obsessive Compulsive Scale (Y-BOCS); Better indicated by lower values)											
30 (1 study) 12 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ^{1,2}	undetected	⊕⊕⊕⊖ LOW ^{1,2} due to imprecision	15	15	-		The mean core autistic symptom (repetitive behaviour) in the intervention groups was 8.20 lower (13.92 to 2.48 lower)
Autistic behaviours (measured with: Ritvo-Freeman Real-Life Rating Scale; Better indicated by lower values)											
30 (1 study) 21 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	15	15	-		The mean autistic behaviours in the intervention groups was 0.82 standard deviations lower (1.56 to 0.07 lower)
Challenging behaviour (aggression) change-from-baseline (measured with: Brown Aggression Scale; Better indicated by lower values)											
30 (1 study) 21 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	15	15	-		The mean challenging behaviour (aggression) change-from-baseline in the intervention groups was 0.92 standard deviations lower

											(1.68 to 0.17 lower)
Maladaptive behaviour (change from baseline) (measured with: Vineland Adaptive Behaviour Scale; Better indicated by lower values)											
30 (1 study) 21 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	15	15	-		The mean maladaptive behaviour (change from baseline) in the intervention groups was 1.61 standard deviations lower (2.43 to 0.79 lower)
Symptom severity/improvement (dichotomous) (assessed with: Clinical Global Impressions (CGI) scale)											
30 (1 study) 21 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	0/15 (0%)	8/15 (53.3%)	RR 17 (1.07 to 270.41)	Study population	
										0 per 1000	-
										Moderate	
0 per 1000	-										
Symptom severity/improvement (continuous) (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
30 (1 study) 21 weeks	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	undetected	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	15	15	-		The mean symptom severity/improvement (continuous) in the intervention groups was 1.94 standard deviations lower (2.8 to 1.07 lower)

¹ Small sample size

² Y-BOCS scale valid and reliable for assessing severity of obsessive-compulsive symptoms in individuals with OCD but reliability and validity for assessing repetitive thoughts in autism is unknown

1.2.8.3 Open-label fluoxetine for behaviour management in adolescents with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Open-label fluoxetine for behaviour management in adults with autism		Risk with Control	Risk difference with Open-label fluoxetine for behaviour management in adults with autism (95% CI)
Symptom severity/improvement (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
23 (1 study) 189 days	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	23	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Compulsive behaviour (measured with: Clinical Global Impressions (CGI) scale; Better indicated by lower values)											
23 (1 study) 189 days	very serious ¹	no serious inconsistency	very serious ^{2,3}	serious ⁴	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	23	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group and efficacy data cannot be extracted

² The mean age is above 15 years but this is predominantly a child and adolescent sample

³ Participants also had coexisting psychiatric disorders

⁴ Small sample size

1.2.8.4 Open-label sertraline for autistic behaviours in adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Open-label sertraline for behaviour management in adults with autism		Risk with Control	Risk difference with Open-label sertraline for behaviour management in adults with autism (95% CI)
Core autistic symptom (repetitive behaviour) (measured with: Yale-Brown Obsessive Compulsive Scale (Y-BOCS); Better indicated by lower values)											
37 (1 study) 12 weeks	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	undetected	⊕⊕⊕⊖ VERY LOW ^{1,2} due to risk of bias, imprecision	-	37	-	See comment	See comment
Autistic behaviours (measured with: Ritvo-Freeman Real-Life Rating Scale; Better indicated by lower values)											
37 (1 study) 12 weeks	very serious ¹	no serious inconsistency	no serious indirectness	serious ³	undetected	⊕⊕⊕⊖ VERY LOW ^{1,3} due to risk of bias, imprecision	-	37	-	See comment	See comment
Maladaptive behaviour (measured with: Vineland Adaptive Behaviour Scale; Better indicated by lower values)											
37 (1 study) 12 weeks	very serious ¹	no serious inconsistency	no serious indirectness	serious ³	undetected	⊕⊕⊕⊖ VERY LOW ^{1,3} due to risk of bias, imprecision	-	37	-	See comment	See comment

Symptom severity/improvement (measured with: Clinical Global Impressions global improvement item; Better indicated by lower values)											
37 (1 study) 12 weeks	very serious ¹	no serious inconsistency	no serious indirectness	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,3} due to risk of bias, imprecision	-	37	-	See comment	See comment

¹ No control group and efficacy data cannot be extracted

² Y-BOCS scale valid and reliable for assessing severity of obsessive-compulsive symptoms in individuals with OCD but reliability and validity for assessing repetitive thoughts in autism is unknown

³ Small sample size

1.2.9 Restrictive diets, vitamins, minerals and supplements

1.2.9.1 Gluten-and-casein-free diet versus treatment as usual for autistic behaviours in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Gluten-and-casein-free diet		Risk with Treatment as usual	Risk difference with Gluten-and-casein-free diet (95% CI)
Autistic behaviours (social isolation and bizarre behaviours) (measured with: Diagnosis of Psychotic Behaviour in Children; Better indicated by lower values)											
20 (1 study) 1 years	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	10	10	-		The mean autistic behaviours (social isolation and bizarre behaviours) in the intervention groups was 5.60 lower (9.04 to 2.16 lower)

¹ Risk of performance bias as unclear if intervention groups received same care apart from treatment, and participants receiving care and individuals administering care were not blind to group allocation

² Extrapolating from children with autism spectrum conditions

³ Small sample size

1.2.9.2 Open-label ketogenic diet for autistic behaviours in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Ketogenic diet		Risk with Control	Risk difference with Ketogenic diet (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale; Better indicated by lower values)											
30 (1 study) 6 months	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	30	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational study with no control group so high potential for bias and not possible to extract efficacy data

² Extrapolating from children with autism spectrum conditions

³ Small sample size

1.2.9.3 L-carnosine versus placebo for autistic behaviours in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With L-Carnosine		Risk with Placebo	Risk difference with L-Carnosine (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale; Better indicated by lower values)											
31 (1 study) 8 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	17	14	-		The mean autistic behaviours in the intervention groups was 4.01 lower (9.03 lower to 1.01 higher)
Symptom improvement (measured with: Clinical Global Impressions improvement scale; Better indicated by higher values)											
31 (1 study) 8 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	17	14	-		The mean symptom improvement in the intervention groups was 2.14 higher (0.99 lower to 5.27 higher)

¹ Baseline group differences in autistic behaviours as measured by the Gilliam Autism Rating Scale (GARS)

² Extrapolating from children with autism spectrum conditions

³ Small sample size

1.2.9.4 Micronutrient versus standard medication for autistic behaviours in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Standard medication	With Micronutrient		Risk with Standard medication	Risk difference with Micronutrient (95% CI)
Autistic behaviours (measured with: Childhood Autism Rating Scale; Better indicated by lower values)											
88 (1 study ¹) 3-98 months	serious ²	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3} due to risk of bias, indirectness	44		-		The mean autistic behaviours in the intervention groups was 0.50 higher (5.62 lower to 6.62 higher)
Challenging behaviour (irritability) (measured with: Aberrant Behaviour Checklist; Better indicated by lower values)											
88 (1 study ¹) 3-98 months	serious ²	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3} due to risk of bias, indirectness	44		-		The mean challenging behaviour (irritability) in the intervention groups was 7.40 lower (9.91 to 4.89 lower)
Symptom severity (measured with: Clinical Global Impressions severity scale; Better indicated by lower values)											
88 (1 study ¹) 3-98 months	serious ²	no serious inconsistency	serious ³	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{2,3} due to risk of bias, indirectness	44		-		The mean symptom severity/improvement in the intervention groups was 1.38 lower (2.04 to 0.72 lower)

¹ case-control

² This is a non-randomized and non-blinded study so there is a high risk of bias

³ Extrapolating from children with autism spectrum conditions

1.2.9.5 Open-label iron supplementation for coexisting sleep problems in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Iron supplement		Risk with Control	Risk difference with Iron supplement (95% CI)
Sleep patterns (measured with: Restless Sleep score; Better indicated by lower values)											
33 (1 study) 8 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	33	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Challenging behaviour (measured with: Clinical Global Impressions - Irritability; Better indicated by lower values)											
33 (1 study) 8 weeks	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	33	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Observational study with no control group, no blinding, and a high attrition rate so there is potential for bias. It is also not possible to extract efficacy data

² Extrapolating from children with autism spectrum conditions

³ Small sample size

1.2.9.6 Open-label magnesium-vitamin B6 supplementation for core autistic symptoms in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Magnesium-vitamin B6		Risk with Control	Risk difference with Magnesium-vitamin B6 (95% CI)
Core ASC symptoms (social interaction, communication, stereotyped behaviour) (measured with: DSM-IV clinical evaluation; Better indicated by lower values)											
33 (1 study) 24 months	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	33	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Symptom severity/improvement (measured with: Behaviour Summarized Evaluation; Better indicated by lower values)											
11 (1 study) 14 weeks	very serious ^{1,4}	no serious inconsistency	very serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3,4} due to risk of bias, indirectness, imprecision	-	11	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group results in high risk of bias and efficacy data cannot be extracted

² Extrapolating from children with autism spectrum conditions

³ Small sample size

⁴ Sample selected for their previous sensitivity to the treatment

1.2.9.7 Digestive enzyme supplementation versus placebo for behaviour management in children with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Placebo	With Digestive enzyme supplementation		Risk with Placebo	Risk difference with Digestive enzyme supplementation (95% CI)
Autistic core symptom (communication) (measured with: Language Development Survey (LDS) Vocabulary score; Better indicated by lower values)											
43 (1 study) 6 months	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	22	21	-		The mean autistic core symptom (communication) in the intervention groups was 1.36 higher (15.74 lower to 18.46 higher)
Gastrointestinal symptoms (measured with: Parent-rated Additional Rating Scale (ARS) gastrointestinal symptoms subscale; Better indicated by lower values)											
43 (1 study) 6 months	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	22	21	-		The mean gastrointestinal symptoms in the intervention groups was 0.18 higher (0.27 lower to 0.63 higher)
Challenging behaviour (measured with: Parent-rated Global Behaviour Rating Scale (GBRS); Better indicated by higher values)											
43 (1 study) 6 months	no serious risk of bias	no serious inconsistency	serious ¹	serious ²	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to indirectness, imprecision	22	21	-		The mean challenging behaviour in the intervention groups was 0.14 higher (0.19 lower to 0.47 higher)

¹ Extrapolating from children with autism spectrum conditions

² Small sample size

1.3 SETTINGS FOR CARE

1.3.1 Community based teams

1.3.1.1 Current living compared to developmental group home training environment for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Developmental centre group home training environment	With Current living		Risk with Developmental centre group home training environment	Risk difference with Current living (95% CI)
Community living skills (measured with: Average number of skills gained across community living skills behavioural domains; Better indicated by lower values)											
20 (1 study) 1 years	very serious ¹	no serious inconsistency	serious ²	very serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	10	10	-		The mean community living skills in the intervention groups was 8.90 higher (8.06 to 9.74 higher)

¹ Non-randomised allocation and non-blind assessment of outcome increasing the risk of selection and detection bias

² Extrapolating from adults with learning disabilities

³ The precision and reliability and validity of the outcome measure is unclear as under-specified and the sample size is small

1.3.1.2 Specialist behaviour therapy team compared with treatment as usual for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Specialist behaviour therapy team		Risk with Treatment as usual	Risk difference with Specialist behaviour therapy team (95% CI)
Challenging behaviour (lethargy/hyperactivity) (measured with: Aberrant Behaviour Checklist (ABC); Better indicated by lower values)											
63 (1 study) 6 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	31	32	-	See comment	See comment
Challenging behaviour (irritability) (measured with: Aberrant Behaviour Checklist (ABC); Better indicated by lower values)											
63 (1 study) 6 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, indirectness	31	32	-	See comment	See comment

¹ Cannot extract data for efficacy as median values and interquartile ranges were reported. This may also imply that the data was skewed. We are thus restricted to analysing the results from this study via narrative review

² Extrapolating from adults with learning disabilities

1.3.1.3 Observational studies of specialist assessment and treatment units for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Specialist assessment and treatment unit		Risk with Control	Risk difference with Specialist assessment and treatment unit (95% CI)
Challenging behaviour (measured with: Adaptive Behaviour Scale Part II violent behaviour domain; Better indicated by lower values)											
16 (1 study) 6 months	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	16	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ Small sample size and ABS data only available for half of the participants. There was also no control group and efficacy data could not be extracted

² Extrapolating from adults with learning disabilities

³ Small sample size

1.3.1.4 Liaison worker compared with treatment as usual for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Treatment as usual	With Liason worker		Risk with Treatment as usual	Risk difference with Liason worker (95% CI)
Access to services (measured with: Number of contacts with services; Better indicated by lower values)											
26 (1 study) 9 months	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	14	12	-	See comment	See comment

¹ Efficacy data could not be extracted

² Extrapolating from adults with learning disabilities

³ Small sample size

1.3.2 Residential accommodation and related services

1.3.2.1 Residential institution compared with community housing for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Community housing	With Residential institution		Risk with Community housing	Risk difference with Residential institution (95% CI)
Residential satisfaction - social life (measured with: Satisfaction Questionnaire of Seltzer and Seltzer's (1978) Community Adjustment Scale; Better indicated by lower values)											
29 (1 study) 0.1-8 years	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	15	14	-		The mean residential satisfaction - social life in the intervention groups was 5.80 higher (3.14 to 8.46 higher)
Residential satisfaction - autonomy (measured with: Satisfaction Questionnaire of Seltzer and Seltzer's (1978) Community Adjustment Scale; Better indicated by lower values)											
29 (1 study) 0.1-8 years	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	15	14	-		The mean residential satisfaction - autonomy in the intervention groups was 1.20 lower

												(2.28 to 0.12 lower)
Residential satisfaction - total (measured with: Satisfaction Questionnaire of Seltzer and Seltzer's (1978) Community Adjustment Scale; Better indicated by lower values)												
29 (1 study) 0.1-8 years	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	15	14	-			The mean residential satisfaction - total in the intervention groups was 5.60 higher (1.1 to 10.1 higher)
Adaptive behaviour (measured with: Adaptive Behaviour Scale (ABS), Vineland Adaptive Behaviour Scales or a modified version of the Behaviour Development Survey; Better indicated by lower values)												
224 (3 studies) 12-48 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	103	121	-			The mean adaptive behaviour in the intervention groups was 0.48 standard deviations lower (0.75 to 0.2 lower)
Social skills (measured with: Staff-rated social skills; Better indicated by lower values)												
100 (1 study) 30 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	50	50	-			The mean social skills in the intervention groups was 5.10 lower (14.31 lower to 4.11 higher)
Quality of life (measured with: Behavioural observations of quality of life ; Better indicated by lower values)												
100 (1 study) 30 months	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	50	50	-			The mean quality of life in the intervention groups was

												12.90 lower (16.05 to 9.75 lower)	
Activity outside the home (measured with: Diary self-report on the number of trips outside the home; Better indicated by lower values)													
36 (1 study) 18 months	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	18	18	-				The mean activity outside the home in the intervention groups was 3.00 lower (6.99 lower to 0.99 higher)

¹ Non-randomised allocation and non-blind assessment of outcome increases the risk of selection and detection bias

² Extrapolating from adults with learning disabilities

³ Small sample size

1.3.2.2 Small residential homes compared with institutions for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Institution	With Small residential homes		Risk with Institution	Risk difference with Small residential homes (95% CI)
Quality of life (measured with: Quality of Life Questionnaire (QOLQ); Better indicated by lower values)											
179 (1 study)	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	76	103	-		The mean quality of life in the intervention groups was 11.40 higher (8.79 to 14.01 higher)
Choice making (measured with: Residence Choice Assessment Scale (RCAS); Better indicated by lower values)											
179 (1 study)	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	76	103	-		The mean choice making in the intervention groups was 36.60 higher (30.89 to 42.31 higher)
Community inclusion (measured with: Use of Community Facilities Scale (UCFS); Better indicated by lower values)											
179 (1 study)	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	76	103	-		The mean community inclusion in the intervention groups was 7.40 higher (4.86 to 9.94 higher)

Contact with family (measured with: Frequency of face-to-face visits; Better indicated by lower values)											
179 (1 study)	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	76	103	-		The mean contact with family in the intervention groups was 0.60 higher (0.36 to 0.84 higher)

¹ Non-randomised allocation of participants and significant group differences in adaptive/maladaptive behaviour

² Extrapolating from adults with learning disabilities

1.3.2.3 Dispersed supported living compared with residential homes for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Residential homes	With Dispersed supported living		Risk with Residential homes	Risk difference with Dispersed supported living (95% CI)
Social inclusion (measured with: Number of community amenities used in past months; Better indicated by lower values)											
241 (1 study)	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	138	103	-		The mean social inclusion in the intervention groups was 0.90 higher (0.43 to 1.37 higher)

¹ Limited data could be extracted from the study as a measure of variation (SD) was only reported for one scale item. Non-randomised allocation and non-blind assessment of outcome also increases the risk of selection and detection bias

² Extrapolating from adults with learning disabilities

1.3.2.4 Group homes compared with semi-independent apartments for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Semi-independent apartments	With Group home		Risk with Semi-independent apartments	Risk difference with Group home (95% CI)
Resident satisfaction (measured with: Lifestyle satisfaction scale (LSS); Better indicated by lower values)											
204 (1 study) 1 years	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	147	57	-		The mean resident satisfaction in the intervention groups was 8.72 lower (12.61 to 4.83 lower)

¹ Differences in sample sizes across groups, and significant differences in demographic factors found between groups, e.g. group home residents oldest, and participants in independent apartments had the highest mean score for adaptive behaviour and the lowest mean score for challenging behaviour which were not controlled for in statistical analysis. Non-randomisation and non-blind assessment of outcome also increases the risk of selection and detection bias

² Extrapolating from adults with learning disabilities

1.3.2.5 Intermediate care placement between institution and community compared with direct community placement for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Direct community placement	With Intermediate care placement between institution and community		Risk with Direct community placement	Risk difference with Intermediate care placement between institution and community (95% CI)
Adaptive behaviour (measured with: AAMD Adaptive Behaviour Scale; Better indicated by lower values)											
57 (1 study) 1 years	serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, indirectness	39	18	-		The mean adaptive behaviour in the intervention groups was 5.89 higher (12.24 lower to 24.02 higher)

¹ Discrepancy in sample size between groups. Also non-randomised allocation and non-blind assessment of outcomes increases the risk of selection and detection bias

² Extrapolating from adults with learning disabilities

1.3.2.6 Person-centred compared with system-centred planning for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With System-centred planning	With Person-centred planning		Risk with System-centred planning	Risk difference with Person-centred planning (95% CI)
Movement into community (assessed with: Number of participants moving into community)											
37 (1 study) 3 years	serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	5/18 (27.8%)	18/19 (94.7%)	RR 3.41 (1.61 to 7.24)	Study population	
										278 per 1000	669 more per 1000 (from 169 more to 1000 more)
										Moderate	
											-

¹ Allocation was not randomised increasing the risk of selection bias

² Extrapolating from adults with learning disabilities

³ Small sample size

1.3.2.7 Observational studies of the TEACCH approach in a residential setting for adults with autism

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With TEACCH approach in residential setting		Risk with Control	Risk difference with TEACCH approach in residential setting (95% CI)
Social abilities (measured with: staff-report questionnaire (based on Vineland Adaptive Behaviour Scales) and observation checklist; Better indicated by lower values)											
12 (1 study) 6 months	very serious ¹	no serious inconsistency	no serious indirectness	serious ²	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, imprecision	-	12	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Functional communication (measured with: staff-report questionnaire (based on Vineland Adaptive Behaviour Scales) and observation checklist; Better indicated by lower values)											
12 (1 study) 6 months	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	undetected	⊕⊖⊖⊖ VERY LOW ¹ due to risk of bias	-	12	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group and efficacy data could not be extracted. This study also used a small sample size

² Small sample size

1.3.2.8 Observational studies of the move from institutional to community settings for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Move from institutional to community settings		Risk with Control	Risk difference with Move from institutional to community settings (95% CI)
Challenging behaviour (measured with: Modified Overt Aggression Scale (MOAS) and Problems Questionnaire (PQ); Better indicated by lower values)											
329 (3 studies) 12-24 months	very serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of bias, indirectness	-	329	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Quality of Life (measured with: The Questionnaire on Quality of Life; Better indicated by lower values)											
29 (1 study) 53 months	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	29	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Family contact (measured with: Developmental Disabilities Quality Assurance Questionnaire (DDQAQ); Better indicated by lower values)											
177 (1 study) 5 years	very serious ¹	no serious inconsistency	serious ²	no serious imprecision	undetected	⊕⊕⊕⊕ VERY LOW ^{1,2} due to risk of	-	177	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

						bias, indirectness					
Adaptive Behaviour (measured with: AAMD's Adaptive Behaviour Scale (ABS) Part I total score; Better indicated by lower values)											
32 (1 study) 5.5 years	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	32	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group and efficacy data could not be extracted

² Extrapolating from adults with learning disabilities

³ Small sample size

1.3.2.9 Observational studies of the move from more restrictive to less restrictive work or living environments for adults with intellectual disability

Quality assessment							Summary of Findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With Control	With Move from more restrictive to less restrictive work or living environments		Risk with Control	Risk difference with Move from more restrictive to less restrictive work or living environments (95% CI)
Self-determination (measured with: Arcs’s Self-Determination Scale: Adult Version; Better indicated by lower values)											
31 (1 study) 1 years	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	31	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted
Autonomous functioning (measured with: Autonomous Functioning Checklist (AFC); Better indicated by lower values)											
31 (1 study) 1 years	very serious ¹	no serious inconsistency	serious ²	serious ³	undetected	⊕⊖⊖⊖ VERY LOW ^{1,2,3} due to risk of bias, indirectness, imprecision	-	31	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

¹ No control group and efficacy data could not be extracted

² Extrapolating from adults with learning disabilities

³ Sample size is small

GRADE EVIDENCE PROFILES FOR ECONOMIC EVIDENCE

1.3.2.10 Clinical / economic question: Employment support scheme versus standard care

Evidence profile - economic evidence							
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect	ICER (£/week employed)	Uncertainty
Guideline economic analysis	Potentially serious limitations ¹	Directly applicable	Cost effectiveness analysis of employment support programme. Public sector perspective.	£6,921	44 weeks in employment	£158 per additional week of employment in the supported group	One-way sensitivity analysis to all parameters: Range of ICER: £80 to £338 per week in employment

¹ The data on rates of different types of accommodation of employed and unemployed is assumed. The model is extended to third year under certain assumptions. The standard service received by the control group not reported in MAWHOOD1999, it is assumed same as day service and adult education.

1.3.2.11 Clinical / economic question: Employment support scheme versus standard care

Evidence profile - economic evidence							
Study & country	Limitations	Applicability	Other comments	Incremental cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty
Mawhood and Howlin, 1999, UK	Potentially serious limitations ²	Directly applicable	RCT. NHS Perspective. Intervention costs of employment support only included - intervention costs of control group not estimated	Cost of intervention of additional person in the programme £25,451	38% NA	Cost of intervention per additional adult employed: £33,474N A	Not reported

² Short time horizon, simple cost analysis, resource use or cost of standard service received by the control group not reported.