APPENDIX 19: GRADE EVIDENCE PROFILES

GRADE Evidence Profiles for Clinical Evidence *2*

1.1 Psychosocial interventions *2*

1.1.1 Behavioural therapies aimed at communication 2
1.1.2 Facilitated communication 4
1.1.3 Behavioural therapies aimed at behaviour management 5
1.1.4 Cognitive behavioural therapies 9
1.1.5 Leisure programmes 13
1.1.6 Social learning interventions 14
1.1.7 Supported employment programmes 19
1.1.8 Support for families and carers 24

1.2 Biomedical interventions *27*

1.2.1 Antipsychotics: grade profiles 27
1.2.2 Anticonvulsants 39
1.2.3 Drugs affecting cognition 43
1.2.4 Adrenocorticotrophic hormones 47
1.2.5 Secretin 49
1.2.6 Melatonin 50
1.2.7 Stimulants 51
1.2.8 Antidepressants 52
1.2.9 Restrictive diets, vitamins, minerals and supplements 58

1.3 Settings for care *65*

1.3.1 Community based teams 65
1.3.2 Residential accommodation and related services 69

GRADE Evidence Profiles for Economic Evidence *82*

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 acquition 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 (MAZZUCCHELLI2001) 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

Economic evidence profile

Study & country	Limitations	Applicability	Other comments	Incremental cost (£)[1]	Incremental effect	ICER	Uncertainty
Mawhood & Howlin, 1999, UK	Potentially serious limitations [2]	Directly applicable	Quasi-experimental parallel group controlled trial Only intervention costs of employment support only – intervention costs of control group not estimated Measure of outcome: probability of employment	£13,018	0.38	£34,258	Not reported
Guideline economic analysis	Minor limitations [3]	Directly applicable	Decision-tree followed by Markov model Time horizon: 8 years Costs considered: Main analysis: intervention costs Secondary analysis 1: intervention and accommodation costs Secondary analysis 2: intervention and NHS/PSS costs Measure of outcome: QALY	Main analysis: £157 Secondary analysis 1: -£1,117 Secondary analysis 2: -£611	0.11	Main analysis: £1,467/QALY Secondary analyses: supported employment dominant	One-way sensitivity analysis (main analysis): 50% change in supported employment intervention cost: £15,190/QALY to supported employment dominant 50% change in standard care intervention cost: supported employment dominant to £15,452/QALY Threshold analysis (main analysis): minimum risk ratio of supported employment vs. standard care required for the intervention to be cost-effective: 1.45 (upper NICE threshold); 1.59 (lower NICE threshold) PSA: probability that the intervention is cost-effective at the lower NICE threshold. Main analysis: 77.5% Secondary analysis 1: 80.4% Secondary analysis 2: 80.8%

[1] Costs uplifted to 2011 UK pounds using the UK HCHS inflation index.
[2] Short time horizon, only intervention costs of supported employment considered, resource use or costs of control not estimated
[3] Efficacy data based on Quasi-experimental parallel group controlled trial, time horizon 8 years, cost data based on published sources, national unit costs used, probabilistic sensitivity analysis conducted.

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 placments (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] Learrning 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 (5.3 %) 5/24 (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] Learrning 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] HELLINGS2005 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] Obervational 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 symtpoms (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 Abberant 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 autsim**		**Risk with Control**	**Risk difference with Open-label sertraline for behaviour management in adults with autsim** (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 spectum 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)
Autsitic 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 autsitic 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 detction 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] Erfficacy 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 Qustionnaire 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 Qustionnaire 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 Qustionnaire 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 bias, indirectness	-	177	-	Efficacy data cannot be extracted	Efficacy data cannot be extracted

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
Autonmous 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

1.3.3 Clinical care pathways - Multi-disciplinary teams

Economic evidence profile

Study & country	Limitations	Applicability	Other comments	Incremental[4] cost (£)	Incremental effect (QALYs)	ICER (£/QALY)	Uncertainty[5]
Clark et al., 2009, UK	Potentially serious limitations[6]	Partially applicable[7]	Snapshot approach with annutised costs and outcomes Public sector perspective; costs the NHS reported separately	Per 1,000 working-age population: £859 cost to the NHS £215 saving to the public purse	NA	NA	**For a range of identification rate range achieved by multi=-disciplinary team 2% to 14%:** Cost to the NHS: £752 to £1,181 per 1,000 working-age population (Cost to public purse £752 to -£5,370 (saving) per 1,000 working-age population

[4] Costs converted to 2010/11 prices using HCHS.
[5] Costs converted to 2010/11 prices using HCHS.
[6] Cost analysis; key input parameters based on a survey, local unpublished data and expert opinion
[7] Perspective broader than NHS and PSS