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Abbreviations

|  |  |
| --- | --- |
| AAMD | American Association on Mental Deficiency |
| ADHD | attention deficit hyperactivity disorder |
| A-PS | assertiveness then social problem-solving |
| BDI(-II) | Beck Depression Inventory (revised) |
| CBT | cognitive behavioural therapy |
| CES-D | Center for Epidemiologic Studies - Depression scale |
| CGI | Clinical Global Impression scale |
| CI | confidence interval |
| GRADE | Grades of Recommendation Assessment, Development and Evaluation |
| GSI | Global Severity Index |
| HAM-A | Hamilton Anxiety Rating Scale |
| ITT | intention to treat |
| MD | mean difference |
| NCBRF | Nisonger Child Behavior Rating Form |
| PS-A | social problem-solving then assertiveness |
| PSI | Parenting Stress Index |
| PTSD | post-traumatic stress disorder |
| RCT | randomised controlled trial |
| RR | risk ratio |
| SAS-ID | Zung Self-Rating Anxiety Scale for Adults with Intellectual Disabilities |
| SCL-90-R | Symptom CheckList-90-Revised |
| SF-12 | 12-Item Short Form Health Survey |
| SIB-R | [Scales of Independent Behavior-Revised](http://www.hmhco.com/hmh-assessments/other-clinical-assessments/sib-r) |
| SMD | standardised mean difference |
| SNAP-IV | Swanson, Nolan and Pelham Questionnaire - revised |
| TAU | treatment as usual |

* 1. Psychological/psychosocial interventions
     1. Psychological interventions versus control for mental health problems

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **psychological interventions** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health – RCTs (follow up: mean 13.25 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 3 | randomised trials | very serious 1 | serious 2 | not serious | serious 3 | none | 41 | - | - | SMD **1.24 SD lower** (2.31 lower to 0.18 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Mental health – Controlled before-and-after studies (follow up: 12 weeks; assessed with: Brief Symptom Inventory: Global Severity Index [GSI]) | | | | | | | | | | | | |
| 1 | observational studies | very serious 4 | not serious | not serious | serious 3 | none | 12 | 12 | - | MD **0.83 lower** (1.29 lower to 0.37 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Low problem behaviour (follow up: 10 weeks; assessed with: Role-play test of anger arousing situations) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 5 | none | 18 | 10 | - | MD **11.69 more** (7.06 more to 16.32 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Maladaptive functioning (follow up: 10 weeks; assessed with: Adaptive Behaviour Scale – revised – part II) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 3 | none | 18 | 10 | - | MD **21.74 lower** (36.45 lower to 7.02 lower) | ⨁⨁◯◯ LOW | IMPORTANT |
| Interpersonal skills (follow up: 18 weeks; assessed with: Social Performance Survey Schedule) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | very serious 6 | none | 22 | 10 | - | MD **20.45 more** (9.74 fewer to 50.74 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection and performance bias
2. I2 suggests considerable heterogeneity
3. Confidence intervals cross minimally important difference in one direction. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
4. Risk of selection and performance bias and unclear risk of selective outcomes, attrition and detection bias
5. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
6. Confidence intervals cross two minimally important differences. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Social problem-solving than assertiveness training (PS-A) versus assertiveness then social problem-solving (A-PS) for mental health problems

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **social problem-solving, then assertiveness training (PS-A)** | **assertiveness, then social problem-solving (A-PS)** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Psychiatric/psychological symptoms (follow up: 23 weeks; assessed with: Brief Symptom Inventory) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1,2 | not serious | not serious | serious 3 | none | 9 | 9 | - | MD 0.02 more (0.43 fewer to 0.47 more) | ⨁⨁◯◯ LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Psychological distress (follow up: 23 weeks; assessed with: Subjective Unit of Distress Scale) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1,2 | not serious | not serious | very serious 4 | none | 9 | 9 | - | MD 0.22 fewer (2.82 fewer to 2.38 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Low problem behaviour – Follow-up (follow up: 23 weeks; assessed with: Role-play test of anger arousing situations) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1,2 | not serious | not serious | serious 3 | none | 9 | 9 | - | MD 4.11 more (1.07 fewer to 9.29 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Adaptive behaviour (follow up: 23 weeks; assessed with: Adaptive Behavior Scale – Revised) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1,2 | not serious | not serious | very serious 4 | none | 9 | 9 | - | MD 2.02 fewer (18.88 fewer to 14.84 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Adaptive behaviour (follow up: 23 weeks; assessed with: Problem-Solving Task) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1,2 | not serious | not serious | very serious 4 | none | 9 | 9 | - | MD 4 fewer (20.7 fewer to 12.7 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection bias (unclear allocation method, no details of allocation concealment)
2. Risk of performance bias (not blind)
3. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
4. Confidence intervals cross minimally important difference in both directions (downgrade 2). Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Psychodynamic psychotherapy (8 sessions) versus psychodynamic psychotherapy (12 or 24+ sessions) for mental health problems

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **psychodynamic psychotherapy (8 sessions)** | **psychodynamic psychotherapy (12 or 24+ sessions)** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health (follow up: ?; assessed with: SCL-90-R) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | No statistically signiﬁcant differences were found between arms with differing lengths of treatment | | | | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Interpersonal problems (follow up: ?; assessed with: Inventory of Interpersonal Problems-32) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | No statistically signiﬁcant differences were found between arms with differing lengths of treatment | | | | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection, detection and performance bias.
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Psychological interventions versus control for substance misuse

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **psychological interventions** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Alcohol misuse (follow up: 34 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | very serious 2 | none | 42 | 42 | - | MD **0.12 fewer** (1.01 fewer to 0.77 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection bias (no details of allocation method or concealment but, most importantly and not comparable risk at baseline), risk of performance bias
2. Confidence intervals cross minimally important difference in both directions (downgrade 2). Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Assertiveness training versus modelling and social inference for substance misuse

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **assertiveness training** | **modelling and social inference** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Alcohol misuse (follow up: mean 34 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | very serious 2 | none | 21 | 21 | - | MD **0.07 fewer** (0.82 fewer to 0.68 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection bias (no details of allocation method or concealment but, most importantly, not comparable risk at baseline), Risk of performance bias
2. Confidence intervals cross minimally important difference in both directions (downgrade 2). Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Psychological intervention versus control for anxiety symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **psychological intervention** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Anxiety symptoms (RCTs) (follow up: mean 42 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 2 | randomised trials | very serious 1 | serious 2 | not serious | very serious 3 | none | 29 | - | - | SMD **0.87 SD fewer** (1.14 fewer to 1.36 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Anxiety symptoms (Controlled before-and-after) (follow up: 12 weeks; assessed with: Brief Symptom Inventory: anxiety symptom dimension) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 4 | not serious | not serious | serious 5 | none | 12 | 12 | - | MD **0.4 SD lower** (1.23 lower to 0.43 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| In paid employment after treatment (follow up: 16 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 6 | not serious | not serious | serious 5 | none | 1/16 (6.3%) | 4/14 (28.6%) | RR 0.22 (0.03 to 1.73) | **223 fewer per 1000** (from 209 more to 277 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Voluntary work (follow up: 16 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 6 | not serious | not serious | very serious 3 | none | 6/16 (37.5%) | 4/14 (28.6%) | RR 1.31 (0.46 to 3.72) | **89 more per 1000** (from 154 fewer to 777 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Risk of selection, performance and detection bias
2. I2 suggests considerable heterogeneity
3. Confidence intervals cross minimally important difference in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
4. Risk of selection and performance bias and unclear risk of attrition and detection bias
5. Confidence intervals cross minimally important difference in one direction. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
6. Risk of performance and selection bias
   * 1. Relaxation training versus control for anxiety symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **relaxation training** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Anxiety symptoms (Group relaxation training versus control) (follow up: range 2.29 weeks to unclear; assessed with: various tools) | | | | | | | | | | | | |
| 2 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 35 | - | - | SMD **2.31 lower** (2.92 lower to 1.7 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Anxiety symptoms (Individual relaxation training versus control) (follow up: 2.29 weeks; assessed with: 5-point scale on 10 ratings; Scale from: relaxed to very anxious) | | | | | | | | | | | | |
| 2 | randomised trials | very serious 3 | serious 4 | not serious | serious 2 | none | 20 | - | - | SMD **2.97 SD lower** (4.36 lower to 1.57 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life (relaxation versus story-telling) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation (relaxation versus story-telling) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection, performance and possible detection bias
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
3. Risk of selection bias (no details of allocation method or concealment); Risk of performance bias (no blinding); Possible risk of detection bias (unclear if outcome assessors blind to treatment and confounding)
4. I2 suggests substantial heterogeneity.
   * 1. Dating skills versus control for social anxiety symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **dating skills training** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Social anxiety symptoms (follow up: 24 weeks; assessed with: Social Avoidance and Distress Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 13 | 12 | - | MD **0.39 lower** (1.18 lower to 0.4 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Proportion with significant change in social anxiety symptoms (follow up: 20 weeks; assessed with: Social Avoidance and Distress Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | -/13 | -/12 | not estimable |  | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection and detection bias
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Cognitive behavioural therapy versus ABA/IBI for post-traumatic stress disorder

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **CBT** | **ABA/IBI** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Somatic symptoms (follow up: not reported; assessed with: Achenbach: somatic subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | serious 2 | none | 42 | 45 | - | MD **3.74 more** (0.69 more to 6.79 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Withdrawn symptoms (follow up: not reported; assessed with: Achenbach: withdrawn subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | serious 2 | none | 42 | 45 | - | MD **4.58 more** (1.12 more to 8.04 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Anxious/depressed symptoms (follow up: not reported; assessed with: Achenbach: anxious/depressed subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | serious 2 | none | 42 | 45 | - | MD **6.89 more** (3.68 more to 10.1 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Thought problems (follow up: not reported; assessed with: Achenbach: thought problems subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | very serious 3 | none | 42 | 45 | - | MD **7.53 more** (4.83 more to 10.23 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Attention subscale (follow up: not reported; assessed with: Achenbach: attention subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | serious 2 | none | 42 | 45 | - | MD **4.58 more** (1.56 more to 7.6 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Social problems (follow up: not reported; assessed with: Achenbach: social problems subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | serious 2 | none | 42 | 45 | - | MD **2.97 more** (0.38 fewer to 6.32 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Aggressive behaviour (follow up: not reported; assessed with: Achenbach: Aggressive behaviour subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | very serious 3 | none | 42 | 45 | - | MD **7.22 more** (4.66 more to 9.78 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Rule breaking symptoms (follow up: not reported; assessed with: Achenbach: Rule breaking subscale) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 1 | not serious | not serious | very serious 3 | none | 42 | 45 | - | MD **9.18 more** (6.95 more to 11.41 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection bias, performance bias (no blinding) and unclear risk of attrition bias
2. Confidence intervals cross minimally important difference in one direction. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
3. Confidence intervals cross minimally important difference in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
   * 1. Cognitive behavioural therapy versus control for depressive symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **CBT** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Depressive symptoms (RCT) (follow up: range 6 weeks to 42 weeks; assessed with: BDI) | | | | | | | | | | | | |
| 3 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 68 | - | - | SMD **0.82 fewer** (1.64 fewer to 0 ) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Depressive symptoms (Controlled before-and-after) (follow up: range 12 weeks to 46.7 weeks; assessed with: various) | | | | | | | | | | | | |
| 3 | observational studies | very serious 3 | not serious | not serious | serious 2 | none | 84 | - | - | SMD **0.81 lower** (1.39 lower to 0.23 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Depression: at least small improvement (follow up: 12 weeks; assessed with: BDI) | | | | | | | | | | | | |
| 1 | randomised trials | serious 4 | not serious | not serious | serious 2 | none | 19/20 (95.0%) | 17/27 (63.0%) | RR 1.51 (1.11 to 2.05) | **321 more per 1000** (from 69 more to 661 more) | ⨁⨁◯◯ LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| In paid employment after treatment (follow up: 16 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 5 | not serious | not serious | serious 2 | none | -/16 | 4/14 (28.6%) | RR 0.22 (0.03 to 1.73) | **223 fewer per 1000** (from 209 more to 277 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| In voluntary work after treatment (follow up: 16 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 5 | not serious | not serious | very serious 6 | none | -/16 | 4/14 (28.6%) | RR 1.31 (0.46 to 3.72) | **89 more per 1000** (from 154 fewer to 777 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Problem behaviour (Controlled before-and-after) (follow up: 23 weeks; assessed with: SIB-R) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 3 | not serious | not serious | serious 2 | none | 16 | 8 | - | MD **7 fewer** (18.58 fewer to 4.58 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Social skills (mild to moderate learning disabilities) (follow up: 6-12 weeks; assessed with: Social comparison scale) | | | | | | | | | | | | |
| 2 | randomised trials | very serious 5 | serious 7 | not serious 8 | serious 2 | none | 54 | 42 | - | MD **1.24 more** (0.66 more to 1.82 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Social behaviours (Controlled before-and-after) (follow up: 23 weeks; assessed with: Social performance survey schedule) | | | | | | | | | | | | |
| 1 | before-after studies | very serious 3 | serious 8 | not serious | serious 9 | none | 16 | 8 | - | MD **11.12 fewer** (17.11 fewer to 5.13 fewer) | ⨁◯◯◯ VERY LOW | IMPORTANT |

; **RR:** Risk ratio; **MD:** Mean difference

1. Risk of selection and performance bias in studies contributing to >50% weighting in analysis
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Risk of selection, performance and detection bias
4. Risk of selection bias
5. Risk of selection and performance bias
6. Confidence intervals cross minimally important differences in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
7. No explanation was provided
8. Inconsistency in the impact on social skills between RCTs and controlled before-and-after studies.
9. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Cognitive behavioural therapy versus behavioural strategies for depressive symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **CBT** | **behavioural strategies only** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Depressive symptoms (follow up: 38 weeks; assessed with: BDI-II) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | 23 | 24 | - | MD **1.56 fewer** (6.57 fewer to 3.45 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Improvement in those with clinical depression at baseline (follow up: 38 weeks; assessed with: BDI-II [reduced score]) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | 14/14 (100.0%) | 14/17 (82.4%) | RR 1.20 (0.94 to 1.53) | **165 more per 1000** (from 49 fewer to 436 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Recovery in those with clinical depression at baseline (follow up: 38 weeks; assessed with: BDI-II [score 12 or less]) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | very serious 3 | none | 8/14 (57.1%) | 12/17 (70.6%) | RR 0.81 (0.47 to 1.40) | **134 fewer per 1000** (from 282 more to 374 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection, performance and detection bias
2. Confidence intervals cross minimally important difference in one direction. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
3. Confidence intervals cross minimally important difference in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
   * 1. Cognitive behavioural therapy versus cognitive strategies for depressive symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **CBT** | **cognitive strategies only** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Depressive symptoms (follow up: 38 weeks; assessed with: BDI-II) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | 23 | 23 | - | MD **1.3 fewer** (5.89 fewer to 3.29 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Improvement in those with clinical depression at baseline (follow up: 38 weeks; assessed with: BDI-II [reduced score]) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | serious 2 | none | 14/14 (100.0%) | 11/15 (73.3%) | RR 1.34 (0.98 to 1.85) | **249 more per 1000** (from 15 fewer to 623 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Recovery in those with clinical depression at baseline (follow up: 38 weeks; assessed with: BDI-II [score 13 or less]) | | | | | | | | | | | | |
| 1 | observational studies | very serious 1 | not serious | not serious | very serious 3 | none | 8/14 (57.1%) | 7/15 (46.7%) | RR 1.22 (0.60 to 2.48) | **103 more per 1000** (from 187 fewer to 691 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection, performance and detection bias
2. Confidence intervals cross minimally important difference in one direction. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
3. Confidence intervals cross minimally important difference in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
   * 1. Psychodynamic psychotherapy versus no treatment for sexually inappropriate behaviour

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **psychodynamic psychotherapy** | **no treatment** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Recidivism (follow up: 208 weeks) | | | | | | | | | | | | |
| 1 | observational studies | serious 1 | not serious | serious 2 | very serious 3 | none | 2/13 (15.4%) | 3/5 (60.0%) | **RR 0.26** (0.06 to 1.11) | **444 fewer per 1000** (from 66 more to 564 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection bias, performance bias
2. Participants are only those who were arrested by the criminal justice system and, therefore, are unlikely to represent all individuals with learning disabilities who present with sexually inappropriate behaviour as not all will be in contact with the criminal justice system.
3. Confidence intervals cross minimally important difference in both directions. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes)
   * 1. Parent training versus control

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **parent training** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Behavioural and emotional problems (severity) – post-treatment (assessed with: various scales) | | | | | | | | | | | | |
| 13 | randomised trials | serious 1 | not serious | not serious | not serious | none | 349 | - | - | SMD **0.4 SD lower** (0.55 lower to 0.24 lower) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Behavioural and emotional problems (severity) – follow-up (follow up: range 26- 52 weeks to 0; assessed with: various scales) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | publication bias strongly suspected | 86 | - | - | SMD **0.13 fewer** (0.45 fewer to 0.19 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Problem behaviour (severity, non-improvement) – post-treatment (assessed with: various scales) | | | | | | | | | | | | |
| 8 | randomised trials | serious 1 | not serious | not serious | not serious | none | 131/231 (56.7%) | 174/197 (88.3%) | RR 0.67 (0.59 to 0.77) | **291 fewer per 1000** (from 203 fewer to 362 fewer) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| Problem behaviour (frequency) – post-treatment (assessed with: various scales) | | | | | | | | | | | | |
| 8 | randomised trials | serious 1 | serious 4 | not serious | not serious | none | 237 | - | - | SMD **0.6 fewer** (0.9 fewer to 0.3 fewer) | ⨁⨁◯◯ LOW | IMPORTANT |
| Problem behaviour (frequency) – follow-up (follow up: mean 26 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | not serious | very serious 6 | publication bias strongly suspected | 35 | - | - | SMD **0.36 fewer** (0.85 fewer to 0.14 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Problem behaviour (frequency, non-improvement) – post-treatment (assessed with: various scales) | | | | | | | | | | | | |
| 6 | randomised trials | serious 1 | not serious | serious 2 | not serious | none | 105/188 (55.9%) | 147/155 (94.8%) | RR 0.63 (0.55 to 0.73) | **351 fewer per 1000** (from 256 fewer to 427 fewer) | ⨁⨁◯◯ LOW | IMPORTANT |
| Adaptive functioning (communication) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 6 | none | 75 | - | - | SMD **0.47 more** (0.11 more to 0.84 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Adaptive functioning (total) – post-treatment | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | 82 | - | - | SMD **0.51 more** (0.15 more to 0.86 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Most information is from studies at moderate risk of bias
2. Concerns with applicability – different populations
3. Optimal information size not met
4. I2 > 40%
5. Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
6. Optimal information size not met; small, single study
7. Publication bias strongly suspected

For the full GRADE evidence profiles for other pairwise comparisons relating to the quality of evidence for parent training, please refer to the NICE guideline [Challenging Behaviour and Learning Disabilities, NG11](https://www.nice.org.uk/guidance/ng11).

* 1. Pharmacological interventions
     1. Amphetamine versus placebo

| **Quality assessment** | | | | | | | **Impact** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| Overall effect of treatment on bespoke form (follow up: mean 23 weeks; assessed with: 14-item 'patient evaluation form') | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | The differences between groups on 10 subscales (hyperkinesis, concentration, attention, aggressiveness, sociability, interpersonal relationship, mood, work capacity, reading, spelling, arithmetic and class standing) were reported as not significant; however, the comprehension and work interest subscales were reported to be significantly better in the amphetamine group than the placebo group (p < 0.05). | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | |
| - | - | - | - | - | - | - |  | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | |
| - | - | - | - | - | - | - |  | - | CRITICAL |

1. Risk of selection and selective outcomes bias; unclear risk of detection, attrition and performance bias.
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Methylphenidate versus placebo

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Methylphenidate** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| ADHD (follow up: mean 16 weeks; assessed with: Connors' ADHD index [parent rated]) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 61 | 61 | - | MD **3.3 fewer** (6.79 fewer to 0.19 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| ADHD (follow up: mean 16 weeks; assessed with: Connors' ADHD index [teacher rated]) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 61 | 61 | - | MD **4.1 fewer** (7.57 fewer to 0.63 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Hyperactivity (follow up: mean 16 weeks; assessed with: Conners' hyperactivity scale [parent rated]) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 2 | none | 61 | 61 | - | MD **1.5 fewer** (3.44 fewer to 0.44 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Hyperactivity (follow up: mean 16 weeks; assessed with: Conners' hyperactivity scale [teacher rated]) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 61 | 61 | - | MD **2.6 fewer** (4.68 fewer to 0.52 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| 'Improved' or 'better' (follow up: mean 16 weeks; assessed with: Clinical Global Impressions-Improvement) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 24/61 (39.3%) | 4/61 (6.6%) | RR 6.00 (2.21 to 16.26) | **328 more per 1000** (from 79 more to 1000 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Weight (follow up: mean 16 weeks; assessed with: kg) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 2 | none | 61 | 61 | - | MD **4.2 kg fewer** (10.25 fewer to 1.85 more) | ⨁⨁⨁◯ MODERATE | IMPORTANT |

1. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Clonidine versus placebo

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Clonidine** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| ADHD symptoms: conduct (follow up: 6 weeks; assessed with: Parent Connor’s score – conduct scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 9 | 10 | - | MD **7.4 fewer** (10.34 fewer to 4.46 fewer) | ⨁◯◯◯ VERY LOW |  |
| ADHD symptoms: impulsive hyperactivity (follow up: 6 weeks; assessed with: Parent Connor’s score – Impulsive hyperactive scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | 9 | 10 | - | MD **2.6 fewer** (6.54 fewer to 1.34 more) | ⨁◯◯◯ VERY LOW |  |
| ADHD symptoms: overall (follow up: 6 weeks; assessed with: Parent Connor’s score – Total score) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | 9 | 10 | - | MD **24.7 fewer** (49.35 fewer to 0.05 fewer) | ⨁◯◯◯ VERY LOW |  |
| ADHD symptoms (clinician rated) (follow up: 6 weeks; assessed with: CGI) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | 9 | 10 | - | MD **1.8 fewer** (3.11 fewer to 0.49 fewer) | ⨁◯◯◯ VERY LOW |  |
| Much or very much improved (follow up: 6 weeks; assessed with: CGI) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 7/9 (77.8%) | 0/10 (0.0%) | RR 16.50 (1.07 to 253.40) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW |  |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - |  |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - |  |

1. Risk of selection and selective outcome reporting bias
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Risperidone versus methylphenidate

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Risperidone** | **methylphenidate** | **Relative (95% CI)** | **Absolute (95% CI)** |
| ADHD symptoms (follow up: mean 4 weeks; assessed with: SNAP-IV total score) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 22 | - | - | SMD **0.54 lower** (1.14 lower to 0.06 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Hyperactivity (NCBRF) (follow up: mean 4 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | No significant between-group differences in change scores. | | | | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Side effects (Barkley's Side Effects Rating Scale) (follow up: mean 4 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | very serious 2 | none | 22 | - | - | SMD **0.08 higher** (0.54 lower to 0.69 higher) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Weight (follow up: 4 weeks; assessed with: kg) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 3 | none | Mean reduction of 0.53 kg in the methylphenidate group compared with a weight increase of 1.01 kg in the risperidone group (reported to be significant). | | | | ⨁◯◯◯ VERY LOW |  |

1. Risk of selection and selective outcome reporting bias
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   1. Pharmacological interventions for dementia in Down’s syndrome
      1. Donepezil versus placebo for prevention of dementia

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Comparison 1a: donepezil** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Cognitive abilities (follow up: 12 weeks; assessed with: Severe Impairment Battery) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | very serious 1 | not serious 2 | very serious 1 | none | 68 | - | - | SMD **0.34 higher** (0.65 lower to 1.33 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Behavioural problems (follow up: 12 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious 3 | none | 62 | - | - | SMD **0.28 higher** (0.07 lower to 0.63 higher) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| Serious adverse events (follow up: 12 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | serious 4 | none | 0/71 (0.0%) | 0/70 (0.0%) | not estimable |  | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| Severe adverse events (follow up: 12 weeks) | | | | | | | | | | | | |
| 1 | randomised trials 5 | not serious | not serious | not serious | very serious 2 | none | 2/62 (3.2%) | 0/61 (0.0%) | RR 4.92 (0.24 to 100.43) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁⨁◯◯ LOW | IMPORTANT |
| Any adverse event (follow up: 12 weeks) | | | | | | | | | | | | |
| 1 | randomised trials 6 | not serious | not serious | not serious | serious 3 | none | 46/62 (74.2%) | 29/61 (47.5%) | RR 1.56 (1.15 to 2.11) | **266 more per 1000** (from 71 more to 528 more) | ⨁⨁⨁◯ MODERATE | IMPORTANT |

1. Downgraded two levels for imprecision (wide confidence interval) and inconsistency (I² = 73%).
2. Downgraded two levels for serious imprecision (wide confidence interval) and small number of events.
3. Downgraded one level for imprecision (wide confidence interval).
4. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
5. Serious adverse events: hypertension and emotional lability.
6. Most common side effects were asthenia, anorexia, dyspepsia, nausea, vomiting, and insomnia.
   * 1. Donepezil versus placebo for treatment of dementia

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Comparison 1b: donepezil** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Cognitive abilities (follow up: 24 weeks; assessed with: Severe Impairment Battery) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 14 | - | - | SMD **0.93 higher** (0.13 higher to 1.73 higher) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Proportion with improved impression of quality of life (follow up: 24 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 11/11 (100.0%) | 4/10 (40.0%) | RR 2.34 (1.14 to 4.81) | **536 more per 1000** (from 56 more to 1000 more) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Behavioural problems (follow up: 24 weeks; assessed with: American Association of Mental Retardation Adaptive Behaviour Scale) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 14 | - | - | SMD **0.99 higher** (0.18 higher to 1.79 higher) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| Serious adverse events (follow up: 24 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 8/16 (50.0%) | 3/14 (21.4%) | RR 2.33 (0.76 to 7.13) | **285 more per 1000** (from 51 fewer to 1000 more) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| At least one serious event (follow up: 24 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | serious 1 | none | 12/16 (75.0%) | 7/14 (50.0%) | RR 1.50 (0.83 to 2.72) | **250 more per 1000** (from 85 fewer to 860 more) | ⨁⨁⨁◯ MODERATE | IMPORTANT |
| Minor adverse reaction (follow up: 24 weeks) | | | | | | | | | | | | |
| 1 | randomised trials 2 | not serious | not serious | not serious | very serious 3 | none | 2/11 (18.2%) | 3/10 (30.0%) | RR 0.61 (0.13 to 2.92) | **117 fewer per 1000** (from 261 fewer to 576 more) | ⨁⨁◯◯ LOW | IMPORTANT |

1. Downgraded one level for imprecision (wide confidence interval).
2. Included soft stool and skin rash (donepezil, one placebo) or mild skin rash only (2 placebo).
3. Downgraded two levels for serious imprecision (wide confidence interval).
   * 1. Memantine versus placebo for dementia in Down’s syndrome

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Comparison 2: memantine** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Cognitive abilities (follow up: range 16 weeks to 52 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | serious 1 | not serious | serious 1 | none | 91 | - | - | SMD **0.05 more** (0.43 fewer to 0.52 more) | ⨁⨁◯◯ LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Behavioural problems (follow up: range 16 weeks to 52 weeks; assessed with: various scales) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | very serious 2 | none | 94 | - | - | SMD **0.17 fewer** (0.46 fewer to 0.11 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Clinically significant/serious adverse events (follow up: range 16 weeks to 52 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | not serious | not serious | not serious | very serious 2 | none | 12/107 (11.2%) | 6/104 (5.8%) | RR 1.79 (0.72 to 4.50) | **46 more per 1000** (from 16 fewer to 202 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Any adverse event (follow up: mean 16 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious 2 | none | 4/19 (21.1%) | 1/19 (5.3%) | RR 4.00 (0.49 to 32.57) | **158 more per 1000** (from 27 fewer to 1000 more) | ⨁⨁◯◯ LOW | IMPORTANT |

1. Downgraded two levels due to imprecision (wide confidence intervals) and inconsistency (I² = 48%).
2. Downgraded two levels for serious imprecision (wide confidence interval) and small number of events.
   * 1. Simvastatin versus placebo for dementia in Down’s syndrome

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Comparison 3: simvastatin** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Cognitive abilities (follow up: 52 weeks; assessed with: Neuropsychological Assessment of Dementia in Intellectual Disabilities battery) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious 1 | none | 10 | 11 | - | MD **10 higher** (0.4 lower to 1.6 higher) | ⨁⨁◯◯ LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Adaptive functioning (follow up: 52 weeks; assessed with: AAMR: ABS) | | | | | | | | | | | | |
| 1 | randomised trials | not serious | not serious | not serious | very serious 1 | none | 10 | 11 | - | MD **0.7 higher** (0 to 1.4 higher) | ⨁⨁◯◯ LOW | IMPORTANT |

1. Downgraded two levels for serious imprecision (wide confidence interval) and small number of events.
   1. Other interventions
      1. Annual health check versus treatment as usual

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Annual health check** | **treatment as usual** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Psychosis (Identification of mental health needs; all levels of learning disabilities) (follow up: mean 39 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | 4/83 (4.8%) | 6/66 (9.1%) | **RR 0.53** (0.16 to 1.80) | **43 fewer per 1000** (from 73 more to 76 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Psychiatric consultation/ visit (Identification of mental health needs; all levels of learning disabilities) (follow up: range 39 weeks to 52 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 4 | not serious | serious 2 | very serious 5 | none | 26/287 (9.1%) | 31/287 (10.8%) | **RR 0.83** (0.50 to 1.36) | **18 fewer per 1000** (from 39 more to 54 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Psychiatric disorders (Identification of mental health needs; all levels of learning disabilities) (follow up: mean 52 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 5 | none | 2/234 (0.9%) | 0/219 (0.0%) | **RR 4.68** (0.23 to 96.96) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Newly detected health issues (all levels of learning disabilities) (follow up: range 39 weeks to 52 weeks) | | | | | | | | | | | | |
| 3 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | -/367 | -/352 | **OR 1.69** (1.08 to 2.64) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Newly detected health monitoring needs (all levels of learning disabilities) (follow up: mean 39 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | serious 6 | none | -/83 | -/66 | **OR 2.38** (1.31 to 4.32) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Newly detected health promotion needs (all levels of learning disabilities) (follow up: mean 39 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 5 | none | -/83 | -/66 | **OR 0.98** (0.73 to 1.32) | **0 fewer per 1000** (from 0 fewer to 0 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Obesity (Identification of health needs; all levels of learning disabilities) (follow up: range 39 weeks to 52 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | serious 7 | serious 2 | serious 6 | none | 74/317 (23.3%) | 43/285 (15.1%) | **RR 1.41** (1.09 to 1.82) | **62 more per 1000** (from 14 more to 124 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of performance bias
2. Indirect outcome
3. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
4. Risk of performance, selection, attrition bias
5. Confidence intervals cross two minimally important differences. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
6. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
7. I2 suggests considerable heterogeneity
   * 1. Acetyl-L-carnitine versus placebo for attention deficit hyperactivity disorder

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Acetyl-L-carnitine** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| ADHD (follow up: mean 52 weeks; assessed with: Conners' Parents ) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 24 | 27 | - | MD **2.8 fewer** (7.58 fewer to 1.98 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| ADHD (follow up: mean 52 weeks; assessed with: Conners' Teachers) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 24 | 27 | - | MD **0.5 more** (5.08 fewer to 6.08 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Adaptive functioning (post-treatment) (follow up: mean 52 weeks; assessed with: VABS – full scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 24 | 27 | - | MD **8.2 more** (0.04 fewer to 16.44 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Adaptive functioning (follow up: mean 52 weeks; assessed with: VABS – socialization scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 24 | 27 | - | MD **11.3 more** (2.18 more to 20.42 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection and detection bias
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Acetyl-L-carnitine versus placebo for dementia

| **Quality assessment** | | | | | | | **Impact** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| Cognitive functioning (mild to moderate learning disabilities) (follow up: mean 39 weeks; assessed with: Multiple measures) | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | No significant difference between Acetyl-L-Carnitine and placebo groups for all measures. | ⨁◯◯◯ VERY LOW | CRITICAL |
| Dementia: (mild to moderate learning disabilities) (follow up: mean 39 weeks; assessed with: Emotional disorder rating scale) | | | | | | | | | |
| 1 | randomised trials | very serious 3 | not serious | not serious | serious 2 | none | No significant difference between Acetyl-L-Carnitine and placebo groups | ⨁◯◯◯ VERY LOW | CRITICAL |
| Dementia (mild to moderate learning disabilities) (follow up: mean 39 weeks; assessed with: Child behaviour checklist) | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | No significant difference between Acetyl-L-Carnitine and placebo groups | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | |
| - | - | - | - | - | - | - |  | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | |
| - | - | - | - | - | - | - |  | - | CRITICAL |

1. Risk of selection, selective outcomes and attrition bias.
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Risk of selection, selective outcomes, detection bias and attrition bias.
   * 1. Antioxidant plus acetylcholinesterase inhibitor versus placebo plus acetylcholinesterase inhibitor for dementia

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Antioxidant** | **placebo** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: DMR [sum of cognitive scores]) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | No significant differences in DMR cognitive scores scores between antioxidant and placebo groups | | | | ⨁⨁◯◯ LOW | CRITICAL |
| Mental health (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: Severe impairment battery) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | No significant differences in Severe Impairment Battery scores between antioxidant and placebo groups | | | | ⨁⨁◯◯ LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Adaptive functioning (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: Brief Praxis Test) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | No significant differences in Brief Praxis Test scores between antioxidant and placebo groups | | | | ⨁⨁◯◯ LOW | IMPORTANT |
| Adaptive functioning (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: DMR [sum of social skills]) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | No significant differences in DMR sum of social scores scores between antioxidant and placebo groups | | | | ⨁⨁◯◯ LOW | IMPORTANT |
| Adaptive functioning (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: Bristol Activities of Daily Living Scale ) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | No significant differences in Bristol Activities of Daily Living Scale scores between antioxidant and placebo groups | | | | ⨁⨁◯◯ LOW | IMPORTANT |
| Any serious adverse event (incapacitation and/or inability to sustain daily activities) (all levels of learning disabilities) (follow up: mean 104 weeks; assessed with: [ITT/analysed as randomised]) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | 14/29 (48.3%) | 11/29 (37.9%) | RR 1.27 (0.70 to 2.32) | **102 more per 1000** (from 114 fewer to 501 more) | ⨁⨁◯◯ LOW | IMPORTANT |

1. Risk of selective outcomes bias.
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Exercise versus any control for anxiety symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Exercise** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Anxiety (mild learning disabilities) (follow up: mean 39 weeks; assessed with: Hamilton Anxiety Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1,2 | not serious | not serious | serious 3 | none | Significant decrease in total HAM-A scores in the aerobic and leisure groups only (no significant decrease was found for the vocational activities control group.) | | | | ⨁◯◯◯ VERY LOW | CRITICAL |
| Anxiety (mild to moderate learning disabilities) (follow up: mean 12 weeks; assessed with: Zung Self-rating anxiety scale (adapted for learning disabilities and named Self-rated Anxiety Scale or SAS-ID) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 4 | none | 14 | 13 | - | MD 6.62 fewer (7.97 fewer to 5.27 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection, performance and detection bias
2. Risk of selective outcome (no variance reported so not possible to use in meta-analysis), performance and selection bias
3. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes). Not possible to assess confidence without variance.
4. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Exercise versus painting control for depressive symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Exercise** | **painting control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Depressive symptoms (mild to moderate learning disabilities) (follow up: mean 12 weeks; assessed with: Zung Self-rating Depression Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 14 | 13 | - | MD **6.06 fewer** (7.25 fewer to 4.87 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |

1. Risk of selection, performance and detection bias
2. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Exercise and education versus control for depressive symptoms

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Exercise and education** | **control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Depressive symptoms (mild to moderate learning disabilities) (follow up: mean 12 weeks; assessed with: Child Depression Inventory) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 32 | 21 | - | MD **1.53 fewer** (3.29 fewer to 0.23 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Community participation and meaningful occupation (mild to moderate learning disabilities) (follow up: mean 12 weeks; assessed with: Communication integration scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 32 | 21 | - | MD **0.78 fewer** (2.06 fewer to 0.5 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life (mild-moderate learning disabilities) (follow up: mean 12 weeks; assessed with: Life Satisfaction Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 32 | 21 | - | MD **2.52 more** (0.87 fewer to 5.91 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Selection and detection bias
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   1. Organisation and Service Delivery
      1. Assertive community treatment versus standard community treatment

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Assertive community treatment** | **standard community treatment** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health (service user) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Healthcare practitioner health and well-being – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Quality of life (follow up: range 13 weeks to 26 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | 25 | - | - | SMD **0.2 fewer** (0.75 fewer to 0.36 more) | ⨁⨁◯◯ LOW | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Problem behaviours – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Global assessment of function (symptomatology) (follow up: range 13 weeks to 26 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | 25 | 25 | - | MD **0.76 fewer** (6.07 fewer to 4.55 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Global assessment of function (Disability) (follow up: range 13 weeks to 26 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | not serious | serious 2 | none | 25 | 25 | - | MD **1.05 more** (4.05 fewer to 6.16 more) | ⨁⨁◯◯ LOW | IMPORTANT |
| Carer uplift/burden (follow up: range 13 weeks to 26 weeks) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | serious 3 | not serious | very serious 4 | none | 25 | 25 | - | MD **0.03 more** (3.48 fewer to 3.54 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of performance bias.
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. I-squared = 36% and may represent moderate heterogeneity.
4. Confidence intervals cross two minimally important differences. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Active case management model versus standard model

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Active treatment case management model** | **standard model of service delivery** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health (service user) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Healthcare practitioner health and well-being – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Quality of life (service user) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Maladaptive behaviour (follow up: 3 years; assessed with: AAMD Maladaptive Behaviour Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | serious 2 | serious 3 | none | 23 | 23 | - | MD **12.91 fewer** (27.37 fewer to 1.55 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Adaptive behaviour (follow up: 3 years; assessed with: AAMD Adaptive Behaviour Scale) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | serious 2 | serious 3 | none | 23 | 23 | - | MD **10.56 more** (6.77 fewer to 27.89 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Move to more staff intensive residential programming (follow up: 3 years) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | serious 2 | very serious 4 | none | 1/23 (4.3%) | 4/23 (17.4%) | RR 0.25 (0.03 to 2.07) | **130 fewer per 1000** (from 169 fewer to 186 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Move to more staff intensive day programming (follow up: 3 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | serious 2 | very serious 4 | none | 0/23 (0.0%) | 2/23 (8.7%) | RR 0.20 (0.01 to 3.95) | **70 fewer per 1000** (from 86 fewer to 257 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selection, performance and detection bias
2. American study so service structures less applicable to UK population
3. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
4. Confidence intervals cross two minimally important differences. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   * 1. Liaison worker versus no liaison worker

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Liaison worker model** | **no liaison worker** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Mental health (follow up: 39 weeks; assessed with: Strength and Difficulties Questionnaire) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 14 | - | - | SMD **1.12 SD lower** (1.95 lower to 0.29 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Quality of life (service user) – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Community participation and meaningful occupation – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Problem behaviours – not reported | | | | | | | | | | | | |
| - | - | - | - | - | - | - |  | | | | - | CRITICAL |
| Carer quality of life – physical (follow up: 39 weeks; assessed with: SF-12-physical) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | serious 2 | none | 14 | - | - | SMD **0.8 lower** (1.6 lower to 0 ) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Care quality of life – mental (follow up: 39 weeks; assessed with: SF-12-mental) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | very serious 3 | none | 14 | - | - | SMD **0.26 fewer** (1.03 fewer to 0.51 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |
| Carer mental health (follow up: 39 weeks; assessed with: General Health Questionnaire-30) | | | | | | | | | | | | |
| 1 | randomised trials | very serious 1 | not serious | not serious | very serious 3 | none | 14 | - | - | SMD **0.11 fewer** (0.88 fewer to 0.66 more) | ⨁◯◯◯ VERY LOW | IMPORTANT |

1. Risk of selective outcome, performance, and detection bias
2. Confidence intervals cross one minimally important difference. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
3. Confidence intervals cross two minimally important differences. Sample size less than optimal information size (<400 for continuous outcomes or <300 for dichotomous outcomes).
   1. Interventions to enhance carer well-being
      1. Interventions informed by cognitive behavioural principles versus control for family carers

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Cognitive behavioural intervention** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Carer health and well-being (depression) – post-treatment | | | | | | | | | | | | |
| 5 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | 251 | - | - | SMD **0.35 fewer** (0.54 fewer to 0.15 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (depression) – follow-up (follow up: range 46 to 104 weeks to) | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | 64 | - | - | SMD **0.41 fewer** (0.79 fewer to 0.04 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (clinically depressed) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 4 | none | 3/53 (5.7%) | 13/58 (22.4%) | RR 0.25 (0.08 to 0.84) | **168 fewer per 1000** (from 36 fewer to 206 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (anxiety, trait) – post-treatment | | | | | | | | | | | | |
| 2 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | 37 | - | - | SMD **0.5 fewer** (1.03 fewer to 0.03 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (anxiety, state) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 4 | none | 18 | - | - | SMD **0.46 fewer** (1.12 fewer to 0.2 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (mental ill health) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 4 | none | 29 | - | - | SMD **2.19 fewer** (2.85 fewer to 1.53 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (quality of life) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 4 | none | 29 | - | - | SMD **0.87 more** (0.33 more to 1.41 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (stress) – post-treatment | | | | | | | | | | | | |
| 3 | randomised trials | serious 1 | serious 6 | serious 2 | serious 3 | none | 225 | - | - | SMD **0.45 fewer** (0.78 fewer to 0.12 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (stress) – follow-up (follow up: mean 104 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 4 | none | 49 | - | - | SMD **0.43 fewer** (0.9 fewer to 0.05 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (clinically stressed) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 5 | not serious | serious 2 | very serious 4 | none | 2/53 (3.8%) | 17/58 (29.3%) | RR 0.13 (0.03 to 0.53) | **255 fewer per 1000** (from 138 fewer to 284 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Most information is from studies at moderate risk of bias
2. Population not family carers of people with learning disabilities with no mental health problems.
3. Optimal information size not met
4. Optimal information size not met; small, single study
5. Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
6. I2 > 40%
   * 1. Psychosocial support interventions versus control for parents

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Psychosocial support interventions** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Carer health and well-being (stress) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 16 | - | - | SMD **1.21 fewer** (2.04 fewer to 0.39 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
2. Population not family carers of people with learning disabilities with no mental health problems.
3. Optimal information size not met; small, single study
   * 1. Psychoeducation versus control for parents

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Psychoeducation** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Carer health and well-being (depression) – follow-up (follow up: mean 4 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 40 | - | - | SMD **0.84 fewer** (1.31 fewer to 0.36 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (burnout) – follow-up (follow up: mean 8 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 45 | - | - | SMD **0.35 fewer** (0.77 fewer to 0.06 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
2. Population not family carers of people with learning disabilities with no mental health problems.
3. Optimal information size not met; small, single study
   * 1. Mindfulness versus control for staff

| **Quality assessment** | | | | | | | **Number of patients** | | **Effect** | | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Mindfulness interventions** | **any control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| Carer health and well-being (mental well-being) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 66 | - | - | SMD **0.17 more** (0.19 fewer to 0.53 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (mental well-being) – follow-up (follow up: mean 6 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 66 | - | - | SMD **0.28 more** (0.08 fewer to 0.64 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (mental ill health) – post-treatment | | | | | | | | | | | | |
| 2 | randomised trials | serious 4 | serious 5 | serious 2 | serious 3 | none | 84 | - | - | SMD **0.54 fewer** (1.06 fewer to 0.02 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (mental ill health) – follow-up (follow up: range 6-13 weeks to) | | | | | | | | | | | | |
| 2 | randomised trials | serious 4 | serious 5 | serious 2 | serious 3 | none | 84 | - | - | SMD **0.24 fewer** (0.72 fewer to 0.24 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (stress) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 66 | - | - | SMD **0.17 more** (0.19 fewer to 0.53 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (stress) – follow-up (follow up: mean 6 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 66 | - | - | SMD **0.05 fewer** (0.41 fewer to 0.31 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (burnout) – post-treatment | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 18 | - | - | SMD **0.18 fewer** (0.86 fewer to 0.49 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (burnout) – follow-up (follow up: mean 13 weeks) | | | | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | very serious 3 | none | 18 | - | - | SMD **0.08 fewer** (0.76 fewer to 0.59 more) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect
2. Population not family carers of people with learning disabilities with no mental health problems.
3. Optimal information size not met; small, single study
4. Most information is from studies at moderate risk of bias
5. I2 > 40%
   * 1. Mindfulness versus control for parents

| **Quality assessment** | | | | | | | **Impact** | **Quality** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Number of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** |
| Carer health and well-being (mental well-being) – post-treatment (follow up: 8 weeks; assessed with: CES-D Total depression score) | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | Parent depression appeared to decrease in the intervention group from baseline (from 17.86 to 11.67) and increase after treatment in the control group from baseline (from 17.53 to 22.0). (no variance reported) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (mental ill health) – post-treatment (follow up: 8 weeks; assessed with: PSI Parental Distress Subscale) | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | Parent distress appeared to decrease in the intervention group from baseline (from 35.17 to 31.72) and also in the control group from baseline (from 38.28 to 37.61). However, the control group appeared to have higher distress at baseline. (no variance reported) | ⨁◯◯◯ VERY LOW | CRITICAL |
| Carer health and well-being (satisfaction with life) – post-treatment (follow up: 8 weeks) | | | | | | | | | |
| 1 | randomised trials | serious 1 | not serious | serious 2 | serious 3 | none | Satisfaction with life appeared to increase in both groups but the increased appeared larger in the intervention group (19.8 to 24.65 in the intervention group versus from 18.41 to 19.42 in the control group). (no variance reported) | ⨁◯◯◯ VERY LOW | CRITICAL |

1. Risk of selection, selective outcomes bias.
2. Population not family carers of people with learning disabilities with no mental health problems.
3. Optimal information size not met; small, single study

Appendices

1. <Insert first appendix heading here>