Appendix I - eTables

eTable 1. Risk of bias

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **S** | **C** | **B** | **A** | **I** | **R** | **O** | **Total risk of bias** |
| Alvarez et al (2008) | - | ? | - | + | + | + | + | Low risk of bias |
| Anguera et al (2017) | + | + | ? | + | + | + | + | Low risk of bias |
| Bowie et al (2013) | + | + | - | + | ? | + | + | Low risk of bias |
| Elgamal et al (2007) | - | - | - | ? | + | + | + | High risk of bias |
| Hoorelbeke et al (2017) | + | + | + | + | + | + | + | Low risk of bias |
| Hoorelbeke et al (2021) | + | + | ? | + | + | + | + | Low risk of bias |
| Listunova et al (2020) | + | + | - | + | + | + | + | Low risk of bias |
| Morimoto et al (2014) | - | - | - | ? | + | ? | ? | High risk of bias |
| Morimoto et al (2020) | ? | ? | + | + | ? | + | - | Low risk of bias |
| Moshier et al (2015) | + | ? | ? | + | + | + | + | Low risk of bias |
| Moshier et al (2017) | + | ? | ? | + | ? | + | + | Low risk of bias |
| Naismith et al (2011) | - | + | - | + | + | + | + | Low risk of bias |
| Owens et al (2013) | ? | ? | ? | - | ? | + | + | High risk of bias |
| Pratap et al (2018) | ? | ? | ? | + | ? | + | + | Low risk of bias |
| Semkovska et al (2015) | + | + | - | + | ? | + | + | Low risk of bias |
| Semkovska et al (2017) | + | + | - | + | + | + | + | Low risk of bias |
| Trapp et al (2016) | + | + | - | + | ? | + | + | Low risk of bias |
| Twamley et al (2019) | + | + | - | + | ? | + | - | Low risk of bias |
| Wanmaker et al (2014) | + | + | + | + | + | + | + | Low risk of bias |
| Wanmaker et al (2015) | + | + | + | + | ? | + | + | Low risk of bias |
| Yamaguchi et al (2017) | + | + | - | - | + | + | + | Low risk of bias |

*Note:* S=sequence generation. C=concealment of allocation. B=blinding of participants and personnel. A=blinding of outcome assessors. I=incomplete outcome data. R=selective reporting. O=other sources of bias. -=high risk of bias (2 points). ?=unclear risk of bias (1 point). +=low risk of bias (0 points). Total risk of bias is scored as >6 points = high risk of bias; <6 points = low risk of bias.

eTable 2. Categorization of outcome measures

|  |  |  |
| --- | --- | --- |
| **Category** |  | **Outcome measures** |
| DS |  |  |
|  |  | Beck Depression Inventory  Beck Depression Inventory-II  Hamilton Depression Rating Scale-17  Patient Health Questionnaire  Positive and Negative Affectivity Scale – Negative Scale  Visual Analogue Scale  Ruminative Response Scale  Remission of Depression Questionnaire  10-item Montgomery-Asberg Depression Rating Scale |
| CF | Cognitive domain |  |
|  | Attention | D2 attention test  Test of variables of attention – Sustained Attention  Continuous Performance Test Identical Pairs Version  Degraded Continuous Performance Test  Ruff’s 2&7 Selective Attention Test  WAIS-R/III / WMS-R – Digit Span Forward  WMS-R/III – Spatial Span Forward  Spanboard Task Forward  Vienna Test System – WAF-A; WAF-G; WAF-S |
|  | Processing speed | Trail Making Test part A  D-KEFS Trails 2 number sequencing  WAIS-III – Digit-Symbol Coding  D-KEFS – Stroop Color-Word Test reading scale (I) and color naming scale (II)  BACS – Symbol Coding Task  Vienna Test System – Trail Making Test-Langensteinbach version part A  Zahlen-Symbol-Test (Digit Symbol Coding) |
|  | Motor speed | BACS Token motor |
|  | Working memory | Clapp’s Working memory/delayed recognition task  WAIS-R/III / WMS-R – Digit Span Backward  WMS-R/III – Spatial Span Backward  Non-adaptive Paced Auditory Serial Addition Task  Change detection task  Gold’s Letter Number Sequencing test  University of Maryland Letter-Number Span  BACS – Digit Sequencing Task  Internal Shift Task  Reading Span  Vienna Test System – N-Back-verbal |
|  | Verbal learning and memory | Hopkins Verbal Learning Test  California Verbal Learning Test  Rey Auditory Verbal Learning Test  WMS – Logical Memory  BACS – Verbal Memory |
|  | Visual learning and memory | Rey/Taylor Complex Figure Test, 3 min delayed recall  Rey- Osterrieth Complex Figure test immediate and delayed recall  WMS-R – Visual reproduction  Brief Visual Memory Test-Revised  Vienna Test System – Figural Memory Test |
|  | Executive functioning | Trail Making Test part B  (D-KEFS) Stroop Color-Word Test inhibition scale (III)  WAIS-R Similarities  D-KEFS – Trails 4 number-letter sequencing  D-KEFS – Towers  D-KEFS – Sorting  D-KEFS – 20 questions Wisconsin Card Sorting Test  Neuropsychological Assessment Battery – Mazes  Vienna Test System – Trail Making Test- Langensteinbach version part B  Vienna Test System – Response inhibition  Vienna Test System – Tower of London-Freiburg version |
|  | Verbal fluency | Controlled Oral Word Association Test – (letter and/or category fluency)  Category switching fluency  BACS – Word fluency  BACS – Letter fluency |
|  | Global/intellectual functioning | WAIS – Verbal intelligence quotient  WAIS – performance intelligence quotient |
| DF | Sub-category |  |
|  | Subjective | World Health Organization Disability Assessment Schedule II  Sheehan Disability Scale  Longitudinal Interval Follow-up Evaluation Range of Impaired Functioning Tool  Behavior Rating Inventory of Executive Function Adult Version - global executive scale  Quality of Life in Depression Scale  Resilience Scale  Brief Disability Questionnaire  Independent Living Skills Survey  Quality of Life Interview  Cognitive Failures Questionnaire  Hot plates repeated knob-checking task – memory confidence; memory vividness; memory detail  Mini – Internal Classification of Functioning, Disability and Health  Specific Level of Functioning Scale |
|  | Objective | Social Skills Performance Assessment  Advanced Finances task  American Psychiatric Association - Global Assessment of Functioning  University of California, San Diego, Performance-Based Skills Assessment-Brief  Memory for Intentions Test  Hot plates repeated knob-checking task - memory accuracy |

*Note:* DS=Depressive Symptomatology. CF=Cognitive Functioning. DF=Daily Functioning. WAIS=Wechsler Adult Intelligence Scale. WMS=Wechsler Memory Scale. R=revised. D-KEFS=Delis-Kaplan Executive Functioning System. BACS=Brief Assessment of Cognition in Schizophrenia.

**Appendix II – Search strategy**

**Database: PubMed**

(((((((((((((((((((((((((((("Cognitive training"[Title/Abstract]) OR "Cognitive remediation"[Title/Abstract]) OR "Cognitive rehabilitation"[Title/Abstract]) OR "Cognitive stimulation"[Title/Abstract]) OR "Cognitive revalidation"[Title/Abstract]) OR "Neurocognitive training"[Title/Abstract]) OR "Neurocognitive remediation"[Title/Abstract]) OR "Neurocognitive rehabilitation"[Title/Abstract]) OR "Neurocognitive stimulation"[Title/Abstract]) OR "Neurocognitive revalidation"[Title/Abstract]) OR "Neurocognitive intervention"[Title/Abstract]) OR "Memory training"[Title/Abstract]) OR "Memory remediation"[Title/Abstract]) OR "Memory rehabilitation"[Title/Abstract]) OR "Memory stimulation"[Title/Abstract]) OR "Memory intervention"[Title/Abstract]) OR "Attention training"[Title/Abstract]) OR "Attention remediation"[Title/Abstract]) OR "Attention rehabilitation"[Title/Abstract]) OR "Attention stimulation"[Title/Abstract]) OR "Attention intervention"[Title/Abstract]) OR "Cognitive control training"[Title/Abstract]) OR "Cognitive control interventions"[Title/Abstract]) OR "Cognitive control intervention"[Title/Abstract]) OR "Brain training"[Title/Abstract]) OR Neurorehabilitation[Title/Abstract]) OR "Neuropsychological training"[Title/Abstract]) OR "Neuropsychological remediation"[Title/Abstract]) OR "Neuropsychological rehabilitation"[Title/Abstract]) OR "Neuropsychological stimulation"[Title/Abstract]) OR "Neuropsychological revalidation"[Title/Abstract]) OR "Neuropsychological intervention"[Title/Abstract]

*And*

(((((((((Depress\*[Title/Abstract]) OR Dysphor\*[Title/Abstract]) OR Dysthym\*[Title/Abstract]) OR "Affective disorder"[Title/Abstract]) OR "Affective disorders"[Title/Abstract]) OR "Mood disorder"[Title/Abstract]) OR "Mood disorders"[Title/Abstract])) OR (("Depression"[Mesh]) OR "Mood Disorders"[Mesh])

**Database: PsycINFO trough OVID**

Neuropsychological rehabilitation/ or Brain training/ or Neurorehabilitation/ or (Cognitive training or Cognitive remediation or Cognitive rehabilitation or Cognitive stimulation or Cognitive revalidation or Neurocognitive training or Neurocognitive remediation or Neurocognitive rehabilitation or Neurocognitive stimulation or Neurocognitive revalidation or Neurocognitive intervention or Memory training or Memory remediation or Memory rehabilitation or Memory stimulation or Memory intervention or Attention training or Attention remediation or Attention rehabilitation or Attention stimulation or Attention intervention or Cognitive control training or Cognitive control interventions or Cognitive control intervention or Brain training or Neurorehabilitation or Neuropsychological training or Neuropsychological remediation or Neuropsychological rehabilitation or Neuropsychological stimulation or Neuropsychological revalidation or Neuropsychological intervention).ab,ti

*And*

"depression (emotion)"/ or major depression/ or affective disorders/ or (Depress\* or Dysphor\* or Dysthym\* or Affective disorder\* or Mood disorder\*).ab,ti

**Database: Embase trough OVID**

Cognitive remediation therapy/ or cognitive rehabilitation/ or Neurorehabilitation/ or (Cognitive training or Cognitive remediation or Cognitive rehabilitation or Cognitive stimulation or Cognitive revalidation or Neurocognitive training or Neurocognitive remediation or Neurocognitive rehabilitation or Neurocognitive stimulation or Neurocognitive revalidation or Neurocognitive intervention or Memory training or Memory remediation or Memory rehabilitation or Memory stimulation or Memory intervention or Attention training or Attention remediation or Attention rehabilitation or Attention stimulation or Attention intervention or Cognitive control training or Cognitive control interventions or Cognitive control intervention or Brain training or Neurorehabilitation or Neuropsychological training or Neuropsychological remediation or Neuropsychological rehabilitation or Neuropsychological stimulation or Neuropsychological revalidation or Neuropsychological intervention).ab,ti

*And*

depression/ or major depression/ or mood disorder/ or (Depress\* or Dysphor\* or Dysthym\* or Affective disorder\* or Mood disorder\*).ab,ti

**Database: Cochrane Library**

“Cognitive training” or “Cognitive remediation” or “Cognitive rehabilitation” or “Cognitive stimulation” or “Cognitive revalidation” or “Neurocognitive training” or “Neurocognitive remediation” or “Neurocognitive rehabilitation” or “Neurocognitive stimulation” or “Neurocognitive revalidation” or “Neurocognitive intervention” or “Memory training” or “Memory remediation” or “Memory rehabilitation” or “Memory stimulation” or “Memory intervention” or “Attention training” or “Attention remediation” or “Attention rehabilitation” or “Attention stimulation” or “Attention intervention” or “Cognitive control training” or “Cognitive control interventions” or “Cognitive control intervention” or “Brain training” or Neurorehabilitation or “Neuropsychological training” or “Neuropsychological remediation” or “Neuropsychological rehabilitation” or “Neuropsychological stimulation” or “Neuropsychological revalidation” or “Neuropsychological intervention”

*And*

Depress\* or Dysphor\* or Dysthym\* or “Affective disorder\*” or “Mood disorder\*”

**Appendix III – Grading of Recommendations Assessment, Development and Evaluation (GRADE) for DS, CF and DF**

| **Certainty assessment** | | | | | | | **№ of patients** | | **Effect** | | **Certainty** | **Importance** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **Cognitive Remediation** | **Control** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Depressive Symptomatology (DS)** | | | | | | | | | | | | |
| 21 | observational studies a | not serious | not serious | not serious | serious b | none | 389 | 510 | Hedges’s g **0**.**28**  (0.09, 0.46) | .. | ⨁◯◯◯ VERY LOW | IMPORTANT |
| **Cognitive Functioning (CF)** | | | | | | | | | | | | |
| 19 | observational studies a | not serious | not serious | not serious | not serious | none | 318 | 279 | Hedges’s g **0**.**60**  (0.37, 0.83) | .. | ⨁⨁◯◯ LOW | IMPORTANT |
| **Daily Functioning (DF)** | | | | | | | | | | | | |
| 12 | observational studies a | not serious | not serious | not serious | serious b | none | 275 | 371 | Hedges’s g **0**.**22**  (0.06, 0.39) | .. | ⨁◯◯◯ VERY LOW | IMPORTANT |

a. Although the majority of studies was randomized, a substantial part of the included studies was not randomized or had unclear sequence generation.

b. Any recommendation based on the evidence, would be different if the lower versus the upper boundary of the confidence interval represented the true effect.