

## Supplementary Online Content

Wei J, Hou J, Mu T, et al. Evaluation of computerized cognitive training and cognitive and daily function in patients living with HIV: a meta-analysis. *JAMA Netw Open*. 2022;5(3):e220970. doi:10.1001/jamanetworkopen.2022.0970

**eTable 1.** Full Search Strategy

**eTable 2.** Supplementary Search Strategy

**eTable 3.** Reasons for Exclusion in Full-text Assessment

**eTable 4.** Categorization of Outcome Measures

**eTable 5.** Study Quality of Evidence According to GRADE Guidelines

**eTable 6.** Full Results of Sensitivity Analyses

**eFigure.** Risk of Bias Summary

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Full Search Strategy

| Database       | Time       | Strategy  | Outcome |
|----------------|------------|---|---------|
| Web of science | 2020.12.15 | ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training") AND ("PLWH" OR "HIV" OR "AIDS")   | 271     |
| PubMed         | 2020.12.15 | ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training") AND ("PLWH" OR "HIV" OR "AIDS")   | 92      |
| PsycINFO       | 2020.12.15 | ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training") AND ("PLWH" OR "HIV" OR "AIDS")   | 140     |
| Cochrane       | 2020.12.15 | "cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training" in Title Abstract Keyword AND "PLWH" OR "HIV" OR "AIDS" in Title Abstract Keyword | 501     |

**eTable 2.** Supplementary Search Strategy

| Database       | Time       | Strategy   | Outcome |
|----------------|------------|--|---------|
| Web of science | 2021.11.18 | ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training" OR "attention training" OR "reasoning training" OR "computer game" OR "video game" OR "computerized training" OR "computerized intervention" OR "cognitive exercise" OR "brain exercise" OR "cognitive stimulation" OR "cognitive enhancement") AND ("PLWH" OR "HIV" OR "AIDS")       | 512     |
| PubMed         | 2021.11.18 | ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training" OR "attention training" OR "reasoning training" OR "computer game" OR "video game" OR "computerized training" OR "computerized intervention" OR "cognitive exercise" OR "brain exercise" OR "cognitive stimulation" OR "cognitive enhancement") AND ("PLWH" OR "HIV" OR "AIDS")       | 153     |
| PsycINFO       | 2021.11.18 | TX ("cognitive training" OR "cognitive intervention" OR "cognitive rehabilitation" OR "non-pharmacology intervention" OR "mnemonic training" OR "processing speed training" OR "working memory training" OR "N-back training" OR "attention training" OR "reasoning training" OR "computer game" OR "video game" OR "computerized training" OR "computerized intervention" OR "cognitive exercise" OR "brain exercise" OR "cognitive stimulation" OR "cognitive enhancement") AND TX ("PLWH" OR "HIV" OR "AIDS") | 199     |
| Cochrane       | 2021.11.18 | “cognitive training” OR “cognitive intervention” OR “cognitive rehabilitation” OR “non-pharmacology intervention” OR “mnemonic training” OR “processing speed training” OR “working memory training” OR “N-back training” in Title Abstract Keyword AND “PLWH” OR “HIV” OR “AIDS” in Title Abstract Keyword<br><br>AND   | 379     |

|                |            |   |        |
|----------------|------------|---|--------|
|                |            | "attention training" OR "reasoning training" OR "computer game" OR "video game" OR "computerized training" OR "computerized intervention" OR "cognitive exercise" OR "brain exercise" OR "cognitive stimulation" OR "cognitive enhancement" in Title Abstract Keyword AND “PLWH” OR “HIV” OR “AIDS” in Title Abstract Keyword |        |
| Google Scholar | 2021.11.18 | HIV AND cognitive training  | 314000 |

**eTable 3.** Reasons for Exclusion in Full-text Assessment

| No. | Full text being excluded  | Reasons   |
|-----|---|---|
| 1   | Avci G, Woods SP, Verduzco M, Sheppard DP, Sumowski JF, Chiaravalloti ND, DeLuca J; HIV Neurobehavioral Research Program (HNRP) Group. Effect of Retrieval Practice on Short-Term and Long-Term Retention in HIV+ Individuals. <i>J Int Neuropsychol Soc.</i> 2017 Mar;23(3):214-222. | Not having computerized cognitive training            |
| 2   | Bai F, Allegrini M, Falcinella C, et al. Efficacy of a computerised cognitive rehabilitation training in improving HIV-associated neurocognitive disorders. <i>Journal of the international AIDS society.</i> 2018, 21.   | Being a conference report                             |
| 3   | Bailey M D, Lohaugen G, Hanna-Pladdy B, et al. Adaptive working memory training on cognitive performance in HIV-1 patients. <i>Journal of neuroimmune pharmacology.</i> 2019, 14(2): 352-352.   | Being a conference report                             |
| 4   | Becker JT, Dew MA, Aizenstein HJ, Lopez OL, Morrow L, Saxton J, Tárraga L. A pilot study of the effects of internet-based cognitive stimulation on neuropsychological function in HIV disease. <i>Disabil Rehabil.</i> 2012;34(21):1848-52.   | Not having extracted data                             |
| 5   | Casaleto KB, Moore DJ, Woods SP, Umlauf A, Scott JC, Heaton RK. Abbreviated Goal Management Training Shows Preliminary Evidence as a Neurorehabilitation Tool for HIV-associated Neurocognitive Disorders among Substance Users. <i>Clin Neuropsychol.</i> 2016;30(1):107-30.         | Not having computerized cognitive training            |
|     | Chan, T., Marta, M., Hawkins, C., & Rackstraw, S. (2020). Cognitive and Neurologic Rehabilitation Strategies for Central Nervous System HIV Infection. <i>Current HIV/AIDS reports</i> , 17(5), 514–521.  | Being a review  |
| 6   | Chang L, Løhaugen GC, Douet V, Miller EN, Skranes J, Ernst T. Neural correlates of working memory training in HIV patients: study protocol for a randomized controlled trial. <i>Trials.</i> 2016 Feb 2; 17:62.   | Having the same dataset published in previous studies |
| 7   | Cody SL, Fazeli PL, Vance DE. Feasibility of a Home-Based Speed of Processing Training Program in Middle-Aged and Older Adults With HIV. <i>J Neurosci Nurs.</i> 2015 Aug;47(4):247-54.   | Not having computerized cognitive training            |
| 8   | Frain JA, Chen L. Examining the effectiveness of a cognitive intervention to improve cognitive function in a population of older adults living with HIV: a pilot study. <i>Ther Adv Infect Dis.</i> 2018 Jan;5(1):19-28.  | Not having extracted data                             |

|    |   |   |
|----|---|---|
| 9  | Ownby RL, Acevedo A. A pilot study of cognitive training with and without transcranial direct current stimulation to improve cognition in older persons with HIV-related cognitive impairment. <i>Neuropsychiatr Dis Treat</i> . 2016 Oct 25;12:2745-2754.  | Not being RCT design                                  |
|    | van der Heijden, I., Abrahams, N., & Sinclair, D. (2017). Psychosocial group interventions to improve psychological well-being in adults living with HIV. The Cochrane database of systematic reviews, 3(3), CD010806.  | Being a review  |
|    | Vance, D. E., Fazeli, P. L., Grant, J. S., Slater, L. Z., & Raper, J. L. (2013). The role of neuroplasticity and cognitive reserve in aging with HIV: recommendations for cognitive protection and rehabilitation. The Journal of neuroscience nursing: journal of the American Association of Neuroscience Nurses, 45(5), 306–316. | Being a review  |
| 10 | Vance DE, Gakumo CA, Childs GD, Enah C, Fazeli PL. Feedback on a Multimodal Cognitive Intervention for Adults Aging With HIV: A Focus Group Study. <i>J Assoc Nurses AIDS Care</i> . 2017 Sep-Oct;28(5):685-697.  | Having the same dataset published in previous studies |
| 11 | Vance D, Fazeli P, Shacka J, Nicholson W, McKie P, Raper J, Azuero A, Wadley V, Ball K. Testing a Computerized Cognitive Training Protocol in Adults Aging With HIV-Associated Neurocognitive Disorders: Randomized Controlled Trial Rationale and Protocol. <i>JMIR Res Protoc</i> . 2017 Apr 26;6(4):e68.                         | Having the same dataset published in previous studies |
| 12 | Vance DE, Jensen M, Tende F, Raper JL, Morrison S, Fazeli PL. Individualized-Targeted Computerized Cognitive Training to Treat HIV-Associated Neurocognitive Disorder: An Interim Descriptive Analysis. <i>J Assoc Nurses AIDS Care</i> . 2018 Jul-Aug;29(4):604-611.   | Not being RCT design                                  |
|    | Weber, E., Woods, S. P., Kellogg, E., Grant, I., Basso, M. R., & HIV Neurobehavioral Research Program (HNRP) Group (2012). Self-generation enhances verbal recall in individuals infected with HIV. Journal of the International Neuropsychological Society: JINS, 18(1), 128–133.  | Not having computerized cognitive training            |
|    | Woods, S. P., Morgan, E. E., Loft, S., Matchanova, A., Verduzco, M., & Cushman, C. (2021). Enhancing cue salience improves aspects of naturalistic time-based prospective memory in older adults with HIV   | Unpublished   |

|  |   |                                   |
|--|---|-----------------------------------|
|  | disease. Neuropsychology, 35(1), 111–122.   |                                   |
|  | Woods, S. P., Morgan, E. E., Loft, S., Matchanova, A., Verduzco, M., & Cushman, C. (2020). Supporting strategic processes can improve time-based prospective memory in the laboratory among older adults with HIV disease. Neuropsychology, 34(3), 249–263. | Not a standard intervention study |

**eTable 4.** Categorization of Outcome Measures

|   | Study name                          | Categorization of outcome measures  |
|---|-------------------------------------|---|
| 1 | Chang et.al. (2016), United States  | Digit span (A/WM); Spacial span (A/WM)  |
| 2 | Cody et.al. (2019), United States   | Digit copy test (MS); Letter comparison test (SIP); UFOV (A/WM)   |
| 3 | Ezeamama et.al. (2020), Uganda      | Color trails (SIP); Finger tapping (MS); Grooved pegboard test (Dominant hand) (SIP); Symbol digit modality (SIP); Timed gait (MS); Verbal fluency (V/L); WHO UCLA verbal learning test Delayed recall and recognition (M); WHO UCLA verbal learning test Delayed recall of first list (M); WHO UCLA verbal learning test Interference list recalls (M); WHO UCLA verbal learning test Post interference list recall (M); WHO UCLA verbal learning test Sum of immediate recalls (M)  |
| 4 | Fazeli et.al. (2017), United States | Digit symbol substitution (SIP); Dimensional card change (A/E); Flanker computed (A/WM); Letter and pattern comparison (SIP); List sorting raw (A/WM); Oral reading recognition (V/L); Pattern comparison raw (SIP); Picture sequence memory (M); Picture vocabulary computed (V/L); UFOV 1 (SIP); UFOV 2 (A/WM); UFOV 3 (A/WM); UFOV risk (SIP); UFOV total (SIP)  |
| 5 | Livelli et.al. (2015), Italy        | Trail making test part A (SIP); Stroop color test-time (SIP); Rey auditory verbal learning test immediate recall (M); Rey auditory verbal learning test delayed recall (M); Rey-osterrieth complex figure delayed recall (M); Tower of London simplified version (A/E); Stroop color test-errors (A/E); Trail making test part B (A/E); Frontal assessment battery (A/E); Rey-osterrieth complex figure copy (A/E); Phonemic fluency (V/L); Verbal span (V/L); Corsi's block-Tapping test (A/WM); Digit span (A/WM); Trail making test part BA (A/WM); Grooved pegboard test dominant and non-dominant hands (MS); IADL test (DF) |
| 6 | Ownby et.al. (2016), United States  | Digit span backward (A/WM); Digit span forward (A/WM); Digit span scaled score (A/WM); Digit span sequencing (A/WM); HVLT-R delayed recall (M); HVLT-R recognition (M); HVLT-R total (M); Pegs dominant hand (MS); Pegs nondominant hand (MS); Trails A (SIP); Trails B (A/E)   |
| 7 | Pope et.al. (2018), United States   | STISIM driving simulator (A/E)  |
| 8 | Towe et.al. (2017), United States   | Working memory (A/WM)   |
| 9 | Towe et.al. (2020), United States   | Paced auditory serial addition task-50 (A/WM); WAIS-IV Digit span subtest (A/WM); WAIS-IV Letter (A/WM); Trail making test part A (SIP); WAIS-IV Coding subtest (SIP); Stroop color and word test color naming score (SIP); HVLT-revised (M); BVMT-   |



|    |                                     |  |
|----|-------------------------------------|--|
|    |                                     | revised (M); Stroop color and word test interference score (A/E); Trail making test part B (A/E); WCST (A/E); FAS letter fluency (V/L); Category fluency (V/L); Grooved pegboard test dominant and non-dominant hand (MS)  |
| 10 | Vance et.al. (2012), United States  | Finger tapping test (MS); UFOV® test (A/WM); Wisconsin card sort test (A/E); TIADL test (DF)   |
| 11 | Vance et.al. (2021a), United States | Stroop Color Naming Test, Trails A (SIP); Paced Auditory Serial Attention Test (A/WM); Stroop Interference, Trails B (A/E); Benton Visual Retention Test—Revised (M); Benton Visual Retention Test Delayed—Revised (M); WAIS IV Block Design (S-P); Hopkins Verbal Learning Test—Revised (M); Hopkins Verbal Learning Test Delayed—Revised (M) |
| 12 | Vance et.al. (2021b), United States | Stroop Color Naming Test, Trails A (SIP); Paced Auditory Serial Attention Test (A/WM); Stroop Interference, Trails B (A/E); Benton Visual Retention Test—Revised (M); Benton Visual Retention Test Delayed—Revised (M); WAIS IV Block Design (S-P); Hopkins Verbal Learning Test—Revised (M); Hopkins Verbal Learning Test Delayed—Revised (M) |

A/E = Abstraction/executive; A/WM = Attention/working memory; M = Memory; MS = Motor skill; SIP = Speed of information processing; S-P = Sensory-perceptual; V/L = Verbal/language; DF = Daily function

eTable 5. Study Quality of Evidence According to GRADE Guidelines

| CCT for HAND                    |  |   |                                |  |
|---------------------------------|--|---|--------------------------------|--|
| Bibliography:                   |  |   |                                |  |
| Outcomes                        | No of Participants<br>(studies)<br>Follow up | Quality of the evidence<br>(GRADE)  | Relative<br>effect<br>(95% CI) | Anticipated absolute effects<br>Risk with Control Risk difference with CCT (95% CI)  |
| Abstraction/Executive           | 240<br>(6 studies)<br>3-24 weeks             | ⊕ ⊕ ⊕ ⊖<br><b>MODERATE</b> <sup>1,2,3</sup><br>due to risk of bias, imprecision, large effect                       |                                | See comment See comment  |
| Attention/Working memory        | 376<br>(9 studies)<br>3-24 weeks             | ⊕ ⊕ ⊕ ⊖<br><b>MODERATE</b> <sup>1,2,3</sup><br>due to risk of bias, imprecision, large effect                       |                                | The mean attention/working memory in the intervention groups was<br><b>0.62 standard deviations higher</b><br>(0.33 to 0.91 higher)        |
| Memory                          | 245<br>(5 studies)<br>3-24 weeks             | ⊕ ⊕ ⊕ ⊖<br><b>MODERATE</b> <sup>1,3</sup><br>due to risk of bias, imprecision, large effect                         |                                | The mean memory in the intervention groups was<br><b>0.59 standard deviations higher</b><br>(0.20 to 0.97 higher)                          |
| Motor skill                     | 229<br>(5 studies)<br>3-10 weeks             | ⊕ ⊕ ⊕ ⊖<br><b>MODERATE</b> <sup>1,2,3</sup><br>due to risk of bias, imprecision, large effect                       |                                | The mean motor skill in the intervention groups was<br><b>0.50 standard deviations higher</b><br>(0.24 to 0.77 higher)                     |
| Speed of information processing | 246<br>(5 studies)<br>3-12 weeks             | ⊕ ⊕ ⊕ ⊖<br><b>MODERATE</b> <sup>1,2,3</sup><br>due to risk of bias, imprecision, large effect                       |                                | The mean speed of information processing in the intervention groups was<br><b>0.65 standard deviations higher</b><br>(0.37 to 0.94 higher) |
| Sensory-perceptual              | 88<br>(1 study)<br>12 weeks                  | ⊕ ⊖ ⊖ ⊖<br><b>VERY LOW</b> <sup>1,2,4</sup><br>due to risk of bias, inconsistency, imprecision,<br>publication bias |                                | The mean sensory-perceptual in the intervention groups was<br><b>0.06 standard deviations higher</b><br>(0.36 lower to 0.48 higher)        |

|                 |             |   |  |
|-----------------|-------------|---|--|
| Verbal/Language | 204         | ⊕ ⊕ ⊕ ⊕   | The mean verbal/language in the intervention groups was<br><b>0.46 standard deviations higher</b><br>(0.07 lower to 0.99 higher) |
|                 | (4 studies) | <b>VERY LOW</b> <sup>1,2,3,5</sup>              |  |
|                 | 4-24 weeks  | due to risk of bias, inconsistency, imprecision |  |
| Daily function  | 187         | ⊕ ⊕ ⊕ ⊕   | The mean daily function in the intervention groups was<br><b>0.44 standard deviations higher</b><br>(0.02 to 0.86 higher)        |
|                 | (3 studies) | <b>MODERATE</b> <sup>1,2,3</sup>                |  |
|                 | 5-24 weeks  | due to risk of bias, imprecision, large effect  |  |

\*The basis for the **assumed risk** (eg. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval;

GRADE Working Group grades of evidence

**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.

**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low quality:** We are very uncertain about the estimate.

<sup>1</sup> Random sequence generation, allocation concealment, or blinding of outcome assessors were poorly described in 50% or more of included studies.

<sup>2</sup> Small sample size

<sup>3</sup> No explanation was provided

<sup>4</sup> Only one study, cannot be assessed.

<sup>5</sup> Large confidence intervals

**eTable 6.** Full Results of Sensitivity Analyses

Age

| Outcomes                        | Age        | SMD   | 95% CI       | Z     | <i>p</i> | <i>Q</i> | <i>p</i> |
|---------------------------------|------------|-------|--------------|-------|----------|----------|----------|
| Abstraction/Executive           |            |       |              | 4.030 | <0.001   | 2.373    | 0.123    |
|                                 | young(n=1) | 1.137 | 0.390-1.884  | 2.984 | 0.003    |          |          |
|                                 | old (n=5)  | 0.500 | 0.186-0.814  | 3.117 | 0.002    |          |          |
| Attention/Working memory        |            |       |              | 3.983 | <0.001   | 0.699    | 0.403    |
|                                 | young(n=2) | 0.976 | -0.036-1.987 | 1.890 | 0.059    |          |          |
|                                 | old (n=7)  | 0.527 | 0.241-0.814  | 3.605 | <0.001   |          |          |
| Daily function                  |            |       |              | 2.480 | 0.013    | 3.170    | 0.075    |
|                                 | young(n=1) | 0.982 | 0.248-1.715  | 2.623 | 0.009    |          |          |
|                                 | old (n=2)  | 0.255 | -0.065-0.575 | 1.562 | 0.118    |          |          |
| Memory                          |            |       |              | 4.167 | <0.001   | 5.747    | 0.017    |
|                                 | young(n=1) | 1.446 | 0.667-2.224  | 3.641 | <0.001   |          |          |
|                                 | old (n=4)  | 0.437 | 0.164-0.710  | 3.138 | 0.002    |          |          |
| Motor skill                     |            |       |              | 3.739 | <0.001   | 2.421    | 0.120    |
|                                 | young(n=1) | 0.153 | -0.362-0.688 | 0.582 | 0.561    |          |          |
|                                 | old (n=4)  | 0.630 | 0.322-0.938  | 4.008 | <0.001   |          |          |
| Speed of information processing | NA         |       |              |       |          |          |          |

Proportion of women(%)

| Outcomes                 | Sex       | SMD   | 95% CI       | Z     | <i>p</i>         | <i>Q</i> | <i>p</i>     |
|--------------------------|-----------|-------|--------------|-------|------------------|----------|--------------|
| Abstraction/Executive    |           |       |              | 3.070 | <i>0.002</i>     | 0.002    | <i>0.965</i> |
|                          | <50(n=4)  | 0.584 | 0.143-1.025  | 2.594 | <i>0.009</i>     |          |              |
|                          | ≥ 50(n=2) | 0.566 | -0.110-1.241 | 1.642 | <i>0.101</i>     |          |              |
| Attention/Working memory |           |       |              | 4.125 | <i>&lt;0.001</i> | 3.226    | 0.072        |
|                          | <50(n=7)  | 0.738 | 0.411-1.066  | 4.424 | <i>&lt;0.001</i> |          |              |
|                          | ≥ 50(n=2) | 0.202 | -0.282-0.687 | 0.818 | <i>0.413</i>     |          |              |
| Daily function           | NA        |       |              |       |                  |          |              |
| Memory                   |           |       |              | 2.564 | <i>0.010</i>     | 0.531    | <i>0.466</i> |
|                          | <50(n=3)  | 0.775 | 0.031-1.520  | 2.040 | <i>0.041</i>     |          |              |
|                          | ≥ 50(n=2) | 0.441 | -0.063-0.945 | 1.716 | <i>0.086</i>     |          |              |
| Motor skill              |           |       |              | 3.448 | <i>0.001</i>     | 0.022    | 0.882        |
|                          | <50(n=3)  | 0.496 | -0.001-0.993 | 1.957 | 0.050            |          |              |

|                                 |           |       |             |       |        |       |       |
|---------------------------------|-----------|-------|-------------|-------|--------|-------|-------|
|                                 | ≥ 50(n=2) | 0.543 | 0.169-0.918 | 2.843 | 0.004  |       |       |
| Speed of information processing |           |       |             | 4.974 | <0.001 | 2.640 | 0.104 |
|                                 | <50(n=2)  | 0.926 | 0.510-1.343 | 4.357 | <0.001 |       |       |
|                                 | ≥ 50(n=3) | 0.486 | 0.157-0.815 | 2.898 | 0.004  |       |       |

#### Years of Education (years)

| Outcomes                 | Education | SMD   | 95% CI       | Z     | p      | Q     | p     |
|--------------------------|-----------|-------|--------------|-------|--------|-------|-------|
| Abstraction/Executive    |           |       |              | 3.714 | <0.001 | 1.273 | 0.259 |
|                          | ≤ 12(n=3) | 0.762 | 0.328-1.196  | 3.443 | 0.001  |       |       |
|                          | > 12(n=3) | 0.405 | -0.038-0.848 | 1.793 | 0.073  |       |       |
| Attention/Working memory |           |       |              | 3.927 | <0.001 | 0.279 | 0.597 |
|                          | ≤ 12(n=4) | 0.727 | 0.246-1.208  | 2.960 | 0.003  |       |       |
|                          | > 12(n=5) | 0.556 | 0.142-0.969  | 2.634 | 0.008  |       |       |
| Daily function           |           |       |              | 1.914 | 0.056  | 0.043 | 0.836 |

|                                 |          |       |              |       |        |       |       |
|---------------------------------|----------|-------|--------------|-------|--------|-------|-------|
|                                 | ≤12(n=2) | 0.520 | -0.251-1.290 | 1.322 | 0.186  |       |       |
|                                 | >12(n=1) | 0.418 | -0.167-1.002 | 1.399 | 0.162  |       |       |
| Memory                          |          |       |              | 2.850 | 0.004  | 2.011 | 0.156 |
|                                 | ≤12(n=4) | 0.694 | 0.265-1.124  | 3.168 | 0.002  |       |       |
|                                 | >12(n=1) | 0.110 | -0.573-0.793 | 0.316 | 0.752  |       |       |
| Motor skill                     |          |       |              | 3.739 | <0.001 | 2.856 | 0.091 |
|                                 | ≤12(n=3) | 0.344 | 0.021-0.667  | 2.089 | 0.037  |       |       |
|                                 | >12(n=2) | 0.829 | 0.369-1.289  | 3.532 | <0.001 |       |       |
| Speed of information processing |          |       |              | 3.697 | <0.001 | 0.005 | 0.945 |
|                                 | ≤12(n=3) | 0.642 | 0.158-1.126  | 2.601 | 0.009  |       |       |
|                                 | >12(n=2) | 0.666 | 0.170-1.163  | 2.629 | 0.009  |       |       |

#### CD4<sup>+</sup>T Cell Counts (cells/ul)

| Outcomes | CD4 | SMD | 95% CI | Z | p | Q | p |
|----------|-----|-----|--------|---|---|---|---|
|----------|-----|-----|--------|---|---|---|---|

|                          |            |       |              |       |              |       |              |
|--------------------------|------------|-------|--------------|-------|--------------|-------|--------------|
| Abstraction/Executive    |            |       |              | 3.878 | <0.001       | 2.233 | <i>0.135</i> |
|                          | <500(n=1)  | 0.181 | -0.399-0.761 | 0.613 | <i>0.540</i> |       |              |
|                          | ≥ 500(n=5) | 0.689 | 0.361-1.018  | 4.110 | <0.001       |       |              |
| Attention/Working memory |            |       |              | 4.166 | <0.001       | 4.776 | <i>0.029</i> |
|                          | <500(n=2)  | 0.198 | -0.185-0.580 | 1.013 | <i>0.311</i> |       |              |
|                          | ≥ 500(n=7) | 0.755 | 0.433-1.078  | 4.594 | <0.001       |       |              |
| Daily function           |            |       |              | 2.127 | <i>0.033</i> | 1.904 | <i>0.168</i> |
|                          | <500(n=2)  | 0.654 | 0.109-1.200  | 2.350 | <i>0.019</i> |       |              |
|                          | ≥ 500(n=1) | 0.185 | -0.197-0.567 | 0.951 | <i>0.342</i> |       |              |
| Memory                   |            |       |              | 3.048 | <i>0.002</i> | 0.779 | <i>0.377</i> |
|                          | <500(n=1)  | 0.297 | -0.213-0.807 | 1.140 | <i>0.254</i> |       |              |
|                          | ≥ 500(n=5) | 0.585 | 0.198-0.972  | 2.962 | <i>0.003</i> |       |              |
| Motor skill              |            |       |              | 3.150 | 0.002        | 2.137 | 0.144        |
|                          | <500(n=1)  | 0.855 | 0.251-1.460  | 2.774 | 0.006        |       |              |



|                                 |            |       |              |       |       |       |       |
|---------------------------------|------------|-------|--------------|-------|-------|-------|-------|
|                                 | ≥ 500(n=3) | 0.344 | 0.021-0.667  | 2.089 | 0.037 |       |       |
| Speed of information processing |            |       |              | 3.276 | 0.001 | 1.657 | 0.198 |
|                                 | < 500(n=1) | 0.209 | -0.299-0.718 | 0.807 | 0.420 |       |       |
|                                 | ≥ 500(n=4) | 0.616 | 0.264-0.968  | 3.426 | 0.001 |       |       |

#### HIV suppression rate (%)

| Outcomes                 | HIV suppression rate | SMD   | 95% CI       | Z     | <i>p</i> | <i>Q</i> | <i>p</i> |
|--------------------------|----------------------|-------|--------------|-------|----------|----------|----------|
| Abstraction/Executive    |                      |       |              | 3.035 | 0.002    | 3.391    | 0.066    |
|                          | < 100(n=4)           | 0.357 | -0.007-0.720 | 1.924 | 0.054    |          |          |
|                          | ≥ 100(n=1)           | 1.137 | 0.390-1.884  | 2.984 | 0.003    |          |          |
| Attention/Working memory |                      |       |              | 5.494 | <0.001   | 4.521    | 0.033    |
|                          | < 100(n=6)           | 0.631 | 0.355-0.907  | 4.484 | <0.001   |          |          |
|                          | ≥ 100(n=1)           | 1.537 | 0.749-2.326  | 3.821 | <0.001   |          |          |
| Daily function           |                      |       |              | 2.730 | 0.006    | 1.390    | 0.238    |

|                                 |           |       |              |       |                  |       |              |
|---------------------------------|-----------|-------|--------------|-------|------------------|-------|--------------|
|                                 | <100(n=1) | 0.418 | -0.167-1.002 | 1.399 | <i>0.162</i>     |       |              |
|                                 | ≥100(n=1) | 0.982 | 0.248-1.715  | 2.623 | <i>0.009</i>     |       |              |
| Memory                          |           |       |              | 3.977 | <i>&lt;0.001</i> | 4.755 | <i>0.029</i> |
|                                 | <100(n=3) | 0.493 | 0.136-0.850  | 2.705 | <i>0.007</i>     |       |              |
|                                 | ≥100(n=1) | 1.446 | 0.667-2.224  | 3.641 | <i>&lt;0.001</i> |       |              |
| Motor skill                     | NA        |       |              |       |                  |       |              |
| Speed of information processing | NA        |       |              |       |                  |       |              |

#### Session

| Outcomes                 | session  | SMD   | 95% CI       | Z     | <i>p</i>         | <i>Q</i> | <i>p</i>     |
|--------------------------|----------|-------|--------------|-------|------------------|----------|--------------|
| Abstraction/Executive    |          |       |              | 3.140 | <i>0.002</i>     | 2.090    | <i>0.148</i> |
|                          | ≥22(n=3) | 0.465 | -0.057-0.987 | 1.747 | <i>0.081</i>     |          |              |
|                          | <22(n=1) | 1.137 | 0.390-1.884  | 2.984 | <i>0.003</i>     |          |              |
| Attention/Working memory |          |       |              | 3.698 | <i>&lt;0.001</i> | 1.341    | <i>0.247</i> |
|                          | ≥22(n=4) | 0.509 | -0.002-1.021 | 1.950 | <i>0.051</i>     |          |              |

|                                 |          |       |              |       |       |       |       |
|---------------------------------|----------|-------|--------------|-------|-------|-------|-------|
|                                 | <22(n=3) | 0.958 | 0.397-1.519  | 3.348 | 0.001 |       |       |
| Daily function                  | NA       |       |              |       |       |       |       |
| Memory                          |          |       |              | 2.098 | 0.036 | 2.236 | 0.135 |
|                                 | ≥22(n=2) | 0.230 | -0.365-0.826 | 0.758 | 0.449 |       |       |
|                                 | <22(n=2) | 0.978 | 0.200-1.756  | 2.463 | 0.014 |       |       |
| Motor skill                     |          |       |              | 2.809 | 0.005 | 1.445 | 0.229 |
|                                 | ≥22(n=2) | 0.751 | 0.138-1.363  | 2.403 | 0.016 |       |       |
|                                 | <22(n=2) | 0.323 | -0.012-0.658 | 1.887 | 0.059 |       |       |
| Speed of information processing |          |       |              | 3.008 | 0.003 | 0.831 | 0.362 |
|                                 | ≥22(n=3) | 0.641 | 0.182-1.101  | 2.737 | 0.006 |       |       |
| <                               | <22(n=1) | 0.346 | -0.094-0.785 | 1.545 | 0.122 |       |       |

Session hours (minutes)

| Outcomes              | Session hours | SMD | 95% CI | Z     | p     | Q     | p     |
|-----------------------|---------------|-----|--------|-------|-------|-------|-------|
| Abstraction/Executive |               |     |        | 2.130 | 0.033 | 0.213 | 0.644 |

|                          |           |       |              |       |                  |              |              |
|--------------------------|-----------|-------|--------------|-------|------------------|--------------|--------------|
|                          | <60(n=2)  | 0.679 | -0.396-1.754 | 1.239 | <i>0.216</i>     |              |              |
|                          | ≥60(n=3)  | 0.405 | -0.038-0.848 | 1.793 | <i>0.073</i>     |              |              |
| Attention/Working memory |           |       |              | 4.325 | <i>&lt;0.001</i> | 9.410        | <i>0.002</i> |
|                          | <60 (n=3) | 1.150 | 0.712-1.589  | 5.138 | <i>&lt;0.001</i> |              |              |
|                          | ≥60 (n=3) | 0.249 | -0.123-0.622 | 1.312 | <i>0.189</i>     |              |              |
| Daily function           |           |       |              | 2.480 | <i>0.013</i>     | <i>3.170</i> | <i>0.075</i> |
|                          | <60 (n=1) | 0.982 | 0.248-1.715  | 2.623 | <i>0.009</i>     |              |              |
|                          | ≥60 (n=2) | 0.255 | -0.065-0.575 | 1.562 | <i>0.118</i>     |              |              |
| Memory                   |           |       |              | 2.703 | <i>0.007</i>     | 3.016        | 0.082        |
|                          | <60 (n=3) | 0.882 | 0.341-1.423  | 3.198 | 0.001            |              |              |
|                          | ≥60 (n=1) | 0.110 | 0.161-1.009  | 0.316 | <i>0.752</i>     |              |              |
| Motor skill              |           |       |              | 4.008 | <i>&lt;0.001</i> | 1.305        | 0.253        |
|                          | <60 (n=2) | 0.468 | 0.053-0.882  | 2.212 | 0.027            |              |              |

|                                 |            |       |              |       |        |       |       |
|---------------------------------|------------|-------|--------------|-------|--------|-------|-------|
|                                 | ≥ 60 (n=2) | 0.829 | 0.369-1.289  | 3.532 | <0.001 |       |       |
| Speed of information processing |            |       |              | 3.008 | 0.003  | 0.847 | 0.358 |
|                                 | <60 (n=2)  | 0.363 | -0.049-0.776 | 1.727 | 0.084  |       |       |
|                                 | ≥ 60 (n=2) | 0.666 | 0.170-1.163  | 2.629 | 0.009  |       |       |

Frequency (times/week)

| Outcomes                 | frequency | SMD   | 95% CI       | Z     | p      | Q     | p     |
|--------------------------|-----------|-------|--------------|-------|--------|-------|-------|
| Abstraction/Executive    | NA        |       |              |       |        |       |       |
| Attention/Working memory |           |       |              | 3.703 | <0.001 | 0.375 | 0.540 |
|                          | <3(n=2)   | 0.578 | -0.586-1.741 | 0.973 | 0.330  |       |       |
|                          | ≥ 3(n=2)  | 0.977 | 0.449-1.505  | 3.625 | <0.001 |       |       |
| Daily function           | NA        |       |              |       |        |       |       |
| Memory                   |           |       |              | 2.979 | 0.003  | 0.002 | 0.961 |
|                          | <3(n=1)   | 0.641 | 0.194-1.088  | 2.813 | 0.005  |       |       |
|                          | ≥ 3(n=1)  | 0.609 | -0.605-1.822 | 0.983 | 0.326  |       |       |

|                                 |         |       |              |       |              |       |              |
|---------------------------------|---------|-------|--------------|-------|--------------|-------|--------------|
| Motor skill                     |         |       |              | 3.015 | <i>0.003</i> | 0.017 | <i>0.895</i> |
|                                 | <3(n=2) | 0.543 | 0.169-0.918  | 2.843 | <i>0.004</i> |       |              |
|                                 | ≥3(n=1) | 0.629 | -0.587-.844  | 1.014 | <i>0.311</i> |       |              |
| Speed of information processing |         |       |              | 2.299 | <i>0.021</i> | 0.001 | <i>0.970</i> |
|                                 | <3(n=2) | 0.519 | 0.047-0.992  | 2.154 | 0.031        |       |              |
|                                 | ≥3(n=1) | 0.495 | -0.710-1.699 | 0.805 |              |       |              |

#### Total training hours (hours)

| Outcomes                 | hours    | SMD   | 95% CI       | Z     | <i>p</i>         | <i>Q</i> | <i>p</i>     |
|--------------------------|----------|-------|--------------|-------|------------------|----------|--------------|
| Abstraction/Executive    | NA       |       |              |       |                  |          |              |
| Attention/Working memory |          |       |              | 3.635 | <i>&lt;0.001</i> | 1.854    | <i>0.173</i> |
|                          | <12(n=4) | 0.478 | -0.018-0.974 | 1.890 | <i>0.059</i>     |          |              |
|                          | ≥12(n=1) | 1.011 | 0.427-1.595  | 3.391 | <i>0.001</i>     |          |              |
| Daily function           | NA       |       |              |       |                  |          |              |
| Memory                   | NA       |       |              |       |                  |          |              |

|                                 |    |  |  |  |  |  |  |
|---------------------------------|----|--|--|--|--|--|--|
| Motor skill                     | NA |  |  |  |  |  |  |
| Speed of information processing | NA |  |  |  |  |  |  |

Time since training (weeks)

| Outcomes                 | Follow-up | SMD   | 95% CI       | Z     | <i>p</i>         | <i>Q</i> | <i>p</i>     |
|--------------------------|-----------|-------|--------------|-------|------------------|----------|--------------|
| Abstraction/Executive    |           |       |              | 3.842 | <i>&lt;0.001</i> | 5.326    | <i>0.021</i> |
|                          | <10(n=3)  | 0.183 | -0.232-0.598 | 0.865 | <i>0.387</i>     |          |              |
|                          | ≥10(n=2)  | 0.841 | 0.466-1.216  | 4.397 | <i>&lt;0.001</i> |          |              |
| Attention/Working memory |           |       |              | 3.956 | <i>&lt;0.001</i> | 1.040    | <i>0.308</i> |
|                          | <10(n=5)  | 0.487 | 0.121-0.854  | 2.605 | <i>0.009</i>     |          |              |
|                          | ≥10(n=4)  | 0.812 | 0.306-1.318  | 3.147 | <i>0.002</i>     |          |              |
| Daily function           |           |       |              | 1.914 | <i>0.056</i>     | 0.043    | <i>0.836</i> |
|                          | <10(n=1)  | 0.418 | -0.167-1.002 | 1.399 | <i>0.162</i>     |          |              |
|                          | ≥10(n=2)  | 0.520 | -0.251-1.290 | 1.322 | <i>0.186</i>     |          |              |
| Memory                   |           |       |              | 3.136 | <i>0.002</i>     | 0.495    | <i>0.482</i> |

|                                 |          |       |              |       |                  |       |       |
|---------------------------------|----------|-------|--------------|-------|------------------|-------|-------|
|                                 | <10(n=6) | 0.454 | 0.136-0.771  | 2.803 | <i>0.005</i>     |       |       |
|                                 | ≥10(n=2) | 0.851 | -0.210-1.912 | 1.573 | <i>0.116</i>     |       |       |
| Motor skill                     |          |       |              | 3.739 | <i>&lt;0.001</i> | 2.421 | 0.120 |
|                                 | <10(n=4) | 0.630 | 0.322-0.938  | 4.008 | <i>&lt;0.001</i> |       |       |
|                                 | ≥10(n=1) | 0.153 | -0.362-0.668 | 0.582 | 0.561            |       |       |
| Speed of information processing |          |       |              | 4.974 | <i>&lt;0.001</i> | 3.200 | 0.074 |
|                                 | <10(n=4) | 0.487 | 0.170-0.804  | 3.008 | 0.003            |       |       |
|                                 | ≥10(n=1) | 0.985 | 0.541-1.429  | 4.347 | <i>&lt;0.001</i> |       |       |

#### Type of participants

| Outcomes                 | Type of participants      | SMD   | 95% CI       | Z     | <i>p</i>         | <i>Q</i> | <i>p</i>     |
|--------------------------|---------------------------|-------|--------------|-------|------------------|----------|--------------|
| Abstraction/Executive    |                           |       |              | 3.714 | <i>&lt;0.001</i> | 1.272    | <i>0.259</i> |
|                          | Cognitive normal(n=3)     | 0.405 | -0.038-0.848 | 1.793 | <i>0.073</i>     |          |              |
|                          | Cognitive impairment(n=3) | 0.762 | 0.328-1.196  | 3.443 | <i>0.001</i>     |          |              |
| Attention/Working memory |                           |       |              | 3.891 | <i>&lt;0.001</i> | 0.625    | <i>0.429</i> |



|                                 |                           |       |              |       |        |       |       |
|---------------------------------|---------------------------|-------|--------------|-------|--------|-------|-------|
|                                 | Cognitive normal(n=6)     | 0.540 | 0.219-0.862  | 3.295 | <0.001 |       |       |
|                                 | Cognitive impairment(n=3) | 0.880 | 0.102-1.658  | 2.216 | 0.027  |       |       |
| Daily function                  |                           |       |              | 1.914 | 0.056  | 0.043 | 0.836 |
|                                 | Cognitive normal(n=1)     | 0.418 | -0.167-1.002 | 1.399 | 0.162  |       |       |
|                                 | Cognitive impairment(n=2) | 0.520 | -0.011-0.921 | 1.322 | 0.186  |       |       |
| Memory                          |                           |       |              | 2.564 | 0.010  | 0.531 | 0.466 |
|                                 | Cognitive normal(n=2)     | 0.441 | -0.063-0.945 | 1.716 | 0.086  |       |       |
|                                 | Cognitive impairment(n=3) | 0.775 | 0.031-1.520  | 2.040 | 0.041  |       |       |
| Motor skill                     |                           |       |              | 3.390 | 0.001  | 0.035 | 0.852 |
|                                 | Cognitive normal(n=4)     | 0.510 | 0.201-0.818  | 3.240 | 0.001  |       |       |
|                                 | Cognitive impairment(n=1) | 0.629 | -0.587-1.844 | 1.014 | 0.311  |       |       |
| Speed of information processing |                           |       |              | 4.972 | <0.001 | 2.640 | 0.104 |
|                                 | Cognitive normal(n=3)     | 0.486 | 0.157-0.815  | 2.898 | 0.004  |       |       |
|                                 | Cognitive impairment(n=2) | 0.926 | 0.510-1.343  | 4.357 | <0.001 |       |       |

**eFigure.** Risk of Bias Summary

|                      | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|----------------------|---|---|---|---|--|--------------------------------------|------------|
| Chang et al, 2016    | +   | ?                                       | ?   | ?   | +  | -                                    | +          |
| Cody et al, 2019     | +   | +                                       | +   | -   | ?  | +                                    | -          |
| Ezeamama et al, 2020 | -   | -                                       | ?   | ?   | +  | +                                    | +          |
| Fazeli et al, 2017   | +   | ?                                       | +   | +   | +  | +                                    | +          |
| Livelli et al, 2015  | +   | ?                                       | ?   | ?   | +  | +                                    | +          |
| Ownby et al, 2016    | +   | +                                       | +   | +   | -  | +                                    | +          |
| Pope et al, 2018     | +   | +                                       | +   | +   | -  | +                                    | +          |
| Towe et al, 2017     | +   | ?                                       | -   | -   | +  | +                                    | -          |
| Towe et al, 2020     | +   | +                                       | ?   | +   | +  | -                                    | +          |
| Vance et al, 2012    | +   | ?                                       | ?   | ?   | -  | +                                    | +          |
| Vance et al, 2021a   | +   | +                                       | ?   | ?   | +  | +                                    | +          |
| Vance et al, 2021b   | +   | +                                       | ?   | ?   | +  | +                                    | +          |