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Title:

The effects of virtual reality training on cognition in older adults: a systematic review, meta-analysis, and meta-regression of randomized controlled trials.

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Running head:

Effects of VRBT on cognition in older adults

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- 1 **The effects of virtual reality training on cognition in older adults: a systematic review, meta-**
- 2 **analysis, and meta-regression of randomized controlled trials**

1 The aim of this systematic review, meta-analysis, and meta-regression was to examine the effects of
2 virtual reality-based training (VRBT) on global cognition and executive function compared with
3 conventional training or information-based treatment in older adults, regardless of cognitive level. A
4 systematic literature search was conducted using four databases. A total of 31 randomized controlled
5 trials (RCT) were identified. Pooled effect sizes were calculated, the risk of bias was assessed, and
6 evidence was graded. The primary analyses showed a small but statistically significant effect of
7 VRBT compared with control on global cognition (Hedges' g 0.42, 95% CI 0.17 to 0.68, $I^2=70.1\%$,
8 $n=876$, 20 RCTs, low evidence) and executive function (Hedges' g 0.35, 95% CI 0.06 to 0.65,
9 $I^2=68.4\%$, $n=810$, 16 RCTs, very low evidence). Meta-regression yielded inconclusive results. VRBT
10 may be more effective than control in improving cognition in older adults; however, more high-
11 quality studies are needed.

12

13 Keywords: Virtual Reality, Aged, Cognition, Meta-Analysis, Randomized Controlled Trial

1 INTRODUCTION

2

3 Cognitive health is an important part of functional performance that enables independence and the
4 management of daily living in older age (WHO, 2019). Biological aging is an important factor that
5 causes changes in brain structure and, together with other risk factors, such as lifestyle and family
6 history, may influence the onset of cognitive impairment (WHO, 2019). To date, more than 55 million
7 people have dementia worldwide, and millions of new cases occur each year (WHO, 2023).
8 Therefore, prevention and rehabilitation of cognitive impairment are essential.

9 In recent years, cognitive rehabilitation has shifted to the increasing use of virtual reality (VR)
10 (Maggio et al., 2019), as it provides multisensory stimulation, increases adherence to training
11 (Valenzuela et al., 2018), and often allows for simultaneous motor-cognitive or dual-task challenges
12 (Monteiro-Junior et al., 2016; Pichierri et al., 2011), which have been shown to benefit cognition and
13 brain function through neuroplasticity (Cramer et al., 2011).

14 VR is often described as a computer-simulated 3D environment that provides a sense of presence and
15 real-time interaction in virtual space (Steuer, 1992; Wilson et al., 1997). VR can be divided into three
16 different levels of immersion (non-immersive, semi-immersive, fully immersive) (Mujber et al.,
17 2004), depending on the hardware used, the experience and feeling of presence gained by replacing
18 the physical environment with the virtual world, and the amount of sensory information available
19 (Rizzo & Koenig, 2017; Steuer, 1992; Wilson et al., 1997). Different levels of virtual reality can also
20 be identified through the concept of a virtuality continuum, which expresses a fusion of real and
21 virtual environments with different levels of virtuality (Milgram & Kishino, 1994). However, a
22 unified definition of virtual reality in rehabilitation research is lacking.

23 Recent meta-analyses have supported the beneficial effects of virtual reality-based training (VRBT)
24 in improving cognitive function in older adults with MCI or dementia (Gómez-Cáceres et al., 2022;
25 Kim et al., 2022; Papaioannou et al., 2022; Yan et al., 2022; Yu et al., 2022; Zhong et al., 2021; Zhu

1 et al., 2021), or over 60-year-olds with undefined cognitive level and other neurological disorders
2 (Yen & Chiu, 2021). These studies included many different cognitive outcomes, of which overall
3 cognitive performance, that is, global cognition, and executive function, are considered particularly
4 important for this review, as they have been found to predict dependence (Gill et al., 1996), functional
5 decline, and mortality (Johnson et al., 2007). With regard to these outcomes, the results of recent
6 meta-analyses have varied. VRBT was found to improve global cognition and executive function in
7 older persons with mild cognitive impairment (MCI) in one study (Gómez-Cáceres et al., 2022),
8 induce no differences between intervention and control groups in another study (Kim et al., 2022),
9 and have beneficial effects only on global cognition but not on executive function in a third study
10 (Papaioannou et al., 2022). These findings are inconclusive. Only one meta-analysis with meta-
11 regression analysis of VRBT in older adults has been published before; in that study the participants
12 had other neurological disorders, and in study selection process, the primary outcome was depressive
13 symptoms (Yen & Chiu 2021).

14 Grading of evidence was seen in only one recent meta-analysis, which found moderate evidence for
15 global cognition and very low evidence for executive function in older adults with MCI or dementia
16 (Papaioannou et al., 2022). However, Papaioannou et al. included other digitized forms of
17 rehabilitation, such as computerized cognitive training, in the control group, making it difficult to
18 separate the true effects of VRBT. In addition, none of the recent meta-analyses assessed the risk of
19 bias separately for each outcome, which may have led to more biased assessments. Some adverse
20 events have been reported with VRBT in older adults (Papaioannou et al., 2022; Yen & Chiu, 2021).
21 These include dizziness, fatigue, mild symptoms of cybersickness, and delayed muscle soreness.
22 However, reports on adverse events associated with VRBT are scarce.

23 This review aimed to address these limitations. The objectives of this systematic review, meta-
24 analysis, and meta-regression were 1) to examine the effects of virtual reality-based training (VRBT)
25 on global cognition and executive function compared with conventional training with physical and/or

1 cognitive exercises or information-based treatment in people aged 60 years and older (defined here
2 as older adults); 2) to examine whether the covariates of the study factors were associated with these
3 effects; 3) to grade the level of evidence; and 4) to assess the safety of VRBT by considering adverse
4 events reported in the original studies. To reliably determine the effects of VRBT, this review was
5 based on randomized controlled trials (RCTs). In this study, the focus was on medical rehabilitation,
6 and interventions using interactive virtual reality or video game technology that simulated real-life
7 situations or environments and provided a sense of presence were considered VR.

8

9 **METHODS**

10

11 This meta-analysis and meta-regression review was conducted according to the guidelines of the
12 Cochrane Handbook for Systematic Reviews of Interventions (Cochrane, 2021). The report
13 corresponds with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses
14 (PRISMA-2020) (Page et al., 2021). The PRISMA checklist is provided in the Supplementary
15 Material S1. This review was prospectively registered in the International Prospective Register of
16 Systematic Reviews
17 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022319227).

18

19 **Search strategy**

20

21 The data for this study were collected as part of a larger research project investigating the
22 effectiveness and meanings of robotics, virtual reality, and augmented reality in medical rehabilitation
23 (Ilves et al., 2022a), due to which a two-phase literature search and screening took place. A
24 comprehensive systematic literature search was carried out using the Ovid MEDLINE, CINAHL,
25 PsycINFO and ERIC databases. The first phase of the search was conducted from inception to

1 September 16, 2020. An updated literature search was conducted after the registration of this review
2 using the same databases from September 2020 to March 25, 2022. The reference lists of previous
3 systematic reviews were hand-searched to obtain all relevant literature. The search strategy consisted
4 of a Cochrane filter for RCTs (Lefebvre et al., 2011), along with MeSH terms and keywords related
5 to rehabilitation, virtual reality including exergaming and video gaming, and augmented reality. No
6 language limitations were implemented during the database search. The search strategy for the Ovid
7 MEDLINE database is presented in Supplementary Material S1.

8

9 **Eligibility criteria**

10

11 A two-phase screening process was used in this review, as described above. In the first phase, the
12 records identified in the larger project (Ilves et al., 2022b) were screened according to the pre-
13 specified PICOS strategy; participants (P) included both children and adults, regardless of age, in
14 need of medical rehabilitation; intervention (I) included rehabilitation robots, virtual reality or
15 augmented reality; and the control (C) group received different approaches or implementation of
16 rehabilitation, usual care, or waiting list treatment. Outcomes (O) included any parameter related to
17 the International Classification of Functioning, Disability, and Health (ICF) classification of bodily
18 functions and structures, performance and participation, quality of life, physical and mental well-
19 being, need for assistance, and ability to study and work. Eligible studies were limited to parallel and
20 cross-over RCT designs (S).

21 In the second phase of screening, more specific PICOS criteria were applied. Original peer-reviewed
22 studies were eligible for this review if they met the following PICOS criteria: participants (P) were at
23 least 60 years of age regardless of cognitive level; and intervention (I) was delivered as VRBT
24 involving either only VR training or VR training in addition to conventional training or information-
25 based treatment. Interventions using interactive virtual reality or video game technology that

1 simulated real-life situations or environments and provided a sense of presence were considered as
2 VR. Control (C) group received conventional training with physical and/or cognitive exercises, or
3 information-based treatment, where participants received health education or written instructions.
4 Outcomes (O) included global cognition or executive function, and the study design (S) was a parallel
5 or cross-over RCT.

6 Conference abstracts without full text, letters to the editor, studies with participants having
7 neurological disorders other than cognitive decline, or studies with a control group that received
8 another type of VRBT, computerized training or no treatment, were excluded from this review.
9 Studies published in English, German, Swedish, or Finnish were included because of the language
10 skills of the research group.

11

12 **Study selection process**

13

14 Screening of abstracts and full texts was performed by two independent reviewers (MK, AK, RYI,
15 EA, OI, SH) using the Covidence systematic review software (Covidence, 2022). All conflicting
16 decisions of the two independent reviewers were discussed and resolved between these reviewers. If
17 no consensus was reached, a third opinion was obtained (EA).

18

19 **Data extraction**

20

21 Data for this review were extracted independently by two researchers (MK, SH) using a pre-
22 customized format in Covidence (Covidence, 2022). The extraction included the identification
23 information of the included study, funding source, study aims and setting, population group, inclusion
24 and exclusion criteria, baseline characteristics of the participants, details of the experimental
25 intervention and control groups, and the outcome measures used. Quantitative data of mean values

1 with standard deviations or standard errors and the number of participants at baseline and post-
2 intervention were extracted for statistical analyses according to the predefined priority list of
3 measures. Priority lists for both global cognition and executive function are presented in
4 Supplementary Material S1. In cases of insufficient quantitative data, the corresponding author was
5 contacted three times by e-mail. If adequate data were not received after three requests, the study was
6 excluded from meta-analyses. The results of these studies are reported narratively in Supplementary
7 Material S2.

8

9 **Risk of bias assessment**

10

11 The included studies were appraised separately for each outcome by two independent assessors (MK,
12 SH) using the Cochrane Risk of Bias 2 tool (RoB 2) for randomized and cluster-randomized (C-RCT)
13 trials (Sterne et al., 2019). Potential conflicts between the assessors were resolved to reach a
14 consensus. If no consensus was reached, a third opinion (EA) was obtained. The tool assesses five
15 different domains: the process of randomization and concealment, deviations from intended
16 interventions, missing outcome data, appropriate outcome measurements used, and possible selection
17 of reported results (Higgins et al., 2019). A variant for C-RCT addresses additional considerations
18 when assessing risk of bias in trials with groups of individuals randomized in clusters (Higgins et al.,
19 2023). Overall risk of bias is estimated across five domains. The level of the risk of bias ranges from
20 low (green) to unclear (yellow) or high (red). For the overall risk to be low, all domains must be rated
21 as low. To gain understanding of the assessment tool and achieve reliable assessments, the use of the
22 tool was practiced within the research team prior to implementation.

23

24 **Data analysis**

25

1 A meta-analysis was conducted to synthesize and pool data on global cognition and executive
2 function. For the random-effects meta-analysis, R software with the Metafor package was used to
3 calculate the effect sizes and variances (Viechtbauer, 2010). The post-intervention values of the mean,
4 standard deviation (SD), and number of participants (n) were used in the analyses. When quantitative
5 data were available as median, interquartile range (IQR), standard error (SE), or 95% confidence
6 interval (CI), they were converted to mean and SD assuming a normal distribution. The direction of
7 outcome measures (from low to high) was harmonized by multiplying the measures by -1 when
8 necessary.

9 When there were multiple group comparisons within a study, all comparisons were analyzed
10 simultaneously in the same meta-analysis (Htut et al., 2018; Karssemeijer et al., 2019; Manenti et al.,
11 2020). This leads to a correlation within the meta-analysis, which is acknowledged here using a
12 correlated effects model. Thus, the correlated effects model with robust variance estimation (RVE)
13 was implemented using the Robumeta package in R (Fisher et al., 2017), as it considers the possible
14 dependent effect of the studies used multiple times in the same meta-analysis. Cluster-randomized
15 trials were included in the same meta-analysis with randomized controlled trials when cluster-
16 randomization had been considered in analyses of the original studies (Higgins et al., 2023). If a
17 correction due to cluster-randomization was not made in the original study or an intraclass correlation
18 coefficient was not reported for the correction to be made for meta-analysis, the study was excluded
19 from statistical analyses of this review (Higgins et al., 2023).

20 A user-specified within-study effect size correlation ρ was set to 0.80 to conduct the analyses (Tanner-
21 Smith et al., 2016). The intervention effect size (Hedges' g) and its' 95% CI were visualized using a
22 forest plot. The Hedges' g scale was evaluated as follows: 0.20–0.49 was considered as a small effect,
23 0.50–0.79 as a medium effect, and 0.80 or more as a large effect (Cohen, 1992). Statistical
24 heterogeneity (I^2) was assessed as follows: 0–40% may not represent important heterogeneity, 30–

1 60% may represent moderate heterogeneity, 50–90% may represent substantial heterogeneity, and
2 75–100% represents considerable heterogeneity (Deeks et al., 2021).

3 Subgroup analyses were performed according to the cognitive level for each outcome to reduce
4 statistical heterogeneity. The level of cognition was categorized as normal, MCI, or dementia
5 according to the characteristics or baseline cognitive scores of the participants by identifying the level
6 when comparing the scores with the appropriate cut-off point of the measurement tests. Sensitivity
7 analyses were carried out by excluding studies with a high risk of bias to assess the reliability of the
8 results. Publication bias was assessed using funnel plots separately for both cognitive outcomes
9 (Egger et al., 1997). Finally, despite the small number of participants and included studies, a meta-
10 regression model was fitted to find out whether covariates of different study factors (age, baseline
11 level of cognition, intervention duration in weeks, number of sessions per week, session duration in
12 minutes per session, intervention volume, commercial versus customized technology, exercise-
13 versus information-based treatment of control groups, supervision of intervention), and RoB
14 domains with a high risk of bias could influence the results.

15

16 **Certainty of evidence**

17

18 Evidence was graded separately for global cognition and executive function according to the Grading
19 of Recommendations, Assessment, Development, and Evaluations (GRADE) (Guyatt et al., 2011;
20 Schünemann et al., 2013). Five categories were assessed: risk of bias of the original studies,
21 inconsistency, indirectness, imprecision, and publication bias (Schünemann et al., 2013). The
22 certainty of evidence varies among very low, low, moderate, and high levels of evidence (Balshem et
23 al., 2011). According to the GRADE guidelines, RCTs start with high-quality evidence and the level
24 is lowered if serious limitations are identified in the categories described (Guyatt et al., 2011).

1 Formulated statements were used to describe the findings of this systematic review and meta-analysis
2 (Santesso et al., 2020).

3

4 **RESULTS**

5

6 **Study selection and characteristics**

7

8 The literature search yielded a total of 4 921 records (Figure 1). After exclusion of duplicates, a first
9 phase of study selection was applied by screening titles and abstracts of 3 621 studies and then
10 skimming through the full text of 1 175 studies. A total of 802 studies were re-screened in the
11 specified second phase using the PICOS criteria of this review, and 771 studies were excluded
12 because their titles and abstracts did not meet the criteria. This left 61 full text articles for further
13 evaluation. Finally, 31 original peer-reviewed studies published between 2010 and 2022 were
14 included in this review. A list of the excluded full texts with justification (n=30) is presented in
15 Supplementary Material S1.

16 All included studies were published in English, of which 26 were RCTs and five were C-RCTs. Two
17 published articles were based on the same RCT (Liao et al., 2019; Liao et al., 2020). A total of 26
18 studies were included in the meta-analysis because four studies (Anderson-Hanley et al., 2012; Gunst
19 et al., 2022; Optale et al., 2010; Padala et al., 2017) did not have sufficient data (see Supplementary
20 Material S2) and one study (Ramnath et al. 2021) was unclear in taking cluster-randomization into
21 account in the original analyses. The detailed characteristics of the selected studies that were included
22 and excluded from the analyses are described in Table 1.

23

24 ***Participants***

25

1 The mean age of the participants was 76 (SD 6) years (mean range 60–88 years), and 64% were
2 female. Gender distribution was not reported in onestudy (Amjad et al., 2019). Cognitive levels varied
3 between normal (five studies), mild cognitive impairment (16 studies), and dementia (five studies).
4 The level was unclear in three studies (Bacha et al., 2018; Gomes et al., 2018; Stanmore et al., 2019),
5 in which baseline cognitive scores were compared with the corresponding cut-off values of the
6 measurement tests, revealing cognition as mildly impaired. Another study reported a normal level of
7 cognition according to the Mini-Mental State Examination (MMSE), but the results from Montreal
8 Cognitive Assessment (MoCA) showed values below normal limits (Htut et al., 2018). As these
9 studies included participants with mild cognitive impairment, they were presented and analyzed
10 according to MCI.

11

12 *Interventions*

13

14 The study setting was described in 22 studies (85%), varying from the home environment to the
15 hospital, senior gymnasium, laboratories or research institutes, care homes, assisted living facilities
16 or geriatric outpatient facilities, and welfare or other community centers.

17 The interventions included different VR technologies, of which 85% (22 studies) were described as
18 non-immersive (e.g., Xbox 360 Kinect, Nintendo Wii) and 11% (3 studies) as immersive (VR
19 headsets). One study (4%) classified the intervention as VR but did not specify the technology
20 (Hwang & Lee, 2017). The length of an intervention session, number of training sessions per week,
21 and length of the intervention period varied widely between studies. Virtual reality-based training
22 was delivered an average of 48 (SD 20) minutes per session (range of variation 18–100 minutes) and
23 3 (SD 1) times per week (range 1–5 times). The mean length of the intervention period was 11 (SD
24 5) weeks (range 3–24 weeks). Follow-up was performed in 7 studies with post-intervention periods
25 ranging from 4 weeks to 12 months. Where reported, the intensity and progression of experimental

1 interventions were generally based on the games played and, in some cases, Borg's scale, rate of
2 perceived exertion (RPE), or heart rate. Interventions were performed either individually, in pairs, or
3 in groups.

4 The reporting of adherence to the intervention varied, and the participation rate was reported either
5 as a percentage, mean total exercise time, or mean number of sessions attended. According to studies
6 that reported group-based adherence, participants were slightly more committed to VRBT than to the
7 control treatment in five RCTs (Guimarães et al., 2018; Hughes et al., 2014; Karssemeijer et al., 2019;
8 Moreira et al., 2021; Padala et al., 2017). The details of the study settings and adherence to the
9 interventions are described in Table 1.

10

11 ***Control groups***

12

13 The control groups received traditional physical and/or cognitive training or information-based
14 treatment with health education or written instructions. In 16 studies, the amount of training and
15 guidance received in the control group corresponded to that of the intervention group. In other studies,
16 the training or guidance received by the control group was either less than that in the intervention
17 group or was not described. Implementations in the control groups were executed individually, in
18 pairs, or in groups.

19

20 ***Outcomes***

21

22 The primary outcomes were global cognition and executive function, measured with various tests.
23 For meta-analyses, results of global cognition were analyzed using the Montreal Cognitive
24 Assessment (MoCA, n=9), Mini-Mental State Examination (MMSE, n=7), Addenbrooke's Cognitive
25 Examination (ACE-III, n=1), Computerized Assessment of Mild Cognitive Impairment (CAMCI,

1 n=1), Cognitive Telephone Screening Instrument (COGTEL, n=1), and Loewenstein Occupational
2 Therapy Cognitive Assessment –Geriatric (LOTCA-G, n=1). Executive function was measured with
3 the Trail Making Test Part B (TMT-B, n=12), Stroop Color Word Test (SCWT, n=1), Frontal
4 Assessment Battery (FAB, n=2), and CogState (n=1).

5

6 *Adverse events*

7

8 Mild adverse events were reported in three (10%) studies (Anderson-Hanley et al., 2012; Bacha et
9 al., 2018; Gomes et al., 2018) related to exercise-induced pain or muscle soreness, dizziness, fatigue,
10 or frustration with the technology used (Table 1). Other adverse events unrelated to the study were
11 also reported in one study, including acute upper respiratory illness, cancer diagnosis, back pain due
12 to lifting, or a car accident (Anderson-Hanley et al., 2012). In 14 (45%) studies, experimental
13 intervention did not cause any adverse events. The last 14 studies (45%) did not consider and report
14 adverse events at all.

15

16 **Risk of bias**

17

18 The overall risk of bias was assessed as unclear or high for each study, in terms of both global
19 cognition and executive function. No study had a low overall risk of bias. The high risk originated
20 mainly from deviations from the intended interventions, missing outcome data, and inappropriate
21 outcome measures. Uncertainty was also found in the concealment of allocation in the randomization
22 process and the lack of research protocols for statistical analyses. Detailed tables for the risk of bias
23 are provided in the Supplementary Material S1.

24

1 **Meta-analysis of intervention effects**

2

3 A total of 26 studies were included in the meta-analyses (Table 1). Meta-analyses were performed for
4 global cognition (20 RCT, n=876) and executive function (16 RCT, n=810). Two studies were
5 included twice in the meta-analysis for both global cognition (Htut et al., 2018; Manenti et al., 2020)
6 and executive function (Karssemeijer et al., 2019; Manenti et al., 2020) because two appropriate
7 control groups were compared with an intervention group and vice versa. The effect of the
8 intervention was balanced using a correlated effects model, as described in the Methods section.

9

10 ***Global cognition***

11

12 The measures included in the meta-analysis of global cognition were MoCA (n=9), MMSE (n=7),
13 ACE-III (n=1), CAMCI (n=1), COGTEL (n=1), and LOTCA-G (n=1). The higher the measured
14 score, the better the outcome and performance in global cognition.

15 According to the meta-analysis, VRBT appeared to be more efficient than the control in improving
16 global cognition, although the effect size was small (Hedges' g 0.42, 95% CI 0.17 to 0.68, 876
17 participants, 20 studies, low-quality evidence) (Figure 2). Statistical heterogeneity was high
18 ($I^2=70.1\%$). Subgroup analysis by cognitive level showed that VRBT was more effective in persons
19 with normal cognition with a small effect size (Hedges' g 0.23, 95% CI 0.03 to 0.44, $I^2=0\%$) and in
20 MCI with a moderate effect size (Hedges' g 0.54, 95% CI 0.22 to 0.86, $I^2=73\%$) compared with the
21 control (Supplementary Material S2). No differences between the intervention and control groups
22 were observed in older adults with dementia (Hedges' g 0.06, 95% CI -1.94 to 2.06, $I^2=73\%$).

23

24 ***Executive function***

25

1 The measures included in the meta-analysis of executive function were the TMT-B (n=12), SCWT
2 (n=1), CogState battery with an executive function test (n=1), and FAB (n=2). Most of the measures
3 involved completion of time, meaning that the faster the performance, the better the result.

4 According to the meta-analysis, VRBT was more effective in improving executive function when
5 compared with control, but the effect size was small (Hedges' g 0.35, 95% CI 0.06 to 0.65, 810
6 participants, 16 studies, very low-quality evidence) (Figure 3). Statistical heterogeneity was
7 considered high ($I^2=68.4\%$). Subgroup analysis by cognitive level showed no difference between the
8 intervention and control groups in older adults with either normal cognition (Hedges' g 0.52, 95% CI
9 -0.61 to 1.66, $I^2=86\%$), MCI (Hedges' g 0.40, 95% CI -0.03 to 0.83, $I^2=57\%$) or dementia (Hedges'
10 g 0.01, 95% CI -0.59 to 0.60, $I^2=29\%$).

11

12 **Sensitivity analyses**

13

14 In global cognition, a statistically significant small effect in favor of the intervention group remained
15 after excluding 9 studies from the meta-analysis owing to a high overall risk of bias (Hedges' g 0.44,
16 95% CI 0.14 to 0.75, $I^2=71.3\%$). However, the levels of effect (confidence intervals) were seen to
17 enlarge. Regarding executive function, the meta-analysis was no longer statistically significant
18 between the groups when 10 studies were excluded owing to a high risk of bias (Hedges' g 0.28, 95%
19 CI -0.05 to 0.62, $I^2=0\%$). The sensitivity analyses are presented in Supplementary Material S2.

20

21 **Meta-regression**

22

23 Meta-regression models were fitted separately for age, baseline level of cognition, intervention
24 duration in weeks, number of sessions per week, session duration in minutes per session, intervention
25 volume, supervision of intervention, combined intervention vs. pure VRBT, customized vs.

1 commercial technology, fully immersive vs. non-immersive VR, type of the control group
2 intervention, and RoB 2 domains with a high risk of bias. Supervision of the intervention increased
3 the effect on executive function (SMD 0.51, 95% CI 0.18 to 0.84, p=0.005) whereas high risk of bias
4 in the selection of reported results decreased the effect on executive function (SMD -0.48, 95% CI -
5 0.79 to -0.17, p=0.005) (Table 2).

6

7 **Publication bias**

8

9 Some degree of publication bias is possible with smaller studies favoring intervention in both global
10 cognition (Figure 4) and executive function (Figure 5); however no strong conclusions can be drawn
11 due to the small number of included studies. There were more studies on MCI than on dementia or
12 cognitively healthy older adults. However, studies with large sample sizes are scarce. It is also
13 possible that high statistical heterogeneity is confounded with the interpretation of publication bias
14 (Sterne et al., 2011).

15

16 **Certainty of evidence (GRADE)**

17

18 The GRADE of evidence was low for global cognition and very low for executive function. The level
19 was lowered due to the high risk of bias in individual studies, inconsistency with high statistical
20 heterogeneity and different directions in the results of individual studies, and imprecision with wide
21 confidence intervals in executive function. The certainty of evidence is presented as a Summary of
22 Findings in Table 3.

23

24 **DISCUSSION**

25

1 Our findings show that virtual reality-based training may be more effective in improving global
2 cognition and executive function than conventional physical and/or cognitive exercise training or
3 information-based treatment in older adults, regardless of cognitive level. This means that VRBT
4 could also be a potential preventative option by increasing cognitive reserve, although its long-term
5 effects should be studied. The certainty of evidence was graded as low for global cognition and very
6 low for executive function indicating uncertainty in the results of this review. Nevertheless, the
7 reliability of the results was increased by including all cognitive levels to ensure correct
8 categorization of the studies in the analyses. We also aimed to reduce statistical heterogeneity and
9 identify covariates behind the clinical heterogeneity affecting the results by performing subgroup
10 analyses, sensitivity analyses, and meta-regression. These results showed that VRBT was particularly
11 beneficial in improving global cognition in older adults with MCI when compared with the control
12 group.

13 Similar results regarding the positive effects of VRBT on global cognition in older adults with MCI,
14 have been reported in recent meta-analyses (Gómez-Cáceres et al., 2022; Papaioannou et al., 2022;
15 Yan et al., 2022; Yu et al., 2022; Zhong et al., 2021; Zhu et al., 2021). However, differing results
16 have also been published regarding the statistical significance of VRBT compared with active or
17 passive controls, which may be due to a very small number of studies analyzed (Kim et al., 2022).

18 Our subgroup analysis showed the significant benefits of VRBT in improving global cognition in
19 older adults with normal cognition and MCI. This may indicate the potential of VRBT as a
20 preventative means in cognitive impairment to delay the clinical onset of cognitive decline (Chao &
21 Chen, 2022) by increasing cognitive reserve (Song et al., 2022; Tucker et al., 2011) or as an early
22 intervention to manage the increasing need for rehabilitation in primary care once the condition is
23 diagnosed (Cieza et al., 2021). No subgroup reached statistically significant effect in executive
24 function though main analysis favored VRBT. This is probably due to the smaller number of studies
25 and participants analyzed per subgroup.

1 Mild adverse events were reported in three studies. As no serious adverse events were identified and
2 the number of mild events was low, VRBT appears to be a safe training alternative for use either alone
3 or as part of conventional rehabilitation. Nevertheless, the use of virtual reality should always be
4 considered individually according to the goals and preferences of the user.

5 Although this review found positive results for the effects of VRBT on cognition, the certainty of
6 evidence was either low or very low according to GRADE. This differs from the gradings of a
7 previous meta-analysis by Zhong et al., which assessed the evidence medium for both outcomes of
8 global cognition and executive function, although the effect sizes of their analyses were smaller. This
9 was because Zhong et al. rated the inconsistency of the results of individual studies and the level of
10 statistical heterogeneity as not serious. This may in part be due to the fact that the meta-analyses were
11 conducted per measurement tests. In addition, publication bias was not considered serious, although
12 funnel plots were not performed because of the small number of studies included (Zhong et al., 2021).

13 The aim of this review was to ensure high-quality evidence of the effects of VRBT and to reduce the
14 clinical heterogeneity associated with the studies by accepting only RCTs. The original studies were
15 appraised by two independent reviewers for both global cognition and executive function to
16 strengthen the quality assessment of this review. However, in this assessment, the included original
17 studies mainly had an unclear or high risk of bias. Therefore, the Cochrane Risk of Bias 2 tool is often
18 considered strict and more demanding than the previous version (Minozzi et al., 2020), which is why
19 it is important to ensure that the interpretation of the appraised domains is consistent among assessors.
20 In this review, the appraisal tool was practiced within the research team prior to implementation and
21 was supported with written notes to ensure consistency.

22 High statistical heterogeneity was observed in the results, which may originate from a wide range of
23 clinical heterogeneity, such as the age range of participants; different levels of education; and varying
24 content, duration, intensity, or progression of training with different length of intervention periods.
25 Although two moderators were found to influence the results according to the statistical significance

1 of the covariate, the small number of studies analyzed in our meta-regression (20 RCTs in global
2 cognition, 16 RCTs in executive function) makes the interpretation difficult and unreliable. However,
3 it is important to investigate the effects of different study factors and high risk of bias domains on the
4 results obtained from the meta-analyses. Therefore, the results of this meta-regression should be
5 confirmed in future reviews, as high-quality RCTs will be published.

6 As various tests are used to measure global cognition and executive function, an important question
7 revolves around the sensitivity of a test in discriminating small improvements in cognitive
8 performance after a short training period. For example, the MMSE was used as a global cognitive
9 measure in two studies with cognitively healthy participants (Guimarães et al., 2018; Moreira et al.,
10 2021) and in two studies with MCI (Manenti et al., 2020; Thapa et al., 2020). This may influence the
11 direction or magnitude of the effect size calculated owing to its high ceiling effect and low sensitivity
12 when used with cognitively healthy persons or with MCI (Hoops et al., 2009). Some researchers have
13 suggested VR as a potential measurement tool through digital tests and games alongside training (e.g.,
14 Cabinio et al., 2020; Kourtesis et al., 2021; Liu et al., 2023) to contribute to this issue.

15 In this review, meta-analysis was justified by an adequate number of RCTs included, with a consistent
16 PICO strategy used during screening. Although several similar meta-analyses of RCTs have been
17 published recently, many discrepancies remain evident. Of the eight most recent meta-analyses
18 published between 2021 and 2022, only one review (Papaioannou et al., 2022) observed most
19 important methodological items when following the appraisal tool for systematic reviews (Shea et
20 al., 2017). Our review also reported the funding sources of the included RCTs and evaluated the
21 results using a clearly defined control group. In addition, the inclusion of older adults regardless of
22 their cognitive level allowed a more accurate assessment of the cognitive category of participants by
23 considering the cut-off values of the measurement tests, rather than analyzing participants in
24 subgroups based only on the inclusion criteria of the original study. In three original studies, the
25 cognitive level of participants remained unclear when cognition was evaluated according to inclusion

1 criteria (Bacha et al., 2018; Gomes et al., 2018; Stanmore et al., 2019). In another study, the cognitive
2 level of participants was evaluated as normal with the MMSE at the inclusion stage (Htut et al., 2018).
3 When the results were critically evaluated, the baseline cutoff values with the MoCA test revealed
4 MCI in all participants in the described studies. Thus, the original RCTs were assessed according to
5 the appropriate cognitive subgroups strengthening the reliability of the results of this review.

6 Although the results support the use of VR in training, clear evidence of the best intervention program
7 remains unclear. That is, no optimal intensity, amount, or duration of VRBT has been identified,
8 although in a previous meta-analysis, VRBT with a total duration of at least 15 h resulted in a greater
9 efficacy in improving global cognition than interventions with less than 15 h (Gómez-Cáceres et al.,
10 2022). However, this only shows the overall training time, rather than the optimal weekly or daily
11 dose. There are also varying results regarding the preference for fully immersive, semi-immersive or
12 non-immersive VR (Yu et al., 2022; Zhu et al., 2021), which may emphasize an individualized
13 approach to VRBT. The possibility of improved accessibility and reduced loneliness through
14 technology has long been suggested (White et al., 2002). Attitudes toward digitalization may vary
15 among older adults (Hill et al., 2015), which is important to consider before implementing VRBT. In
16 addition, cost-effectiveness should be examined when evaluating the overall benefits of VRBT as it
17 could serve as an important implication for future rehabilitation, as learned from the COVID-19
18 pandemic.

19

20 **Strengths and limitations**

21

22 This review had several strengths. First, high-quality research methods were used with grading of
23 evidence and reporting of adverse events, which were often lacking in previous meta-analyses.
24 Second, a comprehensive review protocol was followed by conducting an extensive literature search
25 and careful screening of records to provide sufficient data to justify this meta-analysis, by pre-

1 specifying the PICOS strategy and planning the outcome preference lists to obtain new and reliable
2 information about the study phenomenon in question, and by including only RCTs that provided a
3 basis for high-quality evidence. Third, the included original peer-reviewed studies were appraised
4 with an updated tool independently by two assessors and separately for both examined outcomes,
5 providing a reliable assessment of the risk of bias. Fourth, the conduction of sensitivity analyses and
6 meta-regression, and the assessment of publication bias provided important information for
7 interpreting the results as well as acted as an essential effort to observe statistical heterogeneity.
8 Finally, all cognitive levels were included in the meta-analysis, and by subgrouping the effects, it was
9 possible to identify whether VRBT could serve as a beneficial training alternative for postponing
10 cognitive impairment in cognitively healthy older adults or as an effective treatment for already
11 reduced cognitive performance.

12 Some limitations are also evident. The systematic literature search could have been more extensive
13 when considering the guidelines of Cochrane Handbook (Lefebvre et al., 2022). However, compared
14 with previous reviews, the literature search of RCTs was considered sufficient for the purpose of this
15 review, and no new studies were found through reference and hand searches. The publication
16 language in the eligibility criteria can be seen as a limitation of a review. However, no studies were
17 excluded in the full-text phase of this review due to language limitations. In this review, medians and
18 IQR were converted to means and SDs assuming a normal distribution. As medians are more likely
19 to be reported when the data are skewed, this conversion may have resulted in biased pooled effects
20 of outcomes. Furthermore, some individual studies included a small number of participants, which
21 may have biased the effect size or the statistical significance of the results. Very little research has
22 been conducted on the long-term effects of VRBT, which is why it was not studied in this review.
23 Although subgroup analyses were conducted, this review could not determine an optimal dose of
24 VRBT. Finally, despite the attempt to reveal moderators influencing the results of meta-analyses, the

1 meta-regression may have been unreliable because of the small number of studies included in the
2 model.

3

4 **CONCLUSIONS**

5

6 Virtual reality-based training may be more effective compared with conventional training or
7 information-based treatment in improving global cognition in older adults. The evidence is uncertain.
8 Similar results are obtained with executive function with very uncertain evidence. For global
9 cognition the effect was mostly evident for older adults with normal cognition and MCI. Though two
10 covariates influenced the effect on executive function, the reliability of the association remains
11 inconclusive. The reported adverse events suggest that VR is a safe training alternative. However,
12 individual assessments, goals, and preferences must be noticed when VRBT is considered as part of
13 rehabilitation. There is a further need for high-quality studies to confirm this evidence, as new studies
14 may influence the direction and magnitude of the effect of the current results. Meta-regression
15 analyses should be repeated as more studies are being published. Implications for future research
16 should also include investigating the long-term effects of VRBT using RCTs with longer intervention
17 and follow-up periods.

18

19 **Conflict of interest**

20

21 The authors declare no conflicts of interest.

22

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2

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7

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1 **Table Legend**

2 Table 1. Summary of included RCT studies

3 Table 2. Results of meta-regression analysis for global cognition and executive function on covariates
4 of study factors and the high risk of bias domains

5 Table 3. Summary of Findings

6

7 **Figure Legend**

8 Figure 1. PRISMA 2020 flow diagram for identification and selection of studies

9 Figure 2. Forest plot with estimated effect of VRBT compared with control on global cognition

10 Figure 3. Forest plot with estimated effect of VRBT compared with control on executive function

11 Figure 4. Publication bias assessed by funnel plots for global cognition

12 Figure 5. Publication bias assessed by funnel plots for executive function

1 Table 1. Summary of included RCT studies

Study	Participants	Intervention (I)	Control (C)	Outcome ^{1,2}	Study setting Follow-up Adverse events	Main results Risk of bias (RoB2)	Funding
INCLUDED IN META-ANALYSIS							
<i>Normal cognition</i>							
Gouveia et al. 2021 Portugal RCT	Community-dwelling older adults. n=31 (37 randomized, 31 analyzed) I: 67.6 (SD 5) y C: 69.1 (SD 4.2) y 22 F / 9 M (71% / 29%)	Multicomponent functional fitness with exergaming and traditional physical exercise. Technology: Kinect V2. 2 x 45 min./week 12 weeks Intensity: moderate to vigorous. Progression: depending on participants' perceived exertion and performance achieved in games. Adherence: No group-based adherence level. Total rate 79%–89% out of 24 sessions. n=15	Functional fitness exercise in groups. 2 x 45 min. / week 12 weeks Intensity: moderate to vigorous. Progression: NI Adherence: No group-based adherence level. Total rate 79%–89% out of 24 sessions. n=16	Cognition: COGTEL ¹	Local senior gymnasium. Follow-up at 4 weeks after intervention. No adverse events.	Both groups improved in global cognition after intervention. Memory was improved in intervention group only after follow-up. Exergaming demonstrated a more beneficial effect on cognition compared with traditional physical exercise. RoB2 (GC): Unclear.	Portuguese Foundation for Science and Technology and Swiss National Science Foundation.
Gschwind et al. 2015 Australia, Spain, Germany RCT (Registered: ACTRN12614000 096651)	Community-dwelling older adults (MCI excluded). n=136 (153 randomized, 136 analyzed) Mean age 74.7 (SD 6.3) y. 93 F / 60 M (61% / 39%)	Exergaming with balance and strength exercise + evidence-based booklet. Technology: TV + Kinect. Balance: 3 x 40 min./week Strength: 3 x 15–20 min./week 16 weeks Intensity: NI Progression: by reducing upper limb support, narrowing the base of support, adjusting speed of movement, increasing gaming duration and number of repetitions, sets and the difficulty level. Adherence: iStoppFalls system used median 42 times (IQR 57) at a game level of median 2.1 (IQR 3.9) for a total duration of median 11.7 h (IQR 22.0) when including and median 7.0 h (IQR 12.8) when excluding instructions. n=71	Evidence-based booklet about general health and fall prevention. Control group was encouraged to follow their habitual exercise routines if applicable. Intensity: NI Progression: NI Adherence: NI n=65	Executive function: TMT-B ² , VST, DSB, DSC	Home. No follow-up. No adverse events.	No difference was found between groups concerning cognitive performance. RoB2 (EF): High.	European Union's Seventh Framework Program, Australian National Health and Medical Research Council (NHMRC), Margarete and Walter Lichtenstein Foundation.

Guimarães et al. 2018 Brazil RCT (Registered: RBR-9crpzc)	Older adults n=27 (36 randomized, 27 analyzed) I: 60 (SD 4) y C: 60.7 (SD 3.6) y 16 F / 11 M (59% / 41%)	Active videogame-based physical activity program. Technology: Xbox 360 Kinect. 3 x 60 min./week 12 weeks Intensity: moderate. Progression: gradually increased, not detailed. Adherence: 90.6%, with 424 sessions completed out of 468 sessions (13 participants x 36 sessions). n=13	Aerobic exercise with treadmill and cycle ergometer. 3 x 60 min./week 12 weeks Intensity: moderate. Progression: gradually increased, not detailed. Adherence: 86.9%, with 438 sessions completed out of 504 sessions (14 participants x 36 sessions). n=14	Cognition: MMSE ¹ Executive function: CogState Battery (Groton Maze Learning Test) ²	Laboratory. No follow-up. Adverse events: NI.	Training effects were positive for both groups. No difference between groups was found. RoB2 (GC): High. RoB2 (EF): High.	Federal University of Santa Catarina.
Moreira et al. 2021 Brazil RCT (Registered: RBR-97jm74)	Pre-frail older adults (reduced cognitive capacity excluded). n=66 (99 randomized, 66 analyzed) I: 70.8 (SD 4.5) y C: 70.8 (SD 5.6) y 66 F (100%)	Exergaming. Technology: Xbox 360 Kinect. 3 x 50 min./week 12 weeks Intensity: Borg's Scale 10 to 15. Progression: as proposed within the game. Adherence: Exercise attendance rate 83.1%. n=32	Strength, balance and cardiorespiratory exercises. 3 x 50 min./week 12 weeks Intensity: Borg's Scale 10 to 15. Progression: weight increment was 3% body mass on the first week, followed by gradual increases thereafter. Adherence: Exercise attendance rate 81.2%. n=34	Cognition: MMSE ¹ Executive function: TMT-B ²	Setting not reported. No follow-up. Adverse events: NI.	Intervention group improved more in MMSE, processing speed and TMT-B than control group. Both groups decreased the number of errors. RoB2 (GC): High. RoB2 (EF): High.	Federal University of Paraná, CAPES Foundation.
Wang et al. 2021 Taiwan RCT (Registered: ACTRN 12617000095369)	Community-dwelling older adults (MMSE at least 24 points). n=20 I: 71.30 (SD 5.33) y C: 73.50 (SD 5.66) y 13 F / 7 M (65% / 35%)	Exergaming. Technology: Kinect sensor with TANO and PAPAMAMA software system with treadmill. 3 x 60 min./week 12 weeks Intensity: walking self-selected speed on the treadmill. Progression: by increasing the treadmill speed and the difficulty of the motor or cognitive tasks progressively. Adherence: Attendance rate 100% out of 36 exercise sessions. n=10	Home-based multicomponent exercise training with aerobic, strengthening and balance exercise. 3 x 60 min./week 12 weeks Intensity: RPE 12 to 14. Progression: Record kept on the exercise sessions and physical therapist checking the progress once in 2-3 weeks. Adherence: Attendance rate 100% out of 36 exercise sessions. n=10	Executive function: TMT-B ² , EXIT-25, SCWT	Setting not reported for intervention group (supervised). Home for control group. No follow-up. No adverse events.	Experimental group improved significantly in measures of general executive function and inhibitory control compared with control group. RoB2 (EF): Unclear.	Ministry of Science and Technology of the Republic of China.

Mild cognitive impairment (MCI)

Amjad et al. 2019 Pakistan RCT	MCI n=38 (44 randomized, 38 analyzed) I: 62.8 (SD 5.1) y C: 65.6 (SD 5.,0) y Gender distribution not reported.	Exergaming. Technology: Xbox 360 Kinect. 5 x 25–30 min./week 6 weeks Intensity: NI Progression: according to game difficulty. Adherence: NI n=20	Range of motion (ROM) exercises. 5 x 25–30 min./week 6 weeks Intensity: NI Progression: NI Adherence: NI n=18	Cognition: MoCA ¹ , MMSE Executive function: TMT-B ²	Hospital, under the supervision of a therapist. No follow-up. Adverse events: NI.	MMSE, MoCA and TMT improved significantly. These changes were not observed in the control group. RoB2 (GC): High. RoB2 (EF): High.	Possible funders were Riphah College of Rehabilitation Sciences, Atta-ur-Rahman School of Applied Biosciences, National University of Sciences and Technology, and Railway General Hospital.
Bacha et al. 2018 Brazil RCT (Registered: RBR-4z4f48)	Community dwelling older adults (MoCA baseline < 26 points). n=46 Mean age 69.3 (SD 5.3) y. 34 F / 12 M (74% / 26%)	Virtual reality -based training. Technology: Xbox 360 Kinect. 2 x 60 min./week 7 weeks Intensity: moderate. Progression: according to performance and game difficulty. Adherence: 91.3% (assessed by frequency of the number of elderly individuals who completed the interventions and safety through the presence of adverse effects). n=23	Conventional physical therapy. 2 x 60 min./week 7 weeks Intensity: moderate. Progression: NI Adherence: 91.3% (assessed by frequency of the number of elderly individuals who completed the interventions and safety through the presence of adverse effects). n=23	Cognition: MoCA ¹	Clinics Hospital of the School of Medicine of the University of São Paulo. Follow-up at 4 weeks after intervention. Adverse events: Delayed muscle pain in the lower limbs after the first session, 34% in VR group and 26% in comparison group.	Both groups presented a significant improvement in cognition (MoCA) posttreatment that was maintained at fourth week after treatment. There were no significant differences between groups. RoB2 (GC): Unclear.	According to register: Faculty of Medicine at University of São Paulo and CAPES Foundation.
Delbroek et al. 2017 Belgium RCT	MCI n=17 (20 randomized, 17 analyzed) I: 86.9 (SD 5.6) y C: 87.5 (SD 6.6) y 13 F / 7 M (65% / 35%)	Virtual reality -based training + usual care. Technology: BioRescue. 2 x 18–30 min./week 6 weeks Intensity: A training session consisted of several 3-minute exercises. The level of exertion not described. Progression: gradually increasing training time from 18 min. to 30 min. Adherence: NI n=8	Standard of usual care including physical therapy. 6 weeks Intensity: NI Progression: NI Adherence: NI n=9	Cognition: MoCA (Dutch version) ¹	Nursing home, supervised by a therapist. No follow-up. No adverse events.	No changes were detected over time for either group with regards to MoCA. RoB2 (GC): Unclear.	NI
Gomes et al. 2018 Brazil RCT (Registered: RBR-823rst)	Frail and pre-frail older adults (MoCA baseline < 26 points). n=30 84 (SD 6.0) y 28 F / 2 M (93% / 7%)	Interactive videogaming. Technology: Nintendo Wii Fit Plus. 2 x 50 min./week 7 weeks	Booklet of physical activity. Intensity: NI Progression: NI Adherence: No group-based adherence reported. Out of all 30	Cognition: MoCA ¹	Geriatric outpatient facility. Follow-up 30 days after intervention. Adverse events: Four participants (33%)	No significant effect on MoCA was found. No difference between groups. RoB2 (GC): Unclear.	No external funding.

		Intensity: motor-cognitive demand varied in games (blocks A and B). The level of exertion not described. Progression: NI Adherence: No group-based adherence reported. Out of all 30 participants enrolled in the study, 26 completed the full protocol (14 sessions). n=15	participants enrolled in the study, 26 completed the full protocol. n=15		reported fatigue and one participant (8%) reported muscle soreness in the legs after the first session.		
Htut et al. 2018 Thailand RCT (Registered: NCT03118414)	Older adults living at homes for the aged (normal cognition according to MMSE, but MoCA scores reveal MCI). n=84, (n=63 when passive control group excluded) Mean age 75.8 (SD 5.2) y. 37 F / 47 M (44% / 56%)	Virtual reality -based exercise (VRE). Technology: Xbox 360. 3 x 30 min./week 8 weeks Intensity: In 30 min of playing, participants chose 6 games involving upper and lower limb movements, and balance training. The level of exertion not described. Progression: according to game performance and difficulty. Adherence: NI n=21	Physical exercise (PE). 3 x 30 min./week 8 weeks Intensity: NI Progression: increasing intensity and resistance with elastic TheraBand® or decreasing support after 4 weeks. Adherence: NI n=21 Brain exercise (BE) with board and card games. 3 x 30 min./week 8 weeks Intensity: 10 min./game. Progression: from 2-player games to 4-player games. Adherence: NI n=21 Passive control with no exercise and conducting their lives as usual. n=21	Cognition: MoCA ¹ , TUG-Cog	Homes for the aged. No follow-up. Adverse events: NI.	VRE and BE improved MoCA more compared with PE or passive control group. RoB2 (GC): Unclear.	Norway Government and Mahidol University.
Hughes et al. 2014* USA RCT	MCI n=20 (For CAMCI-test, n=19) Mean age 77.4 (SD 5.8) y. 14 F / 6 M (70% / 30%)	Interactive videogaming. Technology: Nintendo Wii. 1 x 90 min./week 24 weeks Intensity: Players used their arms and/or bodies to simulate actions required for each game. Brief health education at the beginning of each session (10–15 min), followed by interactive videogaming (75–80	Health education. 1 x 90 min./week 24 weeks Intensity: NA Progression: On week 10 and 20 a Jeopardy® style tournament was held in small groups to encourage retention of the health information and to match the	Cognition: CAMCI ¹ , CSRQ	Centrally located church within the study area. 1-year follow-up. Adverse events: NI.	No statistically significant improvement was found concerning cognition, although medium effect sizes were found for cognitive functioning in favor of interactive	The National Institute on Aging at NIH (The National Institute of Health).

		min). The level of exertion not described. Progression: The first 6 weeks focused on training and developing competence with the Wii system. On week 7 new games were introduced. On week 10 and 20 a Wii tournament was held in small groups. Adherence: Participants attended an average of 23 (SD 1.1; range 21–24) sessions out of 24 sessions. n=10	level of friendly competition in the Wii group. Adherence: Participants attended on average 22 (SD 3.3; range 14–24) sessions out of 24 sessions. n=10			video gaming compared with health education. RoB2 (GC): Unclear.	
Hwang & Lee 2017 South Korea RCT	MCI n=24 I: 74.2 (SD 6.1) y C: 70.2 (SD 5.4) y 17 F / 7 M (71% / 29%)	Virtual reality (VR) program. Technology: NI. 5 x 30 min./week 4 weeks Intensity: NI Progression: NI Adherence: NI n=12	Traditional occupational therapy. 4 weeks (not detailed) Intensity: NI Progression: NI Adherence: NI n=12	Executive function / attention: (Stroop) Word Color Test (WCT) ²	Welfare center. No follow-up. Adverse events: NI.	VR-training was significantly more effective than traditional occupational therapy in improving performance in WCT. RoB2 (EF): High.	NI
Liao et al. 2019** Taiwan RCT (Registered: TCTR20180531001)	MCI n=34 (42 randomized, 34 analyzed) I: 75.5 (SD 5.2) y C: 73.1 (SD 6.8) y 23 F / 11 M (68% / 32%)	Virtual reality -based physical and cognitive training. Technology: Microsoft Kinect + HTC VIVE VR-glasses. 3 x 60 min./week 12 weeks Intensity: physical training for 40 min. and cognitive training for 20 min. The level of exertion not described. Progression: according to game performance and difficulty. Adherence: NI n=18	Combined physical and cognitive (CPC) training meeting the ACSM standards for seniors. 3 x 60 min./week 12 weeks Intensity: MHR 50–75%, Borg’s Scale 13 to 14. Progression: by adding more weights, increasing the number of repetitions or the difficulty of the performance. Adherence: NI n=16	Executive function: TMT-B ² , SCWT	Setting not reported. No follow-up. No adverse events.	VR-group showed more improvement in TMT-B than CPC-group. Both groups improved in SCWT. RoB2 (EF): Unclear.	Ministry of Science and Technology.
Liao et al. 2020** Taiwan RCT (Registered: TCTR20181001001)	MCI n=34 (42 randomized, 34 analyzed) I: 75.5 (SD 5.2) y C: 73.1 (SD 6.8) y 23 F / 11 M (68% / 32%)	Virtual reality -based physical and cognitive training. Technology: Microsoft Kinect + HTC VIVE VR-glasses. 3 x 60 min./week 12 weeks Intensity: physical training for 40 min. and cognitive training for 20	Combined physical and cognitive (CPC) training meeting the ACSM standards for seniors. 3 x 60 min./week 12 weeks Intensity: MHR 50–75%, Borg’s Scale 13 to 14. Progression: by adding more weights, increasing the number of	Cognition: MoCA ¹ Executive function: EXIT-25	Setting not reported. No follow-up. No adverse events.	Both groups showed improvement in cognitive performance and executive function but no differences between groups were observed. RoB2 (GC): Unclear.	Ministry of Science and Technology.

		min. The level of exertion not described. Progression: according to game performance and difficulty. Adherence: NI n=18	repetitions or the difficulty of the performance. Adherence: NI n=16				
Liao et al. 2021 Taiwan RCT (Registered: TCTR201805310 01)	Frail older adults (MoCA baseline < 26 points). n=46 (61 randomized, 46 analyzed) I: 79.6 (SD 9.0) y C: 83.8 (SD 5.1) y 31 F / 15 M (67% / 33%)	Exergaming with resistance, aerobic, balance and Tai Chi exercise. Technology: Kinect system. 3 x 60 min. 12 weeks Intensity: HR and RPE monitored during training to ensure consistency between intervention and control groups. Progression: resistance applied by TheraBand from 1.1 to 3.1 kg gradually. Adherence: 27 out of 31 participants randomized completed all exercise sessions. n=25	Combined physical training including resistance, aerobic and balance exercises, meeting ACSM standards for older population. 3 x 60 min. 12 weeks Intensity: intensity of aerobic exercise was 50-75% of participants MHR and targeted RPE 13 to 14. Progression: resistance was applied by TheraBand from 1.1 to 3.1 kg gradually. Adherence: 25 out of 30 participants randomized completed all exercise sessions. n=21	Cognition: MoCA ¹ Executive function: TMT-B ² , SCWT, EXIT-25	Care centers. No follow-up. No adverse events.	Both groups improved in global cognition and executive function. Intervention group significantly enhanced global cognition more than the control group. RoB2 (GC): Unclear. RoB2 (EF): Unclear.	Ministry of Science and Technology.
Liu et al. 2022 Taiwan RCT (Registered: TCTR2021 0530003)	MCI n=50 (54 randomized, 50 analyzed, n=33 when passive control group excluded) I: 74.6 (SD 6.1) y C1: 73.2 (6.3) y C2: 73.4 (6.5) y 35 F / 15 M (70% / 30%)	Exergaming-based Tai Chi Technology: Kinect system. 3 x 50 min. 12 weeks Intensity: RPE 12 to 14 Progression: NI Adherence: 16 out of 18 randomized participants completed all intervention. n=16	Traditional Tai Chi 3 x 50 min. 12 weeks Intensity: RPE 12 to 14 Progression: NI Adherence: 17 out of 18 randomized participants completed the whole intervention. n=17 Passive control with no exercise and maintaining their usual daily physical activities. n=17	Cognition: MoCA ¹ , MMSE Executive function: TMT-B ² , SCWT	Setting not reported. No follow-up. No adverse events.	Both experimental and active comparison groups performed significantly better in executive function than passive control group. Only the experimental group gained significant benefits in MoCA. RoB2 (GC): High. RoB2 (EF): High.	Taipei City Hospital and Cheng Hsin General Hospital.
Manenti et al. 2020 Italy RCT (Registered: NCT03486704)	MCI with memory complaints but absence of dementia n=49 I1: 75.3 (SD 3.3) y I2: 76.3 (SD 4.9) y	Face-to-face cognitive virtual reality rehabilitation (VRRS) + home-based virtual rehabilitation Technology: VRRS by Khymeia. 3 x 60 min./week 4 weeks + 12 weeks	Face-to-face cognitive treatment as usual 60 min./session 12 sessions Intensity: NI Progression: NI	Cognition: MMSE ¹ , CDT (in the study categorized as a test for	Research institutes and participants' home. No follow-up. Adverse events: NI.	No significant differences were found in global cognition or executive function between the groups.	Italian Ministry of Health.

C: 78.1 (SD 4.1) y
25 F / 24 M (51% / 49%)

Intensity: starting level and number of trials adjusted according to the participant's performance level using an adaptive staircase procedure.
Progression: task difficulty adaptively progressed. In home-based treatment, individualized cognitive training exercises adjusted by the therapist once a week.
Adherence: All 18 participants completed the 12 sessions of face-to-face VRRS treatment, 6 participants completed all 36 sessions of at-home VRRS training, whereas all other subjects completed more than 70% of the telerehabilitation sessions.
n=18

Face-to-face VRRS + home-based unstructured cognitive stimulation
Technology: VRRS by Khymeia.
3 x 60 min./week
4 weeks + 12 weeks
Intensity: starting level and number of trials adjusted according to the participant's performance level using an adaptive staircase procedure
Progression: task difficulty adaptively progressed.
Adherence: All 14 participants completed the 12 sessions of face-to-face VRRS treatment, 7 subjects completed the 36 sessions of at-home unstructured cognitive stimulation, and the other subjects completed more than 70% of the at-home unstructured cognitive stimulation sessions.
n=14

Adherence: 8 participants completed the 12 sessions, whereas all the other subjects completed more than 70% of the usual treatment sessions.
n=17

visuo-
construction
al abilities)

Executive
function:
TMT-B²

RoB2 (GC): High.
RoB2 (EF): Unclear.

Park et al.
2020
South Korea

MCI
n=35

Virtual reality -based cognitive-
motor rehabilitation.
Technology: MOTOCOG@.

Conventional cognitive
rehabilitation (CCR)

Cognition:
MoCA¹

Setting not reported.
No follow-up.
Adverse events: NI.

VR-intervention
showed a significantly
greater improvement

The National
Research Foundation
of Korea (NRF)

RCT	(40 randomized, 35 analyzed) I: 75.8 (SD 8.5) y C: 77.2 (SD 7.2) y 18 F / 17 M (51% / 49%)	5 x 30 min./week 6 weeks Intensity: NI Progression: NI Adherence: NI n=18	(e.g. puzzles, card games, paper-pencil table activities). 5 x 30 min./week 6 weeks Intensity: NI Progression: Chosen by experienced occupational therapists to match the patient's cognitive function. Adherence: NI n=17	Executive function: TMT-B ² , DST		in MoCA, TMT and DST compared with CCR. In addition, subjects in VR-group had significantly higher interest and motivation compared with CCR-group. RoB2 (GC): High. RoB2 (EF): High.	funded by the Ministry of Education.
Stanmore et al. 2019 UK C-RCT (Registered: NCT02634736)	Older adults in assisted living facilities (ACE-III baseline < 88 points). n=92 (106 randomized, 92 analyzed), 18 living facilities included. I: 77.8 (SD 10.2) y C: 77.9 (SD 8.9) y 83 F / 23 M (78% / 22%)	Exergaming + Standard care. Technology: Microsoft Kinect. 3 x 30 min./week 12 weeks Intensity: individually prescribed program of standardized exergames suiting the participant's starting level of ability. Level of exertion not described. Progression: tailored progression with more exergames within a session, greater challenge and longer duration. Adherence: Participants attended a mean number of 25 (SD 8.5) out of 36 sessions offered over the 12-week study period. Attendance rate at 12 weeks was 87.5% for the intervention group. The mean total exercise time at the end of the 12 weeks was 359 (SD 151.2) min. n=49	Standard care with a community fall prevention advice comprising the Age UK Staying Steady leaflet and the OTAGO strength and balance home exercise program leaflet. 3 times per week 12 weeks Intensity: 3 preselected exercises from the OTAGO list over the 12-week period. Details of exertion not described. Progression: NI Adherence: NI n=43	Cognition: ACE-III ¹	Assisted living facilities. No follow-up. No adverse events.	No statistically significant result concerning cognitive function. RoB2 (GC): Unclear.	Innovate UK and Medical Research Council (MRC).
Thapa et al. 2020 South Korea RCT (Registered: UMIN000040107)	MCI n=66 (68 randomized, 66 analyzed) Mean age 72.5 (SD 5.3) y. 52 F / 16 M (76% / 24%)	Virtual reality -based intervention + health education. Technology: VR-glasses Oculus HMD. VR: 3 x 100 min./week Education: 1 x 30–50 min. per week 8 weeks Intensity: NI Progression: NI Adherence: Participants strongly adhered to the intervention. Further	Health education. 1 x 30–50 min./week 8 weeks Intensity: NA Progression: NA Adherence: NI n=33	Cognition: MMSE-DS ¹ Executive function: TMT-B ² , SDST	Setting not reported. No follow-up. No adverse events.	TMT-B improved significantly in the intervention group compared with the control group. Positive changes were observed in MMSE and SDST that were not significant. RoB2 (GC): High. RoB2 (EF): Unclear.	Dong-A University research grant.

information on the rate not reported.
n=33

Torpil et al. 2021 Turkey RCT	MCI n=61 (64 randomized, 61 analyzed) I: 70.12 (SD 2.57) y C: 70.30 (SD 2.73) y 36 F / 25 M (59% / 41%)	Virtual reality -based rehabilitation + conventional cognitive rehabilitation. Technology: Microsoft Kinect. 2 x 45 min./week 12 weeks Intensity: NI Progression: according to game challenge levels. Adherence: NI n=30	Conventional cognitive rehabilitation. 2 x 45 min./week 12 weeks Intensity: NI Progression: the first 8 weeks featured interventions for one of the cognitive domains of the LOTCA-G test. The last 4 weeks included interventions involving all cognitive functions. Adherence: NI n=31	Cognition: LOTCA-G ¹	Setting not reported. No follow-up. No adverse events.	Experimental group gained significantly greater improvements in several domains of LOTCA-G test compared with conventional group. RoB2 (GC): Unclear.	No funding.
Dementia							
Karssemeijer et al. 2019 Netherlands RCT (Registered: NTR5581)	Mild or moderate dementia (AD n=59, vascular n=11, mixed n=24, not specified n=21) MMSE baseline 22.4 (SD 3.2) points. n=115 Mean age 79.9 (SD 6.5) y. 53 F / 62 M (46% / 54%)	Exergaming Technology: Bike Labyrinth. 3 x 30–50 min./week 12 weeks Intensity: 65–75% HRR or RPE 12–15. Progression: Gradually increasing the level of exertion in addition to training duration. Start of training with 50–60% HRR or RPE 12–15 and 20 min. duration. Adherence: 87.3% (SD 13.6) by dividing the attended sessions with total offered sessions. n=38	Aerobic exercise with a stationary bike. 3 x 30–50 min./week 12 weeks Intensity: 65–75% HRR or RPE 12–15. Progression: Gradually increasing the level of exertion in addition to training duration. Start of training with 50–60% HRR or RPE 12–15 and 20 min. duration. Adherence: 81.1% (SD 13.7). n=38 Active control with relaxation and flexibility exercises. 3 x 30–50 min./week 12 weeks Intensity: NI Progression: NI Adherence: 85.4% (SD 12.9) n=39	Executive function: TMT-B ² , SCWT, LF, RSCT	Community centers. Follow-up 3 months after intervention. No adverse events.	No significant differences between the intervention and control groups were found for executive function. RoB2 (EF): High.	Netherlands Organisation for Health Research and Development, (ZonMw).
Oliveira et al. 2021 Portugal	Mild to moderate dementia	Virtual reality -based cognitive stimulation.	Traditional cognitive stimulation using paper-and-pencil materials.	Cognition: MMSE ¹ , CDT	Residential care homes. No follow-up.	A marginally significant effect found for global	No external funding, but a research unit supporting the

Pilot RCT	(AD, questionable dementia n= 2, mild dementia n=7, moderate dementia n=8). n=17 (18 randomized, 17 analyzed) I: 82.60 (SD 5.42) y C: 84.14 (SD 6.30) y 12 F / 5 M (71% / 29%)	Technology: Systemic Lisbon Battery virtual reality platform. 2 x 45 min./week 6 weeks Intensity: NI Progression: The exercise sessions presented different difficulty levels for progression throughout the intervention. Progression not detailed. Adherence: NI n=10	Intensity: NI Progression: NI Adherence: NI n=7	Executive function: FAB ² , TMT-B (no data available for TMT)	Adverse events: NI.	cognition (MMSE) favoring experimental group, yet no differences found for improving executive function between groups. RoB2 (GC): Unclear. RoB2 (EF): High.	project was funded by the Foundation for Science and Technology (FCT) of Portugal.
Padala et al. 2012 USA Pilot RCT	Mild dementia (AD, MMSE ≥ 17 points). n=22 I: 79.3 (SD 9.8) y C: 81.6 (SD 5.2) y 16 F / 6 M (73% / 27%)	Exergaming. Technology: Nintendo Wii Fit. 5 x 30 min./week 8 weeks Intensity: NI Progression: NI Adherence: Mean exercise time 11.1 (SD 3.5) hours of maximum 20 hours. n=11	Walking. 5 x 30 min./week 8 weeks Intensity: self-paced indoor walking. Progression: NI Adherence: Mean exercise time 13.1 (SD 4.3) hours of maximum 20 hours. n=11	Cognition: MMSE ¹	Assisted living facility. No follow-up. No adverse events.	No statistically significant difference between groups in MMSE. RoB2 (GC): High.	AMDA Foundation / Pfizer Quality Improvement Award and Alzheimer's Association New Investigator Award.
Serino et al. 2017 Italy RCT	Older adults with AD and probable dementia (MODS < 85,5 points). n=20 I: 86.6 (SD 6.1) y C: 88.7 (SD 3.6) y 17 F / 3 M (85% / 15%)	Virtual reality -based training with navigation and recalling. Technology: Computer + NeuroVirtual 3D software. 3 x 20 min./week 3-4 weeks Intensity: NI Progression: NI Adherence: NI n=10	Traditional cognitive rehabilitative activities (e.g. cards games, naming, fluency, and music listening). 3 times per week 3-4 weeks Intensity: NI Progression: NI Adherence: NI n=10	Executive function: FAB ²	Social senior center. No follow-up. Adverse events: NI.	No significant difference between groups in improving executive function (FAB). RoB2 (EF): Unclear.	Supported by several Italian research projects and the Cariplo Foundation.
van Santen et al. 2020 Netherlands C-RCT (Registered: NTR5537/NL5420)	Mild or moderate dementia (AD n=37, vascular n=9, mixed n=7, other n=13, unknown n=46). n=112 (112 randomized, 84 analyzed) 23 day-care centers. I: 79 (SD 6.0) y C: 79 (SD 7.0) y 52 F / 60 M (46% / 54%)	Exergaming + regular activity program. Technology: interactive cycling with e.g. speed-syncing SilverFit Mile -system. 2-5 x 20-30 min./week 6 months Intensity: NI Progression: NI Adherence: NI n=52	Activity program (e.g. arts and crafts, music and physical exercise such as walking outdoors). 5 times per week 6 months Intensity: NI Progression: NI Adherence: NI n=32	Cognition: MMSE ¹ Executive function: TMT-B ²	Psychogeriatric day-care centers. No follow-up. No adverse events.	Exergaming showed positive effects on MMSE at 6 months compared with control group. Effect size was small but clinically relevant. RoB2 (GC): High. RoB2 (EF): High.	ZonMw-Memorabel programme/ Alzheimer Netherlands, Stichting Dioraphte and the EU.

EXCLUDED FROM META-ANALYSIS

<p>Anderson-Hanley et al. 2012 USA C-RCT (Registered: NCT01167400)</p>	<p>MCI and healthy older adults. n=79 I: 75.7 (SD 9.9) y C: 81.6 (SD 6.2) y 62 F / 17 M (78% / 22%)</p>	<p>Cybercycling. Technology: Stationary bikes + virtual reality display for 3D-tour. Gradually 5 x 45 min./week 12 weeks Intensity: mid-intervention adjustments made to maintain HRR of 60%. Progression: gradually increasing exercise time and frequency. Adherence: The frequency of rides (n) was 51.3 (SD 3.32). n=38</p>	<p>Stationary cycling. Gradually 5 x 45 min. /week, 12 weeks Intensity: mid-intervention adjustments made to maintain HRR of 60%. Progression: gradually increasing exercise time and frequency. Adherence: The frequency of rides (n) was 53.3 (SD 3.14). n=41</p>	<p>Executive function: Stroop C, DSB, CTT</p>	<p>Independent living facilities. No follow-up. Adverse events: In VR group, a total of 7 adverse events reported: Knee or sciatica pain while cycling n=2, other injuries (hurt back lifting, car accident) n=1, cancer diagnosis and treatment n=2, frustrated interacting with bike computer n=1, vertigo while cycling n=1. In comparison group, a total of 6 adverse events reported: Knee or sciatica pain while cycling n=2, acute illness (upper respiratory) n=1, other injuries (hurt back lifting, car accident) n=1, frustrated interacting with bike computer n=2.</p>	<p>Cybercycling was more effective on improving cognitive function than stationary cycling. RoB2 (EF): High.</p>	<p>Robert Wood Johnson Foundation, Union College and Skidmore College.</p>
<p>Gunst et al. 2022 Belgium C-RCT</p>	<p>Residents in a nursing home (MMSE > 20 points). n=32 3 residential care centers included. Age varied between 76-80 years in both groups. 22 F / 10 M (69% / 31%)</p>	<p>Exergaming + other planned activities. Technology: Xbox 360 Kinect Sport. 2 x 60 min./week 13 weeks Intensity: Borg's Scale at baseline was on average 10.9. Progression: Borg's Scale at 3 months was 11.6. Adherence: Mean 23.3 exergame sessions were organized in the three residential care centers and an average participation rate was 88%.</p>	<p>Planned activities (usual care). 13 weeks Intensity: NI Progression: NI Adherence: NI n=17</p>	<p>Cognition: CDT Executive function: SCWT</p>	<p>Residential care centers. Follow-up at 3 months after intervention. Adverse events: NI.</p>	<p>The median time difference for SCWT slightly increased at 3 months for intervention group but decreased with the control group. Results remained inconclusive due to unavailable comparative data. In addition, the direction of the CDT test remained unclear.</p>	<p>NI</p>

		n=15				RoB2 (GC): High. RoB2 (EF): High.	
Optale et al. 2010 Italy Pilot RCT	Older adults with memory deficits n=31 (36 randomized, 31 analyzed) Median age 80 y. 24 F / 12 M (67% / 33%)	Virtual reality memory training (VRMT) + auditory sessions + recreational activities (e.g. reading, painting). Technology: VR-glasses HMD V6. Initial phase (IP) 3 months: 3 x 30 min./week Booster phase (BP) 3 months: 2 x 30 min./week Total of 6 months Intensity: IP with 3 auditory sections alternating with 3 VR sessions every 2 weeks. BP with 1 auditory and 1 VR session every week. The level of exertion not described. Progression: gradually increasing the complexity of the stimuli. Adherence: NI n=15	Music therapy + recreational activities (e.g. reading, painting). Initial phase 3 months: 3 x 30 min./week Booster phase 3 months: 2 x 30 min./week Total of 6 months Intensity: NI Progression: NI Adherence: NI n=16	Cognition: MMSE, MSN Executive function: CET, DTP, PVF	Rest-care home. No follow-up. Adverse events: NI.	VRMT-group showed significant improvements in several aspects of cognition. Control group showed a progressive decline. RoB2 (GC): High. RoB2 (EF): High.	Consorzio Sociale CPS and The Scientific Institute (IRCCS) Eugenio Medea.
Padala et al. 2017 USA Pilot RCT (Registered: NCT01002586)	Mild dementia (AD, MMSE \geq 18 points). n=30 Mean age 73 (SD 6.2) y. 11 F / 19 M (37% / 63%)	Exergaming. Technology: Nintendo Wii Fit. 5 x 30 min./week 8 weeks Intensity: based on prior studies with respect to ability and safety. Progression: according to performance in games. Adherence: Total number of exercise sessions was mean 38 (SD 2) out of maximum 40 sessions (adherence 95%). n=15	Walking. 5 x 30 min./week 8 weeks Intensity: self-paced indoor or outdoor walking. Progression: NI Adherence: Total number of exercise sessions was mean 37 (SD 6) out of maximum 40 sessions (adherence 93%). n=15	Cognition: 3MS, MMSE	Home-based, supervised by caregivers. Follow-up 8 weeks after intervention. No study-related adverse events.	No difference between groups found concerning cognition. RoB2 (GC): High.	New Investigator grant from Alzheimer's Association.
Ramnath et al. 2021 South Africa C-RCT (Registered: PACTR20200854 7335106)	Older adults with memory complaints (Adapted Petersen criteria). n=45 6 different retirement homes included. I: 70.8 (SD 4.52) y C: 74.14 (SD 5.8) y	Interactive video gaming. Technology: Xbox Kinect Sport. 2 x 60 min./week 12 weeks Intensity: Borg's RPE Scale from 1 to 10. Researchers ensured that the individuals participated within their limit. Progression: NI	Conventional multimodal exercise. 2 x 60 min./week 12 weeks Intensity: Borg's RPE Scale from 1 to 10. Researchers ensured that the individuals participated within their limit.	Cognition: MMSE ¹ Executive function: Stroop (modified) ²	Retirement homes. No follow-up. No adverse events.	Experimental group showed significant improvement in the total number of correct responses and reaction time of correct color-words on the Stroop test	No funding.

Gender distribution not reported.

Adherence: 100% for both groups with all 45 participants completing 24 one-hour sessions over the 12-week intervention period.
n=23

Progression: body weight used during first 6 weeks. Intensity of upper body strength training for weeks 7-12 increased by using external weights.
Adherence: 100% for both groups with all 45 participants completing 24 one-hour sessions over the 12-week intervention period.
n=22

compared with conventional group.
RoB2 (GC): High.
RoB2 (EF): High.

1 Outcome measures considered in quantitative analyses for global cognition are expressed as upper index number one (1).

2 Outcome measures considered in quantitative analyses for executive function are expressed as upper index number two (2).

*In Hughes et al. 2014 all participants were analyzed except for CAMCI, in which one participant was unable to complete the test. Thus, the number of analyzed participants (n=20) reported differs from the number of participants included in meta-analysis for CAMCI-test (VR n=9, Control n=10).

**Liao et al. 2019 and Liao et al. 2020 are different publications from the same RCT. Thus, the overall number of participants reported in this review are counted once for this RCT.

Abbreviations: ACE-III = Addenbrooke's Cognitive Examination III, ACSM = American College of Sports Medicine, AD = Alzheimer's Disease, C = Control group, CAMCI = The Computerized Assessment of Mild Cognitive Impairment, CDT = The Clock Drawing Test, CET = Cognitive Estimation Test, COGTEL = Cognitive Telephone Screening Instrument, C-RCT = Cluster-Randomized Controlled Trial, CSRQ = The Cognitive Self-Report Questionnaire 25, CTT = Color Trails Test, DSB = Digit Span Backwards, DSC = Digit Symbol Coding Test, DST = Digit Span Test, DTP = Dual Task Performance, EF = Executive function, e.g. = for example, EXIT-25 = The Executive Interview 25, F = Female, FAB = Frontal Assessment Battery, GC = Global cognition, HMD = Head-Mounted Display, HR = Heart Rate, HRR = Heart Rate Reserve, I = Intervention group, LF = Letter Fluency, LOTCA-G = Loewenstein Occupational Therapy Cognitive Assessment -Geriatric, M = Male, MCI = Mild Cognitive Impairment, MHR = Maximum Heart Rate, MMSE = Mini-Mental State Examination, MMSE-DS = Mini-Mental State Examination-Dementia screening test, MoCA = Montreal Cognitive Assessment, MODS = Milan Overall Dementia Scale, MSN = Mental Status in Neurology, n = number of participants, NA = Not Applicable, NI = No Information, PVF = Phonemic Verbal Fluency, RCT = Randomized Controlled Trial, RPE = Rate of Perceived Exertion, RSCT = Rule Shift Cards Test, SCWT = Stroop Color Word Test, SD = Standard Deviation, SDST = Symbol Digit Substitution Test, TMT = Trail Making Test, TMT-B = Trail Making Test Part B, TUG-Cog = Timed Up and Go Cognition, VST = Victoria Stroop Test, y = age in years, 3MS = Modified Mini-Mental State Examination.

1 Table 2. Results of meta-regression analysis for global cognition and executive function on covariates of study factors and the high risk of bias
2 domains

Covariates	Global cognition						Executive function					
	Estimated Effect Size	SE	Lower CI	Upper CI	<i>p</i>	sig.	Estimated Effect Size	SE	Lower CI	Upper CI	<i>p</i>	sig.
<i>Study factors</i>												
Age (years)	-0.029	0.026	-0.091	0.033	0.305		-0.032	0.030	-0.112	0.048	0.343	
Level of cognition at baseline												
Normal	-0.230	0.154	-0.748	0.287	0.240		0.206	0.400	-0.822	1.234	0.629	
MCI	0.392	0.239	-0.148	0.932	0.135		0.104	0.283	-0.504	0.712	0.718	
Dementia	-0.430	0.441	-1.990	1.130	0.414		-0.357	0.247	-1.004	0.291	0.213	
Intervention duration (weeks)	-0.018	0.020	-0.076	0.040	0.414		-0.049	0.018	-0.103	0.004	0.062	*
Number of sessions per week	-0.009	0.225	-0.566	0.548	0.969		0.201	0.214	-0.423	0.826	0.406	
Session duration (min/session)	-0.003	0.005	-0.017	0.011	0.588		-0.002	0.006	-0.022	0.017	0.745	
Intervention volume (min/week)	-0.002	0.001	-0.006	0.002	0.209		0.000	0.001	-0.005	0.006	0.798	
Supervision of intervention	0.086	0.125	-0.176	0.349	0.500		0.507	0.151	0.179	0.835	0.005	***
Combined intervention (ref. pure VRBT)	0.002	0.253	-0.545	0.550	0.993		-0.435	0.231	-1.006	0.136	0.110	
Customized technology (ref. commercial)	-0.195	0.232	-0.683	0.294	0.412		-0.378	0.399	-1.307	0.551	0.372	
Fully immersive (ref. non-immersive)	-0.287	0.142	-1.412	0.838	0.251		-0.119	0.271	-2.011	1.773	0.720	
Control group intervention (ref. all other types)												
Physical exercise	0.025	0.292	-0.590	0.641	0.933		0.364	0.294	-0.272	1.001	0.237	
Cognitive exercise	0.366	0.378	-0.565	1.296	0.372		0.130	0.254	-0.539	0.800	0.632	
Combined exercise (physical+cognitive)	-0.209	0.178	-0.679	0.261	0.298		-0.211	0.320	-2.336	1.914	0.601	
Information	-0.334	0.135	-1.394	0.726	0.200		-0.535	0.177	-1.105	0.035	0.058	*
<i>High Risk of Bias</i>												
Overall	-0.044	0.259	-0.590	0.502	0.867		0.077	0.244	-0.466	0.621	0.759	
Randomization process	NA						NA					
Deviations from intended interventions	0.172	0.426	-0.947	1.292	0.704		0.095	0.345	-0.667	0.856	0.789	
Missing outcome data	0.261	0.293	-0.393	0.915	0.395		0.566	0.361	-0.269	1.400	0.156	
Measurement of the outcome	-0.494	0.283	-1.247	0.259	0.148		0.093	0.144	-0.217	0.403	0.528	
Selection of the reported results	-0.008	0.129	-0.278	0.263	0.952		-0.479	0.145	-0.790	-0.168	0.005	***

3 SE: Standard Error; CI: 95 % Confidence Interval; VRBT: virtual reality-based training; NA: not applicable; *** $p \leq 0.01$; * $p \leq 0.10$

1 Table 3. Summary of Findings

Virtual reality-based training (VRBT) compared with conventional training or information-based treatment				
Patient or population: Older adults at least 60 years of age regardless of the cognitive level				
Setting: Varied between home, hospital, laboratory and research institutes, senior gymnasium, recreational or community settings, and different living facilities				
Intervention: Virtual reality-based training				
Comparison: Conventional training or information-based treatment				
Outcomes	Hedges' g with 95% CI*	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
Global cognition	Hedges' g 0.42 higher (CI 0.17 to 0.68)	876 (20 RCTs)	⊕⊕○○ Low ^{1,2}	Global cognition was assessed with valid or otherwise widely used measures of Montreal Cognitive Assessment, Addenbrooke's Cognitive Examination, Computerized Assessment of Mild Cognitive Impairment, Cognitive Telephone Screening Instrument, Loewenstein Occupational Therapy Cognitive Assessment –Geriatric and Mini-Mental State Examination.
Executive function	Hedges' g 0.35 higher (CI 0.06 to 0.65)	810 (16 RCTs)	⊕○○○ Very low ^{1,2,3}	Executive function was assessed with valid or otherwise widely used measures of Trail Making Test Part B, Stroop Color Word Test, CogState and Frontal Assessment Battery.

*CI: confidence interval

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

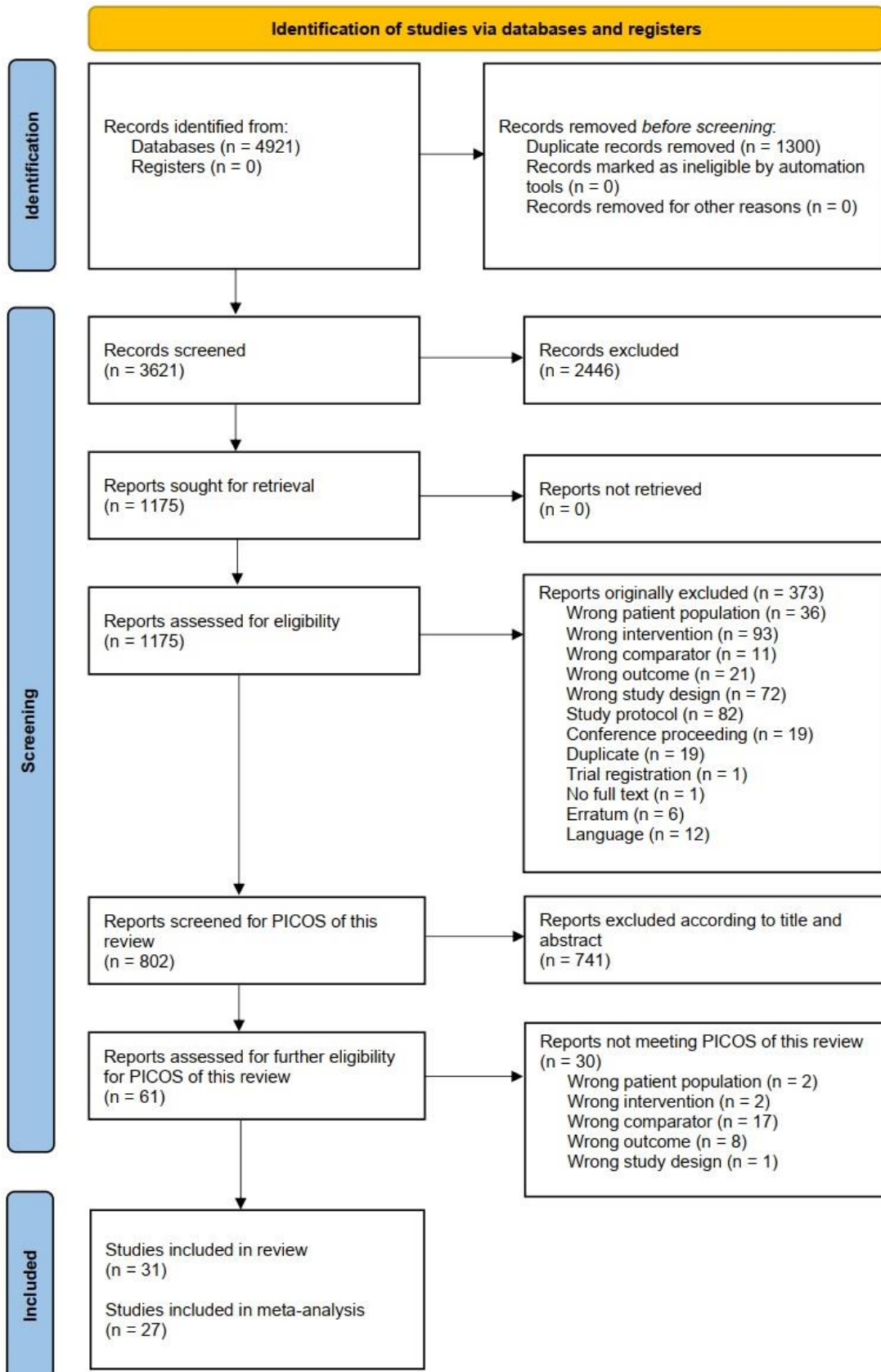
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

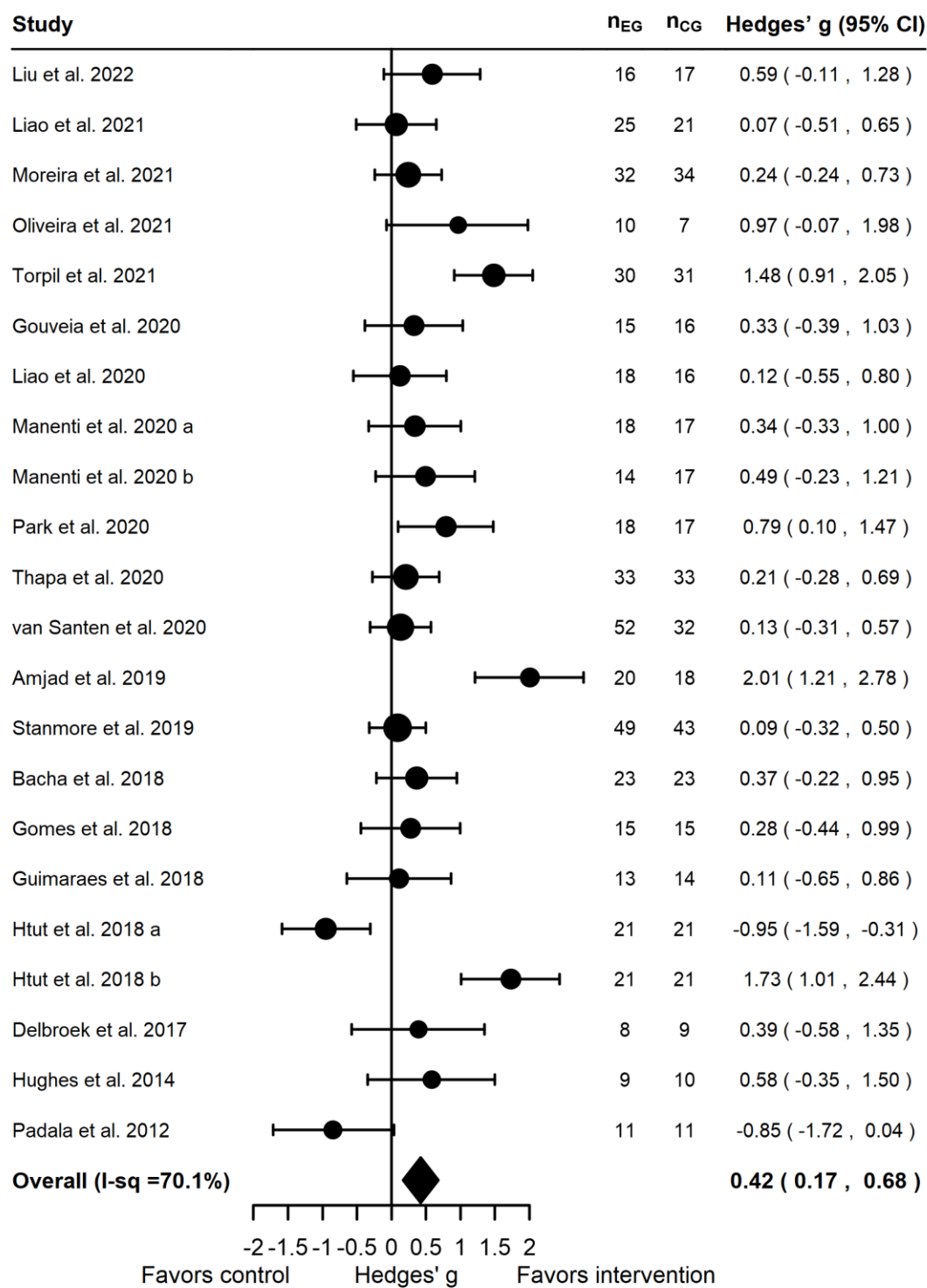
2 **Explanations**

- 3 1. Study limitations: Downgraded by one level due to high risk of bias in individual studies. Results of meta-regression were
4 inconclusive due to a small number of studies analyzed, and there was a high number of unclear and high risk of bias found in all the
5 domains assessed. For global cognition, high risk of bias was identified in randomization process (1), deviation from intended
6 intervention (5), missing outcome data (7), measurement of the outcome (9) and selection of the reported results (1). For executive
7 function, high risk of bias was identified in randomization process (2), deviation from intended intervention (8), missing outcome data
8 (7), measurement of the outcome (1) and selection of the reported results (1).
- 9 2. Inconsistency of results: Downgraded by one level due to inconsistency in individual studies and high heterogeneity (I^2).
- 10 3. Imprecision: Downgrading by one level due to imprecision. The number of participants both in intervention and control groups are
11 over 200 per group (intervention n=433, control n=422) but the number of studies is small and confidence interval wide.
- 12 4. Indirectness: No downgrading due to indirectness, as the review follows the specified PICOS criteria well.
- 13 5. Publication bias: No downgrading due to publication bias. Slight asymmetry indicated in funnel plots, but publication bias was not
14 seen serious.



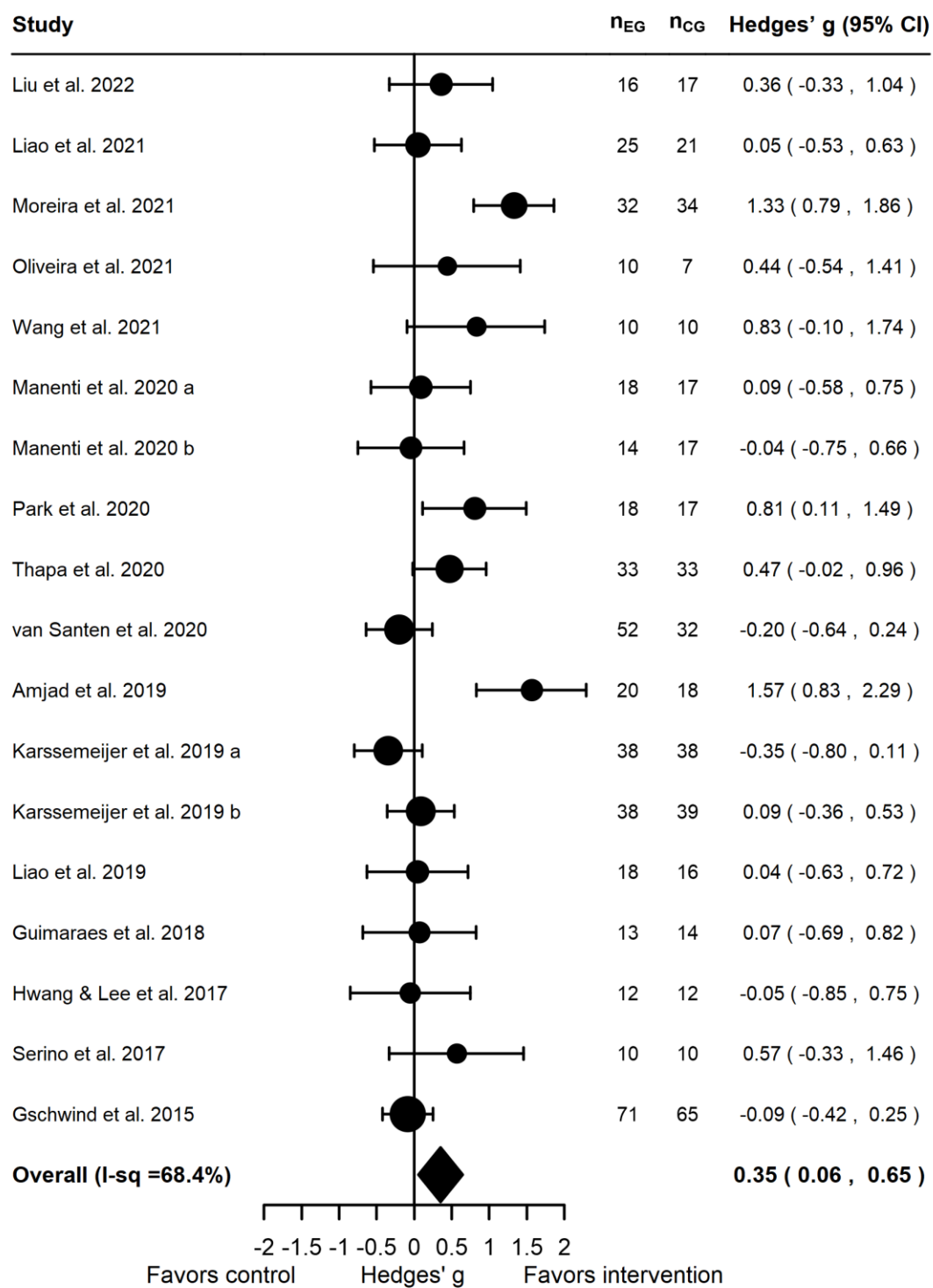
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Figure 1. PRISMA 2020 flow diagram for identification and selection of studies.



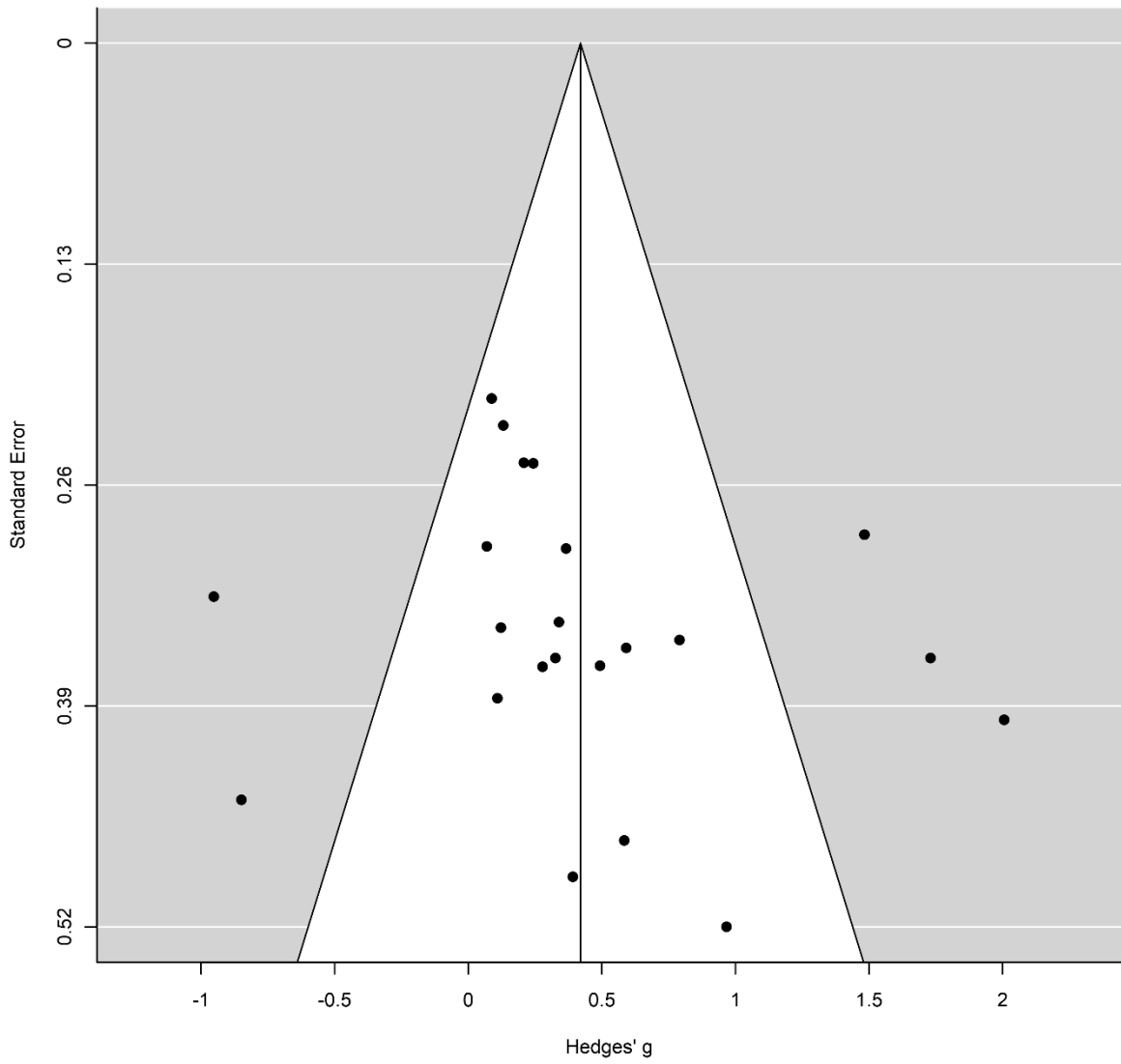
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Figure 2. Forest plot with estimated effect of VRBT compared with control on global cognition. The size of the circle in Hedges' g value shows the emphasis of an individual study in the pooled effect.

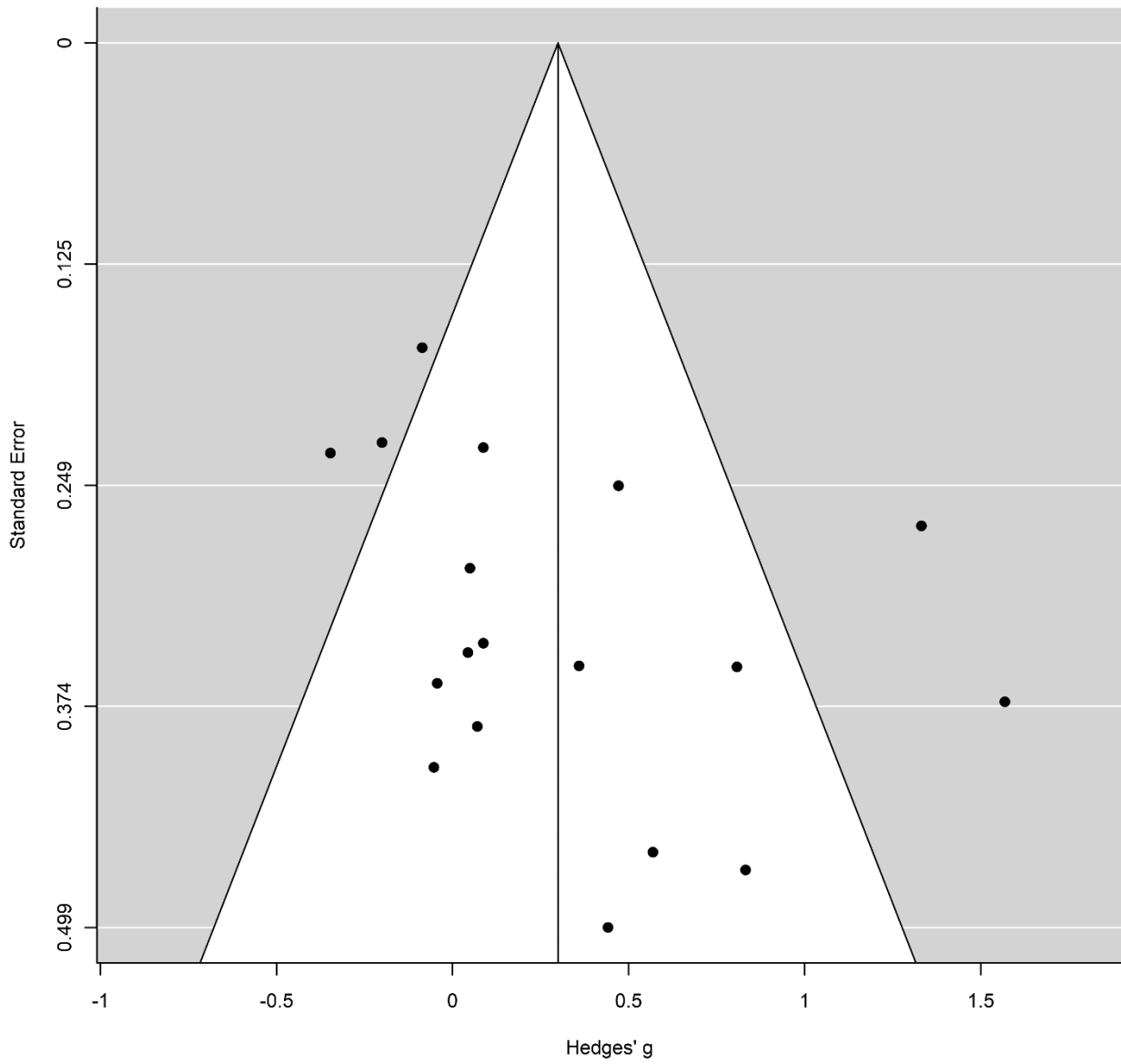


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Figure 3. Forest plot with estimated effect of VRBT compared with control on executive function. The size of the circle in Hedges' g value shows the emphasis of an individual study in the pooled effect.



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 2
 3 Figure 4. Publication bias assessed by funnel plot for global cognition.



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2
3 Figure 5. Publication bias assessed by funnel plot for executive function.

Supplementary Material S1

Appendix 1: PRISMA 2020 Checklist

Appendix 2: Search strategy for Ovid MEDLINE database

Appendix 3: Priority lists of measurements for global cognition and executive function

Appendix 4: A list of excluded studies (n=30) with justification for exclusion

Appendix 5: Tables of risk of bias for global cognition and executive function

Appendix 1.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	JAPA abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary Material S1 (Appendix 2)
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods, Table 1
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Methods
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Methods
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Methods
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Methods
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results (Figure 1)
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Results, Supplementary Material S1 (Appendix 4)
Study characteristics	17	Cite each included study and present its characteristics.	Results (Table 1)
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary Material S1 (Appendix 5)
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Results
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Results
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Results, Supplementary Material S2 (Appendix 2)

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Supplementary Material S1 (Appendix 5)
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results (Table 2)
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion
	23b	Discuss any limitations of the evidence included in the review.	Discussion
	23c	Discuss any limitations of the review processes used.	Discussion
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion, Conclusions
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	/
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	/
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Acknowledgements
Competing interests	26	Declare any competing interests of review authors.	Conflict of interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	/

PRISMA 2020 Checklist from: Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., McGuinness, L. A., ... Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ (Clinical research ed.)*, 372, n71. <https://doi.org/10.1136/bmj.n71>

Appendix 2.

Search strategy for Ovid MEDLINE database

- 1 Randomized Controlled trial.pt.
- 2 Controlled clinical trial.pt.
- 3 (Randomized or Randomised).ab.
- 4 Placebo.ab.
- 5 clinical trials as topic.sh.
- 6 randomly.ab.
- 7 trial.ti.
- 8 OR/1-7
- 9 rehabilitec*.mp.
- 10 Therapist/ or therapist*.mp.
- 11 exp Disabled Persons/ or disabled person.mp.
- 12 Caregivers/ or caregiver*.mp.
- 13 exp Rehabilitation/ or rehab*.mp.
- 14 exp Exercise/ or exercise.mp.
- 15 exp Exercise therapy/ or exercise therapy.mp.
- 16 therapeutic exercise.mp.
- 17 (Physical therap* or Physiotherap*).mp.
- 18 exp Physical Therapy Modalities/ or physical therapy modalities.mp.
- 19 physical rehabilitation.mp.
- 20 exp Occupational Therapy/ or occupational therap*.mp.
- 21 exp "Rehabilitation of Speech and Language Disorders"/
- 22 exp Speech Therapy/ or speech therap*.mp.
- 23 speech-language therap*.mp.
- 24 logoped*.mp.
- 25 exp Audiology/ or audiolog*.mp.
- 26 exp Sign Language/
- 27 exp Psychotherapy/ or psychotherap*.mp.
- 28 Neuropsychotherap*.mp.
- 29 exp Neuropsychology/ or neuropsychol*.mp.
- 30 (riding therap* or equine facilitated therap* or hippotherap* or horse riding therap* or horse back riding therap*).mp.
- 31 exp Dance Therapy/ or dance therap*.mp.
- 32 exp Music Therapy/ or music therap*.mp.
- 33 exp Art Therapy/ or art therap*.mp.
- 34 exp Optometry/ or optomet*.mp.
- 35 exp Orthoptics/ or orthoptic*.mp.
- 36 orthotic*.mp.
- 37 orthopedic techn*.mp.
- 38 exp Podiatry/ or podiat*.mp.
- 39 exp "Physical Education and Training"/ or physical education*.mp.
- 40 mobility special*.mp.
- 41 Rehabilitation Nursing/ or rehabilitation nurs*.mp.
- 42 (practical nurs* or practice nurs*).mp.
- 43 (asthma nurs* or respiratory nurs*).mp.
- 44 (diabetes nurs* or diabetes specialist nurs*).mp.
- 45 (geriatric nurs* or gerontological nurs* or gerontology nurs*).mp.
- 46 (sexual health therap* or sexual therap*).mp.
- 47 exp Sexology/
- 48 Exp Nutritionists/ or nutritionist.mp.
- 49 leisure activit*.mp.
- 50 play therap*.mp.
- 51 (drama therap* or psychodrama therap*).mp.
- 52 psychodram*.mp.
- 53 creative art therap*.mp.
- 54 (expression skills or expressive art therap*).mp.
- 55 (youth counselor* or youth leader*).mp.
- 56 OR/9-55
- 57 exp Augmented Reality/ or augmented realit*.mp.
- 58 exp Virtual Reality/ or virtual realit*.mp.
- 59 exp Video Games/
- 60 (video gam* or videogam*).mp.
- 61 serious gam*.mp.
- 62 exergam*.mp.
- 63 kinect*.mp.
- 64 nintendo*.mp.
- 65 (play station* or playstation*).mp.
- 66 wii*.mp.
- 67 xbox*.mp.
- 68 avatar*.mp.
- 69 OR/57-68
- 70 8 AND 56 AND 69
- 71 animal/
- 72 human/
- 73 71 NOT (71 AND 72)
- 74 70 NOT 73

Appendix 3.

Priority lists of measurements at outcome level

Global cognition

1. Montreal Cognitive Assessment (MoCA)
 - high sensitivity (90 %) and specificity (87 %) for detecting MCI ¹
 - lower ceiling effect compared to MMSE ²
 2. The Addenbrooke Cognitive Examination (ACE)
 - valid and reliable (alpha coefficient 0.8) dementia screening test that is sensitive to early cognitive dysfunction ³
 3. The Computer Assessment of Mild Cognitive Impairment (CAMCI)
 - highly sensitive (86 %) and specific (94 %) for the identification of MCI among community-dwelling older adults ⁴
 4. Cognitive Telephone Screening Instrument (COGTEL)
 - reliable (test-retest reliability 0.85) and valid instrument for assessing cognitive function with inter-individual differences and performance level among healthy older adults ⁵, MCI and dementia ⁶
 5. The Loewenstein Occupational Therapy Cognitive Assessment – Geriatric (LOTCA-G)
 - valid and reliable version of a LOTCA-test for geriatric population distinguishing differences in cognitive performance between mild or moderate dementia and people with normal level of cognition among older adults 70-90 years old ⁷
 6. The Cognitive Self-Report Questionnaire 25 (CSRQ)
 - a self-report questionnaire ⁸
 - found to be an appropriate measure for assessing hearing, cognition, and auditory processing among older adults with or without probable MCI ⁹
 7. Modified Mini-Mental State Examination (3MS)
 - developed to acknowledge the limitations of MMSE in recognizing mild dementia ^{10*}
 - found to be superior to MMSE with higher alpha internal consistency (0.87) though not sensitive for detecting MCI ¹⁰
 8. The Clock-Drawing Test (CDT)
 - quick and easy test for assessing global cognition ¹¹, however scoring and direction of the test can vary ^{12, 13}
 - suites better for screening moderate or severe dementia as the test is not sensitive for detecting mild dementia ¹⁴
 - validity acceptable compared with MMSE ¹⁵
 9. Mini-Mental State Examination (MMSE)
 - high ceiling effect lowering the sensitivity to detect differences in cognitive performance among healthy older adults and ones with MCI ^{16, 17}
-

Executive function

1. Trail Making Test, Part B (TMT-B)
 - widely used measure for executive function that is included in the Halstead-Reitan Neuropsychological Battery ^{18, 19}
 2. Stroop Color Word Test (SCWT, WCT, Stroop C, VST)
 - commonly known measure of attention and inhibition ²⁰ that is also suitable for detecting mild dementia ²¹
 3. Digit Span Backward (DSB)
 - usable measure especially with major cognitive impairment ²²
 - performance in DSB strongly related to gray matter volume of the brain among healthy older adults ²³
 4. Symbol Digit Substitution Test (SDST, DSST, DSC)
 - valid, reliable and sensitive measure for cognitive dysfunction with low impact of language, culture and education on test performance ²⁴
 - apparently measures several cognitive domains such as executive function
 5. Color Trails Test (CTT)
 - developed as equivalent version of TMT test with universal sign language symbols instead of cultural-based language ²⁵, but some distinction has been found between CTT-2 and TMT-B ²⁶
 - age and education level seem to influence on CTT results ²⁵
 6. Executive Interview (EXIT-25)
 - a measure with adequate reliability that is often used for measuring executive function, although studies show its usability also for global cognition ²⁷
 - correlates well with other measurements of executive function ²⁸
 7. CogState Battery
 - game-like computerized test battery with several cognitive tests ²⁹
 - valid and reliable test in detecting cognitive decline among healthy older adults, adults with aMCI or Alzheimer's disease ³⁰
 - learning is shown to affect results in some tests ^{16, 29, 31, 32}
 8. Cognitive Estimation Test (CET)
 - includes both quantitative and qualitative questions rated from 0 to 3 ^{33**}
 - sensitivity uncertain
 9. The Frontal Assessment Battery (FAB)
 - test-retest and interrater reliabilities found to be satisfactory in screening of global executive dysfunction ³⁴
 10. Rule Shift Cards Test (RSCT)
 - a promising measure of executive function, though test-retest reliability has proven to be weak ³⁵
 11. The Dual Task Performance (DTP)
 - measures performance of two tasks simultaneously and division of attention ^{36, 37}
 - apparently no standardized DTP-measure available
 - paper-pencil assessment of DTP identifies impairment in Alzheimer's disease but sensitivity to recognize changes in cognitive performance between healthy and MCI is not clear ³⁸
-

* Original reference according to McDowell et al. 1997: Teng, E. L., & Chui, H. C. (1987). The Modified Mini-Mental State (3MS) examination. *The Journal of clinical psychiatry*, 48(8), 314–318.

** Original reference according to Wagner et al. 2011: Shallice, T., & Evans, M. E. (1978). The involvement of the frontal lobes in cognitive estimation. *Cortex; a journal devoted to the study of the nervous system and behavior*, 14(2), 294–303. [https://doi.org/10.1016/s0010-9452\(78\)80055-0](https://doi.org/10.1016/s0010-9452(78)80055-0)

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Appendix 4.

A list of excluded studies (n=30) with justification for exclusion.

Study	Title	Reason for exclusion
Adcock et al. 2020	Effects of an in-home multicomponent exergame training on physical functions, cognition, and brain volume of older adults: a randomized controlled trial.	Wrong comparator
Anderson-Hanley et al. 2017	Neuropsychological benefits of neuro-exergaming for older adults: a pilot study of an interactive physical and cognitive exercise system (iPACES).	Wrong comparator
Anderson-Hanley et al. 2018	The aerobic and cognitive exercise study (ACES) for community-dwelling older adults with or at-Risk for mild cognitive impairment (MCI): neuropsychological, neurobiological and neuroimaging outcomes of a randomized clinical trial.	Wrong comparator
Barcelos et al. 2015	Aerobic and cognitive exercise (ACE) pilot study for older adults: executive function improves with cognitive challenge while exergaming.	Wrong comparator
Belchior et al. 2019	Computer and videogame interventions for older adults' cognitive and everyday functioning.	Wrong intervention
Hsieh et al. 2014	Virtual reality system based on Kinect for the elderly in fall prevention.	Wrong outcome
Huang et al. 2020	Exergaming executive functions: an immersive virtual reality-based cognitive training for adults aged 50 and older.	Wrong comparator
Kang et al. 2021	Effect of Cognitive Training in Fully Immersive Virtual Reality on Visuospatial Function and Frontal-Occipital Functional Connectivity in Predementia: Randomized Controlled Trial.	Wrong comparator
Karssemeijer et al. 2019	Exergaming as a physical exercise strategy reduces frailty in people with dementia: a randomized controlled trial.	Wrong outcome
Kim et al. 2021	Effects of ICT-Based Multicomponent Program on Body Composition and Cognitive Function in Older Adults: A Randomized Controlled Clinical Study.	Wrong comparator
Liu et al. 2021	Study on Adjuvant Medication for Patients with Mild Cognitive Impairment Based on VR Technology and Health Education.	Wrong patient group
Maillot et al. 2012	Effects of interactive physical-activity video-game training on physical and cognitive function in older adults.	Wrong comparator
Man et al. 2012	Evaluation of a virtual reality-based memory training programme for Hong Kong Chinese older adults with questionable dementia: A pilot study.	Wrong outcome
McCord et al. 2020	Short video game play improves executive function in the oldest old living in residential care.	Wrong intervention
Micarelli et al. 2019	Vestibular rehabilitation in older adults with and without mild cognitive impairment: Effects of virtual reality using a head-mounted display.	Wrong outcome
Mirelman et al. 2016	Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial.	Wrong outcome
Monteiro-Junior et al. 2017	Virtual reality-based physical exercise with exergames (PhysEx) improves mental and physical health of institutionalized older adults.	Wrong study design

Mrakic-Sposta et al. 2018	Effects of combined physical and cognitive virtual reality-based training on cognitive impairment and oxidative stress in MCI patients: A pilot study.	Wrong comparator
Ordnung et al. 2017	No overt effects of a 6-week exergame training on sensorimotor and cognitive function in older adults. A preliminary investigation.	Wrong comparator
Padala et al. 2017	Efficacy of Wii-Fit on static and dynamic balance in community dwelling older veterans: a randomized controlled pilot trial.	Wrong comparator
Park & Park 2018	Does cognition-specific computer training have better clinical outcomes than non-specific computer training? A single-blind, randomized controlled trial.	Wrong comparator
Park Eunhee et al. 2019	Effects of a mixed reality-based cognitive training system compared to a conventional computer-assisted cognitive training system on mild cognitive impairment: A pilot study.	Wrong comparator
Park Jin-Hyuck 2020	Effects of virtual reality-based spatial cognitive training on hippocampal function of older adults with mild cognitive impairment.	Wrong comparator
Park Jin-Hyuck 2022	Does the virtual shopping training improve executive function and instrumental activities of daily living of patients with mild cognitive impairment?	Wrong comparator
Park Jong-Hwan et al. 2020	Feasibility and tolerability of a culture-based virtual reality (VR) training program in patients with mild cognitive impairment: a randomized controlled pilot study.	Wrong comparator
Rica et al. 2020	Effects of a Kinect-based physical training program on body composition, functional fitness and depression in institutionalized older adults.	Wrong outcome
van Santen et al. 2021	Cost-effectiveness of exergaming compared to regular day-care activities in dementia: results of a randomised controlled trial in the Netherlands.	Wrong outcome
Schwenk et al. 2016	Sensor-based balance training with motion feedback in people with mild cognitive impairment.	Wrong comparator
Taylor et al. 2018	Exergames to improve the mobility of long-term care residents: a cluster randomized controlled trial.	Wrong outcome
Wittelsberger et al. 2013	The influence of Nintendo-Wii® bowling upon residents of retirement homes.	Wrong patient group

Appendix 5.

Tables of risk of bias for RCT and C-RCT studies in (a) global cognition and (b) executive function.

(a) Global cognition with RCT studies:

Study (RCT)	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Amjad et al. 2019	?	-	-	+	?	-
Bacha et al. 2018	+	?	+	+	?	!
Delbroek et al. 2017	?	?	+	+	?	!
Gomes et al. 2018	+	?	?	+	?	!
Gouveia et al. 2020	+	?	?	+	?	!
Guimarães et al. 2018	?	-	?	-	?	-
Htut et al. 2018	?	+	+	+	?	!
Hughes et al. 2014	?	+	+	+	?	!
Liao et al. 2020	?	?	?	+	?	!
Liao et al. 2021	?	?	?	+	?	!
Liu et al. 2022	?	?	-	+	?	-
Manenti et al. 2020	?	+	+	-	-	-
Moreira et al. 2021	?	-	-	-	?	-
Oliveira et al. 2021	?	?	+	?	?	!
Optale et al. 2010	?	?	-	-	?	-
Padala et al. 2012	?	?	?	-	?	-
Padala et al. 2017	?	?	?	-	?	-
Park et al. 2020	+	?	-	+	?	-
Thapa et al. 2020	?	?	+	-	?	-
Torpil et al. 2021	?	+	+	+	?	!

 Low risk
 Some concerns
 High risk

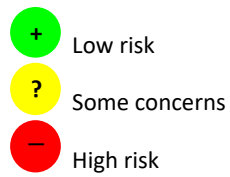
Global cognition with C-RCT studies:

Study (C-RCT)	Randomisation process	Timing of identification or recruitment of participants	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Gunst et al. 2022	!	+	-	-	-	!	-
Ramnath et al. 2021	-	+	+	+	-	!	-
Stanmore et al. 2019	!	+	!	+	+	!	!
van Santen et al. 2020	+	!	-	-	!	+	-

- + Low risk
- ! Some concern
- High risk

(b) Executive function with RCT studies:

Study (RCT)	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Amjad et al. 2019	?	-	-	+	?	-
Gschwind et al. 2015	?	?	?	+	-	-
Guimarães et al. 2018	?	-	?	+	?	-
Hwang & Lee 2017	?	-	+	?	?	-
Karssemeijer et al. 2019	+	-	+	+	+	-
Liao et al. 2019	?	?	?	+	?	!
Liao et al. 2021	?	?	?	+	?	!
Liu et al. 2022	?	?	-	+	?	-
Manenti et al. 2020	?	+	+	+	?	!
Moreira et al. 2021	?	-	-	+	?	-
Oliveira et al. 2021	?	?	+	-	?	-
Optale et al. 2010	?	?	-	+	?	-
Park et al. 2020	+	?	-	+	?	-
Serino et al. 2017	?	?	+	?	?	!
Thapa et al. 2020	?	?	+	+	?	!
Wang et al. 2021	?	+	+	+	?	!



Executive function with C-RCT studies:

Study (C-RCT)	Randomisation process	Timing of identification or recruitment of participants	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Anderson-Hanley et al. 2012	-	+	-	!	+	!	-
Gunst et al. 2022	!	+	-	-	+	!	-
Ramnath et al. 2021	-	+	+	+	+	!	-
van Santen et al. 2020	+	!	-	-	!	+	-

+ Low risk
! Some concerns
- High risk

Supplementary Material S2

Appendix 1: Subgroup analyses

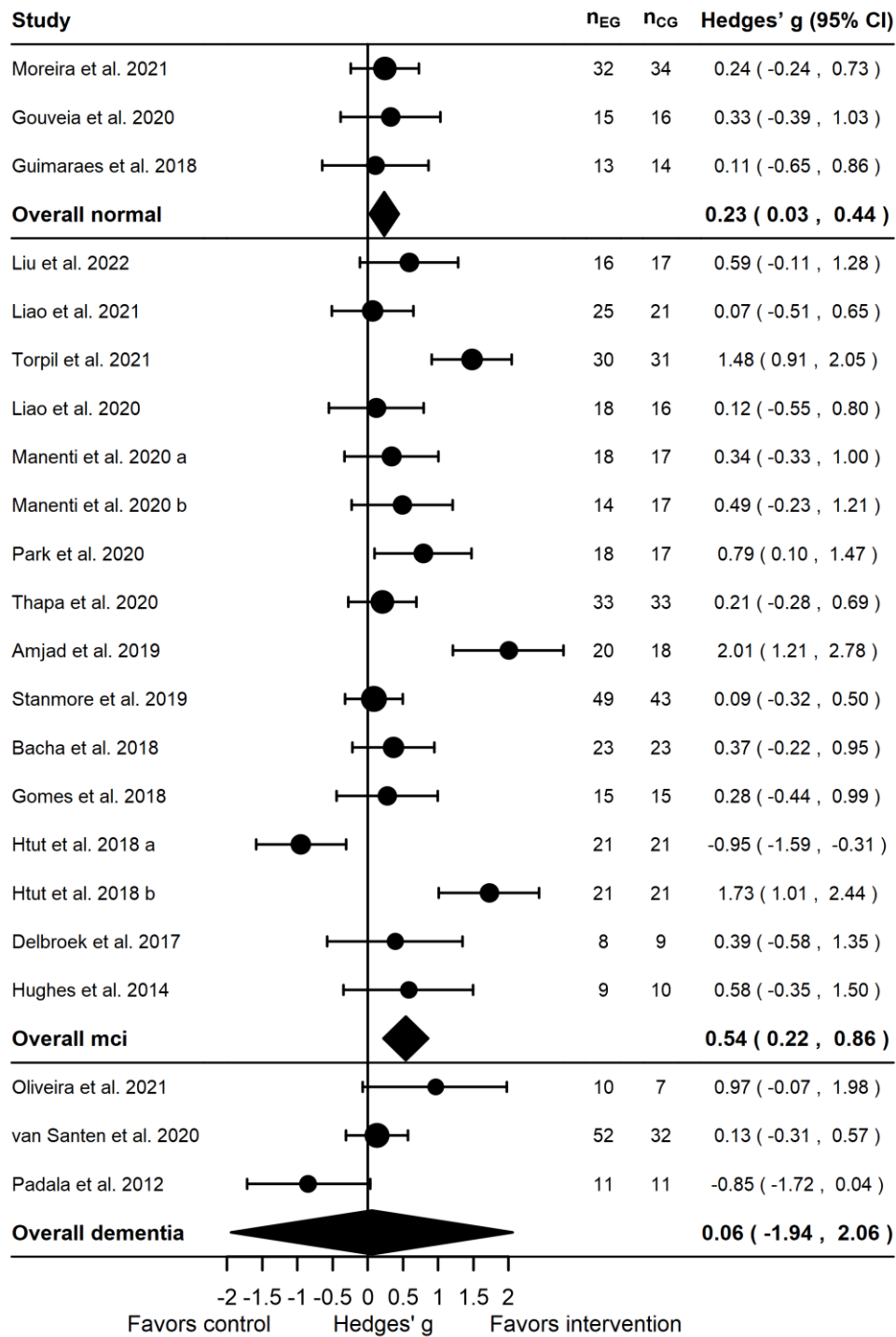
Appendix 2: Sensitivity analyses

Appendix 3: Narrative synthesis of results

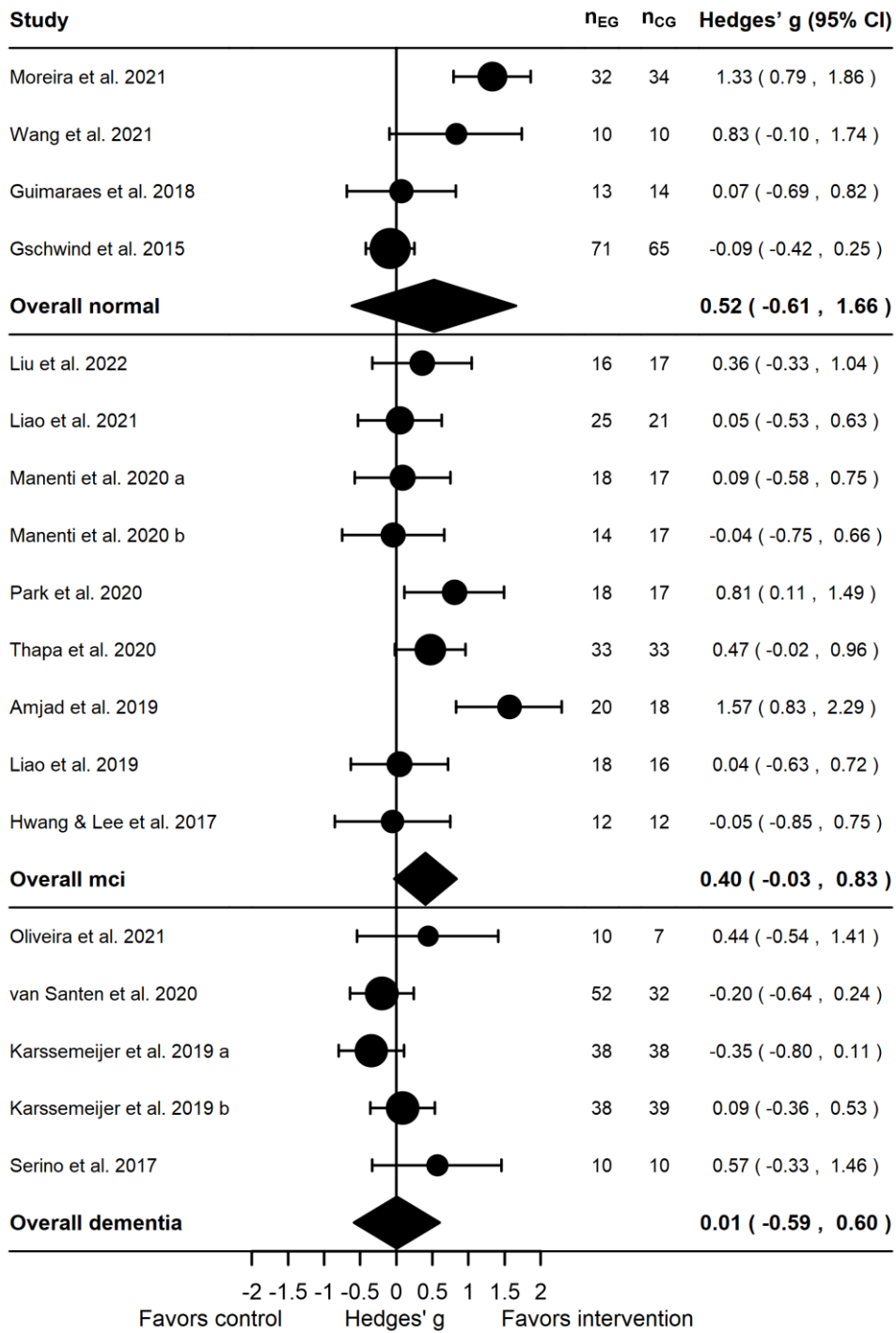
Appendix 1

Subgroup analyses for (a) global cognition and (b) executive function. The size of the circle in Hedges' g value shows the emphasis of an individual study in the pooled estimated effect.

(a)



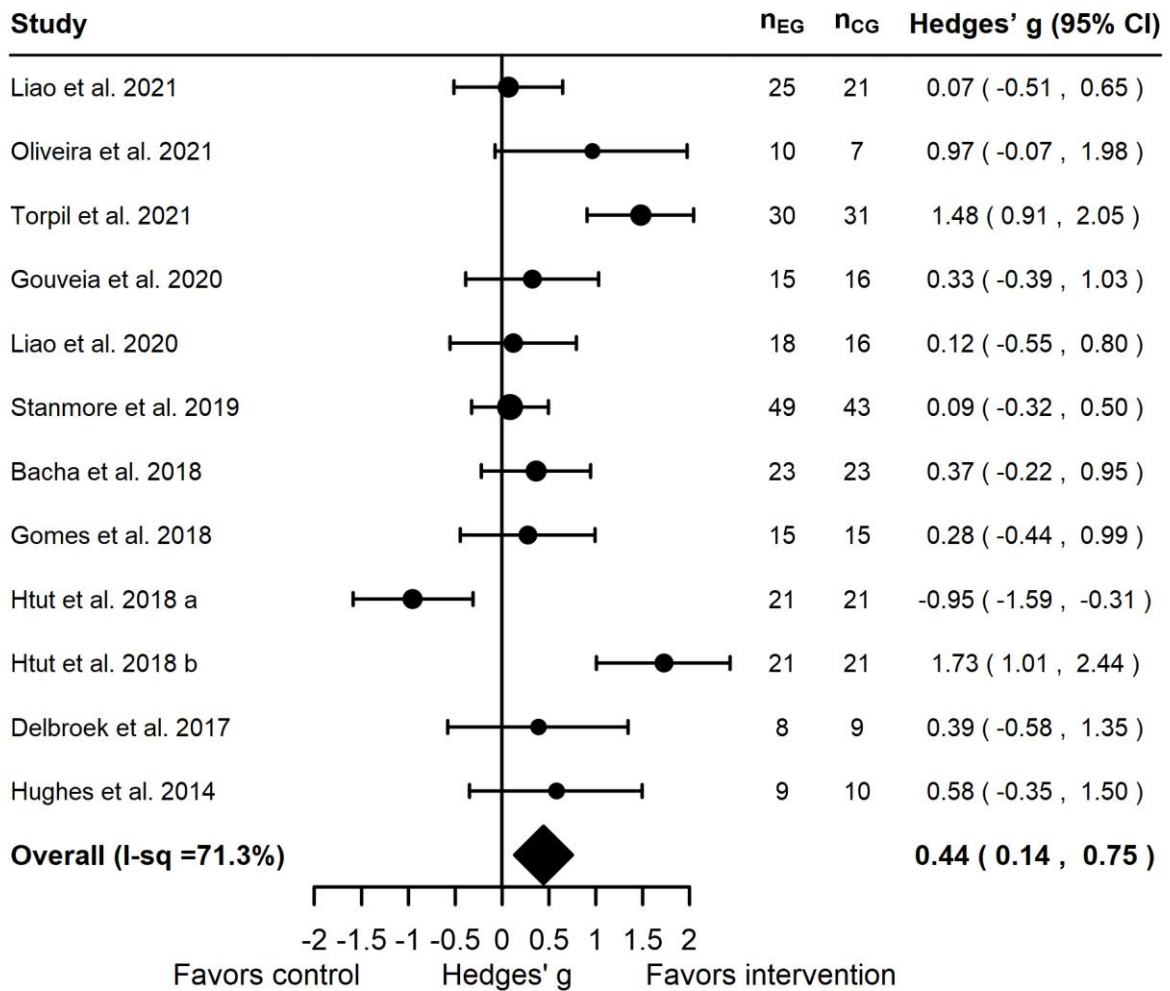
(b)



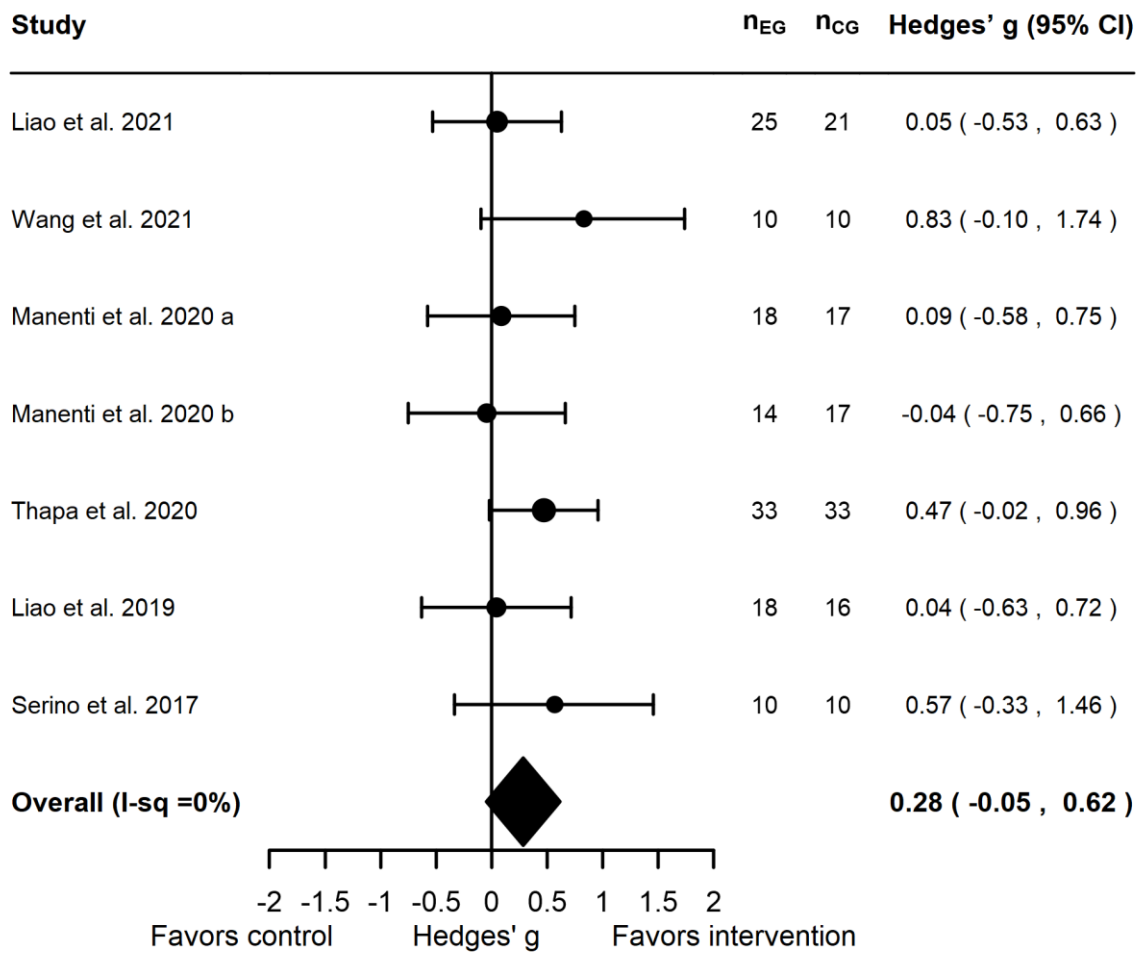
Appendix 2

Sensitivity analyses for (a) global cognition and (b) executive function

(a)



(b)



Appendix 3

Narrative synthesis of results

Five studies were excluded from meta-analysis due to insufficient numerical data (Anderson-Hanley et al. 2012, Gunst et al. 2022, Optale et al. 2010, Padala et al. 2017) and unclarity of cluster-randomization taken into account in the original analyses (Ramnath et al. 2021). Among MCI, intervention group with head-mounted display was observed to be more efficient in improving global cognition than music therapy and recreational activities (Optale et al. 2010). VR-training implemented as cyber cycling seemed to be more effective in improving executive function than stationary cycling (Anderson-Hanley et al. 2012). Interactive video gaming with Xbox Kinect Sport induced statistically significant improvement in global cognition and executive function compared with conventional multimodal physical exercise (Ramnath et al. 2021). Also some improvements were found in cognition by Xbox 360 Kinect Sport training compared with usual care of planned activities among older residents living in a residential care center (Gunst et al. 2022). However, the effect remained otherwise unclear and cognition level of participants was not reported nor was it able to be estimated from results as the direction of the outcome measure was not defined (Gunst et al. 2022).

Among people with mild dementia of Alzheimer's disease, no difference was found between VR-training and walking in global cognition (Padala et al. 2017).