Title:

Effects of cognitive remediation on cognition and psychosocial functioning in schizophrenia: are they durable? A systematic review and meta-analysis of randomized clinical trials

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Abstract (250 words)

Objective: Cognitive Remediation (CR) provides substantial improvements in cognitive performance and real-world functioning for people living with schizophrenia, but the durability of these benefits needs to be reassessed and better defined.

Aims were to provide a comprehensive assessment of CR durability benefits for cognition and functioning for people living with schizophrenia and evaluating potential moderators of effects.

Methods: The systematic search was conducted on three electronic databases (PubMed, Scopus, PsycInfo) on August 08, 2023. Reference lists of included articles and Google Scholar were manually inspected. Eligible studies were randomized clinical trials of CR in patients diagnosed with schizophrenia spectrum disorders including follow-up assessments. Screening and data extraction was performed by at least 2 independent reviewers. Cohen's d was used to measure outcomes. Primary outcomes were changes in cognition and functioning from baseline to follow-up conclusion. Moderators of effects durability were assessed.

Results: Of 2840 identified reports, 281 full texts were assessed and 130 reports on 67 studies with 5334 participants were included. CR produced positive effects that persisted at the end of follow-up in global cognition ($d=0.23$, $p<0.001$) and in global functioning ($d=0.26$, $p<0.001$). Smaller study samples and single-center studies positively influenced cognitive outcomes; longer treatment and follow-up duration, techniques to transfer cognitive gains to the real-world, integration with psychiatric rehabilitation, group format of delivery, and more women participants positively influenced functional outcomes.

Conclusions: CR provides durable improvements in cognition and functioning in schizophrenia. This corroborates the notion that CR should be implemented more widely into clinical and rehabilitation practice.

Keywords: Cognitive remediation; durability; evidence-based; follow-up; meta-analysis; persistence; schizophrenia

Introduction

Background

Cognitive deficits are a core feature of schizophrenia and are important determinants of functional impairment (1, 2), real-world outcomes (3, 4), quality of life (5–7), and limit recovery in the context of psychiatric rehabilitation (8–10).

Cognitive remediation (CR) interventions provide substantial improvements in cognitive performance and in functional outcomes (11–15) and have a good acceptability profile, comparable to that of other evidence-based interventions (16). Given its well-documented effectiveness, CR is currently the psychosocial intervention with the highest level of recommendation in the European Psychiatric Association Guidance for the treatment of cognitive impairment in people living with schizophrenia (17), and is mentioned as a valid intervention in other relevant guidelines dedicated to the global treatment of schizophrenia (18, 19). Despite these recommendations and suggestions, CR is still unevenly implemented into rehabilitation services, even in contexts with high levels of available resources (20, 21).

One potential barrier is durability of effects. If benefits of CR, particularly on functioning, are durable, then this provides further argument for its inclusion in mental health services. Several studies have reported that CR treatment has long-lasting positive effects (22–25). However, the most recent and comprehensive meta-analyses on CR effectiveness (12, 14) did not directly explore the issue of durability, which has only been taken into account in one of the earliest meta-analyses (26). We know that the four core ingredients of CR (27), (I) presence of an active and trained therapist, (II) repetition of exercises, (III) development of cognitive strategies, and (IV) techniques to transfer cognitive gains into the real world affect whether CR has a benefit and how large that benefit is. These ingredients may also affect treatment durability. Integration with psychiatric rehabilitation programs and longer durations of CR programs also have a positive impact on functioning, and it is also possible that demographic and clinical factors of participants affect the outcome.

An understanding of the durability of benefits and factors that contribute to the persistence of CR effects could also provide valuable information for clinical practice, especially on how to deliver and optimize personalized treatment programs.

Aims

This systematic review and meta-analysis complements previous meta-analyses (14, 16) by investigating the durability of CR benefits and assesses potential moderators, including treatment components and patient characteristics by exploring the results of randomized clinical trials that include follow-up assessments. The main hypotheses are that the positive effects of CR can persist over time and that factors with an impact on post-treatment effectiveness, such as the implementation of core ingredients, integration with psychiatric rehabilitation and longer duration of CR programs, may also act as moderators of effect duration.

Materials and Methods

Search Strategy and Selection Criteria

The review was conducted in accordance with the Preferred Reported Items for Systematic Review and Meta-analysis (PRISMA) guidelines (28, 29). The systematic literature search, completed on August 08, 2023, comprised 3 electronic databases (PubMed, Scopus and PsycInfo) using the search string [("cognitive" or "cognit*") AND ("training" or "remediation" or "rehabilitation" or "enhancement") AND ("schizophrenia" or "psychosis") AND ("random*" or "randomized control trial" or "clinical trial")], together with a manual search of Google Scholar (progressively updated) and of reference lists of emerging reviews and included papers.

Eligible studies were randomized trials recruiting participants with a diagnosis of schizophrenia spectrum disorders (at least 70% of the total sample), comparing CR interventions fulfilling the standard Experts Workshop definition (2010) to any control condition other than CR. Only studies that included a follow-up assessment of cognitive or functional performance were considered and no limitation concerning the minimal or maximal length of follow-up was applied. Duration of follow-up was considered as a continuous variable measured in weeks and as a categorical variable, dividing studies in the following length-based groups: (I) ≤ 1 month, (II) 1-3 months, (III) 4-6 months, (IV) >6 months, to establish whether a threshold of positive effects expiration or increase could be identified.

CR could be either delivered as a stand-alone treatment or integrated with other adequately controlled psychosocial interventions. No restriction was applied either to treatment setting, treatment duration or delivery mode.

As social cognitive training interventions usually show substantially different targets than other CR interventions, a subgroup analysis comparing intervention targeting social cognitive outcomes and those not considering social cognition as a treatment target was performed.

Studies investigating the effects Metacognitive Training (MCT) were included in previous meta-analyses (14, 16) and, in line with these works, have also been considered in the present analyses. However, since the classification of MCT as CR raised discussion among reviewers, and trials investigating its effectiveness often present only psychotic symptoms severity as main outcome (30), sensitivity analyses were conducted excluding these trials.

Screening was conducted by 2 independent reviewers with disagreements resolved by a third author. Only articles published in English in peer-reviewed journals were considered. Data extraction was also performed by 2 independent reviewers.

Quality Assessment

Methodological rigor of included studies was evaluated using the Clinical Trials Assessment Measure (CTAM) (31) by at least 2 reviewers. Study authors were not contacted to directly confirm CTAM scoring, but quality ratings were compared with those of other review groups reported in available publications (26, 32, 33), as in previous meta-analyses (14, 16). A cutoff score of 65 out of 100 total points was used to compare studies with adequate and inadequate methodology (34).

Outcomes of interest

The main outcomes were changes in global cognitive performance and overall psychosocial functioning from baseline (T0) to the end of the follow-up period (T2) to estimate the overall durability of effect. Changes from the early post-treatment phase (T1) to the end of the follow-up period (T2) were assessed as a sensitivity analysis in order to assess "sleeper effects", i.e. changes that might occur after the active intervention phase during the follow-up period.

Outcome measures

Cognition: Following Vita et al. (2021) we extracted data on all validated cognitive tasks and classified them in the 7 categories recognized by National Institute of Mental Health–Measurement and Treatment Research to Improve Cognition in Schizophrenia Neurocognition Committee (MATRICS)(35) (see Table S1). For each study, domain-specific effect sizes (ES) were calculated by averaging available ES of the individual measures referring to that specific domain; then, a composite global cognition ES was calculated by averaging the available domain-specific ES, following previous recommendations and studies (14, 26, 36). To address the important issue of synthesizing the results of studies with more thorough and more limited batteries, a metaregression analysis exploring the effect of the number of investigated MATRICS cognitive domains on global cognition outcomes was performed.

Psychosocial functioning: Self-, caregiver- and investigator-rated instruments were all eligible, independently from the area of functioning (e.g. daily life, education, work, interpersonal relationships). Both direct and indirect measures of functioning, such as functional capacity, and living and social skills, were included to obtain a comprehensive picture. Accordingly, quality of life measures were also included (see Table S1). To address the heterogeneity resulting from this approach, a subgroup analysis comparing studies using measures of real-world outcomes and those using performance-based instrument was performed. Another subgroup analysis was performed comparing studies including measures of quality of life and those that did not.

Potential moderators: The list of moderator variables explored is available in Appendix 1. We included all potential moderators explored in the analyses on early post-treatment effects (14). Moderator effects were explored one at a time.

Meta-analytic procedures

For each outcome, we calculated Cohen's *d* with the Carlson & Schimdt formula (37), while Standard Errors (SE) were calculated according to Cooper et al. (38). If raw group means, z-scores, and SDs were not directly available, the group × time interaction F values were used to derive ES and SE according to the suggestions of Thalheimer & Cook (39). If this was also not available, group scores and SD were extracted from available figures using WebPlotDigitizer version 4.2 (Rohatgi), which is a is a semi-automated tool that allows to extract numerical data form plot and images. Missing data were treated using an available-case approach; data resulting from intention-to-treat approaches were preferred.

For studies with multiple treatment arms, each eligible comparison was considered separately. Sensitivity analyses restricted to one ES per study were performed to rule out the issue of dependent ES (40, 41). For each study, outcome data for the longest follow-up assessment were included in the meta-analyses. A supplementary analysis was conducted for single categories of follow-up periods (≤1, 1-3, 3-6, >6 months), using all available outcome data for the specific timepoints (max 1 ES per category for each study).

A random-effects approach was applied considering the expected differences between studies, while a fixed-effect approach was adopted in sensitivity analyses. Meta-analyses and sub-group analyses were performed using Review Manager version 5.4 (The Cochrane Collaboration), meta-regressions were performed using Comprehensive Meta-Analysis version 4.0 (Biostat). Descriptive statistics and

analyses were performed using SPSS version 22 (SPSS Inc.). P-values < 0.05 (2-tailed) were considered significant for all analyses. Corrections for multiple comparison were not applied, and as such, only nominal p-values are reported.

Moderator effects and assessment of heterogeneity

Moderator effects were assessed in the baseline to end of follow-up analyses (T0-T2) using subgroup analyses for categorical variables and using metaregressions for continuous variables. Statistical heterogeneity was investigated through visual inspection of forest plots and assessment of Q-test and I^2 statistic. Sensitivity analyses excluding outliers (42) were performed for the main outcomes and relevant secondary analyses. Studies were defined as outliers for each outcome if their confidence interval did not overlap with the confidence interval of the pooled effect (i.e. their 95% CI lay outside the 95% CI of the pooled effect) (43). Sensitivity analyses are listed in Appendix 2.

Certainty of the evidence

Risk of publication bias was assessed by visual inspection of funnel plots and with the Egger test for asymmetry (44). If significant asymmetry emerged, adjustment of effect estimates was investigated with the trim-and-fill method, using both a random-random and a fixed-random effects model (45, 46). Other important determinants of the global quality of the evidence such as consistency, precision, and directness were explored according to experts' recommendations (47).

Results

The study selection procedure is shown in Figure 1. One hundred and thirty records, reporting data on 67 studies for a total of 75 CR-control comparisons and 5334 participants, were included; 4 ongoing studies were also identified. A complete list of included studies is provided in Appendix 3.

Included studies

Thirty-two studies were conducted in Europe, 17 in the USA, 14 in Asia, 3 in Canada and 1 in Australia. Twenty-five (37.3%) studies had a multicenter design, and 18 (26.9%) were conducted in research-oriented centers and not in a real-world clinical context. Most studies (46, 68.7%) included outpatients specifically. The mean sample size was 79.6±56.6 participants, with a wide range (10-377). Methodological quality was, overall, appropriate with an average CTAM score of 68.8±13.3 with 46 (68.7%) studies with a score ≥65. Included participants were representative of people living with schizophrenia and using mental health services, from individuals experiencing first episodes to those with a long-standing illness, with different clinical outcomes. Participants were aged 36.9±7.8

years, with a 23.5±2.3 years mean age of onset and a 13.8±7.3 years mean duration of illness. More than a third of the participants (35.8%) were women. These characteristics, computed over studies, are summarized in Table 1 and more detail can be found in Table S2. Scores for individual CTAM items for each included study are reported in Table S3.

CR interventions had a mean duration of 14.6±15.8 weeks (range 2-104) with a mean of 2.5±1.2 weekly sessions. Thirty-six (48.0%) interventions were delivered in a group format, and 54 (72.0%) included a computer presentation. CR core elements (27) were well represented, but only a limited number of programs, 35 (46.7%), included all 4 elements. The mean duration of follow-up was 24.9±15.2 weeks (range 3-65), with ≤1 month (4 studies), 2-3 months (18 studies), 4-6 months (26 studies) and ≥7 months (19 studies). The mean drop-out rate at the end of follow-up was 25.4±14.6% (range 0-64.4). The CR programs adopted in the included studies are listed in Table S4.

Durability of CR effects

CR produced a small and durable positive effect on global cognition (d=0.23, 95%CI 0.17-0.29, p<0.001; 70 comparisons, Figure S1) and on global functioning (d=0.26, 95%CI 0.15-0.36, p<0.001; 49 comparisons, Figure S2) compared to controls. Overall heterogeneity was low and non-significant for global cognition (Q=71.9, p=0.38; I^2=4.1%), while a higher level of heterogeneity was observed for global functioning (Q=102.0, p<0.001; I^2=52.9%).

In the sensitivity analyses investigating post-treatment to follow-up (T1-T2) effects, no significant increase or decrease in benefits for either global cognition (Figure S3) or global functioning emerged (Figure S4), with low levels of heterogeneity in both cases. No significant moderator effects were observed for T1-T2 analyses apart from a superior effect of pen-and-paper interventions on cognition (Table S5).

Moderator effects (see Table 2 and Table 3)

Quality of evidence: As expected, larger effects on global cognition were found if the study had a smaller sample size (p=0.020) and was conducted in a single center (p=0.041).

The number of included MATRICS domains in each study had no significant impact on global cognition (coefficient=0,004, 95%CI -0.023-0.037, p=0.754).

Study characteristics: Larger effects on functioning were observed in studies with longer follow-up duration (p= 0.003).

No significant moderator effect was observed for global cognition (p=0.730, Figure S5) in the subgroup analysis comparing different categories of follow-up duration; no significant effect was also observed on functioning, but a trend-level effect was observed suggesting a positive effect of longer follow-up observations (p=0.090, Figure S6).

No significant effect was observed in the subgroup analysis comparing studies using measures of real-world outcomes and those using performance-based instruments, but a trend-level difference was observed suggesting a greater effect size for real-world functional outcome measures (real world outcome measures: d=0.31, 95%CI 0.18-0.44, 33 comparisons; performance-based measures: d=0.14, 95%CI -0.01-0.28, 16 comparisons; χ^2=3.032, p= 0.082).

No substantial difference was observed between studies including measures of quality of life and those that did not (quality of life measures: d=0.15, 95%CI -0.05-0.34, 14 comparisons; no quality of life measures d=0.30, 95%CI -0.16-0.42, 35 comparisons; χ^2=1.664, p= 0.197).

Studies specifically targeting social cognition provided smaller effects as regards global cognition outcomes (p= 0.021), but no significant difference was observed on functioning (p=0.268, see Table 2).

Treatment components affecting durable benefits: Larger benefits were found for functioning if the CR intervention was integrated with psychiatric rehabilitation (p=0.038), included techniques for the transfer of cognitive gains to the real-world (p=0.025), had longer treatment duration (p=0.002) and group format of delivery (p=0.004).

Patient characteristics: Having a sample with more women participants (p=0.047) increased functioning at follow-up.

Certainty of the evidence

The main results were robust to sensitivity analyses, including those removing outliers. The results of all sensitivity analyses are reported in Table S6. Excluding the 7 studies on MCT interventions did not substantially change the main results (global cognition: d=0.25, 95%CI 0.18-0.31, p<0.001, 65 comparisons; global functioning: d=0.26, 95%CI 0.14-0.37, p<0.001, 45 comparisons). Statistical heterogeneity across studies was low, with negligible risk for inconsistency. Potential funnel plot asymmetry was observed for cognition (Egger's test p=0.004, see Figure S7). However, the adjustment of effect estimates performed using the trim-and-fill method showed resilience to this asymmetry, which was therefore not considered a significant cause for concern. No evidence of publication bias or funnel plot asymmetry emerged for functioning (see Figure S8).

Discussion

Durability of CR effects

The conclusion of our analyses is that CR has durable positive effects on cognition and functioning of people living with schizophrenia, with follow-up effect sizes comparable to those observed at post-treatment assessments (12, 14, 15). Also, no major changes between post-treatment and follow-up emerged, further confirming the durability of CR benefits.

The observed effects are slightly smaller than those observed in the previous comprehensive meta-analysis that also considered follow-up assessments (26). This could be due to the inclusion of several more recent and methodologically rigorous articles, and it can be also explained by the wider heterogeneity of the included participants and interventions.

Durability of effects represents one of the fundamental aims of CR (27): the results of these analyses confirm that CR programs actually fulfil this aim, thus confirming the role of CR as an evidence-based intervention that, if properly implemented in rehabilitation settings, could consistently help people living with schizophrenia in achieving their recovery goals (17).

Moderator effects

For global cognition, significant moderator effects were mostly related to study quality elements such as the sample size and the single- or multi-center organization of the study. Studies investigating interventions that specifically targeted social cognition outcomes provided smaller effects on global cognition compared to other CR interventions: this is an expected outcome, which in part could also be due to the heterogeneous nature of included assessment instruments. However, no difference was observed as regards functional outcomes, confirming that both types of interventions can provide durable functional benefits for participants.

Several moderators of effects emerged as significant for durable improvements in global functioning, with important clinical implications. The presence of techniques to transfer cognitive gains into the real-world and integration with structured psychiatric rehabilitation programs produced a durable positive effect on global functioning. Moreover, the observed size of positive effects increased from small to moderate if only studies including a psychiatric rehabilitation program were considered. This was an expected result, as these elements also increases effectiveness early after active treatment (14) and our results suggest they are essential to promote durability of functional gains: considering these findings, providing CR interventions that foster the transfer of cognitive gains in real-world contexts

and are integrated within a structured psychiatric rehabilitation program might represent an important step to improve the participants' recovery process.
The fact that the durability of CR effects remains robust in the face of differences in sample age and symptoms severity is also important and confirms that CR represents a valuable intervention even in older subjects and in participants with a more severe clinical condition (14).

Other specific CR core ingredients did not appear to provide superior durability of positive effects compared to those that did not include them. These factors have been demonstrated to have great importance in CR effectiveness (14, 27). However, the current results could also be due to the characteristics of the sub-group analysis, performed on a very limited number of studies, which often did not consider each CR core element.

Providing the intervention in a group produced greater effects on functioning which has also been found in other recent meta-analytic studies (12) and is expected as these settings are often integrated into rehabilitation services. A group setting might also offer more opportunities for peer-based learning as well as offering opportunities for supporting implementation of social skills. Independent learning here also includes those who receive one-to-one learning as well as independent CR at home. In fact, in the included studies, group interventions were delivered by an active and trained therapist in almost all cases, so there might be a partial overlap between these two factors.

Functional improvements increased with longer treatment duration, which is also found at post-treatment (14) and although no threshold for optimal treatment duration has been identified more sessions may be important. These positive effects also do not fade over time, but instead they are considerably durable.
The finding that longer follow-up was associated with larger functional improvements, observed both considering follow-up duration as a continuous variable in a metaregression and at a trend level considering different follow-up lengths as categories in a subgroup analysis, could also better reflect the ability to use available opportunities, for instance in community activities and employment. Functional improvement might therefore take more time to become evident compared to cognitive gains and might require several months for cognitive gains to be transferred to real-life settings. This suggests that formal interventions could be implemented after and beside CR programs that could further facilitate this transfer process.

Despite these findings, it must be noted that most of the included studies presented a follow-up of relatively short duration: in this regard, little is known about the long-term durability of CR effects in schizophrenia, and more studies with longer follow-up observations are currently needed.

The subgroup-analysis comparing studies using measures of real-world outcomes and those using performance-based instruments did not yield statistically significant results, suggesting that CR interventions provides durable functional benefits regardless of the instrument used to assess participants' functioning. However, a trend-level effect was observed suggesting that measures of real-world outcomes provided larger effect sizes: indeed, these measures may better reflect participants' real-world improvements.

Female gender has emerged as a significant element only in a few studies (48), and not consistently (32). A substantial body of evidence has described a better course of schizophrenia in women compared with men, in terms of better psychosocial functioning, higher achievement of recovery and better response to treatment on the whole (49–52), and this could also influence the durability of the effects of psychosocial interventions such as CR. These differences could be explained by both biological and social factors (53) (54, 55) although as yet there is little agreement on this balance and it may depend on the phase of the illness, and on the recovery measures used (56–60). Interest on the topic is growing and further investigation could yield promising inputs for the development and administration of individualized rehabilitative interventions.

Strength and limitations

The large number of included studies, the representativeness of included samples and the robustness of findings can be considered relevant points of strength of the present work. However, potential between-moderators interactions could not be explored. This is of clinical relevance as identifying the most impactful moderators could be of great practical use in mental health services to optimize and personalize treatment programs. In this regard, a network meta-analysis approach could represent an interesting perspective for future research. While including large samples and applying rigorous method to conduct the analyses consistently reduce the likelihood of this occurrence, the possibility of incurring in Type I errors has to be taken into account in randomized clinical trials as well as in meta-analytical studies. Single study Authors were not directly contacted to confirm the CTAM scoring used in the present work; however, were available, quality ratings were compared with those of other review groups reported in other systematic literature assessments. Finally, direct measures of real-world outcomes such as obtaining a job and days worked, which may be considered

significantly more important than validated scale-based measures, could not be included in the present analyses. This is quite regrettable, as indeed these outcomes are of considerable importance, but as they were not measured with validated scales, and were measured in very different ways across studies, it was not possible to combine results across different studies. Future research conducted with a methodological approach that is specifically designed to better analyze the impact of CR interventions on direct real-world outcomes could be of considerable clinical and scientific interest.

Conclusions

The results of this comprehensive systematic review and meta-analysis show that CR interventions in schizophrenia not only produce positive effects on cognitive performance and psychosocial functioning, but also provide improvements that are small but durable. The most clinically useful recommendation is not only to provide CR to help patients reach their recovery goals but to allow patients to receive longer treatments as these are more likely to be cost-effective for functional gains. The evidence is now overwhelming that CR should be more widely implemented into clinical and rehabilitation practice so our patients can receive an effective intervention.

Author Contributions:
Prof. Vita had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Vita, Barlati, Ceraso, Nibbio, Deste, Wykes.

Acquisition, analysis, or interpretation of data: Vita, Barlati, Ceraso, Nibbio, Durante, Facchi, Deste, Wykes.

Drafting of the manuscript: Vita, Ceraso, Nibbio, Deste, Wykes.

Critical revision of the manuscript for important intellectual content: Vita, Barlati, Ceraso, Nibbio, Deste, Wykes.

Statistical analysis: Ceraso, Nibbio, Deste, Wykes.

Administrative, technical, or material support: Wykes.

Supervision: Vita, Barlati.

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References

1. Galderisi S, Rossi A, Rocca P, et al.: The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. World Psychiatry 2014; 13:275–287

2. Green MF, Horan WP, Lee J: Nonsocial and social cognition in schizophrenia: current evidence and future directions. World Psychiatry 2019; 18:146–161

3. Galderisi S, Rucci P, Kirkpatrick B, et al.: Interplay Among Psychopathologic Variables, Personal Resources, Context-Related Factors, and Real-life Functioning in Individuals With Schizophrenia: A Network Analysis. JAMA Psychiatry 2018; 75:396–404

4. Maj M, van Os J, De Hert M, et al.: The clinical characterization of the patient with primary psychosis aimed at personalization of management. World Psychiatry 2021; 20:4–33

5. Maat A, Fett A-K, Derks E: Social cognition and quality of life in schizophrenia. Schizophrenia Research 2012; 137:212–218

6. Matsui M, Sumiyoshi T, Arai H, et al.: Cognitive functioning related to quality of life in schizophrenia. Progress in Neuro-Psychopharmacology and Biological Psychiatry 2008; 32:280–287

7. Tolman AW, Kurtz MM: Neurocognitive predictors of objective and subjective quality of life in individuals with schizophrenia: a meta-analytic investigation. Schizophr Bull 2012; 38:304–315

8. Spaulding WD, Sullivan ME: Treatment of Cognition in the Schizophrenia Spectrum: The Context of Psychiatric Rehabilitation. Schizophr Bull 2016; 42 Suppl 1:S53-61

9. Vita A, Barlati S: Recovery from schizophrenia: is it possible? Curr Opin Psychiatry 2018; 31:246–255

10. Wykes T, Dunn G: Cognitive deficit and the prediction of rehabilitation success in a chronic psychiatric group. Psychol Med 1992; 22:389–398

11. Kambeitz-Ilankovic L, Betz LT, Dominke C, et al.: Multi-outcome meta-analysis (MOMA) of cognitive remediation in schizophrenia: Revisiting the relevance of human coaching and elucidating interplay between multiple outcomes. Neurosci Biobehav Rev 2019; 107:828–845

12. Lejeune JA, Northrop A, Kurtz MM: A Meta-analysis of Cognitive Remediation for Schizophrenia: Efficacy and the Role of Participant and Treatment Factors. Schizophrenia Bulletin 2021; 47:997–1006

13. van Duin D, de Winter L, Oud M, et al.: The effect of rehabilitation combined with cognitive remediation on functioning in persons with severe mental illness: systematic review and meta-analysis. Psychol Med 2019; 49:1414–1425

14. Vita A, Barlati S, Ceraso A, et al.: Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia: A Systematic Review and Meta-analysis of Randomized Clinical Trials. JAMA Psychiatry 2021; 78:848–858

15. Yeo H, Yoon S, Lee J, et al.: A meta-analysis of the effects of social-cognitive training in schizophrenia: The role of treatment characteristics and study quality. British Journal of Clinical Psychology 2022; 61:37–57

16. Vita A, Barlati S, Ceraso A, et al.: Acceptability of cognitive remediation for schizophrenia: a systematic review and meta-analysis of randomized controlled trials. Psychological Medicine 2022; 1–11

17. Vita A, Gaebel W, Mucci A, et al.: European Psychiatric Association guidance on treatment of cognitive impairment in schizophrenia. European Psychiatry 2022; 65:e57

18. Keepers GA, Fochtmann LJ, Anzia JM, et al.: The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia. AJP 2020; 177:868–872

19. National Institute for Health and Care Excellence: Rehabilitation for adults with complex psychosis NICE guideline [Internet]2020; Available from: https://www.nice.org.uk/guidance/ng181/resources/rehabilitation-for-adults-with-complex-psychosis-pdf-66142016643013

20. Vita A, Barlati S: The Implementation of Evidence-Based Psychiatric Rehabilitation: Challenges and Opportunities for Mental Health Services [Internet]. Frontiers in Psychiatry 2019; 10[cited 2022 Jul 28] Available from: https://www.frontiersin.org/articles/10.3389/fpsyt.2019.00147

21. Wykes T: Cognitive remediation – where are we now and what should we do next? Official Journal of the Italian Society of Psychopathology 2018; 24:57–61

22. Deste G, Barlati S, Cacciani P, et al.: Persistence of effectiveness of cognitive remediation interventions in schizophrenia: a 1-year follow-up study. Schizophr Res 2015; 161:403–406

23. Horan WP, Dolinsky M, Lee J, et al.: Social Cognitive Skills Training for Psychosis With Community-Based Training Exercises: A Randomized Controlled Trial. Schizophr Bull 2018; 44:1254–1266

24. Tan S, Zhu X, Fan H, et al.: Who will benefit from computerized cognitive remediation therapy? Evidence from a multisite randomized controlled study in schizophrenia. Psychol Med 2020; 50:1633–1643

25. Vaskinn A, Løvgren A, Egeland MK, et al.: A randomized controlled trial of training of affect recognition (TAR) in schizophrenia shows lasting effects for theory of mind. Eur Arch Psychiatry Clin Neurosci 2019; 269:611–620

26. Wykes T, Huddy V, Cellard C, et al.: A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. Am J Psychiatry 2011; 168:472–485

27. Bowie CR, Bell MD, Fiszdon JM, et al.: Cognitive remediation for schizophrenia: An expert working group white paper on core techniques. Schizophrenia Research 2020; 215:49–53

28. Moher D, Liberati A, Tetzlaff J, et al.: Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Medicine 2009; 6:e1000097

29. Page MJ, McKenzie JE, Bossuyt PM, et al.: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71

30. Penney D, Sauvé G, Mendelson D, et al.: Immediate and Sustained Outcomes and Moderators Associated With Metacognitive Training for Psychosis: A Systematic Review and Meta-analysis. JAMA Psychiatry 2022; 79:417–429

31. Tarrier N, Wykes T: Is there evidence that cognitive behaviour therapy is an effective treatment for schizophrenia? A cautious or cautionary tale? Behav Res Ther 2004; 42:1377–1401

32. Seccomandi B, Tsapekos D, Newbery K, et al.: A systematic review of moderators of cognitive remediation response for people with schizophrenia. Schizophr Res Cogn 2020; 19:100160

33. Grant N, Lawrence M, Preti A, et al.: Social cognition interventions for people with schizophrenia: a systematic review focussing on methodological quality and intervention modality. Clin Psychol Rev 2017; 56:55–64

34. Wykes T, Steel C, Everitt B, et al.: Cognitive behavior therapy for schizophrenia: effect sizes, clinical models, and methodological rigor. Schizophr Bull 2008; 34:523–537

35. Nuechterlein KH, Barch DM, Gold JM, et al.: Identification of separable cognitive factors in schizophrenia. Schizophr Res 2004; 72:29–39

36. Van den Noortgate W, López-López JA, Marín-Martínez F, et al.: Meta-analysis of multiple outcomes: a multilevel approach. Behav Res Methods 2015; 47:1274–1294

37. Carlson KD, Schmidt FL: Impact of experimental design on effect size: Findings from the research literature on training. Journal of Applied Psychology 1999; 84:851–862

38. Cooper H, Hedges LV, Valentine JC: The handbook of research synthesis and meta-analysis. Russell Sage Foundation, 2019

39. Thalheimer W, Cook S: How to calculate effect sizes from published research: A simplified methodology. Work-Learning Research 2002; 1

40. Rücker G, Cates CJ, Schwarzer G: Methods for including information from multi-arm trials in pairwise meta-analysis. Res Synth Methods 2017; 8:392–403

41. Van den Noortgate W, López-López JA, Marín-Martínez F, et al.: Three-level meta-analysis of dependent effect sizes. Behav Res Methods 2013; 45:576–594

42. Viechtbauer W, Cheung MW-L: Outlier and influence diagnostics for meta-analysis. Res Synth Methods 2010; 1:112–125

43. Harrer M, Cuijpers P, Furukawa T, et al.: Doing meta-analysis with R: A hands-on guide. Chapman and Hall/CRC, 2021

44. Egger M, Smith GD, Schneider M, et al.: Bias in meta-analysis detected by a simple, graphical test. BMJ 1997; 315:629–634

45. Duval S, Tweedie R: Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000; 56:455–463

46. Peters JL, Sutton AJ, Jones DR, et al.: Performance of the trim and fill method in the presence of publication bias and between-study heterogeneity. Stat Med 2007; 26:4544–4562

47. Schünemann H: The GRADE Handbook. Cochrane Collaboration, 2013

48. Nijman SA, Veling W, van der Stouwe ECD, et al.: Social Cognition Training for People With a Psychotic Disorder: A Network Meta-analysis. Schizophr Bull 2020; sbaa023

49. Ayesa-Arriola R, Setién-Suero E, Neergaard KD, et al.: Premorbid IQ subgroups in first episode non affective psychosis patients: Long-term sex differences in function and neurocognition. Schizophr Res 2018; 197:370–377

50. Prat G, Escandell MJ, Garcia-Franco M, et al.: Gender differences in social functioning in people with schizophrenia in psychosocial rehabilitation services using one-dimensional and multidimensional instruments. Compr Psychiatry 2018; 87:120–122

51. Santesteban-Echarri O, Paino M, Rice S, et al.: Predictors of functional recovery in first-episode psychosis: A systematic review and meta-analysis of longitudinal studies. Clin Psychol Rev 2017; 58:59–75

52. Thorup A, Albert N, Bertelsen M, et al.: Gender differences in first-episode psychosis at 5-year follow-up--two different courses of disease? Results from the OPUS study at 5-year follow-up. Eur Psychiatry 2014; 29:44–51

53. Weickert TW, Allen KM, Weickert CS: Potential Role of Oestrogen Modulation in the Treatment of Neurocognitive Deficits in Schizophrenia. CNS Drugs 2016; 30:125–133

54. Li AWY, Hui CLM, Lee EHM, et al.: Gender differences in correlates of cognition in first-episode psychosis. Psychiatry Res 2019; 271:412–420

55. Mazza M, Caroppo E, De Berardis D, et al.: Psychosis in Women: Time for Personalized Treatment. Journal of Personalized Medicine 2021; 11:1279

56. Dubreucq M, Plasse J, Gabayet F, et al.: Sex Differences in Recovery-Related Outcomes and Needs for Psychiatric Rehabilitation in People With Schizophrenia Spectrum Disorder. J Clin Psychiatry 2021; 82:20m13732

57. Giordano GM, Bucci P, Mucci A, et al.: Gender Differences in Clinical and Psychosocial Features Among Persons With Schizophrenia: A Mini Review. Front Psychiatry 2021; 12:789179

58. Jääskeläinen E, Juola P, Hirvonen N, et al.: A systematic review and meta-analysis of recovery in schizophrenia. Schizophr Bull 2013; 39:1296–1306

59. Ochoa S, Usall J, Cobo J, et al.: Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review. Schizophr Res Treatment 2012; 2012:916198

60. Seeman MV: Does Gender Influence Outcome in Schizophrenia? Psychiatr Q 2019; 90:173–184

Figure 1: Prisma Study Flow Diagram

Table 1: Descriptive characteristics of 67 included studies reporting data on 75 intervention-control comparisons (5334 participants)

Variable	N	Mean /n	±SD/%	Range, Lower	Range, Upper
Study characteristics					
Study design (N multicentric studies)	67	25	37,31		
Setting	67				
Real-world		49	73,13		
Research-oriented		18	26,87		
Setting	67				
Outpatients		46	68,66		
Inpatients		13	19,40		
Both		8	11,94		
Sample Size (N randomized)	67	79,61	± 56,56	10	377
Methodological quality	67				
CTAM total score (score 0-100)		68,79	± 13,34	27	94
Studies with adequate quality (score ≥65)		46	68,66		
Blinding of outcome assessments (N blind studies)	67	53	79,10		
Only subjects with schizophrenia included	67	24	35,82		
Comparison categories	75				
TAU		22	29,33		
Active TAU		10	13,34		
Active non-specific interventions		21	28,00		
Active evidence-based interventions		22	29,33		
Follow-up attrition rate (%)	67	25,44	± 14,60	0	64,44
Follow-up duration (weeks)	67	24,91	± 15,23	3	65
Patient and illness characteristics					
Age (years)	67	36,93	± 7,80	15,29	50,56
Gender (% female subjects)	65	35,84	± 12,86	0	70
Education (years)	40	11,98	± 1,64	6,49	14,94
IQ	30	96,89	± 6,60	85,23	107,70
Age of onset (years)	44	23,51	± 2,28	17,03	27,56
Duration of illness (years)	44	13,80	± 7,30	1,17	34,48
Baseline treatment dose (CPZeq)	37	466,04	± 196,84	182,50	1067,60
Baseline symptoms severity (PANSS score)	46	64,34	± 15,22	39,94	118,40
Baseline positive symptoms (PANSS positive scale)	34	14,96	± 4,58	8,41	28,92
Baseline negative symptoms (PANSS negative scale)	34	17,46	± 4,50	10,70	32,32
Treatment characteristics					
Treatment duration (weeks)	75	14,65	± 15,82	2	104
Treatment intensity (sessions/week)	72	2,49	± 1,20	1	6
Treatment intensity (hours/week)	69	2,47	± 1,29	0,67	6
Format of delivery (N group sessions)	75	36	48,00		
Computer presentation (N computerized)	75	54	72,00		
Targeting social cognition (N with target)	75	28	37,33		
Core elements according to Bowie et al.	75				
1. Active and trained therapist		64	85,33		
2. Repetitive practice of cognitive exercises (≥20 hours)		53	70,67		
3. Development of cognitive strategies		61	81,33		
4. Techniques of transfer to real-world		60	80,00		
4bis. Integration with rehabilitation		28	37,33		
Interventions including all core elements		35	46,67		

Table 2: Effects of moderators on cognitive and functional outcomes, metaregressions (T0-T2)

Moderator	Global Cognition					Global Functioning				
	N	Coefficient	95% CI, Lower	95% CI, Upper	p	N	Coefficient	95% CI, Lower	95% CI, Upper	p
Study characteristics										
Publication year	70	-0,008	-0,019	0,002	0,132	49	-0,009	-0,029	0,011	0,361
Methodological Quality (CTAM score)	70	-0,004	-0,009	0,001	0,102	49	-0,004	-0,012	0,004	0,338
Follow-up duration (weeks)	70	-0,001	-0,004	0,004	0,949	49	0,011	0,004	0,019	**0,003**
Sample size (N randomized)	70	-0,002	-0,003	-0,001	**0,020**	49	0,001	-0,002	0,003	0,759
Treatment characteristics										
Treatment duration (weeks)	70	0,001	-0,003	0,005	0,603	49	0,008	0,003	0,012	**0,002**
Treatment intensity (sessions/week)	68	0,015	-0,035	0,065	0,560	47	-0,038	-0,124	0,047	0,380
Treatment intensity (hours/week)	65	0,013	-0,033	0,059	0,579	47	-0,014	-0,099	0,072	0,751
Patient and illness characteristics										
Age (years)	70	0,003	-0,005	0,010	0,498	49	0,004	-0,008	0,017	0,513
Gender (% female subjects)	67	-0,001	-0,007	0,005	0,715	47	0,010	0,001	0,019	**0,047**
Education (years)	42	-0,004	-0,059	0,051	0,887	30	-0,063	-0,139	-0,013	0,103
IQ	31	0,003	-0,009	0,015	0,642	25	0,001	-0,020	0,021	0,966

Moderator	Global Cognition					Global Functioning				
	N	Coefficient	95% CI, Lower	95% CI, Upper	p	N	Coefficient	95% CI, Lower	95% CI, Upper	p
Age of onset (years)	44	-0,027	-0,061	0,007	0,124	32	-0,004	-0,058	0,051	0,900
Duration of illness (years)	44	0,002	-0,007	0,012	0,632	32	-0,003	-0,021	0,014	0,711
Baseline treatment dose (CPZeq)	38	-0,001	-0,001	0,000	0,189	31	-0,001	-0,001	0,001	0,346
Baseline symptoms severity (PANSS score)	48	0,003	-0,002	0,008	0,284	35	-0,001	-0,009	0,007	0,790
Baseline positive symptoms (PANSS-P)	35	-0,002	-0,023	0,020	0,881	26	-0,011	-0,045	0,022	0,503
Baseline negative symptoms (PANSS-N)	36	0,013	-0,010	0,036	0,281	26	-0,007	-0,047	0,032	0,718

Coefficients values in metaregressions indicate that a one-unit increase in the moderator corresponds to an increase in the effect size by the amount indicated by the corresponding regression coefficient.

Table 3: Effects of moderators on cognitive and functional outcomes, subgroup analyses (T0-T2)

Moderator	Global Cognition							Global Functioning						
	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p
Study characteristics														
Methodological Quality														
Adequate (CTAM ≥ 65)	51	0,25*	0,18	0,32				35	0,21*	0,10	0,33			
Inadequate (CTAM < 65)	19	0,17*	0,05	0,30				14	0,39*	0,17	0,61			
Test for subgroup differences					1,125	1	0,289					1,985	1	0,159
Blinding														
Open trials	13	0,33*	0,14	0,52				8	0,46*	0,14	0,79			
Blind trials	57	0,21*	0,15	0,28				41	0,22*	0,11	0,32			
Test for subgroup differences					1,363	1	0,243					1,941	1	0,164
Setting														
Outpatients	50	0,24*	0,16	0,31				34	0,28*	0,15	0,40			
Inpatients	14	0,29*	0,16	0,43				8	0,30	-0,03	0,62			
Both	6	0,12	-0,07	0,30				7	0,14	-0,08	0,36			
Test for subgroup differences					2,329	2	0,312					1,223	2	0,543
Setting														
Single centre	45	0,29*	0,21	0,37					0,30*	0,13	0,46			
Multi-centre	25	0,17*	0,08	0,25					0,22*	0,09	0,35			

Moderator	Global Cognition							Global Functioning						
	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p
Test for subgroup differences					4,191	1	**0,041**					0,440	1	0,507
Setting														
Real-world	49	0,24*	0,16	0,33				34	0,28*	0,15	0,41			
Research	21	0,22*	0,13	0,32				15	0,22*	0,05	0,39			
Test for subgroup differences					0,102	1	0,750					0,292	1	0,589
Comparison category														
TAU	21	0,19*	0,09	0,30				15	0,22*	0,04	0,39			
Active TAU	8	0,17*	0,02	0,33				7	0,33*	0,09	0,57			
Active non-specific interventions	21	0,22*	0,10	0,34				14	0,27*	0,03	0,51			
Active evidence-based interventions	20	0,34*	0,19	0,48				13	0,26*	0,05	0,48			
Test for subgroup differences					3,202	3	0,361					0,572	3	0,903
Diagnosis for inclusion														
Only subjects with schizophrenia	24	0,30*	0,16	0,44				17	0,26*	0,03	0,48			
Including other diagnoses	46	0,21*	0,14	0,28				32	0,26*	0,15	0,38			
Test for subgroup differences					1,259	1	0,262					0,005	1	0,944
Treatment characteristics														
Active and trained therapist (Core element 1)														
Present	59	0,23*	0,17	0,30				44	0,28*	0,17	0,39			

Moderator	Global Cognition							Global Functioning						
	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p
Absent	11	0,23*	0,07	0,40				5	0,05	-0,17	0,27			
Test for subgroup differences					0,000	1	0,982					3,364	1	0,067
Repeated practice of cognitive exercises (Core element 2)														
Present	52	0,25*	0,18	0,31				38	0,25*	0,13	0,37			
Absent	18	0,17*	0,03	0,31				11	0,27*	0,06	0,48			
Test for subgroup differences					0,989	1	0,320					0,013	1	0,910
Development of cognitive strategies (Core element 3)														
Present	56	0,24*	0,17	0,31				42	0,29*	0,17	0,40			
Absent	14	0,20*	0,07	0,33				7	0,08	-0,09	0,26			
Test for subgroup differences					0,307	1	0,580					3,696	1	0,055
Techniques of transfer to real-world (Core element 4)														
Present	55	0,20*	0,14	0,27				40	0,30*	0,18	0,42			
Absent	15	0,36*	0,20	0,52				9	0,06	-0,11	0,23			
Test for subgroup differences					3,078	1	0,079					5,013	1	**0,025**
Integration with rehabilitation (Core element 4bis)														
Present	24	0,22*	0,13	0,32				16	0,41*	0,23	0,58			

Moderator	Global Cognition							Global Functioning						
	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p
Absent	46	0,24*	0,16	0,32				33	0,18*	0,06	0,30			
Test for subgroup differences					0,063	1	0,802					4,305	1	**0,038**
Interventions including all core elements (1,2,3,4)														
All core elements	34	0,24*	0,16	0,32				26	0,34*	0,19	0,49			
Not all core elements	36	0,23*	0,13	0,32				23	0,15*	0,02	0,28			
Test for subgroup differences					0,032	1	0,857					3,754	1	0,053
Format of delivery														
Individual format	38	0,28*	0,18	0,37				26	0,12	-0,01	0,25			
Group format	32	0,19*	0,11	0,27				23	0,40*	0,26	0,54			
Test for subgroup differences					1,872	1	0,171					8,242	1	**0,004**
Computer presentation														
Computerized intervention	52	0,21*	0,15	0,28				35	0,28*	0,15	0,40			
Pencil-and-paper intervention	18	0,33*	0,16	0,49				14	0,20*	0,02	0,38			
Test for subgroup differences					1,593	1	0,207					0,536	1	0,464
Social cognition among CR targets														
Target on social cognition	45	0,14*	0,05	0,24				20	0,33*	0,16	0,08			
No target	25	0,29*	0,2	0,37				29	0,21*	0,08	0,34			

Moderator	Global Cognition							Global Functioning						
	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p	N	Effect Size	95% CI, Lower	95%CI, Upper	χ^2	dF	p
Test for subgroup differences					5,309	1	**0,021**					1,226	1	0,268

*: statistically significant effect ($p<0.05$)

Figure 1: Prisma Study Flow Diagram

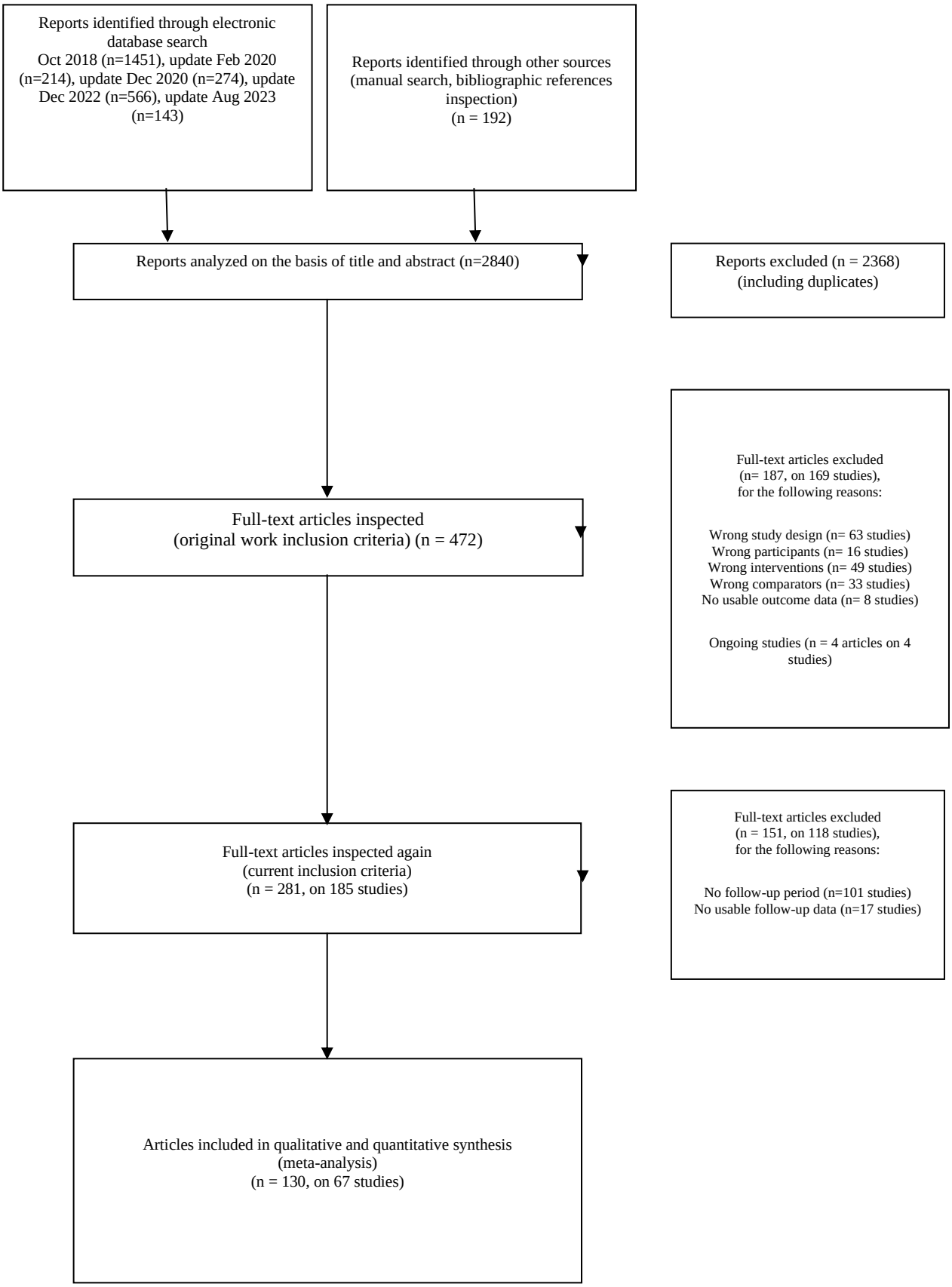


Table S1. List of rating scales and corresponding cognitive domains

Attention/Vigilance Continuous Performance Tests (CPT) D2 Letter Cancellation Test Sustained Attention Test (SAT) Test of Sustained and Selective Attention (TASS) Digit Vigilance Test Triads Test Backward Masking Test (BMT) Span of Apprehension tests **Processing Speed** Trail Making Test, Part A (TMT-A) Digit Symbol Substitution Test Symbol Digit Modalities Test (SDMT) WAIS Digit Symbol BACS Symbol Coding BACS Token Motor Controlled Oral Word Association Test (COWAT- FAS) Other Verbal Fluency tests (Category and Letter) Stroop Test, Color and Word conditions Reaction Time tests **Working Memory** Trail Making Test, Part B (TMT-B) WAIS or WMS Letter-Number Sequencing WMS Visual/Spatial Span Sentence Span tests WAIS, WISC or WMS Digit Span Digit Span Distractibility Test BACS Digit Sequencing Other Digit Span tasks RBANS Attention CANTAB Spatial Working Memory WAIS Arithmetic Other arithmetic tasks Dual Span N-back Self Ordered Pointing Task (SOPT) Neurobehavioural Cognitive Status Examination (NCSE) Attention, Calculating	**Verbal Learning and Memory** Hopkins Verbal Learning Test (HVLT) Rey Auditory Verbal Learning Test (RAVLT) California Verbal Learning Test (CVLT) Complutense Verbal Learning Test (TAVEC) WMS Logical Memory WMS Memory Passages BACS Verbal Memory Hong Kong List Learning Test (HKLLT) NCSE Memory RBANS Learning Other Word List recall tests **Visual Learning and Memory** Brief Visuospatial Memory Test (BVMT) Rey Osterrieth Complex Figure WMS Visual Reproduction WMS Memory for Faces Kimura Recurring Figures Test **Reasoning and Problem Solving** Behavioral Assessment of the Dysexecutive Syndrome (BADS) Mazes test Wisconsin Card Sorting Test (WCST) or COGLAB Card Sorting Test - Categories achieved and Perseverative Errors Trail Making Test, Part B- A (TMT B- A) Stroop Test, Interference condition Response Inhibition Test BACS Tower of London Delis-Kaplan Executive Function System (D- KEFS) Tower Test RBANS Visuospatial NCSE Construction NCSE Reasoning Proverb Interpretation tasks Six Elements Test WAIS Picture Arrangement WAIS Matrix Reasoning	**Social Cognition** Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) Bell Lysaker Emotion Recognition Task (BLERT) Facial Emotion Identification Test (FEIT) Face Emotion Discrimination Task (FEDT) Penn Emotion Recognition Test (ER 40) Elkman 60 Faces test Emotion Recognition Questionnaire (EMOREC) Emotion Recognition Test Faces (ERTF) Pictures of Facial Affect (PFA) Emotion in Biological Motion (EmoBio) The Awareness of Social Inference Task (TASIT) Reading the Mind in the Eyes Test (RMET) Reading the Mind in the Voices (RMVT) Hinting Task Movie for the Assessment of Social Cognition (MASC) Metaphor and Irony test Cartoon test TOM Picture Stories Social Cognition Screening Questionnaire – Theory of Mind and Attributional Style Profile of Non-Verbal Sensitivity (PONS) Schema Component Sequencing Task (SCST) Script Test Relationships Across Domains (RAD) Faux Pas Detection Test Davos Assessment of Cognitive Biases (DACOBS) Social Cognition Problems Ambiguous Intentions Hostility Questionnaire (AIHQ) Internal Personal and Situational Attribution Questionnaire (IPSAQ) Attributional Style Questionnaire (ASQ) Empathic Accuracy Test	**Psychosocial Functioning** UCSD Performance-Based Skills Assessment (UPSA) Medication Management Ability Assessment (MMAA) Social Skills Performance Assessment (SSPA) Independent Living Skills Survey (ILSS) Life Skills Profile (LSP) Maryland Assessment of Social Competence Work Behavior Inventory (WBI) Assessment of Interpersonal Problem Solving Skills (AIPSS) Global Assessment of Functioning (GAF; GAF-f) Global Assessment Scale (GAS) Global Functioning Role/Social Goal Attainment Scale (GAS) Social Functioning Scale (SFS) Personal and Social Performance (PSP) Specific Levels of Functioning (SLOF) Role Functioning Scale (RFS) WHO Disability Assessment Scale (WHO-DAS) Social and Occupational Functioning Assessment Scale (SOFAS) Health of the Nation Outcome Scale (HoNOS) Social Adjustment Scale (SAS) Social Behavior Scale (SBS) Major Role Adjustment Inventory (MRAI) Multnomah Community Ability Scale (MCAS) Time use survey Heinrichs Carpenter Quality of Life Scale (QLS) WHO Quality of Life (WHOQOL; WHOQOL-BREF) EUROHIS Quality of Life (EUROHIS-QOL) Personal Well-Being Index (PWI) Quality of Life Interview (QoLI) Lancashire Quality of Life Profile (LQoLP) Satisfaction Life Domains Scale (SLDS)

Appendix 1. List of moderators investigated (metaregressions and subgroup analyses)

Study characteristics	Publication year, Methodological quality (CTAM total score, CTAM >< 65 points), Blinding of outcome assessment (blind/open), Setting (outpatients/inpatients/both), Setting (real-world/research-oriented), Duration of follow-up (weeks, categories based on time intervals), Sample size (N randomized), Comparison category (as specified in the Methods), Diagnostic composition of included sample (Only subjects with schizophrenia/Including other diagnoses), Number of cognitive domains assessed*, Psychosocial functioning measures assessed (real-world/performance-based outcomes)*, Evaluation of quality of life (yes/no)*.
Treatment characteristics	Presence of single active ingredients (yes/no), Integration with rehabilitation (yes/no), Presence of all active ingredients (yes/no), Treatment duration (weeks), Treatment intensity (sessions/week, hours/week), Format of delivery (individual/group), Computer presentation (computerized/pencil-and-paper), Target on social cognition (yes/no)*.
Patient and illness characteristics	Age (years), Gender (% female subjects), Education (years), Premorbid IQ, Age at onset (years), Duration of illness (years), Baseline treatment dose (CPZeq), Baseline symptoms severity (PANSS total score, PANSS positive scale, PANSS negative scale).

*Analyses added *post-hoc* according to suggestions from Reviewers.

Appendix 2. List of sensitivity analyses

Fixed effects model
Only one effect size per study (both randomly and choosing the most substantial comparison)
Removing outliers
Removing studies with insufficient details on allocation
Removing studies providing only completers data
Removing studies with attrition rate >50% at follow-up*
Removing studies evaluating interventions designed for trial purpose
Removing studies evaluating Metacognitive Training (MCT)

*Analyses added *post-hoc* according to suggestions from Reviewers.

Appendix 3. References of included studies

1. Au DWH, Tsang HWH, So WWY, et al. Effects of integrated supported employment plus cognitive remediation training for people with schizophrenia and schizoaffective disorders. Schizophr Res. 2015;166(1-3):297-303. doi:10.1016/j.schres.2015.05.013

1b. Tsang HWH, Bell MD, Cheung V, Tam KL, Yeung WS. Integrated supported employment plus cognitive remediation training for people with schizophrenia. Hong Kong Med J. 2016;22 Suppl 2:S15-18.

2. Bell M, Bryson G, Greig T, Corcoran C, Wexler BE. Neurocognitive enhancement therapy with work therapy: effects on neuropsychological test performance. Arch Gen Psychiatry. 2001;58(8):763-768. doi:10.1001/archpsyc.58.8.763

2b. Bell M, Fiszdon J, Greig T, Wexler B, Bryson G. Neurocognitive enhancement therapy with work therapy in schizophrenia: 6-month follow-up of neuropsychological performance. J Rehabil Res Dev. 2007;44(5):761-770. doi:10.1682/jrrd.2007.02.0032

3. Bowie CR, McGurk SR, Mausbach B, Patterson TL, Harvey PD. Combined cognitive remediation and functional skills training for schizophrenia: effects on cognition, functional competence, and real-world behavior. Am J Psychiatry. 2012;169(7):710-718. doi:10.1176/appi.ajp.2012.11091337

4. Bryce SD, Rossell SL, Lee SJ, et al. Neurocognitive and Self-efficacy Benefits of Cognitive Remediation in Schizophrenia: A Randomized Controlled Trial. J Int Neuropsychol Soc. 2018;24(6):549-562. doi:10.1017/S1355617717001369

5. Cavallaro R, Anselmetti S, Poletti S, et al. Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. Psychiatry Res. 2009;169(3):191-196. doi:10.1016/j.psychres.2008.06.027

5b. Poletti S, Anselmetti S, Bechi M, et al. Computer-aided neurocognitive remediation in schizophrenia: durability of rehabilitation outcomes in a follow-up study. Neuropsychol Rehabil. 2010;20(5):659-674. doi:10.1080/09602011003683158

6. Choi J, Taylor B, Fiszdon JM, et al. The synergistic benefits of physical and cognitive exercise in schizophrenia: Promoting motivation to enhance community effectiveness. Schizophr Res Cogn. 2020;19:100147. doi:10.1016/j.scog.2019.100147

7. Dai Y, Ding H, Lu X, et al. CCRT and aerobic exercise: a randomised controlled study of processing speed, cognitive flexibility, and serum BDNF expression in schizophrenia. Schizophrenia (Heidelb). 2022 Oct 20;8(1):84. doi: 10.1038/s41537-022-00297-x.

8. D'Souza DC, Radhakrishnan R, Perry E, et al. Feasibility, safety, and efficacy of the combination of D-serine and computerized cognitive retraining in schizophrenia: an international collaborative pilot study. Neuropsychopharmacology. 2013;38(3):492-503. doi:10.1038/npp.2012.208

9. de Pinho LMG, Sequeira CA da C, Sampaio FMC, Rocha NB, Ozaslan Z, Ferre-Grau C. Assessing the efficacy and feasibility of providing metacognitive training for patients with schizophrenia by mental health nurses: A randomized controlled trial. J Adv Nurs. 2021;77(2):999-1012. doi:10.1111/jan.14627

10. Dickinson D, Tenhula W, Morris S, et al. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. Am J Psychiatry. 2010;167(2):170-180. doi:10.1176/appi.ajp.2009.09020264

11. Donohoe G, Dillon R, Hargreaves A, et al. Effectiveness of a low support, remotely accessible, cognitive remediation training programme for chronic psychosis: cognitive, functional and cortical outcomes from a single blind randomised controlled trial. Psychol Med. 2018; 48(5):751-764. doi: 10.1017/S0033291717001982.

12. Drake RJ, Day CJ, Picucci R, et al. A naturalistic, randomized, controlled trial combining cognitive remediation with cognitive-behavioural therapy after first-episode non-affective psychosis. Psychol Med. 2014;44(9):1889-1899. doi:10.1017/S0033291713002559

13. Eack SM, Greenwald DP, Hogarty SS, et al. Cognitive enhancement therapy for early-course schizophrenia: effects of a two-year randomized controlled trial. Psychiatr Serv. 2009;60(11):1468-1476. doi:10.1176/appi.ps.60.11.1468

13b. Eack SM, Greenwald DP, Hogarty SS, Keshavan MS. One-year durability of the effects of cognitive enhancement therapy on functional outcome in early schizophrenia. Schizophr Res. 2010;120(1-3):210-216. doi:10.1016/j.schres.2010.03.042

14. Farreny A, Aguado J, Ochoa S, et al. REPYFLEC cognitive remediation group training in schizophrenia: Looking for an integrative approach. Schizophr Res. 2012;142(1-3):137-144. doi:10.1016/j.schres.2012.08.035

15. Fekete Z, Vass E, Balajthy R, et al. Efficacy of metacognitive training on symptom severity, neurocognition and social cognition in patients with schizophrenia: A single-blind randomized controlled trial. Scand J Psychol. 2022 Aug;63(4):321-333. doi: 10.1111/sjop.12811.

16. Fisher M, Holland C, Merzenich MM, Vinogradov S. Using neuroplasticity-based auditory training to improve verbal memory in schizophrenia. Am J Psychiatry. 2009;166(7):805-811. doi:10.1176/appi.ajp.2009.08050757

15b. Fisher M, Holland C, Subramaniam K, Vinogradov S. Neuroplasticity-based cognitive training in schizophrenia: an interim report on the effects 6 months later. Schizophr Bull. 2010;36(4):869-879. doi:10.1093/schbul/sbn170

15c. Fisher M, Mellon SH, Wolkowitz O, Vinogradov S. Neuroscience-informed Auditory Training in Schizophrenia: A Final Report of the Effects on Cognition and Serum Brain-Derived Neurotrophic Factor. Schizophr Res Cogn. 2016;3:1-7. doi:10.1016/j.scog.2015.10.006

17. Fisher M, Loewy R, Carter C, et al. Neuroplasticity-based auditory training via

laptop computer improves cognition in young individuals with recent onset schizophrenia. Schizophr Bull. 2015;41(1):250-258. doi:10.1093/schbul/sbt232

17b. Loewy R, Fisher M, Ma S, et al. Durable Cognitive Gains and Symptom Improvement Are Observed in Individuals With Recent-Onset Schizophrenia 6 Months After a Randomized Trial of Auditory Training Completed Remotely. Schizophr Bull. 2022;48(1):262-272. doi:10.1093/schbul/sbab1

18. Fiszdon JM, Choi KH, Bell MD, Choi J, Silverstein SM. Cognitive remediation for individuals with psychosis: efficacy and mechanisms of treatment effects. Psychol Med. 2016;46(16):3275-3289. doi:10.1017/S0033291716001951

19. García S, Fuentes I, Ruíz JC, Gallach E, Roder V. Application of the IPT in a Spanish sample: Evaluation of the "Social perception subprogramme". Int J Psychol Psychol Ther 2003; 3: 299–310.

18b. Fuentes I, García S, Ruiz JC, Soler MJ, Roder V. Social perception training in schizophrenia: a pilot study. International Journal of Psychology and Psychological Therapy, vol. 7, núm. 1, april, 2007, pp. 1-12, Universidad de Almería, España.

20. García-Fernández L, Cabot-Ivorra N, Rodríguez-García V, et al. Computerized cognitive remediation therapy, REHACOM, in first episode of schizophrenia: A randomized controlled trial. Psychiatry Res. 2019;281:112563. doi:10.1016/j.psychres.2019.112563

21. Garrido G, Barrios M, Penadés R, et al. Computer-assisted cognitive remediation therapy: cognition, self-esteem and quality of life in schizophrenia. Schizophr Res. 2013; 150(2-3):563-9. doi: 10.1016/j.schres.2013.08.025.

21b. Garrido G, Penadés R, Barrios M, et al. Computer-assisted cognitive remediation therapy in schizophrenia: Durability of the effects and cost-utility analysis. Psychiatry Res. 2017 Aug;254:198-204. doi: 10.1016/j.psychres.2017.04.065.

22. Hegde S, Rao SL, Raguram A, Gangadhar BN. Addition of home-based cognitive retraining to treatment as usual in first episode schizophrenia patients: a randomized controlled study. Indian J Psychiatry. 2012;54(1):15-22. doi:10.4103/0019-5545.94640

23. Hogarty GE, Flesher S, Ulrich R, et al. Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior. Arch Gen Psychiatry. 2004;61(9):866-876. doi:10.1001/archpsyc.61.9.866

23b. Hogarty GE, Greenwald DP, Eack SM. Durability and mechanism of effects of cognitive enhancement therapy. Psychiatr Serv. 2006;57(12):1751-1757. doi:10.1176/ps.2006.57.12.1751

24. Horan WP, Dolinsky M, Lee J, et al. Social Cognitive Skills Training for Psychosis With Community-Based Training Exercises: A Randomized Controlled Trial. Schizophr Bull. 2018;44(6):1254-1266. doi:10.1093/schbul/sbx167

25. Ishikawa R, Ishigaki T, Shimada T, et al. The efficacy of extended metacognitive training for psychosis: A randomized controlled trial. Schizophr Res. 2020;215:399-407.

doi:10.1016/j.schres.2019.08.006

26. Katsumi A, Hoshino H, Fujimoto S, et al. Effects of cognitive remediation on cognitive and social functions in individuals with schizophrenia. Neuropsychol Rehabil. 2019;29(9):1475-1487. doi:10.1080/09602011.2017.1409639

27. Kern RS, Liberman RP, Becker DR, Drake RE, Sugar CA, Green MF. Errorless learning for training individuals with schizophrenia at a community mental health setting providing work experience. Schizophr Bull. 2009;35(4):807-815. doi:10.1093/schbul/sbn010

28. Kidd SA, Kaur J, Virdee G, George TP, McKenzie K, Herman Y. Cognitive remediation for individuals with psychosis in a supported education setting: a randomized controlled trial. Schizophr Res. 2014;157(1-3):90-98. doi:10.1016/j.schres.2014.05.007

29. Kidd SA, Herman Y, Virdee G, et al. A comparison of compensatory and restorative cognitive interventions in early psychosis. Schizophr Res Cogn. 2020;19:100157. doi:10.1016/j.scog.2019.100157

30. Kukla M, Bell MD, Lysaker PH. A randomized controlled trial examining a cognitive behavioral therapy intervention enhanced with cognitive remediation to improve work and neurocognition outcomes among persons with schizophrenia spectrum disorders. Schizophr Res. 2018;197:400-406. doi:10.1016/j.schres.2018.01.012

31. Lado-Codesido M, Rey Varela RM, Larios Quiñones M, et al. Voices 2: Improving Prosodic Recognition in Schizophrenia With an Online Rehabilitation Program. Front Psychol. 2021 Dec 24;12:739252. doi: 10.3389/fpsyg.2021.739252.

32. Lo PMT, Lui SSY, Law CKM, et al. A randomized controlled trial of social cognition and interaction training for persons with first episode psychosis in Hong Kong. Front Psychiatry. 2023; 14:1098662. doi: 10.3389/fpsyt.2023.1098662.

33. Lopez-Morinigo JD, Martínez AS, Barrigón ML, et al. A pilot 1-year follow-up randomised controlled trial comparing metacognitive training to psychoeducation in schizophrenia: effects on insight. Schizophrenia (Heidelb). 2023; 9(1):7. doi: 10.1038/s41537-022-00316-x.

33b. Lopez-Morinigo JD, Ruiz-Ruano VG, Martínez ASE, et al. Study protocol of a randomised clinical trial testing whether metacognitive training can improve insight and clinical outcomes in schizophrenia. BMC Psychiatry. 2020; 20(1):30. doi: 10.1186/s12888-020-2431-x.

34. Man DWK, Law KM, Chung RCK. Cognitive training for Hong Kong Chinese with schizophrenia in vocational rehabilitation. Hong Kong Med J. 2012;18 Suppl 6:18-22.

35. Matsui M, Arai H, Yonezawa M, Sumiyoshi T, Suzuki M, Kurachi M. The effects of cognitive rehabilitation on social knowledge in patients with schizophrenia. Appl Neuropsychol. 2009;16(3):158-164. doi:10.1080/09084280903098414

36. McGurk SR, Mueser KT, Xie H, et al. Cognitive remediation for vocational

rehabilitation nonresponders. Schizophr Res. 2016;175(1-3):48-56. doi:10.1016/j.schres.2016.04.045

37. Meichenbaum D, Cameron R. Training schizophrenics to talk to themselves: A means of developing attentional controls. Behav Ther 1973; 4: 515–34.

38. Mueller DR, Schmidt SJ, Roder V. One-year randomized controlled trial and follow-up of integrated neurocognitive therapy for schizophrenia outpatients. Schizophr Bull. 2015;41(3):604-616. doi:10.1093/schbul/sbu223

39. Mueller DR, Khalesi Z, Benzing V, Castiglione CI, Roder V. Does Integrated Neurocognitive Therapy (INT) reduce severe negative symptoms in schizophrenia outpatients? Schizophr Res. 2017;188:92-97. doi:10.1016/j.schres.2017.01.037

40. Mueller DR, Khalesi Z, Roder V. Can Cognitive Remediation in Groups Prevent Relapses?: Results of a 1-Year Follow-up Randomized Controlled Trial. J Nerv Ment Dis. 2020;208(5):362-370. doi:10.1097/NMD.0000000000001146

41. Nijman SA, Pijnenborg GHM, Vermeer RR, et al. Dynamic Interactive Social Cognition Training in Virtual Reality (DiSCoVR) versus Virtual Reality Relaxation (VRelax) for People With a Psychotic Disorder: A Single-Blind Multicenter Randomized Controlled Trial. Schizophr Bull. 2022 Nov 22:sbac166. doi: 10.1093/schbul/sbac166.

42. O'Reilly K, Donohoe G, O'Sullivan D, et al. A randomized controlled trial of cognitive remediation for a national cohort of forensic patients with schizophrenia or schizoaffective disorder. BMC Psychiatry. 2019;19(1):27. doi:10.1186/s12888-019-2018-6

43. Ochoa S, López-Carrilero R, Barrigón ML, et al. Randomized control trial to assess the efficacy of metacognitive training compared with a psycho-educational group in people with a recent-onset psychosis. Psychol Med. 2017;47(9):1573-1584. doi:10.1017/S0033291716003421

43b. Ruiz-Delgado I, Moreno-Küstner B, García-Medina M, et al. Is Metacognitive Training effective for improving neurocognitive function in patients with a recent onset of psychosis? Psychiatry Res. 2022 Dec;318:114941. doi: 10.1016/j.psychres.2022.11494

44. Østergaard Christensen T, Vesterager L, Krarup G, et al. Cognitive remediation combined with an early intervention service in first episode psychosis. Acta Psychiatr Scand. 2014;130(4):300-310. doi:10.1111/acps.12287

45. Penadés R, Catalán R, Salamero M, et al. Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. Schizophr Res. 2006;87(1-3):323-331. doi:10.1016/j.schres.2006.04.019

46. Pijnenborg GHM, de Vos AE, Timmerman ME, et al. Social cognitive group treatment for impaired insight in psychosis: A multicenter randomized controlled trial. Schizophr Res. 2019;206:362-369. doi:10.1016/j.schres.2018.10.018

47. Rakitzi S, Georgila P, Efthimiou K, Mueller DR. Efficacy and feasibility of the

Integrated Psychological Therapy for outpatients with schizophrenia in Greece: Final results of a RCT. Psychiatry Res. 2016;242:137-143. doi:10.1016/j.psychres.2016.05.039

48. Rass O, Forsyth JK, Bolbecker AR, et al. Computer-assisted cognitive remediation for schizophrenia: a randomized single-blind pilot study. Schizophr Res. 2012;139(1-3):92-98. doi:10.1016/j.schres.2012.05.016

49. Reeder C, Huddy V, Cella M, et al. A new generation computerised metacognitive cognitive remediation programme for schizophrenia (CIRCuiTS): a randomised controlled trial. Psychol Med. Published online September 4, 2017:1-11. doi:10.1017/S0033291717001234

50. Roberts DL, Combs DR, Willoughby M, et al. A randomized, controlled trial of Social Cognition and Interaction Training (SCIT) for outpatients with schizophrenia spectrum disorders. Br J Clin Psychol. 2014;53(3):281-298. doi:10.1111/bjc.12044

51. Rodríguez Pulido F, Caballero Estebaranz N, González Dávila E, Melián Cartaya MJ. Cognitive remediation to improve the vocational outcomes of people with severe mental illness. Neuropsychol Rehabil. 2021 Mar;31(2):293-315. doi: 10.1080/09602011.2019.1692671.

52. Tan BL, King R. The effects of cognitive remediation on functional outcomes among people with schizophrenia: a randomised controlled study. Aust N Z J Psychiatry. 2013;47(11):1068-1080. doi:10.1177/0004867413493521

53. Tan S, Zhu X, Fan H, et al. Who will benefit from computerized cognitive remediation therapy? Evidence from a multisite randomized controlled study in schizophrenia. Psychol Med. 2020;50(10):1633-1643. doi:10.1017/S0033291719001594

53b. Zhu X, Fan H, Zou Y, et al. Computerized or manual? Long term effects of cognitive remediation on schizophrenia. Schizophr Res. 2022 Jan;239:47-54. doi: 10.1016/j.schres.2021.11.019.

54. Twamley EW, Savla GN, Zurhellen CH, Heaton RK, Jeste DV. Development and Pilot Testing of a Novel Compensatory Cognitive Training Intervention for People with Psychosis. Am J Psychiatr Rehabil. 2008;11(2):144-163. doi:10.1080/15487760801963678

54b. Twamley EW, Vella L, Burton CZ, Heaton RK, Jeste DV. Compensatory cognitive training for psychosis: effects in a randomized controlled trial. J Clin Psychiatry. 2012;73(9):1212-1219. doi:10.4088/JCP.12m07686

55. Ueland T, Rund BR. A controlled randomized treatment study: the effects of a cognitive remediation program on adolescents with early onset psychosis. Acta Psychiatr Scand. 2004;109(1):70-74. doi:10.1046/j.0001-690x.2003.002

55b. Ueland T, Rund BR. Cognitive remediation for adolescents with early onset psychosis: a 1-year follow-up study. Acta Psychiatr Scand. 2005;111(3):193-201. doi:10.1111/j.1600-0447.2004.00503.x

56. van Oosterhout B, Krabbendam L, de Boer K, et al. Metacognitive group training for schizophrenia spectrum patients with delusions: a randomized controlled trial. Psychol Med. 2014;44(14):3025-3035. doi:10.1017/S0033291714000555

57. Vaskinn A, Løvgren A, Egeland MK, et al. A randomized controlled trial of training of affect recognition (TAR) in schizophrenia shows lasting effects for theory of mind. Eur Arch Psychiatry Clin Neurosci. 2019;269(5):611-620. doi:10.1007/s00406-019-00997-z

58. Vass E, Simon V, Csukly G, et al. Virtual reality-based theory of mind intervention in schizophrenia: Preliminary efficacy results. Compr Psychiatry. 2022 Nov;119:152350. doi: 10.1016/j.comppsych.2022.152350.

59. Vita A, De Peri L, Barlati S, et al. Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: a prospective study in a real-world setting. Schizophr Res. 2011;133(1-3):223-231. doi:10.1016/j.schres.2011.08.010

59b. Deste G, Barlati S, Cacciani P, et al. Persistence of effectiveness of cognitive remediation interventions in schizophrenia: a 1-year follow-up study. Schizophr Res. 2015;161(2-3):403-406. doi:10.1016/j.schres.2014.12.004

60. Wang Y, Roberts DL, Xu B, Cao R, Yan M, Jiang Q. Social cognition and interaction training for patients with stable schizophrenia in Chinese community settings. Psychiatry Res. 2013;210(3):751-755. doi:10.1016/j.psychres.2013.08.038

61. Wang C, Chong Y, Zhang J, et al. The Efficacy of Extended Metacognitive Training on Neurocognitive Function in Schizophrenia: A Randomized Controlled Trial. Brain Sci. 2022 Mar 21;12(3):413. doi: 10.3390/brainsci12030413.

62. Wykes T, Reeder C, Corner J, Williams C, Everitt B. The effects of neurocognitive remediation on executive processing in patients with schizophrenia. Schizophr Bull. 1999;25(2):291-307. doi:10.1093/oxfordjournals.schbul.a033379

62b. Wykes T, Reeder C, Williams C, Corner J, Rice C, Everitt B. Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. Schizophr Res. 2003;61(2-3):163-174. doi:10.1016/s0920-9964(02)00239-6

63. Wykes T, Newton E, Landau S, Rice C, Thompson N, Frangou S. Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. Schizophr Res. 2007;94(1-3):221-230. doi:10.1016/j.schres.2007.03.030

64. Wykes T, Reeder C, Landau S, et al. Cognitive remediation therapy in schizophrenia: randomised controlled trial. Br J Psychiatry. 2007;190:421-427. doi:10.1192/bjp.bp.106.026575

65. Wykes T, Stringer D, Boadu J, et al. Cognitive Remediation Works But How Should We Provide It? An Adaptive Randomized Controlled Trial of Delivery Methods Using a Patient Nominated Recovery Outcome in First-Episode Participants. Schizophr

Bull. 2023; 49(3):614-625. doi: 10.1093/schbul/sbac214.

66. Zhu X, Fan H, Fan F, et al. Improving social functioning in community-dwelling patients with schizophrenia: a randomized controlled computer cognitive remediation therapy trial with six months follow-up. Psychiatry Res. 2020;287:112913. doi:10.1016/j.psychres.2020.112913

67. Zhu X, Song H, Chang R, et al. Combining compensatory cognitive training and medication self-management skills training, in inpatients with schizophrenia: A three-arm parallel, single-blind, randomized controlled trial. Gen Hosp Psychiatry. 2021 Mar-Apr;69:94-103. doi: 10.1016/j.genhosppsych.2020.12.012

Table S2. Summary of individual characteristics of included studies

Study	Country, Design and Setting	Characteristics of included sample	Sample and attrition rate	Treatment Program, Duration, Format and Schedule	Comparison	Follow-up duration (weeks)	Quality Rating (CTAM)	Outcome measures (included in the analyses)
Au 2015	Hong Kong, single center Outpatients	Gender: 36.7% F Age: 36.1 years Illness duration: 11.2 years Onset: 24.9 years Education: 14.9 years QI: n.i. Diagnosis: schizophrenia (58%), schizoaffective Baseline PANSS: 41.9 Daily drug dose (CPZeq): n.i.	N=90, 10% dropouts (global)	Captain's Log, 3 sessions/week 2h each + Integrated Supported Employment, 12 weeks, N=45 Group sessions	Watching TV + Integrated Supported Employment, N=45	48	73	Cognition Functioning
Bell 2001	USA, multicenter Outpatients	Gender: 22.4% F Age: 42.8 years Illness duration: 20.7 years Onset: 22 years Education:13.3 years QI: 87.6 Diagnosis: schizophrenia (69%), schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): 698.4 mg/day	N=151, 23% dropouts at follow-up	Neurocognitive Enhancement Therapy (NET), 3-4 sessions/week, + work therapy, 22 weeks, N=53 Group sessions	Work therapy, N=63	26	60	Cognition
Bowie 2012	USA, multicenter Outpatients	Gender: n.i. Age: 40,6 years Illness duration: 20.2 years Onset: 20.4 years Education:13.1 years QI: n.i. Diagnosis: schizophrenia, schizoaffective Baseline PANSS:	N=114, 27% dropouts	Thinking Skills for Work, 2 hours/week 12 weeks, N=36 Thinking Skills for Work + Functional Adaptation Skills Training, N=36	Functional Adaptation Skills Training, N=38	12	75	Cognition Functioning

		n.i. Daily drug dose (CPZeq): n.i.		Individual sessions				
Bryce 2018	Australia, Single center Inpatients and outpatients	Gender: 30% F Age: 41 years Illness duration: 14.1 years Onset: 26.9 years Education:13.1 years QI: 98.1 Diagnosis: schizophrenia (71%), schizoaffective Baseline PANSS: 61.1 Daily drug dose (CPZeq): 703.8 mg/day	N=56, 23% dropouts at end of treatment, 41% at follow-up	Cogpack, 2 sessions/week 1h each, 10 weeks, N=29 Individual sessions	Computer games, N=27	12	72	Cognition Functioning
Cavallaro 2009-Poletti 2010	Italy, multicenter Inpatients	Gender: 40% F Age: 34.3 years Illness duration: 10 years Onset: 24.2 years Education:11.7 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 67.7 Daily drug dose (CPZeq): n.i.	N=100, 14% at end of treatment, 46% at follow-up	Cogpack, 12 weeks, 3 sessions/week 1h each, + Standard Psychiatric Rehabilitation, 12 weeks, N=32 Individual sessions	Computer activities + Standard Psychiatric Rehabilitation, N=22	38	51	Cognition Functioning
Choi 2019	USA, single center Outpatients	Gender: 44.9% F Age: 34.8 years Illness duration: 12.5 years Onset: 22.4 years Education: 11.4 years QI: n.i. Diagnosis: schizophrenia (56.3%), schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=85, 2.4% dropouts at end of treatment, 4.7% at follow-up	Computerized training OR Computerised training + Physical exercise, 13 weeks, 3 sessions/week, 2.5 hours/week, N=27+29 Group sessions	Physical exercise, N=29	10	69	Cognition
Dai 2022	China, Single center	Gender: 17,65% F Age: 41.4 years	N=96, unknown	Computerized cognitive	Physical exercise,	4	77	Cognition

	Outpatients	Illness duration: 18,3 years Onset: 23,1 years Education: 9,5 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS:64,8 Daily drug use (CPZeq): 343,14	dropout rate	remediation therapy (CCRT)+Aerobic Exercise, 2 sessions/week in 8 weeks, N=26 Group sessions	N=25			
D'Souza 2013	USA, multicenter Outpatients	Gender: 25% F Age: 37.2 years Illness duration: 10.7 years Onset: 26.5 years Education:12.7 years QI: 91.2 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: 56.9 Daily drug dose (CPZeq): 272.5 mg/day	N=53, 15% dropouts at end of treatment, 36% at follow-up	PSS CogRehab, 5 hours/week, 12 weeks, N=22 * Only the arm taking serine-placebo was included in the analysis Individual sessions	Watching TV, N=23 * Only the arm taking serine-placebo was included in the analysis	24	62	Cognition Functioning
De Pinho 2020	Portugal, multicenter, Inpatients and outpatients	Gender: 46.4 % F Age: 50.6 years Illness duration and Onset: n.i. Education: 7.7 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq):n.i.	N=56, 7.1% dropouts (global)	Metacognitive Training (MCT), 2 sessions/week 1h each, 4 weeks, N=27 Group sessions	Treatment as usual, N=29	12	73	Functioning
Dickinson 2010	USA, multicenter Outpatients	Gender: 35% F Age: 47.6 years Illness duration and Onset: n.i. Education:12.5 years QI: n.i. Diagnosis: schizophrenia (78%),	N=69, 9% dropouts at end of treatment, 30% at follow-up	Computerised training, 3 sessions/week 1h each, 15 weeks, N=28 Individual sessions	Computer games, N=20	12	82	Cognition Functioning

		schizoaffective Baseline PANSS: 66.5 Daily drug dose (CPZeq): n.i.						
Donohoe 2018	Ireland, multicenter Outpatients	Gender: 60% F Age: 43.3 years Illness duration: 17.1 years, Onset: 26.2 years Education:14 years QI: n.i. Diagnosis: SSD Baseline PANSS: n.i. Daily drug dose (CPZeq): 490.4 mg/day	N=90, 64% dropouts at follow-up	Computerised, low-support Working memory training, 6 sessions/week, 8 weeks, N=15 Individual sessions	Sham intervention, N=17	20	79	Cognition Functioning
Drake 2014	Great Britain, multicenter Outpatients	Gender: 39.3 % F Age: 24.1 years Illness duration and Onset: n.i. Education: 17.7 years QI: 104.4 Diagnosis: schizophrenia (85%), other from schizophrenia spectrum disorders Baseline PANSS: 70.4 Daily drug dose (CPZeq): n.i.	N=62, 48.4% dropouts at end of treatment, 43.6% at follow-up	CIRCuiTS, 4 sessions/week, 3 hours/week, 12 weeks, N=31 Individual sessions	Time-matched social contact (SC), N=30	30	83	Cognition Functioning
Eack 2009-2010	USA, single center Outpatients Recent onset (<5 years)	Gender: 31% F Age: 28.9 years Illness duration: 3.2 years Onset: 22.7 years Education:n.i. QI: 98.1 Diagnosis: schizophrenia (66%), schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): 418.2	N=58, 27% dropouts at follow-up	Cognitive Enhancement Therapy (CET) + Enriched Supportive Therapy, 104 weeks, N=31 Group sessions	Enriched Supportive Therapy, N=27	52	56	Functioning

		mg/day						
Farreny 2012	Spain, single center Outpatients	Gender: 32% F Age: 40,6 years Illness duration: 17.5 years Onset: 23.1 years Education:n.i. QI: n.i. Diagnosis: schizophrenia (89%), schizoaffective Baseline PANSS: 65.0 Daily drug dose (CPZeq): 475 mg/day	N=62, 14,5% dropouts at end of treatment, 24% at follow-up	Problem Solving and Cognitive Flexibility Training (REPYFLEC), 2 sessions/week 1h each, 17 weeks, N=29 Group sessions	Leisure activities, N=24	26	76	Cognition Functioning
Fekete 2022	Hungary, multicenter Outpatients	Gender: 46% F Age: 41,3 years Illness duration: 13,7 years Onset: 27,6 years Education: n. i. QI: 105,65 Diagnosis: schizophrenia Baseline PANSS: 80.2 Daily drug use (CPZeq): 388,79 mg/day	N=46, dropout 21,7% dropout at follow-up	Metacognitive Training (MCT), 1 session/week, 16 weeks. N=23 Group sessions	Treatment as usual, N=13	26	58	Cognition
Fisher 2009-2010	USA, single center Outpatients	Gender: 21.9% F Age: 46.2 years Illness duration and Onset: n.i. Education:13.1 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq): 495.5 mg/day	N=32 (completers), dropouts n.i.	Posit Science (Auditory training), 5 sessions/week 1h/week, 10 weeks 50 hours tot, N=12 100 hours tot, N=10 Individual sessions	Computer games, N=10	26	70	Cognition Functioning
Fisher 2015-2021	USA, multicenter Outpatients	Gender: 25.5% F Age: 21.2 years Illness duration: 1. 9 years Onset: 19.3 years Education: 12.7	N=147, 29.3% dropouts at end of treatment, 47.6% at	Posit Science, Auditory training, 5 sessions/week 1h each, 8 weeks, N=80	Computer games, N=65	26	68	Cognition Functioning

		years QI: 102.8 Diagnosis: schizophrenia, schizophreniform or schizoaffective. Baseline PANSS: 59.6 Daily drug dose (CPZeq): 328.1 mg/day	follow-up	Individual sessions				
Fiszdon 2016	USA, single center Outpatients	Gender: 26.7% F Age: 47.8 years Illness duration and Onset: n.i. Education:12.4 years QI: 93.6 Diagnosis: psychotic disorder, including affective (81% schizophrenia) Baseline PANSS: 52.7 Daily drug dose (CPZeq): n.i.	N=75, 17% dropouts at end of treatment, 28% at follow-up	PSS CogRehab, 5 sessions/week 1h each, 9 weeks, N=50 Individual sessions	Treatment as usual, N=25	9	39	Cognition Functioning
Garcia 2003-Fuentes 2007	Spain, single center Outpatients	Gender: 33% F Age: 39.2 years Illness duration: 18.7 years Onset: 20.5 years Education:n.i. QI: n.i. Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=23, 13% dropouts at end of treatment, 22% at follow-up	Integrated Psychological Therapy (IPT), Social perception module, 2 sessions/week 30-60min each, 12 weeks, N=10 Group sessions	Treatment as usual, N=8	26	27	Cognition Functioning
Garcia-Fernandez 2019	Spain, single center Outpatients Recent onset (<1 year)	Gender: 31.4% F Age: 25.5 years Illness duration and Onset: n.i. Education:13.4 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 108.8 Daily drug dose	N=110, 22% dropouts (global)	Rehacom, 2 sessions/week 1h each, 12 weeks, N=36 Individual sessions	Computer activities, N=50	26	73	Cognition Functioning

		(CPZeq): 1067.6 mg/day						
Garrido 2013-2017	Spain, single center Outpatients	Gender: 26.8% F Age: 33.3 years Illness duration: 11.4 years, Onset: 21.9 years, Education: 9.9 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 55.9 Daily drug dose (CPZeq): 317 mg/day	N=67, 51% dropouts at follow-up	Computer assisted cognitive remediation (various tools), 2 sessions/week 1h each, 26 weeks, N=20 Individual sessions	Watching videos, N=13	20	70	Cognition Functioning
Hegde 2012	India, single center Outpatients Recent onset (<2 years) or first episode	Gender: 17% F Age: 29.3 years Illness duration and Onset: n.i. Education:12.8 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 89.7 Daily drug dose (CPZeq): 204 mg/day	N=45, 31% dropouts at end of treatment, 49% at follow-up	Home-based training with flexible schedule, 9 weeks, N=13 Individual sessions	Treatment as usual including psychoeducation, N=18	17	35	Cognition
Hogarty 2004-2006	USA, single center Outpatients	Gender: 41% F Age: 37.2 years Illness duration: 15.7 years Onset: 21.5 years Education:n.i. QI: 97.2 Diagnosis: schizophrenia (70%), schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=121, 11,5% dropouts at end of treatment, 12% at follow up	Cognitive Enhancement Therapy (CET) 2,5 hours/week, + Enriched supportive therapy, 104 weeks, N=60 Group sessions	Enriched Supportive Therapy, N=46	52	63	Cognition Functioning
Horan 2018	USA, single center Outpatients	Gender: 30.4% F Age: 47.3 years Illness duration: 25.6 years Onset: 21.7 years Education:12.4 years QI: n.i. Diagnosis: non affective psychosis	N=139, 6.5% dropouts	Social Cognitive Skills Training (SCST), flexible schedule, 2-3 sessions/week 1h each, 12 weeks, in vivo N=41, in clinic	UCLA Illness Management Skills Training, N=49	12	85	Cognition Functioning

		Baseline PANSS: 50.9 Daily drug dose (CPZeq): n.i.		N=49 Group sessions				
Ishikawa 2020	Japan, multicenter Inpatients and outpatients	Gender: 70% F Age: 47.6 years Illness duration: 21.1 years Onset:26.5 years Education: n.i. QI: n.i. Diagnosis: schizophrenia, schizotypal, psychosis NOS Baseline PANSS: n.i. Daily drug dose (CPZeq): 764.6 mg/day	N=50, 10% dropouts	MCT-10 modules, 10 weeks, 1 weekly session lasting 1h, N=24 Group sessions	Treatment as usual, N=26	4	76	Functioning
Katsumi 2019	Japan, single center Outpatients	Gender: 40.9% F Age: 37.8 years Illness duration: 13.9 years Onset: 23.9 years Education:12 years QI: 90.7 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: 56.3 Daily drug dose (CPZeq): 664.4 mg/day	N=44, no dropout	Neuropsychological e Educational Approach to Remediation (NEAR), 4 sessions/week, 40-60min each, 5 weeks, N=22 Group sessions	Treatment as usual with multidisciplinary rehabilitation, N=22	34	42	Functioning
Kern 2009	USA, single center Inpatients	Gender: 70% F Age: 47.6 years Illness duration: 25.2 years Onset: 22.4 years Education:12.4 years QI: n.i. Diagnosis: schizophrenia, schizoaffective Baseline PANSS: 77.6 Daily drug dose (CPZeq): n.i.	N=40, dropouts 47.5% at follow-up	Errorless Learning, 15-20min sessions, 2 weeks, N=20 Individual sessions	UCLA Illness Management Skills Training, N=20	10	55	Functioning
Kidd 2014	Canada, single center	Gender: 54% F Age: 34.2 years Illness duration:	N=37, 16% dropouts , at end of	Cogpack, 2 sessions/week 50min each +	Supported education, N=9	17	65	Cognition

	Students	6.9 years Onset: 27.3 years Education:12.5 years QI: n.i. Diagnosis: psychosis including affective (56% schizophrenia) Baseline PANSS: 65.1 Daily drug dose (CPZeq): n.i.	treatment, 35% at follow-up	Group discussions 50min/week + Supported education, 20 weeks, N=15 Group sessions				
Kidd 2020	Canada, single center Inpatients and outpatients	Gender: 37.7% F Age: 27.1 years Illness duration: 5.5 years Onset: 21.6 years Education: n.i. QI: n.i. Diagnosis: schizophrenia (77%), Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=56, 30.4% at end of treatment, 44.6% at follow-up	Action Based Cognitive Remediation (ABCR) with Scientific Brain Traiing Pro, 16 weeks, 1 session/week lasting 1,5h, N=24 Group sessions	Cognitive Adaptation Training (CAT), N=32	22	72	Cognition Functioning
Kukla 2018	USA, single center Outpatients	Gender: 8% F Age: 48.5 years Illness duration and Onset: n.i. Education:12.9 years QI: n.i. Diagnosis: schizophrenia (70%), schizoaffective Baseline PANSS: 75.1 Daily drug dose (CPZeq): n.i.	N=50, 14% dropouts at end of treatment, 50% at follow-up	Posit Science (Fitness e Insight), 1 session/week + Cognitive Behavioral Therapy (CBT), 26 weeks, N=23 Individual sessions	Cognitive Behavioral Therapy (CBT), N=22	26	67	Cognition
Lado-Codesido 2021	Spain, multicenter Outpatients	Gender: 39% F Age: 43,2 years Illness duration:19,4 years Onset: 23,9 years Education: n.i. QI: 98.12 Diagnosis: schizophrenia and schizoaffective disorder.	N= 44, 6,81% dropout at follow-up	Lyrics Training music program - Voices 2, 2 sessions/week in 8 weeks. N=22 Individual sessions	Auditory Training, N=19	4	53	Cognition

		Baseline PANSS: 73.82 Daily drug dose (CPZeq): 971.36 mg/day						
Lo 2023	China, single center Outpatients First-episode	Gender: 55.8% F Age: 25.8 years Illness duration: 1.7 years Onset: 24.1 years, Education: n.i. QI: 95.3 Diagnosis:SSD Baseline PANSS: 39.9 Daily drug dose (CPZeq): 444.0 mg/day	N=72, 14% dropouts at end of treatment, 25% at follow-up	Social Cognition and Interaction Training, 2 sessions/week, 10 weeks, N=39 Group sessions	Treatment as usual, including active rehabilitative components, N=33	12	73	Cognition
Lopez-Morinigo 2023	Spain, single center Outpatients	Gender: 47.2% F Age: 47.7 years Illness duration: 34.5 years Onset: 24 years. Education: 6.5 years QI: 104.6 Diagnosis: SSD Baseline PANSS: 41.9 Daily drug dose (CPZeq): 451.6 mg/day	N=77, 56% dropouts at end of treatment, 64% at follow-up	Metacognitive Training, 3 sessions/week,, 8 weeks, N=39 Group sessions	Psychoeducation, N=38	52	74	Cognition Functioning
Man 2012	Hong Kong, single center Inpatients	Gender: 37.5% F Age: 36.9 years Illness duration, Onset and Education:n.i. QI: 89.7 Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=90, 11% dropouts at end of treatment, 34% at follow-up	Errorless learning training, 12 sessions, 4 weeks, computer-assisted N=18, therapist-assisted N=15 Individual sessions	Treatment as usual, N=24	12	57	Cognition
Matsui 2009	Japan, single center Outpatients	Gender: n.i. Age: 32.3 years Illness duration: 8.3 years Onset: 24 years Education:12.7 years	N=20, no dropouts at end of treatment, 25% at follow-up	Social Perception Training, 40 minutes/week, 12 weeks, N=11 Individual	Treatment as usual (drugs only), N=9	12	47	Cognition

		QI: 99.9 Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq): 182.5 mg/day		sessions				
McGurk 2016	USA, single center Outpatients, refractory to previous rehabilitation	Gender: 30% F Age: 37.7 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: psychosis including affective (81% schizophrenia) Baseline PANSS: 70.3 Daily drug dose (CPZeq): n.i.	N=54, 5.5% dropouts at end of treatment, 35% at follow-up	Thinking Skills for Work + Vocational Rehabilitation, 1-2 sessions/week 45-60min each, 12 weeks, N=28 Individual sessions	Enhanced Vocational Rehabilitation , N=23	35	79	Cognition
Meichenbaum 1973	Canada, single center Outpatients 50% acute phase	Gender: 100% M Age: 36 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: schizophrenia Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=10, no dropout	Self-instructional training group, 8 sessions 45 min each, 3 weeks, N=5 Individual sessions	Yoked practice group, N=5	3	65	Cognition
Müller 2015	Germany, Austria and Switzerland, multicenter Outpatients	Gender: 31% F Age: 34.2 years Illness duration: 10.6 years Onset: 24.2 years Education:11 years QI: 104 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): 438.5 mg/day	N=156, 10% dropouts at end of treatment, 22% at follow-up	Integrated Neurocognitive Therapy (INT), 2 sessions/week 90 min each, 15 weeks, N=81 Group sessions	Treatment as usual, N=75	37	87	Cognition Functioning
Müller 2017	Switzerland, single center Outpatients, predominant negative	Gender: 22.9% F Age: 35.5 years Illness duration: 10.8 years Onset: 24.7 years Education:10.8	N=61, 20% dropouts at follow-up	Integrated Neurocognitio n Therapy (INT), 2 sessions/week 90 minuti each, 15 weeks, N=28	Treatment as usual, N=33	37	71	Cognition Functioning

	symptoms	years QI: 101.4 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: 78 Daily drug dose (CPZeq): 405.4 mg/day		Group sessions				
Müller 2020	Switzerland, single center Outpatients	Gender: 41.4% F Age: 31 years Illness duration: 8 years Onset: 23.6 years Education:12.6 years QI: 107.7 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: 54 Daily drug dose (CPZeq): 336 mg/day	N=58, 10% dropouts at follow-up	Integrated Neurocognitio n Therapy (INT), 2 sessions/week 90 minutes each, 15 weeks, N=32 Group sessions	Treatment as usual, N=26	37	78	Cognition Functioning
Nijman 2022	Netherlands, multicenter Inpatients and outpatients	Gender: 30,9% F Age: 37.8 years Illness duration, Onset, Education, CPZeq, QI: n.i. Diagnosis: schizophrenia (59,25%), schizoaffective disorder (22,22%), Brief psychotic disorder (1,23%), schizophreniform disorder (1,23%), delusional disorder (1,23%), other psychotic disorder (4,9%). Baseline PANSS: 65.2	N=81, 17,3% dropout rate at follow-up	DiSCoVR, 2 sessions/week, 8 weeks, N=33 Individual sessions	VRrelax, N=34.	12	87	Cognition Functioning
O'Reilly 2019	Ireland, single center Forensic	Gender: 15.4% F Age: 41 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: schizophrenia	N=65, 11% dropouts at end of treatment, 25% at follow-up	Own program, 4 sessions/week, 14 weeks, N=32 Group sessions	Treatment as usual, waiting list, N=33	35	87	Cognition Functioning

		(76%), schizoaffective Baseline PANSS: 51.2 Daily drug dose (CPZeq): 488.5 mg/day						
Ochoa 2017	Spain, multicenter Outpatients Recent onset (< 5 years)	Gender: 30.3% F Age: 27.6 years Illness duration: 2.3 years Onset: 25.6 years Education:n.i. QI: n.i. Diagnosis: schizophrenia spectrum Baseline PANSS: 54.3 Daily drug dose (CPZeq): 494.3 mg/day	N=122; 27% dropouts at end of treatment, 34% at follow-up	Metacognitive Training (MCT), 1 session/week, 8 weeks, N=41 Group sessions	Psychoeducation, N=40	26	71	Cognition Functioning
Østergaard Christensen 2014	Denmark, multicenter Inpatients First episode	Gender: 46.2% F Age: 24.9 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: first episode of psychosis (schizophrenia 84%) Baseline PANSS: 54.2 Daily drug dose (CPZeq): n.i.	N=117, 16% dropouts at end of treatment, 21% at follow-up	Computerised training (NEUROCOM) ,2 sessions/week 1h each, integrated with OPUS program, 16 weeks, N=60 Individual sessions	Treatment as usual consisting in multidisciplinary rehabilitation (OPUS), N=57	36	84	Cognition Functioning
Penadés 2006	Spain, single center Outpatients Predominant negative symptoms	Gender: 42.5% F Age: 35.1 years Illness duration: 13.8 years Onset: 21.3 years Education:11.6 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 67 Daily drug dose (CPZeq): 361.3 mg/day	N=40, 17.5% dropouts	Frontal/Executive Program, 2-3 sessions/week 1h each, 17 weeks, N=20 Individual sessions	Cognitive Behavioral Therapy for psychosis (CBTp), N=20	26	67	Cognition Functioning
Pijnenborg 2019	The Nederlands, multicenter Inpatients and outpatients	Gender: 21.5% F Age: 39.7 years Illness duration: 12.7 years Onset: 27 years Education:n.i. QI:	N=121, 13% dropouts at end of treatment, 22% at follow-up	Cognitive Remediation Therapy (CRT), 2 sessions/week 1h each, 6 weeks, N=30	REFLEX program, N=55	20	72	Cognition Functioning

		n.i. Diagnosis: schizophrenia Baseline PANSS: 62.6 Daily drug dose (CPZeq): n.i.		Group sessions				
Rakitzi 2016	Greece, single center Outpatients	Gender: 33% F Age: 32.6 years Illness duration: 5.7 years Onset: 26.9 years Education:n.i. QI: 89.8 Diagnosis: schizophrenia Baseline PANSS: 118.4 Daily drug dose (CPZeq): 527.1 mg/day	N=48, 25% dropouts at end of treatment, 31% at follow-up	Integrate Psychological Therapy (IPT), cognitive subprograms, 2 sessions/week 1h each, 10 weeks, N=18 Group sessions	Treatment as usual, N=24	12	65	Cognition Functioning
Rass 2012	USA, single center Outpatients	Gender: 38% F Age: 41.3 years Illness duration: 20.3 years Onset: 21 years Education:n.i. QI: 96.3 Diagnosis: schizophrenia (41%), schizoaffective Baseline PANSS: 57.6 Daily drug dose (CPZeq): n.i.	N=38, 6% dropouts at end of treatment, 8% at follow-up	Posit Science, 2 sessions/week 2h each, 10 weeks, N=17 Individual sessions	Watching TV, N=17	10	65	Cognition
Reeder 2017	Great Britain, single center Inpatients and outpatients	Gender: 35.5% F Age: 38.3 years Illness duration e Onset: n.i. Education:13.2 years QI: 93.5 Diagnosis: schizophrenia, schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): 333.3 mg/day	N=93, 6.5% dropouts at end of treatment, 12% at follow-up	CIRCuiTS, 3 sessions/week 1h each, 12 weeks, N=46 Individual sessions	Treatment as usual, N=47	14	80	Cognition Functioning
Roberts 2014	USA, single center Outpatients	Gender: 33% F Age: 39.7 years Illness duration: 16.8 years Onset: 23 years Education:n.i. QI: 99.2 Diagnosis:	N=66, 9% dropouts	Social Cognition and Interaction Training (SCIT), 1h/week, 26 weeks, N=30	Treatment as usual, N=30	12	64	Cognition Functioning

		schizophrenia spectrum (42% schizophrenia) Baseline PANSS: 65.3 Daily drug dose (CPZeq): 632.6 mg/day		Group sessions				
Rodriguez Pulido 2021	Spain, single center Outpatients	Gender: 32% F Age: 33 years Illness duration, Onset, Education, CPZeq, QI: n.i. Diagnosis: schizophrenia (74,46 %), Bipolar disorder (14,89%), Personality Disorder (8,51%), Depression (2,12%). Baseline PANSS: 53,53	N=57, 17,54% dropout rate at follow-up	Cognitive Remediation and Individual Placement and Support, Cogpack program; 9 weeks; 1 session/week; 1h/week. N=21 Individual sessions	Individual placement and Support, N=19	52	74	Cognition
Tan 2013	China, single center Outpatients	Gender: 43% F Age: 34.7 years Illness duration: 10.6 years Onset: 24.1 years Education:11.1 years QI: n.i. Diagnosis: schizophrenia (96%), schizoaffective Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=70, 34% dropouts	Computerised training, 3 sessions/week (5 hours/week), 12 weeks, N=36 Group sessions	Physical exercise, N=34	52	79	Cognition
Tan 2019-Zhu 2022	China, single center Inpatients	Gender: 27,3% F Age: 48,7 years Illness duration: 22,6 years Onset: 23,8 years Education:10,8 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 61,5 Daily drug dose (CPZeq): 379,3 mg/day	N=270, dropout rate 32,96% at follow-up	Computerised Cognitive remediation therapy, 4-5 sessions/week 45min each, 12 weeks, N=144; Cognitive Remediation Therapy, 4-5 sessions/week 45min each, 12 weeks, N=72	Leisure activities (playing easy instrument and learning dancing), N=67	65	83	Cognition

				Group sessions				
Twamley 2008-2012	USA, multicenter Outpatients	Gender: 35% F Age: 46.3 years Illness duration: 23.3 years Onset: 23.1 years Education:12.9 years QI: 106.9 Diagnosis: psychosis including affective (54% schizophrenia) Baseline PANSS: n.i. Daily drug dose (CPZeq): 383.8 mg/day	N=69, 26% dropouts	Compensatory Cognitive Training (CCT), 2 hours/week, 12 weeks, N=38 Group sessions	Treatment as usual (drugs only), N=31	12	55	Cognition Functioning
Ueland 2004-2005	Norway, single center Inpatients Adolescents	Gender: 46.2% F Age: 15.3 years Illness duration, Onset and Education:n.i. QI: 88.6 Diagnosis: psychosis including affective (62% schizophrenia) Baseline PANSS: 73.2 Daily drug dose (CPZeq): n.i.	N=26, dropouts n.i.	Own program based on IPT, 30h tot, + Psychoeducation, 12 weeks, N=14 Individual sessions	Psychoeducation, N=12	52	50	Cognition Functioning
Van Oosterhout 2014	The Nederlands, multicenter Inpatients and outpatients Active positive symptoms	Gender: 28.6% F Age: 37.5 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: psychosis including affective (64% schizophrenia) Baseline PANSS: n.i. Daily drug dose (CPZeq): n.i.	N=154, 28% dropouts	Metacognitive Training (MCT), 1 session/week lasting 1h, 8 weeks, N=51 Group sessions	Treatment as usual, N=60	16	84	Cognition
Vaskinn 2019	Norway, single center Outpatients	Gender: 33.3% F Age: 30.4 years Illness duration: 7.9 years Onset: 22.5 years Education:12.2	N=48, 17% dropouts at end of treatment, 33% at follow-up	Training of Affect Recognition (TAR), 2 sessions/week, 8 weeks, N=17	Treatment as usual, N=15	12	62	Cognition Functioning

		years QI: 101.9 Diagnosis: schizophrenia (81%), schizoaffective Baseline PANSS: 43,7 Daily drug dose (CPZeq): n.i.		Individual sessions				
Vass 2022	Hungary single center Outpatients	Gender: 47,6 F Age: 39,6 years Illness duration: 18,5 years Onset: 21,1 years Education: 14,6 years QI: 101,8 Diagnosis: Schizophrenia and schizoaffective disorder. Baseline PANSS: 51,93 Daily drug dose (CPZeq): 521,88 mg/day	N=43, 6,97% dropout rate at follow-up	VR-ToMIS 1-h/session; 1 preparative session and 8 virtual sessions, 9 weeks, N=21 Individual sessions.	VR treatment,with only exploration of the virtual environment, N=19	12	65	Cognition Functioning
Vita 2011 a-Deste 2015	Italy, multicenter Inpatients	Gender: 37% F Age: 39.8 years Illness duration: 15.6 years Onset: 24.7 years Education:10.2 years QI: 85.2 Diagnosis: schizophrenia Baseline PANSS: 85.2 Daily drug dose (CPZeq): 670 mg/day	N=84, 2% dropouts at end of treatment, 36% at follow-up	Integrated Psychological Therapy (IPT), cognitive subprograms, OR Cogpack, 2 sessions/week 45min each, 24 weeks, N=37 Group sessions	Treatment as usual + adjunctive rehabilitation, N=17	52	72	Cognition Functioning
Wang 2013	China, single center Inpatients	Gender: 49% F Age: 42.6 years Illness duration and Onset: n.i. Education:10.4 years QI: 98.6 Diagnosis: schizophrenia Baseline PANSS: 66.6 Daily drug	N=43, 9% dropouts at follow-up	Social Cognition and Interaction Training (SCIT), 1h/week, 20 weeks, N=22 Group sessions	Treatment as usual, N=17	26	63	Cognition Functioning

		dose (CPZeq): 308.6 mg/day						
Wang 2022	China single center Inpatients	Gender: 56% F Age: 44,5 years Illness duration, Onset, Education, QI, Baseline PANSS, Daily drug dose (CPZeq): i.n. Diagnosis: schizophrenia	N=100, 8% dropout at follow-up	Metacognitive Training for Psychosis (MCT), 45-60 min/session, 2 sessions/week, 4 weeks, N=50 Group sessions	Treatment as usual, N=50	12	69	Cognition
Wykes 1999-2003	Great Britain, multicenter Outpatients	Gender: 24.2% F Age: 38.4 years Illness duration and Onset: n.i. Education:12.3 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 59.3 Daily drug dose (CPZeq): n.i.	N=33, 12% dropouts at end of treatment, 15% at follow-up	Cognitive Remediation Therapy (CRT), 3 sessions/week 1h each, 12 weeks, N=17 Individual sessions	Occupational therapy , N=16	26	68	Cognition Functioning
Wykes 2007 a	Great Britain, single center Inpatients Adolescents or recent onset (<5 years)	Gender: 35% F Age: 18.2 years Illness duration: 1.2 years Onset: 17 years Education:n.i. QI: 85.3 Diagnosis: schizophrenia Baseline PANSS: 67.9 Daily drug dose (CPZeq): n.i.	N=40, 22.5% dropouts	Cognitive Remediation Therapy (CRT), 3 sessions/week 1h each, 14 weeks, N=21 Individual sessions	Treatment as usual, N=19	12	60	Cognition Functioning
Wykes 2007 b	Great Britain, multicenter Outpatients Severe funcional impairment	Gender: 27% F Age: 36 years Illness duration, Onset and Education:n.i. QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 59.9 Daily drug dose (CPZeq): 334.4 mg/day	N= 85, 8% dropouts at end of treatment, 21% at follow-up	Cognitive Remediation Therapy (CRT), 3 sessions/week, 12 weeks, N=39 Individual sessions	Treatment as usual, N=39	26	87	Cognition Functioning
Wykes 2023	Great Britain, multicenter Outpatients	Gender: 27% F Age: 25.7 years Illness duration, Onset and Education:n.i. QI: 88.18	N= 377, 33% dropouts at end of treatment, 45% at follow-up	CIRCuiTS, different treatment schedules with different therapist	Treatment as usual (comprehensive case management at EIS care),	26	94	Cognition Functioning

	Early intervention service	Diagnosis: SSD Baseline PANSS: 56.7 Daily drug dose (CPZeq): 217.5 mg/day		support, 12 weeks, N=311 One-to-one, group or independent sessions	N=66			
Zhu 2020	China, multicenter Outpatients	Gender: 45.9% F Age: 43.7 years Illness duration: 18.6 years Onset: 25.4 years Education: 11.6 years QI: n.i. Diagnosis: schizophrenia Baseline PANSS: 49.2 Daily drug dose (CPZeq): 266.1 mg/day	N=157, 11.5% dropouts at end of treatment, 19.8% at follow-up	Computerized Cognitive Remediation Therapy (CCRT), +social cognition, 12 weeks, 4-5 sessions/week, N=73 Group sessions	Treatment as usual, N=66	26	76	Cognition Functioning
Zhu 2021	China single center Inpatients	Gender: 47,8% F Age: 32,1 years Illness duration: 9,1 years Onset: 23 years Education: 11 years QI: n.i. Diagnosis: schizophrenia Daily drug dose: 461,9 mg/day Baseline PANSS: n.i.	N=55, 16,4% dropout rate at follow-up	Compensatory Cognitive training (CCT), 4 weeks, 2 sessions/week; N=29 Group sessions	Treatment as usual, N=26	12	89	Cognition

Table S3. Methodological quality and Clinical Trial Assessment Measure scores in included studies

Study ID	Sample	Allocation	Assessment	Comparison	Analysis	Treatment	Overall
Au 2015	7	16	26	10	11	3	**73**
Bell 2001	7	16	6	10	15	6	**60**
Bowie 2012	7	10	26	10	11	11	**75**
Bryce 2018	0	16	26	10	9	11	**72**
Cavallaro 2009-Poletti 2010	7	13	6	10	9	6	**51**
Choi 2019	7	10	16	10	15	11	**69**
D'Souza 2013	2	13	26	10	5	6	**62**
Dai 2022	7	13	29	16	9	3	**77**
De Pinho 2020	10	10	26	6	15	6	**73**
Dickinson 2010	7	16	29	10	9	11	**82**
Donohoe 2018	10	16	32	10	5	6	**79**
Drake 2014	7	16	29	10	15	6	**83**
Eack 2009-2010	7	16	6	10	11	6	**56**
Farreny 2012	7	16	26	10	11	6	**76**
Fekete 2022	2	16	29	6	9	6	**68**
Fisher 2009-2010	7	10	26	10	9	6	**70**
Fisher 2015-Loewy 2021	7	10	26	10	11	6	**68**
Fiszdon 2016	2	10	6	6	9	6	**39**
Garcia 2003-Fuentes 2007	2	10	3	6	0	6	**27**
Garcia-Fernandez 2019	7	10	26	10	9	11	**73**
Garrido 2013-2017	10	16	26	10	5	3	**70**
Hegde 2012	2	10	6	6	5	6	**35**
Hogarty 2004-2006	7	10	16	10	9	11	**63**
Horan 2018	10	13	26	10	15	11	**85**
Ishikawa 2020	2	16	26	6	15	11	**76**
Katsumi 2019	0	13	6	6	11	6	**42**
Kern 2009	2	10	26	10	9	8	**55**
Kidd 2014	2	16	26	10	5	6	**65**
Kidd 2020	5	10	26	10	15	6	**72**
Kukla 2018	2	13	26	10	5	11	**67**
Lado Codesido 2021	2	10	26	6	5	6	**55**
Lo 2023	7	13	26	6	15	6	**73**
Lopez-Morinigo 2023	7	16	26	10	9	6	**74**
Man 2012	2	10	26	16	0	3	**57**
Matsui 2009	2	10	16	6	5	8	**47**
McGurk 2016	2	16	29	6	15	11	**79**
Meichenbaum 1973	2	10	26	10	11	6	**65**
Mueller 2015	10	16	29	6	15	11	**87**
Mueller 2017	7	10	26	6	11	11	**71**
Mueller 2020	7	13	26	6	15	11	**78**
Nijman 2022	7	16	32	10	11	11	**87**
O'Reilly 2019	7	16	32	6	15	11	**87**

Ochoa 2017-Ruiz Delgado 2022	7	13	26	10	9	6	**71**
Østergaard Christensen 2014	7	16	29	6	15	11	**84**
Penades 2006	2	16	16	16	11	6	**67**
Pijnenborg 2019	7	10	26	10	11	8	**72**
Rakitzi 2016	2	16	26	6	9	6	**65**
Rass 2012	2	13	26	16	5	3	**65**
Reeder 2017	10	16	26	6	11	11	**80**
Roberts 2014	7	10	29	6	4	8	**64**
Rodriguez Pulido 2021	7	13	29	10	9	6	**74**
Tan 2013	7	16	29	10	11	6	**79**
Tan 2019-Zhu 2022	10	16	26	10	15	6	**83**
Twamley 2008-2012	7	10	26	6	0	6	**55**
Ueland 2004-2005	0	13	6	10	15	6	**50**
Van Oosterhout 2014	10	16	32	6	9	11	**84**
Vaskinn 2019	2	13	26	6	9	6	**62**
Vass 2022	2	16	26	10	5	6	**65**
Vita 2011a-Deste 2015	5	16	26	10	9	6	**72**
Wang 2013	2	13	26	6	5	11	**63**
Wang 2022	10	13	29	6	15	6	**79**
Wykes 1999-2003	5	16	16	10	15	6	**68**
Wykes 2007a	10	16	6	6	11	11	**60**
Wykes 2007b	10	16	29	6	15	11	**87**
Wykes 2023	10	16	26	16	15	11	**94**
Zhu 2020	10	13	26	6	15	6	**76**
Zhu 2021	10	16	26	16	15	6	**89**

Table S4. Cognitive remediation programs adopted in included studies.

Categories of CR programs	Specific CR programs applied in studies
Computer-based neurocognitive interventions (CACR)	Au 2015 (Captain's Log) Drake 2014 (CIRCuiTS) Reeder 2017 (CIRCuiTS) Wykes 2023 (CIRCuiTS, different therapist support) Cavallaro 2009-Poletti 2010 (Cogpack) Kidd 2014 (Cogpack) Vita 2011a-Deste 2015 (Cogpack) Bryce 2018 (Cogpack) Rodriguez Pulido 2021 (Cogpack) Fisher 2009-2010 (Posit Science, Auditory) Fisher 2015-2021 (Posit Science, Auditory) Kukla 2018 (Posit Science, Brain fitness) Rass 2012 (Posit Science, multiple tasks) D'Souza 2013 (PSSCogrehab) Tan 2013 (PSSCogrehab) Fiszdon 2016 (PSSCogrehab) Garcia-Fernandez 2019 (RehaCom) Kidd 2020 (Scientific Brain Training PRO) Østergaard Christensen 2014 (NEUROCOM) Garrido 2013-2017 (multiple tools) Donohoe 2018 (low-support working memory training) Dickinson 2010 (unspecified) Man 2012 (unspecified) Choi 2019 (unspecified) Tan 2019-Zhu 2022 (unspecified) Dai 2022 (unspecified)
Pencil-and-paper neurocognitive interventions	Wykes 1999-2003 (CRT) Wykes 2007a (CRT) Wykes 2007b (CRT) Pijnenborg 2019 (CRT-based) Tan 2019-Zhu 2022-2 (CRT) Penades 2006 (Frontal/Executive Program) Twamley 2008-2012 (Compensatory Cognitive Training) Zhu 2021 (Compensatory Cognitive Training) Hegde 2012 (home-based, study-specific) Man 2012-2 (unspecified)
Interventions targeting Social Cognition	Wang 2013 (SCIT) Roberts 2014 (SCIT) Lo 2023 (SCIT) Horan 2018 (SCST) Vaskinn 2019 (TAR) Matsui 2009 (Social Perception Training) Lado Codesido 2021 (Voices 2) Nijman 2022 (DISCoVR) Vass 2022 (VR-TOMIS)
Interventions based on an integrative approach	Hogarty 2004-2006 (CET) Eack 2009-2010 (CET) Müller 2015 (INT) Müller 2017 (INT) Müller 2020 (INT) Garcia 2003-Fuentes 2007 (IPT) Vita 2011a-Deste 2015 (IPT) Rakitzi 2016 (IPT)

	Ueland 2004 (IPT-based, study-specific) Bowie 2012 (Thinking Skills for Work) McGurk 2016 (Thinking Skills for Work) Katsumi 2019 (NEAR) Bell 2001-2007 (NET) Farreny 2012 (REPYFLEC) O'Reilly 2019 (study-specific) Zhu 2020 (CACR+ social cognition training)
Metacognitive Training (MCT)	van Oosterhout 2014 Ochoa 2017 de Pinho 2020 Ishikawa 2020 Fekete 2022 Wang 2022 Lopez-Morinigo 2023
Other interventions	Meichenbaum 1973 (Self-instructional Training) Kern 2009 (Errorless learning training)

Figure S1: Forest plot for the effects of cognitive remediation on global cognition (T0-T2)

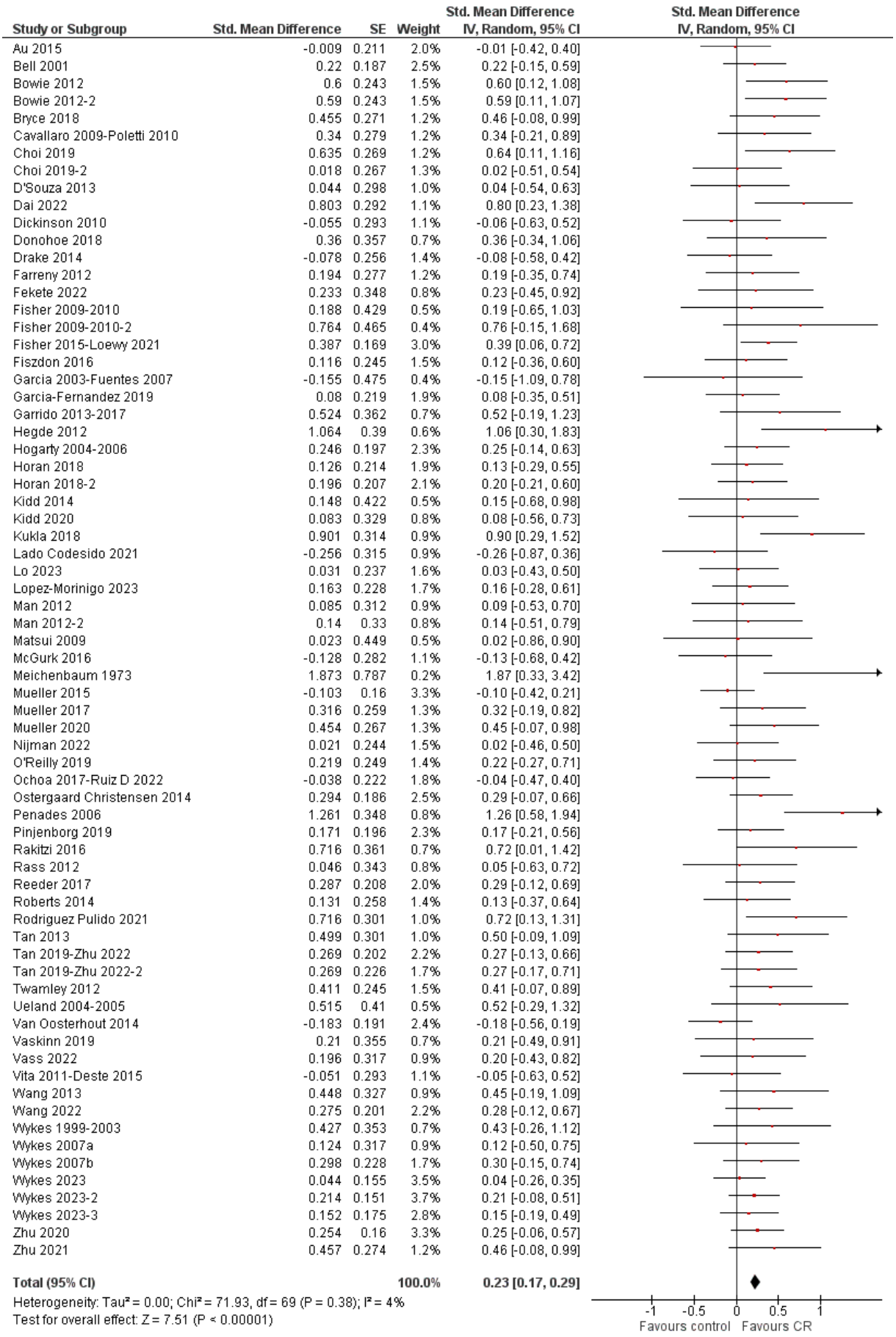


Figure S2: Forest plot for the effects of cognitive remediation on global functioning (T0-T2)

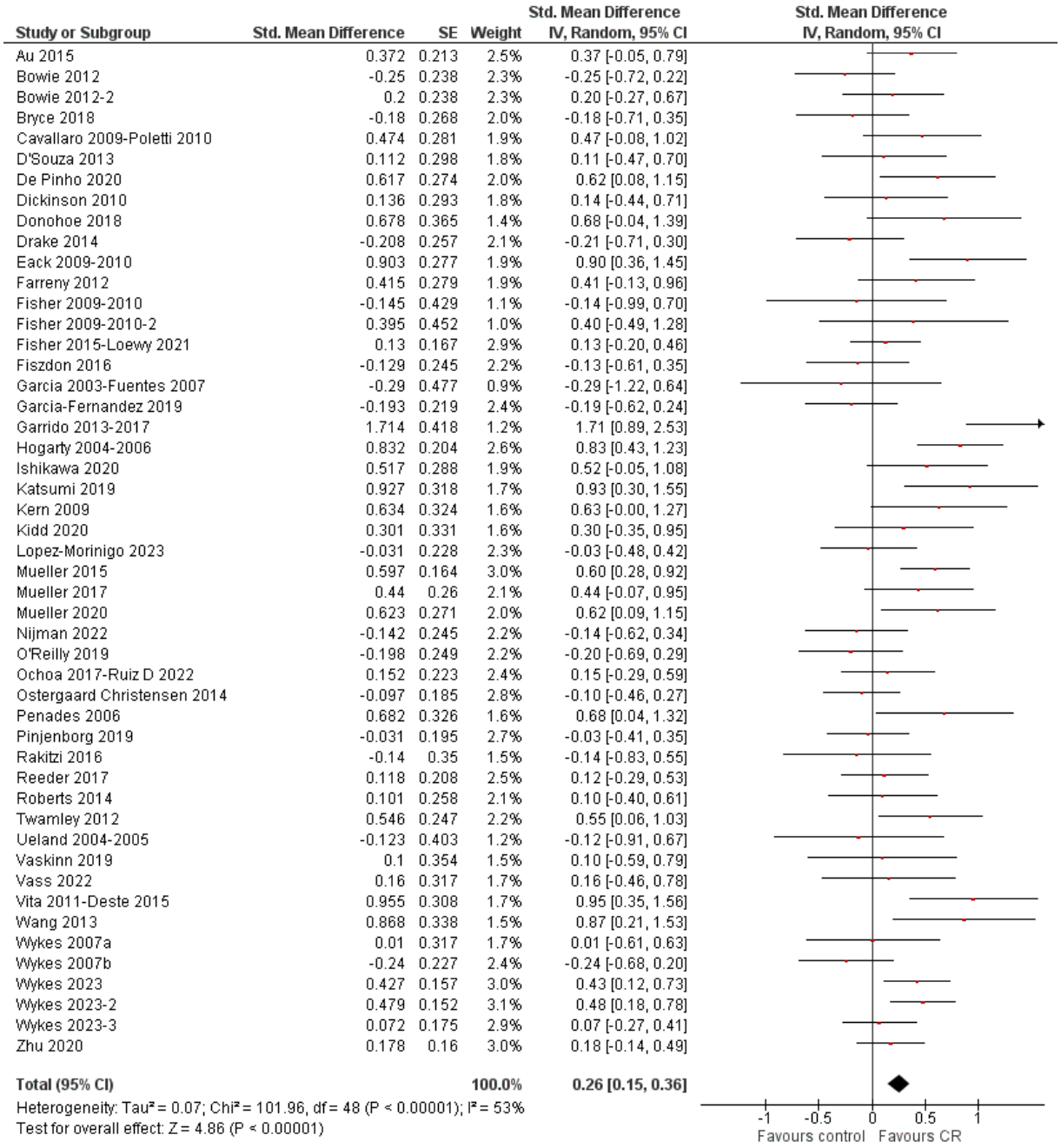


Figure S3: Forest plot for the effects of cognitive remediation on global cognition (T1-T2)

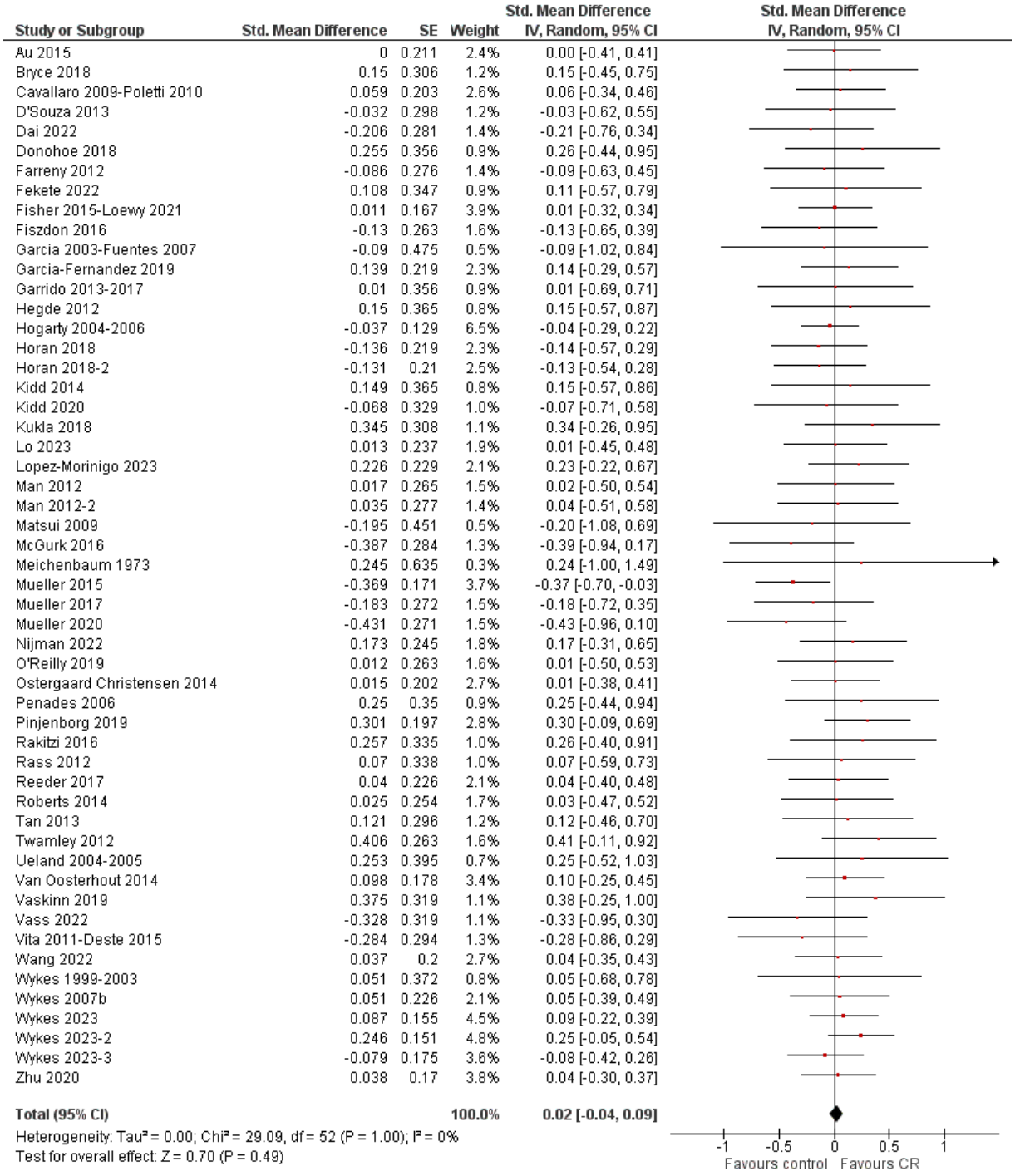


Figure S4: Forest plot for the effects of cognitive remediation on global functioning (T1-T2)

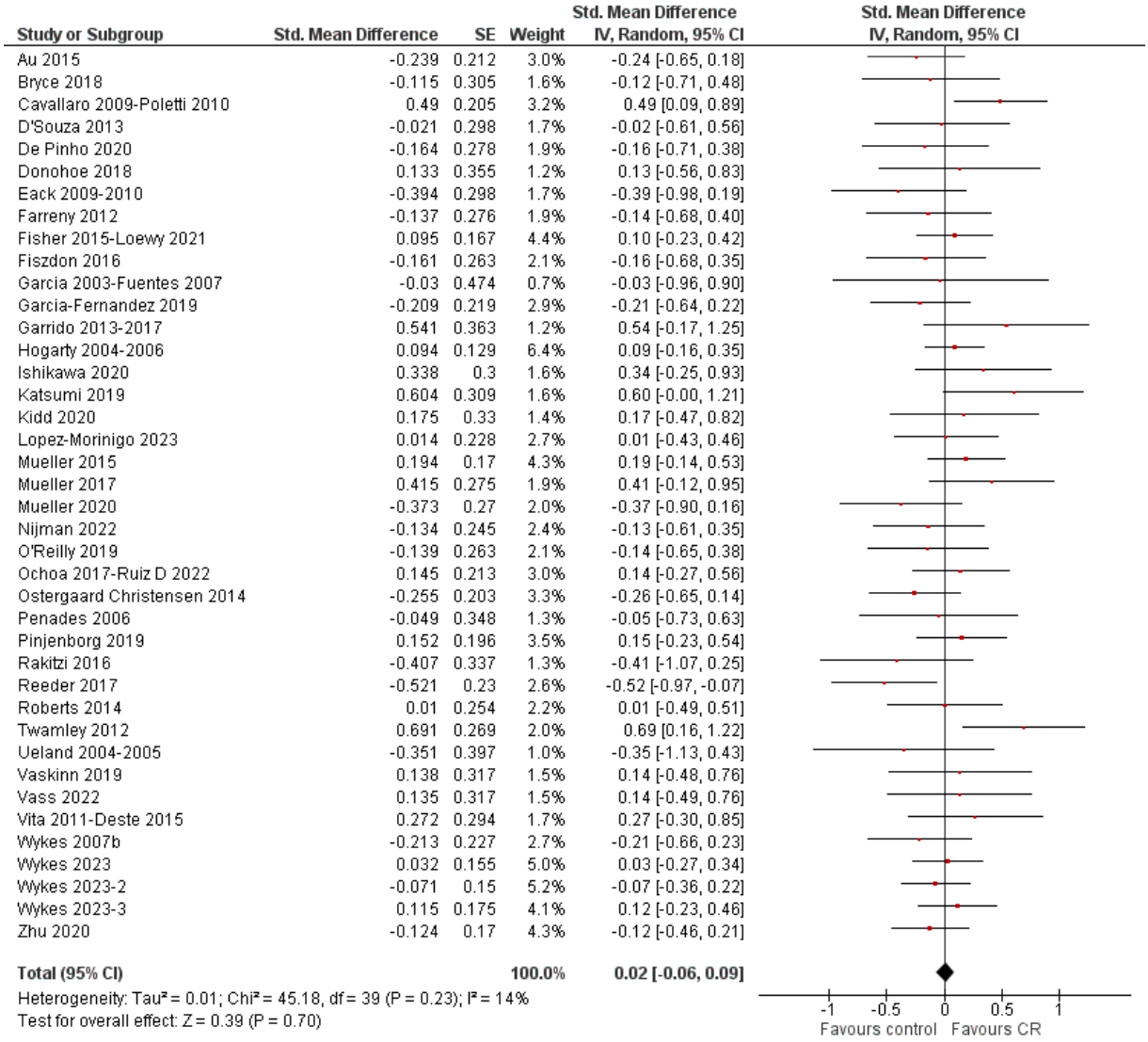


Figure S5: Subgroup analysis for the effects of interventions based on duration of follow-up (global cognition, T0-T2)

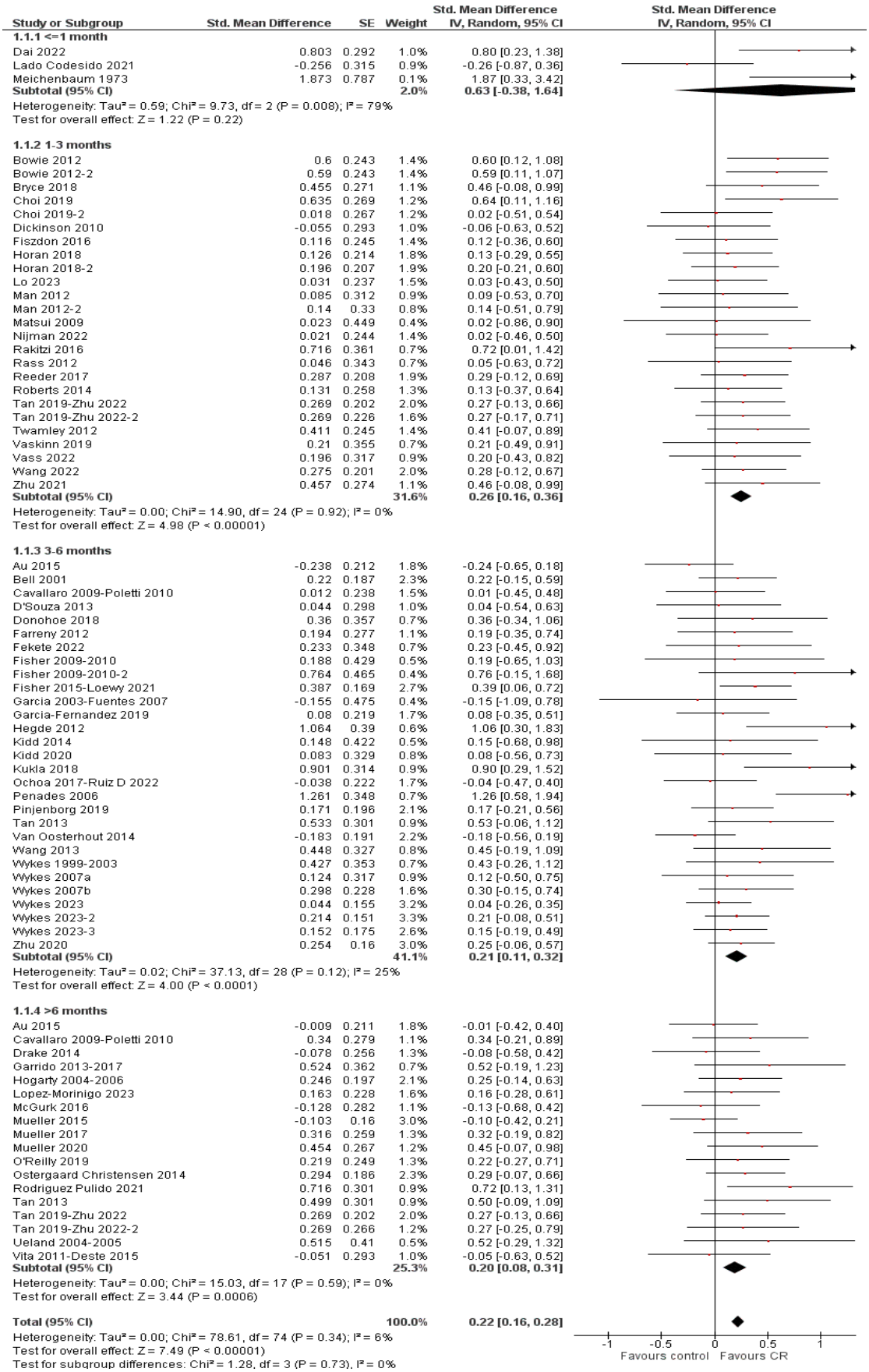


Figure S6: Subgroup analysis for the effects of interventions based on duration of follow-up (global functioning, T0-T2)

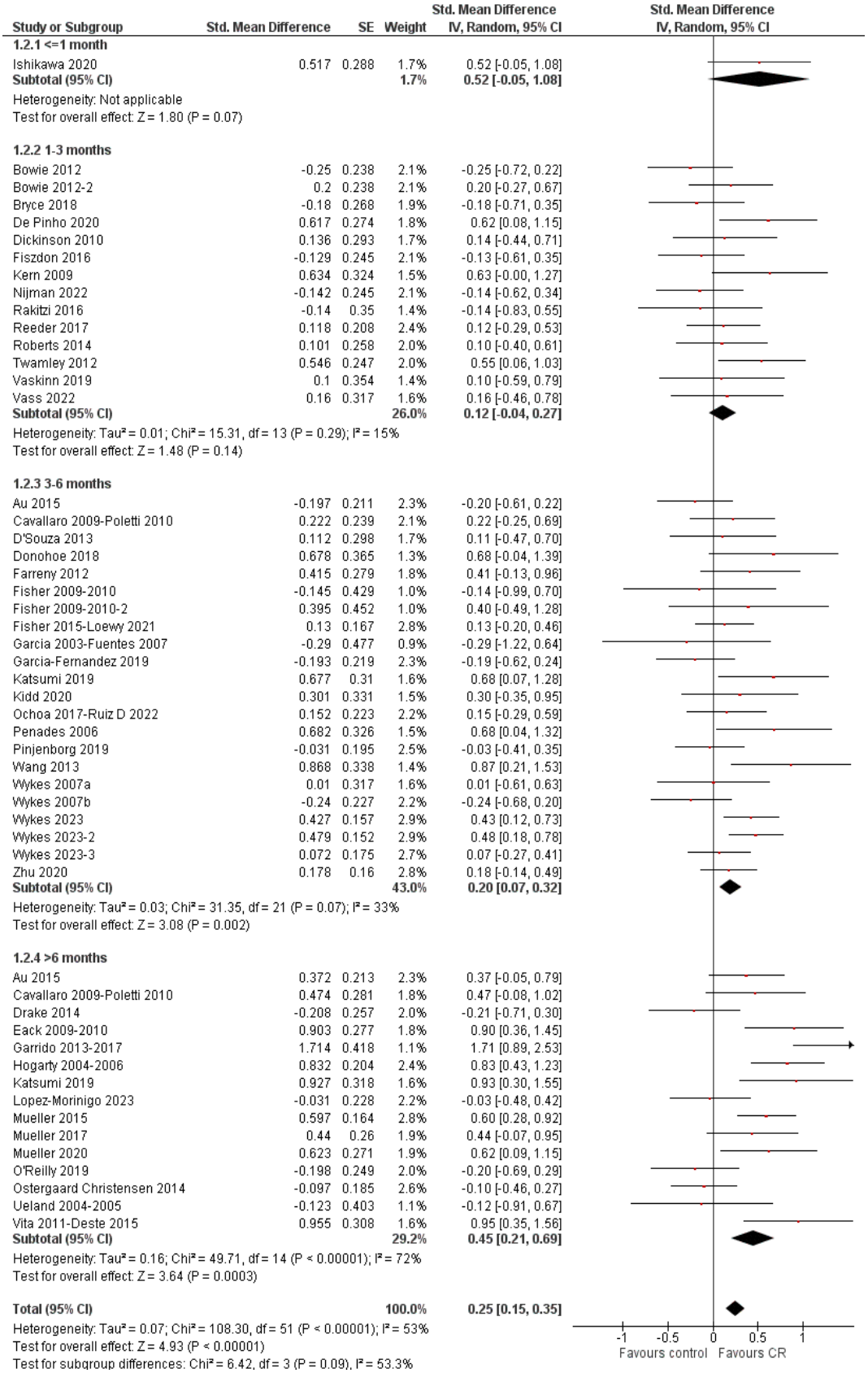


Table S5: Effects of moderators on cognitive and functional outcomes (T1-T2)

Moderator	Global Cognition			Global Functioning		
	N	Coefficient/ Effect Size (95%CI)	p	N	Coefficient/ Effect Size (95%CI)	p
Study characteristics						
Publication year	53	0,001 (-0,009 to 0,012)	0,794	40	-0,002 (-0,016 to 0,011)	0,725
Methodological Quality (CTAM score)	53	-0,001 (-0,006 to 0,004)	0,695	40	-0,004 (-0,010 to 0,001)	0,097
Methodological Quality **Adequate (CTAM ≥ 65)** **Inadequate (CTAM < 65)** **Test for subgroup differences**	 38 15	 d = 0,01 (-0,06 to 0,09) d = 0,05 (-0,07 to 0,18) χ^2 = 0,314 (dF =1)	 0,575	 29 11	 d = -0,02 (-0,11 to 0,06) d = 0,12 (-0,07 to 0,32) χ^2 =1,862 (dF =1)	 0,172
Blinding **Open trials** **Blind trials** **Test for subgroup differences**	 9 44	 d = 0,01 (-0,16 to 0,17) d = 0,03 (-0,04 to 0,10) χ^2 =0,066 (dF =1)	 0,797	 7 33	 d = 0,10 (-0,13 to 0,33) d = -0,01 (-0,09 to 0,08) χ^2 =0,703 (dF =1)	 0,402
Setting **Outpatients** **Inpatients** **Both** **Test for subgroup differences**	 38 9 6	 d = 0,01 (-0,07 to 0,09) d = -0,01 (-0,17 to 0,16) d = 0,14 (-0,05 to 0,32) χ^2 =1,691 (dF =2)	 0,429	 28 5 7	 d = 0,03 (-0,06 to 0,11) d = 0,02 (-0,29 to 0,33) d = -0,06 (-0,28 to 0,16) χ^2 =0,471 (dF =2)	 0,790
Setting **Single centre** **Multi-centre** **Test for subgroup differences**	 35 18	 d = -0,01 (-0,09 to 0,09) d = 0,05 (-0,04 to 0,15) χ^2 =0,757 (dF =1)	 0,384	 27 22	 d = -0,06 (-0,17 to 0,06) d = 0,07 (-0,03 to 0,16) χ^2 =2,378 (dF =1)	 0,123
Setting **Real-world** **Research** **Test for subgroup differences**	 38 15	 d = -0,02 (-0,10 to 0,07) d = 0,08 (-0,02 to 0,19) χ^2 =2,039 (dF =1)	 0,153	 28 12	 d = -0,02 (-0,12 to 0,08) d = 0,06 (-0,07 to 0,18) χ^2 =0,925 (dF =1)	 0,336
Follow-up duration (weeks)	53	-0,002 (-0,007 to 0,003)	0,384	40	0,003 (-0,003 to 0,009)	0,279
Sample size (N randomized)	53	0,000 (-0,001 to 0,002)	0,813	40	0,000 (-0,002 to 0,002)	0,924
Comparison category **TAU** **Active TAU** **Active non-specific interventions** **Active evidence-based interventions** **Test for subgroup differences**	 18 8 13 14	 d = -0,02 (-0,14 to 0,09) d = 0,07 (-0,08 to 0,21) d = 0,01 (-0,14 to 0,16) d = 0,05 (-0,07 to 0,18) χ^2 =1,218 (dF =3)	 0,749	 13 7 10 10	 d = -0,03 (-0,21 to 0,16) d = 0,01 (-0,15 to 0,17) d = 0,10 (-0,06 to 0,26) d = 0,00 (-0,14 to 0,14) χ^2 =1,293 (dF =3)	 0,731
Diagnosis for inclusion **Only subjects with schizophrenia** **Including other diagnoses** **Test for subgroup differences**	 18 35	 d = 0,07 (-0,06 to 0,20) d = 0,01 (-0,07 to 0,08) χ^2 =0,686 (dF =1)	 0,408	 13 27	 d = 0,01 (-0,13 to 0,14) d = 0,02 (-0,08 to 0,11) χ^2 =0,015 (dF =1)	 0,903
Treatment characteristics						
Active and trained therapist (Core element 1) **Present**	 46	 d = 0,02 (-0,05 to 0,09)		 37	 d = 0,01 (-0,08 to 0,09)	

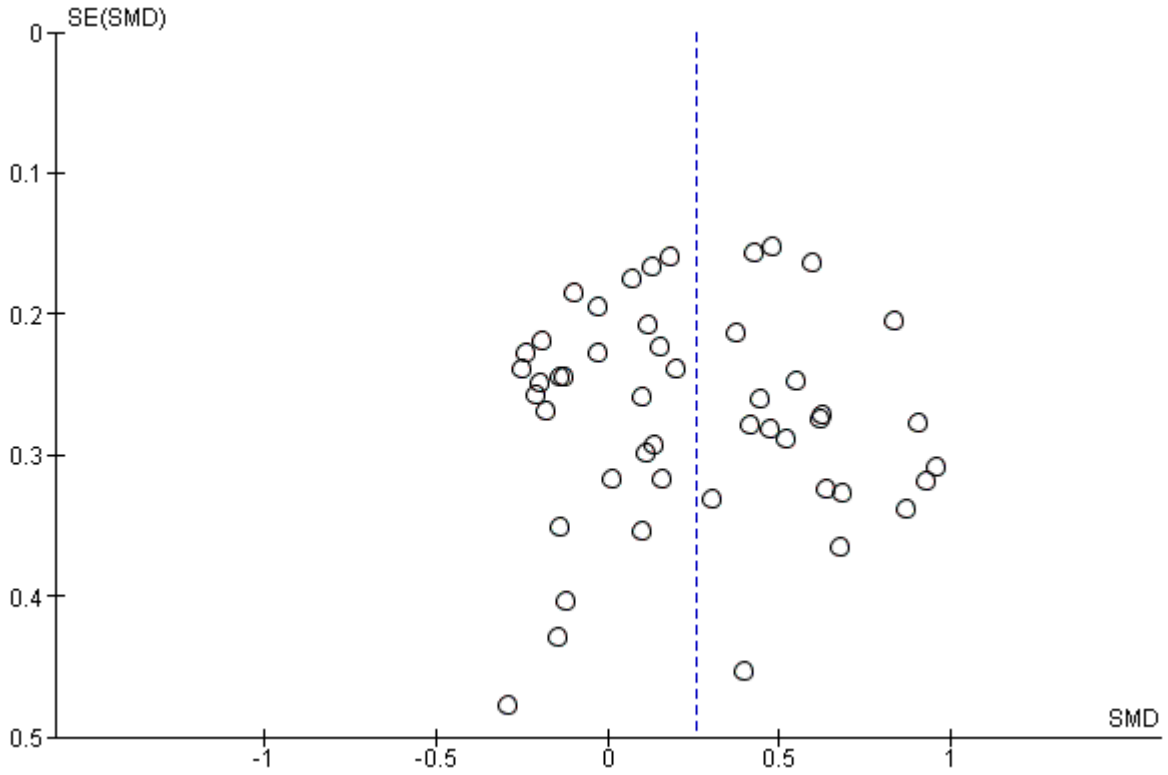
Moderator	Global Cognition			Global Functioning		
	N	Coefficient/ Effect Size (95%CI)	p	N	Coefficient/ Effect Size (95%CI)	p
Absent **Test for subgroup differences**	7	d = 0,06 (-0,12 to 0,25) χ^2 =0,218 (dF =1)	0,641	3	d = 0,11 (-0,13 to 0,34) χ^2 =0,660 (dF =1)	0,416
Repeated practice of cognitive exercises (Core element 2) **Present** **Absent** **Test for subgroup differences**	 39 14	 d = 0,01 (-0,07 to 0,08) d = 0,10 -(0,04 to 0,24) χ^2 =1,462 (dF =1)	0,227	 30 10	 d = -0,02 (-0,10 to 0,06) d = 0,16 (-0,01 to 0,33) χ^2 =3,380 (dF =1)	0,050
Development of cognitive strategies (Core element 3) **Present** **Absent** **Test for subgroup differences**	 44 9	 d = 0,01 (-0,06 to 0,08) d = 0,08 (-0,07 to 0,24) χ^2 =0,677 (dF =1)	0,411	 35 5	 d = 0,02 (-0,07 to 0,11) d = -0,02 (-0,20 to 0,16) χ^2 =0,168 (dF =1)	0,682
Techniques of transfer to real-world (Core element 4) **Present** **Absent** **Test for subgroup differences**	 43 10	 d = 0,02 (-0,05 to 0,09) d = 0,06 (-0,11 to 0,23) χ^2 =0,247 (dF =1)	0,619	 34 5	 d = 0,01 (-0,08 to 0,10) d = 0,03 (-0,16 to 0,22) χ^2 =0,029 (dF =1)	0,866
Integration with rehabilitation (Core element 4bis) **Present** **Absent** **Test for subgroup differences**	 17 36	 d = 0,04 (-0,06 to 0,10) d = 0,01 (-0,07 to 0,10) χ^2 =0,146 (dF =1)	0,702	 14 26	 d = 0,01 (-0,12 to 0,14) d = 0,02 (-0,08 to 0,12) χ^2 =0,011 (dF =1)	0,917
Interventions including all core elements (1,2,3,4) **All core elements** **Not all core elements** **Test for subgroup differences**	 27 26	 d = -0,01 (-0,09 to 0,08) d = 0,06 (-0,04 to 0,16) χ^2 =1,107 (dF =1)	0,293	 21 19	 d = 0,04 (-0,07 to 0,15) d = -0,01 (-0,12 to 0,10) χ^2 =0,413 (dF =1)	0,520
Treatment duration (weeks)	53	-0,001 (-0,004 to 0,002)	0,500	40	-0,001 (-0,003 to 0,003)	0,936
Treatment intensity (sessions/week)	51	0,001 (-0,059 to 0,061)	0,984	39	-0,023 (-0,093 to 0,034)	0,364
Treatment intensity (hours/week)	48	-0,020 (-0,073 to 0,033)	0,451	39	-0,027 (-0,088 to 0,034)	0,386
Format of delivery **Individual format** **Group format** **Test for subgroup differences**	 27 26	 d = 0,04 (-0,05 to 0,14) d = 0,01 (-0,08 to 0,09) χ^2 = 0,311 (dF =1)	0,577	 18 22	 d = -0,02 (-0,13 to 0,09) d = 0,04 (-0,07 to 0,15) χ^2 =0,688 (dF =1)	0,407
Computer presentation **Computerized intervention** **Pencil-and-paper intervention** **Test for subgroup differences**	 38 15	 d = -0,01 (-0,09 to 0,06) d = 0,14* (0,01 to 0,28) χ^2 =3,884 (dF =1)	**0,049**	 28 12	 d = 0,01 (-0,08 to 0,10) d = 0,02 (-0,15 to 0,18) χ^2 =0,005 (dF =1)	0,944
Social cognition among CR targets **Target on social cognition** **No target** **Test for subgroup differences**	 22 31	 d = -0,04 (-0,13 to 0,06) d = 0,07 (-0,02 to 0,16) χ^2 = 2,610 (dF =1)	0,106	 19 21	 d = 0,01 (-0,10 to 0,11) d = 0,03 (-0,09 to 0,15) χ^2 =0,104 (dF =1)	0,747

Moderator	Global Cognition			Global Functioning		
	N	Coefficient/ Effect Size (95%CI)	p	N	Coefficient/ Effect Size (95%CI)	p
Patient and illness characteristics						
Age (years)	53	-0,001 (-0,010 to 0,007)	0,756	40	0,004 (-0,006 to 0,013)	0,466
Gender (% female subjects)	52	-0,004 (-0,007 to 0,006)	0,899	40	0,000 (-0,008 to 0,008)	0,993
Education (years)	29	0,006 (-0,050 to 0,061)	0,843	22	-0,029 (-0,095 to -0,038)	0,400
IQ	26	-0,007 (-0,020 to 0,006)	0,320	22	0,007 (-0,007 to 0,021)	0,318
Age of onset (years)	33	0,022 (-0,018 to 0,062)	0,276	28	-0,009 (-0,051 to 0,033)	0,671
Duration of illness (years)	33	0,003 (-0,009 to 0,014)	0,636	28	0,004 (-0,009 to 0,017)	0,565
Baseline treatment dose (CPZeq)	29	0,000 (-0,001 to 0,004)	0,858	28	0,000 (-0,001 to 0,001)	0,759
Baseline symptoms severity (PANSS score)	39	0,001 (-0,004 to 0,006)	0,718	30	0,000 (-0,006 to 0,006)	0,999
Baseline positive symptoms (PANSS-P)	26	0,007 (-0,013 to 0,028)	0,491	23	-0,001 (-0,023 to 0,022)	0,976
Baseline negative symptoms (PANSS-N)	27	0,002 (-0,020 to 0,024)	0,835	23	-0,009 (-0,035 to 0,017)	0,503

*: statistically significant effect ($p<0.05$)

Coefficients values in metaregressions indicate that a one-unit increase in the moderator corresponds to an increase in the effect size by the amount indicated by the corresponding regression coefficient.

Figure S7: Analysis of publication bias – Funnel plot for global cognition



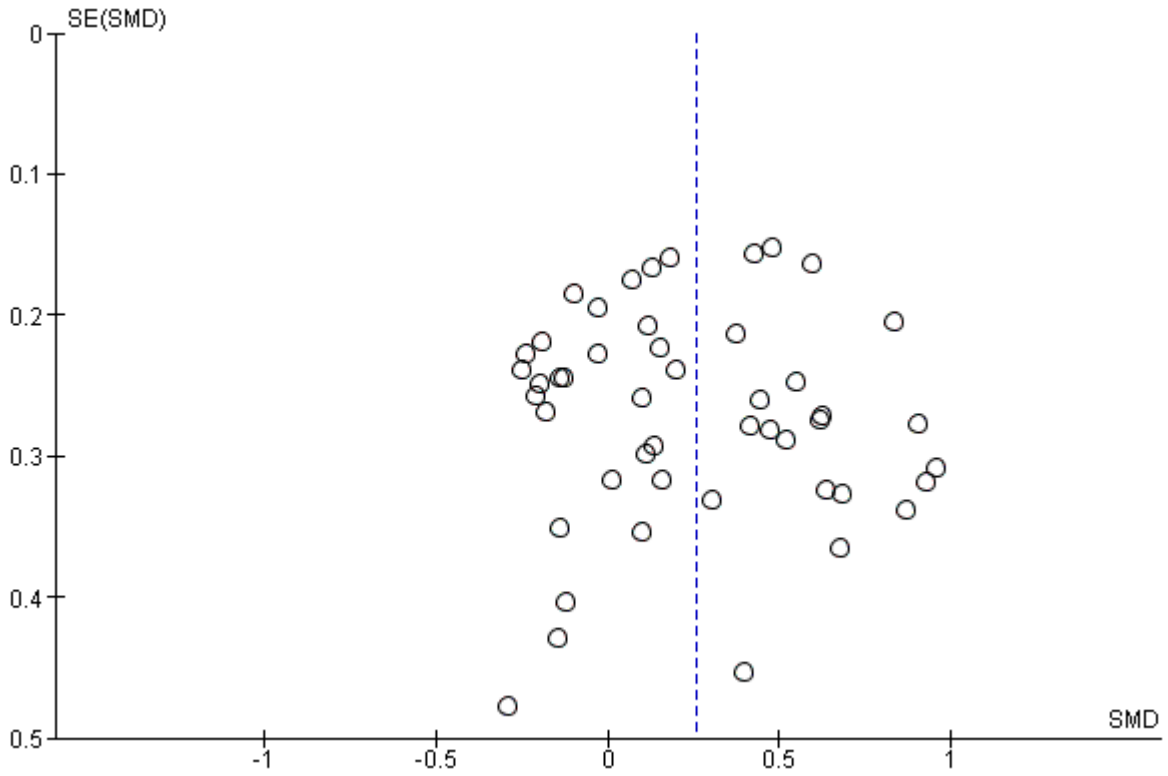
Test for asymmetry of funnel plot (linear regression of effect estimates on their standard errors weighted by their inverse variance – Egger's test):

	N	Coefficient	SE	95% CI (lower limit)	95% CI (upper limit)	p value
Intercept	70	1.240	0.411	0.420	2.059	0.004

Adjustment of effect estimates using the Duval and Tweedie's trim and fill method (studies missing to the left of the mean; random-random effects model):

	N	Point Estimate	95% CI (lower limit)	95% CI (upper limit)
Observed	70	0.230	0.170	0.290
Adjusted	+1	0.192	0.122	0.262

Figure S8: Analysis of publication bias – Funnel plot for global functioning



Test for asymmetry of funnel plot (linear regression of effect estimates on their standard errors weighted by their inverse variance – Egger's test):

	N	Coefficient	SE	95% CI (lower limit)	95% CI (upper limit)	p value
Intercept	49	0.542	0.763	-0.994	2.077	0.241

Table S6. Sensitivity analyses for primary outcomes

Analysis	Global cognition (T0-T2)	Global functioning (T0-T2)
Original meta-analysis (random effects model)	**d=0.23 (95%CI 01.7-0.29) (70 comparisons)**	**d=0.26 (95%CI 0.15-0.36) (49 comparisons)**
Fixed effects model	d=0.23 (95%CI 0.17-0.29) (70 comparisons)	d=0.25 (95%CI 0.18-0.32) (49 comparisons)
One effect size per study (randomly selected)	d=0.23 (95%CI 0.16-0.29) (62 comparisons)	d=0.27 (95%CI 0.16-0.38) (45 comparisons)
One effect size per study (most substantial comparison)	d=0.24 (95%CI 0.17-0.31) (62 comparisons)	d=0.26 (95%CI 0.15-0.37) (45 comparisons)
Removing outliers	d=0.21 (95%CI 0.15-0.27) (66 comparisons)	d=0.21 (95%CI 0.11-0.30) (46 comparisons)
Removing studies with insufficient details on allocation	d=0.21 (95%CI 0.14-0.28) (47 comparisons)	d=0.29 (95%CI 0.15-0.42) (32 comparisons)
Removing studies providing only completers data	d=0.23 (95%CI 0.16-0.31) (37 comparisons)	d=0.24 (95%CI 0.11-0.36) (27 comparisons)
Removing studies with attrition rate >50% at follow-up	d=0.23 (95%CI 0.17-0.29) (67 comparisons)	d=0.24 (95%CI 0.14-0.34) (46 comparisons)
Removing studies of interventions designed for trial purpose	d=0.22 (95%CI 0.16-0.29) (57 comparisons)	d=0.29 (95%CI 0.17-0.41) (41 comparisons)
Removing studies evaluating Metacognitive Training	d=0.25 (95%CI 0.18-0.31) (65 comparisons)	d=0.26 (95%CI 0.14-0.37) (45 comparisons)