

Review Article

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A meta-analysis of cognitive interventions for patients with recent onset psychosis: are they effective for improving functioning?

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Abstract

The increasing popularity of cognitive interventions for patients with psychosis calls for further exploration on how these interventions may benefit functional outcomes. We conducted a meta-analysis of randomized controlled trials (RCTs) to examine the effectiveness of cognitive interventions (i.e. Cognitive Remediation, Cognitive Training, Social Cognition, and their combination) on functioning of patients with recent onset psychosis, established as the period within the first five years from the first episode. The following databases were searched: Proquest, PUBMED/MEDLINE, PsycINFO, WOS, Scopus for research published until January 2022. In total, 12 studies were eligible. The total number of participants was 759, of which 32.2% in the intervention and 30.8% in the control group were female. We extracted data to calculate the standardized mean change from pre-test to post-test comparing the intervention with the control conditions. Overall, there was no effect of any of the cognitive intervention types on functioning. None of the examined factors (intervention type, length, and modality; control condition, follow-up time; cognitive functions; medication; symptoms) seemed to moderate these findings. Our results indicate that cognitive interventions as standalone interventions do not appear to improve functioning in patients with recent onset psychosis. Given the small number of eligible studies, further RCTs with larger and more refined samples are needed to test whether these interventions should be applied as single interventions with these patients.

Introduction

The first five years after a first episode of psychosis are considered the most critical time for determining a patient's long-term outcomes (Crumlish et al., 2009). This is the period when most functional and cognitive impairments are observed (Coentre, Levy, & Figueira, 2011) and when patients show the highest relapse rates throughout the course of the disorder (Kaleda, 2009). Psychosis onset coincides with the completion of brain maturation (Paus, Keshavan, & Giedd, 2008), and the following five years are considered a period of maximum cognitive and psychosocial plasticity (Birchwood, Todd, & Jackson, 1998). Therefore, a unique opportunity arises for offering appropriate biopsychosocial care (International Early Psychosis Association Writing Group, 2005). This is also reflected in the Mental Health Action Plan 2013–2030 guidelines (World Health Organization, 2021), that prioritize early identification and management of such patients.

Thus, when designing recovery services for patients with recent onset psychosis, it is essential to include interventions that target outcomes beyond symptomatic remission, such as functioning (Calvo et al., 2018). Impaired functioning is consistently found to be associated with cognitive deficits (Halverson et al., 2019; Kharawala et al., 2022). Importantly, for patients within the first five years of the onset of psychosis, cognitive deficits arise as strong and independent predictors of functional outcomes, even after accounting for the contribution of symptoms, duration of untreated psychosis (DUP), and duration of illness (Cowman et al., 2021). Therefore, interventions targeting these deficits may potentially improve functioning.

There are several types of cognitive interventions used with patients with psychosis. The most widely used are Cognitive Remediation (CR) interventions, defined by the Cognitive Remediation Experts Workshop (April 2010, Florence) as 'behavioural training-based interventions that aim to improve cognitive processes (attention, memory, executive function, social cognition or metacognition) with the goal of durability and generalisation' (Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). CR interventions are seen to adopt a

restorative approach of cognitive functioning and attempt to reduce impairments. The rationale behind these interventions is that improvement in the targeted cognitive factors will also be associated with improved functioning. A previous meta-analysis focusing only on CR interventions for patients with early psychosis (Revell, Neill, Harte, Khan, & Drake, 2015) suggested a non-significant positive effect on global cognition, and significant moderate effects on functioning. Another recent meta-analysis on psychosocial interventions used with these patients also reported a modest significant positive impact of CR interventions on functioning (Frawley, Cowman, Lepage, & Donohoe, 2023). However, both meta-analyses included studies of patients with more than five years since the first onset of psychotic symptoms, studies with samples at risk of psychosis, and samples with mixed diagnoses (i.e. patients with psychosis and other severe mental illnesses such as bipolar disorder).

Though conceptualized as part of CR interventions, some studies employ interventions based solely on Social Cognition strategies (SC) (Horan & Green, 2019), targeting emotional and social perception and processing, Theory of Mind, and attributional style (Savla, Vella, Armstrong, Penn, & Twamley, 2013). A recent meta-analysis considering samples at any stage of psychosis, suggested that interventions that adopt a wide social cognition approach, which target almost all the above-mentioned social cognition elements, improve emotional processing, Theory of Mind, and functioning (Nijman, Veling, van der Stouwe, & Pijnenborg, 2020).

On the other hand, Compensatory or Cognitive Training (CT) interventions aim to counterbalance cognitive impairments by relying on intact cognitive skills having a direct influence on functioning (Twamley, Jeste, & Bellack, 2003). These interventions usually include techniques such as internal self-management strategies, external strategies/environmental modification, and errorless learning. A recent meta-analysis on CT effectiveness for patients with severe mental illness proposed robust and durable effects on functioning (Allott et al., 2020).

Considering the previous evidence and given the lack of systematic evidence-based conclusions on whether cognitive interventions improve functioning in patients with recent onset psychosis, there is a need to examine the effectiveness of these interventions in a systematic way.

Therefore, the aims of the present meta-analysis were (1) to examine the available evidence on the range of cognitive interventions destined to patients with recent onset psychosis and determine the effect size of their impact on functioning (performance or capacity-based, global, social), based on results from randomized controlled trials (RCTs); (2) to identify any factors that may be moderating the effectiveness of such interventions, such as (a) the type of cognitive intervention (Cognitive Remediation, Cognitive Training, Social Cognition, or any combination of those), (b) type of control intervention (treatment as usual (TAU), other intervention, other control condition), (c) length of interventions and follow-up, (d) type of sessions (i.e. group or individual), (e) intervention format (non-computerized, computerized with supplementary human guidance/therapist-provided strategy coaching) (f) medication dosage, (g) improvement in cognitive functions and (h) symptoms.

Methods

The meta-analysis was conducted adhering to the PRISMA guidelines (Page et al., 2021) and was registered in the PROSPERO database (CRD42022314045).

Search strategy

We searched the following databases: Proquest, PUBMED/MEDLINE, PsycINFO (EBSCO), Web of Science, and Scopus, for documents published in English until January 2022, with no restriction in terms of publication period. We also performed reference checking by hand searching the reference list of included articles and relevant reviews/meta-analyses to identify potentially eligible studies.

Separate searches were run in each database and included a combination of key words related to the population, intervention types, design of studies and outcomes, based on Abstract, Title, and Keyword (when available). Terms were as follows: 'First episode' OR 'First-episode' OR 'FEP' OR 'Early' AND 'Psychosis' OR 'Psychoses' OR 'Psychotic' OR 'severe mental illness' OR 'schizophrenia' AND 'Cognit*'

AND 'Functioning' AND 'intervention' OR 'therapy' OR 'training' OR 'program*' OR 'service' AND 'Randomised' OR 'Randomized' OR 'RCT'.

Inclusion and exclusion criteria

To be able to provide refined conclusions, we adopted a strict application of the -five years since onset- criteria to define recent onset psychosis (Crumlish et al., 2009; Kaleda, 2009), we excluded studies of interventions applied to samples with several diagnoses, and we carefully considered the potential impact of having different types of interventions used as the control condition. Studies were included if they: (a) described RCTs of interventions targeting (or measuring as an outcome) functioning; (b) focused on patients with recent onset psychosis (within the last 5 years) of any gender and age; (c) examined programs of Cognitive Interventions of any type (i.e. Cognitive Remediation (CR), Cognitive Training (CT), Social Cognition Training (SC), the combination of those) of any length, modality (i.e. group or individual) and format (non-computerized, computerized with supplementary human guidance/therapist-provided strategy coaching) in any inpatient or outpatient mental health setting; (d) included control conditions such as TAU (i.e. early intervention services components), being on the waiting list (scheduled to receive the intervention under study at a later stage), or any other intervention; (e) assessed functioning through standardized instruments (i.e. with properly established psychometric properties).

Studies were excluded when (a) targeting or including population of patients that suffered from psychosis for more than five years; (b) had mixed diagnoses (i.e. patients with psychosis and mood disorders) or drug induced psychosis; (c) were at ultra-high risk for psychosis; (d) had a design other than RCT, (e) presented non primary data of functioning outcomes (f) were published as comments, letters, editorials, conference reports/posters, or books, (g) did not report enough statistical parameters to allow the calculation of effect sizes (i.e. mean, standard deviation, sample size for intervention and control group, or standardized mean difference), or data were not available by authors.

Screening and data extraction

Two reviewers (NMM, EP) conducted screening of titles and abstracts based on the inclusion criteria, and then accessed full texts for eligibility. Discrepancies were discussed with two of the other authors (AC, TSG). Seven authors were contacted to request

missing data, with only one (Wykes *et al.*, 2007) (14.0%) responding to the request. Data from each eligible study were extracted by the same two reviewers (NMM, EP) and included the following: study year and country; participant characteristics: population size and demographics (sex, age, diagnosis); intervention characteristics: length, type (CR, CT, SC, combination of any of those), modality (group-individual); medication (Chlorpromazine equivalents-CPZE mg/day); study follow-up time. To account for heterogeneity due to the different types of control group intervention/conditions, we reshaped the approach of Vita *et al.* (2021), creating three categories as follows: (a) Active TAU: i.e. early intervention services, pharmacological therapy-case management, waiting lists (scheduled to receive the intervention under study at a later stage), TAU not specified; (b) other evidence-based intervention; (c) other control condition specifically designed for the study, matching the intervention condition in modality and duration, such as computerized games. Lastly, we collected means and SDs for functioning, cognitive functions, and symptoms (see section below).

Outcomes and moderators

The primary outcome was change in functioning. All types and standardized measures of functioning were included (global, social, self-rated, clinician rated or performance-based).

Changes in the cognitive functions were considered as moderators. As the neuropsychological instruments used to measure the cognitive domains were different in some of the studies, we grouped the subtest into six domains, following previous research (Cuesta *et al.*, 2015; Sánchez-Gutiérrez *et al.*, 2020): attention, executive functioning (considering working memory separately), processing speed, verbal memory and learning, visual memory, and social cognition (online Supplementary Table 1).

Symptom severity scores as measured by the PANSS (Positive, Negative, General, and Overall; Kay, Fiszbein, and Opler, 1987), and medication doses measured as CPZE mg/day at baseline were also included to check for their contribution as moderators.

Quality assessment

Two authors (NMM, EP) checked for the quality of RCTs included in the review based on the Effective Public Health Practice Project Quality Assessment Tool (Thomas, Ciliska, Dobbins, & Micucci, 2004). A study was considered strong based on the following criteria: absence of selection bias by including a sample that is representative of the target population; RCT design, control of confounders, appropriate blinding procedures (participants and outcome assessors unaware of the research question); data collection based on validated instruments; and low withdrawals and drop-outs. Disagreements were resolved upon discussion with a third author (AC).

Statistical analyses

A meta-analysis was performed using Cohen's *d* standardized mean changes as the effect size (Becker, 1988). The standardized mean change is an effect size that indicates the mean change in the intervention group (from pre-test to post-test measures) relative to the mean change in the control group. First, we calculated the mean change of the intervention group (using the pre-test standard deviation as the denominator), and then the mean change of the control group (using the pre-test standard

deviation of the control group as the denominator). These two Cohen's *d* were corrected for small sample bias, resulting in Hedges' *g* (Hedges, 1981). Then, these two effect sizes were subtracted to obtain the standardized mean change. To calculate the sampling variance of the standardized mean change, we used the formulas provided by Morris and DeShon (2002, see Table 2 in their article for single-group pre-test-post-test formulas). As the correlation between the pre- and post-test measure was not reported in any of the studies, we imputed an average correlation of 0.40.

Some of the studies included several measures of functioning, which led to obtaining multiple effect sizes from the same study based on the same sample. This statistical dependency among effect sizes was modelled using three-level models to obtain the overall effect in order to avoid inflated Type I errors (Cheung, 2014; Van den Noortgate, López-López, Marín-Martínez, & Sánchez-Meca, 2013, 2015). A three-level model considers that observed effect sizes (Level 1) are nested within different outcomes (Level 2), which are at the same time nested within studies (Level 3). In addition, the Robust Variance Estimation (RVE) method (Tipton, Pustejovsky, & Ahmadi, 2019) was applied a posteriori to the three-level model results to correct potential shrunk standard errors, and therefore obtain adequate Type I error rates (Fernández-Castilla *et al.*, 2021).

Meta-regressions were performed to check for differences based on cognitive intervention type (i.e. CR, CT, SC, and combination of those) and control group interventions. Three-level meta-regression analyses were performed to examine the influence of baseline medication, symptoms, change in cognitive functions, length of intervention, intervention modality (group-individual), intervention format (non-computerized, computerized with supplementary human guidance/therapist-provided strategy coaching) and length of follow up. These variables were first entered in the meta-regression alone, and then together with the variable 'cognitive intervention type' to control for potential differences in these study variables across type of interventions. The standard errors obtained from these three-level meta-regressions were also corrected using RVE methods.

Funnel plots were generated for each type of intervention to check for the possible presence of publication bias. However, since there were less than 10 studies for interventions, funnel plots should be interpreted with caution.

Results

Study selection

A total of 783 studies were initially identified, and 12 studies were finally included in the meta-analysis (See online Supplementary Figure 1 for the study selection procedure based on the PRISMA checklist).

Study and sample characteristics

Study, sample, and intervention characteristics of each included study can be seen at Table 1. There were four studies conducted in Spain, two in the USA, UK, and Denmark respectively, and one in Canada and Iceland respectively.

The total number of participants was $N = 759$, with $n = 393$ (32.2% female) in the intervention group and $n = 366$ (30.8% female) in the control group. The mean age of participants in

Table 1. Cognitive functions and symptoms as moderators of the intervention effects on functioning

Moderators	Effects (studies)	<i>B</i>	<i>p</i> -value
Cognitive functions			
Attention	20 (9)	0.022	0.507
Executive functions	27 (11)	0.170	0.360
Working memory	15 (9)	-0.146	0.149
Processing speed	11 (8)	-0.052	0.867
Social cognition	40 (8)	0.049	0.557
Verbal memory and learning	21 (9)	-0.029	0.900
Visual memory	15 (9)	-0.334	0.540
Symptoms			
Positive	9 (7)	-0.440	0.429
Negative	9 (7)	0.106	0.825
General psychopathology	2	-	-
Total symptoms	10 (7)	0.387	0.273

B = regression coefficient that represents the effect of the Cohen's *d* that summarizes the effectiveness of cognitive interventions on cognitive functions and symptom outcomes on the Cohen's *d* that summarizes the effect of cognitive interventions on functioning.

the control group was 24.17 (s.d. = 4.65) and in the intervention group was 24.13 (s.d. = 4.49).

Type, format and modality of interventions

Eight interventions were held on individual basis and four had a group format. Five interventions were delivered without computer software and seven were computerized. Of those computerized, two were delivered with supplementary human guidance and five with therapist-provided strategy coaching.

There were six studies implementing interventions of CR, three studies implementing CT, two implementing interventions that combined CR with SC and one that combined CT with SC. Further details on the content of each intervention are displayed in Table 1. The duration of the interventions ranged from eight to 48 weeks, with an average of 19. Five studies included a follow-up assessment, and the mean follow-up time was 19 weeks, ranging from 0 to 52 weeks.

Type of comparison interventions

There were six studies comparing the experimental interventions with TAU, one comparing them with other evidence-based therapy and five using other control conditions (see Table 1 for details).

Type of outcome

To measure functioning, two of the included studies based their assessment solely on the UPSA-B, two used the GAF, three used the SBS, the GIFS and the SCORSS respectively, whereas five studies included a combination of measurements (see Table 1 for details).

Study quality and risk of bias

Based on the quality assessment, most of the studies had a global score of strong quality ($k = 10$), with only two studies having a moderate score. There were no studies with an overall weak score. However, some of the studies scored weakly in the areas of selection bias, for instance reporting less than 60% agreement to participate in the study ($k = 2$), lack of complete blinding ($k = 2$), and high percentage of withdrawals/dropouts ($k = 2$) (online Supplementary Table 2).

The visual inspection of the funnel plots revealed no publication bias, except for the detection of one outlier, which was considered in the meta-analysis.

Overall effect of cognitive interventions on functioning

The 12 studies reported 18 effect sizes of functioning (global or social functioning). Most effect sizes were within -1 and 1 , except for one potential outlier ($g = 3.5$). The overall effect of the interventions on functioning as compared to the control conditions was not significant ($g = -0.029$; $p = 0.639$, 95% CI -0.165 to 0.107). This remained not significant when removing the potential outlier: ($g = -0.048$; $p = 0.417$, 95% CI -0.176 to 0.081). See Forest plots (Figs 1–3) for details.

Effect on functioning based on type of intervention

From the 18 effect sizes of the reported functioning outcomes, CR interventions were used in nine. The overall effect for this type of intervention was not significantly different from zero ($g = -0.081$; $p = 0.543$); four outcomes were reported in studies implementing CT interventions, and the overall effect for this intervention type was not significantly different from zero ($g = 0.048$; $p = 0.646$). Finally, a combination of interventions (CR or CT with SC) were used in studies for the remaining five functioning outcomes, and the overall effect was not statistically different from zero ($g = -0.025$; $p = 0.754$). A moderator analysis using 'type of intervention' as a predictor variable showed that there were no statistical differences between the overall intervention effects. Therefore, none of these interventions worked better than the control conditions to improve functioning. Sensitivity analyses were performed, and analyses were repeated after removing the potential outlier. The overall effect of the CT interventions changed to $g = -0.126$ but remained not significantly different from zero ($p = 0.325$).

Effect on functioning based on control group intervention type

The different types of intervention used in control groups did not seem to influence the findings. TAU was used as a control group in relation to 10 of the 18 functioning outcomes ($g = -0.020$; $p = 0.839$), other evidence-based therapy was used in a study for one outcome ($g = -0.052$; $p = 0.800$), and 'other control condition' was used in studies for seven outcomes ($g = -0.035$; $p = 0.755$). There were no differences among the overall effects from each control group intervention category, and none of these overall effects were statistically different from zero. After removing the potential outlier, the overall effect of the category 'other control condition' changed to $g = -0.085$, however it remained not significantly different from zero ($p = 0.178$; see online Supplementary File 1 for details).

Forest plot with all interventions

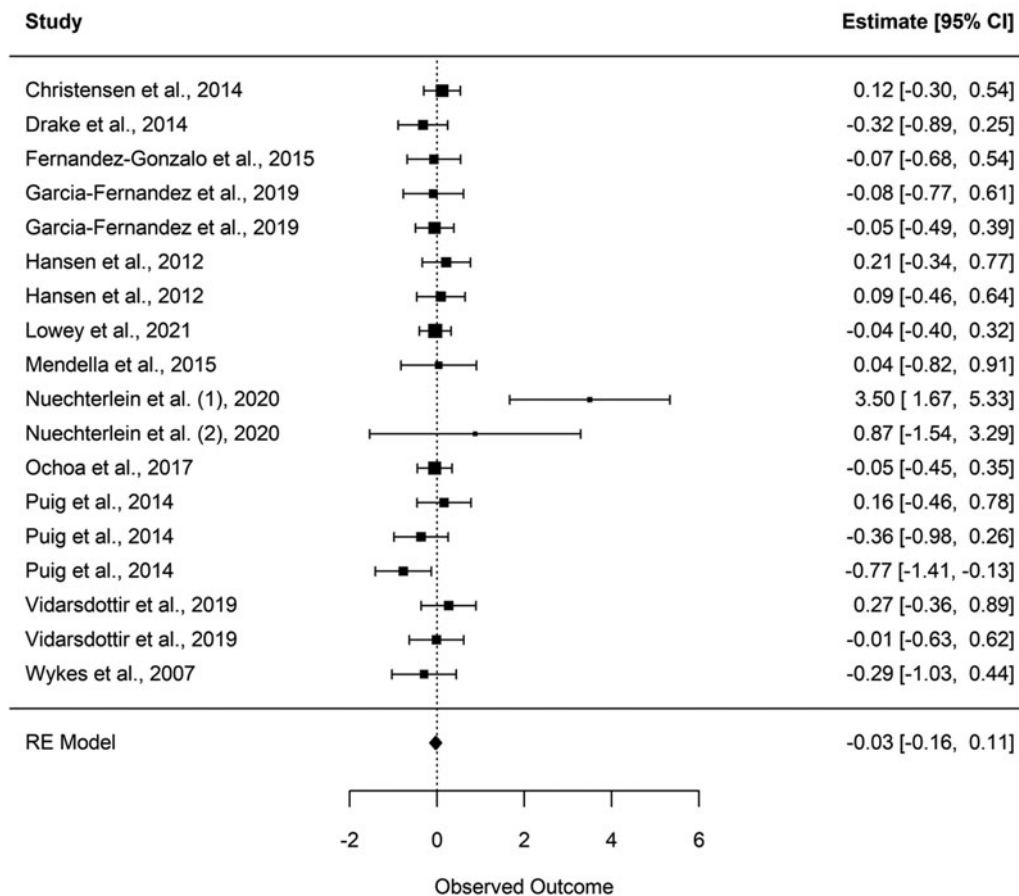


Figure 1. Forest plot of the effect of all cognitive interventions on functioning.

Effect on functioning based on intervention format and modality

The overall effect for studies with interventions applied in individual format was $g = -0.075$ ($p = 0.328$) and the overall effect of studies with group intervention was $g = 0.120$ ($p = 0.493$). No significant differences were found between these categories ($t = -1.07$, $p = 0.328$). Removing the outlier did not change the results. Intervention format was not statistically significant when entered together with the variable 'type of cognitive intervention' (See online Supplementary File 1 for details).

Results showed that the overall effect of studies that used no computer software ($g = -0.09$, $s.e. = 0.12$, $k = 8$) was not statistically different from the overall effect of those studies that used supplementary human guidance or therapist-provided strategy coaching ($g = 0.02$, $s.e. = 0.06$, $k = 10$; difference = 0.11, $s.e. = 0.134$, $t = 0.832$, $p = 0.435$). The same results were found when the outlying effect size was removed. This variable was not statistically significant when it was entered together with type of intervention.

The overall effect size for those studies that used supplementary human guidance was -0.05 ($s.e. = 0.01$, $k = 3$), whereas the overall effect for studies that included no computer software was -0.09 ($s.e. = 0.12$, $k = 8$), and for those with a therapist-provided strategy coaching intervention was 0.08 ($s.e. = 0.11$,

$k = 7$). No statistical differences were found across categories, even when the outlying effect was removed and when type of intervention was added as a control variable in the meta-regression.

Duration of the intervention and follow-up

The intervention duration did not seem to influence the results ($B = 0.032$, $p = 0.152$) across interventions. The same results were found when the outlying effect size was removed ($B = 0.015$, $p = 0.073$). When entered together with type of intervention (CR, CT, combination of any) the intervention duration remained non-significant. (See online Supplementary File 1 for details).

Similarly, follow-up assessment time did not seem to influence the results. Five studies reported seven effect sizes with follow-up data and the overall effect for these standardized mean changes (from pre-test to follow up) was not statistically significant ($g = -0.08$, $p = 0.228$).

Cognitive functions

The standardized mean changes of the variables examining cognitive functions (attention, working memory, executive functions, etc.) were independently introduced as moderators in the meta-regression to test whether the intervention effectiveness on

Forest plot by intervention type

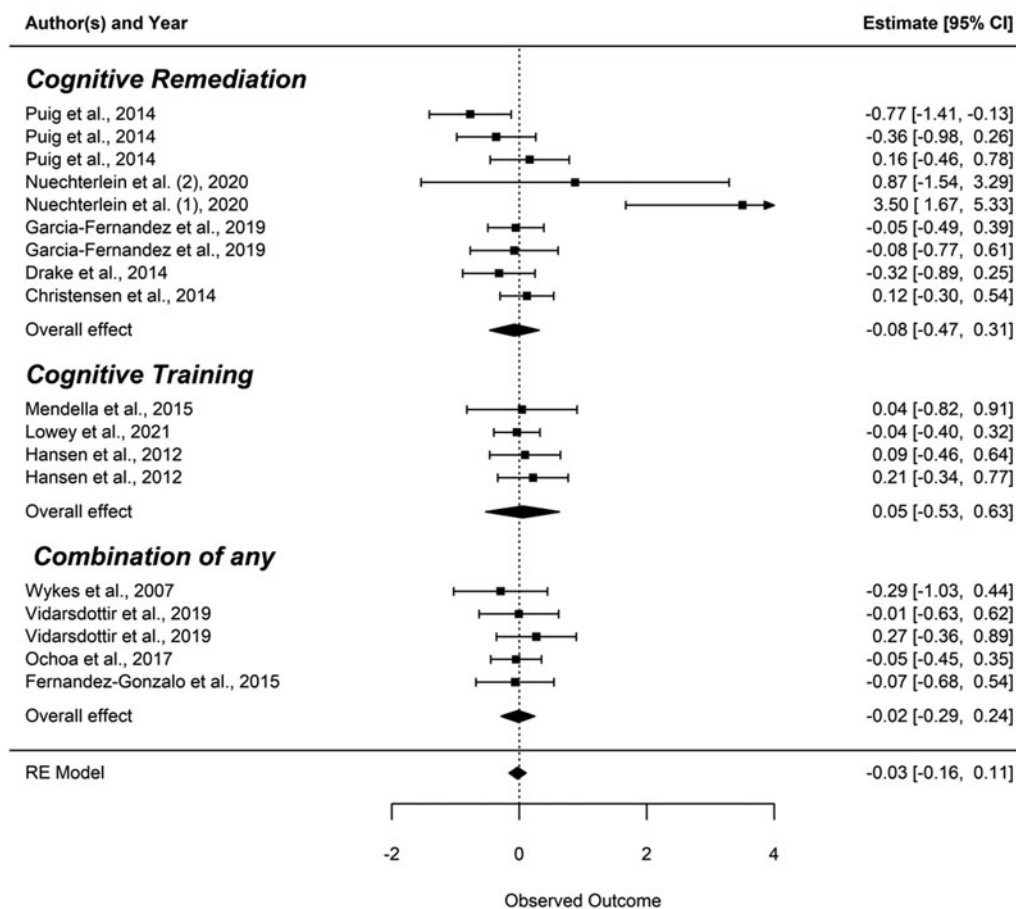


Figure 2. Forest plot of the effect of cognitive interventions on functioning by type of intervention.

functioning was partially explained by the intervention effectiveness on cognitive domains. As shown in Table 2, none of the cognitive functions significantly explained the standardized mean changes in functioning. Results on the effect of interventions on cognitive functions showed no significant improvement on any of the cognitive functions (online Supplementary Table 3).

Symptoms

Similarly, the standardized mean change in positive, negative, general psychopathology and total symptoms was introduced as a moderator in the meta-regression and revealed non-significant effects of symptoms on the intervention outcomes (see Table 2 for details).

Medication

Participants in the intervention group had a mean of 534.184 (s.d. = 387.50) CPZE mg/day and participants in the control group had a mean of 516.02 (s.d. = 272.85) CPZE mg/day. The mean doses of medication of the intervention group did not moderate the results ($B = 0.00006$, $p = 0.727$), similar to the medication of the control group ($B = 0.00006$, $p = 0.795$). Removing the outlying effect size did not seem to influence the results. There were not

enough data to enter this moderator variable together with type of intervention.

Discussion

This is the first meta-analysis that examined the effectiveness of different cognitive interventions for improving functioning in patients with recent onset psychosis. The findings indicate that none of the cognitive interventions used with these patients performed better than the control conditions for improving functioning, and none of the patient or intervention characteristics proposed as potential moderators seemed to explain these results.

Our findings differ from those reported in the previous meta-analyses published in 2015 by Revell et al., and 2023, by Frawley et al., which focused only on CR interventions for patients with early psychosis and found a moderate effect on functioning. Revell et al. (2015) suggest that CR interventions may have little impact because of the reduced scope of improvement in early psychosis compared to chronic schizophrenia patients, whose baseline impairment provides them a wider range for improvement. Baseline functioning levels in the sample included in our meta-analysis seemed to be relatively low, therefore our findings cannot be explained by this hypothesis. The discrepancy in our findings may be explained by the different inclusion criteria

Forest plot by control group type

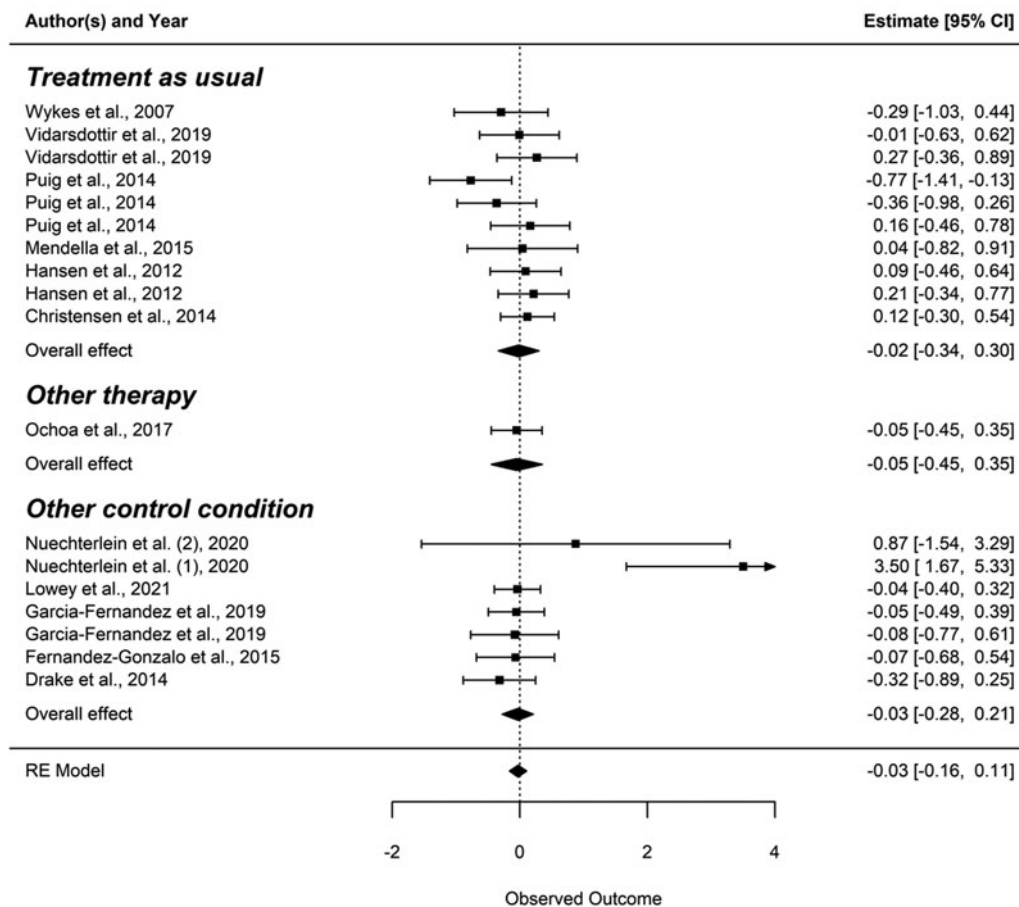


Figure 3. Forest plot of the effect of cognitive interventions on functioning by type of control intervention.

used, as both previous meta-analyses (Frawley et al., 2023; Revell et al., 2015) included studies targeting patients with a psychosis course of more than five years since onset, participants at risk for psychosis, and patients with mixed diagnoses. Thus, our results indicate that when adopting a more refined approach in terms of the target population, and including studies published until 2022, the previously reported CR moderate effect seems to fade, with these interventions showing no significant effect on functioning. Earlier work suggested that for a CR intervention to be effective, it should be delivered together with other types of interventions that are oriented towards the practice of everyday skills (Wykes et al., 2011). This may explain why these interventions do not seem to improve functioning when examined in a standalone format. However, a recent meta-analysis revealed that CT combined with psychosocial rehabilitation programs improved vocational functioning and social skills, but not everyday functioning (van Duin et al., 2019). To increase the effectiveness of these interventions, the working group on CR has recently recommended the inclusion of a treatment component that helps translate cognitive gain to everyday functioning (Bowie et al., 2020).

When it comes to CT interventions, a recent meta-analysis suggested a moderate effect on functioning in patients with schizophrenia; however, this does not seem to apply in samples with recent onset (Allott et al., 2020). The authors proposed

that further work was needed to confirm whether the phase of illness is relevant with respect to functioning outcomes. We expand their suggestions further, encouraging research on the effects of CT interventions on the functioning of patients with recent onset psychosis, as only three studies applying CT were included in our meta-analysis.

In the same line, in a recent network meta-analysis Nijman et al. (2020), suggested that SC interventions with and without CR improved functioning in schizophrenia. Like Allott et al. (2020), the authors only included one study with recent onset schizophrenia patients, therefore, their findings may not apply to these patients. Again, we found that interventions including SC combined with other types of cognitive interventions did not improve functioning in recent onset psychosis. However, for the present meta-analysis, there was no eligible study that tested the effects of a standalone SC intervention. Given that social cognition is strongly associated with functioning in recent onset psychosis, representing a potential candidate for treatment (Cowman et al., 2021) further research is essential for making conclusions on the effectiveness of SC interventions with these patients.

In an earlier study, Allott, Liu, Proffitt, and Killackey (2011) proposed that change in baseline cognition may be related to changes in functional outcomes following pharmacological, cognitive, and psychosocial treatments, and the strength of these

Table 2. Sample and measure characteristics of the RCTs included in the meta-analysis

Number	Authors	Country, sample, mean age (s.d.), % female (n)	Diagnosis	Psychosis duration	Primary Intervention type	Intervention Group: description, modality, and format	Control Group: description	Intervention Duration	Medication	Functioning outcome, cognitive domains, symptoms, and corresponding measure(s)	Assessment time-points	Main conclusions
1	Østergaard Christensen et al. (2014)	Denmark NEUROCOM N = 60 Age = 25.0 (3.3) Female = 41.7% (25) Early Intervention Service (EIS) N = 57 Age = 24.9 (3.3) Female = 50.9% (29)	Schizophrenia spectrum	First episode	Cognitive Remediation	NEUROCOM:CR + EIS Included four modules: attention, executive functions, learning/memory, and cognitive domains that the participant needed to improve. Also include work, self-experienced cognitive, and social competencies Computerized therapist-provided strategy coaching Individual basis	EIS alone Antipsychotic medication; group treatment; psychoeducation; case management; contact with job consultant; multi-family group	1-hour sessions, twice a week for 16 weeks (32 sessions)	Type not specified NEUROCOM 93.3% EIS alone 84.2%	Functioning outcome: UPSA-B Cognitive domains and measure(s): -Attention: CPT-IP -Executive function: substest mazes from NAB, TMT-B >Working memory: Number Sequencing WAIS-III -Processing speed: PMR, BACS, category fluency (animal naming) and TMT-A substests from MCCB, digit symbol coding substest from WAIS-IV, logical memory substests from the WMS-II -Verbal memory and learning: HVL-T-R, WMS-III -Visual memory: BVMT-R -Social cognition: MSCEIT Symptoms: PANSS	Pre Post 12 months	No significant differences between the groups in functioning
2	Drake et al. (2014)	United Kingdom CIRCUITS (Computerized Cognitive Remediation) N = 31 Age: 24.7 (5.2) Female = 32.0% (10) Social Contact (SC) N = 30 Age: 23.4 (4.4) Female = 47.0% (14)	Schizophreniform disorder Schizophrenia Schizoaffective disorder Delusional disorder	First episode	Cognitive Remediation	CIRCUITS + Cognitive-Behavioural Therapy for Psychosis(CBTp) A virtual town as an environment guiding participants through a sequence of tasks. Each task requiring a specific mixture of skills (e.g. sustained attention, working memory, registration and recall, planning) and with specific criteria for progression Computerized therapist-provided strategy coaching Individual basis	SC + CBTp: Social contact with support workers: social activity (e.g. conversation, neurocognitively undemanding recreations) Both conditions provided interpersonal contact, warmth, and unconditional positive regard within a professional relationship	12 weeks (12 sessions) CIRCUITS session length (10-60 min) according to attention (usually 4-8 tasks)	CIRCUITS -No antipsychotics: 22.6% -First-generation: 3.0% -Second-generation: 74.4% SC -No antipsychotics: 14.0% -First-generation: 6.0% -Second-generation: 80.0%	Functioning outcome: SOFAS Cognitive domains and measure(s): -Attention: CPT-II -Executive functions:WCST -Processing speed: TMT-A -Social cognition: TMT-B -Visual memory:RPCF (reproduction) Symptoms: PANSS	Pre Post (after CR; 12 weeks) After CBTp (42 weeks)	No significant differences between the groups in functioning

(Continued)

Table 2. (Continued.)

Number	Authors	Country, sample, mean age (s.d.), % female (n)	Diagnosis	Psychosis duration	Primary Intervention type	Intervention Group: description, modality, and format	Control Group: description	Intervention Duration	Medication	Functioning outcome, cognitive domains, symptoms, and corresponding measure(s)	Assessment time-points	Main conclusions
3	Fernandez-Gonzalo et al. (2015)	Spain Neuro Personal Trainer-Mental Health (NP-MH) N = 28 Age: 30.9 (5.9) Female = 39.3% (11) Control group (CG) N = 25 Age: 30.2 (7.4) Female = 32.0% (8)	Schizophrenia Schizoaffective disorder	First episode	Cognitive Remediation and Social Cognition	NP-MH Included two modules: the cognition module, that comprises attention, memory and executive functions tasks; and the social cognition module, working different aspects of emotional processing, theory of mind and cognitive biases Computerized therapist-provided strategy coaching Individual basis	CG Non-specific computer training group. One of three: (a) a course focused on text editing, spreadsheet management and creation of dynamic presentations, (b) playing non-specific internet games previously selected by therapists, and (c) watching documentary videos about the functioning of the brain and the human body	1-hour sessions, twice per week for 16-20 weeks (32-40 sessions)	CPZE mg/day: NP-MH 269.7 ± 195.2 CG 244.1 ± 202.6	Functioning outcomes: SFS, GAF Cognitive domains and measure(s): -Attention: digits forward subtest from the WAIS-III, CPT-II -Executive function: SWCT, TOL, HT, TMT-B >Working memory: digits backward subtest from WAIS-III, spatial span backward subtest of the WMS-III -Processing speed: index of reaction time from the CPT-II, TMT-A -Verbal memory and learning: logical memory and visual reproduction subtests from WMS-III, RAVLT, PMR -Visual memory: BVMT-R -Social cognition: HT, RMET, TOM, IPSAQ, PFA Symptoms: PANSS	Pre Post	No significant differences between the groups in functioning
4	Garcia-Fernandez et al. (2019)	Spain Cognitive Remediation Therapy (CRT)-REHACOM N = 36 Age: 24.0 (6.7) Female = 22.2% (8) Computerized Control (CC) N = 50 Age: 26.6 (7.9) Female = 38.0% (19)	Schizophrenia Schizophreniform disorder	First episode	Cognitive Remediation	REHACOM + TAU Includes tasks on vigilance, divided attention, attention and concentration, logical reasoning, topological memory and shopping TAU: individual multidisciplinary approach designed to achieve clinical remission, reduce medication doses and treat associated comorbidity and family impact; psychoeducation Computerized with supplementary human guidance Group intervention	CC + TAU A specifically designed computerized active control group: free computer activities available in Internet	1-hour sessions, twice a week for 12 weeks (24 sessions)	CPZE mg/day: REHACOM 1210.5 ± 599.2 CC 964.7 ± 489.6	Functioning: GAF, UPSA Cognitive domains and measure(s): -Attention: MCCB -Executive function: MCCB >Working memory: MCCB -Processing speed: MCCB -Verbal memory and learning: MCCB -Visual memory: MCCB -Social cognition: MCCB Symptoms: PANSS	Pre Post 6 months	No significant differences between the groups in functioning

5	Hansen, Østergaard, Nordentoft, and Hounsgaard (2012)	Denmark Cognitive Adaptation Training (CAT) + Assertive community treatment (ACT) <i>N</i> = 31 Age: 33.2 (11.4) Female = 39.0% (12) ACT alone <i>N</i> = 31 Age: 32.8 (10.3) Female = 32.0% (10)	Schizophrenia spectrum	First episode	Cognitive Training	CAT + ACT Solving of concrete problems related to daily life using tools such as schedules, schemes, and signs. Non computerized Individual basis	ACT alone Regular contact with a physician, a community mental health nurse, and a social worker; medications and weekly contact with professionals; psychoeducation; social skill training; psychosocial intervention with relatives	Every 14 days for a period of 24 weeks (12 sessions)	N/A	Functioning outcomes: GAF, HoNOS, CANSAS Cognitive domains and measure(s): no measures Symptoms: PANSS	Pre Post 9 months	No significant differences between the groups in functioning
6	Loewy et al. (2022)	United States of America Auditory Training (AT) <i>N</i> = 80 Age: 21.7 (4.0) Female = 23.8% (19) Computer Games <i>N</i> = 65 Age: 20.5 (3.5) Female = 27.7% (18)	Schizophrenia Schizophreniform disorder Schizoaffective disorder	Maximum five years since onset	Cognitive Training	AT + TAU Computerized exercises designed to improve speed and accuracy of auditory information processing while engaging auditory and verbal working memory TAU: medication case management, psychotherapy; adjustments in medications Computerized with supplementary human guidance Individual basis	CG + TAU Subjects were given laptop computers to take home and were asked to perform 20–40 h of commercial computer games	1-hour sessions day, 5 days/week for 8 weeks (40 sessions)	CPZE mg/day: AT 295.3 ± 290.8 CC 369.9 ± 382.1	Functioning outcomes: SCORSS Cognitive domains and measure(s): -Executive function: D-KEFS >Working memory: letter-number sequencing WAIS-III, spatial span backward subtest of the WMS-III; WASI -Processing speed: CFAN, TMT-A -Verbal memory and learning: HVL-T-R -Visual memory: BVMT-R Symptoms: PANSS	Pre Post 6 months	No significant differences between the groups in functioning
7	Mendella et al. (2015)	Canada Compensatory Cognitive Training (CCT) <i>N</i> = 16 Age: 25.0 (3.9) Female = 31.2% (5) TAU <i>N</i> = 11 Age: 24.8 (2.6) Female = 18.2% (2)	Schizophreniform disorder Schizophrenia Schizoaffective disorder	First Episode	Cognitive Training	CCT Included four domains: prospective memory, attention and vigilance, learning and memory, and executive functioning Non computerized Group intervention	TAU Routine psychiatric care; regular access to treatment providers from other disciplines (e.g. psychology, social work, nursing, occupational therapy)	2-hour sessions, weekly, for 12 weeks (12 sessions)	N/A	Functioning outcome: UPSA-B Cognitive domains and measure(s): -Attention: MCCB, CPT-IP -Executive function: MCCB >Working memory: MCCB -Processing speed: MCCB, TMT-A -Verbal memory and learning: MCCB, HVL-T-R, WMS-III -Visual memory: MCCB, BVMT-R -Social cognition: MCCB, MSCEIT Symptoms: PANSS	Pre Post	No significant differences between the groups in functioning

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Table 2. (Continued.)

Number	Authors	Country, sample, mean age (s.d.), % female (n)	Diagnosis	Psychosis duration	Primary Intervention type	Intervention Group: description, modality, and format	Control Group: description	Intervention Duration	Medication	Functioning outcome, cognitive domains, symptoms, and corresponding measure(s)	Assessment time-points	Main conclusions
8	Nuechterlein et al. (2022)	United States of America Cognitive Remediation (CR) + injectable risperidone N = 12 Age: 21.7 (2.9) Female = 17% (2) CR + oral risperidone N = 17 Age: 21.4 (3.5) Female = 29% (5) Healthy behaviors training (HBT) + injectable risperidone N = 17 Age: 22.8 (4.8) Female = 18% (3) Healthy behaviors training (HBT) + oral risperidone N = 14 Age: 20.9 (4.0) Female = 29% (4)	Schizophrenia Schizoaffective disorder Schizophreniform disorder	First psychotic episode beginning within the last 2 years	Cognitive Remediation	4 conditions: CR computer-assisted cognitive training program. It combined restorative approaches from Neurocognitive Enhancement Therapy (NET) and Neuropsychological Educational Approach to Remediation (NEAR) that targeted cognitive skills ranging from processing speed and attention to memory and problem solving or Healthy behaviors training Development of holistic well-being through strength-based interventions that build resilience and increase self-determination. <i>Combined with oral or injectable risperidone</i> Computerized therapist-provided strategy coaching Group intervention	All patients received TAU Case management and supportive, skills-focused therapy. Individual placement and support	CR 2 h/week sessions for 24 weeks, followed by 1 h/week for 12 weeks and then 1 hour every other week for 12 weeks HBT 3 h/week for 24 weeks, followed by 2 h/week for 12 weeks and then 2 h every other week for the last 12 weeks	N/A	Functioning outcome: GFS Cognitive domains and measure(s): -Attention: MCCB -Executive function: MCCB >Working memory: MCCB -Processing speed: MCCB -Verbal memory and learning: MCCB -Visual memory: MCCB -Social cognition: MCCB Symptoms: BPRS	Pre Post 12 months	CR was superior to HBT. Significant differential improvements were evident at 6 and 12 months
9	Ochoa et al. (2017)	Spain Metacognitive training (MCT) N = 65 Age: 27.1 (7.9) Female = 32.3% (21) Psycho-educational intervention (PEI) N = 57 Age: 28.2 (6.7) Female = 28.1% (16)	Schizophrenia Psychotic disorder not otherwise specified Delusional disorder Schizoaffective disorder Brief psychotic disorder Schizophreniform disorder	Recent onset of psychosis, less than 5 years from the onset of symptoms	Cognitive Training And Social Cognition	MCT Included eight modules: Attributional style (1), jumping to conclusions (2, 7), changing beliefs (3), empathy (4, 6), memory (5), and depression and self-esteem (8) Non computerized Group intervention	PEI + cognitive-behavioral elements The modules were: healthy habits (1), risk behaviors (2), prevention of relapse (3), video forum (4, 5), resources of work (6), leisure activities (7), and resources available in the community (8)	8 weekly sessions for both groups	CPZE mg/day: MTC 472.5 ± 703.9 PEI 519.5 ± 534.6	Functioning outcome: GAF Cognitive domains and measure(s): -Attention: MCCB -Executive function: MCCB >Working memory: MCCB -Processing speed: MCCB -Verbal memory and learning: MCCB -Visual memory: MCCB -Social cognition: HT, IPSAQ, ERT, TCI Symptoms: PANSS	Pre Post 6 months	No significant differences between the groups in functioning

10	Puig et al. (2014)	Spain Cognitive Remediation Therapy (CRT) N = 25 Age: 16.7 (1.6) Female = 48.0% (12) TAU N = 25 Age: 16.8 (1.6) Female = 48.0% (12)	Schizophrenia Schizoaffective disorder	Adolescents with onset before 17 years old	Cognitive Remediation	CRT + TAU The program addresses flexibility in thinking and information-set maintenance, executive processes central to both memory control and planning, and set/schema formation and manipulation Non computerized Individual basis	TAU alone Psychoeducation medical reviews case management (No psychotherapy)	2 sessions per week for 20 weeks (40 sessions)	CPZE mg/day: CRT 422.9 ± 314.8 TAU alone 481.9 ± 373.3	Functioning outcomes: C-GAS, LSP, VABS Cognitive domains and measure(s): MCCB -Executive function: WCST, TMT-B >Working memory: digits and letter number sequencing subtests from WISC-IV/WAIS-III -Processing speed: TMT-A -Verbal memory and learning: logical memory subtests from the WMS-III, RAVLT, verbal fluency subtest from the COWAT -Visual memory: visual reproduction subtests from WMS-III. -Social cognition: HT, IPSAQ, ERT, TCI Symptoms: PANSS	Pre Post 3 months (only CRT)	Patients in the CRT group made greater improvements in daily-living skills (LSP), and in global functioning (VABS). No significant differences were found in C-GAS. Functional gains were not maintained at 3-month follow-up
11	Vidarsdottir et al. (2019)	Iceland Integrative Cognitive Remediation (ICR) N = 25 Age: 23.6 (3.4) Female = 8.0% (2) TAU N = 24 Age: 24.8 (2.9) Female = 16.7% (4)	Schizophrenia Psychosis not otherwise specified Bipolar with psychotic features	Five years or less	Social Cognition and Cognitive Remediation	Three interventions making ICR + TAU: Social Cognition (SC): targeting emotion recognition, theory of mind, and attributions as well as metacognitive overconfidence and interaction skills to improve social functioning Compensatory Cognitive Training (CCT): a strategy-based compensatory approach designed to target prospective memory, attention, learning/memory, and executive functioning Neuropsychological Educational Approach to Remediation (NEAR): content enhancing motivation and reward Computerized therapist-provided strategy coaching Individual basis	TAU Case-management supportive counseling, medication management, socialization at the early intervention service (lunch, board games) occupational therapy, education about psychosis, individual or group-based exercise, and/or family support	2-hour sessions, twice per week over a 12-week period (24 sessions)	IRC -No antipsychotics: 8.3% -First-generation: 16.0% -Second-generation: 88.0% TAU -No antipsychotics: 4.0% -First-generation: 4.2% -Second-generation: 91.7%	Functioning outcomes: LSP, OSA Cognitive domains and measure(s): -Executive function: WASI, BRIEF-A,D-KEFS, SWCT, TMT-B >Working memory: digits backward subtest of the WAIS-IV -Processing speed: digit symbol coding from WAIS-III, TMT-A -Verbal memory and learning: logical memory subtests from the WMS-III -Social cognition: TOM, HT, AIHQ-A, FEIT Symptoms: PANSS	Pre Post	No significant differences between the groups in functioning
12	Wykes et al. (2007)	United Kingdom Cognitive Remediation Therapy (CR) N = 21	Schizophrenia	3 years or less	Cognitive Remediation	CRT + TAU Includes component processes in remembering, complex planning,	TAU alone Not specified	1-hour sessions at average rate of 3 per	CR -No antipsychotics: 0.0% -First-	Functioning outcome: SBS Cognitive domains and measure(s): -Executive function: WCST,	Pre Post 7 months	No significant differences between the groups in functioning

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Table 2. (Continued.)

Number	Authors	Country, sample, mean age (s.d.), % female (n)	Diagnosis	Psychosis duration	Primary Intervention type	Intervention Group: description, modality, and format	Control Group: description	Intervention Duration	Medication	Functioning outcome, cognitive domains, symptoms, and corresponding measure(s)	Assessment time-points	Main conclusions
		Age: 18.8 (2.6) Female = 38.0% (8) TAU alone N = 19 Age: 17.5 (2.2) Female = 32.0% (6)				and problem solving Non computerized Individual basis		week (40 sessions)	generation: 29.0% -Second-generation: 67.0% TAU -No antipsychotics: 5.0% -First-generation: 11.0% -Second-generation: 89.0%	MSET >Working memory: digit span from WAIS-IV Symptoms: BPRS		

Names of interventions and outcomes measured are in bold.

Abbreviations: CPZE, Chlorpromazine Equivalent; TAU, Treatment as Usual. Questionnaires: **AIHQ-A**, Ambiguous Intentions Hostility Questionnaire-ambiguous situations; **BACS**, Brief Assessment of Cognition in Schizophrenia; **BRIEF-A**, Behavior Rating Inventory of Executive Function-Abbreviated form; **BVMT-R**, Brief Visuospatial Memory Test-Revised; **CANSAS**, Camberwell Assessment of Need; **CFAN**, Category Fluency Animal Naming; **C-GAS**, Children's Global Assessment Scale; **CPT-II**, Continuous Performance Test-II; **CPT-IP**, Continuous Performance Test Identical Pair Version; **COWAT**, Controlled Oral Word Association Tests; **D-KEFS**, Delis-Kaplan Executive Function System; **ERT**, Emotional Recognition Task; **FEIT**, Facial Emotion Identification Test; **GAF**, Global Assessment of Functioning; **HoNOS**, Health of the Nation Outcome Scales; **HT**, Hinting Task; **HVLT-R**, Hopkins Verbal Learning Test Revised; **IPSAQ** externalizing and personalizing, Internal, Personal, and Situational Attributions Questionnaire; **LSP**, Life Skills Profile; **MCCB**, MATRICS (National Institute of Mental Health's Measurement and Treatment Research to Improve Cognition in Schizophrenia) Consensus Cognitive Battery; **MSCEIT**, Mayer-Salovey-Caruso Emotional Intelligence Test; **MSET**, Modified Six Elements Test; **NAB**, Neuropsychological Assessment Battery; **OSA**, Occupational Self-Assessment; **PANSS**, Positive And Negative Symptoms Scale; **PFA**, Pictures of Facial Affect; **PMR**, Spanish version of the Verbal Fluency Test; **RAVLT**, Rey Auditory Verbal Learning Test; **RMET**, Reading the Mind in the Eyes Test; **ROCF**, Rey-Osterrieth Complex Figure; **SBS**, Social Behavior Schedule; **SCORSS**, Strauss-Carpenter Outcome Role and Social Scales; **SFS**, Social Functioning Scale; **SOFAS**, Social and Occupational Functional Assessment Scale; **SWCT**, Stroop Word and Color Test; **TCI**, Temperament and Character Inventory; **TOL**, Tower Of London Test; **TOM**, Theory Of Mind Test; **TMT-A**, Trail Making Test-A; **TMT-B**, Trail Making Test-B; **UPSA-B**, University of California San Diego (UCSD) Performance-based Skills Assessment Brief Version; **VABS**, Vineland Adaptive Behavior Scales; **WAIS-III**, Wechsler Adult Intelligence Scale 3rd edition; **WASI**, Wechsler Abbreviated Scale Intelligence; **WCST**, Wisconsin Card Sort Task; **WISC-IV**, Wechsler Intelligence Scale for Children 4th edition; **WMS-III**, Wechsler Memory Scale 3rd edition; **WRAT**, Wide Range Achievement Test.

relationships may vary depending on the assessment length. Also, recent reports suggested that both neurocognitive functioning and social cognition were significantly associated with functioning in patients with schizophrenia with recent onset (Cowman et al., 2021), and at any stage (Kharawala et al., 2022). In line with this, Wykes et al. (2007) proposed a mediation or moderation hypothesis to explain the absence of direct intervention effects on functioning. As cognitive interventions target cognitive functions and not functioning directly, it is expected that improvement in cognitive functions will lead to functional improvement, or that the interventions will boost the effect of cognitive change on functioning. Following these recommendations, we checked whether improvement in cognitive functions could be moderating the intervention effects on functioning. Our findings suggested that none of the cognitive functions significantly explained the absence of significant change in functioning. A potential explanation may come by the fact that functioning was considered as a whole, and was not disentangled to further dimensions (i.e. social, occupational, global, community functioning). Some previous evidence suggests a moderating role of cognitive functions on improving social functioning (Wykes et al., 2007), but most studies report no benefit for occupational or global functioning (Pantelis, Wannan, Bartholomeusz, Allott, & McGorry, 2015). Another explanation may be that the included interventions did not improve cognitive functions, therefore there was no improvement that could be translated to functional gains. In this sense, Pantelis et al. (2015) propose that for functional improvement to take place, interventions for people with early persistent cognitive deficits should combine restorative and adaptive techniques, together with other elements that directly target functional outcomes. However, there was no study combining cognitive remediation with cognitive training techniques included in the present meta-analysis, calling for further evidence-based testing of this hypothesis.

Interventions using computer software were compared to those exclusively delivered by the therapists, but this did not influence the findings. Importantly, following previous evidence (Kambeitz-Illankovic et al., 2019; Lejeune, Northrop, & Kurtz, 2021), we examined whether the effect of computerized interventions differs depending on the amount of human involvement; that is, whether human guidance is offered as a supplement to the computerized techniques, or the therapist has an active role proposing strategies and applying coaching techniques. Again, the intervention modality did not seem to determine the results.

We also checked whether cognitive functioning changes are translated to functional gains when functioning is assessed on a later time point after the study completion; still, our results were not significant. Given the small number of studies included in this meta-analysis that provided follow-up assessments, results on the potential effect of cognitive changes on functioning in the long run should be interpreted with caution.

This meta-analysis has several strengths. To our knowledge, this is the first meta-analysis that evaluates the effectiveness of available cognitive interventions for improving functioning in patients with recent onset psychosis. We performed a comprehensive and systematic search including a variety of databases combined with manual searching, using a broad range of search terms, and covering all years. To provide refined conclusions, we adopted a strict application of the -five years since onset- criteria to define recent onset psychosis and excluded studies of interventions applied to samples with several diagnoses.

Moreover, we considered the potential impact of having different types of interventions used as the control condition. The quality of studies was strong in most cases, revealing no publication bias, except for the detection of one outlier.

Our results should nevertheless be interpreted in the light of the following limitations. First, only a small number of studies fulfilled the inclusion criteria, which shows that literature studying the effectiveness of cognitive interventions for patients with recent onset psychosis is still scarce. Also, six out of seven potentially eligible studies could not be included, as the statistical parameters were not publicly available and the authors were unresponsive. Despite this limitation, we performed meta-regressions to explore the influence of potential moderators, as well as sensitivity analyses by excluding the outlier study, to support the robustness of the main pooled estimates. Second, it was not possible to calculate intervention effects for different functioning outcomes (i.e. community *v.* social functioning) due to the limited number of studies, and the variety of instruments used to examine functioning. Similarly, the effect of other variables that may be relevant early in the course of the disease, such as DUP, treatment adherence or diagnosis within the psychosis-spectrum could not be examined due to underreporting. Third, differences across countries and ethnicities have not been addressed in detail in the literature, and there were no included studies performed in countries outside Europe and the USA/Canada regions. Therefore, it remains unclear whether the results can be generalized across the globe.

Conclusion

The existing evidence as observed through this meta-analysis suggests that cognitive interventions in a standalone format may not be a suitable candidate for improving functioning in patients with early onset of psychosis. Given the small amount of the existing studies on this field to the date, further RCTs with larger samples, wider follow-up periods, and more refined sample criteria are essential for extracting more robust conclusions. Further research should aid the establishment of cost-effective interventions that can be easily implemented with these patients and can potentially lead to an optimal everyday life.

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