Neuropsychology Review
https://doi.org/10.1007/s11065-026-09699-5

REVIEW

Efficacy of Cognitive Training for Treating Cancer-related Cognitive Impairment: Systematic Review and Meta-analysis by Cognitive Domain

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Received: 22 April 2025 / Accepted: 30 March 2026

Abstract

Cognitive Training (CT) is proposed to improve cancer-related cognitive impairment (CRCI), but its effect on objective cognition remains unclear. This systematic review and meta-analysis (PROSPERO ID: CRD42023426761) aimed to examine the efficacy of CT on objective CRCI using neuropsychological tests categorised into cognitive domains following international classifications. Secondary objectives were to assess CT effects on self-reported variables. A systematic search was conducted in PubMed, PsycINFO and Cochrane Library (last search in May 2024). Controlled trials performing CT and reporting neuropsychological outcomes were included. Risk of bias was assessed with RoB-2 and certainty of evidence with the GRADE approach. Hedges' g at post-intervention was the primary outcome of the multivariate meta-analysis, calculated as the standardized mean difference between groups at post-intervention. Hedges´ g at pre-intervention was included as a fixed covariate. Fifteen studies were included in the systematic review and 12 in the meta-analysis (control group $n=507$; intervention group $n=578$). The meta-analysis showed a small, significant effect of CT on executive functioning (Hedges' $g=0.15$, 95% CI [0.00, 0.29], $p=.047$). This result warrants cautious interpretation due to low-quality evidence. No significant effects were found in other cognitive domains or self-reported indices. Although these results contrast with previous meta-analyses, this study includes a larger dataset, enhancing the robustness of the results, and introduces a novel analysis strategy by grouping neuropsychological tests according to international classifications. In conclusion, CT shows a small benefit for executive functioning in CRCI, but high-quality studies are needed to confirm its efficacy.

Keywords Cognitive dysfunction · Chemotherapy-related cognitive impairment · Cancer-related cognitive impairment (CRCI) · Chemobrain · Cognitive training (CT) · Cognitive rehabilitation · Neuropsychological tests

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Published online: 04 May 2026

Cancer-related cognitive impairment (CRCI), also referred to as cancer-related cognitive decline (CRCD) (Binarelli et al., 2023), is one of the most common long-term effects observed in cancer survivors[1] (European Society for Medical Oncology [ESMO], 2017; National Comprehensive Cancer Network [NCCN], 2024; Runowicz et al., 2016). CRCI can be understood as the patient's subjective perception of cognitive decline (known as cognitive complaints) or as an objective deterioration in several cognitive functions assessed by neuropsychological testing (Ahles & Root, 2018; Chao et al., 2021; Dias-Carvalho et al., 2022; Onzi et al., 2022; Pendergrass et al., 2018; Yang & Von Ah, 2024). Neuroimaging studies also detected CRCI-related brain alterations (Bradley-Garcia et al., 2022; Leskinen et al., 2025; Sousa et al., 2020). Regardless of its severity (subtle or severe) or course (permanent or transient), CRCI negatively impacts survivors' daily functioning, work status, emotional well-being and medical outcomes, and thus their quality of life (QoL) (Chao et al., 2021; Haywood et al., 2023; Henderson et al., 2019; Klaver et al., 2020; Lange et al., 2019a; Maeir et al., 2023a; Yang & Von Ah, 2024).

Research on CRCI began in the mid-1980s and interest has grown over the last decade (Schweppe et al., 2025). Studies are mainly conducted in women with breast cancer, in whom CRCI is highly prevalent. It is estimated that one-third of them experience cognitive difficulties, as reported by different subjective and objective criteria, throughout the cancer care continuum: 25–30% experience CRCI before cancer treatments, 75% during the treatment, and 24–60% experience it months or years after treatment completion (Dijkshoorn et al., 2021; Whittaker et al., 2022). CRCI is also very frequent in other types of cancer, either affecting the central nervous system (CNS) or not (Chan et al., 2021; Chieffo et al., 2023; Hess et al., 2015; Ho et al., 2024; Skurlova et al., 2023; Wefel et al., 2022). CRCI can be related to the cancer itself or to the various different treatments (Dias-Carvalho et al., 2022; Fleming et al., 2023; Ibrahim et al., 2023; Murillo et al., 2023; Oppegaard et al., 2021; Országhová et al., 2021). Cancer survivors have expressed a need for cognitive intervention (Lange et al., 2019b; Le Fel et al., 2013), and the World Health Organization has identified cognitive functioning as an intervention target in cancer rehabilitation (Hart et al., 2024; Signorelli et al., 2024). Guidelines for CRCI management state that the first therapeutic option for those reporting cognitive complaints should be non-pharmacological, even if there is no evidence of objective cognitive decline assessed by neuropsychological tests (Duivon et al., 2024; Innovative partnership for action against cancer [iPAAC], 2021; Sanft et al., 2023; Sleurs et al., 2022). Recommended treatments include cognitive training (CT), psycho-education, and cognitive rehabilitation (CR), among others (Binarelli et al., 2023; Duivon et al., 2024; Mayo et al., 2021; Runowicz et al., 2016; Sleurs et al., 2022). Previous systematic reviews and meta-analyses have shown these interventions to be effective for improving subjective cognitive function and objective performance in attention, memory, executive functions, and processing speed tasks (Binarelli et al., 2021; Cáceres et al., 2025; Cheng et al., 2022; Fernandes et al., 2019; Kim & Kang, 2019; Mackenzie & Marshall, 2022; Merceur et al., 2024; Morean et al., 2015; Nakamura et al., 2024; Oldacres et al., 2023; Park et al., 2023; Sánchez-Gómez et al., 2025; Syed Alwi et al., 2021; Von Ah et al., 2014; Von Ah & Crouch, 2020; Yan et al., 2023; Yang et al., 2025; Zeng et al., 2016, 2020). In some of these studies, the effects were maintained for months after the intervention and, in general, a high level of satisfaction with the interventions was reported. CT has several advantages over other interventions. For example, it is often computerized and therefore widely accessible, and can be conducted at home and tailored to individual performance levels (Binarelli et al., 2023; Yan et al., 2023). Strong adherence to CT programmes and high satisfaction is generally observed (ranging from 65 to 95%). Considering all the above advantages and results of previous reviews, experts in the field are advocating for funding to develop and implement this intervention in clinical settings (Binarelli et al., 2021, 2023).

Nevertheless, despite the positive considerations, there is great heterogeneity in prior literature in the definition of cognitive interventions, the outcomes measured, and the observed efficacy. In terms of definition, very few studies have used the definition proposed by experts. In this vein, Duivon et al. (2024) defined CT as interventions aimed at "improving cognitive difficulties using repetitive and sustained exercises (frequently computerized) with incremental difficulty based on the patient's performance" and CR as "interventions combining psychoeducation, cognitive training, and/or cognitive behavioural therapy, in order to improve cognitive difficulties observed in daily life. Cognitive behavioural therapy (CBT) proposes new behaviours to adopt, improve or compensate for a specific function" (p. 1976). Based on those definitions, previous research has not clearly differentiated between CT and CR (Binarelli et al., 2023; Cáceres et al., 2025; Mackenzie & Marshall, 2022; Merceur et al., 2024; Park et al., 2023; Sánchez-Gómez et al., 2025), has used vague definitions of CT (Yan et al., 2023; Zeng et al., 2016), has not clearly defined which studies were considered CT (Yang et al., 2025), or has used different terms to refer to CR (i.e., strategy training, compensatory strategies, and CBT) (Cheng et al., 2022; Fernandes et al., 2019; Nakamura et al., 2024; Oldacres et al., 2023; Syed Alwi et al., 2021; Von Ah & Crouch, 2020; Zeng

[1] Cancer survivor refers to individuals from the time of diagnosis onwards (National Cancer Institute, n.d.)

et al., 2020). In addition, despite the International Cognition and Cancer Task Force (ICCTF) efforts to systematised neuropsychological assessment in CRCI (Wefel et al., 2011), ongoing research barely follow these recommendations (Capetti et al., 2025). As a result, a wide range of measures has been used when objective cognitive performance was the outcome addressed to assess the intervention efficacy. For instance, Oldacres et al. (2023) reported up to 100 different measures, while Mackenzie and Marshall (2022) reported 51 measures. Additionally, there was no agreement on how to categorize tests by cognitive domain, so a consensus on classification of neuropsychological tests is needed (Capetti et al., 2025). Finally, different conclusions were reached regarding the efficacy of CRCI interventions depending on the procedure used and the cognitive functions assessed. Oldacres et al. (2023) and Mackenzie and Marshall (2022) concluded that while CT shows promise as an intervention for improving CRCI, the variability in results across studies hampers definitive conclusions being drawn about its overall effectiveness. Despite the variable findings, the available meta-analyses have reported positive results for CT, reporting improvements in processing speed, verbal memory, working memory, and subjective cognitive function (Cheng et al., 2022; Kim & Kang, 2019; Nakamura et al., 2024; Syed Alwi et al., 2021; Yan et al., 2023; Yang et al., 2025; Zeng et al., 2016, 2020). In addition to heterogeneity in methods and measures, which can lead to difficulties when evaluating the effects of CT, the existing research on the efficacy of CT in improving objective cognitive functioning in cancer survivors has several limitations: 1) low-quality studies, such as pilot studies or single-arm studies without control groups, and with a high risk of bias (Binarelli et al., 2021; Cheng et al., 2022; Fernandes et al., 2019; Kim & Kang, 2019; Mackenzie & Marshall, 2022; Morean et al., 2015; Nakamura et al., 2024; Park et al., 2023; Sánchez-Gómez et al., 2025; Syed Alwi et al., 2021; Von Ah & Crouch, 2020); 2) scarce meta-analysis, due to the heterogeneity of study designs and objective cognitive outcomes (Binarelli et al., 2021; Fernandes et al., 2019; Kim & Kang, 2019; Merceur et al., 2024; Nakamura et al., 2024; Oldacres et al., 2023; Syed Alwi et al., 2021); 3) lack of studies with objective cognitive performance as the main outcome (most assess subjective cognitive functioning) and inconsistent classification of tests by cognitive domain (Cáceres et al., 2025; Cheng et al., 2022; Fernandes et al., 2019; Nakamura et al., 2024; Oldacres et al., 2023; Park et al., 2023; Sánchez-Gómez et al., 2025; Syed Alwi et al., 2021; Yan et al., 2023; Yang et al., 2025; Zeng et al., 2020); 4) studies mostly focused on breast cancer populations (Cáceres et al., 2025; Merceur et al., 2024; Morean et al., 2015; Park et al., 2023; Sánchez-Gómez et al., 2025; Syed Alwi et al., 2021; Yan et al., 2023; Yang et al., 2025), which limits generalization of findings across different cancer types; 5) studies including CNS cancer survivors, who may manifest cognitive difficulties different from those associated with non-CNS cancers (Binarelli et al., 2021; Nakamura et al., 2024; Von Ah & Crouch, 2020); 6) lack of consideration of the impact of CT on anxiety, depression and fatigue, although the evidence indicates that CRCI is associated with these conditions (Bai & Yu, 2021; Cáceres et al., 2025; Chao et al., 2021; Lange et al., 2019a; Lee & Oh, 2019; Merriman et al., 2013; Mounier et al., 2020; Murillo et al., 2023; Oliveira et al., 2023; Zhou et al., 2023).

Considering all the gaps identified in previous reviews and meta-analyses, the main aim of this systematic review and meta-analysis was to analyse the effectiveness of CT in improving objective cognitive functioning in non-CNS cancer survivors by assessing its impact in different cognitive domains. In the included studies reviewed, objective cognitive function should be measured by neuropsychological tests classified according to international standards. Secondary objectives were 1) to assess the effects of CT on subjective cognitive function assessed by self-report questionnaires and 2) to assess the impact of CT on other outcomes such as anxiety, depression, fatigue, and QoL. Additionally, this review will serve to update previous findings.

Materials and Methods

This review and meta-analysis followed the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (2020 statement) (Page et al., 2021) (Supplementary Material 1-Table S1 and S2). The protocol was registered in the PROSPERO database (an international prospective register of systematic reviews) (registration number, CRD42023426761). Minor changes in the protocol are available in PROSPERO.[2]

Eligibility Criteria and Information Sources

The PubMed and PsycINFO databases and the Cochrane Library were searched from the first data available until April 2023. A further search was re-run prior to final data analyses to retrieve any recent eligible study for inclusion (27 May 2024). For a comprehensive search, the PICO approach was applied (Methley et al., 2014). The Population (P) comprised adults with cancer (except for CNS cancer); the Intervention (I) was Cognitive Training applied independently (CT) or as a part of a more extensive Cognitive Rehabilitation program (CR + CT); the Comparison (C)

[2] Minor changes: 1) changes in authorship and 2) including information on the APA and ICF classifications to group the neuropsychological outcomes.

groups were cancer survivors receiving treatment as usual, on a waiting list or receiving any intervention except the CT carried out by the experimental group; and the Outcome (O) was objective cognitive performance on neuropsychological tests.

Search Strategy and Selection Process

The keywords and search query applied included (cancer OR CRCI OR chemobrain OR chemofog OR oncolog*) AND ("cognitive rehabilitation" OR "cognitive training"). Detailed search strategies and terms can be consulted in Supplementary Material 2-Table S3. The filters applied to each database were sample (adult) and language (English, French, Spanish, Portuguese).

Before the titles and abstracts were screened, duplicate articles were removed using the Zotero Reference Manager. Two independent researchers (CSB and an independent collaborator) then assessed the eligibility of the remaining reports according to their title and abstract, using RAYYAN (https://www.rayyan.ai/), a software that manages review projects (by sorting the records by inclusion/exclusion criteria in parallel by two researchers, with blinded option). The following exclusion criteria were applied: 1) articles out of topic (e.g., involving population other than cancer survivors, participants under 18 years old, and interventions other than CR or CT); and 2) wrong publication type. Only randomized, quasi-, or non-randomized controlled trials (RCT), with pre-post assessment and control group, were included, while study protocols, reviews, meta-analyses, qualitative studies, and case reports were excluded. Duplicate articles that were not detected in the previous step were now removed. The full texts were then retrieved. The full text of each paper was then evaluated (by CSB and AFO). Rejected papers were classified according to the following exclusion criteria: 1) wrong population (e.g., CNS or paediatric cancer); 2) wrong intervention type (e.g., not including CT); 3) wrong outcome (e.g., not reporting cognitive outcomes measured by neuropsychological tests); and 4) wrong design (e.g., no control group, no pre-post intervention assessment). Researchers were blind to each other's decisions, and conflicts were resolved by consultation with other researchers (MTC, CF) and consensus. Finally, CSB checked previous systematic reviews and meta-analyses conducted on this topic to identify any missing article.

Data Collection Process and Data Items

The data collected from each report were stored in an Excel© (Microsoft Office, USA) file. The following items were retrieved from each study: 1) first author, country, and year of publication; 2) study design; 3) sample criteria (i.e., cognitive complaints as inclusion criteria or neurological conditions affecting cognition as exclusion criteria); 4) sociodemographic and medical data of the experimental and control groups; 5) intervention description (type and format); 6) assessment period; 7) attrition rate in the intervention group (number of missing participants in the post-treatment assessment /number of participants initially randomised); 8) objective cognitive outcomes and trends in data; 9) subjective cognitive outcomes and trends in data; 10) other outcomes (depression, anxiety, fatigue, QoL) and trends in data. CSB extracted the data from each study, and AFO checked for possible missing or wrongly extracted data. Both researchers then conferred to confirm the final data extracted. When important information was not included in the full text (e.g., results of each group at each time point assessed), the authors were asked to provide the missing data.

Regarding intervention, two experimental groups were included: 1) CT applied alone or 2) CT + CR (based on the definition of Duivon et al., (2024)). CR interventions could include, in addition to CT, psychoeducation, compensatory strategy training, CBT, coping strategies, or homework between sessions. Experimental groups receiving CR without CT were not considered.

Concerning the main outcome, neuropsychological tests were categorized by cognitive domains following two different classifications: 1) the American Psychiatric Association (APA, 2013) classification, which establishes the functions of complex attention, executive functioning, learning and memory, and working memory. For categorizing tests according to the APA domains, we followed the classification proposed in a recent meta-analysis (Poppe et al., 2024); 2) the International Classification of Functioning, Disability and Health (ICF) framework proposed by the World Health Organization (World Health Organization [WHO], 2001). For categorizing tests according to the ICF domains, we used the classification proposed in a recent review study (Saita et al., 2023), which differentiates psychomotor functions, attention, higher-level functions, language, and memory. To avoid heterogeneity in the meta-analysis, we did not consider tests not included in either of these classifications. In addition, we reviewed the tests included in the APA classification used by Poppe et al. (2024) and the tests included in the ICF classification used by Saita et al. (2023) and only considered the tests with at least two uses in previous studies. For the meta-analysis, we extracted means and standard deviations of each group at pre- and post-treatment in all outcome variables.

Risk of Bias Assessment

We used the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) (Sterne et al., 2019) to assess the risk of bias of each study. This tool separately evaluates the risk of bias of studies considering an intention-to-treat effect (ITT) and that of studies considering a per-protocol effect (PP) strategy. Rob 2 provides an overall risk estimation and the specific biases arising from 5 domains: 1) randomisation process; 2) deviations from the intended intervention; 3) missing outcome data; 4) measurement of the outcome; and 5) selection of the reported result. MTC and CSB analysed each article independently, using the RoB2 Excel tool available on the web page (22 August 2019 version) (https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2). The judgements were pooled, and controversies were solved by agreement.

Meta-analysis: Effect Size Measures, Synthesis, and Bias Assessment

For calculation of effect size in between-group analyses, sample size (n), means (*M*), and standard deviations (*SD*) were extracted for each group at pre-intervention and post-intervention. When critical data for the effect size calculation were requested to the author and not provided, they were not included in the meta-analysis. Comparisons with missing values were excluded. Any inconsistencies after verification were clarified with the original authors or addressed in a meeting with the research team.

A multilevel (multivariate) random-effects meta-analysis with correlated effect sizes within studies was conducted, with outcome measures categorized into cognitive domains according to the APA and ICF classifications. Self-report outcomes were analysed in a separate multivariate meta-analysis. All analyses were conducted (by CF and CSB) in R (version 4.3.3; R Core Team, 2021) using the packages metafor (version 4.6.0; Viechtbauer, 2010), and clubSandwich (version 0.6.1; Pustejovsky, 2025). Hedges' *g* at post-intervention was the primary outcome of the multivariate meta-analysis, calculated as the standardized mean difference between experimental and control groups at post-intervention using the pooled post-test SD and applying Hedges´*g* correction factor (*J*) for small sample bias (Borenstein et al., 2009). To account for baseline imbalances, a meta-regression approach was followed by calculating Hedges´*g* at pre-intervention for each comparison and including it as a fixed covariate in the multivariate model (Morris, 2008). Baseline effect size uncertainty was not propagated in the meta-regression. To account for the non-independence of multiple effect sizes reported within the same study, we employed the Robust Variance Estimation (RVE) with a working correlation of $\rho = 0.50$ when constructing the within-study variance–covariance matrix. Sensitivity analyses with alternative values ($\rho = 0.30$ and $\rho = 0.70$) confirmed that the overall results were robust to this assumption. We specified a multivariate random-effects model estimated by restricted maximum likelihood (REML) with a nested random-effects structure (Cheung, 2019; Pustejovsky & Tipton, 2022). Domain-specific estimates were obtained from this model, and RVE with CR2 small-sample corrections was applied to derive confidence intervals and significance tests. Between- and within-study heterogeneity were quantified using τ^2 (REML estimator), the I^2 statistic, and Cochran's Q test with its associated degrees of freedom. For reporting domain-level heterogeneity statistics (I^2, τ^2, Q, df), auxiliary models were also fit with REML. Statistical significance was determined at a threshold of $p < .05$.

To assess potential publication bias, domain-specific PET/PEESE meta-regressions were conducted (Bartoš et al., 2022) using post-intervention Hedges´*g* while controlling for baseline Hedges´*g* All models were estimated using REML and RVE with CR2 small-sample corrections. PET models included the standard error as predictor, while PEESE models included the sampling variance. We followed the standard PET – PEESE decision rule: if the PET intercept was statistically significant ($\alpha = .05$), the PEESE intercept was taken as the adjusted effect. Otherwise, the adjusted effect was considered approximately zero. If convergence issues occurred in PET/PEESE models, alternative optimizers were used to achieve convergence, without changing the model specification.

Finally, to examine whether CT effects differed across cognitive domains within APA and ICF classifications, as well as within self-reported outcomes, an omnibus Wald test was applied on the domain coefficients of the multilevel model using CR2 and Satterthwaite-adjusted degrees of freedom.

Certainty Assessment

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to rate the certainty of evidence for each outcome of interest (i.e., the cognitive domains proposed by the APA and ICF). To make this decision, the GRADE system classifies the risk of bias, inconsistency, indirectness, and imprecision into four categories (very low, low, moderate, and high) (Schünemann et al., 2013). The quality of the evidence was assessed in the Summary of Findings table provided by the GRADE profiler Guideline Development TOOL (GRADEpro GDT) (https://www.gradepro.org/). CSB analysed each outcome independently, and MTC checked each judgement. Controversies were resolved by discussion and consensus.

Results

Study Selection

A PRISMA flow diagram represents the search process and results (Fig. 1). In total, 272 articles were obtained from the different databases. After excluding duplicates, 239 records were screened by title and abstract following the inclusion and exclusion criteria explained above. The interrater agreement was very large (Cohen's Kappa = 0.894), indicating high consistency when applying the mentioned criteria. This yielded 80 articles eligible for full-text assessment; however, 13 of these were not able to be retrieved even though the authors were requested to supply the texts. After applying the above-mentioned inclusion and exclusion criteria, 13 studies were included (the paper by Chapman et al., (2023) was included after the re-run search). Similarly, in the full-text assessment, the interrater agreement was very large (3 conflicts, Cohen's Kappa = 0.868). In addition, two studies (Meneses et al., 2018; Poppelreuter et al., 2009) were

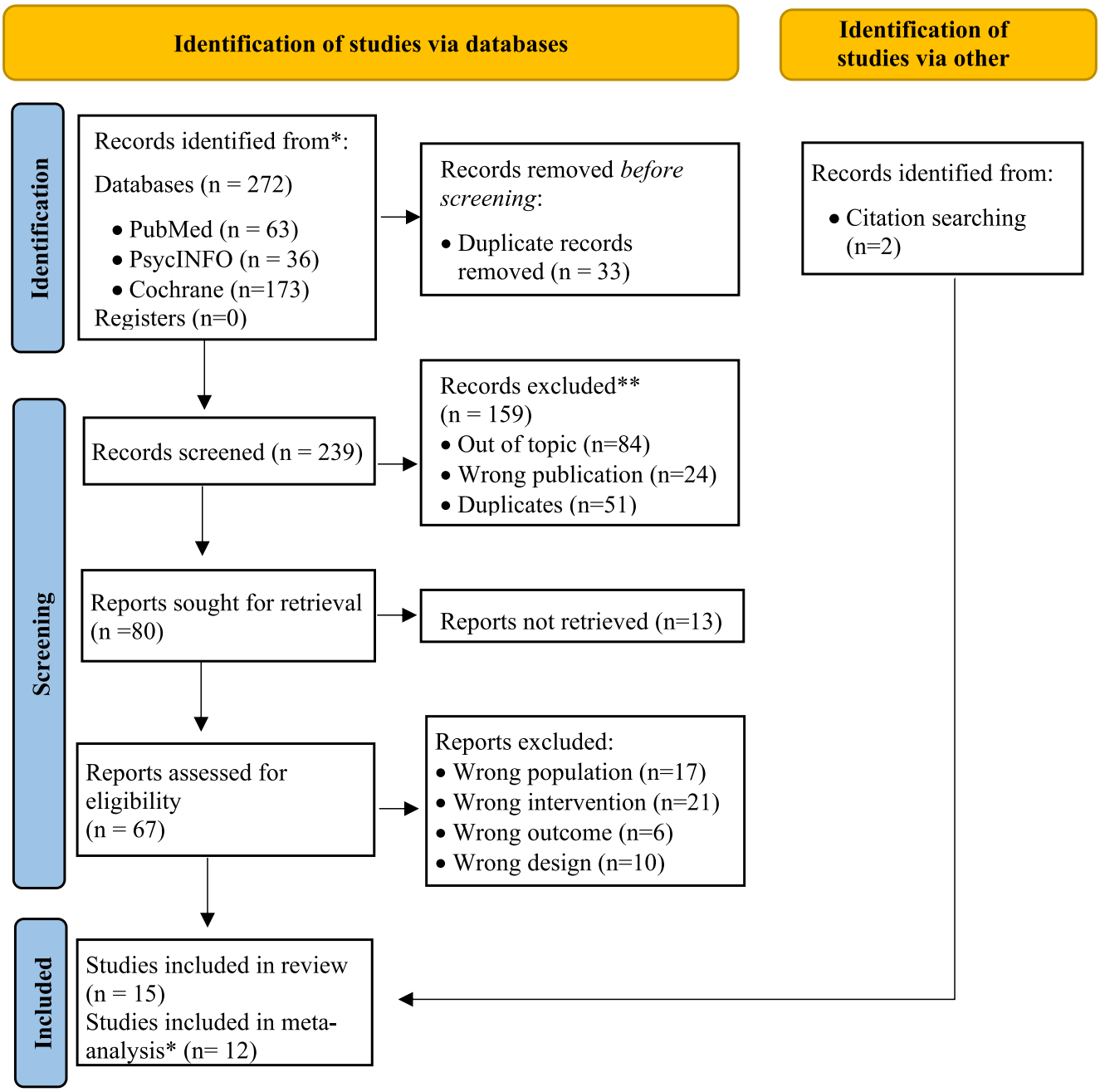

Fig. 1 PRISMA 2020 flow diagram for the search process

identified by searching through the references of previous reviews exploring therapeutic interventions for CRCI. Thus, 15 studies were finally included in the systematic review. To perform a meta-analysis with data as homogeneous as possible, the data reported by Chapman et al., (2023) were not included, as the tests used did not fit into the APA or ICF classifications. In addition, Peterson et al., (2018) and Von Ah et al. (2022) included an active control group, while all other studies included a passive control group (waiting lists), so these studies were not included. Thus, only 12 studies were finally considered in the meta-analysis.

* The data reported by Chapman et al. (2023) were not included for the main outcome because the neuropsychological tests used did not fit into the APA or ICF classification. For secondary variables (self-reported measures), these data were included.

Characteristics of Included Articles

Table Supplementary Material S4 (Supplementary Material 2) summarizes the principal characteristics of the 15 studies included.

All the papers were published between 2009 and 2023. Seven studies were conducted in the USA, and the others were conducted in several European countries, Australia or Israel. Thirteen studies were RCTs, and two were quasi-RCTs, and most of them considered the presence of cognitive complaints as inclusion criteria (with the exception of the studies by Kesler et al., (2013); Meneses et al., (2018) and Peterson et al., (2018)) and excluded participants presenting neurological conditions affecting cognition. The control groups consisted of patients who were either on a waiting list or receiving standard medical care, except in three studies, which included active control groups (Chapman et al., 2023; Peterson et al., 2018; Von Ah et al., 2022).

Demographics and Medical Data

The sample size of the control group was 507 participants, of whom 92.11% were women. The mean age was 55 years (excluding Peterson et al. (2018) and Poppelreuter et al., (2009) studies, who did not provide these data) and most of them were highly educated. Of the participants, 87.77% were women with breast cancer, 93.33% were receiving or had received chemotherapy and 67.94% were receiving or had received hormone therapy. The participants were recruited while undergoing chemotherapy or until 72 months after its completion. The sample size of the experimental group was 578, and 91% were women. The mean age was 54.63 years (excluding Peterson et al. (2018) and Poppelreuter et al., (2009) studies, who did not provide data) and most of them were highly educated. Of these participants, 87% were women with breast cancer, 78.37% were receiving or had received chemotherapy and 66.6% % were receiving or had received hormone therapy. These participants were recruited while undergoing chemotherapy or until 78 months after its completion. Three studies did not provide oncological treatment data for any of the groups (Peterson et al., 2018; Poppelreuter et al., 2009; Wu et al., 2018).

Intervention Type and Format

CT was usually offered via commercially available computerized programs (e.g., BrainHQ program), aimed at different cognitive functions. Thirteen studies carried out only individualized CT intervention. Eight studies applied computerized CT at home, and five studies performed it in a clinical setting. The length of the interventions ranged from two to 15 weeks, and the total number of sessions ranged from nine to 60. Sessions lasted between 25 min and 1 h. Some studies did not indicate the duration of the sessions but specified the number of hours to be spread over a specified time.

Two studies carried out a CR + CT intervention, combining CT with other cognitive and functional strategies. One study applied computerized intervention in the clinical setting, and one study carried out the treatment in group format and provided pencil-and-paper CT. The length of the interventions ranged from five to 12 weeks, and the total number of sessions ranged from five to nine. Sessions lasted 1 h or combined 20 min of CT and 2 h of CR weekly. For more details, see Supplementary Material 2-Table S5.

Finally, the study by Maeir et al. (2023b) included two experimental groups (CT and CT + CR). The CT + CR group (named CRAFT) was not included in this work due to the differences in content between this CR programme (focused only on problem-solving and generalization to real life) and the content of the other two included CR programmes. In addition, methodological difficulties could arise in the meta-analysis if the CT and the CT + CR groups were compared with the same control group.

Assessment Periods and Attrition Rates

All studies assessed cognitive function before and after the intervention. Six studies conducted follow-up assessments from two to 12 months post-intervention. Attrition rates ranged from 0 to 57%.

Risk of Bias

Concerning the risk of bias of the included articles, we assessed 10 studies that followed an ITT approach (Chapman et al., 2023; Damholdt et al., 2016; Ercoli et al., 2015; Kesler et al., 2013; Meneses et al., 2018; Poppelreuter et

al., 2009; Vardy et al., 2023; Von Ah et al., 2012, 2022; Wu et al., 2018) and five based on the PP effect (Bellens et al., 2020; Bray et al., 2017; Dos Santos et al., 2020; Maeir et al., 2023b; Peterson et al., 2018) (see Supplementary Material 2-Table S6). In the first group, none of the studies were classified as low risk (see Supplementary Material 2-Figure F1a): Seven articles presented "some concerns" on the overall bias, and three were classified as "high risk". Considering the domains analysed, the main risk of bias arose from selection of the reported results, as 90% of the studies lacked a pre-specified data analysis plan before recruitment was started (although some of them were pre-registered studies). Another important source of risk concerns deviations from the intended intervention, as neither participants nor people delivering the intervention were blinded in 90% of the studies. The third critical domain concerns missing outcome data: 70% of the studies had some missing outcome data for more than 5% of randomized participants. Measurement of the outcome variables was the fourth critical domain: only 50% of the outcome variables were classified as low risk in this domain. For the remaining domain- randomization—most of the studies presented low risk; the study with the highest risk was a quasi-RCT (Poppelreuter et al., 2009).

Risk of bias was more critical in studies using a per-protocol strategy, as four out of five of these studies obtained an overall high-risk assessment (see Supplementary Material 2-Figure F1b). The main source of risk was again deviation from the intended intervention. The second critical domain was also selection of the reported results. Finally, in 60% of the studies, measurement of the outcome was not appropriate, and 40% of the studies performed inadequate randomization and allocation to the intervention groups (randomization domain). The percentage of missing data was not as important a source of risk as in the case of ITT studies: only 40% of the studies had some missing outcome data for more than 5% of randomized participants.

Qualitative Synthesis: Results of Individual Studies

Table S7 (Supplementary Material 2) summarizes the principal outcomes and results of the 15 studies included in the systematic review.

Objective Cognitive Outcomes and Results

Overall, 53 different neuropsychological tests were identified, including both traditional paper-and-pencil measures and computerized assessment. The included studies had an average of four tests, with a range of three to ten tests per study. Of the 53 tests, only 29 fitted in the ICF and/or APA classification by cognitive domains (for more details, see Supplementary Material 2-Table S8). The most applied tools were the Trail Making Test (TMT A and B forms), the Symbol-Digit Coding, the Digit Span Forwards and Backwards, verbal fluency tasks, and word list learning and remembering. Concerning the outcomes reported for each test, four studies (Ercoli et al., 2015; Maeir et al., 2023b; Peterson et al., 2018—only for COWAT scores-; Wu et al., 2018) provided age-corrected scores, while other three (Vardy et al., 2023; Von Ah et al., 2012, 2022) provided age and education corrected scores. The remaining studies provided raw data (correct responses, speed…) in their full text or when contacting the authors. However, all the studies (with the exception of Peterson et al., 2018 and Poppelreuter et al., 2009) reported no significant differences between groups in age or educational level at baseline.

Four studies reported improvement in memory (assessed by word list learning), three in complex attention (assessed by Useful Field of View-UFOV-), two in working memory/attention (assessed by Digit Span Backwards), one in verbal fluency, executive functions (assessed by Wisconsin Card Sorting Test -WCST-) and symbol search, and another one in working memory (assessed by the Change Detection Task -CDT-).

Subjective Cognitive Outcomes and Results

Thirteen studies included subjective cognitive function questionnaires. Seven tests were administered, with the Functional Assessment of Cancer Therapy Cognitive Function (FACT-Cog) being the most used. Papers reported the total score or the Perceived Cognitive Impairment subscale (PCI) score. Eight studies reported a significant improvement in subjective cognition after the intervention.

Other Outcomes and Results

Ten studies assessed the impact of CT in QoL mainly through the FACT-General or the 36-Item Short-Form Health Survey (SF-36) but did not find any improvement after CT intervention. Depression and anxiety were assessed in 10 and eight studies, respectively, and two studies found an improvement in depressive symptoms as assessed by the Center for Epidemiologic Studies Depression Scale (CES-D). Five studies assessed the impact of CT on fatigue applying different questionnaires and two studies found significant improvement.

Meta-analysis Results: Impact of CT by Cognitive Domains

The raw data, the script, and the codebook used to perform the meta-analysis, as well as the results exported from R, can be found in Supplementary Material 3, as recommended by Sandoval-Lentisco et al. (2024).

Cognitive Domains Categorized According to APA

Complex Attention Ten studies involving a total of 647 participants (294 controls and 353 from the experimental group) provided data to analyse the effects of CT on tests assessing complex attention. The meta-analysis did not show a significant effect of CT in complex attention (Hedges' g=0.07, 95% CI [−0.06, 0.19], p=.248). Overall heterogeneity was moderate (I^2 total=48.36%), primarily attributable to within-study variability (τ^2 between=0.000; τ^2 within=0.083). Evidence of statistically significant heterogeneity was found (Q (27)=74.08, p<.001). Regarding potential publication bias, the PET intercept was not statistically significant (g=0.12, p=.829), nor the PEESE model (g=0.10, p=.724), indicating no evidence of small-study effects.

Executive Functioning Nine studies involving a total of 784 participants (371 controls and 413 from the experimental group) were included. The meta-analysis showed a statistically significant effect of CT on this domain (Hedges' g=0.15, 95% CI [0.00, 0.29], p=.047). Heterogeneity was negligible (I^2 total=0.0%, τ^2 between=0.000; τ^2 within=0.000; Q (19)=14.40, p=.760). PET (g=0.10, p=.611) and PEESE models (g=0.13, p=.162) provided no evidence of small-study effects.

Learning and Memory Seven studies involving a total of 644 participants (290 controls and 354 from the experimental group) provided data to analyse the effects of CT on tests assessing learning and memory. The meta-analysis did not show a significant effect of CT on this domain (Hedges' g=0.11, 95% CI [−0.13, 0.36], p=.318). Overall heterogeneity was moderate (I^2 total=44.22%, τ^2 between=0.047; τ^2 within=0.015) and there was evidence of statistically significant heterogeneity (Q (16)=26.33, p=.050). Neither the PET (g=−0.11, p=.807) nor the PEESE model (g=−0.02, p=.924) provided evidence of small-study effects.

Working Memory Five studies involving a total of 597 participants (285 controls and 312 from the experimental group) were included. The meta-analysis did not show a significant effect of CT on this domain (Hedges' g=0.24, 95% CI [−0.07, 0.55], p=.105). Overall heterogeneity was moderate (I^2 total=34.12%), driven mainly by between-study variability (τ^2 between=0.044; τ^2 within=0.000; Q (4)=8.19, p=.085). Neither the PET (g=0.85, p=.125) nor the PEESE model (g=0.495, p=.117) showed evidence of small-study effects.

The omnibus test assessing whether the effects of CT differed across domains did not reach statistical significance [F (3, 4.96)=0.99, p=.471].

The forest plot obtained for each cognitive domain categorized according to APA are shown in Fig. 2.

Cognitive Domains Categorized According to ICF

Attention Six studies involving a total of 449 participants (199 controls and 250 from the experimental group) provided data for analysing the effects of CT on tests assessing attention functions. The meta-analysis showed a trend towards improvement (Hedges' g=0.17, 95% CI [−0.01, 0.35], p=.055). Overall heterogeneity was low (I^2 total=16.20%), mainly driven by within-study heterogeneity (τ^2 between=0.000; τ^2 within=0.012; Q (11)=13.20, p=0.280). Neither the PET model (g=0.43, p=.163) nor the PEESE model (g=0.290, p=.108) showed evidence of small-study effects.

Higher-Level Functions Six studies involving a total of 327 participants (158 controls and 169 from the experimental group) provided data for analysing the effects of CT on tests assessing higher-level functions. The meta-analysis did not show a significant effect of CT on this domain (Hedges' g=0.14, 95% CI [−0.04, 0.33], p=.105). Heterogeneity was negligible (I^2 total=0.00%, τ^2 between=0.000; τ^2 within=0.000; Q (9)=3.73, p=.928). No evidence of small-study effects was detected [PET model (g=0.15, p=.676) and PEESE model (g=0.17, p=.373)].

Language Six studies involving a total of 443 participants (200 controls and 243 from the experimental group) were included. The meta-analysis did not show a significant effect of CT on this domain (Hedges' g=0.12, 95% CI [−0.07, 0.31], p=.175). Heterogeneity was negligible (I^2 total=0.0%, τ^2 between=0.000; τ^2 within=0.000; Q (7)=6.08, p=.530) and no evidence of small study effects was found [PET model (g=0.04, p=.870) and PEESE model (g=0.05, p=.697)].

Memory Five studies involving a total of 344 participants (149 controls and 195 from the experimental group) provided data for analysing the effects of CT on tests assessing memory. The meta-analysis did not show a significant effect CT on this domain (Hedges' g=0.21, 95% CI [−0.02, 0.45], p=.067). Overall heterogeneity was low (I^2 total=15.79%), primarily attributable to between-study heterogeneity (τ^2 between=0.016; τ^2 within=0.000; Q (12)=11.03, p=.526). Neither the PET model (g=0.066, p=.902) nor the PEESE model (g=0.13, p=.674) showed evidence of small study effects.

Psychomotor Functions Six studies involving a total of 343 participants (158 controls and 185 from the experimental group) were included. The meta-analysis did not show a significant effect of CT on this domain

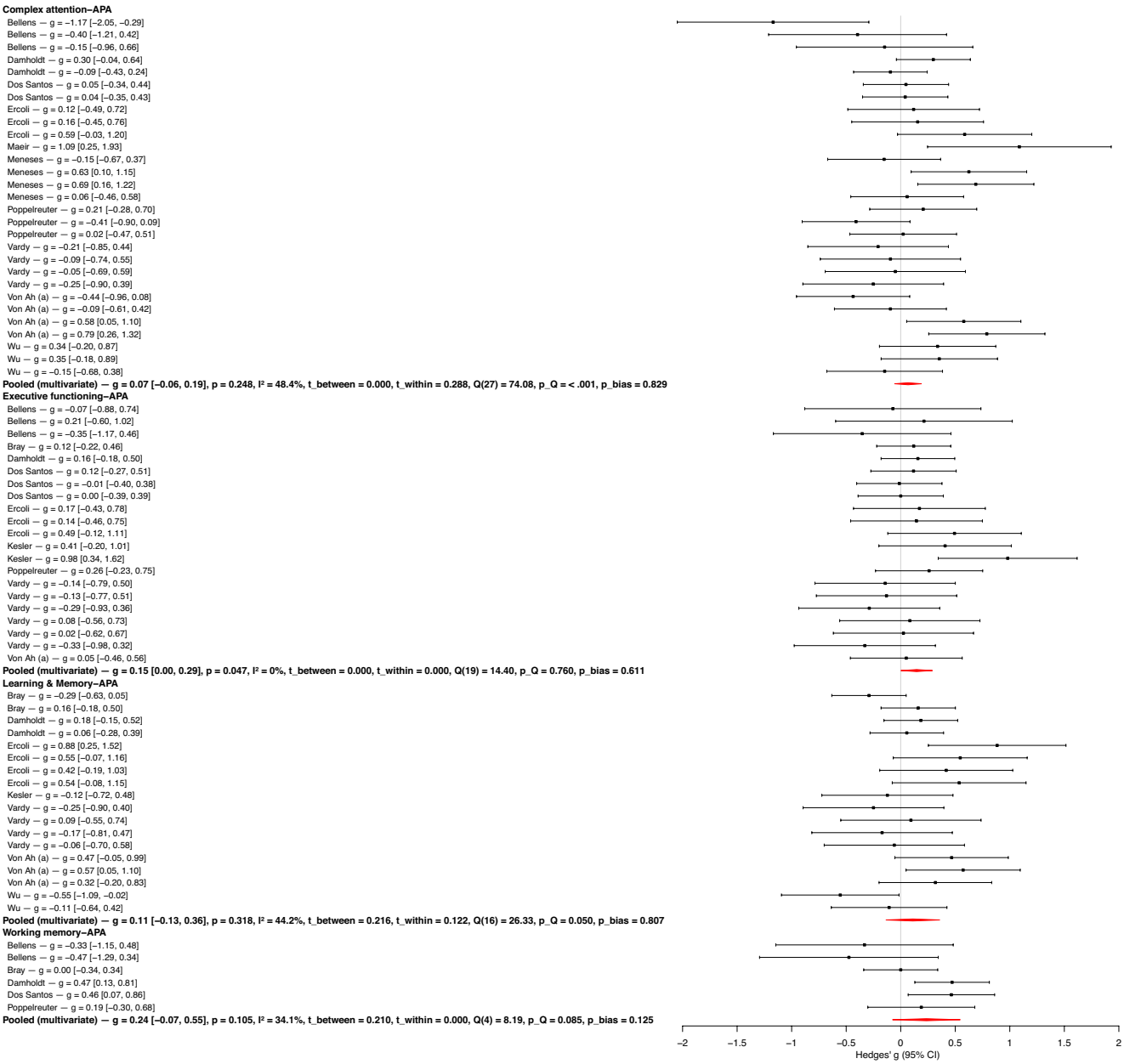

Fig. 2 Forest plot for cognitive domains according to APA classification

(Hedges' $g = -0.12$, 95% CI [−0.49, 0.26], $p = .462$). Overall heterogeneity was substantial (I^2 total = 60.34%), largely attributable to between-study heterogeneity (τ^2 between = 0.151; τ^2 within = 0.000). There was evidence of statistically significant heterogeneity (Q (6) = 13.19, $p = .040$). No evidence of small study effects was found for this domain [PET model ($g = 0.64$, $p = .498$) and PEESE model ($g = 0.18$, $p = .638$)].

The omnibus test assessing whether the effects of CT differed across domains did not reach statistical significance [F (4, 1.32) = 0.42, $p = .795$].

The forest plots obtained for each cognitive domain categorized according to ICF are shown in Fig. 3.

Self-report Outcomes

Subjective Cognitive Function Ten studies involving a total of 836 participants (389 controls and 447 from the experimental group) provided data for analysing the effects of CT on subjective cognitive function. The meta-analysis did not show a significant effect of CT on this outcome (Hedges' $g = 0.06$, 95% CI [−0.22, 0.34], $p = .622$). Overall heterogeneity was moderate (I^2 total = 58.32%, τ^2 between = 0.057; τ^2

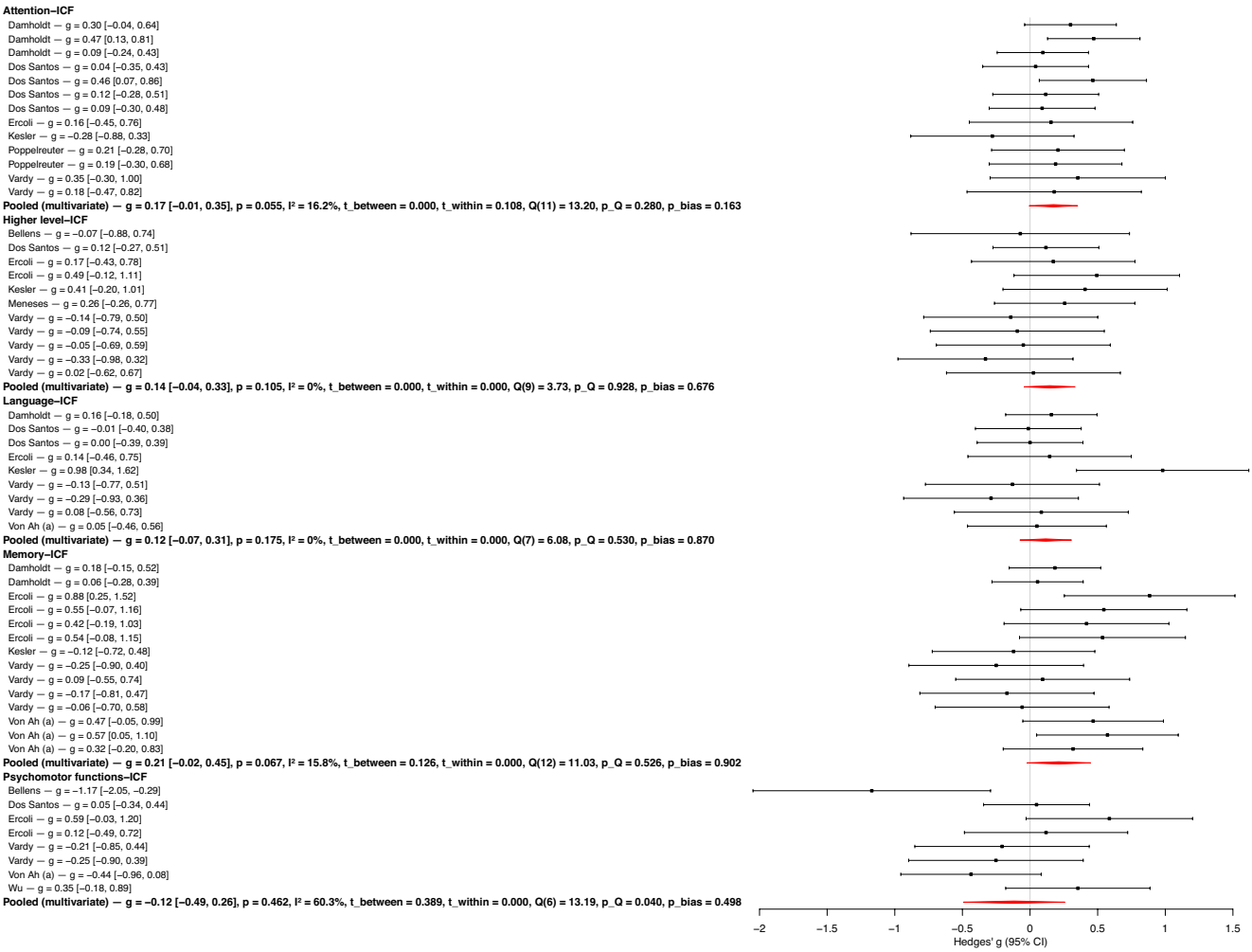

Fig. 3 Forest plot for cognitive domains according to ICF classification

within = 0.057) and evidence of statistically significant heterogeneity was found (Q (8) = 21.20, $p = .007$). There was no evidence of small study effects [PET model ($g = 0.028$, $p = .959$) and PEESE model ($g = -0.06$, $p = .847$)].

Anxiety Seven studies involving a total of 524 participants (246 controls and 278 from the experimental group) were included. The meta-analysis results showed that CT did not have a significant effect on anxiety (Hedges' $g = -0.08$, 95% CI [−0.26, 0.10], $p = .303$). Heterogeneity was negligible (I^2 total = 0%, τ^2 between = 0.000; τ^2 within = 0.000; Q (5) = 3.25, $p = .662$) and there was no evidence of small study effects [PET model ($g = 0.12$, $p = .908$) and PEESE model ($g = 0.11$, $p = .801$)].

Depression Eight studies involving a total of 564 participants (265 controls and 299 from the experimental group) provided data for analysing the effects of CT on depression. The results showed that CT did not have a significant effect on depression (Hedges' $g = -0.13$, 95% CI [−0.38, 0.12], $p = .247$). Overall heterogeneity was moderate (I^2 total = 26.19%, τ^2 between = 0.014; τ^2 within = 0.014; Q (6) = 9.01, $p = .173$). Neither the PET model ($g = -0.11$, $p = .922$) nor the PEESE model ($g = -0.08$, $p = .906$) showed evidence of small study effects.

Fatigue Four studies involving a total of 460 participants (230 controls and 230 from the experimental group) were included. The results did not show significant effects of CT on fatigue (Hedges' $g = 0.22$, 95% CI [−0.09, 0.53], $p = .110$), pointing to a reduction in the self-reported fatigue in the experimental group. Heterogeneity was negligible (I^2 total = 0%, τ^2 between = 0.000; τ^2 within = 0.000; Q (2) = 0.74, $p = .629$). Neither the PET model ($g = -0.03$, $p = .944$) nor the PEESE model ($g = 0.08$, $p = .698$) showed evidence of small study effects.

Quality of Life (QoL) Seven studies involving a total of 574 participants (280 controls and 294 from the experimental

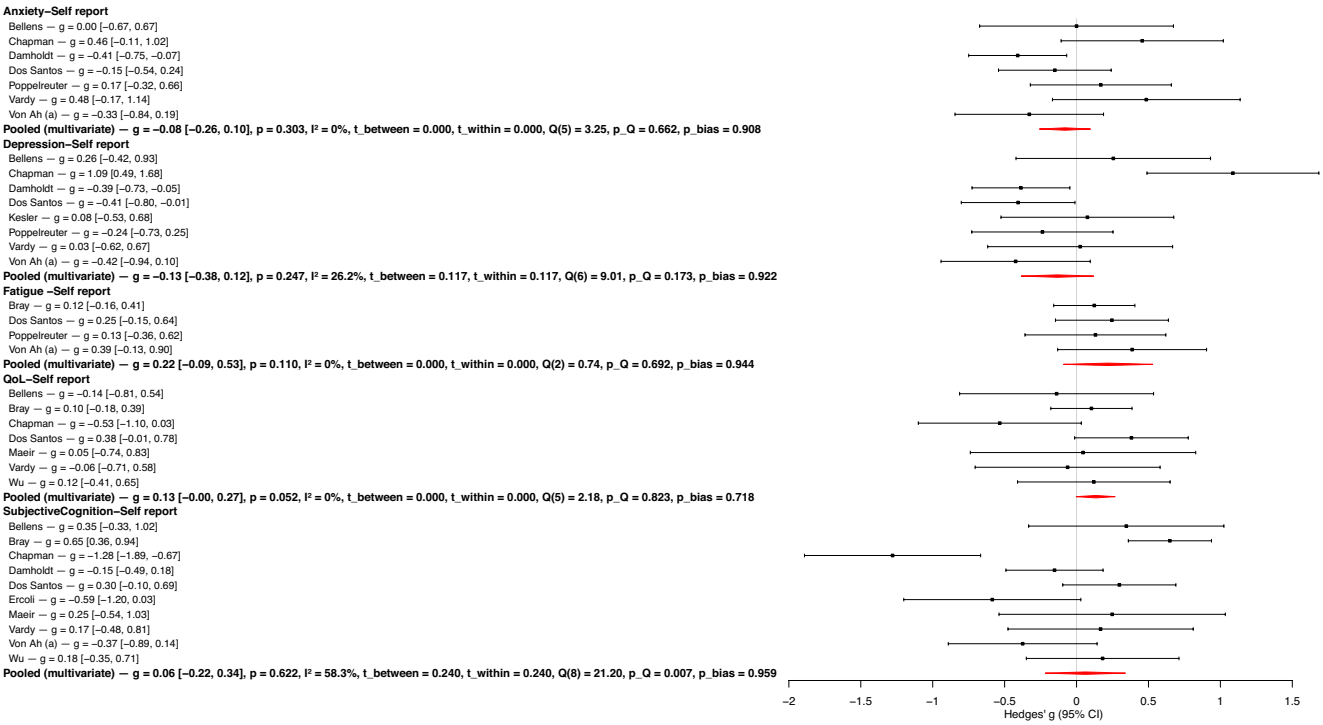

Fig. 4 Forest plot for self-reported measures

group) were included. The meta-analysis results showed a trend to improvement (Hedges' g=0.13, 95% CI [−0.00, 0.27], p=.052). Heterogeneity was negligible (I^2 total=0%, τ^2 between=0.000; τ^2 within=0.000; Q (5)=2.18, p=.823). Neither the PET model (g=0.08, p=.718) nor the PEESE model (g=0.08, p=.635) showed evidence of small study effects.

The omnibus test assessing whether the effects of CT on self-report outcomes differed across domains did not reach statistical significance [F (4, 3.32)=1.17, p=.456].

The forest plots obtained for each self-reported measure are shown in Fig. 4.

Certainty of Evidence

There were no conflicts between researchers when assessing the quality of the evidence. The certainty of the evidence for the efficacy of CT on all cognitive domains was rated as low, except for complex attention and learning and memory – APA – and psychomotor functions – ICF –, where it was rated as very low. The GRADE Summary of Findings is provided in Supplementary Material 2-Table S9. The main reason for downgrading the quality of the evidence was the risk of bias of each study, which was rated as serious for all the outcomes, according to the ROB-2 assessment for individual studies. The other important reason for downgrading was imprecision, as small and non-significant effects were found for almost all the outcomes, and CI intervals were moderate, including possible harm, benefit, and no effect. Most outcomes (except psychomotor, memory and higher-level functions -ICF) complied with the optimal information size (at least 200 participants per group). Inconsistency (assessed by I^2 total Cochran's Q test) was a significant reason for downgrade the certainty of evidence for complex attention and learning and memory – APA – and psychomotor functions – ICF –. Publication bias (small study effects) and indirectness were not significant reasons for downgrading the quality of the evidence.

Discussion

Cognitive training (CT) has been used for treating cancer-related cognitive impairment (CRCI). However, current evidence of its efficacy for improving objective cognitive function is weak, and the existent data have not been aggregated to analyse the overall efficacy of this intervention. To our knowledge, this is the first systematic review and meta-analysis assessing the efficacy of CT in cancer survivors with CRCI by using performance in neuropsychological tests as the main outcome variable. One of the strengths of this work is that tests are categorised by cognitive domains following the proposal of two international health organisations, the

APA and the WHO (ICF classification), to aid comparison between studies and to provide greater robustness to the results. This approach helped to determine the cognitive functions that improve after CT, which is more meaningful than examining specific test scores.

The qualitative synthesis of the results from individual studies provides some positive evidence on the effect of CT on a few objective and subjective cognitive function indices. However, in contrast to previous reports (Cheng et al., 2022; Sánchez-Gómez et al., 2025; Yan et al., 2023; Yang et al., 2025; Zeng et al., 2016, 2020), this meta-analysis only threw a small, significant effect on executive functioning (APA domain) and a marginally significant trend towards improvement on attention (ICF domain). As for the other cognitive domains (both APA and ICF), no beneficial effect of CT can be concluded from the meta-analysis. Results were also negative for self-reported outcomes (subjective cognitive function, anxiety, depression, and fatigue), except for QoL, for which a marginally significant effect of CT was found.

Previous research has shown inconsistent results regarding the effects of CT on executive functioning, with some works providing favourable results (Sánchez-Gómez et al., 2025; Yang et al., 2025) and others failing to find them (Cheng et al., 2022; Yan et al., 2023). Our positive results may be explained by the fact that several of the CT programmes included tasks targeting executive functions, which can contribute to enhance cognitive efficiency and, ultimately, cognitive performance (Von Bastian et al., 2022). In addition, near transfer effects of CT could be reflected in these results, as the large majority of the studies included executive functioning assessment ("training to the test") (Simons et al., 2016; Von Bastian et al., 2022). In fact, this is one of the domains with the highest number of included studies and the domain with the highest number of participants.

However, these results should be interpreted with caution for several reasons. First, low GRADE evidence was found for this executive functioning (APA) due to the high risk of bias in five of the nine studies included, as well as imprecision. In addition, this APA domain included tests that were divided into the ICF domains of higher-level functions and language, for which no significant effects were found.

The marginally significant trend towards improvement on attention (ICF domain) should also be interpreted with caution as low GRADE evidence was found due to the risk of bias of included studies and imprecision.

Previous systematic reviews and meta-analyses have reported a positive effect of CT on other cognitive domains (Binarelli et al., 2021; Cheng et al., 2022; Kim & Kang, 2019; Nakamura et al., 2024; Oldacres et al., 2023; Sánchez-Gómez et al., 2025; Syed Alwi et al., 2021; Yan et al., 2023; Yang et al., 2025; Zeng et al., 2016, 2020). Differences in terms of the population, intervention, comparator, and outcomes included can explain the different patterns of results obtained in this work. Specifically, we excluded the CNS-cancer population, in contrast to previous works (Binarelli et al., 2021; Nakamura et al., 2024). Concerning the intervention, prior research used the labels CR or CT interchangeably in some of the reviewed studies (Bray et al., 2017; Dos Santos et al., 2020; Ercoli et al., 2015) or considered as CT some interventions that did not meet previously established criteria (i.e., in a meta-analysis, Mackenzie and Marshall (2022) classified the studies by King and Green (2015), Mihuta et al. (2018); Park et al. (2017) as CT). Related to the comparison, previous reviews have included single-arm or pilot studies (Binarelli et al., 2021; Fernandes et al., 2019; Nakamura et al., 2024; Sánchez-Gómez et al., 2025; Von Ah & Crouch, 2020), while we only considered clinical trials with a waiting list control group as this provides the best-quality evidence. Finally, referring to the outcome variables, we observed remarkable differences between previous literature and our study in relation to the classification of neuropsychological tests (which we did in accordance with the ICF and APA standards). The discrepancy between the findings of previous meta-analyses (Cheng et al., 2022; Yan et al., 2023; Yang et al., 2025) and those of the present study regarding the effects of CT on working memory, verbal memory, and processing speed can also be due to the greater dataset of our meta-analyses. For example, Yan et al. (2023) found an improvement in verbal memory, but this result was based on only four studies (229 participants) and one measure (the Rey Auditory Verbal Learning Test -RAVLT-). In our meta-analysis, we considered seven studies in the APA classification (644 participants) and five studies in the ICF (344 participants), which adds robustness to our results. Finally, the previous meta-analyses included two studies (Tan et al., 2020; Wyant, 2017) that we were not included in this work because important data were not available (despite having requested the authors for them). However, it is unlikely that the different pattern of results can be explained by the omission of those studies, as Tan et al. (2020) did not apply CT independently, and Wyant (2017) did not observe any significant improvement in neuropsychological performance.

In addition to methodological differences relative to previous reviews, other factors may help in understanding the negative results on CT efficacy obtained in the present study. First, although the ICCTF recommends neuropsychological tests for assessing CRCI (Wefel et al., 2011), these have several sensitivity limitations to the cognitive changes faced by oncological population. On one hand, they were designed to diagnose severe brain conditions or neurodegenerative processes, which differ from the mild and subtle

difficulties present in CRCI (Capetti et al., 2025). In addition, they may lack ecological validity, as they are applied in a controlled and distraction-free laboratory setting. On the other hand, practice effects (i.e., better performance when testing with the same task repeatedly, especially when there are no parallel forms), the Hawthorne effect (i.e., better performance when participants are aware that they are being assessed), and ceiling effects (i.e., impairments not detected in a highly educated sample, as examined in this work) are other limitations of these tools to detect CRCI (Chao et al., 2021; Horowitz et al., 2018; Mayo et al., 2021; Nelson & Suls, 2013; Oldacres et al., 2023). A clear reflection of this lack of sensitivity is that many participants—in both the experimental and control groups—of the studies included in the meta-analysis showed average performance in the pre-intervention assessment, although they reported cognitive complaints, a reliable indicator of CRCI (Chen et al., 2024; Durán-Gómez et al., 2022; Kesler et al., 2023; Sousa et al., 2020). In addition, neuropsychological tests also do not allow differentiation between CRCI trajectories (Colaes et al., 2025) and they are not always related to neuroimaging findings (Sousa et al., 2020). Thus, as cancer survivors frequently perform within normal limits in neuropsychological tests, it may be difficult to capture any improvement after CT. In addition, the sample of this study included highly educated and middle-aged survivors (around 55 years old), which increases the difficulty in detecting cognitive decline in neuropsychological testing. Some authors suggested that older women with a lower level of education (a proxy for cognitive reserve) may be more vulnerable to CRCI (Ahles & Root, 2018; Ahles et al., 2010; Kao et al., 2023; Kerstens et al., 2023; Lange et al., 2019a).

Another factor that may explain the lack of effects of CT in CRCI is the time elapsed between the end of chemotherapy, and the application of CT. Longitudinal neuroimaging studies detected brain structural and functional changes mainly in the subacute period after chemotherapy (approximately up to 5 to 7 months), and these were not necessarily correlated with objective cognitive outcomes. One year after the end of chemotherapy, partial recovery of some brain structures and functions has been reported, even in patients undergoing hormone therapy (Chen et al., 2024; Li & Caeyenberghs, 2018; Sousa et al., 2020; Yang et al., 2025). Supporting this, premature brain aging of about 5.4 months was observed in the 4-month period after chemotherapy, while this aging process improved over time (De Ruiter et al., 2023). Similar observations were obtained regarding objective cognitive outcomes: 30% of breast cancer survivors receiving chemotherapy or who had received it in the previous year were labelled as cognitively impaired, while 2–3 years later, this percentage dropped to 20% (very low GRADE evidence), as reported by Whittaker et al. (2022). Considering these findings, the moment at which CT is applied is critical. Five of the 15 included studies applied CT approximately 2 years after the end of chemotherapy, and three studies delayed it by 6 years, and therefore the lack of improvement after CT reported in this work may be related to the spontaneous recovery that occurs months after the end of this treatment. However, it is important to note that the two studies in which CT was started during chemotherapy or two months after its end did not find any improvement in objective cognitive function (Peterson et al., 2018; Poppelreuter et al., 2009). To understand this result, it should be considered that the study by Peterson et al. (2018) included only 5 participants, so it could be underpowered and may not have been able to detect any beneficial effects of CT. In addition, the participants stated that the CT tasks were too difficult, and they felt overwhelmed as the software provided high-difficulty exercises.

To date, there are no recommendations about the best time to deliver cognitive intervention. Although some authors suggest early cognitive interventions as a prevention strategy (Schagen et al., 2022; Shelton et al., 2025), others do not recommend starting the intervention during chemotherapy, although this may depend on the survivors´ condition and available healthcare resources (Fardell et al., 2011; Merceur et al., 2024; Poppelreuter et al., 2009). Some researchers argue that cognitive intervention should be offered when neural stabilization is achieved, suggesting a broad time frame of between 6 to 24 months after chemotherapy (Merceur et al., 2024; Wefel et al., 2015). Finally, it is important to note that in a subset of survivors, CRCI may appear shortly after the first cycles of chemotherapy and then improve or remain for months or years after its end, as well as suddenly appear after the end of chemotherapy (Agelink Van Rentergem et al., 2024; Bender et al., 2015; Bi et al., 2025; Colaes et al., 2025; Dijkshoorn et al., 2021; Janelsins et al., 2018; Kreukels et al., 2008; Smith et al., 2026; Wefel et al., 2010; Whittaker et al., 2022).

Regarding our secondary aim, studying the impact of CT on subjective cognitive function, mood, and fatigue, the results were similar to those of objective cognitive performance: CT did not have a significant effect on any of these outcomes. Although eight of the included studies reported an improvement on subjective cognitive function after CT, the findings of the meta-analysis did not support significant effects. In addition, moderate heterogeneity was found in this domain, both within and between studies. This result contrasts with previous meta-analysis supporting the efficacy of CT to improve subjectively reported cognitive function (Sánchez-Gómez et al., 2025; Yan et al., 2023). This discrepancy may be due to several factors. Altogether, the number of articles included in the present study was greater than in previous research, supporting the robustness of our findings.

In addition, the questionnaires used for subjective cognition are focused on difficulties in everyday tasks, although the transfer of CT to daily activities has little support (Sala & Gobet, 2019; Simons et al., 2016). For this reason, previous research suggested complementing CT with other strategies, such as psychoeducation, CBT, or strategy-based interventions to improve subjective cognitive function (Cheng et al., 2022; Nakamura et al., 2024; Yang et al., 2025).

Concerning the other secondary outcome variables, although CRCI is closely related to anxious-depressive symptoms (Bai & Yu, 2021; Zhou et al., 2023), and these conditions usually involve problems in executive functioning and attentional control (Pan et al., 2019; Snyder, 2013; Volel et al., 2018; Wei et al., 2023), CT does not seem to be an appropriate intervention for mood alterations related to cancer. Alternative therapeutic options such as psychotherapy, acceptance and commitment therapy, physical exercise, relaxation, medication, or a combination of CT and these therapies may be better alternatives (Grinberg et al., 2021; Hu et al., 2025; Reis et al., 2020; Smith, 2015; Tavares et al., 2024). In the same vein, although fatigue is an important side-effect of cancer and treatments, and has been related to CRCI (Bai & Yu, 2021; Lange et al., 2019a), other pharmacological and non-pharmacological interventions should be considered for fatigue (Bower, 2014; Escalante & Manzullo, 2009).

The marginally significant results of CT on QoL may be related to the improvement of executive functioning, which could have a positive effect on daily life tasks. However, the impact of CT in QoL warrants further research, as it is a multidimensional and complex construct, and previous findings are inconsistent (Sánchez-Gómez et al., 2025).

Regarding the risk of bias of the included studies, it is important to note that none of them were considered low risk. The main critical area was the selection of the reported results, as most of the studies did not include a pre-specified data analysis plan before recruitment began or pre-registration, which could have affected the reliability of the results. In addition, the lack of blinding of participants and research staff were other major sources of bias. Finally, more than half of the studies had some missing outcome data for more than 5% of randomized participants, and some studies did not perform adequate analysis of missing data. In addition, adherence to the CT programmes was low, as nine studies reported an attrition rate higher than 10%, and the training time was less than the expected in the original intervention. The certainty of the evidence for the efficacy of CT on objective CRCI was low or very low, mainly due to the risk of bias and imprecision. Inconsistency within and between studies was also important for specific cognitive domains (complex attention and learning and memory -APA-; learning and memory -ICF-; and subjective cognitive functioning).

Limitations

Although we used two types of classification to categorise tests by cognitive domain, the heterogeneity of the neuropsychological measures was so great that some outcomes were not included in the meta-analysis because they did not fit into these classifications (e.g., tests on working memory and complex attention applied in Bray et al., 2017; Chapman et al., 2023; Maeir et al., 2023b; Meneses et al., 2018). Including such data could perhaps contribute to detecting some significant improvement after CT in these cognitive domains, in line with previous research. In addition, there was heterogeneity when reporting the outcomes of the neuropsychological tests: four studies provided age-corrected scores, three studies provided age and education corrected scores and the remaining seven studies provided raw data. Since part of our sample had a high education level, not correcting neuropsychological scores could lead to miss subtle impairment. However, all studies included in the meta-analysis (except Poppelreuter et al., (2009)) reported no significant differences between groups in age or educational level and, of the studies that corrected scores by these characteristics (Vardy et al., 2023; Von Ah et al., 2012), only Von Ah et al., (2012) found an improvement in cognition after CT. Thus, it is unlikely that the heterogeneity in the reporting of neuropsychological outcomes has added error to the results. It is also important to highlight that none of the included studies reported on performance or symptom validity tests, which are recommended to confirm the accuracy of the results (Larrabee, 2012).

Another limitation is that our meta-analysis excluded studies that only considered subjective cognitive function outcomes, which may have affected the findings. However, no study was excluded at the full-text revision stage for this reason. In addition, two studies that met our inclusion criteria were not included, because they were published after the last re-run search. One of these studies reported an improvement in overall cognitive performance and executive functions in women with breast cancer who had completed chemotherapy six months earlier (Kleinknecht et al., 2024), and the other found an improvement in attention, memory, and subjective cognitive function in cervical cancer survivors who had completed chemotherapy eight years earlier (Areklett et al., 2024).

An additional limitation is related to the population and the comparison selected in this work. In total, 90% of the sample were women, mainly women with breast cancer. This may hinder generalization of the results to other cancer populations. The sample size in most of the studies was small, and consequently, the effect size was also small. Relative to the comparison group, most of the included studies used a waiting list control group and, to ensure

homogeneity. studies including an active control group were excluded from the meta-analysis. Thus, it was not possible to differentiate between the effect of CT per se and other associated factors, such as placebo effects. Future studies should analyse both active and waiting list control groups to assess the efficacy of the intervention (Binarelli et al., 2023; Grinberg et al., 2021).

It is also important to highlight that, since none of the included studies were considered as low risk of bias, a sensitivity analyses should be conducted to evaluate to what extent the study quality affected the results. However, this would mean excluding six of the 12 studies, which were rated as high risk of bias, substantially reducing precision, decreasing per-domain sample sizes, and affecting the stability of the multivariate model. Likewise, a meta-regression with RoB-2 as a moderator would be severely underpowered with only 12 study clusters, yielding unreliable inferences.

Finally, two secondary objectives that were initially proposed (see PROSPERO, registration number CRD42023426761) could not be achieved. One of these was to compare the efficacy of CT when applied independently versus as a part of a broader CR program. The rationale for proposing this objective was that some authors suggested that CT should be combined with other strategies (e.g., psychoeducation and compensatory strategies) to be effective (Binarelli et al., 2021; Duivon et al., 2024; Kim & Kang, 2019), but studies applying CT alone have not been compared with studies combining CT and other types of intervention. Among the 15 studies included in our systematic review, only two used a CR + CT intervention. Although these studies detected a significant improvement in different outcomes (one in complex attention and one in learning and memory), these data could not be included in the meta-analysis owing to the small sample size. The other objective was to analyse the long-term impact of the intervention. However, we decided not to perform the corresponding meta-analysis due to the heterogeneity of the follow-up periods considered: Six studies performed a follow-up assessment at 6 months, four studies performed a follow-up at 2–3 months, two studies did a follow-up at 12 months, and three did not perform any follow-up. In addition, few studies that included a follow-up assessment found any improvements on cognitive function months after the intervention (Chapman et al., 2023; Damholdt et al., 2016; Ercoli et al., 2015; Maeir et al., 2023b; Meneses et al., 2018; Von Ah et al., 2012).

Recommendations and Future Directions

Although CT seems to promote cognitive efficiency and functional brain changes (Chapman et al., 2023; Dai et al., 2023; Ercoli et al., 2015; Von Bastian et al., 2022), the results of this meta-analysis do not support its effectiveness, either in objective or subjective cognitive outcomes or self-report measures related to daily life. These findings should not be considered discouraging, as they encompass a reflection on the management of CRCI and current studies on this topic, providing suggestions for improving future research. To date, there is no gold standard treatment for CRCI. Experts recommend one session of psychoeducation for all survivors with cognitive complaints (Duivon et al., 2024). This step makes sense given that cognitive complaints are a valid way of reporting CRCI (Capetti et al., 2025) and a sensitive index of underlying changes in brain functioning (Apple et al., 2018; Chen et al., 2024; Durán-Gómez et al., 2022). In addition, subjective cognitive function seems to be a reliable indicator, as more than 40% of women with breast cancer make complaints immediately after chemotherapy, and this percentage varies very little thereafter (Whittaker et al., 2022).

In addition to psychoeducation, as medical and personal factors are related to CRCI and the survivors' needs vary throughout the cancer care continuum, experts encourage offering a multi-modal intervention (i.e., CR, CT, CBT, physical activity, meditation, psychological therapy, sleep hygiene, nutrition) to improve subjective and objective cognitive function, in line with a comprehensive model of neuropsychological rehabilitation (Binarelli et al., 2023; Cheng et al., 2022; Duivon et al., 2024; Merceur et al., 2024; Nakamura et al., 2024). In this vein, Duivon et al. (2024) stated that CR programs should include psychoeducation and CT, as well as on-site and home-based exercises. Conducting a systematic review and meta-analysis similar to the present one focused on CR interventions should be considered to shed light on the beneficial effects of interventions that include more than one therapeutic strategy for cognitive improvement. Recommendations for researchers developing and assessing the effectiveness of CT are also provided by Simons et al. (2016), while Grinberg et al. (2021) and Sandoval-Lentisco et al. (2024) provided recommendations for conducting a meta-analysis assessing the efficacy of CT. Ongoing studies (NCT06435559, NCT06710639, NCT06686823, NCT06103318, NCT05690828, NCT06686823, NCT05896189, NCT04817566, NCT06053775) will shed some light on whether CT is more beneficial in improving CRCI when combined with other strategies, as some of the CR + CT included studies seem to suggest.

Regarding the duration of the intervention, Yan et al. (2023) found that CT should last at least two months to be effective, while Mackenzie and Marshall (2022) did not find any relationship between the duration of the intervention and its effectiveness. Duivon et al. (2024) mentioned

that each CR session should last at least 45 min (although this may depend on the patient´ condition and healthcare resources). Finally, tailored interventions are important as different profiles of CRCI have been observed (Ahles & Root, 2018; Colaes et al., 2025; Hardy-Leger et al., 2021; Kesler et al., 2020, 2023; Merriman et al., 2019; Mulholland et al., 2024; Poppelreuter et al., 2009).

Although several interventions can be applied in the management of CRCI, sociodemographic, geographic, and economic factors limit their implementation. For this reason, reliance on digital, easily accessible, and home-based interventions is recommended (Binarelli et al., 2021; Merceur et al., 2024; Yan et al., 2023). Thus, CT has several advantages in terms of accessibility and treatment adherence, besides offering rich content for training cognition that can mimic real environments. CT also allows adaptation of task difficulty to the level of participants, which is important to provide tailored interventions and to achieve a balance between challenge and motivation (Grinberg et al., 2021). However, support should be provided by healthcare professionals for the delivery and supervision of the intervention (Binarelli et al., 2023; Kim & Kang, 2019). Adherence to the interventions should also be promoted (Von Ah et al., 2022; Wu et al., 2018), and the acceptability, feasibility, fidelity, and cost of the interventions should be studied to determine which are more beneficial and likely to be sustained in clinical settings (Binarelli et al., 2023).

Additionally, future research should directly compare passive and active control groups within the same trials. This examination will clarify if the nature of the control condition adds some therapeutic effects different from those of the intervention studied. In addition, comparing the same and different interventions at different points during the medical process is as important as assessing their efficacy. This would aid the development of recommendations on the timing of the intervention, as one strategy may be relevant at one point and not at another (Mackenzie & Marshall, 2022; Merceur et al., 2024; Nakamura et al., 2024). Considering that different trajectories of CRCI have been associated with psychological variables (Bi et al., 2025; Colaes et al., 2025; Smith et al., 2026), moderation analyses should be implemented to clarify the effectiveness of the intervention according to the participants` profile (Sánchez-Gómez et al., 2025). Finally, it is also relevant to compare the same intervention across different oncological populations, as different cancers and treatments may affect cognition differently (Onzi et al., 2022). Standardization of cognitive assessment is important to enable these comparisons to be made. Application of the neuropsychological tools proposed by the ICCTF (Wefel et al., 2011) and following the APA classification to assign them to a cognitive domain, which is more comprehensive than the ICF classification, are recommended with purposes of uniformity in neuropsychological CRCI assessment. Capetti et al. (2025) also provided practical recommendations for research conducting cognitive evaluation in oncological population (including neuropsychological measures quality assessment) and Andreotti et al. (2016) provided recommendations for study design and statistical methods to enhance the sensitivity of neuropsychological tests to CRCI. Considering the abovementioned limitations of the neuropsychological tests, other methods that can improve the detection of cognitive changes after intervention include applying computerized tests based on cognitive neuroscience and with neuropsychologist supervision, ecological assessments (daily-task related tests, transfer to real-world or functional outcomes, participation measures, virtual reality tools) and techniques such as neuroimaging and electroencephalography (Binarelli et al., 2021; Chen et al., 2024; Cheng et al., 2025; Cobden et al., 2025; Henneghan et al., 2025; Janelsins et al., 2018; McDonald, 2021; Nakamura et al., 2024; Nelson & Suls, 2013; Sousa et al., 2020; Yao et al., 2023; Zeng et al., 2023).

It is also important to assess the effects of the intervention on subjective cognitive function, as they have been related to alterations in neuroimaging and neurotransmission (Chen et al., 2024; Duivon et al., 2024; iPAAC, 2021; Oppegaard et al., 2025; Pace et al., 2024). Finally, including performance and symptom validity measures is essential to confirm the validity of the data (Larrabee, 2012).

Considering the high risk of bias of the studies included in this review and the low grade of certainty of the evidence, the quality of future studies should be improved by e.g. performing double-blind RCTs, preregistering studies, including waiting list and active control groups, using samples with more than 20 participants per group, reporting all the results and performing ITT analysis (Binarelli et al., 2023; Grinberg et al., 2021; Simons et al., 2016; Sterne et al., 2019). In addition, repeated measures of the same participant before and after the intervention are preferable to comparing control and experimental groups, and a 6-month follow-up after the end of the intervention should be carried out to assess the middle-term effects (Merceur et al., 2024).

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11065-026-09699-5.

Acknowledgements Helena Garcez Martins (HGM), an independent collaborator who participated in the initial search and selection process.
CSB has a research contract funded by the Spanish Ministry of Science, Innovation and Universities (FPU21/00082).

Author Contribution All authors have contributed substantially to the conception and the design of this work. Cristina-Salgado Blanco and Ana F. Oliveira have played an active role in the collection and coding of the data, Carina Fernandes in the data analysis (meta-analysis)

and Cristina Salgado-Blanco and María Carrillo de-la-Pena in the interpretation of results. Cristina Salgado-Blanco and Carina Fernandes drafted the manuscript and Ana F. Oliveira and María Carrillo-de-la-Peña reviewed it critically for important intellectual content. All authors gave the final approval of this version to be published and agreed to be accountable for all aspects of the work, ensuring that the work was carried out in accordance with the principles of research integrity.

Funding Open Access funding provided thanks to the CRUE-CSIC agreement with Springer Nature.

Data Availability The author confirms that all data generated or analysed during this study are included in this published article. Furthermore, data supporting the findings of this study and analytic code are all available at the time of submission.

Declarations

Competing interests The authors have no relevant financial or non-financial interests to declare.

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