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Effect of cognitive training on patients with breast cancer reporting cognitive changes: a systematic review and meta-analysis

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ABSTRACT

Objectives Cognitive training is a non-drug intervention to improve the cognitive function of participants by training them in different cognitive domains. We investigated the effectiveness of cognitive training for patients with breast cancer reporting cognitive changes.

Design Systematic review and meta-analysis.

Data sources PubMed, Embase, Cochrane Library, WOS, CINAHL, CNKI, VIP, SinoMed, Wanfang, Grey literature and trial registries were searched (from inception to 1 October 1, 2022).

Eligibility criteria Inclusion of randomized controlled trials (RCTs) assessing the effects of cognitive training on breast cancer patients reporting cognitive changes The primary outcome was subjective cognitive function. Secondary outcomes were objective cognitive functioning (eg, executive functioning and attention) and psychological outcomes(eg, anxiety, depression, and fatigue).

Data extraction and synthesis Two reviewers worked independently to screen the literature, extract data, and assess the methodological quality and risk bias of the included studies. Results are reported as standardizedstandardised mean differences (SMDs) with 95% confidence intervals(CI). Grades of Recommendation, Assessment, Development, and Evaluation(GRADE) were used to assess the quality of evidence.

Main outcomes and measures The primary outcome was subjective cognitive function. Secondary outcomes were objective cognitive functioning (eg, executive functioning and attention) and psychological outcomes(eg, anxiety, depression and fatigue).

Results A total of 9 RCTs involving 666 patients with breast cancer were included. The frequency of cognitive training varied and the duration was mostly focused on 5–12 weeks. It can be delivered to patients in an individual or group mode, both online and face to face. Meta-analysis revealed that cognitive training aimed at adaptive training in cognitive field has statistically significant effects on improving subjective cognitive function (SMD=0.30, 95% CI (0.08 to 0.51), moderate certainty). Some objective cognitive functions such as processing speed (SMD=0.28, 95% CI (0.02 to 0.54), low certainty), verbal memory (SMD=0.32, 95% CI (0.05 to 0.58), moderate certainty), working memory (SMD=0.39, 95% CI (0.17 to 0.61), moderate certainty) and episodic memory (SMD=0.40, 95% CI (0.11 to 0.69), moderate certainty) were significantly improved after the intervention. In addition, we did not find statistically significant changes in attention, short-term memory, execution function, depression, anxiety and fatigue in patients with breast cancer after the intervention. Subgroup analyses revealed that based on the delivery of individual sessions, the use of web-based cognitive training software may be more beneficial in improving the outcome of the intervention.

Conclusion Evidence of low to moderate certainty suggests that cognitive training may improve subjective cognition, processing speed, verbal memory, working memory and episodic memory in patients with breast cancer reporting cognitive changes. But it did not improve patients' attention, short-term memory, executive function, depression, anxiety and fatigue.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is an up-to-date review that excludes non-randomised studies, follows a preregistered protocol and measures the effects of cognitive training.
⇒ Search included published literature, trial registries and grey literature to reduce the risk of missing potentially eligible data.
⇒ The small number of included studies and the small total sample size limited our ability to meta-analyse the intervention effects.

INTRODUCTION

In a large survey which included mainly breast cancer survivors, 75% of participants reported having cognitive complaints related to cancer.[1] Qualitative interviews about side effects after cancer also showed that breast cancer survivors often reported cognitive impairment, which was the symptom most survivors claimed to be most concerned about.[2] The American Cancer Society defines cognitive decline in patients with cancer from diagnosis to subsequent treatment as 'cancer-related cognitive impairment' (CRCI).[3] It main manifestations are memory loss, concentration and thinking difficulty, calculation and processing ability, and so on.[4 5] Although this

cognitive impairment is mild to moderate, it can persist for months or even years, which would compromise the patients' treatment adherence, reduces work productivity and impacts the quality of daily activities.[6–9]

Studies have shown that some drugs, such as stimulants, antidepressants and dementia drugs, have been shown to help prevent cognitive impairment in patients with cancer.[8 10] However, for cancer survivors, treatment of cognitive impairment using daily medications may be challenging because of drug interactions with chemotherapy and other cancer therapies as well as patients' reluctance to add more drugs to their medicine list.[11] Because of these shortcomings, we sought to assess the impact of non-pharmacological intervention.

Cognitive training typically involves guided practice on a set of standardised tasks designed to reflect particular cognitive functions such as memory or attention.[12] This is a non-drug intervention method that aims at potential neural pathways and hopes to improve cognitive ability through adaptive training in specific cognitive fields.[13] Studies have shown that based on the theory of brain plasticity, cognitive training can induce positive chemical changes in brain structure and function, thereby enhancing cognitive function.[14] Previous reviews have investigated the effectiveness of cognitive training offered in older adults, patients with dementia, traumatic brain injury or stroke.[15–18] Several revealed reviews or systematic reviews have attempted to judge the effects of cognitive training in patients with breast cancer with cognitive changes, but some limitations remain. Lange *et al*[19] study reviewed the management strategies of CRCI and found that cognitive training may be the most promising strategy to improve patients' subjective cognition, but its effect on improving some objective cognitive function and daily function indicators such as emotional state is still unclear. The review by Treanor *et al*[20] included six studies assessing the effects of non-pharmacological interventions on improving or maintaining cognitive or non-cognitive effects in people with cancer, but only two cognitive training interventions were included, so there was limited opportunity to draw reliable conclusions about the effects of cognitive training. In the Chan *et al*[11] study, cognitive training for patients with breast cancer were reported to show self-reported benefits in cognitive function, memory and speech function. But the researchers did not distinguish between compensatory cognitive training and cognitive training, which are collectively referred to as cognitive training. Considering that compensatory cognitive training is to improve cognition by acquiring compensatory strategies to reduce the incidence and impact of cognitive failure on daily activities,[21 22] while cognitive training is hypothesised that repetitive training of cognitive tasks such as processing speed can produce repair of damaged neural circuits to restore memory function. We have reason to believe that there is a difference between the two mechanisms of action,[22 23] which can be divided into two different non-drug interventions and further test their practical benefits for clinical intervention. Because of these limitations, these reviews fail to provide clear conclusions on whether cognitive training has a positive effect on patients with breast cancer with cognitive changes. Therefore, we conducted a systematic study search and meta-analysis to provide relevant evidence-based evidence on this issue.

MATERIAL AND METHODS

This study has been registered in the International Prospective Register of Systematic Reviews.

Study selection

The inclusion criteria followed the PICOS framework: (1) P(population): Patients over 18 years of age who were pathologically diagnosed with breast cancer and had subjectively reported or objectively measured cognitive changes. The study population will be considered eligible if patients with cancer have more than 80% breast cancer. This cut-off is set to select studies that are targeting patients with breast cancer rather than general interventions that simply included a high proportion of patients with breast cancer. (2) I(intervention): the experimental group underwent cognitive training, which was defined as an intervention that trained the patients' memory, attention, executive function, information processing speed or other cognitive dimensions.[18] (3) C(comparison): the control group underwent no treatment, the usual/standard treatment, wait-list control or active control condition. (4) O(outcomes): primary outcome was subjective cognitive function. Secondary outcomes were objective cognitive function (eg, executive functioning and attention) and psychological outcomes (eg, anxiety, depression and fatigue). Online supplemental file 1 provides specific assessment tools for the outcomes, all from the clinical neuropsychological cognitive assessment manual or a validated standard assessment tool.[24] (5) S(study design): Randomised controlled trial (RCT). Reviews, conference abstracts, full text or data not available, not published in Chinese or English, duplicate reports will be excluded.

Search strategy

We searched PubMed, Embase, Cochrane Library, Web of Science, CINAHL, Wanfang Database, China Knowledge Resource Integrated Database(CNKI), SinoMed and Weipu Database(VIP). In addition, trial registries (ChiCTR, ClinicalTrials.gov) and grey literature (OpenGrey) sources were searched. At the same time, the references cited in the included literature were traced back to ensure that all eligible articles were included. The search time was limited from inception to 1 August 2021, and the search was updated on 1 October 2022. The full search strategy is provided in online supplemental file 2.

Data collection and analysis

Selection of studies

After removing duplicate studies, two reviewers (XY and QL) independently assessed the eligible publications by

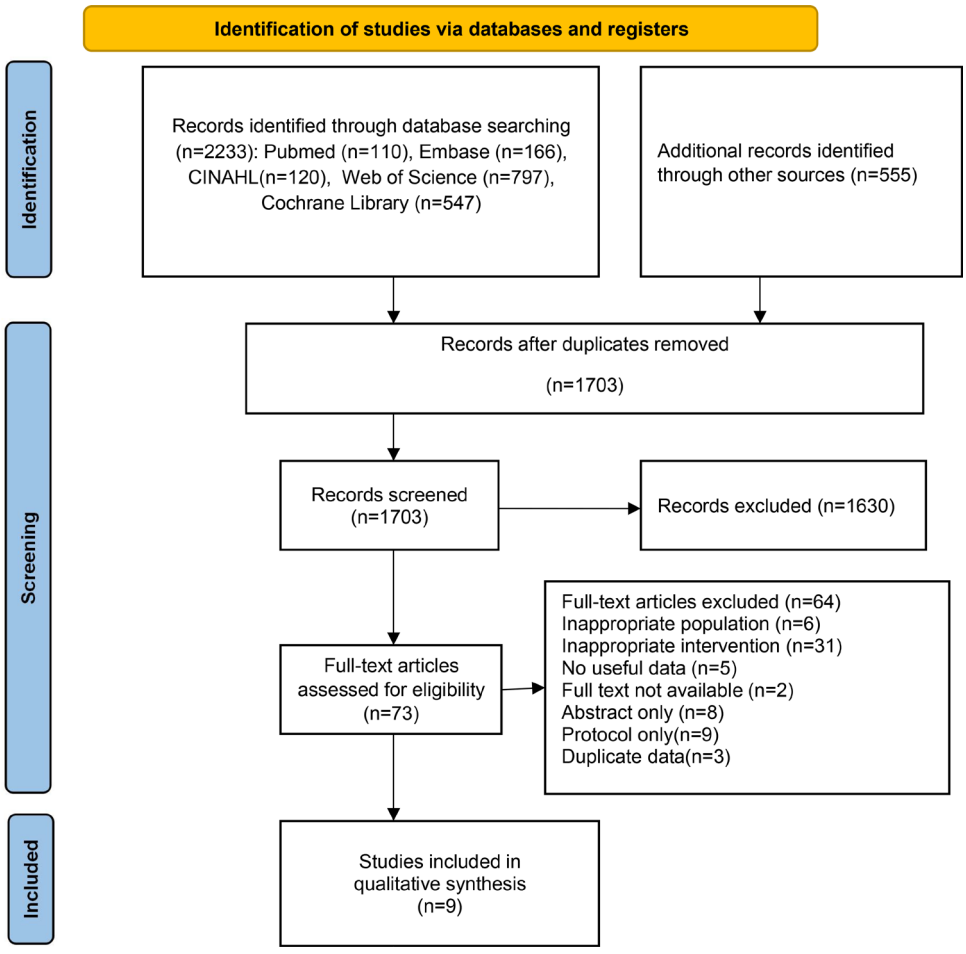

Figure 1 Flow diagram of study selection in the meta-analysis.

screening titles and abstracts according to a previously established protocol. Full-text articles were retrieved when at least one reviewer decided that an abstract was eligible for inclusion.

Data extraction and management

The following details will be extracted into a structured data extraction form developed specifically for this study: first author and year of publication, country, proportion of the total population with breast cancer, sample size, mean age, education level, time since diagnosis or treatment, intervention content, means of intervention, mode of delivery, intervention duration, intervention frequency, comparison content, duration of follow-up, attrition rate, outcome variables of interest and findings.

Two independent reviewers (XY and QL) independently coded outcomes into cognitive domains during data extraction; this was informed by professional experience, test documentation and the wider academic literature. It was common for a given test to yield multiple outcomes, reviewers could code these outcomes into separate domains as appropriate.

Risk of bias and quality of evidence assessment

Two independent reviewers (XY and QL) assessed the risk of bias using the version 2 of the Cochrane risk-of-bias tool for randomised trials.[25] This tool assesses five domains to address different types of bias: randomisation process, deviations from the intended interventions, missing outcome data, measurement of the outcome and selection of the reported result.[26] Based on the established criteria, each domain was rated as low risk, some concerns or high risk of bias.[25] The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to rate the certainty of evidence for each outcome of interest.[27] This approach rates the risk of bias, inconsistency, indirectness, imprecision and publication bias as four grades (very low, low, moderate and high). We adopted the Grading of Recommendations Assessment, Development and Evaluation profiler Guideline Development Tool (GRADEpro) to produce the summarised findings.[28] Disagreements between the reviewers were resolved by discussion.

Data analysis

All statistical analyses were performed using RevMan.[29] The standardised mean difference (SMD) was used to calculate the intervention effect for continuous outcomes.[30] Means with 95% CIs are presented. Heterogeneity was calculated by means of the Q and I^2 statistics. The I^2 values of 0%–40%, 30%–60%, 50%–90% or

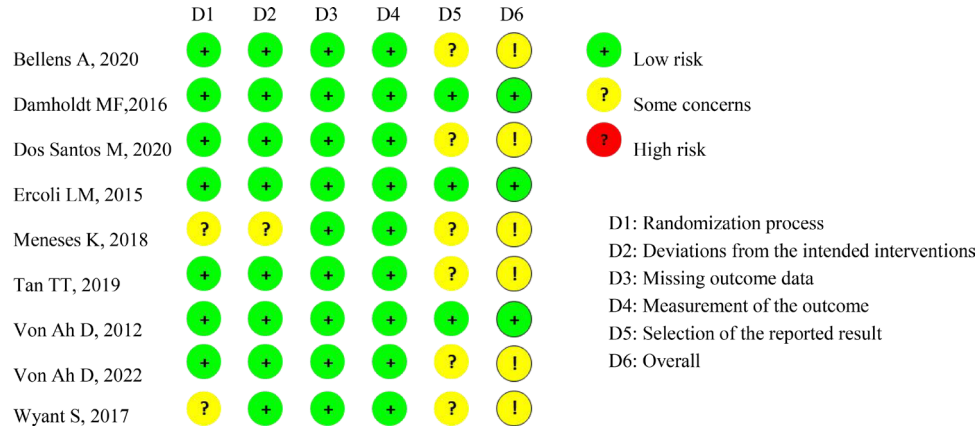

Figure 2 Risk of bias graph.

75%–100% indicated not important, moderate, substantial or considerable heterogeneity.[28] If there was no significant difference (p≥0.1, I^2<50%), a fixed-effects model was used. Otherwise (p<0.1, I^2≥50%), a random-effects model was chosen. For the same outcomes, if some scales increased with outcome severity while others decrease, the reviewer, when extracting the data, multiplied the mean values from one set of studies by −1 to ensure that all the scales point in the same direction, before standardisation.[30] If a study included two intervention groups, the number of participants in the control group was halved to avoid double counting.[31] We explored the contribution of individual studies to the heterogeneity excluding one at a time. Moreover, we conducted a post hoc subgroup analysis of the primary outcome measure, subjective perception, according to the intervention mode, intervention means and intervention duration. The significance of the combined statistics was determined by the Z-test, in which p<0.05 was considered statistically significant. We did not perform publication bias analysis because there were fewer than 10 included studies.

RESULTS

Literature search results

Figure 1 shows the number of manuscripts included in each phase of the review. After importing the articles into EndNote V.X9.1 for deduplication, 1703 articles remained. Of the initial 1703 non-duplicate articles, 73 were assessed for full-text review. Of them, 64 were excluded (online supplemental file 3) with reasons: inappropriate population(n=6), inappropriate intervention (n=31), no useful data (n=5), full text not available (n=2), abstract only (n=8), protocol only (n=9), duplicate date(n=3). Finally, nine full-text studies were found eligible and included in this meta-analysis.

Characteristics of the included studies and participants

Of the nine studies included, five originated from the USA[32–36] and the rest were from China,[37] France,[38] Belgium[39] and Denmark.[40] The sample sizes of each study ranged from 13 to 157 participants, and a total of 666 patients were included. Most of the studies recruited only patients with breast cancer, and only one[38] included patients with multiple cancer types, which accounted for 85%. With the exception of the two studies by Bellens *et al*[39] and Damholdt *et al*,[40] the remaining seven studies reported on the patient's stage of treatment. Of these seven studies,[32–38] only the Tan's[37] study implemented intervention in patients with breast cancer undergoing chemotherapy, and the remaining six studies[32–36 38] were all patients with breast cancer in rehabilitation stage who had completed treatment. All patients included in the study were about 50–60 years old. The time of breast cancer diagnosis or treatment ranged from 9 months to 78 months in the included study. About half of the cognitive training (n=4) delivered the intervention in group format,[32 34 35 40] while the rest (n=5) delivered the interventions in individual format.[33 36–39] The content of cognitive training is to train attention, processing speed, learning, memory, working memory and visuospatial tasks, but different studies may involve different cognitive domains. At the same time, the delivery of cognitive training is different, which can be based on the relevant software to carry out computerised exercises,[33 35 36 38–40] or directly use the compiled cognitive training task workbook.[32 34 37] The frequency and period of the interventions ranged from 3 to 5 times each week, lasting for 20–60 min per session, with the total intervention length ranging from 5 to 12 weeks. In all the included studies, outcomes were measured before the intervention, and at the end of the intervention. Follow-up assessments were conducted in four studies,[32 33 39 40] and the length of follow-up varies from 2 months to 6 months. Attrition rates ranged from 3% to 42%. The characteristics of each of the included studies are shown in online supplemental table 1.

Study quality

Three studies[32 34 40] were assessed as low risk, and the other studies were assessed as some concerns.[33 35–39] Two studies[33 36] did not report the randomisation process. Because there was insufficient information about the analysis strategy, the study by Meneses *et al*[33] was assessed

to have some concern about the risk of bias from the intended intervention area. In six studies,[33 35–39] 'Selection of the reported result' was rated as having some concern because no prespecified analysis plans available for comparison and we were unable to validate the protocol (figure 2).

Meta-analysis

Subjective cognitive function

Six studies[32 36 38–40] involving a total of 369 participants provided available data to analyse the effects of cognitive training on subjective cognition in patients with breast cancer reporting cognitive changes. The pooled result indicated that, in comparison with the control group, cognitive training had a significant effect (SMD=0.30, 95% CI (0.08 to 0.51), I^2=33%) on patients. The results of subgroup analysis with intervention mode (figure 3A), intervention means (figure 3B) and intervention duration (figure 3C) as the grouping variables are shown in the figure 3. The results showed that cognitive training had effect on subjective cognition of patients with cognitive changes when in the individual session mode[36 38 39](SMD=0.45, 95% CI (0.14 to 0.75), I^2=24%), the means of intervention was web-based[36 38–40](SMD=0.27, 95% CI (0.04 to 0.49), I^2=42%) and the intervention duration was more than 2 months[36 38 39](SMD=0.45, 95% CI (0.14 to 0.75), I^2=24%). However, subgroup analysis showed no significant effect of cognitive training when in the group session mode[32 40](SMD=0.15, 95% CI (−0.15 to 0.45), I^2=38%) or the intervention duration was less than 2 months[32 40] (SMD=0.15, 95% CI (−0.15 to 0.45), I^2=38%). The level of certainty of the evidence was moderate because the sample size of participants did not meet the optimal information size as calculated (online supplemental table 2).

Objective cognitive function

Figure 4 shows the results of the objective cognitive tests after coding them into specific cognitive dimensions. The fixed-effects model was used for meta-analysis of all objective cognitive dimensions. Summary result display cognitive training had significant effects on processing speed[32 33 38](SMD=0.28, 95% CI (0.02 to 0.54), I^2=0%), verbal memory[32 35 36 40] (SMD=0.32, 95% CI (0.05 to 0.58), I^2=0%), working memory[33 38 40] (SMD=0.39, 95% CI (0.17 to 0.61), I^2=0%) and episodic memory[33 38](SMD=0.40, 95% CI (0.11 to 0.69), I^2=0%). The effects of cognitive training on attention[32 33 38 40](SMD=0.09, 95% CI (−0.11 to 0.30), I^2=0%) and short-term memory[38 40] (SMD=0.13, 95% CI (−0.11 to 0.38), I^2=0%) were not statistically significant. There was no statistically significant heterogeneity between the studies, except for executive function (I^2=90%, $p < 0.01$). Further sensitivity analysis showed that the heterogeneity mainly came from the study of Tan[37] (details are provided in online supplemental file 4), and there was no heterogeneity after eliminating this study (I^2=0%, p=0.46) (figure 4). In addition, the combined SMD was not altered after sensitivity analyses of the five intervention groups from the other four studies, indicating the robustness of the results. The pooled combined SMDs have no statistically significant effect on executive function favouring cognitive training group[32 33 38 39](SMD=−0.05, 95% CI (−0.30 to 0.20), I^2=0%). Due to sample size, CIs, blindness, detection bias and notable concern about conflicts of interest, we rated the overall quality of 'processing speed' as low, 'execution function' as very low and other objective outcomes as moderate (online supplemental table 2).

Psychological outcomes

We performed data extraction and analysis on the psychometric outcomes commonly mentioned in various studies, such as depression, anxiety and fatigue (figure 5). The pooled mean effect size estimating depression comprised eight cognitive training groups from six studies[34 35 37–40] with large heterogeneity (I^2=51%, p=0.05) using fixed-effects models (details are provided in online supplemental file 4). Sensitivity analysis showed that heterogeneity was mainly due to the Tan's[37] study, which included patients with breast cancer with self-reported cognitive changes and depression. After excluding patients with higher baseline depression, there was no heterogeneity in the remaining studies (I^2=0%, p=0.72), and there was no statistically significant difference in the degree of depression reduction in the cognitive training group (SMD=−0.19, 95% CI (−0.39 to 0.01), I^2=0%). Due to notable concern about conflicts of interest, we rated the quality of the evidence as moderate (online supplemental table 2). The composite mean effect size for assessing anxiety included seven cognitive training groups from five studies,[34 36 38–40] with no heterogeneity across studies (I^2=0%, p=0.80), but the improvement of anxiety was not statistically significant (SMD=−0.08, 95% CI (−0.28 to 0.12), I^2=0%). We rated the quality of the evidence as moderate due to the confidence intervals (online supplemental table 2). In addition, the composite mean effect size for fatigue assessment included five cognitive training groups from three studies,[34 36 38] with no heterogeneity across studies (I^2=0%, p=0.87), but the improvement of fatigue was not statistically significant (SMD=−0.25, 95% CI (−0.51 to 0.02), I^2=0%). We rated the quality of the evidence as low due to the sample size and notable concern about conflicts of interest (online supplemental table 2).

DISCUSSION

The factors influencing cognitive changes in patients with cancer or related interventions have been studied in detail in recent years. However, previous evidence syntheses have been subject to limitations. Bail and Meneses[41] published a narrative review in 2016 concluding computer-based cognitive training may enhance cognitive function in

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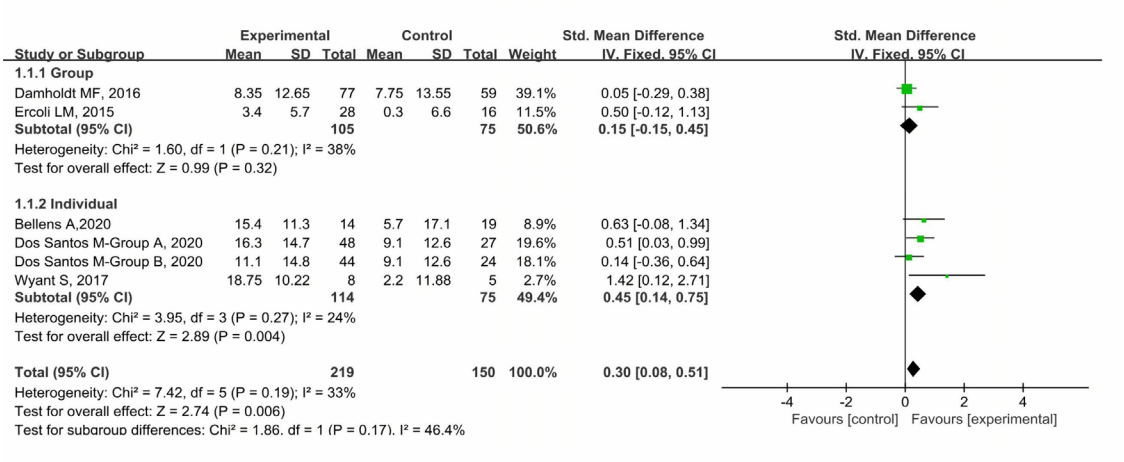

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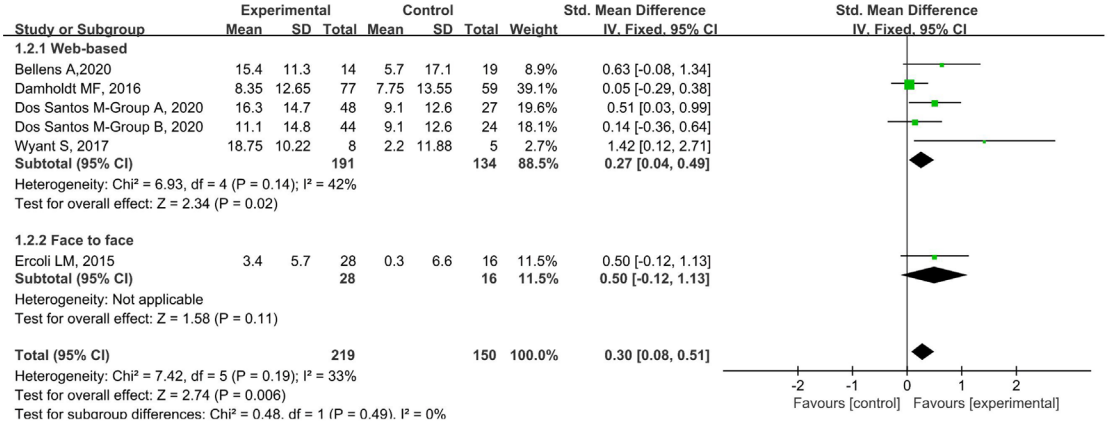

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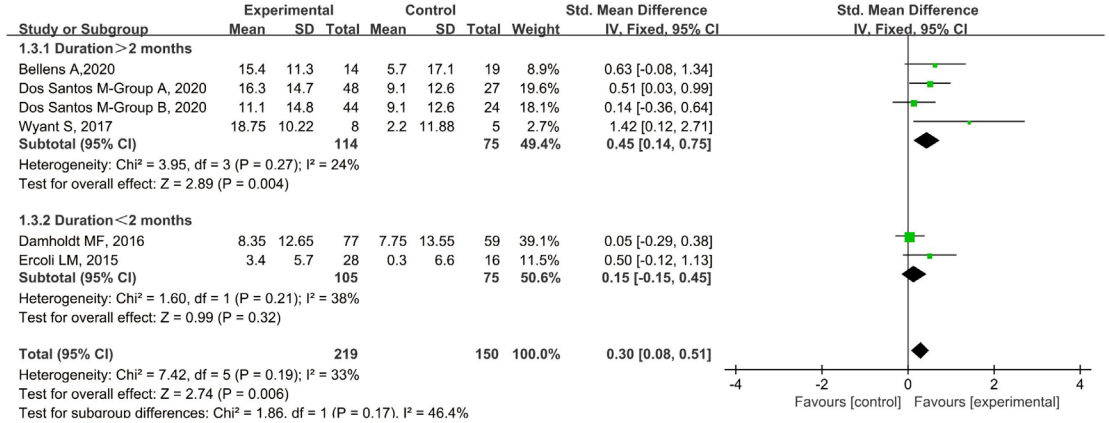

Figure 3 Forest plot of the effects of subjective cognitive function.

patients with breast cancer with CRCI but no attempt has been made to quantitatively summarise this relationship. The latest non-systematic review by Mackenzie and Marshall[42] examined interventions to address CRCI in adults, reporting the effectiveness of cognitive training, which is consistent with our findings. Our comprehensive meta-analysis focused on a more specific population (patients with breast cancer reporting cognitive changes) and covered a wide range of outcome measures. We found that cognitive training had beneficial effects on subjective

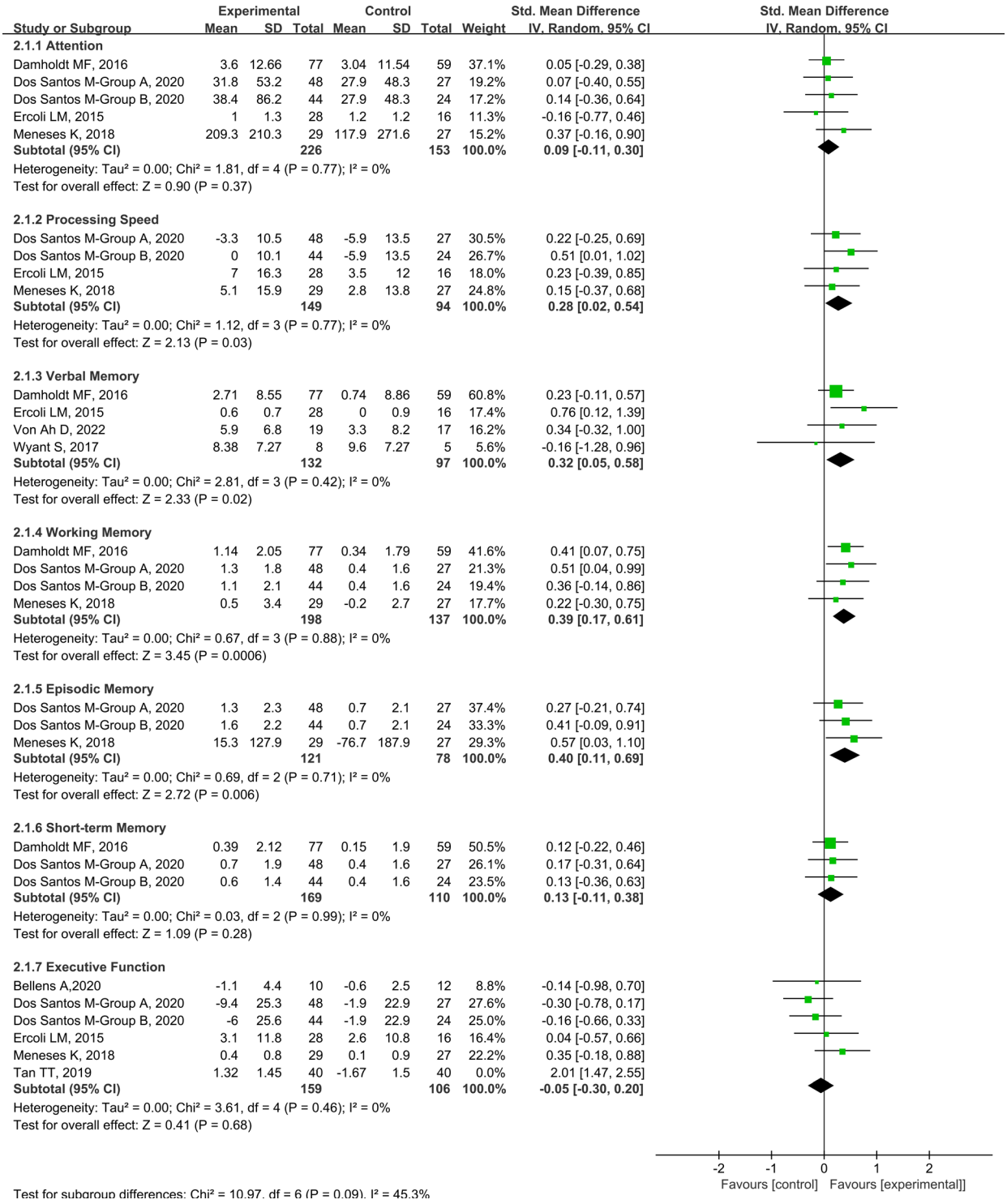

Figure 4 Forest plot of the effects of objective cognitive function.

and some objective cognitive domains in patients with breast cancer reporting cognitive changes, although there was no significant effect on the improvement in anxiety, depression and fatigue.

Effectiveness of cognitive training

Cognitive training is an integrative training method for some cognitive dimensions that can be done through systematic instruction or web-based devices to strengthen patients' cognitive skills.[29 43 44] The pooled results demonstrated that compared with control group, cognitive training improved subjective cognitive function in breast cancer survivors reporting cognitive changes, which was consistent with a previous study.[45] Patients' self-reported subjective cognitive function was more sensitive than neuropsychological assessments, so it can detect the cognitive changes of

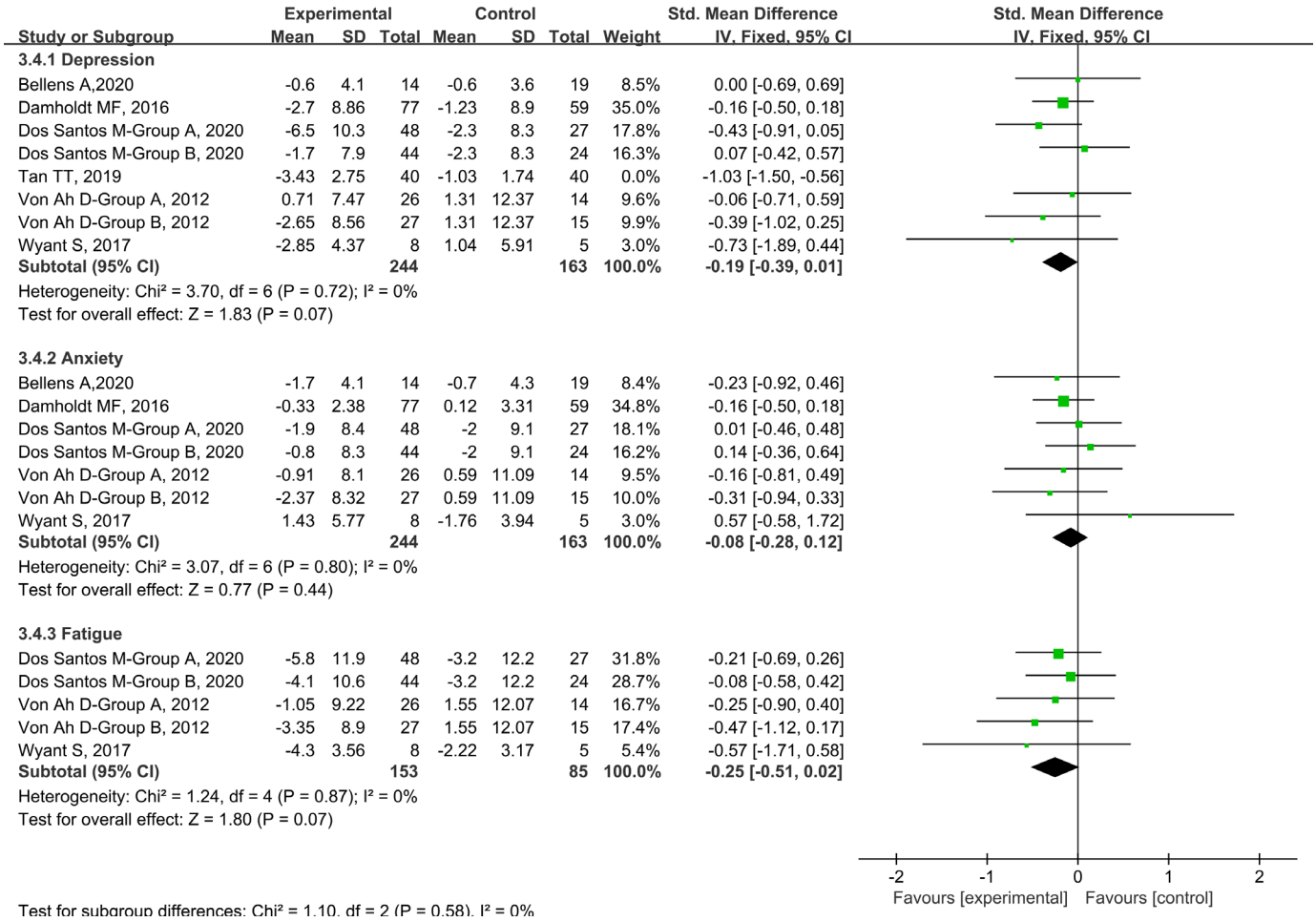

Figure 5 Forest plot of the effects of psychological outcomes.

patients easier. In addition, studies have shown that cognitive training improves perceived CRCI experienced by patients, enhancing their self-confidence and general emotional well-being. These perceived improvements, in turn, can decrease reliance on self-management methods for cognitive impairment, which can be reflected in improved performance on measures of subjective cognitive impairment.[46] Partial objective cognitive dimension makes positive changes, such as processing speed, verbal memory, working memory, episodic memory. Studies have found that cognitive training stimulates neurogenesis in certain parts of the brain by repeatedly training specific cognitive dimensions.[47] And the cognitive training content is very rich, through the combination of listening, speaking, reading and writing various forms of training to strengthen cognition.[48] Unexpectedly, cognitive training did not show effects on attention, executive function and short-term memory. On one hand, results from clinical studies using neuropsychological tests also suggest that attention and executive function are most affected by cancer-related treatments.[49] Therefore, trying to improve these dimensions is inherently challenging. On the other hand, the number of studies included in our review is limited and more RCTs are needed to draw more credible conclusions.

Subgroup analysis

We conducted a post hoc subgroup analysis of the subjective cognitive function, according to intervention mode, intervention means and intervention duration to better understand when and how cognitive training might be beneficial. Subgroup analysis revealed that individual sessions of cognitive training were more effective than group sessions, at the same time, web-based cognitive training is a more preferred intervention in most studies than face-to-face interventions. We carefully examined the specific content of the intervention. Most individual interventions rely on online training software, do not require site-specific training and face-to-face contact, and offer greater flexibility and access to cognitive training. At the same time, the software program can involve algorithmic control of difficulty level to optimise the balance between challenge and motivation, so that the brain always maintains a relatively tense level in the training,[50] which is conducive to more efficient brain training and better intervention effect. In terms of intervention duration, we found that an appropriate

extension of the intervention duration (more than 2 months) may result in better intervention results, which is consistent with the results of Orgeta *et al*.[51] We found attrition rates of 4%–20% in studies with an intervention duration of less than 2 months. Attrition rates ranged from 13% to 42% for all studies with interventions longer than 2 months, except for Tan's study (3% attrition rate).[37] Further analysis revealed that the interventions in this study were cyclical.[37] There were four cycles in total, including 5 days of concurrent intervention during chemotherapy hospitalisation and 21 days of home rest after discharge. The intervention participants were all hospitalised patients in the treatment stage. The other four studies[32 38–40] had a frequency of continuous intervention with a fixed amount of tasks per week or per lesson, all of whom were convalescent patients. Therefore, we suspect that the study of Tan[37] low attrition rate is more likely to be related to the patient's treatment phase, as hospitalised patients may show better adherence.[52] Based on this, we recommend that the duration of cognitive training can be appropriately extended under the premise of ensuring good persistence of survivors to improve the rehabilitation effect of patients. In the future, the relationship between the effectiveness of cognitive training and better adherence can be further explored through dose-reflection models to determine the minimum does of cognitive training.

Effectiveness of psychological outcomes

Depression is characterised by a slowdown in information processing,[53] while anxiety symptoms are mainly characterised by excessive worry and uneasiness about daily chores,[22] both of which are stimulated by brain functions and structures associated with negative emotions, such as the prefrontal cortex and amygdala.[54] Cognitive training can relieve anxiety and depression by stimulating the cerebral cortex, which is involved in emotional responses, and by diverting the patient's attention from being immersed in negative emotions.[55] But surprisingly, our review showed that cognitive training had no significant effect on depression and anxiety. One possible explanation is that cognitive training keeps the brain thinking, increasing sympathetic nervous system activity and psychologically increasing tension. In addition, variability in the use of instruments may bias the effects when assessing some state variables, such as depression and anxiety. In Wyant's study,[36] it is reasonable to believe that the Patient-Reported Outcomes Measurement System (PROMIS) scale selected in this study is an appropriate tool to assess the anxiety state of patients with breast cancer based on the detailed introduction of the context in the risk of bias assessment. However, it is also worth mentioning that other studies have shown that the PROMIS scale can be used to evaluate the health-related outcomes of patients with breast cancer after surgery and during chemotherapy with good reliability and validity, while it may not be very sensitive to other treatment methods of breast cancer, such as targeted therapy, radiotherapy and endocrine therapy.[56] Wyant's study[36] included patients with breast cancer with all types of treatment, only 13.3% of whom received surgery or chemotherapy alone, so it is necessary to rethink whether assessment tools are not sensitive enough to capture the minimal clinical differences in the improvements in depression or anxiety that could have been achieved. Therefore, it is suggested that future researchers should consider whether the scale can be used in the population they want to evaluate, and also consider the baseline demographic characteristics of the study population, so as to select a scale with high sensitivity and specificity.

At the same time, we found that cognitive training did not significantly alleviate fatigue in breast cancer survivors which is consistent with previous study.[57] In both treatment period and recovery period, cancer treatment, such as chemoradiotherapy, mastectomy, breast reconstruction and so on, can lead to breast cancer survivors more frequently encountered many difficulties associated with disease or treatment, such as cancer symptoms and postchemoradiotherapy physical fatigue. This difficulty may persist even after treatment has ended.[58] In addition, some patients undergoing surgery are more likely to have psychological disorders because of the influence of self-image disorder.[59] Fatigue in patients with cancer has been recognised as a multifactorial construct that includes both physical symptoms(ie, fatigue) and psychological disorders.[60] Studies have shown complex interactions among various aetiological mechanisms. Thus, cognitive training that focus on the cognitive health and well-being of patients may not help to improve fatigue, suggesting that multimodal interventions that combine cognitive training with psychosocial approaches may be more appropriate to improve fatigue in breast cancer survivors.

Strengths and limitations

The strength of our review is that, on the one hand, we specifically focused on patients with breast cancer with cognitive changes. In addition, because we found that many studies considered both cognitive training and compensatory cognitive training, such as cognitive behavioural therapy, as cognitive training, we strictly differentiated the two interventions and focused only on cognitive training. On the other hand, not only did we quantify the effects of cognitive training on cognition, but we also included emotional state as a secondary outcome, because studies have shown that anxiety, depression and fatigue are associated with CRCI.

There are several limitations of our study. First, due to limited data from the included studies, no post hoc subgroup analysis of objective cognitive function and psychological outcomes, and few published enough detail in the report to extract data on different participant

demographic characteristics, we were unable to give more specific opinions on how best to implement cognitive training in the clinic. Second, time and cost factors prevent some studies from tracking the long-term effects of cognitive training. We also did not analyse the short-term or medium-term or long-term effects of cognitive training during the follow-up period, mainly considering that there were insufficient data for analysis. Finally, only nine studies were included in the review, and we were unable to further identify the source of heterogeneity by meta-regression. At the same time, each independent meta-analysis for each cognitive domain contained a small sample size and number of studies. This results in limited statistical power and relatively conservative results.

CONCLUSIONS

Our review provides a better understanding on the effect of cognitive training in patients with breast cancer reporting cognitive changes. The results show that cognitive training is mainly implemented in patients with breast cancer at the stage of rehabilitation. Through the adaptive training of each cognitive dimension, the subjective cognitive function and some objective cognitive functions of patients with breast cancer with cognitive changes, such as processing speed and verbal memory, have a significant intervention effect. Delivery based on individual sessions, the use of web-based cognitive training software may be more conducive to improving the outcome of patient interventions. The implementation of cognitive training by web-based mobile medical applications or programmes may be an important way to improve cognitive symptoms of patients with breast cancer in the future. It must be noted, however, that based on the limited research available, we cannot conclude that cognitive training can improve depression, anxiety and fatigue in patients with breast cancer with cognitive changes. It is suggested that future studies should further expand the sample size and conduct randomised controlled studies for further confirmation.

Contributors XY defined the research question as well as inclusion and exclusion criteria for this systematic review. XY and QL were responsible for article screening, data extraction, classifications of adverse events and performed the quality assessment. Questions and discrepancies were discussed among all authors until consent was achieved. XY conducted the meta-analyses and designed the tables and figures. S-QW accepted full responsibility for the work of the study, had access to the data, and controlled the decision to publish as the guarantor. All authors have read and approved the final version of the manuscript.

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