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Review

Impact of nonpharmacological interventions on cognitive impairment in women with breast cancer: A systematic review and meta-analysis

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ABSTRACT

Objective: This study aimed to examine the characteristics of research conducted on nonpharmacological interventions for cognitive impairment in patients with breast cancer and identify the primary effects of nonpharmacological interventions through a systematic review and meta-analysis.

Methods: Five electronic databases were searched to identify all randomized controlled trial studies until September 30, 2022, using the key terms "breast cancer," "cognitive disorders," and their possible variations. The Cochrane Risk of Bias tool was used to assess risk of bias. The effect sizes were calculated in Hedges' g. Potential moderators influencing the intervention effects were explored.

Results: Twenty-three studies were included in the systematic review, and 17 studies were included in the meta-analysis. Among the nonpharmacological interventions for patients with breast cancer, cognitive rehabilitation and physical activity were the most common, followed by cognitive behavioral therapy. The meta-analysis indicated that nonpharmacological interventions had a significant effect on attention ($g = 0.83$; 95% CI: 0.14 to 1.52; $I^2 = 76\%$), immediate recall ($g = 0.33$; 95% CI: 0.18 to 0.49; $I^2 = 0\%$), executive function ($g = 0.25$; 95% CI: 0.13 to 0.37; $I^2 = 0\%$), and processing speed ($g = 0.44$; 95% CI: 0.14 to 0.73; $I^2 = 51\%$) among objective cognitive functions, as well as subjective cognitive function ($g = 0.68$; 95% CI: 0.40 to 0.96; $I^2 = 78\%$). Intervention type and mode of delivery were potential moderators for the effects of nonpharmacological interventions on cognitive functions.

Conclusions: Nonpharmacological interventions can improve subjective and objective cognitive functioning among patients with breast cancer undergoing cancer treatment. Therefore, it is necessary to provide nonpharmacological interventions by screening patients at high risk of cancer-related cognitive impairment.

Systematic review registration: CRD42021251709.

Introduction

Breast cancer is one of the most prevalent cancers among women worldwide.[1] New treatment and early detection have reduced breast cancer recurrence rates and significantly increased survival rates.[1] The improved survival rate, however, leads to concerns regarding side effects from cancer and its treatment. Thus, it has become increasingly important to initiate and implement programs for post-treatment recovery.[1,2]

Patients undergoing breast cancer treatment are exposed to secondary health problems, such as the sudden onset of menopause, sexual dysfunction, cognitive dysfunction, fatigue, and osteoporosis.[3] Cancer-related cognitive impairment (CRCI), which often entails decreased memory and attention/concentration, can occur among patients with cancer, especially those with breast cancer.[4,5] The incidence of CRCI is reported to occur among 12%–82% of patients with breast cancer undergoing chemotherapy, of which 17%–35% have reported experiencing severe cognitive impairment for years after treatment.[4,5] The areas of cognitive function that are commonly affected include attention, verbal memory, executive function, and psychomotor processing speed, which often occur at the end of chemotherapy and, in some cases, can last for more than 10 years.[4–7].

According to previous studies on the health of breast cancer survivors,[3,8] CRCI has been reported to have negative effects on quality of life, autonomy, return to work, social relations, and self-confidence.[6] Owing

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to changes in cognitive function, breast cancer survivors experience decreased capacity to carry out their responsibilities in their families, communities, and workplaces. Furthermore, CRCI decreases treatment adherence and makes it difficult to maintain a social life or adapt to the workplace.[4,5,8–11] Moreover, CRCI adversely affects the ability to adapt to life after breast cancer treatment and increases the likelihood of developing mental health issues such as depression and anxiety.[9]

Nonpharmacological interventions, which have recently emerged as measures for CRCI, are safe and effective in enhancing patient satisfaction and processing speed and memory compared to drug therapy.[12] Currently, nonpharmacological interventions for CRCI include programs that promote cognitive rehabilitation,[13–20] cognitive behavioral therapy (CBT),[21–26] physical activity interventions such as exercise and yoga,[27–34] and acupuncture.[35] Among these interventions, cognitive rehabilitation, including cognitive training, aims to improve cognitive abilities and restore impaired skills through repetitive, standardized, problem-oriented tasks targeting specific cognitive domains.[16] CBT is designed to improve or restore mental function through behaviorally oriented programs that may include retraining lost cognitive abilities, compensatory strategies, or more inclusive behavioral programs.[36,37] Physical activity interventions, including any form of exercise or physical activity, may improve cerebrovascular function by improving oxygenation and blood flow to the brain and reducing stress.[12] Additionally, acupuncture may potentially increase brain structural connectivity and cognitive integrity.[35,38]

According to a recent review and meta-analysis, cognitive training,[39] cognitive behavioral intervention,[39] physical activity,[40] and complementary and integrative interventions[41] for CRCI have been reported as effective in improving cognitive function and reducing symptoms of CRCI in patients. Moreover, as several studies[12,42] have analyzed the effects of nonpharmacological therapy on cognitive function, there have been attempts to integrate individual study results through systematic reviews and meta-analyses. However, these studies have limitations in that they were conducted to identify the effects of nonpharmacological interventions on patients with cancer with different treatment characteristics[12] or used limited databases and search terms.[42] Therefore, it is necessary to integrate the currently available research on nonpharmacological interventions for CRCI and identify their impact on the cognitive function of patients with breast cancer.

This study aims to identify the characteristics of research conducted on nonpharmacological interventions on cognitive impairment in patients with breast cancer and to analyze the effectiveness of nonpharmacological interventions on cognitive function through a systematic review and meta-analysis.

Methods

A systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) statement[43] and registered with the International Prospective Register of Systematic Reviews (No. CRD42021251709).

Inclusion and exclusion criteria

We reviewed all published manuscripts that investigated the effects of nonpharmacological interventions of CRCI in adult patients with breast cancer.

Inclusion criteria

Participants were women aged 18 years or older who were diagnosed with stage 0 to IV breast cancer and who had received previous breast cancer treatment (ie, chemotherapy or hormonal therapy). Interventions were nonpharmacological interventions that were operationalized in previous studies as cognitive rehabilitation (ie, cognitive training, brain training, compensatory strategy training), CBT (ie, cognitive behavioral intervention, psychotherapy, meditation/relaxation), physical activities (ie, exercise, yoga or Tai Chi/Qigong), and acupuncture.[12,42] Comparisons were not restricted; usual routine care, waitlist control, or other intervention types that differed from nonpharmacological interventions were eligible. Outcomes were at least one measure of cognitive function, measured at baseline and follow-up by any validated neuropsychological test of cognition. In this study, cognitive function was classified as either objective (ie, neuropsychological test) or subjective (ie, self-reported questionnaire). Among different study designs, only randomized controlled trials (RCTs) were selected.

Exclusion criteria

Studies were excluded if they were as follows: (1) studies on patients with cancer other than breast cancer; (2) studies without an adequate specification of nonpharmacological interventions; (3) studies in which cognitive functioning was not measured and/or reported as a dependent variable; (4) nonintervention studies; (5) review articles; (6) unpublished studies, abstracts, or dissertations; (7) non-peer-reviewed articles and book chapters; and (8) non-English language studies.

Search strategy

We conducted a systematic literature search using five electronic databases on September 30, 2022: Ovid-MEDLINE, EMBASE, CENTRAL (Cochrane Central Register of Controlled Trials), PsycINFO, and CINAHL. The search strategy was established under the guidance of a librarian. Medical subject headings and keywords included those related to breast cancer (ie, breast neoplasm* OR breast cancer* OR breast tumor* OR breast malignancy), and cognition (ie, cognitive function OR neuropsychological tests OR attention OR mental processes) or cognitive disorder (ie, cognition disorders OR chemo brain OR cognitive impair*) and were combined with an "AND" term. Search terms were modified according to each database and are reported in full in the Supplementary File. Relevant systematic reviews and meta-analyses were also searched for in these databases. In addition, the reference lists of relevant reviews were searched until no further studies were found.

Process of data selection and data extraction

Process of study selection

All studies identified through the electronic databases were downloaded to the Endnote program, a reference management database, and duplicates were removed. After removing duplicate literature, two researchers (PJH and JSJ) independently screened the title and abstract of the studies in the order of relevance. Then, the studies that initially met the inclusion criteria were assessed after a full-text screening. If the complete text was not available or relevant data information was missing, the authors of those studies were contacted via email to obtain relevant data. Any disagreements between the researchers during the study review were resolved by examining the studies according to the selection criteria until a consensus was reached. The reference lists of systematic reviews identified during the search were screened for relevant studies. A PRISMA flow diagram was used to display the search results.

Process of data extraction

After the initial screening of the studies, another researcher independently coded and entered information from each selected study into data extraction forms. The Endnote program was used to manage the extraction of searched studies. Data were extracted to analyze its characteristics (primary author, publication year, country of study), the participants' characteristics (age, cancer stage, number of participants), intervention characteristics (content, length of sessions, mode of delivery [online vs. offline], setting [individual vs. group]), and measurement instruments for objective and subjective evaluation of cognitive function. The outcome data including objectively and/or subjectively assessed cognitive functions were extracted. In the case of objective cognitive function data, scores measured through a verified neuropsychological test were extracted.[44] These neuropsychological measures were categorized into five separate cognitive domains of attention, memory, executive function, processing speed, and language fluency according to the neuropsychological assessment literature.[44,45] Attention assessments included selective and sustained attention tests. Memory was classified as immediate and delayed memory and included verbal test assessments. Executive function assessments were categorized based on previous studies[46–48] and included tests measuring working memory, cognitive flexibility, reasoning, planning, inhibition, and global executive composite. Processing speed included tests that measured reaction time to perform an intellectual task or the amount of work that could be completed in a specific amount of time. Language included assessments of verbal and phonological fluency tests.

For subjective cognitive function data, the total scores on the cognitive measures evaluated using self-report questionnaires (eg, the Cognitive Failures Questionnaire, the Functional Assessment of Cancer Therapy-Cognitive Function, the Multiple Ability Self-report Questionnaire), whose reliability and validity were verified, were extracted.

Assessment of risk of bias in included studies

The risk of bias in the included studies was evaluated independently by two reviewers (PJH and JSJ) according to the Cochrane risk of bias tool of the Review Manager 5.4.1 software, the RoB 2.0.[49] The RoB 2.0 consists of five domains: "bias arising from the randomization process," "bias due to deviations from the intended interventions," "bias due to missing outcome data," "bias in the measurement of the outcome," and "bias in the selection of the reported result." The risk of bias for each study was classified as "low risk," "unclear," or "high risk." Disagreements were resolved through discussions.

Data synthesis and data analysis

All analyses were performed with the Comprehensive Meta-Analysis® 3.0 program (Biostat, Englewood, NJ, USA). The continuous data on cognitive function were extracted from the included studies. The standardized mean difference was expressed as the effect size measure by calculating the mean change from pre- to postintervention in the experimental and control groups, respectively. Owing to heterogeneity between studies, a random-effects model was used for this meta-analysis. The pooled effect sizes were presented in a forest plot, and a positive effect size value reflected a more effective nonpharmacological program. Considering the small sample size of the studies included in the meta-analysis, the effect sizes were calculated in Hedges' *g*.[50] Hedge's *g* value was interpreted as an effect size of 0.2 for small, 0.5 for moderate, and 0.8 for large.[51]

To analyze the effect size, the mean, standard deviation, and sample size for each intervention group and control group before and after the intervention were extracted. However, in the case of studies[20,31] that provide a calculated effect size (eg, Cohen's *d*) rather than these statistics, the calculated effect size was used in the meta-analysis. When the cognitive function was repeatedly measured after the end of the intervention,[14,17,19,20,22,23,26,28,32] the effect size was calculated using data from the most recent follow-up period after the end of the intervention to determine the immediate effect of the nonpharmacological intervention. For studies involving two groups of nonpharmacological interventions,[20,23,32,33] two sets of effect sizes were calculated and matched against controls for each intervention group.

The level of statistical heterogeneity was measured using the I^2 statistic, and substantial heterogeneity was defined as values of > 50%. Sensitivity analyses were carried out by removing studies one by one from the meta-analysis.[52] Finally, the funnel plot and Egger's regression test were employed to examine the publication bias.[53,54] Duvall and Tweedie's trim and fill analysis was used to recalculate a new effect size by adjusting the outlier values.[55,56] The significance level was set at $P <$ 0.05. In addition, we performed subgroup analyses to investigate the confounding factors (intervention type, the mode of delivery of intervention, intervention setting, and intervention length). Among the systematic review literature, the studies that did not fully present the result values were excluded from the meta-analysis.

Results

Search results

For this study, a total of 22,046 studies were initially searched, of which 2993 duplicates were excluded using the Endnote program. Based on the exclusion criteria, 19,030 studies were excluded after reviewing the titles and abstracts. Finally, 23 studies were included in the systematic review, and 17 studies were included in the meta-analysis. In the meta-analysis, we excluded six studies[13,15,26,28,30,32] that did not present statistics for the effect size calculation (Fig. 1).

Characteristics of the studies included

The characteristics of the 23 studies included in the systematic review are summarized in Table 1 and are described in detail in Table 2. Among the included studies, four studies (17.4%) were conducted before 2015, 17 studies (73.9%) were conducted between 2015 and 2020, and two studies (8.7%) were conducted between 2021 and 2022. Fourteen studies (60.9%) were performed in North America. Regarding the types of nonpharmacological interventions, cognitive rehabilitation[13–20] and physical activities[27–34] were used in 34.8% of the studies, followed by CBT (26.1%),[21–26] and acupuncture (4.3%).[35] In 13 studies (56.5%), interventions were delivered individually onsite, whereas in 6 studies (26.1%) interventions were provided online. In addition, the intervention was delivered over 8–12 weeks in 13 studies (56.5%) and over less than 8 weeks in 7 studies (30.4%). Regarding the outcome variable, objective cognitive function was measured in 15 studies (65.2%), and subjective cognitive function was measured in 20 studies (87.0%).

Risk of bias in the included studies

The risk of bias in the 23 studies included in the systematic review was evaluated. "Bias arising from the randomization process" (n = 20, 87.0%), "bias due to missing outcome data" (n = 19, 82.6%), "bias in the measurement of the outcome" (n = 23, 100.0%), and "bias in the selection of the reported result" (n = 20, 87.0%) were considerably low, whereas "bias due to deviations from the intended interventions" (n = 14, 60.9%) was either unclear or high for most cases (Fig. 2).

Effectiveness of nonpharmacological interventions on objective cognitive function

Attention

The pooled result of two comparisons from two studies[14,19] measuring the attention of 190 participants (intervention: 102 vs. control: 88) showed a significant difference (g = 0.83; 95% CI: 0.14 to 1.52; P = 0.018; I^2 = 76%) (Fig. 3A). Because only two studies were included in the analysis, the degree of publication bias could not be judged by the funnel plot. Additionally, Egger's test, Duvall and Tweedie's trim and fill procedure, and subgroup analysis could not be perform.

Verbal memory—immediate recall

The pooled result of 13 comparisons from 11 studies[14,16–20,24,27,31,33,35] measuring verbal memory—the immediate recall of 710 participants (intervention: 366 vs. control: 344)—showed a statistically significant difference and small effect from baseline to postintervention (g = 0.33; 95% CI: 0.18 to 0.49; P < 0.001; I^2 = 0%) (Fig. 3B). A symmetrical funnel plot is shown in Fig. 4A, indicating no publication bias for verbal memory—immediate recall. Egger's test did not detect any asymmetry (P = 0.694) and the trim-and-fill method estimated that no effect size had to be added to restore the symmetry.

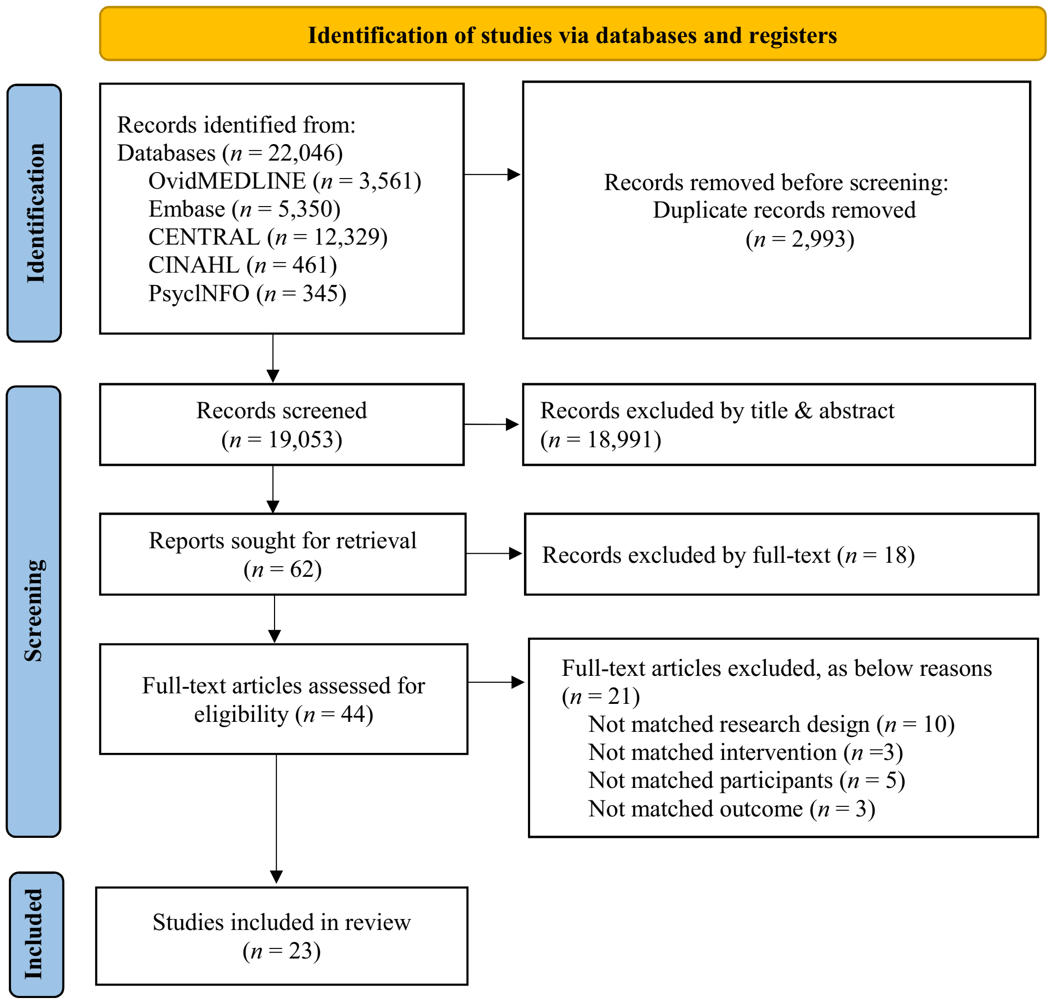


Fig. 1. Flow diagram of the study selection process.

Table 1
Characteristics of studies included in the systematic review (n = 23).

Characteristics	Categories	n (%)	Mean
Publication year	< 2015	4 (17.4)	
	2015–2020	17 (73.9)	
	≥ 2021	2 (8.7)	
Region	North America	14 (60.9)	
	Europe	4 (17.4)	
	Asia	4 (17.4)	
	Australia	1 (4.3)	
Sample size (person)	< 50	10 (43.5)	60.83
	50–100	11 (47.8)	
	≥ 101	2 (8.7)	
Intervention type	Cognitive rehabilitation	8 (34.8)	
	Physical activity	8 (34.8)	
	Cognitive behavioral therapy	6 (26.1)	
	Acupuncture	1 (4.3)	
Mode of delivery	Offline	17 (73.9)	
	Online	6 (26.1)	
Intervention setting	Individual	13 (56.5)	
	Group	10 (43.5)	
Intervention length (weeks)	< 8	7 (30.4)	10.8
	8–12	13 (56.5)	
	> 12	3 (13.0)	

Verbal memory—delayed recall

The pooled result of 8 comparisons from 6 studies[14,20,24,27,33,35] measuring the verbal memory-delayed recall of 435 participants (intervention: 233 vs. control: 202) showed a small effect from baseline to postintervention but not statistically significant results (g = 0.08; 95% CI: −0.11 to 0.26; P = 0.426; I^2 = 0%) (Fig. 3C). The funnel plot suggested an asymmetry skewed to the left. Again, Egger's test was significant (P = 0.040), and the trim-and-fill method estimated that one effect size should be added to restore the symmetry of the funnel plot, reducing the estimated summary effect to 0.06 (95% CI: −0.13 to 0.24) (Fig. 4B).

Executive function

The pooled result of 18 comparisons from 9 studies[14,16,18,19,24,27,29,33,35] measuring the executive function of 1020 participants (intervention: 566 vs. control: 454) showed a statistically significant difference and small effect from baseline to postintervention (g = 0.25; 95% CI: 0.13 to 0.37; P < 0.001; I^2 = 0%) (Fig. 3D). The funnel plot suggested an asymmetry skewed to the left. Egger's test was not significant (P = 0.201), but the trim-and-fill method estimated that three effect size should be added to restore the symmetry of the funnel plot, reducing the estimated summary effect to 0.22 (95% CI: 0.10 to 0.34) (Fig. 4C).

Processing speed

The pooled result of nine comparisons from 8 studies[16–20,27,31,35] measuring the processing speed of 483 participants (intervention: 238 vs. control: 245) showed a statistically significant difference and moderate effect from baseline to postintervention (g = 0.44; 95% CI: 0.14 to 0.73;

Table 2
Descriptive summary of included studies in the systematic review ($n = 23$).

Study	Participants' demographics and time point of follow-up	Delivery/Dosage	Description of intervention	Classification	Control group	Outcome measurement tool
Bellens *et al.*,[13] 2020[a] Belgium	Breast cancer at stages 0-III with intervention ($n = 23$) and control ($n = 23$) groups; mean age was 51.8 years; post-intervention.	The training consisted of game playing for three months, at least three times a week, for a minimum of 60 min or a total minimum of 12 h. (60 min/time, 3 times/week)	Web-based cognitive training (*Aquasnap videogame*) was provided individually online for 24 weeks.	Cognitive rehabilitation	Waist list control	**O:** My clinical cognition **S:** CFQ, Beck Cognitive Insight Scale
Campbell *et al.*,[27] 2018 Canada	Breast cancer at stages II-III with intervention ($n = 10$) and control ($n = 9$) groups; mean age was 52.1 years; post-intervention (48 weeks after baseline).	The 24-week intervention consisted of 150 min/week of moderate to vigorous aerobic exercise with two 45 min supervised sessions per week in a research gym and 2 additional 30-min unsupervised home sessions. (150 min/week: two 45 min/week supervised sessions + two 30 min unsupervised sessions)	Moderate-to-vigorous aerobics was provided individually offline for 24 weeks.	Physical activity	Usual lifestyle	**O:** Animal naming test, Controlled Oral Word Association, Hopkins Verbal Learning Test-Revised, Trail Making Test **S:** FACT-Cog
Damholdt *et al.*,[14] 2016 Denmark	Breast cancer at stages 0-IV with intervention ($n = 94$) and control ($n = 63$) groups; mean age was 54.8 years; post-intervention and 30 weeks after baseline.	Participants were asked to train a minimum of 30 min/day, 5 days/week, for 6 weeks. (30 min/day, 5 days/week)	Web-based scientific brain training was provided individually online for 6 weeks.	Cognitive rehabilitation	Waist list control	**O:** Cognitive Estimation Task, Digit ordering, Digit span-forwards and backward, Paced Auditory Serial Addition Test, Rey's Auditory Verbal Learning Test, the 20 Questions test, the Letter Fluency Test **S:** CFQ
Derry *et al.*,[28] 2015[a] U S A	Breast cancer at stages 0-IIIa with intervention ($n = 10$) and control ($n = 10$) groups; mean age was 51.5 years; post-intervention 24 weeks after baseline.	Trained yoga instructors delivered the yoga intervention, twice weekly, 90-min sessions. (90 min/session, 2 times/week)	Hatha Yoga was given offline in groups for 12 weeks.	Physical activity	Normal activity except for Yoga	**S:** Cognitive problem scale in Breast Cancer Prevention Trial symptom checklist
Ding *et al.*,[21] 2020 China	Breast cancer at stages I-III with intervention ($n = 34$) and control ($n = 40$) groups; mean age was 50.8 years; post-intervention.	During a period of 3–6 months, patients in the intervention group received up to 3 to 6 sessions of individual therapy, each lasting 30 min. (30 min/session*number of sessions)	Psychotherapy (*Cancer and Living Meaningfully, CALM*) was provided individually offline for 12–24 weeks.	Cognitive behavioral therapy	Usual care	**O:** MMSE, Prospective and Retrospective Memory Questionnaire **S:** FACT-Cog
Duval *et al.*,[22] 2022 Canada	Breast cancer at various stages with intervention ($n = 30$) and control ($n = 30$) groups; mean age was 51.7 years; post-intervention and 20 weeks after baseline.	The intervention consisted of eight 2.5-h weekly sessions. (150 min/week)	Mindfulness-based stress reduction was given offline in groups for 8 weeks.	Cognitive behavioral therapy	Waist list control	**O:** CNS Vital Signs **S:** FACT-Cog, Prospective and Retrospective Memory Questionnaire
Ehlers *et al.*,[30] 2018[a] U S A	Breast cancer at stages I-III with intervention ($n = 42$) and control ($n = 43$) groups; mean age was 53.8 years; post-intervention and 24 weeks after baseline	The intervention goal is to gradually increase participants to $\geq$ 150 weekly minutes of moderate-intensity physical activity. (First 6 weeks: 45–200 min/week, Second 6 weeks: $\geq$ 150 min/week)	Home-based exercise-Better Exercise Adherence after Treatment for Cancer was given offline in groups for 12 weeks.	Physical activity	Usual care	**S:** Frequencies of Forgetting
Ercoli *et al.*,[15] 2015[a] U S A	Breast cancer at stages 0-III with intervention ($n = 32$) and control ($n = 16$) groups; mean age was 54.1 years; post-intervention and 13 weeks after baseline.	The 5-week, 2 h per week, manualized group intervention targeted attention (weeks 1–2), executive (week 3), and memory (week 4) functions and review (week 5). (2 h/week)	The cognitive rehabilitation program was given offline in groups for 5 weeks.	Cognitive rehabilitation	Waist list control	**O:** Paced Auditory Serial Addition Test, Rey's Auditory Verbal Learning Test, Trail Making Test
Ferguson *et al.*,[16] 2012 U S A	Breast cancer at stages I-II with intervention ($n = 19$) and control ($n = 21$) groups; mean age was 49.9 years; post-intervention and 16 weeks after baseline.	The intervention consisted of four biweekly individual office visits lasting 30–50 min with phone contacts between visits. (30–50 min/time, 4 times/2 weeks)	Brief CBT Memory and Attention Adaptation Training was provided individually (offline) for 8 weeks.	Cognitive rehabilitation	Waist list control	**O:** California Verbal Learning Test-II, Color-Word-Interference, Color-Word and Switching Trials, Digit Span-Coding, Trail Making Test **S:** MASQ
Ferguson *et al.*,[17] 2016 U S A	Breast cancer at stages I-IIIa with intervention ($n = 27$) and control ($n = 20$) groups; mean age was 54.8 years; post-intervention and 16 weeks after baseline.	Both memory and attention adaptation training and supportive therapy involved 8 weekly visits of 30–45 min each. (30–45 min/week)	Video conference-delivered Brief CBT Memory and Attention Adaptation Training was provided individually online for 8 weeks.	Cognitive rehabilitation	Supportive therapy	**O:** California Verbal Learning Test-II, Symbol Digit Modalities Test **S:** FACT-Cog

(*continued on next page*)

Table 2 (*continued*)

Study	Participants' demographics and time point of follow-up	Delivery/Dosage	Description of intervention	Classification	Control group	Outcome measurement tool
Freeman *et al.*,[23] 2015 U S A	Breast cancer at stages 0-IV with intervention 1 (LD, n = 23), intervention 2 (TD, n = 48), and control (n = 47) groups; mean age was 55.4 years; post-intervention (9 weeks) and 17 weeks after baseline.	The first four sessions were separated into four module searches consisting of 25 min of didactic education followed by 25 min of interaction with the fellow group. (50 min*4 modules/week)	The imagery-based behavioral intervention was provided online (live-delivery, LD) in groups for 5 weeks (Intervention 1). The imagery-based behavioral intervention was provided online (telemedicine-delivery, TD) in groups for 5 weeks (Intervention 2).	Cognitive behavioral therapy Cognitive behavioral therapy	Waist list control	**S:** FACT-Cog
Gokal *et al.*,[29] 2018 U K	Breast cancer at stages I-III with intervention (n = 25) and control (n = 25) groups; mean age was 55.3 years; post-intervention.	Participants began by completing 10 min of walking at any one time and then steadily increasing the duration to 30 min five times a week. (30 min/time, 5 times/week)	Home-based, self-managed moderate intensity walking was provided individually offline for 12 weeks.	Physical activity	Usual care	**O:** Block Design, Digit Span-Forwards and Backwards, Errors of Omission, Stroop Interference **S:** CFQ
Hartman *et al.*,[31] 2018 U S A	Breast cancer at stages I-III with intervention (n = 43) and control (n = 44) groups; mean age was 56.9 years; post-intervention.	Participants had 35–45 min in-person meetings during which they went on a 10-min walk at moderate intensity and set physical activity goals. They performed aerobic exercise over time and met the study goal of at least 150 min per week. (150 min/week)	Moderate to vigorous physical activity plus aerobic with mobile monitoring was provided individually offline for 12 weeks.	Physical activity	Usual care with email education	**O:** Auditory-Verbal Learning Test, NIH toolbox **S:** Patient-Reported Outcomes Measurement Information System
Kesler *et al.*,[18] 2013 U S A	Breast cancer at stages I-III with intervention (n = 21) and control (n = 20) groups; mean age was 55.6 years; post-intervention.	The curriculum in the present study included 48 sessions, each 20–30 min in duration. (20–30 min/session, a total of 48 sessions)	Computerized Executive Function training was provided individually online for 12 weeks.	Cognitive rehabilitation	Waist list control	**O:** Behavioral Rating Inventory of Executive Function, Hopkins Verbal Learning Test-Revised, Digit Span, Letter Fluency Test, Wisconsin Card Sorting Test
Meneses *et al.*,[19] 2018 U S A	Breast cancer at stages 0-III with intervention (n = 30) and control (n = 30) groups; mean age was 54.7 years; post-intervention and 30 weeks after baseline.	Participants were instructed to complete 2 h of Speed of Processing training per week for a total of 10 h within 6–8 weeks. (120 min/week)	Speed of processing-Double Decision program was provided individually online for 6 weeks.	Cognitive rehabilitation	Usual care	**O:** NIH Toolbox Cognition Battery, Useful Field of View Test
Milbury *et al.*,[24] 2013 U S A	Breast cancer at stages I-III with intervention (n = 23) and control (n = 24) groups; mean age was 53.3 years; post-intervention.	Participants participated in two weekly meditation classes (60 min, each) over 6 weeks. (60 min/class, 2 times/week)	The Tibetan Sound Meditation program was given offline in groups for 6 weeks.	Cognitive behavioral therapy	Usual care	**O:** Controlled Oral Word Association, Digit Span, Digit Symbol, Rey's Auditory Verbal Learning Test **S:** FACT-Cog
Myers *et al.*,[32] 2019[a] U S A	Breast cancer at stages I-III with intervention 1 (n = 19), intervention 2 (n = 20), and control (n = 11) groups; mean age was 53.7 years; post-intervention and 12 weeks after baseline.	Participants were instructed to practice for 15 min at home twice a day. Each group met for eight weekly 60-min sessions. (60 min/time, 1 time/week)	Qigong was given offline in groups for 8 weeks (Intervention 1). The gentle exercise was given offline in groups for 8 weeks (Intervention 2).	Physical activity Physical activity	Survivorship support	**O:** Rey's Auditory Verbal Learning Test, Trail Making Test **S:** FACT-Cog
Northey *et al.*,[33] 2019 Australia	Breast cancer at stages I-III with intervention 1 (n = 6), intervention 2 (n = 5), and control (n = 6) groups; mean age was 63.3 years; post-intervention.	The two intervention groups exercised 3 times per week for 12 weeks (up to 36 sessions). (20–30 min/session, 3 times/week)	High-intensity interval exercise training (HIT) was given offline in groups for 12 weeks (Intervention 1). Moderate-intensity interval exercise training (MOD) was given offline in groups for 12 weeks (Intervention 2).	Physical activity Physical activity	Waist list control	**S:** FACT-Cog
Shari *et al.*,[25] 2020 Malaysia	Breast cancer at stages I-III with intervention (n = 32) and control (n = 30) groups; mean age was 47.2 years; post-intervention.	The brief acceptance and commitment therapy intervention has 4 sessions, each lasting 1 h. (60 min/week)	Psychological intervention (brief acceptance and commitment therapy) was provided individually offline for 4 weeks.	Cognitive behavioral therapy	Usual care	**S:** FACT-Cog
Tong *et al.*,[35] 2018 China	Breast cancer at stages 0-II with intervention (n = 40) and control (n = 40) groups; mean age was 42.7 years; post-intervention.	Patients received two 4-week courses of acupuncture with a 3-days of rest between the 2 courses. Every week, patients were treated once a day for 5 days, followed by 2 days of rest. (30 min/time, 5 times/week)	Acupuncture was provided individually offline for 8 weeks.	Acupuncture	Usual care	**O:** Auditory Verbal Learning Test, Clock-Drawing Test, Symbol Digit Modalities Test, Trail Making Test-Part B, Verbal Fluency Test **S:** FACT-Cog

(*continued on next page*)

Table 2 (*continued*)

Study	Participants' demographics and time point of follow-up	Delivery/Dosage	Description of intervention	Classification	Control group	Outcome measurement tool
Van der Gucht *et al.*,[26] 2020[a] Belgium	Early-stage breast cancer with intervention (*n* = 18) and control (*n* = 15) groups; mean age was 45.7 years; post-intervention and 20 weeks after baseline.	It was offered in a blended format, a combination of four 3-h, in-person group sessions spread over 8 weeks and in between online support. (180 min*4 sessions)	Mindfulness-based intervention (mindfulness-based stress reduction + mindfulness-based cognitive therapy) was given offline in groups for 8 weeks.	Cognitive behavioral therapy	Waist list control	**S:** CFQ
Von Ah *et al.*,[20] 2012 U S A	Breast cancer at various stages with intervention 1 (*n* = 29), intervention 2 (*n* = 30), and control (*n* = 29) groups; mean age was 56.3 years; post-intervention and 16 weeks after baseline.	Each intervention included ten 1-h training sessions over 6–8 weeks. (60 min/session, total of 10 sessions)	Cognitive training focused on memory (Advanced Cognitive Training for Independent and Vital Elderly) was given offline in groups for 6–8 weeks (Intervention 1).	Cognitive rehabilitation	Waist list control	**O:** Rey's Auditory Verbal Learning Test, Speed of Processing **S:** FACT-Cog
			Cognitive training focused on processing speed (Posit Science®) was given offline in groups for 6–8 weeks (Intervention 2).	Cognitive rehabilitation		
Wei *et al.*,[34] 2022 China	Breast cancer at stages I-III with intervention (*n* = 35) and control (*n* = 35) groups; mean age was 55.0 years; post-intervention.	Recommended training time was five times a week for half an hour each time during the 12-week exercise period. (30 min/session, 5 times/week)	Physical activity (Qigong) was provided individually offline for 12 weeks.	Physical activity	Usual healthy lifestyle	**S:** FACT-Cog

CFQ, cognitive failure questionnaire; FACT-Cog, Functional Assessment of Cancer Therapy–Cognitive; MASQ, Multiple Ability Self-Report Questionnaire; MMSE, Mini-Mental State Examination.

[a] Not included in the meta-analysis.

$P = 0.004$; $I^2 = 51\%$) (Fig. 3E). When Shari et al.'s[25] study was excluded, they showed moderate and statistically significant results ($g = 0.40$; 95% CI: 0.12 to 0.68; $P = 0.005$; $I^2 = 48\%$). The funnel plot suggested an asymmetry skewed to the left. Also, Egger's test was significant ($P = 0.015$), and the trim-and-fill method estimated that one effect size should be added to restore the symmetry of the funnel plot, reducing the estimated summary effect to 0.35 (95% CI: 0.16 to 0.55) (Fig. 4D).

Language fluency

The pooled result of 5 comparisons from 5 studies[14,18,24,27,35] measuring the language fluency of 339 participants (intervention: 187 vs. control: 152) showed a statistically significant difference and small effect from baseline to post-intervention ($g = 0.23$; 95% CI: −0.01 to 0.47; $P = 0.057$; $I^2 = 13\%$) (Fig. 3F). The funnel plot suggested an asymmetry skewed to the left. Furthermore, the result of the Egger's test was significant ($P = 0.015$), and the trim-and-fill method estimated that two effect size should be added to restore the symmetry of the funnel plot, reducing the estimated summary effect to 0.12 (95% CI: −0.07 to 0.32) (Fig. 4E).

Effectiveness of nonpharmacological interventions on subjective cognitive function

The pooled result of 15 comparisons from 13 studies[14,16,17,20–25,27,29,34,35] measuring the subjective cognitive function of a total of 993 participants (intervention: 502 vs. control: 491) showed a statistically significant difference and moderate effect from baseline to postintervention ($g = 0.68$; 95% CI: 0.40 to 0.96; $P < 0.001$; $I^2 = 78\%$) (Fig. 3G). When the study[21] with an intervention comparison was excluded, they showed moderate and statistically significant results ($g = 0.57$; 95% CI: 0.36 to 0.78; $P < 0.001$; $I^2 = 58\%$). In addition, after excluding Shari et al.'s[25] study, a moderate significance was still observed from postintervention ($g = 0.48$; 95% CI: 0.32 to 0.64; $P < 0.001$; $I^2 = 25\%$). The funnel plot suggested symmetry. Egger's test was not significant ($P = 0.212$), and the trim-and-fill method estimated that no effect size should be added to restore the symmetry of the funnel plot (Fig. 4F).

Moderator analysis

To further explore the intervention effects, we conducted moderator analysis using subgroup analysis (Table 3). Four variables were included as moderators: intervention type (cognitive rehabilitation, CBT, physical activity, acupuncture), the mode of delivery of the intervention (online, offline), intervention setting (individual, group), and intervention length (number of weeks). The analysis revealed a statistically significant difference between groups in processing speed and subjective cognitive function according to the intervention type. Additionally, there was a statistically significant difference between groups in subjective cognitive function according to the mode of delivery of the intervention.

Effect size according to intervention type

In processing speed, there was a statistically significant difference according to the intervention type ($Q_{(2)} = 9.87$, $P = 0.007$). Physical activity (g = 1.66, 95% CI: 0.77 to 2.55) had a greater effect than cognitive rehabilitation (g = 0.36, 95% CI: 0.14 to 0.59) on processing speed. There was no heterogeneity in physical activity ($I^2 = 0\%$), but there was low heterogeneity in cognitive rehabilitation ($I^2 = 21\%$).

In subjective cognitive function, there were significant differences according to the intervention type ($Q_{(3)} = 21.91$, $P < 0.001$). The effect sizes of CBT and physical activity on subjective cognitive function were large to medium (g = 0.98, 95% CI: 0.77 to 1.18; g = 0.66, 95% CI: 0.32 to 1.00, respectively). Contrastingly, the effect size of cognitive rehabilitation on subjective cognitive function was small (g = 0.32, 95% CI: 0.11 to 0.52). The heterogeneity of CBT was high ($I^2 = 86\%$), but the heterogeneity of cognitive rehabilitation was low ($I^2 = 31\%$). There was no heterogeneity in physical activity ($I^2 = 0\%$).

Effect size according to the mode of delivery of the intervention

There were significant differences according to the mode of delivery in subjective cognitive function ($Q_{(1)} = 4.36$, $P = 0.037$). The effect size of offline education on subjective cognitive function (g = 0.73, 95% CI: 0.56 to 0.89) was larger than that of online education on subjective

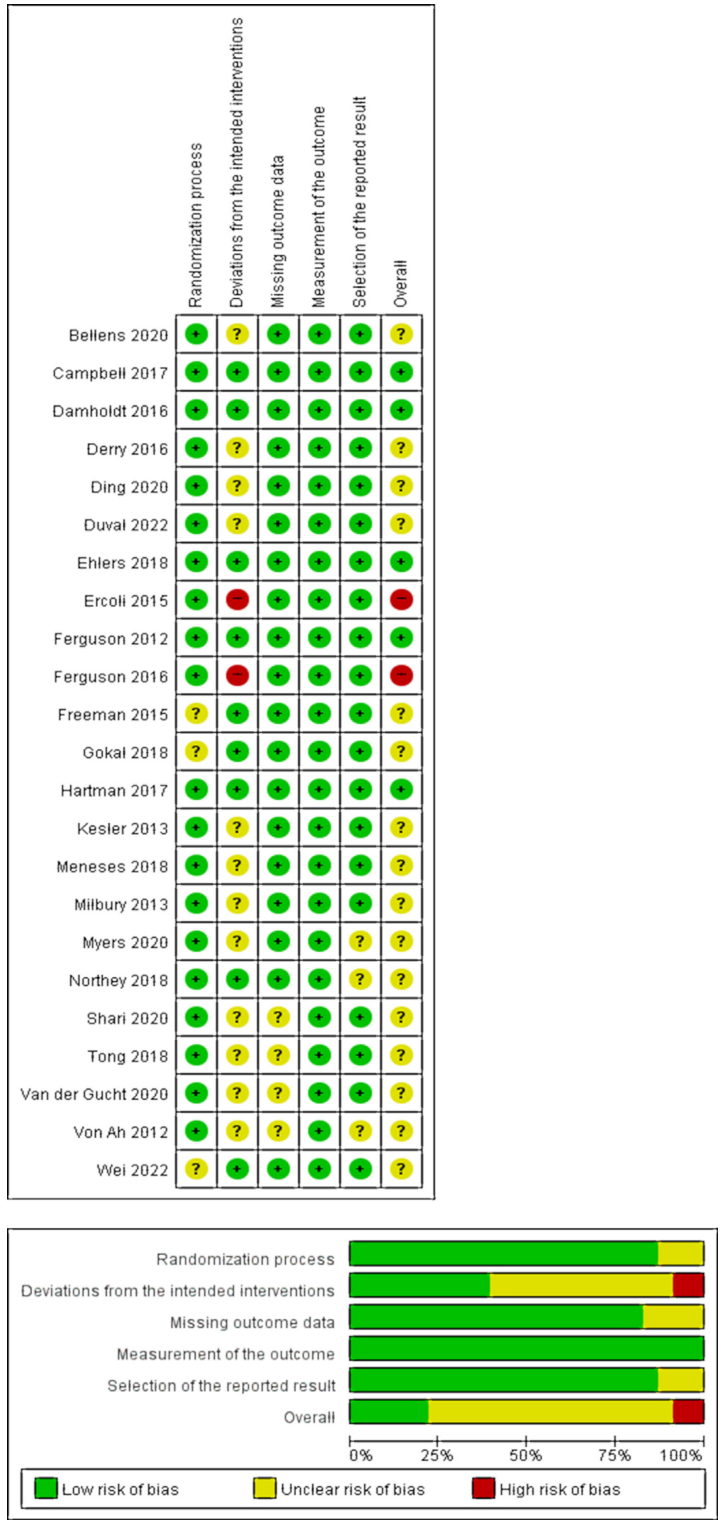


Fig. 2. Risk of bias assessment of included randomized trials.

cognitive function (g = 0.44, 95% CI: 0.23 to 0.65). The heterogeneity of both offline (I^2 = 80%) and online (I^2 = 73%) education was high.

Discussion

Characteristics of the studies included in the systematic review

This study investigated the effects of nonpharmacological interventions on CRCI in patients with breast cancer through a systematic review and meta-analysis. Most studies referring to nonpharmacological interventions, such as CBT for cognitive impairment in patients with breast cancer, were published after 2012.[16] However, for a more comprehensive literature search, literature published before September 30, 2022, was searched. Of the 22,046 studies searched, a total of 23 studies were selected for systematic review according to the inclusion and exclusion criteria. Of these, 17 studies were conducted between 2015 and 2020, indicating that RCT studies with nonpharmacological interventions to improve CRCI in patients with breast cancer have been

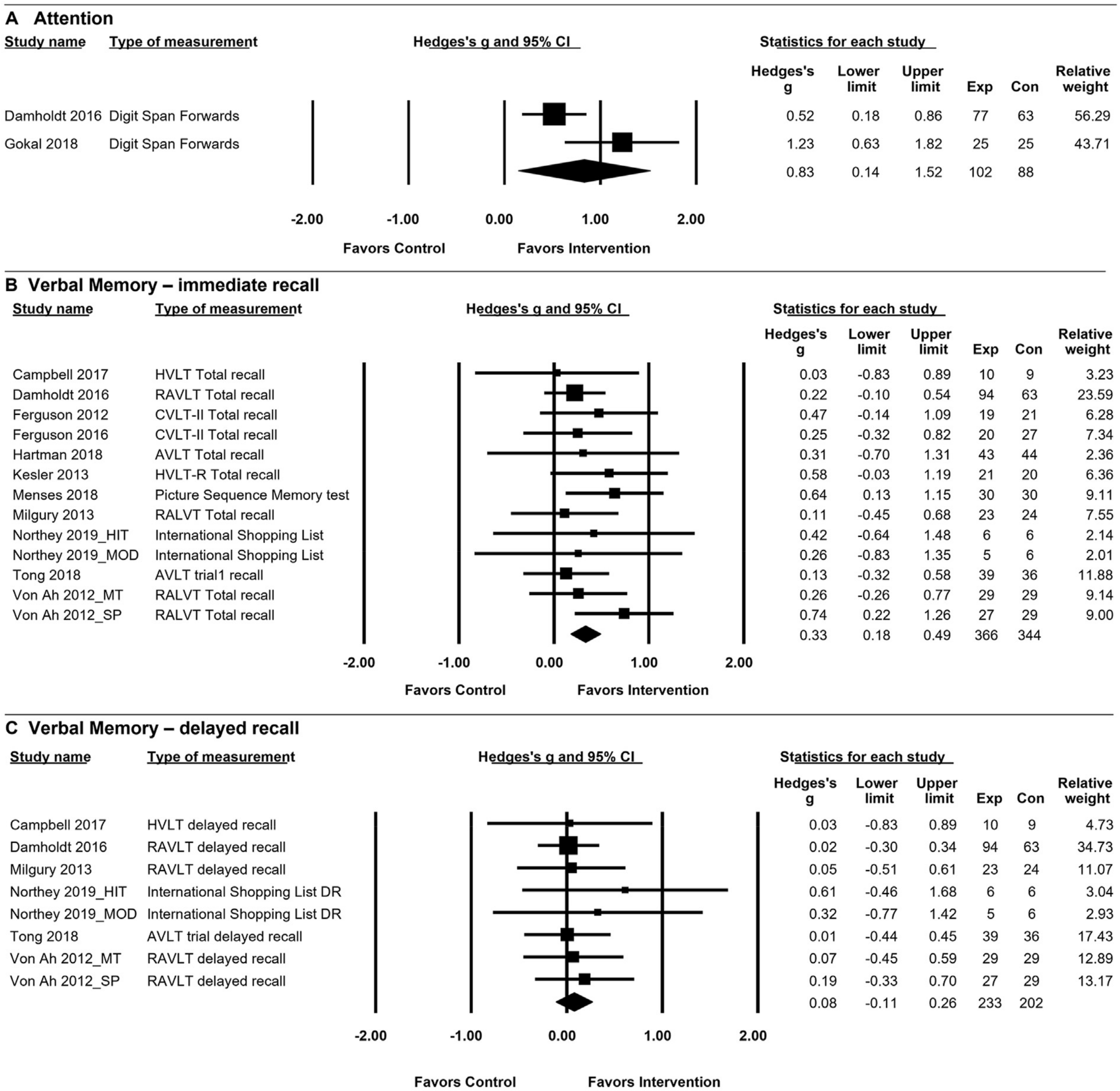


Fig. 3. Pooled effects of cognitive functions after nonpharmacological intervention compared with the control group. (A) Attention; (B) Verbal memory-immediate recal; (C) Verbal memory-delayed recall; (D) Executive function; (E) Processing speed; (F) Language fluency; (G) Subjective cognitive function. AVLT, Audi·tory-Verbal Learning Test; BRIEF, behavioral rating inventory of executive function; CFQ, Cognitive Failures Questionnaire; COWA, Controlled Oral Word Association; CVLT-II, California Verbal Learning Test-II; D-KEFS, Delis-Kaplan Executive Function System; FACT-Cog, Functional Assessment of Cancer Therapy–Cognitive; HVLT-R, Hopkins Verbal Learning Test-Revised; MASQ, Multiple Ability Self-Report Questionnaire; RAVLT, Rey's Auditory Verbal Learning Test; TMT, trail making test; UFOV, Useful Field of View test; WCST, Wisconsin card sorting test.

actively conducted only recently. In terms of region, various studies were conducted in North America, Europe, Asia, and Australia. However, 14 studies were conducted in North America, and only four studies were conducted in Asia.

Among the nonpharmacological interventions for patients with breast cancer, cognitive rehabilitation was common with eight published papers (34.8%). Cognitive rehabilitation involves cognitive training programs that use acquired skills and tasks to improve executive function and teach the brain to bypass damaged cognitive pathways.[20] Cognitive rehabilitation has been employed to improve various cognitive abilities, including CRCI, and has been shown to increase brain function, connectivity, cortical thickness, and neurotransmitter function.[18,57] Cognitive rehabilitation also includes compensatory strategy training.[16,37] Compensatory strategy training has been used to help patients manage or cope with impaired cognitive function through learning techniques such as the use of mnemonics to aid memory.[16]

To understand the degree to which nonpharmacological interventions affect cognitive function improvement, most studies simultaneously evaluated subjective and objective cognitive functions. Neuropsychiatric tests for objective cognitive function evaluation reflect the patients' current state, while self-reported subjective cognitive function evaluation reflects the experience of cognitive function decline over a certain period.[58] These two methods reflect patients' cognitive function status succinctly; however, a difference in sensitivity was noted in the subjective and objective evaluation of cognitive function. The subjective measurement of cognitive function helps determine the extent to which patients with breast cancer are affected by CRCI. Furthermore, this measurement can determine the impact of cognitive function on quality of life. Therefore, subjective and objective cognitive function evaluations should be conducted simultaneously.[7]

The results of a quality evaluation of the selected studies show that most of the five domains of RoB 2.0 were good, but the ratios of

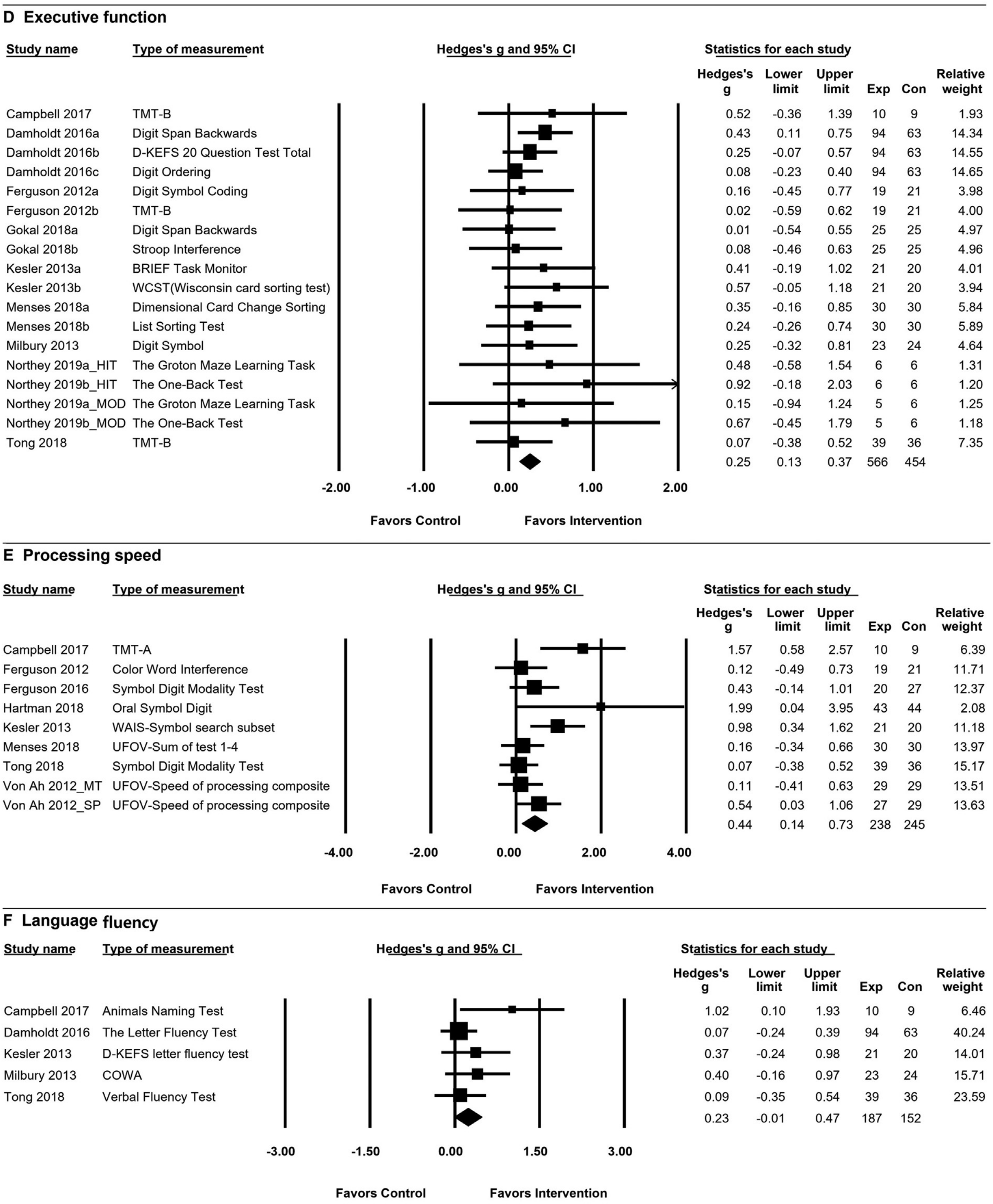
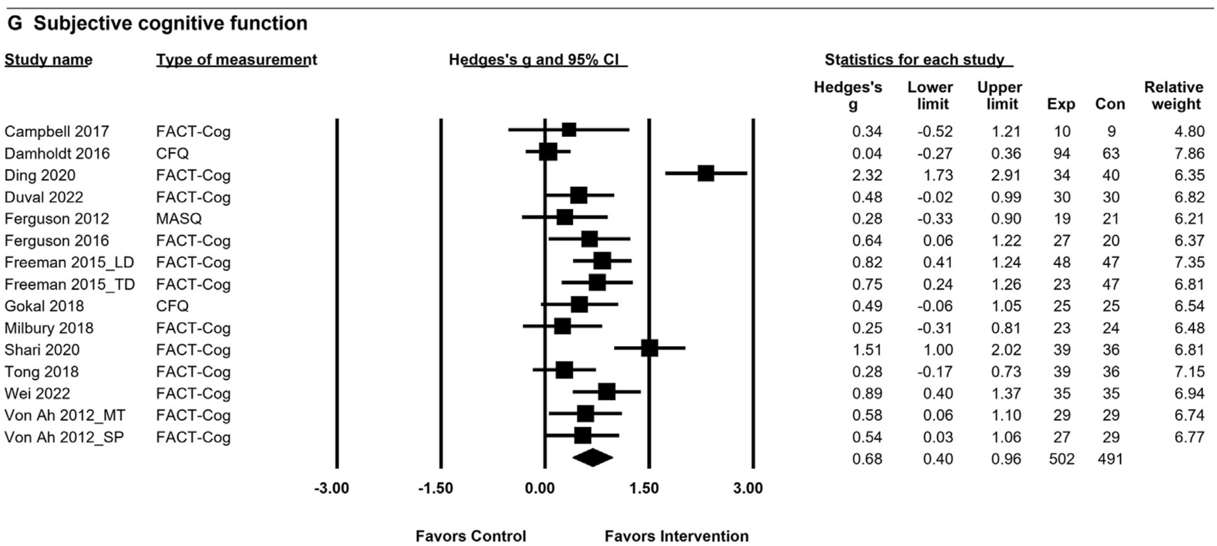


Fig. 3. (*continued*).

"unknown" and "high bias" were high in the bias domain, owing to deviation from the intended intervention. Deviation from the intended interventions is a type of implementation bias, which means that contrary to the intention of the researcher, either the individual was unable to perform the intervention satisfactorily or the intervention allocation effect was not estimated properly.[59] Therefore, in future studies, interventions should be applied accurately based on the intervention protocols so that such biases can be avoided.

Effects of the nonpharmacological intervention

The results of the meta-analysis on the intervention effect found that nonpharmacological interventions had a significant effect on subjective cognitive function and attention, immediate recall, executive function, and processing speed among objective cognitive functions. Subjective cognitive function indicated a medium effect size (g = 0.68), suggesting that nonpharmacological interventions were effective in improving



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subjective cognitive function among patients with breast cancer. Subjective cognitive function was significantly affected by emotional conditions. As a result, the incidence may be high due to physical and emotional symptoms, such as depression, anxiety, and fatigue. This is distinct from the results of neuropsychological tests.[60] However, recent studies suggested that subjective cognitive decline and brain function imaging are closely related[61] and that subjective cognitive decline has a greater adverse effect on the quality of life compared to objective neuropsychological investigations.[7] Therefore, a strategy is required to improve the subjective cognitive function and quality of life of people living with breast cancer by offering them nonpharmacological interventions.

The effect size of nonpharmacological interventions for each area of objective cognitive function was from large to small effect size in attention ($g = 0.83$), processing speed ($g = 0.44$), executive function ($g = 0.25$), and immediate recall of verbal memory ($g = 0.33$). Breast cancer survivors commonly report deficits in attention span and memory functions before, during, and after treatments, which reduce confidence and performance at all occupation levels.[6,7] In this study, we analyzed selective attention tests and found a large and significant effect size. Selective attention is the process of focusing on a specific object in the environment for a specific amount of time, which helps us to ignore unimportant details and focus on what is important.[45] Because breast cancer survivors simultaneously experience various visual and auditory stimuli in daily life, it is necessary to provide selective attention as a basic strategy for nonpharmacological interventions to help with these daily life adjustments.

Verbal memory is an important part of the cognitive domain that is responsible for functions such as encoding and storing information, as well as immediate recall that is related to short-term memory. Breast cancer survivors need to understand the information relevant to breast cancer-related treatment and maintain treatment adherence to prevent reoccurrence. To this end, high cognitive functions such as executive function and immediate recall are required.[7] In this meta-analysis, we analyzed the effect sizes of immediate recall and delayed recall of verbal memory, obtaining a moderately significant effect size for immediate recall but not for delayed recall. Based on the results of this study, it will be possible to contribute to memory improvement by actively providing cost-effective and safe nonpharmacological interventions to patients with breast cancer complaining about short-term memory impairment. In this meta-analysis, we analyzed the effect sizes of processing speed and executive function, obtaining a moderate and small significant effect size. Processing speed plays a central role in cognition and can be important for efficiently performing daily life activities after cancer treatment, especially those related to learning and memory, such as driving and returning to daily life.[19,31] Therefore, improved processing speed could lead to improvements in other cognition aspects.[17] Executive function is a pivotal cognitive area that influences thinking ability, time management, and decision-making.[62] It is also a very common cause of cognitive decline in patients with breast cancer who have undergone cancer treatment.[7] Therefore, executive function after treatment needs to be increased by planning and providing nonpharmacological interventions in advance for cancer survivors scheduled for treatment.

Moderator analysis

In the moderator analysis, there was a significant difference in subjective cognitive function according to the intervention type ($P < 0.001$) and the mode of delivery ($P = 0.037$). In other words, for subjective cognitive function, CBT was found to be more effective than cognitive rehabilitation, and offline education was more effective than online education. Compared with cognitive rehabilitation, which focuses on repetitive training of tasks or skills to improve cognitive function,[16] the goal of CBT is to help individuals understand how their thoughts impact actions and to reframe their perspective and view life's challenges in a new way.[36] Therefore, CBT would have indicated a positive effect on the improvement of subjective cognitive function measured by a self-report questionnaire. However, the moderate to high heterogeneity and limited number of CBT or online education studies make it difficult to draw definitive conclusions about the results of subgroup analyses of intervention types. Therefore, it is necessary to identify effective types and methods of intervention through continuous intervention studies on CRCI.

In addition, there was a significant difference in processing speed according to the intervention type ($P = 0.007$), indicating that physical activity had a more significant effect than cognitive rehabilitation. The relationship between physical activity and cognitive function, including processing speed, has been reported,[19,27,40] and efforts are being made to reveal the mechanism.[12] For example, physical activity is thought to contribute to improved cognitive function by increasing cerebral blood flow and oxygen transport to the brain.[12] However, given the small number of studies included, the generalizability of the findings is limited. Further research investigating the effect of nonpharmacological interventions on improving processing speed is needed.

Publication bias

The study findings revealed a risk of publication bias for the effects of nonpharmacological interventions on objective cognitive functions such as memory delay, executive function, processing speed, and verbal fluency. Therefore, the estimated effect of nonpharmacological intervention in this study and the actual training effect in the corresponding cognitive domain may be different. In particular, summary effect sizes may be overestimated

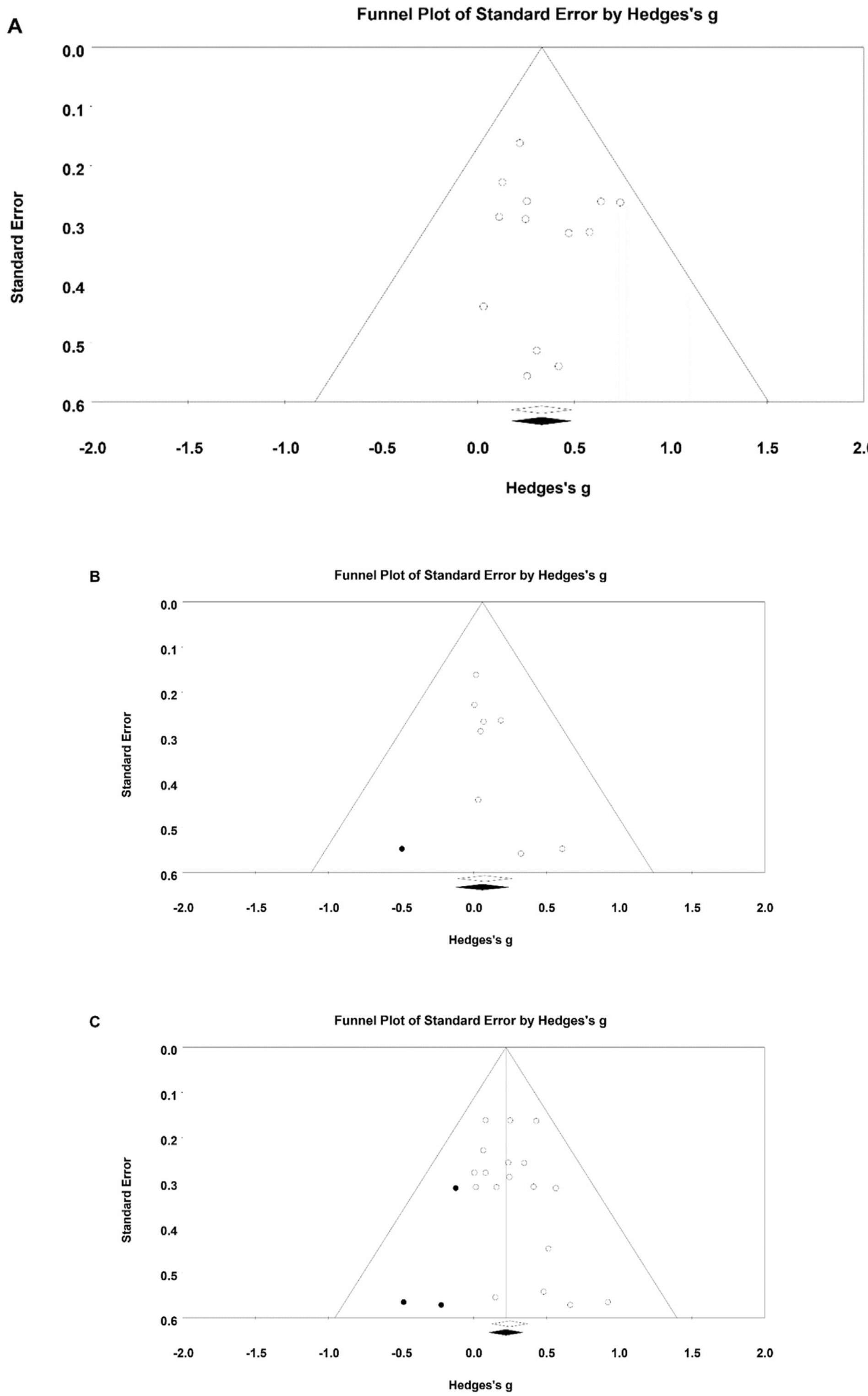

Fig. 4. Funnel plots with effect size on the X-axis and standard error of the effect size on the Y-axis for the estimated summary effects of (A) verbal memory-immediate recall, (B) verbal memory-delayed recall, (C) Executive executive function, (D) processing speed, (E) language fluency, (F) subjective cognitive function.

because small sample studies were included in the analyses. The results must, therefore, be interpreted with caution.

Limitations

Despite the significance of this study, the following limitations should be noted. First, even though there were no limitations on the publication search, only papers published in English were included in this study, thus narrowing the number of studies in the meta-analysis. Second, since this study conducted a systematic review based on studies collected using search engines, there is a possible bias related to the exclusion of unpublished studies. Third, as moderator analysis was used to determine the cause of heterogeneity by cognitive function area, there may be a limitation in terms of insufficient inclusion criteria.[53,63] Finally, five

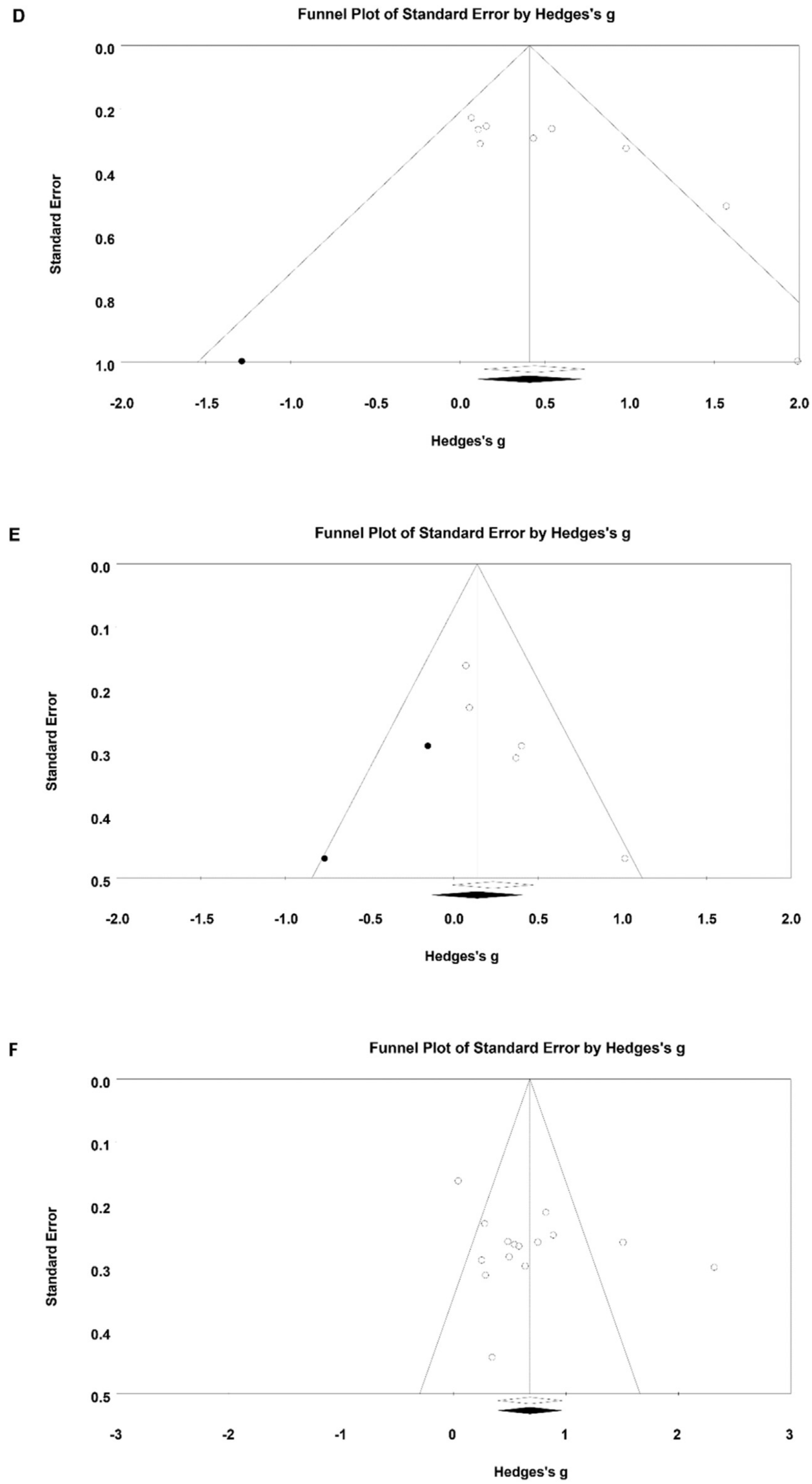

Fig. 4. (*continued*).

papers were excluded from the meta-analysis because they reported insufficient statistics to calculate the effect size or did not report statistics. Therefore, caution is required when interpreting the results of this study.

Clinical implications

This study is significant in that it confirmed the effect of nonpharmacological interventions on CRCI that may occur in patients with breast cancer undergoing systematic treatment. In this study, only RCTs on patients with breast cancer were included, avoiding the effects of bias or population discrepancies in non-RCTs. Nonpharmacological interventions showed moderate improvement in cognitive function, although there were slight differences by cognitive domain. In particular, the results of the sensitivity analysis remained robust. These findings provide a rationale for healthcare providers to offer nonpharmacological interventions to help patients with breast cancer adjust and return to their daily lives after the treatment ends.

Table 3
Results of moderator analyses.

Outcomes	Moderators	Level	*n*	Sub-analysis			Between-group homogeneity		
				Hedges' *g*	95% confidence intervals	I^2	Q-value	df (Q)	*P*
Subjective cognitive function									
	Intervention type	CR	5	0.32	0.11, 0.52	31	21.91	3	< 0.001
		CBT	6	0.98	0.77, 1.18	86			
		PA	3	0.66	0.32, 1.00	0			
		Acupuncture	1	0.28	−0.17, 0.73	0			
	Mode of delivery	Online	4	0.44	0.23, 0.65	73	4.36	1	0.037
		Offline	11	0.73	0.56, 0.89	80			
	Intervention setting	Individual	9	0.60	0.47, 0.80	87	0.05	1	0.816
		Group	6	0.60	0.40, 0.81	0			
	Intervention length	< 8 weeks	7	0.56	0.38, 0.73	79	1.29	1	0.257
		≥ 8 weeks	8	0.71	0.51, 0.90	81			
Objective cognitive function									
Verbal memory – immediate recall	Intervention type	CR	7	0.40	0.22, 0.59	0	2.09	3	0.553
		CBT	1	0.11	−0.45, 0.68	0			
		PA	4	0.23	−0.27, 0.73	0			
		Acupuncture	1	0.13	−0.32, 0.58	0			
	Mode of delivery	Online	4	0.36	0.13, 0.58	0	0.09	1	0.769
		Offline	9	0.31	0.10, 0.52	0			
	Intervention setting	Individual	8	0.31	0.13, 0.50	87	0.15	1	0.703
		Group	5	0.38	0.10, 0.66	0			
	Intervention length	< 8 weeks	5	0.36	0.16, 0.56	18	0.15	1	0.699
		≥ 8 weeks	8	0.30	0.06, 0.54	0			
Verbal memory – delayed recall	Intervention type	CR	3	0.07	−0.17, 0.31	0	0.58	3	0.901
		CBT	1	0.05	−0.51, 0.61	0			
		PA	3	0.28	−0.30, 0.85	0			
		Acupuncture	1	0.01	−0.44, 0.46	0			
	Mode of delivery	Online	1	0.02	−0.30, 0.34	0	0.20	1	0.659
		Offline	7	0.11	−0.13, 0.34	0			
	Intervention setting	Individual	3	0.02	−0.23, 0.26	0	0.53	1	0.469
		Group	5	0.16	−0.13, 0.44	0			
	Intervention length	< 8 weeks	4	0.06	−0.16, 0.28	18	0.05	1	0.827
		≥ 8 weeks	4	0.11	−0.24, 0.46	0			
Executive function	Intervention type	CR	9	0.27	0.12, 0.41	0	0.69	3	0.875
		CBT	1	0.25	−0.32, 0.81	0			
		PA	7	0.24	−0.05, 0.54	0			
		Acupuncture	1	0.07	−0.38, 0.52	0			
	Mode of delivery	Online	7	0.29	0.14, 0.44	0	0.79	1	0.373
		Offline	11	0.18	−0.02, 0.38	0			
	Intervention setting	Individual	13	0.23	0.11, 0.36	0	0.65	1	0.420
		Group	5	0.40	0.01, 0.80	0			
	Intervention length	< 8 weeks	6	0.26	0.10, 0.42	0	0.06	1	0.806
		≥ 8 weeks	12	0.23	0.04, 0.42	0			
Processing speed	Intervention type	CR	6	0.36	0.14, 0.59	21	9.87	2	0.007
		PA	2	1.66	0.77, 2.55	0			
		Acupuncture	1	0.07	−0.38, 0.52	0			
	Mode of delivery	Online	3	0.46	0.13, 0.78	50	0.46	1	0.498
		Offline	6	0.32	0.07, 0.57	58			
	Intervention setting	Individual	7	0.39	0.15, 0.62	60	0.07	1	0.792
		Group	2	0.33	−0.04, 0.69	26			
	Intervention length	< 8 weeks	3	0.27	−0.03, 0.56	0	0.82	1	0.367
		≥ 8 weeks	6	0.45	0.19, 0.71	64			
Language fluency	Intervention type	CR	2	0.14	−0.14, 0.42	1	3.91	3	0.271
		CBT	2	0.40	−0.17, 0.97	0			
		PA	1	1.02	0.10, 1.94	0			
		Acupuncture	1	0.09	−0.36, 0.54	0			
	Mode of delivery	Online	2	0.14	−0.14, 0.42	0	0.65	1	0.420
		Offline	3	0.32	−0.17, 0.97	39			
	Intervention setting	Individual	4	0.18	−0.05, 0.41	27	0.50	1	0.478
		Group	1	0.40	−0.17, 0.97	0			
	Intervention length	< 8 weeks	2	0.15	−0.13, 0.43	0	0.46	1	0.499
		≥ 8 weeks	3	0.30	−0.03, 0.64	37			

CBT, cognitive behavioral training; CR, cognitive rehabilitation; PA, physical activity.

In addition, it was found that specific nonpharmacological interventions such as CBT or physical activity had a beneficial effect compared to cognitive rehabilitation in the case of processing speed or subjective cognitive function. This suggests that it is possible to plan and deliver tailored nonpharmacological interventions for patients with breast cancer that focus on improving specific cognitive functions.

Nurses should be aware that CRCI is a common side effect experienced by individuals following breast cancer diagnosis and treatment.[4,5] Therefore, nurses should be able to integrate a strategy for selecting and managing CRCI to improve patient compliance from the time of cancer diagnosis and promote self-management after the end of treatment.

Conclusions

Based on the study results, nonpharmacological interventions can improve subjective and objective cognitive functioning among patients with breast cancer undergoing cancer treatment. Therefore, it is necessary to provide nonpharmacological interventions by screening patients at high risk of CRCI. Furthermore, breast cancer, which is the type of cancer with the highest incidence among women, is expected to continue to increase in the future alongside lifestyle changes. Thus, active research on interventions to prevent CRCI and relieve symptoms caused by chemotherapy is required worldwide.

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CRediT author statement

Jin-Hee Park: Conceptualization, design, resources, and acquisition of data, analysis and interpretation of data, writing – review and editing, supervision, funding acquisition. **Su Jin Jung:** Analysis and interpretation of data, writing –original draft preparation. **Lena J. Lee:** Writing – review and editing. **Junghyun Rhu:** Writing –original draft preparation. **Sun Hyoung Bae**: Analysis and interpretation of data, writing –original draft preparation, writing – review and editing. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare no conflict of interest.

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Ethics statement

Not required.

Data availability statement

Data availability is not applicable to this article as no new data were created or analyzed in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apjon.2023.100212.

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