Supportive Care in Cancer (2019) 27:3253–3279
https://doi.org/10.1007/s00520-019-04866-2

REVIEW ARTICLE

Cognitive rehabilitation for cancer-related cognitive dysfunction: a systematic review

Holly A. Fernandes[1] · Nadine M. Richard[2] · Kim Edelstein[2,3]

Received: 23 October 2018 / Revised: 23 April 2019 / Accepted: 9 May 2019 / Published online: 30 May 2019

Abstract

Purpose Individuals with non-central nervous system (CNS) cancers can experience cancer-related cognitive dysfunction (CRCD), negatively impacting daily functioning and quality of life. This systematic review examined cognitive rehabilitation programs aimed at improving cognitive function.

Methods PsychInfo and PubMed were searched in February 2019. Eligible studies evaluated a cognitive rehabilitation program for adults with non-CNS cancers and included at least one objective cognitive measure. Across studies, we assessed methodological quality using relevant criteria based on published intervention-related review guidelines and examined findings from performance-based and self-reported outcome measures.

Results 19 studies met inclusion criteria, totalling 1124 participants altogether. These studies included randomized controlled trials ($n = 12$), partial, quasi or non-randomized controlled trials ($n = 3$) and single-arm pilot studies ($n = 4$). All studies found improvements on at least one cognitive measure (performance-based or self-reported). By cognitive domain, objective improvements in memory were most commonly reported, followed by executive functions and processing speed. In terms of methodological quality, studies generally provided clear descriptions of participants and interventions. However, limitations included lack of standardized terminology for interventions, discrepancies in outcome measures, and incomplete statistical reporting.

Conclusions The available evidence supports clinical implementation of cognitive rehabilitation to improve CRCD, with further work in program development, dissemination, and feasibility recommended. We provide specific recommendations to facilitate future research and integration in this field.

Keywords Neuropsychological intervention · Cognitive training · Chemobrain

Individuals diagnosed with cancer, including cancers outside the brain, can develop cognitive difficulties throughout the course of the disease. Cancer-related cognitive dysfunction (CRCD) can affect cognitive abilities including attention, memory, executive functions, language, visuospatial skills and processing speed [1, 2]. For individuals with primary or metastatic brain tumours, CRCD reflects tumour location and treatment [3, 4]. In non-central nervous system (CNS) cancers, a subset of patients experience cognitive changes primarily associated with chemotherapy [2, 5] and endocrine therapy [6, 7], although fatigue, mood and post-traumatic stress may also contribute [8, 9]. The mechanisms underlying CRCD in these patients is likely multi-factorial, including effects of genetics, changes to the blood–brain barrier, cytokine deregulation and inflammation, DNA damage, hormonal alterations and psychosocial factors [10, 11].

CRCD research initially focused on breast cancer but now includes lung, gastrointestinal, haematological, prostate, testicular and head-and-neck cancers [12–17]. The incidence of CRCD in non-CNS cancers varies. The literature suggests that 15–50% of non-CNS cancer patients

Nadine M. Richard and Kim Edelstein share senior authorship.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00520-019-04866-2) contains supplementary material, which is available to authorized users.

✉ Holly A. Fernandes
hfernan2@yorku.ca

[1] Department of Psychology, Faculty of Health, York University, 4700 Keele St., Toronto, ON M3J 1P3, Canada

[2] Department of Supportive Care, Princess Margaret Cancer Centre, Toronto, ON, Canada

[3] Department of Psychiatry, Faculty of Medicine, University of Toronto, Toronto, ON, Canada

have objective cognitive impairments as measured on standardized neurocognitive performance tests following chemotherapy, although rates of patient-reported cognitive dysfunction are often higher on questionnaires [11, 18]. This discrepancy may be due at least in part to emotional distress, pain, fatigue or other factors that exacerbate cognitive concerns [19]. The course of CRCD varies; some individuals improve, whereas others have shown cognitive difficulties months to decades post-treatment [2, 20]. Persistent CRCD adversely affects daily functioning and quality of life (QOL). Survivors may avoid social situations due to problems with word-finding or following conversations, hindering social interactions and relationships [21]. Occupational functioning may be affected, with some survivors taking extended leaves of absence, retiring early and having increased financial concerns [22]. CRCD also associates with diminished self-confidence and role-fulfilment and greater cognitive effort required to complete daily tasks [23].

Given these far-reaching, potentially long-term adverse effects, CRCD has become an important survivorship issue, yet there are no standard treatments. One possibility is cognitive rehabilitation, broadly categorized into two approaches: computer-based training (CT) and strategy training (ST). CT programs, often referred to as "cognitive (re)training" or "brain training", focus on retraining a cognitive skill through practice, using computerized tasks. ST, also called "cognitive behavioural training" or "cognitive behavioural therapy" (CBT) in this literature, refers to behaviourally oriented programs that include retraining of lost cognitive abilities and compensatory strategies and may also include psychoeducation, stress reduction or peer support. Currently, there are no standardized terms for these different approaches. Importantly, the term "cognitive behaviour(al) therapy (CBT)" is widely used to describe an established form of psychotherapy focused on modifying maladaptive thinking and behaviour patterns to improve psychological functioning [24], which is distinct from rehabilitation of cognitive deficits.

The first pilot cognitive rehabilitation study targeting CRCD [25] showed gains in executive functions, processing speed and memory, stimulating interest in this approach. However, publications remain limited, with variable methods and findings. In this systematic review of cognitive rehabilitation for CRCD, we aim to provide a current, comprehensive integration of available evidence, evaluate methodological quality (risk of bias) and compare consistencies and discrepancies (e.g. study designs and outcomes). We evaluate neuropsychological results by cognitive domain to identify potential targeted benefit(s) of cognitive rehabilitation. Finally, we address limitations in the literature, and provide recommendations for clinical implementation and future research.

Methodology

Search strategy

Articles were searched via PubMed and PsychInfo (final search completed in February 2019). Key search terms used to identify cognitive rehabilitation studies for non-CNS cancer survivors were as follows: cancer AND cognitive training OR cognitive rehabilitation OR neuropsychological intervention OR cognitive-behavioural/behavioural (refer to Supplemental Table 1 for full search strategies).

Study selection

Additional inclusion criteria were as follows: published in an English-language peer-reviewed scientific journal (no abstracts, conference proceedings, editorials) intervention targeting cognitive functioning (i.e. cognitive rehabilitation) for adults with non-CNS cancer (primary brain tumours or brain metastases excluded) and included at least one objective cognitive outcome measure.

Titles and abstracts were screened by the first author (HF), and potentially appropriate articles were screened at full-text level by all authors. Discrepancies or uncertainties about article inclusion were resolved by consensus of the 3 authors.

Data collection and analysis

Data from selected articles were abstracted into three tables: (1) study design, (2) study findings and (3) quality assessment. To systematically review study designs and findings, we (HF, NR, KE) abstracted study data including participant information, intervention content and format, outcome measures, and results in the study design and findings tables. Study authors were contacted for additional information as needed (see Table 2). Studies varied in the p value used for statistical significance. For consistency, we considered findings with $p < 0.05$ as significant and reported effect sizes for those findings when available.

Quality assessment criteria relevant to intervention studies were derived from published sources [44–47] based on applicability to cognitive rehabilitation studies. These criteria included the following: level of evidence, participant eligibility criteria specification, outcome assessor and participant blinding, adequate intervention description, appropriate neuropsychological test use, considering effects of baseline group differences on outcomes, considering missing data, appropriate statistical reporting, considering other factors that may affect cognition and acknowledging study limitations. Criteria that were not relevant to cognitive rehabilitation were excluded (e.g. concealed allocation).

Results

From an initial 1166 articles, removal of duplicates ($n = 181$) and studies not meeting inclusion criteria ($n = 966$) yielded 19 articles (see Fig. 1 for full details on study selection). Most articles were excluded because the term "cognitive-behavioural" referred to psychotherapy CBT (i.e. studies examining psychotherapy for other cancer-related difficulties such as pain, fatigue, and sexual functioning), not a cognitive rehabilitation intervention targeting cognitive dysfunction.

Study design and findings

Study design and intervention description

Study design and findings are summarized in Tables 1 and 2, respectively. Twelve studies were randomized control trials (RCTs) (i.e. class I), one study was a quasi-randomised control trial (i.e. class Ia), two studies were a partially randomized or non-randomised control trial (i.e. class II) and four were single-arm pilot studies (i.e. class III) [45].

The 19 studies evaluated 13 intervention programs. Four studies examined different home-based CT interventions targeting various cognitive domains, in which participants completed 4–5 weekly 20–60 min sessions, with 15–40 h recommended total training time; two also offered telephone and/or email contact.

Five ST interventions were assessed across 10 studies. These programs focused on learning internal and external compensatory strategies to improve daily functioning (e.g. use of calendars and lists, verbal rehearsal, imagery). Some programs also provided psychoeducation about cognition or psychosocial functioning (e.g. managing stress). These interventions were delivered individually or in groups and consisted of 4–12 weekly or biweekly 30–120 min sessions.

PRISMA Flow Diagram

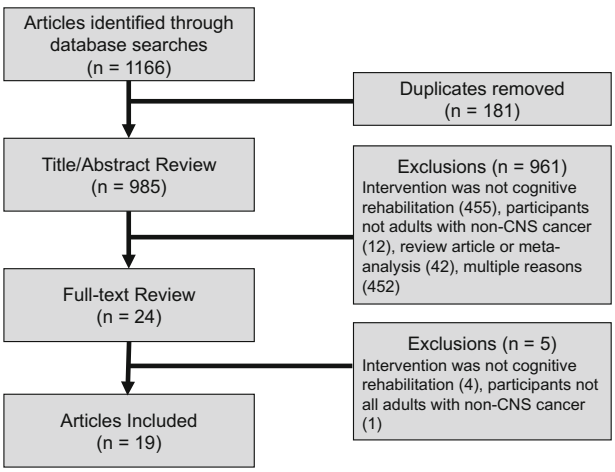

Fig. 1 PRISMA flow diagram

Seven studies primarily had in-person contact, one study examined a video-conference format [28], one study involved a web-based format [39] and one study had an initial in-person session followed by six telephone contacts [31]. Between sessions, 5 studies assigned homework, and 3 studies offered telephone support. One study had booster sessions within 3 months post-intervention.

Five studies examined four different programs that combined ST and CT approaches. Two assessed separate ST and CT interventions against a control group, and three studies combined ST and CT exercises. Program frequency and length were similar to the ST-only interventions described above.

Participants

Participants were fairly homogenous overall; the majority were well-educated, middle-aged (mean age approximately 50–60 years) female breast cancer survivors. Eleven studies (58%) solely recruited females with breast cancer, and it was the most common diagnosis in the remaining studies. Seventeen studies (89%) provided cancer diagnosis and treatment type including chemotherapy, surgery, radiation, endocrine therapy, and/or androgen deprivation therapy. In 18 studies (95%), participants had completed treatment, except for current endocrine therapy in six studies. Thirteen studies (68%) reported the range or mean time since treatment, varying from 2 months to 6 years. One study [31] included participants currently receiving adjuvant chemotherapy. No studies targeted younger adults. Two studies [30, 41] examined an intervention for older adults (age ≥ 65 years).

Outcome assessments

All studies included standardized objective cognitive measures. To facilitate comparisons across studies, we categorized neuropsychological tests into cognitive domains [49]. Most studies assessed memory, attention, executive functions and processing speed; language and visuospatial skills were less commonly evaluated. Five studies (26%) included a measure of "global cognition" through use of a composite score from multiple tests or total score from a screening test (e.g. Mini Mental Status Exam [50], Repeatable Battery of Assessment of Neuropsychological Status [51]). Two studies (11%) included a performance-based measure assessing everyday skills (e.g. managing finances or medication).

All studies included patient-reported measures of cognitive concerns or abilities. Eighteen studies (95%) assessed mood (e.g. depression, anxiety, stress). Eleven studies (58%) assessed health-related QOL (HRQOL), five studies (26%) evaluated fatigue, and one study (5%) assessed patient-reported ability to perform everyday activities.

Four studies (21%) assessed participants at baseline and immediately post-intervention, 12 studies (63%) had three

Table 1 Study design

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
Cherrier et al. [26]	RCT	Waitlist	Overall sample *n* = 28 (93% female) Mean age = 58.9 (2.4) Mean years of education = 17.1 (0.4) Ethnicity NR	Breast Bladder Colon Prostate Uterine (% NR)	Chemotherapy (89.3%) Surgery (78.6%) Radiotherapy (46.4%) Mean years post-chemotherapy = 4.8 (1.0)	ST: - Strategies targeting attention and memory	7 weekly in-person, group sessions (60 min long) plus homework	T1: Baseline T2: Post-intervention	Mixed model repeated measure MANOVA
Ferguson et al. [27]	RCT	Waitlist	Overall sample *n* = 40 (100% female) Mean age = 50.3 (6.4) Mean years of education = 16.4 (2.4) 97.5% Caucasian	Breast (I-II) (100%)	Chemotherapy (100%) Current hormone therapy (57.5%) Mean years post-chemotherapy NR	ST: Memory and Attention Adaptation Training (MAAT) - Psychoeducation - Strategies targeting everyday functioning - Relaxation training	4 bi-weekly in-person, individual sessions (30–50 min long) plus telephone contact	T1: Baseline T2: Post-intervention T3: 2-month follow-up	Repeated measures ANCOVA (full scale IQ and years of education as covariates)
Ferguson et al. [28]	RCT	Active	Overall sample *n* = 35 (100% female) Mean age = 54.6 (12.1) Mean years of education = 15.6 (2.8) 100% Caucasian	Breast (I-IIIA) (100%)	Chemotherapy (100%) Current hormone therapy (~ 75%) Mean years post-chemotherapy = 4.4 (3.9)	ST: MAAT - See Ferguson et al. [27]	8 weekly, videoconference sessions (30–45 min long)	T1: Baseline T2: Post-intervention T3: 2-month follow-up	ANCOVAs (baseline scores as covariates) at POST and 2 months
King, Green [29]	RCT	Waitlist and community sample	Intervention group *n* = 16 (93.8% female) Mean age = 50.4 (8.8) Mean years of education = 15.8 (4.0) Ethnicity NR Cancer control group *n* = 13 (100% female) Mean age = 51.8 (9.4) Mean years of education = 13.8 (3.5) Ethnicity NR Community group *n* = 16 (93.8% female) Mean age = 52.9 (4.3) Mean years of education = 13.9 (3.8) Ethnicity NR	Breast (76%) Hematological (10%) Colorectal (7%) Prostate (3%) Ovarian (3%)	Chemotherapy (89.7%) Surgery (86.2%) Radiotherapy (82.8%) Current hormone therapy (69%) - Other (75.9%) Mean years post-treatment: Intervention = 3.1 (2.1), 6–84 Control = 3.9 (3.8), 6–137	ST: Responding to cognitive concerns (ReCog) [48] - Psychoeducation - Strategies targeting memory and attention - Strategies targeting fatigue, sleep and emotional well-being	4 weekly in-person, group sessions (120 min long) plus homework	T1: Baseline T2: Post-intervention T3: 3-month follow-up (intervention and cancer control groups only)	Mixed factorial ANOVA

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
McDougall et al. [30]	RCT	Active	Overall sample *n* = 22 (59% female) Mean age = 73.9 (4.8) Mean years of education = 16 86% Caucasian	Breast (36%) Prostate (23%) Skin (14%) Uterine (11%) Lymphoma and leukaemia (5%) Throat (5%) Lung (5%)	NR	ST: The Cognitive Behavioural Model of Everyday Memory (CBMEM) - Strategies targeting memory - Health promotion - Addressing fear towards cognitive aging	8 bi-weekly in-person, group sessions (90 min long) and 4 booster sessions (120 min long)	T1: Baseline T2: Post-intervention T3: 2-month follow-up T4: 6-month follow-up T5: 14-month follow-up T6: 26-month follow-up	Mixed factorial ANOVA
Park et al. [31]	RCT	Waitlist	Overall sample *n* = 54 (100% female) Mean age = 44.4 (8.5) Education: ≤ Middle school (16.7%) High School (48.1%) ≥ University (35.2%) Ethnicity NR	Breast (I–II) (100%)	Chemotherapy (current) (100%) Surgery (100%) Radiotherapy (79.6%) Hormone therapy (66.7%) Targeted therapy (11.1%) Mean years post-treatment NR	ST: Promoting Cognitive Health Program (PCHP) - Psychoeducation - Self-awareness training to identify cognitive difficulties - Strategies targeting participants' concerns	1 in-person, individual session (45–60 min long) plus homework and 6 bi-weekly phone contacts	T1: Baseline T2: Post-intervention T3: 6-month follow-up	Repeated measures ANCOVA (age, treatment, WAIS-III vocabulary, and BDI-II score as covariates)
Bray et al. [32]	RCT	Standard medical care	Intervention group *n* = 121 (96% female) Median age = 52, range 23–74 Median yrs. of education = 14, range 8–19 Ethnicity NR Control Group *n* = 121 (94% female) Median age = 54, range 31–74 Median yrs. of education = 12, range 3–19	Breast (89%) Colorectal (5%) Gynecologic (2%) Lymphoma (1%) Thoracic (1%) Other (1%)	Chemotherapy (100%) Radiotherapy (67.5%) Hormone therapy (69.5%) Immunotherapy (22.5%) Mean years post-chemotherapy = 2.3, range 6–60	CT: Insight from Posit Science - Computerized tasks targeting multiple cognitive domains	60 at-home sessions (40 min long for 15 weeks)	T1: Baseline T2: Post-intervention T3: 6-month follow-up	Linear mixed models

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
			Ethnicity NR						
Damholdt et al. [33]	RCT	Waitlist	Intervention group $n = 94$ (100% female) Mean age = 55.0 (8.5) Education: ≤ Middle school (22%) ≥ High school (78%) Ethnicity NR Control group $n = 63$ (100% female) Mean age = 54.6 (8.7), ≤ Middle school (28%) ≥ High school (72%) Ethnicity NR	Breast (100%)	Chemotherapy (82.8%) Surgery (98.7%) Radiotherapy (85.4%) Hormone therapy (69.4%) Mean years post-treatment NR	CT: Happyneuron Pro© - Computerized tasks targeting multiple cognitive domains	30 at-home sessions (30 min/day, 5 days/week, for 6 weeks) plus two telephone contacts	T1: Baseline T2: Post-intervention T3: 5-month follow-up	Linear mixed models
Kesler et al. [34]	RCT	Waitlist	Intervention group $n = 21$ (100% female) Mean age = 55 (7) Mean years of education = 16 (2) Ethnicity NR Control group $n = 20$ (100% female) Mean age = 56 (6) Mean years of education = 16 (3) Ethnicity NR	Breast (I–IIIA) (100%)	Chemotherapy (100%) Surgery (100%) Radiotherapy (67%) Hormone therapy (61%) Mean years post-treatment = 6 (3)	CT: Lumosity - Selected computerized tasks targeting executive functions	48 at-home sessions: (20–30 min long, 4 times/week for 12 weeks) plus telephone or email contact	T1: Baseline T2: Post-intervention	ANCOVA (baseline WCST score, age, education, radiotherapy, hormone therapy, Clinical Assessment of Depression score and time since chemotherapy as covariates)
Wu et al. [35]	RCT	Waitlist	Overall sample $n = 60$ (0% female) Mean age = 66.6 (8.5) Mean years of education = 16.5 (2.8) 91.7% Caucasian	Prostate (100%)	Surgery (48.3%) Radiotherapy (26.6%) Other (11.7%) Androgen deprivation therapy (100%) Mean years post-treatment NR	CT: BrainHQ (PositScience®) - Computerized tasks targeting visual attention and information processing	40 at-home sessions (60 min long for 8 weeks)	T1: Baseline T2: Post-intervention T3: 2-month follow-up	Repeated measure linear mixed models (years of education as covariate)
Ercoli et al. [36]	RCT	Waitlist	Overall sample $n = 48$ (100% female) Mean age = 53.8 (8.2) Education:	Breast (0–III) (100%)	Chemotherapy (77%) Radiotherapy (75%) Current hormone therapy (71%)	ST: - Strategies targeting memory,	5 weekly, in-person, group sessions (120 min	T1: Baseline T2: Post-intervention	Mixed models, controlling for baseline values and

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
			< University (25%) ≥ University (75%) 90% Caucasian		Herceptin (26%) 1.5–5 years post-treatment	attention and execution functions CT: - Non-computerized tasks targeting memory, attention and execution functions	long) plus homework	T3: 2-month follow-up	baseline co-variates (age, employment, BDI-II score, years since diagnosis, current hormone therapy, prior chemotherapy and radiotherapy)
Von Ah et al. [37]	RCT	Waitlist	Overall sample *n* = 82 (100% female) Mean age = 56.5 (8.5) Mean years of education = 15.7 Ethnicity NR	Breast (100%)	Chemotherapy (100%) Surgery (100%) Radiotherapy (74%) Current hormone therapy (46%) Mean yrs. post-treatment = 5.5 (4.2)	ST group: (memory) - Strategies targeting memory adapted from Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) [48] CT group: (processing speed) - Selected computerized tasks from Insight targeting processing speed	10 in-person, group sessions (60 min long) over 6–8 weeks	T1: Baseline T2: Post-intervention T3: 2-month follow-up	General linear mixed models for each intervention group compared to control group, controlling for baseline scores and co-variates (age and education)
Poppelreuter et al. [38]	Quasi-randomized control trial	Standard medical care	Overall sample: *n* = 96 (100% female) Mean age = 49.2 (7.7) Education: Polytechnic/apprenticeship (76.1%) University (16.7%) None/other (7.3%) Ethnicity NR	Breast (I–II) (100%)	Chemotherapy (100%) Radiotherapy (89.6%) Hormone therapy (70.8%) Mean years post-treatment = 0.2 (0.2), 0–1.3	ST group: - Strategies and simulated real-life tasks targeting memory and attention CT group:	4 sessions/week (60 min long) during inpatient stay ST = group sessions CT = individual sessions	T1: Baseline T2: Post-intervention T3: 6-month follow-up	MANOVA

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
						- Computerized tasks from various suppliers targeting memory and attention			
Mihuta et al. [39]	Partially randomized control trial[i]	Waitlist and community sample	Intervention group *n* = 12 (100% female) Mean age = 45.4 (10.3) Mean years of education = 16.1 (3.4) Ethnicity NR Waitlist control community group *n* = 15 (73% female) Mean age = 45.9 (7.4) Mean years of education = 17.2 (2.4) Ethnicity NR Active control community group *n* = 16 (75% female) Mean age = 47.6 (10.0) Mean years of education = 16.1 (3.9) Ethnicity NR	Breast (50%) Bowel (8%) Endometrial (8%) Lymphoma (17%) Pseudomyxoma peritonei Appendix (8%) Squamous cell carcinoma vulva (8%)	Chemotherapy (100%) Surgery (83.3%) Radiotherapy (58.3%) Mean yrs. post-treatment = 4.4 (3.9)	ST: ReCog -See King, Green [29]	4 weekly web-based at-home sessions plus homework	T1: Baseline T2: Post-intervention T3: 3-month follow-up	Mixed factorial ANOVA
Schuurs, Green [40]	Non-randomize control trial	Standard medical care and community sample	Intervention group *n* = 23 (56.5% female) Mean age = 58.2 (11.8) Mean years of education = 15.4 (3.2) Ethnicity NR Control cancer group *n* = 9 (77.8% female) Mean age = 58.3 (8.6) Mean years of education = 13.6 (3.4) Ethnicity NR Community group *n* = 23 (56.5% female) Mean age = 58.5 (11.1)	Breast (50%) Colorectal (22%) Prostate (13%) Mixed (6%) Neck (3%) Ovarian (3%) Testicular (3%)	Chemotherapy (65.6%) Surgery (59.3%) Radiotherapy (59.4%) Other (53.2%) Mean years post-treatment: Intervention = 3.0 (2.7), 0.3–10.3 Control = 4.0 (3.7), 0.9–13.3	ST: ReCog - See King, Green [29]	4 weekly in-person, group sessions (120 min long) plus homework	T1: Baseline T2: Post-intervention T3: 3-month follow-up (intervention group only)	Mixed factorial ANOVA

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
			Mean years of education = 15.7 (3.9) - Ethnicity NR						
Ferguson et al. [25]	Single-arm trial	None	Overall sample *n* = 29 (100% female) Mean age = 56.0 (7.8) Mean years of education = 15.4 (2.3) 100% Caucasian	Breast (I–II) (100%)	Chemotherapy (100%) Mean years post-chemotherapy = 8.2 (4.4)	ST: MAAT - See Ferguson et al. [27]	4 monthly in-person, individual, sessions (30–50 min long) plus homework and 3 telephone contacts	T1: Baseline T2: Post-intervention T3: 2-month follow-up T4: 6-month follow-up	Repeated measures ANOVA
McDougall [41]	Single-arm trial	None	Overall sample *n* = 11 (sex NR) Mean age = 84.8 (6.8) Mean years of education = 15.2 (3.9) Ethnicity NR	NR	NR	ST: CBMEM - See McDougall et al. [30]	8 bi-weekly in-person, group sessions (75 min long)	T1: Baseline T2: Post-intervention	Repeated measures ANOVA
Becker et al. [42]	Single-arm trial	None	Overall sample *n* = 20 (100% female) Mean age = 53.1 (8.2) Mean years of education = 15.4 (1.5) 85% Caucasian	Breast (I–IIIC) (100%)	Chemotherapy (100%) Current hormone therapy (45%) Mean years post-chemotherapy = 1.8 (1.5), 0.2–5.3	ST: - Psychoeducation - Strategies targeting cognitive functioning - Health promotion resources for physical activity, sleep and stress CT: BrainHQ (PositScience®) - Computerized tasks targeting multiple cognitive domains	6 weekly in-person, group sessions (90 min long) plus CT homework (45 min, 3–4 times/week)	T1: Baseline T2: Post-intervention	Paired *t* tests
Ercoli et al. [43]	Single-arm trial	None	Overall sample *n* = 27 (100% female) Mean age = 54.1 (6.3) Mean years of education = 16.4 (1.9) 85% Caucasian	Breast (0–III) (100%)	Chemotherapy (89%) Surgery (100%) Radiotherapy (63%) Hormone therapy (67%) 1.5–5 years post primary treatment	ST and CT - See Ercoli et al. [36]	5 weekly in-person, group sessions 120 min long) plus homework	T1: Baseline T2: Post-intervention T3: 2-month follow-up	Repeated measures ANOVA

Table 1 (continued)

Study	Design	Control group	Participants	Cancer disease site	Cancer treatment	Intervention type and description	Intervention format	Assessments	Statistical procedure for treatment effects
								T4: 4-month follow-up	

NR not reported, *MANOVA* multivariate analysis of variance, *ANCOVA* analysis of covariance, *ANOVA* analysis of variance

assessments (baseline, immediately post-intervention, and 2–6-month follow-up), two studies (11%) had four assessments, and one study (5%) had six assessments (but only analyzed the first four to maximize sample size). Two studies (10%) [26, 42] administered neuropsychological tests twice prior to the intervention, using the second as the baseline score to reportedly control for practice effects, although this approach is not standard. Fourteen studies (74%) did assessments in-person, two studies (11%) used telephone administration [28, 33], and three studies (16%) used an at-home computerized battery [32, 35, 39].

Findings

Of the 15 class I/II studies, 13 (87%) found an intervention effect on at least one objective cognitive measure (i.e. intervention group showed significantly greater improvement(s) than the control group). Memory improvements were most common (9 of 15 studies that assessed memory, 60%). Intervention effects were also reported for executive functions (4/12 studies, 33%), processing speed (5/15 studies, 33%) and "global cognition (2/5 studies, 40%). All class III studies found improvement on at least one objective cognitive measure, including processing speed (2/3 studies, 75%), memory (2/4 studies, 50%) and executive functions (2/4 studies, 50%). Of the 16 studies that included at least three assessments, 10 (63%) reported intervention effects at least 2 months post-intervention. Intervention effect sizes, an established indicator of clinical significance [52], ranged from small (e.g. Cohen s $d \leq 0.2$) to large ($d \geq 0.8$) [53]; when available, specific effect sizes by domain are provided in Table 2.

In addition to comparing mean changes in test performance between intervention and control groups, some authors used reliable change index (RCI) methods [29, 37, 38, 40, 43] and found reliable improvements in a greater percentage of intervention than control participants across cognitive domains including processing speed, memory, visuospatial skills and "global cognition". Another study [38] reported percentage of participants with impaired test scores (≤ 1.5 SD below normal means) and found fewer intervention participants were impaired at 6-month follow-up compared to baseline, although some continued to exhibit cognitive deficits.

For self-reported cognitive function, 10/15 class I/II studies (67%) found greater benefits for the intervention compared to control group. Three studies reported improved subjective cognition across all participants. All class III studies found patient-reported improvements.

Of the eleven studies (58%) that specified one or more objective or self-report measures as primary outcomes (Table 2), 78% reported an intervention effect on one or more of these measures.

Eighteen studies evaluated mood. Two class I/II studies (13%) found improvements, but in many studies, participants had few symptoms at baseline (i.e. minimal room for

Table 2 Study findings

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
Cherrier et al. [26]	- RAVLT - Digit Span - FACT-Cog QOL	Memory: - RAVLT Total Recall and Delayed Recall (raw) Attention: - WAIS-III Digit Span Forward (raw) Executive function (inhibition): - Stroop Interference (raw) Executive function (working memory): - WAIS-III Digit Span Total and Backward (raw) Processing speed: - WAIS-III Digit Symbol Coding (raw)	Intervention effects Improved: - Executive function (working memory; Digit Span Total and Backwards) at POST	Cognitive function: - FACT-Cog (PCA, PCI, QOL) Mood: - Beck Anxiety Inventory - Patient Health Questionnaire-9 Fatigue: - FACIT-F	Intervention effects Improved: - Reported cognitive function (FACT-Cog PCA, PCI, QOL) at POST
Ferguson et al. [27]	- CVLT-II Total Recall - MASQ - QOL-CS	Memory: - CVLT-II Total Recall (SS) Executive function (cognitive flexibility): - D-KEFS TMT Number-Letter (NS) Executive function (inhibition): - DKEFS Colour-Word-Interference Test Colour Word and Colour Word Switching (NS) Processing speed - WAIS-III Digit Symbol-Coding (NS)	Intervention effects Improved: - Memory (CVLT-II Total Recall) at POST ($d_w = 0.4$, $d_c = 0.5$) and 2 months ($d_w = 0.1$, $d_c = 0.6$)	Cognitive function: - MASQ (all subscales) Mood: - CES-D - STAI HRQOL: - QOL-CS (all subscales)	Intervention effects Improved (intervention group): - HRQOL (QOL-CS spiritual well-being) at POST ($d_w = 0.4$, $d_c = 0.5$) and 2 months ($d_w = 0.1$, $d_c = 0.3$) Time effects Improved (both groups): - Reported cognitive function (MASQ total) at POST and 2 months
Ferguson et al. [28]	- FACT-Cog PCA, PCI	Memory: - CVLT-II Total Recall (telephone administration) (NS) Processing speed: - Symbol Digit Modalities (telephone administration) (NS)	Intervention effects: Improved: - Processing speed (Symbol Digit Modalities) at POST ($d_c = 0.5$)	Cognitive function: - FACT-Cog (PCA, PCI) - MIA-A Mood: - Depression Anxiety Stress Scales-21 HRQOL: - FACT-G Fatigue - FACIT-F	Intervention effects Improved: - Reported cognitive function (FACT-COG PCI) at 2 months ($d_c = 0.5$) - Time effects NR
King, Green [29]	- RBANS (all scores) - TMT A and B - FACT-Cog	Memory: - RBANS Immediate and Delayed Memory (NS)	Intervention vs. cancer control Intervention effects Improved (intervention group):	Cognitive function: - FACT-Cog (all subscales)	Intervention vs. cancer waitlist control Time effectsImproved (both cancer groups):

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
	- BAPM	Attention: - RBANS Attention/concentration (NS) Executive function (cognitive flexibility): - TMT B (NS) Processing speed: - TMT A (NS) Language: - RBANS Language (NS) Visuospatial skills: - RBANS Visuospatial/ constructional (NS) Global cognition: - RBANS Total (NS)	- Processing speed (TMT A) at POST ($d_c = 0.4$) and 3 months ($d_c = 0.6$) Time effects Improved (both cancer groups): - Memory (RBANS Immediate and Delayed Memory) - Attention (RBANS attention/concentration) - Language (RBANS Language) - Visuospatial skills (RBANS Visuospatial/constructional) - General cognition (RBANS Total) Intervention vs. cancer control vs. community sample Group effects Improved (intervention and cancer control): - Visuospatial skills (RBANS Visuospatial/constructional) at POST (cancer groups improved, community sample declined) - Global cognition (RBANS Total) at POST Time effects Improved (all groups): - Processing speed (TMT A) at POST - Language (RBANS Language) at POST	- BAPM Mood: - K10 Health-related QOL: - EORTC-QLQ-C30 (all subscales) - BIPQ (total score) Other: - The Benefit Finding Scale - The Traumatic Brain Injury Self-Efficacy Scale	- Reported cognitive function (FACT-Cog all subscales) - HRQOL (EORTC-QLQ-C30 physical, emotional, cognitive, social, global QOL; BIPQ total) - Cognitive self-efficacy (The Traumatic Brain Injury Self-Efficacy Scale) Intervention vs. cancer waitlist control vs. community sample Intervention effects Improved (intervention group): - Reported cognitive function (FACT-Cog PCI) at POST ($d_c = 0.7$) - HRQOL (EORTC-QLQ-C30 social function) at POST ($d_c = 0.6$) Time effects Improved (all groups): - Reported cognitive function (FACT-Cog Comments from Others) at POST - Mood (K10) at POST - HRQOL (EORTC-QLQ-C30 physical, role, emotional, global QoL, fatigue; BIPQ total) at POST
McDougall et al. [30]	NR	Memory: - RBMT (NS) - HVLT-R (NS) - BVMT-R (NS) Global cognition: - MMSE (NS) Daily functioning: - The Direct Assessment of Functional Status (NS)	No intervention or time effects	Cognitive function: - MIA (all subscales) - MSEQ Mood: - STAI - CES-D	Intervention effects Improved: - Reported cognitive function (MIA capacity, change, locus and complaints subscales) Time effects Improved (both groups): - Reported cognitive function (MSEQ)
Park et al. [31]	NR	Memory: - SVLT Immediate Recall, Delayed Recall, Recognition (SS) Attention: - Digit Span Forward (SS) Executive Function (cognitive flexibility): - TMT B (SS) Executive function (working memory): - Digit Span Total and Backward (SS)	Intervention effects Improved: - Memory (composite score; SVLT Immediate and Delayed Recall) at POST ($d_c = 0.6$–0.8) and 6 months ($d_c = 0.6$–0.9) - Executive function (composite score; Verbal Fluency, K-COWAT category and letter; Working Memory, Digit Span Total) at POST ($d_c = 0.4$–0.8) - Global cognition (composite score) at POST ($d_c = 0.7$)	Cognitive function: - FACT-Cog (all subscales) Mood: - BDI-II	Intervention effects: - Reported cognitive function (FACT-Cog PCI) at 6 months: control group declined ($d_c = 0.7$); intervention group was stable

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		Executive function (verbal fluency): - Korean COWAT Category and Letter (SS) Processing speed: - TMT A (SS) Language - Korean WAIS Vocabulary (SS)			
Bray et al. [32]	- FACT-Cog PCI	Memory: - Cogstate Paired Associates Total Errors (NS) - Cogstate One Card Learning Arcsine Proportion Correct (NS) Attention: - Cogstate Identification Speed (NS) Executive function (working memory): - Cogstate One Back and Two Back Task Speed (NS) Executive function (problem solving): - Cogstate Groton Maze Learning Total Errors (NS) Processing speed: - Cogstate Detection task speed (NS) Global cognition: - Cogstate Total (NS)	No intervention effects; time effects NR	Cognitive function: - FACT-Cog (all subscales) Mood: - GHQ - PSS HRQOL: - FACT-G Fatigue: - FACT-Fatigue	Intervention effects Improved: - Reported cognitive function (FACT-Cog all subscales) at POST ($d_c = \sim 0.1$–0.3) and 6 months (FACT-Cog PCI, PCA) ($d_c = \sim 0.3$) - Mood (GHQ, PSS) at POST ($d_c = \sim 0.2$) and 6 months (PSS) ($d_c = \sim 0.2$) - HRQOL (FACT-G) at 6 months ($d_c = \sim 0.2$)
Damholdt et al. [33]	- PASAT	Memory: - RAVLT total recall (SS) Attention: - WAIS-IV Digit Span Forward Maximum Span Length (SS) Executive function (working memory): - PASAT (SS) - WAIS-IV Digit Span Backward and Ordering Maximum Span Length (SS) Executive function (problem solving):	Intervention effects Improved: - Memory (RAVLT Total Recall) at 5 months ($d_c = 0.2$)[iii] - Executive function (working memory; Digit Span Backwards) and POST and 5 months ($d_c = 0.2$)	Cognitive function: - Cognitive Failures Questionnaire Mood: - BDI-II - Anxiety subscale from the Symptoms Checklist-92 - Whitely-7	No intervention effects; time effects NR

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		- D-KEFS 20 Questions Test (SS) - Cognitive Estimation Task (SS) Executive function (verbal fluency): - Letter Fluency (SS)			
Kesler et al. [34]	- WCST	Memory: - HVLT-R (NS) Attention: - WAIS-IV Digit Span (NS) Executive function (cognitive flexibility): - WCST Total Errors (SS)[iv] Executive function (verbal fluency): - D-KEFS Letter Fluency (NS) Processing speed: - WAIS-IV Symbol Search (NS)	Intervention effects Improved: - Executive function (cognitive flexibility, WCST Total Errors; verbal fluency, Letter Fluency) at POST ($d_w = 0.6–0.9$) ($d_c = 0.7–1.0$) - Processing speed (Symbol Search) at POST ($d_w = 0.9$) ($d_c = 1.0$)	Cognitive function: - BRIEF (all subscales) Mood: - Clinical Assessment of Depression	Intervention effects Improved: - Reported cognitive function (BRIEF Planning/organization and Task Monitoring) at POST ($d_w = 0.4$) ($d_c = 0.2–0.4$)
Wu et al. [35]	- CNS Vital Signs Stroop Test, Symbol Digit Coding Test, Continuous Performance Test, Finger Tapping[v]	Memory - CNS Vital Signs Verbal Memory (NS) - CNS Vital Signs Visual Memory (NS) Attention - CNS Vital Signs Continuous Performance Test (NS) Executive function (cognitive flexibility): - CNS Vital Signs Shifting Attention Test (NS) Processing speed: - CNS Vital Signs Stroop Test (NS) - CNS Vital Signs Symbol Digit Coding Test (NS) Motor - CNS Vital Signs Finger Tapping Test (NS)	Intervention effects[vi] Improved: - Processing speed (CNS Vital Signs Stroop) at POST ($d_w = 0.6$) and 2 months ($d_w = 0.6$) Declined: - Memory (CNS Vital Signs Verbal and Visual Memory) at POST ($d_w = 0.7–0.9$) (intervention group declined, control group improved)	Cognitive function: - Frontal Systems Behaviour Scale - PAOFI Health-related QOL: - Functional Assessment of Cancer Therapy-Prostate	No intervention effects; time effects NR
Ercoli et al. [36]	- PAOFI Total	Memory: - RAVLT Total Recall and Delayed Recall (raw and SS)	Intervention effects Improved: - Memory (RAVLT Total and Delayed Recall) at 2 months ($d_c = 0.3–0.6$) (intervention group improved, control group declined)	Cognitive function: - PAOFI (Total and Memory) Mood: - BDI-II	Intervention effects: Improved: - Perceived cognitive function (PAOFI Total and Memory) at 2 months ($d_w = 0.9–1.1$) Time effects:

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		- BVMT-R Total Recall and Delayed Recall (raw and SS) Executive function (cognitive flexibility): - TMT B (raw and SS) Executive function (working memory): - PASAT Trial 2 Number Incorrect (raw and SS) Executive function (inhibition): - CNS Vital Signs Stroop Complex Reaction Time (raw and SS) Executive function (verbal fluency): - COWAT (raw and SS) Processing speed: - CNS Vital Signs Stroop Simple Reaction Time (raw and SS) - CNS Vital Signs Symbol Digit Coding Correct (raw and SS) - TMT A (raw and SS) Motor: - CNS Vital Signs Finger Tapping Dominant and Non-dominant (raw and SS)			Improved (both groups): - Mood (BDI-II) POST and 2 months
Von Ah et al. [37]	- RAVLT - RBMT Story - Useful Field of View	Memory: - Immediate memory composite score: RAVLT Total Recall, Immediate Recall, Recognition; RBMT Story Immediate Recall (SS) - Delayed memory composite score: RAVLT Delayed Recall; RBMT Story Delayed Recall (SS) Processing speed: - Composite score: Useful Field of View Divided	Intervention effects Improved (ST Memory Group): - Memory (Immediate and Delayed Memory composite scores) at 2 months ($d_c = 0.6–0.7$) Improved (CT Processing Speed Group): - Memory at POST (Immediate Memory composite score) ($d_c = 0.8$) and 2 months (Immediate and Delayed Memory composite score) ($d_c = 0.7–0.8$) - Processing speed (composite score) at POST ($d_c = 0.6$) and 2 months ($d_c = 0.7$)	Cognitive function: - FACT-Cog (total) - SSMQ Mood: - CES-D - STAI-State HRQOL: - QOL-CS - SF-36 Fatigue: - FACT-F	Intervention effects Improved (ST Memory Group): - Reported cognitive function (FACT-Cog Total, SSMQ) at POST ($d_c = 0.6–0.7$) and 2 months ($d_c = 0.7–0.8$) - Mood (STAI-State) at 2 months ($d_c = 0.7$) Improved (CT Processing Speed Group) - Reported cognitive function (FACT-Cog total) at POST ($d_c = 0.6$) - Mood (CES-D) at POST ($d_c = 0.6$) and 2 months (CES-D, STAI-State) ($d_c = 0.8–0.9$) - HRQOL (SF-36) at POST ($d_c = 0.7$) and 2 months ($d_c = 0.6$)

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		Attention and Selective Attention (SS)			- Fatigue (FACT-F) at POST ($d_c = 0.7$) and 2 months ($d_c = 0.78$)
Poppelreuter et al. [38]	NR	Memory: - RBMT Story Immediate Recall and Delayed recall (raw) - Learning and Memory-Test City Plan and Objects (raw and SS) Attention: - WMS-R Digit Span Forward (raw and SS) Sustained attention: - TAP Working Memory and Sustained Attention (raw) Executive function (cognitive flexibility): - TAP Reaction Change (raw and SS) Executive function (working memory): - WMS-R Digit Span Backward (raw and SS) Executive function: (divided/selective attention) - TAP Divided Attention (raw) - TAP Go/NoGo (raw) Processing speed: - TAP Alertness (raw and SS)	Intervention effects Improved (both interventions): - Memory (RBMT Story Immediate and Delayed Recall) at POST Time effects Improved (all groups): - Sustained attention (TAP Working Memory and Sustained attention) at POST - Executive function (divided attention, TAP Divided Attention; cognitive flexibility, TAP Reaction Change) at POST - Processing speed (TAP Alertness) at POST - Additional improvements on 6 of 16 measures (NR) at 6 months	Cognitive function: - Select items from EORTC QLQ-C30 - Select items from Multidimensional Fatigue Inventory - Select items from Questionnaire of Self-Perceived Deficits in Attention Mood: - Hospital Anxiety and Depression Scale	Time effects Improved (all groups): - Reported cognitive function (select items from EORTC QLQ-C30) at POST and 6 months
Mihuta et al. [39]	- Fact-Cog PCI	Memory: - WebNeuro Verbal Memory (SS) Attention: - WebNeuro Attention/concentration (SS) Executive function: - WebNeuro Executive Functioning (SS) - WebNeuro Impulsivity (SS) - WebNeuro Working Memory Capacity (SS) Processing speed: - WebNeuro Information Processing Efficiency (SS)	Intervention effects: Improved (cancer group): - Attention (WebNeuro Attention/concentration) at 3 months ($d_c = 0.8$)[vii] (non-cancer waitlist group also improved; non-cancer intervention group declined) Time effects Improved (all groups): - Executive function (WebNeuro Executive Functioning) at POST and 3 months Declined (all groups): - Memory (WebNeuro Verbal Memory) at 3 months	Cognitive function: - FACT-Cog (OTH, PCA, PCI, QOL) - BAPM (BADL and IADL subscales) - EORTC-QLQ-C30 (memory and concentration items) Health-related QOL: - BIPQ Mood: - K10	Intervention effects Improved (non-cancer intervention group): - Reported cognitive function (BAPM BADL) at POST Time effects Improved (all groups): - Reported cognitive function at POST (Fact-Cog PCI) and 3 months (Fact-Cog PCI, BAPM IADL) at 3 months

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		- WebNeuro Response Speed (SS)			
Schuurs, Green [40]	-NR	Memory: - RBANS Immediate and Delayed Memory (NS) Attention: - RBANS Attention/concentration (NS) Executive function (cognitive flexibility): - TMT B (NS) Processing speed: - TMT A (NS) Language: - RBANS Language (NS) Visuospatial skills: - RBANS Visuospatial/ constructional (NS) Global cognition: - RBANS Total (NS)	Intervention effects Improved: - Memory (RBANS Immediate and Delayed Memory) at POST (d_c = 0.5–1.6) (d_w = 0.6–1.5) and 3 months (d_w = 0.7–1.8)[viii] - Visuospatial skills (RBANS Visuospatial/constructional) at POST (d_c = 0.9–1.2) (d_w = 1.4) and 3 months (d_w = 1.7) - Global cognition (RBANS Total) at POST (d_c = 1.0–1.2) (d_w = 1.4) and 3 months (d_w = 1.4) Time effects Improved (all groups): - Processing speed (TMT A) at POST - Language (RBANS Language) at POST	Cognitive function: - FACT-Cog (all subscales) - MASQ (Total Score) Mood: - K10 HRQOL: - EORTC-QLQ-C30 (all subscales) - BIPQ (all subscales)	Intervention effects Improved: - HRQOL (EORTC-QLQ-C30 social, BIPQ Illness Coherence) at POST (d_c = 0.3–0.6) (d_w = 0.4–0.6) and 3 months) (d_w = 0.3–0.8) Time effects Improved (all groups): - Reported cognitive function (FACT-Cog PCI) at POST - Mood (K10) at POST (only for participants with scores in clinical range at baseline)
Ferguson et al. [25]	NR	Memory: - CVLT-II Total Recall (SS) - WMS-III Logical Memory I and II (raw) Executive function (cognitive flexibility): - TMT B (raw) Executive function (inhibition): - Stroop Colour-Word Interference (raw) Processing Speed: - TMT A (raw) - WAIS-III Digit Symbol-Coding (raw)	Improved: - Memory at POST (WMS III Logical Memory I and II) (d_w = 0.9–1.0), 2 months (WMS III Logical Memory I and II, CVLT-II Total Recall) (d_w = 1.1) and 6 months (WMS III Logical Memory I and II, CVLT-II Total Recall) - Executive function (cognitive flexibility, TMT B) at 6 months (d_w = 0.6) - Executive function (inhibition, Stoop Colour-Word Interference) at POST (d_w = 0.6), 2 months and 6 months - Processing speed (Digit Symbol, TMT A) at 2 months (d_w = 0.9–1.2) and 6 months	Cognitive function: - MASQ (all subscales) HRQOL: - QOL-CS (total score) Mood: - CES-D - STAI	Improved: - Reported cognitive function (MASQ total, attention/ concentration spatial memory, verbal memory, language) at POST (d_w = 0.5–0.7), 2 months and 6 months - HRQOL (QOL-CS total score) at 6 months (d_w = 0.5)
McDougall [41]	NR	Memory: - RBMT Belongings, Immediate and Delayed Story Recall, Immediate and Delayed Route Recall (SS)	Improved: - Memory (RBMT Belongings, Immediate and Delayed Story Recall) at POST Declined: - Memory (RBMT Immediate and Delayed route) at POST	Cognitive function: - MEQ - MIA Mood: - Geriatric Depression Scale HRQOL: - Multilevel Assessment	Improved: - Reported cognitive function (MEQ, MIA) at POST

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
				Instrument (Health subscale) Functional ability: - IADL scale	
Becker et al. [42]	NR	Memory: - CVLT-II (NS) Executive function (verbal fluency): - COWAT (NS) Processing speed: - The Symbol Digit Modalities Test (NS) Daily functioning: - Everyday Problems Test–Revised (NS)	Declined: - Memory (CVLT-II) at POST	Cognitive function: - PROMIS (Cognitive Concerns) - MMQ (Strategy) - Compensatory Cognitive Strategies Scale Mood: - PROMIS (Emotional Distress) HRQOL: - FACT-G Fatigue/sleep: - PROMIS (Fatigue and Sleep Disturbance)	Improved: - Reported cognitive function (PROMIS Cognitive Concerns, MMQ Strategy and Compensatory Cognitive Strategies Scale) at POST - Mood (PROMIS Emotional Distress) at POST - Fatigue/sleep (PROMIS Fatigue, Sleep Disturbance) at POST
Ercoli et al. [43]	NR	Memory: - HVLT-R Total and Delayed Recall (NS) - BVMT-R Total Recall and Learning Slope (NS) Attention: - CNS Vital Signs Continuous Performance Test Correct (NS) Executive function (cognitive flexibility): - CNS Vital Signs Shifting Attention Test Correct (NS) - TMT B (NS) Executive function (working memory): - PASAT Trial 1 Total Errors (NS) Executive function (inhibition): - CNS Vital Signs Stroop Complex Reaction Time and Number Correct (NS)	Improved: - Executive function (inhibition, Stroop Complex Reaction Time) at POST ($d_w = 0.6$) and 4 months ($d_w = 0.7$) - Processing speed (Symbol Digit, Stroop Reaction Time, TMT A) at POST ($d_w = 0.3$–0.5) and 4 months ($d_w = 0.4$–0.6)	Cognitive function: - PAOFI (Total, Memory, Higher-level Cognitive Functions) Mood: - BDI-II - STAI	Improved: - Reported cognitive function at POST (PAOFI Total and Memory) ($d_w = 0.5$) and 4 months (PAOFI Total, Memory, and Higher-level Cognitive Functions) ($d_w = 0.6$–0.8)

Table 2 (continued)

Study	Primary outcome measure(s)	Neuropsychological measures	Neuropsychological results[ii]	Self-report measures	Self-report results[i]
		Executive function (verbal fluency): - Verbal fluencies tests (NS) Processing speed - CNS Vital Signs Stroop Simple Reaction Time (NS) - CNS Vital Signs Symbol Digit Test Correct - TMT A (NS) Visuospatial skills: - Judgment of Line Total Correct (NS) Motor - CNS Vital Signs Finger Tapping Dominant and Non-dominant (NS)			

NR not reported, *NS* type of score not specified, *SS* standardized score, d_w Cohen's d within group effect size, d_c Cohen's d corrected effect size, *POST* immediate post-test, *HRQOL* health-related quality of life, *RAVLT* Rey Auditory Verbal Learning Test, *WAIS* Wechsler Adult Intelligence Scale, *CVLT-II* California Verbal Learning Test—Second Edition, *D-KEFS* Delis–Kaplan Executive Function System, *RBANS* Repeatable Battery for the Assessment of Neuropsychological Status, *TMT* Trial Making Test, *RBMT* Rivermead Everyday Behavioural Memory Test, *HVLT-R* Hopkins Verbal Learning Test—Revised, *BVMT-R* Brief Visuospatial Memory Test-Revised, *MMSE* Mini Mental State Examination, *SVLT* Seoul Verbal Learning Test, *COWAT* Controlled Oral Word Association Test, *PASAT* Paced Auditory Serial Addition Test, *WCST* Wisconsin Card Sorting Test, *WMS* Wechsler Memory Scale, *EORTC QLQ-C30* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire QLQ-C30, *TAP* Test Battery for Attentional Performance, *FACT-Cog* Functional Assessment of Cancer Therapy-Cognitive, *QOL* Quality of Life, *OTH* Comments From Others, *PCA* Perceived Cognitive Abilities, *PCI* Perceived Cognitive Impairments, *BAPM* The Brief Assessment of Prospective Memory, *BADL* Basic Activities of Daily Living, IADL Instrumental Activities of Daily Living, *FACIT-F* Functional Assessment of Chronic Illness Therapy-Fatigue, *MASQ* Multiple Ability Self-Report Questionnaire, *CES-D* Centre for Epidemiological Study—Depression, *BDI-II* Beck Depression Inventory-II, *STAI* Spielberger State-Trait Anxiety Inventory, *QOL-CS* Quality of Life-Cancer Survivors, *MIA-A* Metamemory in Adulthood-Anxiety scale, *FACT-G* Functional Assessment of Cancer Therapy-General, *FACT-F* Functional Assessment of Cancer Therapy-Fatigue, *K10* The Kessler Psychological Distress Scale, *EORTC-QLQ-C30* The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire, *BIPQ* The Brief Illness Perception Questionnaire, *MSEQ* The Memory Self-Efficacy Questionnaire, *GHQ* General Health Questionnaire, *PSS* Perceived Stress Scale, *BRIEF* The Behavioural Rating Inventory of Executive Function, *PAOFI* Patient's Assessment of Own Functioning Inventory, *SSMQ* Squire Subjective Memory Questionnaire, *SF-36* Short-form health survey, *MEQ* Memory Efficacy Questionnaire, *PROMIS* Patient-Reported Outcomes Measurement Information System, *PROMIS* Patient-Reported Outcomes Measurement Information System, *MMQ* Multifactorial Memory Questionnaire

[i] All participants with cancer received the intervention. Healthy control participants from the community were randomized to waitlist and intervention groups.

[ii] Only significant results ($p < .05$) are reported

[iii] Authors contacted for additional information about effect sizes

[iv] Authors contacted for additional information about test score

[v] To allow for consistency of test labeling and interpretation across studies, specific test names were added based on authors' description and published information about CNS Vital Signs battery

[vi] Authors also reported ITT analyses and results were comparable

[vii] Corrected effect size reported for cancer intervention group compared to non-cancer intervention group

[viii] Corrected effect sizes (ranges) reported for cancer intervention group compared to cancer control group and healthy community control

improvement). Five (63%) of the class I/II studies assessing HRQOL found an intervention effect, and 1/4 studies (25%) found intervention-related reductions in fatigue.

Quantitative electroencephalography (qEEG) was used as an exploratory biomarker of intervention effects across pilot [43] and RCT [36] studies of a ST program. Increased resting-state alpha power and/or decreased delta power in rehabilitation participants suggested increased general alertness, with some associations to patient-reported cognitive improvements.

Quality assessment

Quality assessment data are summarized in Table 3. Thirteen studies (68%) were class I or Ia (i.e. RCT), two studies (11%) were class II (partially or non-randomized controlled trial) and four studies (21%) were class III (single-arm study) [45]. Three class III studies [25, 41, 43] were pilot studies, for which RCTs were later completed. The other class III study was recently published, with recommendations for a future RCT [42].

Fourteen class I/II studies (93%) and three class III studies (75%) provided clear participant eligibility criteria, including age, diagnosis and treatment details, and excluded CNS tumours/metastases. The remaining two studies [30, 41] retrospectively examined self-identified cancer survivors, who were a subset of participants from a larger cognitive intervention study; their diagnosis and treatment criteria were unspecified. Seven class I/II studies (47%) reported that outcome assessors were blinded. No study adequately blinded participants to group membership. Thirteen class I/II studies (87%) considered effects of baseline group differences on outcomes, including demographic variables and/or pre-intervention questionnaire or test scores.

Studies provided cognitive rehabilitation using CT, ST or a combination. Seventeen studies (89%) adequately described their interventions by specifying session number, frequency, duration and content, homework and phone call support if included and referencing a manual or computer/online program if available. One class I study comparing ST and CT interventions to a standard-care control [38] did not specify which cognitive training exercises were used in the CT group. One class III ST study [41] described the intervention, but the administration procedures and which participants completed it were unclear.

All studies appropriately used objective cognitive measures based on the criteria that they administered standardized neuropsychological tests and assessed cognitive domains targeted by the intervention. However, for three CT studies [32, 38, 42], the degree of similarity between intervention exercises and cognitive outcome measures was unclear; improvements might reflect increased test-specific skills (i.e. training-to-test), rather than more generalizable improvements [54]. Two CT studies not only acknowledged the training-to-test issue [33, 34] but also included tests of untrained cognitive domains. Nine studies (47%) specified the scores used for each measure (i.e. raw vs. standardized); two studies (11%) provided this information for select scores only.

All 19 studies considered factors that could affect cognition, such as fatigue, mood, and psychiatric or neurological conditions, either through exclusion criteria or use of self-report measures to monitor change. All studies acknowledged limitations, which commonly included small sample size and/or lack of an active control group. Other limitations included homogenous participant samples (e.g. results in breast cancer patients may not generalize to other populations), recruitment biases, participants not blinded to group membership, missing data, participants having no/mild cognitive impairment at baseline and lack of long-term follow-up.

For statistical reporting, 17 studies (89%) reported loss to follow-up information and statistical procedures used to address missing data, including completer analysis/exclusion of dropout participants, linear interpolation, multiple imputation, intention-to-treat, and substitution of person-specific means for missing questionnaire items. We assessed whether studies reported significant and non-significant results, p values, means and standard deviations for significant findings, effect sizes and considered the issue of multiple comparisons. Four studies (21%) met all criteria. Ten studies (53%) did not provide complete statistics (e.g. p values, means, standard deviations). Ten studies (52%) addressed the issue of multiple comparisons using adjusted alpha level and/or post-hoc tests [25, 29, 31, 32, 34, 38, 40], multivariate analyses [26], composite scores [37] or justification of no adjustment [42]. Fifteen studies (79%) reported effect sizes; 14 used Cohen's d within-group (i.e. comparing pre-to-post change independently in each group) and/or corrected (i.e. effect size for intervention group controlling for effect size in control group) [55], and one study reported partial eta-squared [30].

Discussion

This systematic review identified 19 cognitive rehabilitation studies for CRCD in individuals with non-CNS cancers. Overall, there is evidence for improvement in objective and patient-reported outcomes. Below we summarize the quality of evidence, consistencies and discrepancies across studies for outcome measures and terminology and make recommendations for future research and clinical implementation.

Improvements following cognitive rehabilitation

Most studies reported improvements on both performance and self-reported cognitive measures after rehabilitation; all studies found improvement on at least one measure. For

performance measures, improved memory was most common. Executive functions, processing speed and visuospatial skills also improved in some studies. Where assessed, performance in real-life tasks did not change [30, 42].

Patients reported fewer cognitive complaints or improved cognitive abilities after rehabilitation in most studies. In many of the remaining studies without intervention-specific effects, all participants reported improvements, suggesting time or other non-specific effects. There was some evidence for improved HRQOL but limited support for improved functioning in other self-reported domains (e.g. mood, fatigue) that were typically included as control variables (i.e. not targets of the interventions).

Taken together, these findings indicate that cognitive rehabilitation programs can positively affect objective and subjective cognitive functioning, although generalization to daily life and other aspects of functioning are understudied.

Quality of evidence

Despite the challenges of conducting this type of research, most studies met criteria for high quality cognitive rehabilitation research [44, 45, 47], including design (i.e. RCTs), methods, data analyses and reporting. However, incomplete results (e.g. not reporting full statistics, not addressing multiple comparisons) were a common limitation.

Selection and reporting of outcome measures

There was variability across studies in choice of objective cognitive tests, reported scores and interpretation. Noting discrepancies in test categorization between studies, we applied a uniform domain categorization to facilitate comparisons. Memory, processing speed, attention and executive functions were generally assessed through domain-specific tests or subscores on a larger screening battery. Only 47% of studies indicated whether raw or standardized scores were used in analyses; this information is necessary for clinical interpretation and between-study comparisons.

There was also variability in selection of patient-reported measures. Some cognitive questionnaires assessed broader cognitive functioning, others specific domains (e.g. memory, executive functions). HRQOL was examined in 57% of studies, most frequently with screening measures commonly used in oncology [56, 57]. These measures assess multiple aspects of QOL but are less reflective of important factors such as participation in valued activities [58], spiritual well-being or social functioning [27, 40] or other determinants of well-being, such as positive affect [29]. Only one study included a self-report measure of everyday functioning [41]. Inclusion of such measures to assess well-being and daily functioning is important and often missing in cancer research [59].

In terms of data analyses and statistical reporting, various approaches to analyzing group-mean differences (e.g. MANOVAs, ANCOVAs, linear mixed models) and varying significance thresholds (e.g. adjusting p values for multiple comparisons) were used, rendering between-study comparisons more challenging. Participant-level analyses were used in 32% of studies, either through RCIs or percent of participants with impaired scores; these additional analyses provide useful information about meaningful change or base rates of impairment, respectively.

Seventy-nine percent of studies reported effect sizes, most commonly Cohen's d, calculated as a within-group (e.g. pre-to-post) or corrected effect size; the latter quantifies the intervention effect controlling for repeat-testing effects [55]. Three studies [27, 34, 40] reported both types as absolute and relative measures of the intervention effect, facilitating comparisons across studies. Effect sizes are also meaningful in the absence of statistically significant results. For example, the moderate effect sizes reported by McDougall et al. [30] and Mihuta et al. [39] support further investigation of the interventions with larger sample sizes enabling adequate statistical power.

Cognitive rehabilitation terminology

We categorized cognitive rehabilitation programs using a common distinction between computer-training (CT) and strategy-training (ST). However, terminology in this literature is inconsistent. One source of confusion arises from referring to ST programs as CBT, the well-established psychotherapy technique. Cognitive rehabilitation programs vary greatly from CBT psychotherapy. The former aims to restore or improve cognitive abilities, the latter focuses on altering dysfunctional beliefs and behaviours to enhance psychological functioning [24].

Many studies examine psychotherapy CBT in cancer populations, but few include cognitive outcomes. For instance, one study [60] hypothesized that psychotherapy CBT would reduce post-cancer fatigue, thereby improving self-reported cognitive functioning. Although CBT psychotherapy positively affects various outcomes in cancer patients including cognition, it differs from cognitive rehabilitation. Some ST cognitive rehabilitation programs include components often used in psychotherapy CBT (e.g. relaxation training) [61], but the overall content and aims of psychotherapy CBT and cognitive rehabilitation are distinct.

Recommendations for future research

Neuropsychological tests

As many tests measure multiple abilities [49], we recommend that researchers consider which cognitive domains to assess,

Table 3 Quality assessment

Study	Level of evidence	Eligibility criteria specified	Outcome assessor blinded	Participants blinded	Adequate intervention and control descriptions	Considered group differences at baseline	Appropriate use of neuropsychological tests	Discussion of missing data and statistical procedure	Missing statistical information	Considered factors that may affect cognition	Considered limitations of study
Cherrier et al. [26]	I	Yes	No	Yes	Yes	Yes	Yes	Yes: completer analyses	Exact *p* values Effect sizes	Yes	Yes
Ferguson et al. [27]	I	Yes	Yes	No	Yes	Yes	Yes	Yes: linear interpolation	Consideration of multiple comparisons	Yes	Yes
Ferguson et al. [28]	I	Yes	Yes	NR	Yes	Yes	Yes	Partial: completer analyses, but NR for missing self-report items	Consideration of multiple comparisons	Yes	Yes
King, Green [29]	I	Yes	Yes	NR	Yes	Yes	Yes	Yes: completer analyses and ITT	None	Yes	Yes
McDougall et al. [30]	I	Partial	NR	NR	Yes	No	Yes	No	Exact *p* values Consideration of multiple comparisons	Yes	Yes
Park et al. [31]	I	Yes	Yes	NR	Yes	Yes	Yes	Yes: completer analyses	None	Yes	Yes
Bray et al. [32]	I	Yes	NR	NR	Yes	Yes	Yes	Yes: multiple imputation	None	Yes	Yes
Damholdt et al. [33]	I	Yes	NR	NR	Yes	Yes	Yes	Yes: ITT	Consideration of multiple comparisons	Yes	Yes
Kesler et al. [34]	I	Yes	Yes	NR	Yes	Yes	Yes	Yes: completer analyses	None	Yes	Yes
Wu et al. [35]	I	Yes	No	No	Yes	Yes	Yes	Yes: completer analyses and ITT	Consideration of multiple comparisons	Yes	Yes
Ercoli et al. [36]	I	Yes	Yes	NR	Yes	Yes	Yes	Yes: ITT	Exact Ms and SDs, *p* values (some measures) Consideration of multiple comparisons	Yes	Yes
Von Ah et al. [37]	I	Yes	Yes	No	Yes	Yes	Yes	Yes: person-specific means substituted for missing items	Ms and SDs (follow-up scores)	Yes	Yes
Poppelreuter et al. [38]	Ia	Yes	NR	NR	Partial	No	Yes	Yes: completer analyses	Exact Ms and SDs, *p* values (some measures)	Yes	Yes

Table 3 (continued)

Study	Level of evidence	Eligibility criteria specified	Outcome assessor blinded	Participants blinded	Adequate intervention and control descriptions	Considered group differences at baseline	Appropriate use of neuropsychological tests	Discussion of missing data and statistical procedure	Missing statistical information	Considered factors that may affect cognition	Considered limitations of study
									Effect sizes		
Mihuta et al. [39]	II	Yes	No	No	Yes	Yes	Yes	Yes: ITT	Consideration of multiple comparisons	Yes	Yes
Schuurs, Green [40]	II	Yes	NR	NR	Yes	Yes	Yes	Yes: completer analyses and ITT	Exact *p* values	Yes	Yes
Ferguson et al. [25]	III	Yes	NA	NA	Yes	NA	Yes	Yes: completer analyses	Exact *p* values	Yes	Yes
McDougall [41]	III	Partial	NA	NA	Partial	NA	Yes	No	Effect sizes Consideration of multiple comparisons	Yes	Yes
Becker et al. [42]	III	Yes	NA	NA	Yes	NA	Yes	Yes: completer analyses and person-specific means substituted for missing self-report items	Exact *p* values Effect sizes	Yes	Yes
Ercoli et al. [43]	III	Yes	NA	NA	Yes	NA	Yes	Yes: completer analyses	Exact Ms and SDs, *p* values (some measures) Consideration of multiple comparisons	Yes	Yes

NA not applicable, *NR* not reported, *ITT* intention-to-treat, *Ms* means, *SDs* standard deviations

based on hypotheses around intervention targets and generalization to untrained domains. Outcome measures should differ from intervention tasks, especially for CT programs wherein training-to-test can be problematic [54]. While encouraging researchers to select sensitive measures appropriate to assessing their intervention effects, batteries should include the standardized neuropsychological tests recommended by the International Cognition and Cancer Task Force [62] to facilitate comparisons across studies.

Self-report measures

Intervention outcome assessments should include patient-reported outcomes that may capture concerns not apparent in objective tests and may be more closely related to everyday functioning and QOL [63, 64].

In addition to HRQOL screening, other determinants of well-being, such as positive emotions (i.e. not just negative affect), should be assessed. Improvements in real-life functioning should also be assessed using standardized questionnaires [65] or procedures for identifying and working toward individually tailored goals [66].

Statistical analyses and reporting

Comprehensive descriptions of statistical analyses (e.g. distinguishing between intervention effects where the intervention group improves more than a control group, and time effects where all participants improve) and full data reporting (i.e. at minimum, group means and standard deviations for each measure, but ideally also effect sizes and patient-level indices such as RCI or percent impaired scores) facilitate interpretation of results and comparisons across studies. Due to the nature of cognitive rehabilitation work (e.g. study duration and time commitment), participant attrition is common, so it is important for studies to acknowledge and account for missing data. Finally, accurate interpretation of results requires clearly specifying which neuropsychological test scores are presented, including the standardization method and source(s) of normative data.

Cognitive rehabilitation terminology

We recommend using computer-training and strategy-training as standard terms to describe cognitive rehabilitation interventions. Use of the term CBT to refer to cognitive rehabilitation is strongly discouraged to avoid confusion with psychotherapy CBT.

Other recommendations

Methods to increase generalizability are recommended for future research. Most CRCD rehabilitation trials have involved middle-aged women with breast cancer. Validation in other cancer populations and other age groups is lacking. Older age poses a risk for CRCD [67, 68], yet only two studies have targeted older adults. Moreover, we are unaware of published cognitive rehabilitation research in younger adults, a group that may be uniquely affected by CRCD as they return to studies, employment or family responsibilities.

Clinical implementation

Participant blinding, large sample sizes and active control groups are commonly lacking in this literature. These criteria typically represent gold-standard qualities in pharmacotherapy trials but are difficult to implement in cognitive rehabilitation research. Active control conditions (e.g. offering support or education without targeted cognitive rehabilitation) enables blinding and controls for "placebo effects, and validation in larger samples (e.g. through multi-site studies) would be informative. Nonetheless, the available evidence supports clinical implementation of cognitive rehabilitation programs for CRCD, as our review suggests these programs have positive effects.

Future research should focus on feasibility of implementation within clinical settings. This might include increasing clinician access to empirically validated programs through collaboration between institutions or dissemination or commercialization of program materials. Comparing similarities and unique benefits between interventions may clarify the contributions of their particular components, allowing sites to tailor programs based on institution-specific resources and best serve patient needs. Technology-enabled program delivery [28] would increase accessibility to participants, and should be examined in future research.

Limitations

Limitations include the following: possible missed relevant articles due to search criteria and/or single author abstract-screening; reporting results as significant at $p < 0.05$ across studies (e.g. unadjusted for multiple comparisons [69]), focusing exclusively on cognitive rehabilitation interventions. While beyond the scope of this review, future meta-analysis as this field develops would synthesize emerging findings and inform future research and clinical implementation. This could incorporate other approaches including exercise, mindfulness and pharmacological interventions that may improve cognition in individuals with cancer [48, 68].

Conclusion

Individuals with non-CNS cancers can experience meaningful cognitive declines that negatively affect QOL and daily

functioning. Cognitive rehabilitation to reduce or manage these deficits appears promising, based on available evidence in this relatively new research area. Both ST and CT programs resulted in benefits on objective cognitive tests and/or self-report measures. While acknowledging limitations in the methodological quality of these studies, the available evidence suggests that dissemination and clinical implementation of these programs, with efforts to study and improve feasibility, are appropriate and important future directions.

Acknowledgments This work was supported in part by the Princess Margaret Cancer Foundation and the Ontario Ministry of Health and Long Term Care.

Compliance with ethical standards

Disclaimer The views expressed do not necessarily reflect those of the OMOHLTC.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Hodgson KD, Hutchinson AD, Wilson CJ, Nettelbeck T (2013) A meta-analysis of the effects of chemotherapy on cognition in patients with cancer. Cancer Treat Rev 39(3):297–304
2. Wefel JS, Lenzi R, Theriault RL, Davis RN, Meyers CA (2004) The cognitive sequelae of standard-dose adjuvant chemotherapy in women with breast carcinoma. Cancer 100(11):2292–2299
3. Meyers CA, Smith JA, Bezjak A, Mehta MP, Liebmann J, Illidge T, Kunkler I, Caudrelier J-M, Eisenberg PD, Meerwaldt J (2004) Neurocognitive function and progression in patients with brain metastases treated with whole-brain radiation and motexafin gadolinium: results of a randomized phase III trial. J Clin Oncol 22(1):157–165
4. Schagen SB, Klein M, Reijneveld J, Brain E, Deprez S, Joly F, Scherwath A, Schrauwen W, Wefel J (2014) Monitoring and optimising cognitive function in cancer patients: present knowledge and future directions. Eur J Cancer Suppl 12(1):29–40
5. Schagen SB, Muller MJ, Boogerd W, Mellenbergh GJ, Van Dam FS (2006) Change in cognitive function after chemotherapy: a prospective longitudinal study in breast cancer patients. J Natl Cancer Inst 98(23):1742–1745
6. Ahles TA, Saykin AJ, McDonald BC, Li Y, Furstenberg CT, Hanscom BS, Mulrooney TJ, Schwartz GN, Kaufman PA (2010) Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: impact of age and cognitive reserve. J Clin Oncol 28(29):4434–4440
7. Schilder CM, Seynaeve C, Beex LV, Boogerd W, Linn SC, Gundy CM, Huizenga HM, Nortier JW, van de Velde CJ, van Dam FS (2010) Effects of tamoxifen and exemestane on cognitive functioning of postmenopausal patients with breast cancer: results from the neuropsychological side study of the tamoxifen and exemestane adjuvant multinational trial. J Clin Oncol 28(8):1294–1300
8. Hermelink K, Bühner M, Sckopke P, Neufeld F, Kaste J, Voigt V, Münzel K, Wuerstlein R, Ditsch N, Hellerhoff K (2017) Chemotherapy and post-traumatic stress in the causation of cognitive dysfunction in breast cancer patients. J Natl Cancer Inst 109(10):djx057
9. Schagen SB, Wefel JS (2017) Post-traumatic stress as the primary cause for cognitive decline—not the whole story, and perhaps no story at all. J Natl Cancer Inst 109(10)
10. Ahles TA, Saykin AJ (2007) Candidate mechanisms for chemotherapy-induced cognitive changes. Nat Rev Cancer 7(3):192–201
11. Janelsins MC, Kesler SR, Ahles TA, Morrow GR (2014) Prevalence, mechanisms, and management of cancer-related cognitive impairment. Int Rev Psychiatry 26(1):102–113
12. Zer A, Pond GR, Razak ARA, Tirona K, Gan HK, Chen EX, O'sullivan B, Waldron J, Goldstein DP, Weinreb I (2018) Association of neurocognitive deficits with radiotherapy or chemoradiotherapy for patients with head and neck cancer. JAMA Otolaryngol Head Neck Surg 144(1):71–79
13. Alibhai SM, Timilshina N, Duff-Canning S, Breunis H, Tannock IF, Naglie G, Fleshner NE, Krahn MD, Warde P, Marzouk S (2017) Effects of long-term androgen deprivation therapy on cognitive function over 36 months in men with prostate cancer. Cancer 123(2):237–244
14. Hoogland AI, Nelson AM, Small BJ, Hyland KA, Gonzalez BD, Booth-Jones M, Anasetti C, Jacobsen PB, Jim HS (2017) The role of age in neurocognitive functioning among adult allogeneic hematopoietic cell transplant recipients. Biol Blood Marrow Transplant 23(11):1974–1979
15. Simó M, Root JC, Vaquero L, Ripollés P, Jové J, Ahles T, Navarro A, Cardenal F, Bruna J, Rodríguez-Fornells A (2015) Cognitive and brain structural changes in a lung cancer population. J Thorac Oncol 10(1):38–45
16. Vardy JL, Dhillon HM, Pond GR, Rourke SB, Bekele T, Renton C, Dodd A, Zhang H, Beale P, Clarke S (2015) Cognitive function in patients with colorectal cancer who do and do not receive chemotherapy: a prospective, longitudinal, controlled study. J Clin Oncol 33(34):4085–4092
17. Wefel JS, Vidrine DJ, Marani SK, Swartz RJ, Veramonti TL, Meyers CA, Hoekstra HJ, Hoekstra-Weebers JE, Gritz ER (2014) A prospective study of cognitive function in men with nonseminomatous germ cell tumors. Psycho-oncology 23(6):626–633
18. Ahles TA, Root JC, Ryan EL (2012) Cancer- and cancer treatment-associated cognitive change: an update on the state of the science. J Clin Oncol 30(30):3675–3686
19. Hutchinson AD, Hosking JR, Kichenadasse G, Mattiske JK, Wilson C (2012) Objective and subjective cognitive impairment following chemotherapy for cancer: a systematic review. Cancer Treat Rev 38(7):926–934
20. Koppelmans V, Breteler M, Boogerd W, Seynaeve C, Gundy C, Schagen S (2012) Neuropsychological performance in survivors of breast cancer more than 20 years after adjuvant chemotherapy. J Clin Oncol 30(10):1080–1086
21. Boykoff N, Moieni M, Subramanian SK (2009) Confronting chemobrain: an in-depth look at survivors' reports of impact on work, social networks, and health care response. J Cancer Surviv 3(4):223–232
22. Munir F, Burrows J, Yarker J, Kalawsky K, Bains M (2010) Women's perceptions of chemotherapy-induced cognitive side affects on work ability: a focus group study. J Clin Nurs 19(9–10):1362–1370
23. Von Ah D, Habermann B, Carpenter JS, Schneider BL (2013) Impact of perceived cognitive impairment in breast cancer survivors. Eur J Oncol Nurs 17(2):236–241
24. Beck JS (2011) Cognitive behavior therapy: basics and beyond. Guilford Press, New York
25. Ferguson RJ, Ahles TA, Saykin AJ, McDonald BC, Furstenberg CT, Cole BF, Mott LA (2007) Cognitive-behavioral management of chemotherapy-related cognitive change. Psycho-Oncology 16(8):772–777. https://doi.org/10.1002/pon.1133

26. Cherrier MM, Anderson K, David D, Higano CS, Gray H, Church A, Willis SL (2013) A randomized trial of cognitive rehabilitation in cancer survivors. Life Sci 93(17):617–622. https://doi.org/10.1016/j.lfs.2013.08.011
27. Ferguson RJ, McDonald BC, Rocque MA, Furstenberg CT, Horrigan S, Ahles TA, Saykin AJ (2012) Development of CBT for chemotherapy-related cognitive change: results of a waitlist control trial. Psychooncology 21(2):176–186. https://doi.org/10.1002/pon.1878
28. Ferguson RJ, Sigmon ST, Pritchard AJ, LaBrie SL, Goetze RE, Fink CM, Garrett AM (2016) A randomized trial of videoconference-delivered cognitive behavioral therapy for survivors of breast cancer with self-reported cognitive dysfunction. Cancer 122(11):1782–1791. https://doi.org/10.1002/cncr.29891
29. King S, Green HJ (2015) Psychological intervention for improving cognitive function in cancer survivors: a literature review and randomized controlled trial. Front Oncol 5:72. https://doi.org/10.3389/fonc.2015.00072
30. McDougall GJ, Becker H, Acee TW, Vaughan PW, Delville CL (2011) Symptom management of affective and cognitive disturbance with a group of cancer survivors. Arch Psychiatr Nurs 25(1):24–35. https://doi.org/10.1016/j.apnu.2010.05.004
31. Park JH, Jung YS, Kim KS, Bae SH (2017) Effects of compensatory cognitive training intervention for breast cancer patients undergoing chemotherapy: a pilot study. Support Care Cancer 25(6):1887–1896. https://doi.org/10.1007/s00520-017-3589-8
32. Bray VJ, Dhillon HM, Bell ML, Kabourakis M, Fiero MH, Yip D, Boyle F, Price MA, Vardy JL (2017) Evaluation of a web-based cognitive rehabilitation program in cancer survivors reporting cognitive symptoms after chemotherapy. J Clin Oncol 35(2):217–225. https://doi.org/10.1200/jco.2016.67.8201
33. Damholdt MF, Mehlsen M, O'Toole MS, Andreasen RK, Pedersen AD, Zachariae R (2016) Web-based cognitive training for breast cancer survivors with cognitive complaints—a randomized controlled trial. Psycho-Oncology 25(11):1293–1300. https://doi.org/10.1002/pon.4058
34. Kesler S, Hadi Hosseini SM, Heckler C, Janelsins M, Palesh O, Mustian K, Morrow G (2013) Cognitive training for improving executive function in chemotherapy-treated breast cancer survivors. Clin Breast Cancer 13(4):299–306. https://doi.org/10.1016/j.clbc.2013.02.004
35. Wu LM, Amidi A, Tanenbaum ML, Winkel G, Gordon WA, Hall SJ, Bovbjerg K, Diefenbach MA (2018) Computerized cognitive training in prostate cancer patients on androgen deprivation therapy: a pilot study. Support Care Cancer 26(6):1917–1926
36. Ercoli LM, Petersen L, Hunter AM, Castellon SA, Kwan L, Kahn-Mills BA, Embree LM, Cernin PA, Leuchter AF, Ganz PA (2015) Cognitive rehabilitation group intervention for breast cancer survivors: results of a randomized clinical trial. Psychooncology 24(11):1360–1367. https://doi.org/10.1002/pon.3769
37. Von Ah D, Carpenter JS, Saykin A, Monahan P, Wu J, Yu M, Rebok G, Ball K, Schneider B, Weaver M, Tallman E, Unverzagt F (2012) Advanced cognitive training for breast cancer survivors: a randomized controlled trial. Breast Cancer Res Treat 135(3):799–809. https://doi.org/10.1007/s10549-012-2210-6
38. Poppelreuter M, Weis J, Bartsch HH (2009) Effects of specific neuropsychological training programs for breast cancer patients after adjuvant chemotherapy. J Psychosoc Oncol 27(2):274–296. https://doi.org/10.1080/07347330902776044
39. Mihuta M, Green H, Shum D (2018) Efficacy of a web-based cognitive rehabilitation intervention for adult cancer survivors: a pilot study. Eur J Cancer Care 27(2):e12805
40. Schuurs A, Green HJ (2013) A feasibility study of group cognitive rehabilitation for cancer survivors: enhancing cognitive function and quality of life. Psycho-Oncology 22(5):1043–1049. https://doi.org/10.1002/pon.3102
41. McDougall GJ (2001) Memory improvement program for elderly cancer survivors. Geriatr Nurs (New York, NY) 22(4):185–190. https://doi.org/10.1067/mgn.2001.117916
42. Becker H, Henneghan AM, Volker DL, Mikan SQ (2017) A pilot study of a cognitive-behavioral intervention for breast cancer survivors. Oncol Nurs Forum 44(2):255–264. https://doi.org/10.1188/17.onf.255-264
43. Ercoli LM, Castellon SA, Hunter AM, Kwan L, Kahn-Mills BA, Cernin PA, Leuchter AF, Ganz PA (2013) Assessment of the feasibility of a rehabilitation intervention program for breast cancer survivors with cognitive complaints. Brain Imaging Behav 7(4):543–553. https://doi.org/10.1007/s11682-013-9237-0
44. Cicerone KD, Azulay J, Trott C (2009) Methodological quality of research on cognitive rehabilitation after traumatic brain injury. Arch Phys Med Rehabil 90(11):S52–S59
45. Cicerone KD, Langenbahn DM, Braden C, Malec JF, Kalmar K, Fraas M, Felicetti T, Laatsch L, Harley JP, Bergquist T (2011) Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. Arch Phys Med Rehabil 92(4):519–530
46. Downs SH, Black N (1998) The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 52(6):377–384
47. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savović J, Schulz KF, Weeks L, Sterne JA (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 343:d5928
48. Milbury K, Chaoul A, Biegler K, Wangyal T, Spelman A, Meyers C, Arun B, Palmer J, Taylor J, Cohen L (2013) Tibetan sound meditation for cognitive dysfunction: results of a randomized controlled pilot trial. Psycho-Oncology 22(10):2354–2363
49. Strauss E, Sherman EM, Spreen O (2006) A compendium of neuropsychological tests: administration, norms, and commentary. American Chemical Society, Washington
50. Folstein MF, Folstein SE, McHugh PR (1975) "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12(3):189–198
51. Randolph C (1998) Repeatable battery for the assessment of neuropsychological status manual. The Psychological Corporation, San Antonio
52. Sullivan G, Feinn R (2012) Using effect size- or why the p value is not enough. J Grad Med Educ 4:279–282. https://doi.org/10.4300/JGME-D-12-00156.1
53. Cohen J (1988) Statistical power analysis for the behavioral sciences, 2nd edn. Erlbaum, Hillsdale
54. Owen AM, Hampshire A, Grahn JA, Stenton R, Dajani S, Burns AS, Howard RJ, Ballard CG (2010) Putting brain training to the test. Nature 465:775–778. https://doi.org/10.1038/nature09042 https://www.nature.com/articles/nature09042 - supplementary-information
55. Morris SB (2008) Estimating effect sizes from pretest-posttest-control group designs. Organ Res Methods 11(2):364–386
56. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Nat l Cancer Inst 85(5):365–376
57. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, Silberman M, Yellen SB, Winicour P, Brannon J (1993) The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol 11(3):570–579
58. Devins GM (2010) Using the illness intrusiveness ratings scale to understand health-related quality of life in chronic disease. J Psychosom Res 68(6):591–602

59. Catt S, Starkings R, Shilling V, Fallowfield L (2017) Patient-reported outcome measures of the impact of cancer on patients' everyday lives: a systematic review. J Cancer Surviv 11(2):211–232
60. Goedendorp MM, Knoop H, Gielissen MF, Verhagen CA, Bleijenberg G (2014) The effects of cognitive behavioral therapy for postcancer fatigue on perceived cognitive disabilities and neuropsychological test performance. J Pain Symptom Manag 47(1): 35–44
61. Kucherer S, Ferguson RJ (2017) Cognitive behavioral therapy for cancer-related cognitive dysfunction. Curr Opin Support Palliat Care 11(1):46–51
62. Wefel JS, Vardy J, Ahles T, Schagen SB (2011) International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. Lancet Oncol 12(7):703–708
63. Downie FP, Mar Fan HG, Houédé-Tchen N, Yi Q, Tannock IF (2006) Cognitive function, fatigue, and menopausal symptoms in breast cancer patients receiving adjuvant chemotherapy: evaluation with patient interview after formal assessment. Psycho-Oncology 15(10):921–930
64. Myers JS (2009) Chemotherapy-related cognitive impairment. Clin J Oncol Nurs 13(4):413–421
65. Mlinac ME, Feng MC (2016) Assessment of activities of daily living, self-care, and independence. Arch Clin Neuropsychol 31(6):506–516
66. Turner-Stokes L (2009) Goal attainment scaling (GAS) in rehabilitation: a practical guide. Clin Rehabil 23(4):362–370
67. Sleight A (2016) Coping with cancer-related cognitive dysfunction: a scoping review of the literature. Disabil Rehabil 38(4):400–408
68. Janelsins MC, Peppone LJ, Heckler CE, Kesler SR, Sprod LK, Atkins J, Melnik M, Kamen C, Giguere J, Messino MJ (2016) YOCAS©® yoga reduces self-reported memory difficulty in cancer survivors in a nationwide randomized clinical trial: investigating relationships between memory and sleep. Integr Cancer Ther 15(3): 263–271
69. Perneger TV (1998) What's wrong with Bonferroni adjustments. BMJ 316(7139):1236–1238