



Cancer-related cognitive impairment in adolescents and young adults with cancer: a scoping review

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Purpose of review

Cancer-related cognitive impairment (CRCI) is a frequent and clinically meaningful consequence of cancer, yet current evidence is largely derived from older adult populations. Adolescents and young adults (AYAs) may be particularly vulnerable due to ongoing neurodevelopment, high cognitive demands, and cancer-related biological and psychosocial stressors. This review is timely given the growing interest in biological mechanisms and preventive models of CRCI, alongside the persistent lack of AYA-specific syntheses addressing cognitive trajectories, mechanisms, and optimal intervention timing.

Recent findings

Approximately 25–30% of AYAs experience CRCI, most commonly affecting attention, processing speed, executive functioning, and working memory. Cognitive alterations may be detectable prior to treatment initiation and can persist across the cancer trajectory. Emerging AYA-specific evidence implicates biological mechanisms such as systemic inflammation and altered neuroplasticity, including changes in brain-derived neurotrophic factor (BDNF). A consistent dissociation between subjective cognitive complaints and objective performance is observed, underscoring the functional impact of subtle inefficiencies in academic and early professional contexts. While non-pharmacological interventions show promise in the general CRCI literature, early and AYA-specific preventive interventions remain scarce.

Summary

CRCI in AYAs should be conceptualized as a dynamic, biologically grounded process embedded within ongoing neurodevelopment. Early, developmentally sensitive, and multimodal interventions may represent a key opportunity to preserve long-term cognitive, functional, and psychosocial outcomes in this vulnerable population.

Keywords

adolescents and young adults (AYAs), cancer-related cognitive impairment, interventions, neurodevelopment and neuroplasticity

INTRODUCTION

Cancer-related cognitive impairment (CRCI) is now widely recognized as a frequent and clinically meaningful consequence of cancer and its treatments across the oncology care continuum [1[¶]]. Over the past year, 18 systematic reviews and meta-analyses addressing CRCI in cancer patients were identified, emphasizing the growing importance of research in this field (see Table 1).

Across the general CRCI literature, large-scale systematic [2[¶]], umbrella reviews [1[¶]] and a meta-analysis [3] consistently report impairments across multiple cognitive domains, including memory, attention, executive functions, and information processing speed. These impairments may be present prior to treatment initiation, worsen during active treatment, and persist long after treatment completion

[1[¶],2[¶]]. Growing attention has been devoted to the biological mechanisms underlying CRCI, with neuroimaging reviews suggesting functional and structural

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KEY POINTS

- Evidence supports the involvement of biological mechanisms underlying cancer-related cognitive impairment (CRCI) in adolescents and young adults (AYAs), including systemic inflammation, alterations in neuroplasticity, and changes in brain-derived neurotrophic factor (BDNF), with cognitive impairments detectable prior to treatment initiation.
- CRCI is a frequent and clinically meaningful condition in AYAs, affecting multiple cognitive domains, including attention, processing speed, executive functioning, and memory.
- CRCI is associated with substantial consequences for quality of life, functional autonomy, educational and occupational trajectories, and psychosocial development in AYAs.
- A marked dissociation between objective cognitive performance and subjective cognitive complaints is consistently observed in AYAs, reinforcing the importance of integrating patient-reported outcomes into CRCI assessment and clinical care.
- Non-pharmacological interventions, including cognitive training, physical activity, and psychological approaches, show promise for improving cognitive and patient-reported outcomes, but AYA-specific and early preventive interventions remain scarce.

alterations in large-scale brain networks, particularly default mode, executive, and attentional networks, following anticancer treatments, albeit with heterogeneous findings largely derived from adult samples [4].

These neural alterations are embedded within neuroplastic processes, defined as the capacity of the brain to reorganize in response to biological and environmental challenges [5^{••}] that may reflect both deleterious mechanisms (e.g., neuroinflammation, oxidative stress, and reductions in neurotrophic factors), and adaptive mechanisms that aim to maintaining cognitive functioning [5^{••}]. Consistent with this framework, systemic inflammation, stress-axis dysregulation, and changes in brain-derived neurotrophic factor (BDNF) levels have been repeatedly associated with CRCI [6].

CRCI is associated with substantial impairments in quality of life, functional autonomy, and social participation, representing a major source of long-term morbidity for cancer survivors from 5 to 75 years old [1[•]]. Meta-analytic evidence indicates that chemotherapy is associated with small-to-moderate declines in objectively measured attention, particularly during the first year post-treatment, although differences between chemotherapy-treated and non-chemotherapy patients

remain less consistent [3]. Qualitative [7] and mixed methods reviews [1[•],2[•]] consistently describe CRCI as a disruptive and often invalidating experience, with persistent effects on return to work, social relationships, personal identity, and self-esteem. Across reviews, a marked dissociation is observed between objective cognitive performance and subjective cognitive complaints, with subjective complaints frequently being more pronounced than impairments detected by standardized neuropsychological tests, underscoring the need to integrate patient-reported outcomes and functional measures into CRCI research, beyond standardized neuropsychological testing alone [1[•],2[•]].

Despite this expanding body of evidence, several reviews converge on important methodological and conceptual limitations [1[•],2[•]]. The CRCI literature remains highly fragmented, with substantial heterogeneity in study design, intervention protocols, outcome measures, and timing of assessments [2[•]]. A recent systematic review identified more than 150 different neuropsychological tools used to assess cognition in non-central nervous system cancer populations, with limited adherence to the recommendations of the International Cancer and Cognition Task Force [8]. This variability limits cross-study comparability, the synthesis of intervention effects, and the identification of reliable cognitive trajectories [8,2[•]].

In response to the growing recognition of CRCI, a range of non-pharmacological interventions has been developed and evaluated, including cognitive remediation and training programs [9–12], physical activity-based interventions [13–15], and mind-body and psychological approaches [16–18]. Syntheses from recent systematic reviews [2[•]] and an umbrella review [1[•]] indicate that these interventions are generally associated with improvements in cognitive and patient-reported outcomes, although effect sizes vary across cognitive domains and intervention modalities [1[•],2[•]]. Cognitive training interventions show the most consistent benefits on objective cognitive performance, particularly in executive functions and memory [9–12]. Physical activity-based interventions have also demonstrated beneficial effects on attention, working memory, and executive functioning, albeit with substantial heterogeneity related to exercise type, duration, and timing relative to cancer treatment [13–15]. In contrast, mind-body and psychological interventions primarily appear to improve subjective cognitive complaints and quality of life rather than objective cognitive performance [16–18]. Recent reviews also highlight digital and computerized cognitive interventions as particularly promising in terms of accessibility, scalability, and feasibility, especially during active treatment [9]. However, most interventions have been implemented after treatment completion, reflecting a predominantly

Table 1. Summary of general CRCI literature

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
1. Treatment-effect and cognitive characterization reviews								
Jung <i>et al.</i> , 2025	Meta-analysis of prospective longitudinal cohort studies	2005–2023 / 18 studies (16 datasets)	Women with breast cancer (adults ≈ 21–88 years)	During and after chemotherapy	To quantify the impact of chemotherapy on objective attention and to identify the time point of greatest impact	NA	Objective attention (TMT; TAP; CPT; Digit Span; SDMT)	Attention is significantly more impaired in patients treated with chemotherapy compared with healthy controls, with the strongest effect observed within the year following chemotherapy; no systematic differences found compared with non-chemotherapy patients
2. Informative reviews on biomarkers and underlying mechanisms								
Boschetti <i>et al.</i> , 2025	Systematic review	NA / NA	Women with non-metastatic breast cancer (adults ≈ 40–70 years)	Before / during / after treatment	To identify blood and genetic biomarkers associated with CRCI	NA	Cognition objective: memory (HVT, RAVIT, verbal memory tests), attention / processing speed (TMT, Digit Symbol), executive functions (TMT, Stroop, verbal fluency), global cognition (composite neuropsychological batteries) Subjective cognition: FACT-Cog, cognitive fatigue scales or associated symptom measures Biochemical biomarkers: inflammatory cytokines (IL-6, TNF-α, CRP, cortisol, BDNF) Genetic biomarkers: DNA repair genes, oxidative stress-related genes, APOE, COMT, BDNF	Cytokines (IL-6 and TNF-α) are mainly associated with subjective cognition; BDNF and cortisol are related to cognitive complaints; Objective and genetic findings are inconsistent
Leskinen <i>et al.</i> , 2025	Systematic review	NA / NA	Adults with non-CNS cancers (predominantly breast cancer; ≈ 40–70 years)	After treatment	To examine brain alterations associated with CRCI	NA	Objective cognition: memory (HVT, RAVIT, CVLT, WMS), attention / working memory (Digit Span, PASAT, Stroop), processing speed (TMT, Digit Symbol), executive functions (TMT, WCST, D-KEFS), language (verbal fluency, Boston Naming Test) Subjective cognition: FACT-Cog, MoCA, MMSE, MASQ Brain connectivity: fMRI, DTI, structural MRI (GMD, volume); indices: white matter integrity, gray matter density, FC, ALFF / fALFF, ReHo; brain networks: DMN, CEN, DAN, fronto-parietal networks, hippocampal networks, salience network Humour: HADS, BDI, STAI Quality of life / fatigue: EORTC QLQ-C30, FACIT, PSQI	Structural and functional alterations of brain networks (DMN, CEN, DAN); Heterogeneous associations between cognition and neuroimaging findings

Table 1 (Continued)

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
3. Qualitative and methodological reviews								
Ibrar <i>et al.</i> , 2025	Qualitative systematic review	2013–2025 / 51 studies	Adults with various cancers (predominantly breast cancer; ≈ 18 to > 70 years)	During and after treatment	To explore the subjective experience of cancer-related cognitive impairment	NA	CRCI experienced as persistent, disabling, and multidimensional: memory, attention, executive functions, language, and processing speed most affected; strong impact on employment, identity, and quality of life	Supports the primacy of subjective complaints; Justifies the dissociation between subjective and objective cognition; Provides a patient-centered and resilience-based foundation
Capetti <i>et al.</i> , 2025	Methodological systematic review	2011–2023 / 178 studies	Adults, non-CNS cancers (18–80 years)	NA	To examine the cognitive assessment tools used in oncology	NA	Extreme variability in cognitive tests; low adherence to ICCTF recommendations; tools often insufficiently sensitive to CRCI; high risk of under-detection	Highlights the limitations of classical neuropsychological tests; Supports the need for ecological and combined assessment tools; Provides strong methodological support
4. Intervention reviews								
Shellon <i>et al.</i> , 2025	Systematic review	1990–2024 / 5 studies	Women with breast cancer (adults ≈ 50 –60 years)	During and after treatment	To examine the effectiveness of neuroprotective interventions implemented during chemotherapy to prevent or reduce CRCI in patients with breast cancer	Preventive interventions during chemotherapy: Exercise Compensatory Cognitive Training (CCT) Memantine Probiotics	Subjective cognition: FACT-Cog, PROMIS Cognitive Function, MDASI cognitive module Objective cognition: memory (HVLT-R, BVMTR), processing speed (TMT, Digit Symbol), executives functions (TMT, Stroop, SCWT), Attention (Digit Span), verbal fluency (VFT, COWAT) Global cognition (CANTAB battery)	Probiotics and CCT are associated with promising preventive effects on global cognition; Exercise mainly improves subjective cognition; Objective effects are heterogeneous; Evidence is limited by small sample sizes.
Ang <i>et al.</i> , 2025	Systematic review + meta-analysis	2008–2023 / 10 studies	Cancer survivors (adults + some children/adolescents)	After treatment	To evaluate the effectiveness of computerized cognitive training (CCT) on cognition and quality of life in cancer survivors with CRCI	Computerized Cognitive Training (CCT): adaptive digital programs (working memory, attention, executive functions), home-based access	Objective cognition: attention (TMT-A, Digit Symbol), tacite attentives informatises (BrainHQ, AquaSnap), executives functions (TMT-B, Stroop, verbal fluency, flexibility tasks, tests executives informatises (HappyNeuron, BrainHQ, RehaCom), working memory (Digit Span, n-back, Letter-Number Sequencing, tests informatises (RehaCom, HappyNeuron) Quality of life: FACT-G, EORTC QLQ-C30, PROMIS Quality of Life	Small improvements in working memory post-intervention and at follow-up. Small improvements in executive functions observed only at follow-up. No significant effects on attention or quality of life

Table 1 (Continued)

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
Pinheiro <i>et al.</i> , 2025	Systematic review + meta-analysis	2014–2022 / 11 studies	Women with breast cancer (adults ≈ 37–71 years)	During and after treatment	To evaluate the effects of physical exercise programs on cognitive functioning in breast cancer survivors	Structured exercise (aerobic, resistance, combined, mind–body)	Subjective cognition: FACT-Cog, PROMIS Cognitive Function, CFQ Objective cognition: attention/vitesse/mémoire de travail (TMT-A, Digit Span, SART, One-Back/N-back) executives functions (TMT-B, Stroop, Groton Maze Learning Task GMLT), memory (HVLT-R, RAVLT, Auditory consonant trigrams), language/fluency (COWAT / Animal Naming), Global cognition (CogState, NIH Toolbox Cognition Battery)	Significant improvements in attention, working memory, executive functions, and perceived cognition; No significant effects on learning/memory, processing speed, or verbal fluency; High heterogeneity of cognitive assessment tools
Sánchez-Gómez <i>et al.</i> , 2025	Systematic review + meta-analysis	2012–2024 / 11 studies in the review, 9 in the meta-analysis	Various cancers (adults 18–80 years)	During and after treatment	To evaluate the effectiveness of cognitive training (CT) interventions to improve CRCI in patients with breast cancer	Cognitive Training (in-person and digital): standardized repeated exercises targeting memory, attention, and executive functions	Subjective cognition: FACT-Cog Objective cognition: global cognition (CogState Battery, Cambridge Brain Sciences, NIH Toolbox Cognition Battery), attention / executives functions (TMT-A&B), memory (RAVLT)	Significant improvement in perceived global cognition (FACT-Cog); No robust evidence for effects on objective cognition; Overall level of evidence is low
Cáceres <i>et al.</i> , 2025	Systematic review + meta-analysis	2020–2024 / 12 studies in the review, 10 in the meta-analysis	Women with breast cancer (adults ≈ 45–65 years)	During and after treatment	To evaluate the effectiveness of cognitive stimulation interventions to reduce or improve CRCI in patients with breast cancer	Cognitive stimulation: Psychotherapies (ACT, CALM, CBT) Group-based interventions	Subjective cognition: FACT-Cog, CFQ, PROMIS Cognitive Function, RRS Objective cognition: global cognition (MMSE, MoCA, RBMT-II, BADS, CDT)	Moderate but non-significant effect on global cognition (mainly assessed using FACT-Cog); High methodological heterogeneity across studies
Wolfe <i>et al.</i> , 2025	Systematic review + network meta-analysis (NMA)	2012–2024 / 18 studies	Non-CNS cancer survivors (adults, mostly >50 years)	After treatment	To evaluate the comparative effectiveness of pharmacological and non-pharmacological interventions to treat CRCI in adults treated for non-CNS cancer	Non-pharmacological and pharmacological interventions: Guided multimodal programs (education + rehabilitation) Mindfulness Medications (e.g., donepezil)	Objective cognition: verbal memory (HVLT-R, RAVLT, Story Recall), mémoire visuelle (BVMTR), Processing speed (TMT-A, Digit Symbol, processing speed tasks), executives functions (TMT-B, Stroop, COWAT, DKEFS 20), attention (Digit Span, Attention tests spécifiques), working memory (LNS)	Guided group-based multimodal programs show the most consistent effects across several objective cognitive domains (learning, memory, processing speed, attention, working memory); More limited effects for mindfulness; No benefit of pharmacological treatments (e.g., donepezil)
Jia <i>et al.</i> , 2025	Systematic review + NMA	2014–2024 / 20 studies	Women with breast cancer (adults ≈ 28–78 years)	During and after treatment	To evaluate the effectiveness of different types of mind–body exercise (MBE) on CRCI in breast cancer patients and identify the optimal MBE intervention	Mind–Body Exercise (MBE): Baduanjin Yoga Tai Chi / Qigong Dance	Subjective cognition: FACT-Cog, EORTC QLQ-C30 - Cognitive Function, BCPT Cognitive Problems Scale, SOSI-CD Objective cognition: WAIS-III, RAVLT, TMT-A1B, Fluence verbale	Baduanjin appears to be the most effective intervention, followed by yoga and Tai Chi/Qigong; Dance does not show significant effects

Table 1 (Continued)

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
Hung <i>et al.</i> , 2025	Systematic review + meta-analysis	2018–2024 / 21 studies	Women with breast cancer (adults >18 years)	During and after treatment	To examine the impact of physical activity interventions on cognitive functioning in patients with breast cancer and survivors, and to analyze exercise parameters as moderators of cognitive effects	Physical exercise: Aerobic Resistance HIIT Multicomponent exercise	Subjective cognition: FACT-Cog, EORTC QLQ-C30 - Cognitive Function, CFQ, PROMIS Cognitive Function, BCPT Symptom Checklist, MDASI cognitive items Objective cognition: memory (HVLTR, RAVLT, Auditory Verbal Learning Test, Rey Complex Figure Test, Corsi Block-Tapping Test), Attention/vitesse de traitement (TMT-A, Digit Vigilance Test, D2 Test, Reaction Time Tasks), executives functions (TMT-B, Stroop, Verbal Fluency (COWAT, FAS, Animal naming), Tower of London, NBack), working memory (Digit Span, Letter-Number Sequencing)	Small but significant overall effect of exercise on cognition ($g \approx 0.22$); Significant effects for subjective cognition, basic and higher-order cognitive functions; HIIT and multicomponent exercise show the largest effects; No clear effect on memory; Quality of evidence: low (GRADE)
Hu <i>et al.</i> , 2025	Umbrella review	2015–2025 / 28 studies	Women with breast cancer (adults $\approx$ 45–65 years)	Before / during treatment	To synthesize evidence from randomized controlled trials evaluating non-pharmacological interventions for cognitive functioning in patients with cancer	Physical exercise: Aerobic Resistance Combined Mind-body	Subjective cognition: FACT-Cog, EORTC QLQ-C30 - Cognitive Function, CFQ, PROMIS Cognitive Function, MDASI cognitive items, BCPT, MASQ, PRMQ, POMQ Objective cognition: Memory/apprentissage (HVLTR, RAVLT, CVLT, AVLT, BVMT-R, WMS), attention/vitesse de traitement (TMT-A, Digit Symbol Substitution Test, SART, UFOV, D2), executives functions (TMT-B, Stroop, COWAT, WCST, FAB), working memory (Digit Span, NBack), globale cognition (MMSE, MoCA)	Robust effects on specific objective cognitive outcomes; Mind-body exercise mainly improves subjective cognition; Limited and heterogeneous evidence for global objective cognition and resistance training
Jiang <i>et al.</i> , 2025	Systematic review + meta-analysis	2005–2024 / 30 studies	Breast cancer survivors (adults $\approx$ 46–63 years)	During and after treatment	To evaluate the effects of mindfulness-based interventions on cognitive functioning in patients with cancer	Mindfulness-based interventions (MBI): MBSR MBCT Meditation Breathing Yoga	Subjective cognition: EORTC QLQ-C30 - Cognitive Function, FACT-Cog Objective cognition: TMT, WAIS-III, RAVLT, verbal fluency	Mindfulness-based interventions significantly improve subjective cognition (post-intervention and follow-up); No significant effects on objective cognition; Moderate effects influenced by intervention context and delivery modalities

Table 1 (Continued)

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
Wang <i>et al.</i> , 2025/2026	Systematic review + meta-analysis + NMA	2010–2025 / 31 studies	Various cancers, predominantly breast cancer (adults ≈ 40–70 years)	Mostly after treatment	To synthesize and compare the effectiveness of different cognitive rehabilitation interventions in adults with cancer	Cognitive rehabilitation: Cognitive Training (CT) Compensatory Strategy Training (CST) Combined interventions (with or without technology)	Subjective cognition: FACT-Cog, EORTC QLQ-C30 - Cognitive function, CFQ, BRIEF, PAOFI, PROMIS - Cognition, CSCW DV, GFS, FEDA, BAPM, FSBE, MMG, AFI, SSMG Objective cognition: global cognition (MoCA, MMSE, Cogstate battery, CNS Vital Signs, WebNeuro, NIH Toolbox Cognition Battery), attention/vitesse de traitement (Digit Span, TMT-A&B, D2 test, SDMT, PASAT, CST, SCWT, Attentive matrices, SART, BrainHQ (Bubble Pop, Double Decision, Sound Sweeps), Processing Speed Tasks (Insight, HappyNeuron), memory (RAVLT, HVLTR, AVLT-H, BVMTR, RBMT, Graber & Buschke Test, VLMT, Rey- Osterrieth Complex Figure), Executive function (WCST, BADS, Letter Fluency, UPS, MWT-A, Hotel Task, COWAT, CET, FAB), Fonctions visuospatiales et matrices (Rey-Osterrieth Complex Figure, PM47, Grooved Pegboard Test, Digit Symbol, Spatial Span), Tâche informatisée (MyCO, TAP, MSI, LDST), autres (MoCA, BrainHQ, RehaCom, ReMind)	Improvements in subjective cognition and several objective cognitive domains, with moderate to large effects for attention/ concentration, executive functions, and learning/memory; CST (especially technology-based) is most effective for subjective cognition; Technology-based CT is most effective for memory/learning
Yang <i>et al.</i> , 2025	Systematic review + NMA	2012–2024 / 42 studies	Women with breast cancer (adults 18–67 years)	During and after treatment	To compare the impact of different non-pharmacological interventions on CRCI in breast cancer patients and identify the most effective interventions	Non-pharmacological interventions (NMA): Psychological interventions (CBT, ACT, psychoeducation) Cognitive training (CT) Cognitive rehabilitation (CR) Exercise / physical activity Meditation / MBSR Tai Chi / Qigong / Baduanjin Acupuncture, music	Subjective cognition: FACT-Cog, EORTC QLQ-C30 - cognitive function Objective cognition: Processing speed (TMT-A, WAIS code), Working memory (Digit Span, TMT-B), Executive functions (TMT-B, Stroop, fluency)	Psychological interventions are most effective for subjective cognition; Cognitive training is best for working memory and executive functions; Cognitive rehabilitation is best for learning memory; Meditation / MBSR is best for processing speed; Overall effects are modest but consistent; quality of evidence is low to very low

Table 1 (Continued)

Author (year)	Type of review	Period / number of studies	Population (age)	Timing	Main objective	Specific interventions	Cognitive outcomes	Main findings
Haywood <i>et al.</i> , 2025	Umbrella review	2012-2024 / 64 reviews	Various cancers (children,AYA, adults)	Before / during / after treatment	To provide a critical overview of systematic reviews on non-pharmacological interventions aiming to improve cognition in people with cancer, inform clinical recommendations, and identify gaps in the literature	Non-pharmacological interventions: Cognitive training / rehabilitation Exercise / physical activity Mind-body / mindfulness Psychological / behavioral interventions Multimodal interventions	Subjective cognition: FACT-Cog, PROMIS Cognitive Function, EORTC QLQ-C30 - Cognitive Function Objective cognition : attention/vitesse (TMT-A&B, Digit Symbol), memory (Auditory Verbal Learning Test, Hopkins Verbal Learning Test, Digit Span), Executive Functions (Wisconsin Car Sorting Test WCST, Stroop), Verbal Fluency (COWAT)	Cognitive training / rehabilitation shows the strongest and most consistent evidence; Exercise is promising but results are heterogeneous; Mind-body and psychological interventions mainly show short-term effects with limited evidence; Multimodal interventions show interesting potential but are poorly defined; Overall methodological quality of reviews ranges from low to moderate

CRCI, cancer related cognitive impairment; TMT, Trail Making Test; CPT, continuous performance test reaction time; SDMT, Symbol Digit Modality Test; HVLT, Hopkins Verbal Learning Test; RAVLT, Rey Auditory-Verbal Learning Test; FACT-Cog, Functional Assessment of Cancer Therapy-Cognitive Function. BDNF, brain-derived neurotrophic factor; CVLT, California Verbal Learning Test; WMS, Wechsler Memory Scale; PASAT, Paced Auditory Serial Addition Test; WCST, Wisconsin Card Sorting Test; D-KEFS, Delis-Kaplan Executive Function System; MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental State Examination; MASQ, Mood and Anxiety Symptom Questionnaire; HADS, Hospital Anxiety and Depression Scale; BDI, Beck Depression Inventory; STAI, State Trait Anxiety Inventory; FACIT, Functional Assessment Of Chronic Illness Therapy; PSQI, Pittsburgh Sleep Quality Index; DTI, diffusion tensor imaging; FC, Connectivité fonctionnelle; DMN, default mode network; CEN, central executive network; ICCTF, International Cognition and Cancer Task Force; MDASI, MD Anderson Symptom Inventory, SCWT, Stroop Color and Word Test; VFT, Verbal Fluency Test; COWAT, Controlled Oral Word Association Test, SART, Sustained Attention to Response Test; RRS, Ruminative Responses Scale; RBMT-II, Rivermead Behavioral Memory Test; BADS, Behavioural Assessment of the Dysexecutive Syndrome; CDT, Clock Drawing Test; ACT, Acceptance and Commitment Therapy; CALM, Managing Cancer and Living Meaningfully; CBT-I, Cognitive Behavioral Therapy for Insomnia; BVMTR, Brief Visuospatial Memory Test-Revised; LNS, Letter-Number Sequencing Test; BCPT, Breast Cancer Prevention Trial; SOSICD, Symptoms of Stress Inventory - Cognitive Disorganization; CFQ, Cognitive Failures Questionnaire. PRMQ, POMQ, Prospective and Retrospective Memory Questionnaire; UFOV, Useful Field of View; FAB, Frontal Assessment Battery; PAOFI, Patients Assessment of Own Functioning Inventory; FEDA, Fragebogen erlebter Defizite der Aufmerksamkeits; BAPM, brief assessment of prospective memory; FrSBE, MMQ, Mini-Mental Question, AFI, assessment of functional Impairment; SSMQ, Squire Subjective Memory Questionnaire.

restorative model that may overlook earlier windows of vulnerability in the cancer trajectory [2[■],5[■]].

Within this emerging neurobiological framework, a recent review has proposed a neuroprotective model of CRCI prevention, emphasizing interventions implemented before or during chemotherapy, including physical activity, cognitive, pharmacological, nutritional, and multimodal approaches [5[■]]. This work marks a shift from a predominantly restorative to a preventive perspective grounded in biological and neurocognitive mechanisms such as neuroinflammation and altered neuroplasticity.

AYAs with cancer represent a distinct and particularly vulnerable population in this context, as the cognitive demands of this developmental period intersect with cancer-related biological and psychological stressors [19[■],20[■]]. Several reviews emphasize CRCI as a central determinant of global functioning and life trajectories in AYAs [19[■]]. Importantly, cancer and its treatments occur during a period of ongoing brain maturation and cognitive development and may therefore alter cognitive functioning in ways that differ qualitatively from those observed in fully mature adult populations. Despite high cognitive reserve, even subtle inefficiencies may result in marked functional consequences in this population, particularly in academic, vocational, and social contexts.

Despite this recognized vulnerability, AYAs remain markedly underrepresented in CRCI research. Most systematic reviews and meta-analyses primarily focus on older adult populations, particularly breast cancer survivors, while AYAs are often excluded, aggregated with broader age groups, or receive limited dedicated attention [1[■],2[■]]. Consequently, the specific cognitive trajectories, biological correlates, and intervention needs of AYAs remain poorly characterized, and preventive approaches tailored to these developmental periods are largely absent from the literature [19[■],20[■]].

The objective of this review is therefore to provide a critical synthesis of the literature on CRCI and interventions designed to prevent or mitigate its effects, with a particular emphasis on intervention timing and the specific needs of AYAs. This review aims to identify key gaps in current knowledge, discuss methodological and clinical implications, and highlight priority directions for the development of early, neuroprotective interventions tailored to this vulnerable population.

METHODS

A targeted literature search was conducted using the following strategy: (“AYA”[Title/Abstract] OR “adolescent and young adult”[Title/Abstract] OR “young adult”[Title/Abstract]) AND (“cancer”[Title/Abstract] OR “neoplasm”[Title/Abstract]) AND (“cognitive

impairment”[Title/Abstract] OR “cancer-related cognitive impairment”[Title/Abstract] OR “CRCI”[Title/Abstract] OR “cognitive dysfunction”[Title/Abstract]) NOT (“older”[Title/Abstract] OR “pediatric”[Title/Abstract] OR “childhood”[Title/Abstract]).

The search identified 13 records. Three primarily medical studies were excluded as they focused on medical rather than psychological outcomes. The final corpus comprised 10 publications focused on AYAs, published between 2022 and 2026 (see Table 2). Most studies were observational in design ($n = 5$) [21–25], complemented by two qualitative investigations ($n = 2$) [26,27], one interventional feasibility study ($n = 1$) [28[■]], and two narrative or systematic reviews synthesizing the available evidence in this population ($n = 2$) [19[■],20[■]].

OVERVIEW OF THE AYA-SPECIFIC LITERATURE ON CRCI

Prevalence and clinical characteristics of CRCI in AYAs

AYA-specific reviews [19[■],20[■]] and observational studies [22,24] indicate that CRCI is a *common* and heterogeneous condition in this population, with prevalence estimates of approximately 25–30% among AYA cancer survivors [19[■],20[■],22,24]. CRCI most frequently affects attention, processing speed, executive functioning, and working memory [24], and is described by AYAs as fluctuating and context-dependent, often exacerbated by fatigue, stress, and emotional burden [26,27]. Importantly, cognitive impairments can be observed early in the cancer trajectory, including prior to treatment initiation. Indeed, a multicenter study conducted shortly after diagnosis demonstrated that approximately 40% of AYAs exhibited objective deficits in attention and executive control before exposure to systemic therapy, as assessed using standardized neuropsychological testing (CANTAB) [22]. Cognitive difficulties often persist beyond treatment completion and exert a significant impact on quality of life, daily functioning, and psychosocial adjustment. Among AYA survivors, CRCI assessed via self-reported measures has been reported on average up to a decade after diagnosis, and in some very long-term survivor populations, up to approximately 25 years following treatment completion, underscoring the long-term persistence of self-reported cognitive difficulties in AYA cancer survivors [19[■],20[■]].

Dissociation between subjective cognitive complaints and objective performance

A consistent finding across AYA-specific studies is the dissociation between subjectively reported cognitive

Table 2. Summary of AYA-focused publications

Author (year)	Type of article	Period / number of studies	Main objective	Age range	Timing	Outcomes	Main findings
1. Reviews							
Vizer <i>et al.</i> , 2022	Scoping review	January 2011 - November 2021 / 21 studies	To describe the prevalence, associated factors, and impacts of CRCI among non-CNS AYA cancer survivors	15–39 years	Post-treatment	Subjective cognition: patient-reported outcomes (PRO); EORTC QLQ-C30 (cognitive functioning); SF-36; Objective cognition (rare): HVLT, TMT, COWA	Prevalence ≈ 25–30% CRCI is more frequent in women and associated with chemotherapy, fatigue, and psychological comorbidities Marked impairment in role functioning (work, studies) and reduced quality of life Substantial unmet needs regarding information, assessment, and management of CRCI Few longitudinal studies and an almost complete lack of AYA-specific interventions
McGrady <i>et al.</i> , 2023	Narrative review	Not specified	To synthesize psychological outcomes among AYA cancer survivors (including CRCI)	15–39 years	Post-treatment	Emotional health (anxiety, depression, psychological distress) Social functioning (relationships, social integration) Health behaviors (physical activity, diet, tobacco/alcohol use) CRCI (subjective complaints and at-risk categories)	AYAs experience a high burden of psychological distress, persistent social difficulties, and unhealthy behaviors CRCI is under-documented but identified as an emerging clinical issue interacting with mental health and overall functioning
2. Observational studies							
Small <i>et al.</i> , 2025	Comparative observational study	NA / NA	To characterize CRCI in AYAs	18–39 years N = 184	Post treatment	Objective cognition: CANTAB (online): attention (RVP, DMS) executive functions (SWM), memory (PAL) Subjective cognition: PROMIS Cognitive Function, PROMIS Cognitive Abilities Quality of life: PROMIS depression, anxiety, fatigue, sleep, physical functioning	No major differences in objective cognition Marked impairment in subjective cognition Significantly lower quality of life Pronounced subjective-objective discordance
Chan <i>et al.</i> , 2023	Cross-sectional observational study	NA / NA	To assess CRCI prior to treatment in AYAs	15–39 years N = 192	Pre-treatment	Objective cognition: CANTAB: multitasking (MTT), memory (PAL), processing speed (RTI), executive functions (SWM), attention (RVP). Subjective cognition: FACT-Cog v3. Associated factors: fatigue (MFSISF), distress (RSCL). Plasma cytokines and BDNF	Approximately 40% present objective CRCI before treatment Lower cognitive performance compared with controls Subjective-objective discordance Lower BDNF and higher cytokine levels in AYAs Biomarkers associated with cognitive performance
Ng <i>et al.</i> , 2023	Longitudinal observational study	NA / NA	To investigate BDNF as a biomarker of CRCI	15–39 years N = 192	Pre / during treatment	Objective cognition: CANTAB: memory (PAL), attention (RVP), executive functions (SWM), response speed (RTI), Reliable Change Index (RCI). Subjective cognition: FACT-Cog. Associated factors: fatigue (MFSISF), distress (RSCL). Plasma BDNF levels and BDNF polymorphism	Lower BDNF levels in AYAs Low BDNF predicts poorer cognitive performance at follow-up Association between BDNF and cognition

Table 2 (Continued)

Author (year)	Type of article	Period / number of studies	Main objective	Age range	Timing	Outcomes	Main findings
Trudeau <i>et al.</i> , 2025	Longitudinal observational study	NA / NA	To examine cytokines and BDNF as predictors of CRCI	15–39 years (AYAs) N = 177	Pre / during / post treatment	Objective cognition: CANTAB: multitasking (MTT), memory (PAL), attention (RVP), response speed (RTI), executive functions (SWM); RCI biomarkers are linked to poorer cognitive functioning Subjective cognition: FACT-Cog distress (RSCI) Associated factors: fatigue (MFSISF) and Biomarkers and BDNF	Objective and subjective CRCI are more frequent in AYAs than in controls Inflammation is associated with cognitive outcomes: increased inflammatory biomarkers are linked to poorer cognitive functioning BDNF is positively associated with cognitive performance: decreased BDNF levels are observed during and after chemotherapy Effects vary according to treatment phase
Brock <i>et al.</i> , 2022	Longitudinal observational study	NA / NA	To examine the relationship between CRCI and work ability/return to work in AYAs	18–39 years N = 502	Posttreatment	Subjective cognition: COPSOQ - sous-échelle cognitive impairments (concentration, memory, mental clarity, decision-making) Work ability: Work Ability Index (WAI) Effort-oriented coping : PACIS	Approximately 20% experience persistent cognitive difficulties Subjective CRCI is strongly associated with reduced work ability Long-term socio-occupational impact Significantly reduced work capacity: 76% at T1 and 57% at T2; significant improvement between T1 and T2.
3. Qualitative studies							
Tomeitch <i>et al.</i> , 2024a	Qualitative study	NA / NA	To describe the lived experience of CRCI	18–30 years N = 20	Posttreatment	Lived cognition, fatigue, stress, coping, mood, social isolation, coping strategies, functional impact	Persistent cognitive difficulties (attention, memory, concentration) CRCI is modulated by fatigue, stress, sleep, and mood Heterogeneous coping strategies with variable effectiveness Impact on daily life, education, and work
Tomeitch <i>et al.</i> , 2024b	Qualitative study	NA / NA	To explore the relationship between CRCI and mental health	18–30 years N = 20	Posttreatment	Lived cognition, depression, anxiety, unmet needs, implications for care	Bidirectional interaction between cognition and psychological distress Anxiety and depression exacerbate CRCI Frustration, self-criticism, and fear of long-term sequelae Lack of structured CRCI management during follow-up
4. Interventional studies							
Gooch <i>et al.</i> , 2022	Prospective controlled pilot study, non-randomized	NA / NA	To test the feasibility of an early cognitive training program	12–25 years N = 14	During treatment	Feasibility: adherence rate, training time completed, assessment completion rate, satisfaction questionnaires Objective cognition: CogState Brief Battery: processing speed (Detection Test), visual attention (Identification Test), visual learning (One Card Learning), working memory (One Back Test), executive function (Groton Maze Learning Test) Biomarkers: serum BDNF	71% of participants in the intervention group completed more than 80% of the planned activities In the control group, a higher prevalence of deficits was observed in processing speed, visual attention, and working memory In the intervention group, fewer deficits were observed in these domains, with improvements across several scores (non-significant) A global decrease in serum BDNF over time was observed in both groups, with no significant between-group differences

CRCI, cancer-related cognitive impairment; AYA, adolescent and young adult; SF-36, Short-Form 36; HVLT, Hopkins Verbal Learning Test; TMT, Trail Making Test; COWA, Controlled Oral Word Association; CANTAB, Cambridge Neuropsychological Test Automated Battery; RVP, rapid visual information; DMS, delayed match to sample; SWM, spatial working memory; PAL, paired associates learning; MTT, Multitasking Test; RTI, reaction time; MFSISF, Multidimensional Fatigue Symptom Inventory; RSCI, Rotterdam Symptom Checklist; BDNF, brain-derived neurotrophic factor; RCI, Reliable Change Index; FACT-Cog, Functional Assessment of Cancer Therapy – Cognitive Function; COPSOQ, Copenhagen Psychosocial Questionnaire; PACIS, Perceived Adjustment to Chronic Illness Scale.

difficulties and objectively measured cognitive performance. Comparative and observational studies demonstrate that AYAs frequently report pronounced cognitive complaints despite neuropsychological performance remaining within normative ranges, a pattern that appears particularly salient in this age group [20[■],24]. Qualitative studies suggest that standard neuropsychological assessments inadequately capture the real-world functional impact of these difficulties, as even subtle cognitive changes may interfere with demanding academic or early professional activities [20[■],24]. Moreover, qualitative data highlight a bidirectional relationship between cognitive complaints and psychological distress, with anxiety and depressive symptoms exacerbating perceived cognitive inefficiencies and persistent cognitive difficulties further undermining emotional well-being [27].

Biological correlates of CRCI in AYAs

AYA-specific evidence supports the presence of biological correlates of CRCI. Prior to treatment initiation, AYAs with objective cognitive deficits show elevated systemic inflammatory markers and reduced BDNF levels, suggesting early neurobiological vulnerability independent of treatment-related neurotoxicity. The study population mainly comprised patients diagnosed with breast (24%) and head and neck (22%) cancers [22]. Longitudinal studies further indicate that fluctuations in inflammatory markers and BDNF are closely associated with changes in cognitive functioning across the cancer trajectory, with lower BDNF linked to poorer cognitive performance and greater subjective cognitive complaints during chemotherapy [23,25]. Together, these findings support a dynamic model of CRCI in AYAs driven by interactions between inflammation and neuroplasticity.

Functional and developmental impact of CRCI in AYAs

Beyond cognitive test performance, CRCI in AYAs is consistently associated with substantial functional and developmental consequences. Longitudinal evidence indicates that cognitive complaints are among the strongest predictors of reduced work capacity and difficulties with workforce reintegration, with effects that may persist for several years after treatment and interfere with key life transitions related to education, employment, and financial independence [21]. Qualitative studies further highlight CRCI as an “invisible” yet destabilizing consequence of cancer, undermining self-confidence, autonomy, and identity formation during a life stage characterized by

high expectations of productivity and cognitive efficiency [26]. These findings are echoed in AYA-focused reviews identifying CRCI as a central determinant of long-term psychosocial outcomes and life trajectories in this population [19[■],20[■]].

AYA-specific CRCI interventional study

The only AYA-specific intervention study identified is a small prospective pilot trial (n = 14) evaluating the feasibility of a computerized cognitive training program delivered during active cancer treatment [28[■]]. Implemented shortly after diagnosis in AYAs aged 12–25 years, the intervention was feasible and acceptable, with approximately 70% of participants completing at least 80% of the prescribed sessions despite ongoing chemotherapy. Exploratory analyses suggested fewer cognitive deficits in the intervention group than in controls, particularly in processing speed, attention, and working memory [28[■]].

DISCUSSION

The AYA-specific evidence synthesized in this review indicates that CRCI is a frequent, heterogeneous, and clinically meaningful condition in AYAs [19[■],20[■]]. In contrast to adult models largely conceptualizing CRCI as treatment-induced neurotoxicity [1[■],2[■]], evidence in AYAs suggests cognitive impairments that may be detectable prior to treatment and that interact with ongoing neurodevelopmental processes [22,23,25]. Although pre-treatment cognitive alterations have also been reported in adults, they appear particularly salient in AYAs given the combination of ongoing brain maturation, heightened neuroplasticity, and high cognitive demands characteristic of this life stage [19[■],20[■]]. In this context, cancer-related biological perturbations may interfere with normative neurodevelopmental trajectories rather than induce transient deficits, as more commonly assumed in adult models. Longitudinal biological data support conceptualizing CRCI in AYAs as a biologically grounded and evolving process. Elevated levels of inflammatory markers and reduced BDNF levels have been observed prior to treatment initiation in some AYAs, indicating early neurobiological vulnerability independent of treatment-related neurotoxicity [22]. Fluctuations in these markers are closely associated with objective and subjective cognitive trajectories across the cancer continuum [23,25]. While similar mechanisms have been described in adults [5[■],6], their interaction with ongoing neurodevelopment confers a distinct profile of vulnerability and intervention opportunity in AYAs.

A dissociation between subjective cognitive complaints and objective performance is a core feature of CRCI and appears especially relevant in AYAs, likely reflecting high premorbid functioning and demanding academic and early professional contexts [1[■],2[■],20[■],24]. Qualitative evidence further suggests that standard neuropsychological assessments insufficiently capture the real-world functional impact of cognitive difficulties in this population [26,27].

Within this framework, CRCI may be understood as the result of modifiable biological mechanisms that evolve across the cancer trajectory, supporting the potential value of earlier, and possibly preventive, interventions initiated at diagnosis or during active treatment [5[■]]. However, AYA-specific interventional research remains extremely limited. To date, only one pilot study has demonstrated the feasibility and acceptability of an early, digitally delivered cognitive intervention during treatment in this population [28[■]].

This perspective is further supported by a recent scoping review conducted by our group, which demonstrated that multicomponent psychological interventions, particularly those integrating physical activity, cognitive-behavioral strategies, and self-regulation processes, improve psychological adjustment and quality of life in AYAs with cancer [29]. Although cognitive outcomes were not the primary focus, many of the targeted mechanisms overlap closely with pathways implicated in CRCI. Considered within a neuroprotective framework, these findings support the development of integrated, early, and multimodal intervention models aimed at preserving both cognitive and psychosocial outcomes in this vulnerable population [5[■]].

Limitations and methodological perspectives

The AYA-specific CRCI literature is constrained by small and heterogeneous samples, broad age ranges, and substantial variability in cognitive assessment methods and assessment timing. Moreover, the available evidence is largely derived from adult populations, with limited consideration of developmental factors and age-specific vulnerabilities. Most studies rely on cross-sectional designs and lack standardized, developmentally sensitive outcome measures, limiting the characterization of cognitive trajectories and the identification of underlying biological mechanisms. These methodological constraints underscore the need for adequately powered, multicenter longitudinal studies using harmonized cognitive assessment frameworks that integrate objective performance, patient-reported outcomes, functional indicators, and biological markers, with assessments initiated early in the cancer trajectory.

Such approaches are essential to inform the development and evaluation of early, developmentally tailored preventive interventions and to optimize long-term educational, occupational, and psychosocial outcomes in AYAs.

CONCLUSION

In conclusion, CRCI in AYAs is a frequent and clinically meaningful condition that reflects a dynamic, biologically grounded process embedded within ongoing neurodevelopment, with cognitive alterations observable as early as diagnosis. The early implementation of developmentally sensitive and multimodal interventions represents a promising strategy to preserve cognitive functioning and long-term psychosocial trajectories in this particularly vulnerable population.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Haywood D, Henneghan AM, Chan A, *et al.* The effect of non-pharmacological interventions on cognitive function in cancer: an overview of systematic reviews. *Support Care in Cancer* 2025; 33:151.

This umbrella review synthesizes systematic reviews on non-pharmacological interventions for cancer-related cognitive impairment (CRCI) across cancer types and stages. Cognitive training and rehabilitation showed the most consistent benefits; physical activity yielded promising but variable effects, while mind-body, psychological, and multimodal approaches demonstrated limited or short-term efficacy, underscoring heterogeneity and the need for harmonized methods and clearer cognitive outcome definitions.

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This pilot prospective study demonstrates the feasibility of early, computer-based cognitive training as a preventive intervention for cancer-related cognitive impairment (CRCI) in adolescents and young adults undergoing chemotherapy. Exploratory remember aims show that patients receiving cognitive training exhibited less cognitive impairment across several domains compared with controls, while serum BDNF levels declined over time in both groups, suggesting potential cognitive benefit independent of detectable biomarker change and highlighting the need for further validation of BDNF in AYA CRCI.

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