Abstract

Strategies for Managing Cancer-Related Cognitive Impairment (CRCI) in Childhood Cancer Survivors: A Systematic Review with Meta-Analysis

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Citation: Belloni, S., Zucca, M., Caruso, R., Conte, G., Magon, A., & Arrigoni, C. (2026). Strategies for managing cancer-related cognitive impairment (CRCI) in childhood cancer survivors: A systematic review with meta-analysis. *International Journal of Health Supplements*, 1(Suppl. 2), 150–151. https://doi.org/10.82051/ijhs-2026-Suppl2

Winner of the Early Bird Abstract Award

Introduction. Advances in cancer treatment have reduced cancer mortality by 70% in children, leading to a growing population of childhood cancer survivors (CCSs). This population experiences a premature onset of ageing-related morbidities, including cancer-related cognitive impairment (CRCI), attributable to epigenetic age acceleration (EAA). The National Cancer Institute (NCI) has highlighted the importance of early non-pharmacological strategies; however, current evidence regarding their efficacy remains limited. The aim of this study was to systematically map non-pharmacological strategies for managing neurocognitive impairment in childhood cancer survivors and assess their efficacy by including randomized controlled trials (RCTs).

Methods. This systematic review with meta-analysis (PROSPERO: CRD420251008299) followed Cochrane guidelines for systematic reviews of interventions. Six databases were searched from inception to September 2025. Two reviewers independently screened the studies, extracted data, and assessed the risk of bias using the RoB 2 tool.

Results. Thirteen publications representing 11 studies were included, among which two were quasi-randomized studies and six were pilot and feasibility studies. Participants were aged 4 to 17 years and included survivors of brain solid tumors and hematological malignancies. The identified strategies included computerized and non-computerized cognitive training interventions, interactive analog tools, traditional interventions aimed at developing academic and mathematical skills, and physical activity programs. Computerized cognitive training using the Cogmed® platform showed

statistically significant post-intervention improvements across several cognitive domains, including working memory, attention, visuospatial memory, and executive functions, as well as academic skills such as reading and mathematics. These benefits tended to persist over time, with the exception of mathematical skills.

Discussion. The findings suggest improvements in intellectual functioning and cognitive abilities following structured cognitive training programs. Integrating these interventions into clinical pathways may contribute to improving the social integration and long-term outcomes of childhood cancer survivors. Further randomized controlled trials are needed to enable rigorous quantitative synthesis of the evidence and to evaluate interventions tailored to specific age groups.

Keywords: Cancer-Related Cognitive Impairment, Childhood Cancer Survivors, Cognitive Training

Funding: This research received no external funding. **Conflict of Interest:** The authors declare no conflict of interest.