Physical activity, cognitive function, psychological well-being, and quality of life in adolescents and young adults treated for cancer

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Thesis submitted to the University of Ottawa in partial fulfillment of the requirements for the Master of Arts degree in Human Kinetics

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Preface

This thesis is original, unpublished work by the author, Sitara Sharma (SS). The study reported herein was granted ethics approval (H-05-21-6889 - REG-6889) for the project "Physical activity, cognitive function, psychological well-being, and quality of life in young persons treated for cancer" on August 2, 2021.

Under the supervision of Dr. Jennifer Brunet (JB), SS was responsible for study conceptualization and design, data collection, data analysis, and writing. JB provided substantial contributions towards the conceptualization and design, data analysis, and editing of this thesis.

Abstract

Background: Many adolescents and young adults (AYAs) aged 15-39 years describe struggling with cancer-related cognitive impairment (CRCI) after treatment. CRCI (e.g., memory, concentration, and learning difficulties) often causes distress, diminishes quality of life (QoL), and impedes young adults' participation in academic, recreational, and social experiences. Yet, CRCI is poorly understood in AYAs and options to prevent or treat this burdensome side effect are lacking. Based on growing evidence suggesting that physical activity (PA) may enhance cognitive function in older adults, individuals with diseases of cognition, and breast cancer survivors, research exploring links between PA and CRCI in AYAs is warranted. Thus, the purpose of this observational, mixed methods thesis was to explore how AYA cancer survivors experience and cope with CRCI, taking into consideration potential predisposing factors (i.e., medical, psychological), interventional strategies (i.e., PA), and outcomes (i.e., QoL). **Methods:** Over a nine-month period, 90 AYAs who had completed primary cancer treatment self-referred; 49 were eligible and enrolled into the study. Of these, 46 participants (M_{age}=31.4±5.4; 91.3% female; 39.1% blood cancer) completed an online survey and three web-based neuropsychological tests; semi-structured interviews were conducted on a rolling basis with a sub-set (n=16) who reported clinically meaningful CRCI. Quantitative data were analyzed descriptively and qualitative data were analyzed thematically. **Results:** Overall, participants were active based on their self-reported moderate-to-vigorous intensity PA (MVPA; M=27.3±20.6) and relative to scale ranges, they reported moderate levels of depressive symptoms, stress, fatigue, and quality of life (M=12.1±5.5; M=21.1±7.2; M=25.2±11.5; M=68.8±18.3, respectively). On average, participants reported clinically meaningful CRCI (M=44.7±17.4), and as compared to normative values, their neuropsychological test scores indicated poor executive

functioning and processing speed, but not working memory. Bivariate correlations between cognitive function (self-reported and objective) and medical characteristics (i.e., time since diagnosis, cancer stage, chemotherapy exposure) had small-to-moderate effect sizes. Small-to-large correlations were observed between cognitive function and psychological factors (i.e., depressive symptoms, stress, fatigue, QoL). Finally, correlations between cognitive function and MVPA were favourable, though effect sizes were small. Moreover, qualitative data provided insight into how AYAs experience and cope with their cognitive impairment, which was summarized within four themes: (1) *descriptions and interpretations of the CRCI phenomenon*, (2) *effects of CRCI on day-to-day life and QoL*, (3) *cognitive-behavioural self-management strategies*, and (4) *recommendations for improving care*. **Conclusion:** Results confirm that cancer can impact AYAs' cognitive function and have detrimental effects for their daily life and overall QoL. AYAs reported using various cognitive-behavioural self-management strategies, including PA; taken together with quantitative data, findings suggest that PA may be a promising strategy to cope with CRCI. However, high-quality experimental research is needed to confirm this association, test the processes by which this may occur, as well as to determine optimal PA dosages/contexts for managing CRCI.

Keywords: Cognitive function; physical activity; cancer; adolescents; young adults; quantitative; qualitative

Acknowledgements

It really does take a village.

To my supervisor, Dr. Jennifer Brunet:

I know that navigating this degree online was not what either of us expected initially, but I am so grateful for all the time and effort that you have invested in me. Thank you for taking me under your wing, sharing your vast insight, constantly seeking opportunities for me to grow, and for challenging me to be the best researcher that I can be. I appreciate your openness, support, and everything you have done for me on both a professional and personal level. Above all, thank you for nurturing my passion for learning and research, and giving me the space to exercise my creativity throughout. It has been a pleasure working together, and I really look forward to continuing this journey with you as I begin my PhD in the Fall.

To my committee, Dr. Andra Smith, Dr. Melanie Sekeres, & (honorarily) Dr. Natalia Jaworska:

Thank you for taking an interest in my project and for offering your expertise throughout this whole process. I appreciate all the fruitful discussions we have had, your thoughtful input and questions, and your continual support and kindness, even when things went awry. Each of you have helped shape and enhance the quality of this thesis and I am very grateful.

To the individuals who participated in this research:

Thank you for your eagerness and for trusting me with your stories, it has been so incredible learning from all of you.

To my funding sources:

Thank you to the *Social Sciences and Humanities Research Council of Canada* as well as the *University of Ottawa* for supporting my research and granting me the opportunity to concentrate fully on my studies and grow as an early scholar.

To my lab-mate, Jenson:

Thank you for making me feel welcome and supported despite us working miles away from one another—our coffee chats were always a breath of fresh air. I appreciate all your help, guidance, and encouragement during this often ambiguous and daunting process, and I am thrilled to finally be able to work together in person.

To my role model, Michelle,

I owe so much of what I know to you. Thank you for taking a chance on me all those years ago and for fostering my passion for learning and teaching. You are such a bright, supportive light and I genuinely hope to follow in your footsteps one day.

To all my fantastic friends:

While there are far too many of you lovely humans to properly thank, please know just how grateful I am to each of you for always believing in me and reminding me to believe in myself as well (as I often struggle with). Thank you for being patient with my busy schedule, for comforting me when things were tough, for encouraging breaks, and for celebrating my successes like your own. Mel, Sangi, and Chris–thank you especially for every phone call, pep talk, each time you listened to me ramble on as I tried to make sense of my thoughts, and above everything, for always being there. I could not have done this without you.

Finally, to my family:

Thank you from the bottom of my heart for your support and everything you do for me, day in, and day out. I owe it all to you (even if you have no idea what I do). I love you!

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List of Abbreviations

AYA	Adolescent and young adult
QoL	Quality of life
EF	Executive functioning
CRCI	Cancer-related cognitive impairment
PA	Physical activity
ICCTF	International Cancer and Cognitive Task Force
SSRI	Selective serotonin reuptake inhibitor
SNRI	Norepinephrine reuptake inhibitor
FACT-Cog	Functional Assessment of Cancer Therapy—Cognition
PCI	Perceived cognitive impairments
SF-36	36-Item Short Form Health Survey
M-WCST	Modified Wisconsin Card Sorting Test
A-LNST	Auditory Letter-Number Sequencing Test
TMT	Trail Making Test
CES-D-10	10-Item Center for Epidemiologic Studies Depression Scale
PSS-10	10-Item Perceived Stress Scale
FACIT-Fatigue	Functional Assessment of Chronic Illness Therapy—Fatigue
FACT-G	Functional Assessment of Cancer Therapy—General
LTEQ	Leisure-Time Exercise Questionnaire
MET	Metabolic equivalent
MVPA	Moderate-to-vigorous intensity physical activity
LSI	Leisure Score Index
SD	Standard deviation
CI	Confidence interval
IADL	Instrumental activities of daily living

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Chapter 1: Introduction

Globally, over one million adolescents and young adults (AYAs) between the ages of 15-39 years are diagnosed with cancer on an annual basis [1]. While the five-year relative survival rate for most cancers has improved over the past several decades in Canada [2], most AYA cancer survivors experience a myriad of debilitating physical and psychological sequelae that severely diminish their quality of life (QoL) [3]. Cognitive impairments are a common adverse effect of cancer treatments [4]. Indeed, cancer survivors across the lifespan (including AYAs) frequently self-report difficulties with their memory, executive functioning (EF), and processing speed [5], all of which may hinder the successful navigation of day-to-day life. Cancer survivors of all ages also tend to perform worse on neuropsychological tests (i.e., performance-based methods used to assess various cognitive domains) as compared to controls [6-9]. Critically, mild-to-severe cognitive impairments can persist long after completion of cancer treatment [4], and are associated with psychological distress [10] and cancer-related fatigue [11-14]. Cognitive impairments can also give rise to considerable challenges in education, employment, and relationships [15]. Consequently, despite bearing financial and social responsibilities, AYA cancer survivors are often unable to work and contribute to society to the same degree as their peers [16].

Research on cancer-related cognitive impairment (CRCI) has burgeoned in recent years, yet noteworthy limitations remain in the extant literature. Primarily, despite a growing awareness of AYA cancer survivors' unique needs, the vast majority of published studies on CRCI have been conducted with either middle-aged or older breast cancer survivors [5]. As such, there has been a recent call-to-action for increased research and clinical attention to CRCI in AYA cancer survivors [17]. Additionally, there is debate surrounding the applicability of the two predominant

methods of cognitive assessment—namely, objective neuropsychological testing (or performance-based methods) and self-report—and they are both poorly correlated throughout the literature [18]. Objective testing is the current gold standard method of assessment, though many researchers rely solely on self-report of cognitive function [19]. The use of self-report is not surprising as it is clinically meaningful [20] and can capture the impact of CRCI on daily functioning and QoL [19, 21, 22]. However, self-report can also inherently capture psychological distress and confound cognitive function scores, highlighting the importance of using a complementary approach to assess cognitive function. To address both of these limitations, we aimed to quantitatively assess AYA cancer survivors' cognitive function using both self-report *and* performance-based methods (objective 1a) and explore its associations with QoL (objective 1b). Concurrently, due to the scarcity of qualitative research in the current corpus of CRCI literature (particularly in AYAs), we aimed to give voice to AYA cancer survivors by qualitatively exploring their lived experiences with CRCI (objective 2). A deeper understanding of AYAs' perspectives (e.g., the meanings that they ascribe to their cognitive function, how they see CRCI affecting their QoL) can offer valuable insight into the development and implementation of supportive care services to help improve cancer-associated outcomes (e.g., cognitive function) and QoL for this population.

A third shortcoming of past studies is a failure to identify factors beyond sociodemographic characteristics that are associated with CRCI. Preliminary data suggests that certain medical and psychological factors may predispose cancer survivors to a higher risk of cognitive impairment [5, 23]. Thus, we aimed to investigate if cognitive function is associated with select medical characteristics (i.e., cancer stage, time since diagnosis, chemotherapy

exposure) and potentially-modifiable psychological factors (e.g., depressive symptoms, perceived stress, fatigue) (objective 3) in AYAs.

Finally, researchers have largely overlooked strategies that may help mitigate CRCI. Emerging evidence suggests that physical activity (PA) may be one such strategy. PA confers numerous benefits for a range of cancer cohorts, and recent reviews of studies largely conducted with breast cancer survivors present preliminary evidence that PA may help to bolster cognitive function [24, 25]. Seeing as AYA cancer survivors are biologically and psychosocially-unique as a population [26, 27], they may respond differently to PA [28]. Therefore, we aimed to describe the association between PA and cognitive function in AYA cancer survivors (objective 4) as a first step towards understanding if PA may be a promising behavioural intervention for CRCI.

Study Purpose and Objectives

In summary, the purpose of this study was to investigate cognitive function in AYA cancer survivors, taking into consideration potential predisposing factors (i.e., medical, psychological), interventional strategies (i.e., PA), and outcomes (i.e., QoL). The specific objectives were to: (1a/1b) describe cognitive function and its association with QoL in AYA cancer survivors using self-report and performance-based methods, (2) understand the lived experiences of AYA cancer survivors who report clinically meaningful CRCI, (3) examine associations between medical/psychological factors and cognitive function, and (4) explore if PA is associated with cognitive function.

Chapter 2: Literature Review

AYA Cancer Survivors and Cognitive Function

During the past several decades, cancer diagnoses in AYAs have been on the rise [1]. AYA cancer survivors comprise a unique population with tumour biology, prognosis, and survivorship that is distinct from other age groups [29]. Although advancements in cancer treatments have drastically improved survival rates [2], treatments often induce adverse physical and psychological side effects [3]. Accordingly, there is a growing number of AYA cancer survivors living with lingering side effects and experiencing subsequent detriments to their QoL. Cognitive impairments are among the most burdensome sequelae reported by this group [16]. Commonly referred to as CRCI and described as "mental cloudiness" or "brain fog," this phenomenon encompasses difficulties in various cognitive domains—namely, memory, EF, and processing speed [5].

While the exact etiology of CRCI is unclear, the literature suggests that cancer treatments contribute to neural toxicity, immune dysfunction, oxidative stress, and changes to central nervous system vascularization and blood flow [30-32]. These putative mechanisms, as well as genetics, may play a role in the development and trajectory of CRCI, but regardless of the mechanisms at play, the prevalence of CRCI in cancer survivors is concerning. Longitudinal studies indicate that up to 30% of cancer survivors experience CRCI prior to undergoing any anti-cancer therapy, with rates escalating to 75% during treatment and often persisting long after treatment is complete [4, 30]. Persistent CRCI is associated with psychological distress [10] and fatigue [11-14], and it is at the root of many emotional, interpersonal, and economic problems [16]. This makes CRCI important to consider in the context of AYA cancer survivors—a population that faces distinct age-related challenges alongside their cancer-related sequelae.

Specifically, AYAs are in a key phase of psychosocial growth and development, tasked with expectations to function in familial, social, educational, and vocational settings [33]. Unmanaged CRCI may disrupt AYA cancer survivors' abilities to attain major developmental milestones and establish functional roles in society [16], yet, most researchers have only targeted middle-aged and older breast cancer survivors in studies on CRCI [5]. To map the burden of CRCI amongst AYA cancer survivors, research aiming to quantify and qualify their cognitive function is warranted. In addition, it is important to explore the methods that AYAs use to manage CRCI and thus improve their QoL.

Assessing CRCI

To inform a comprehensive oncological treatment plan, assessing cognitive function in cancer survivors, including AYAs, is critical [34]. There are two main ways cancer survivors' cognitive function has been assessed in the literature: objective neuropsychological testing (or performance-based approaches) and self-report. Although both methods have their respective strengths and limitations, they are seldom used in concert to assess CRCI; on the rare occasion that they are, both methods are poorly correlated [18].

The International Cancer and Cognitive Task Force (ICCTF) [35] recommends the use of objective neuropsychological tests to assess cognitive function and advises that such tests be administered under controlled, optimal conditions to capture participants' "best" cognitive performances. As such, neuropsychological testing has traditionally been conducted in laboratory settings; however, the ongoing COVID-19 pandemic has necessitated researchers to adapt and provide remote assessment options [36]. While in-person, pen-and-paper methods remain the standard (and for many, the preferred) way of testing, online testing forms (e.g., Inquisit 6 Web, CogState, NIH Toolbox Cognition Battery) are seen as an attractive solution for continuing

cognitive research during this unprecedented time. In many ways, online neuropsychological tests resemble in-person tests and offer advantages such as permitting simultaneous testing of many individuals, increasing convenience (i.e., participants can complete testing at times that suit them and from their own homes) and saving resources like time (i.e., no travel needed to-and-from testing locations) and costs (i.e., related to test administration/scoring) [37]. By reducing barriers (economic and otherwise) for participants, this form of testing may allow for the inclusion of more diverse research samples [38]. Nevertheless, it can also pose some challenges. For example, online testing may be difficult to navigate and require extra time to adjust to the system/software (especially for those who are not computer literate), and external disturbances (e.g., noisy environments) or infrastructure problems (e.g., unstable internet connection; especially for rural-dwelling individuals) may affect participants' performances. More importantly, online testing scores may not be comparable to norms developed from in-person testing, highlighting a need to establish psychometric properties and normative data for computer-based tests [36]. Even so, as the many advantages of online neuropsychological testing can negate the disadvantages of in-person testing, the former should be accepted as a way to assess CRCI so long as researchers acknowledge its limitations. Though a universally-accepted, standardized battery of tests does not currently exist to assess CRCI, it has been recommended to select tests covering memory, EF, and processing speed as longitudinal research with cancer survivors indicates noteworthy deficits in these cognitive domains [35]. Importantly, several studies have demonstrated inferior neuropsychological test performance in middle and older-aged breast cancer survivors in comparison to the general population in such domains [6-9], but few researchers have objectively assessed cognitive function in AYA cancer survivors.

On the other hand, self-report is largely administered in the form of questionnaires (either in-person or online) and it focuses on *perceived* changes in cognitive domains and abilities. Similar to objective testing, self-report has frequently been used to assess cognitive function in middle-aged and older breast cancer survivors [13, 14, 39-43], with sparse research focusing on perceived cognitive impairments in AYA cancer survivors (see [10, 33, 44, 45] for exceptions). Self-report measures generally ask about participants' experiences during the past week or month; thus, they help capture *overall* cognitive function and QoL (unlike objective testing that captures cognitive function at a single time point) [19, 21]. Moreover, self-report is clinically meaningful as cancer survivors' perceptions of their own cognitive function are valuable to healthcare providers in improving patient-centered care [17, 20]. Due to these benefits and other advantages such as lower costs, many researchers predominantly rely on self-report to assess cognitive function [19]. However, it is important to note that self-report has a considerable limitation. That is, some studies in breast cancer survivors have shown associations between self-reported psychological factors (e.g., depression, stress, anxiety, fatigue) and cognitive complaints, though not with objective test scores [46, 47]. This suggests that self-report may inherently capture psychological distress and related symptoms as opposed to actual cognitive impairment [19] and underscores the importance of also using objective measures when assessing cognitive function. Altogether, despite inconsistencies between self-report and objective measures of cognitive function, both types of assessment provide valuable information and should be employed concurrently to inform a more rounded understanding of CRCI in AYA cancer survivors [19].

Beyond assessing cognitive function through quantitative measures, it is important to give AYAs a voice to express their lived experiences with CRCI, though few qualitative studies

have been published on this topic. A review by Selamat and colleagues [48] synthesized the sparse corpus of qualitative research on CRCI; they found that breast cancer survivors often experienced significant emotional, psychological, social, and employment-related struggles due to their cognitive impairments, and that participants faced difficulties with adjusting to and self-managing their CRCI. Similar findings have been reported in more recent qualitative studies exploring CRCI in cervical [49] and breast cancer survivors [50], though AYA cancer survivors have largely been neglected. Therefore, future qualitative research should explore the meanings that AYAs ascribe to their CRCI and how it impacts their QoL. This will allow for a deeper understanding of CRCI and thus help inform a more holistic, patient-centered treatment plan for this population.

Associated Risk Factors

Preliminary data suggest that certain medical characteristics impair neurological function and may predispose cancer survivors to a higher risk of CRCI. [5, 23]. For example, CRCI has been shown to vary based on cancer type [43] and stage [51]. As well, time since diagnosis has been associated with CRCI such that its prevalence often increases during treatment and decreases post-treatment, though remaining higher than at diagnosis. Indeed, longitudinal studies have demonstrated objective cognitive impairment in approximately 40%, 75%, and 60% of cancer patients before, during, and post-treatment, respectively [52]. Further, chemotherapy exposure has a particularly well-established link with CRCI [53]. Last, such characteristics (i.e., cancer type and stage, time since diagnosis, chemotherapy exposure) have been associated with varying levels of neurotoxicity in cancer survivors, further reinforcing the notion that they may be risk factors for CRCI [23].

Although identifying medical correlates of CRCI is an important first step in understanding this phenomenon and was investigated in this study, factors beyond these must also be elucidated. It is speculated that psychological factors may also increase risk of cognitive impairment in cancer survivors. Psychological distress (e.g., depression, stress, fatigue) can adversely affect cognitive function in healthy and ill patient populations [34]. Such factors have received attention in diseases of cognition such as mild cognitive impairment and dementia [54, 55], but they have seldom been explored within a cancer context [56]. This is problematic because psychological well-being is often threatened following a cancer diagnosis [56] as this is a highly stressful event [57, 58]. AYA cancer survivors are at risk for psychological distress since younger age has been consistently associated with higher rates of distress and psychiatric disorders in adult cancer survivors [59-61]. Given that psychological distress is known to be related to cognitive function in persons with a variety of cognitive disorders [62], various psychological factors contributing to psychological distress may also be associated with CRCI in AYAs. Indeed, research conducted in breast cancer survivors has demonstrated associations between cognitive complaints and four modifiable psychological risk factors: anxiety [11, 13, 14, 18, 39, 40], depression [11, 13, 18, 39-41], post-traumatic stress disorder [12], and cancer-related fatigue [11-14]. Such findings suggest that perceived cognitive impairments relate to psychological distress in middle-aged and older breast cancer survivors, however, these associations need to be examined and confirmed in AYA cancer survivors. To this end, it is important to explore how cognitive function (self-report and objective) may relate to psychological factors like depressive symptoms, perceived stress, and fatigue in AYAs. Furnishing a better understanding of associated potentially modifiable factors may help inform interventions to manage effects of CRCI for this population.

Physical Activity and Cognitive Function

Therapeutic options to prevent or treat CRCI remain elusive. While pharmacological therapies have shown some promise in improving cognitive function for neurodevelopmental and psychiatric disorders [63], those tested to reduce the suspected mechanisms of CRCI (e.g., neurotoxic effects on brain morphology, neural inflammation, oxidative stress, and alterations to central nervous system vascularization) have had limited success [30, 64]. Even if such drug therapies were to work, the use of pharmacotherapy may not be optimal in many cases as these treatments are often unable to remediate other adverse effects of cancer and may be contraindicated in some cancer survivors [65]. In this way, since cognitive difficulties have a negative impact on QoL (e.g., independence, return-to-work/school, social role functioning, etc.), it is necessary to investigate other methods of managing or reducing CRCI.

Cognitive benefits of PA have been observed in older adults and individuals with diseases of cognition (i.e., mild cognitive impairment and Alzheimer's disease) [66, 67]. Recent published reviews have also suggested the use of PA to bolster both objective and subjective cognitive function in cancer survivors [24, 25]. For instance, Galiano-Castillo and colleagues [68] reported improved performance on two neuropsychological tests (i.e., Auditory Consonant Trigrams and the Trail Making Test) assessing memory, EF, and processing speed in middle-aged breast cancer survivors following a resistance PA intervention. Similarly, Gokal and colleagues [69] found improvements in self-reported cognitive function in middle-aged breast cancer survivors following a home-based aerobic PA intervention. While encouraging, these trials (and most others) have solely assessed the impact of PA on cognitive function in one cancer cohort (i.e., middle-aged/older breast cancer survivors) and report inconsistent results [5, 70]. Thus, these findings may not be generalizable to AYA cancer survivors—a biologically and

psychosocially-distinct group [26, 27] that may respond differently to PA [28]. Given the deleterious impacts that CRCI has on QoL in AYAs, it is important to confirm the association between cognitive function and PA in this specific group. As a first step, finding evidence that AYA cancer survivors who engage in higher levels of PA report/demonstrate better cognitive function and QoL would encourage future PA-based trials for this population.

Current Study

As summarized in Table 1, the objectives of this study were to: (1a) describe cognitive function using self-report and performance-based methods and (b) its association with QoL in AYA cancer survivors, (2) understand the lived experiences of AYA cancer survivors who report clinically meaningful CRCI, (3) examine whether cognitive function is associated with select medical characteristics (i.e., time since diagnosis, cancer stage, chemotherapy exposure) and psychological factors (i.e., depressive symptoms, perceived stress, fatigue), and (4) explore if PA is associated with cognitive function. Based on recent reviews [5, 22], we anticipated impaired levels of self-reported and objective cognitive function (objective 1a, hypothesis 1a), positive associations between cognitive function and QoL (objective 1b, hypothesis 1b), inverse associations between cognitive function and cancer stage, chemotherapy exposure, depressive symptoms, perceived stress, and fatigue (objective 3, hypothesis 3a), positive associations between cognitive function and time since diagnosis (objective 3, hypothesis 3b), and positive associations between cognitive function and PA (objective 4, hypothesis 4). Of note, no hypotheses were put forward for objective 2 due to its exploratory nature.

Table 1. *Study Objectives and Hypotheses*

	Study Objectives	**Hypotheses**
1.	a) Describe cognitive function using self-report and performance-based methods and; b) Describe its association with QoL in AYA cancer survivors.	a) Impaired levels of self-reported and objective cognitive function. b) Positive associations between cognitive function and QoL.

2.	Understand the lived experiences of AYA cancer survivors who report clinically meaningful CRCI.	No hypotheses formed due to its exploratory nature.
3.	Examine whether cognitive function is associated with select medical characteristics (i.e., time since diagnosis, cancer stage, chemotherapy exposure) and psychological factors (i.e., depressive symptoms, perceived stress, fatigue).	a) Inverse associations between cognitive function and cancer stage, chemotherapy exposure, depressive symptoms, perceived stress, and fatigue. b) Positive associations between cognitive function and time since diagnosis.
4.	Explore if PA is associated with cognitive function.	Positive associations between cognitive function and PA.

Notes. QoL=quality of life; AYA=adolescent and young adult; CRCI=cancer-related cognitive impairment; PA=physical activity.

Chapter 3: Methods

Epistemological Approach and Study Design

This observational study was rooted in a pragmatic epistemology, wherein the underlying belief is that researchers should use the philosophical and/or methodological approach(es) most appropriate for answering their particular research question(s) [71]. Pragmatism enables one to embrace a plurality of data collection methods to both practically and holistically address their research objectives. To address the objectives of this study and gain a broader perspective on the topic, a mixed methods methodology [72] was employed. Specifically, both quantitative and qualitative data were collected concurrently using three methods: a self-report survey, neuropsychological tests, and a semi-structured interview. The quantitative methods provided the data necessary to address objectives 1, 3, and 4, whereas the qualitative method was used to address objective 2.

Participants

Potential participants were screened for eligibility based on the following inclusion criteria: (1) diagnosed with cancer between the ages of 15 to 39 years and *currently* between the ages of 16 to 39 years,[1] (2) completed primary treatment for non-metastatic cancer, (3) have access to the Internet and audio-visual devices, and (4) able to read, speak, and provide written informed consent in English. Exclusion criteria included: (1) traumatic brain injury or concussion with residual symptoms (e.g., dizziness, headaches, loss of concentration) at the time of screening, (2) actively taking selective serotonin reuptake inhibitor (SSRI) or norepinephrine reuptake inhibitor (SNRI) medication to treat a major mood disorder, and (3) having received a

[1] The National Cancer Institute defines AYA cancer survivors as individuals aged 15-39 years who are diagnosed with cancer and living until the end of life (i.e., from diagnosis onwards; www.cancer.gov/types/aya). Since the age of consent in the province of Ontario is 16, individuals between 16-39 years who have been treated for cancer were recruited to reduce recruitment burden.

diagnosis of a substance use disorder (e.g., alcohol, narcotics) by a medical professional within the past year. No restrictions were set for country of residence.

Sample Size

Since the quantitative and qualitative methods in this mixed methods study address separate objectives, the respective sample sizes had to be appropriate to collect and analyze data for each method. The exact number of participants required for quantitative descriptive research can vary. One point of view is that the sample size must be at least 10 times the total number of items/variables to obtain normal distributions in quantitative descriptive research; this would require recruitment of 120 participants since there are 12 variables (i.e., time since diagnosis, cancer type, chemotherapy exposure, self-reported cognitive function, three tests of objective cognitive function, depressive symptoms, perceived stress, fatigue, QoL, and PA). The other point of view is that a relatively small sample size is adequate for such research so long as the sample is representative, though it should not be less than 30. The goal was to get as close as possible to the former, but despite persistent recruitment efforts, the target sample size was not attained. Rather, 49 participants were recruited over a nine-month period, 46 of which provided data for analysis. This means that the margin of error (which indicates how much one can expect their overall population estimates to vary as a function of the observed scores, and thus represents the precision of the estimates) *might* be larger. To inform readers about this, margins of errors (or, equivalently, confidence intervals) were computed and reported for all estimates.

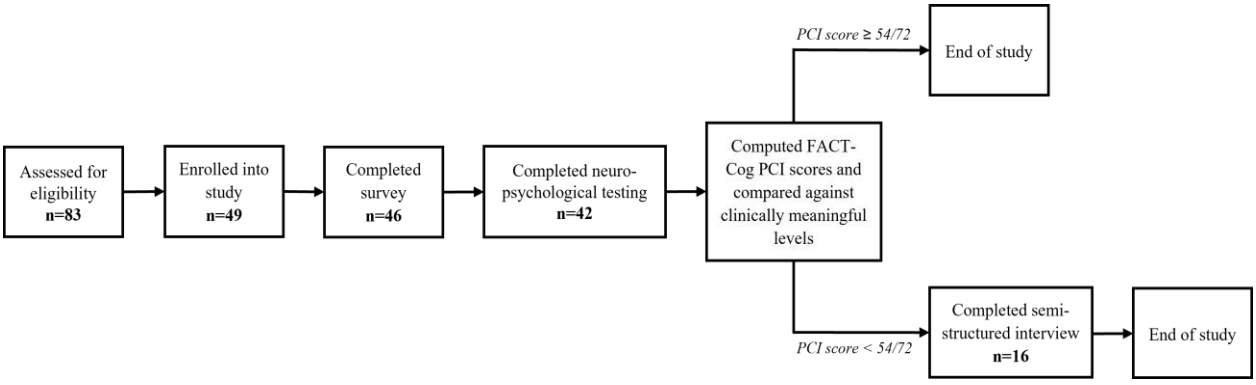
Recommendations for sample sizes in qualitative research are more consistent; they favour smaller sample sizes for conducting in-depth qualitative analyses [73]. Thus, the aim was to interview approximately 10-15 participants who completed the quantitative methods, although recruitment and interviewing continued until theme saturation was met [74].

Data Collection

An overview of the study flow is presented in Figure 1. Following approval from the University of Ottawa Research Ethics Board (**Appendix A**), participants were recruited by: (1) advertising the study using a flyer (**Appendix B**) on social media websites (e.g., Facebook, Twitter, Instagram), (2) posting information about the study on cancer support groups' and organizations' websites (e.g., www.youngadultcancer.ca, www.stupidcancer.org, www.survivornet.ca), and (3) word of mouth. Participants were invited to contact the primary author (SS) via either email (scenario 1) or telephone (scenario 2) if they wished to participate. In scenario 1, SS replied to their email using a recruitment email script (**Appendix C**) containing study details and nine screening questions, to which participants needed to respond (Step 1). If they met eligibility criteria (based on their responses), SS confirmed this with them and sent them an email containing their Participant ID and a "Participant Protocol Document" (Step 2; **Appendix D**); this document contained detailed instructions on how to complete the study, including a SurveyMonkey link to a secure online informed consent form (**Appendix E**). After providing consent (Step 3), participants were automatically directed to a 30–minute survey to complete (Step 4; **Appendix F**), and then directed to the Inquisit 6 Web platform through which they completed a battery of three neuropsychological tests (Step 5). Steps 2-5 were the same for scenario 2; however, for Step 1, SS provided study details and screened potential participants over the phone using a recruitment telephone script (**Appendix G**). In both scenarios, participants were asked to complete Steps 3-5 within one week of screening; up to three reminder emails were sent (i.e., one per week) to those who had not yet provided their informed consent, completed the survey, and completed the neuropsychological tests (unless they indicated that they wished to withdraw from the study).

In addition to quantitative data collection, qualitative data were collected from a sub-sample of participants. Self-report cognitive function scores were used to identify this sub-sample on a rolling basis. Specifically, once participants completed the online survey, the Functional Assessment of Cancer Therapy—Cognition (FACT-Cog; [75]) questionnaire was scored and compared against clinically meaningful levels of cognitive impairment, as determined by Van Dyk and colleagues [76]. Those who scored below 54 (out of a possible 72) on the 18-item Perceived Cognitive Impairments (PCI) subscale of the FACT-Cog were invited to participate in a one-hour semi-structured interview. Guided by an interview guide (**Appendix H**), SS conducted interviews to explore participants' lived experiences with CRCI, as well as the role of PA in their lives. Interviews were conducted online via Zoom and audio-recorded for transcription purposes. Of note, participants were entered into a draw to win a $100 CAD Visa gift card for their time; they received one entry into the draw for each study component that they began (i.e., survey, neuropsychological tests, interview, if applicable), for up to three entries.

Figure 1. *Overview of Study Flow*



Note. FACT-Cog=Functional Assessment of Cancer Therapy—Cognition; PCI=perceived cognitive impairment

Measures

Sociodemographic and Medical Characteristics. Participants self-reported their age, biological sex, gender identity, self-identified ethnicity, civil (relationship) status, highest level

of education attained, household income, employment status, medication and substance-use (if applicable), cancer type and stage, date of cancer diagnosis, and cancer treatment history. Participants also rated their perceived health on a 5-point likert scale ranging from 1 (*excellent*) to 5 (*poor*) using a single item from the 36-Item Short Form Health Survey (SF-36; [77]). These data were used to describe the sample and some were used to address objective 3. Of note, there are additional correlations between cognitive function and the aforementioned characteristics that could have been computed, but a limited number were chosen to reduce the risk of error.

Self-Reported Cognitive Function. The FACT-Cog [75] Version 3 was used to assess self-reported levels of cognitive function and inform who was invited to participate in a semi-structured interview. The FACT-Cog is a 37-item measure designed specifically to assess cognitive impairment and its impact on QoL in cancer survivors. This questionnaire comprises four subscales (i.e., Perceived Cognitive Impairments, Comments from Others, Perceived Cognitive Abilities, and Impact on QoL) and allows cancer survivors to assess their own memory, attention, concentration, language, and thinking abilities over the past week. Responses are given using a 5-point likert scale that spans from 0 (*never/not at all*) to 4 (*several times a day/very much*). Ranging from 0 to 132, FACT-Cog scores are obtained by reverse-scoring negatively-stated items, summing all items, and then summing scores for all subscales; higher scores reflect fewer cognitive difficulties and better QoL. However, based on recommendations from scale developers (see www.facit.org), only the 18-item PCI subscale score (range: 0 to 72) was used for analysis in this study to address objectives 1, 3, and 4, and to help select participants for interviews as described above (to address objective 2). This approach (i.e., limiting analyses to one self-report cognitive function variable) was deemed appropriate given the sample size and a desire to reduce the risk of error. Scores on the FACT-Cog (including PCI

subscale scores) have been found to be highly reliable and valid, and this questionnaire has been used previously with various cancer populations [75].

Neuropsychological Tests. In consideration of the COVID-19 pandemic and to enable wider recruitment, remote neuropsychological testing was conducted using the Inquisit 6 Web platform (www.millisecond.com/products/web) to objectively assess participants' cognitive function. Based on input from a licensed neuropsychologist, three computerized tests (and their specific outcomes) covering memory, EF, and processing speed (i.e., the cognitive domains most vulnerable to the adverse effects of cancer treatments; [5]) were selected and completed by participants in the same order. The first test was the Modified Wisconsin Card Sorting Test (M-WCST; [78]) for EF. Scores reflect the percentage of perseverative errors; higher values indicate worse EF. The second test was the Auditory Letter-Number Sequencing Test (A-LNST; [79]) for working memory. Scores reflect the total points received in reordering digits/letters (i.e., recalling digits in ascending numerical order, followed by letters in alphabetical order); higher scores reflect better working memory. The third test was the Trail Making Test (TMT; [80]) for EF/processing speed. Scores reflect the time taken to complete Trails B (i.e., TMT B) in seconds; higher values reflect worse EF/processing speed. Each test was preceded by clear instructions and a practice test through Inquisit to give participants a chance to familiarize themselves prior to actual assessment. Of note, given the online nature and copyrights, these tests are not presented in the Appendices. Participants were instructed to complete these tests on a computer (rather than a mobile device) in a quiet environment with limited noise and distractions. Participants were also asked to record information regarding the device used (i.e., year and model of computer, size of screen) to help better understand test results in case an ad hoc review is needed. Test results were used alongside self-report results to address objectives 1, 3, and 4.

Psychological Factors. The 10-Item Center for Epidemiologic Studies Depression Scale (CES-D-10; [81]) was used to assess psychological distress. The CES-D-10 is a 10-item self-report checklist which measures depressive symptoms in the past week. Responses are indicated using a 4-point likert scale that spans from 0 (*rarely or none of the time; less than 1 day*) to 3 (*all of the time; 5-7 days*). Ranging from 0 to 30, CES-D-10 scores are obtained by reverse-scoring positively-worded items and then summing all items; higher scores indicate greater depressive symptomology. The CES-D-10 has been used previously with cancer populations [82] and has been shown to be both valid and reliable across diverse groups [83-85].

The 10-Item Perceived Stress Scale (PSS-10; [86]) was used to assess perceived stress. The PSS-10 assesses the degree to which participants appraise situations in their life as stressful over the last month. Responses are given using a 5-point likert scale that spans from 0 (*never*) to 4 (*very often*). Ranging from 0 to 40, PSS scores are obtained by reverse-scoring positively-stated items and then summing all responses; higher scores reflect higher perceived stress. Widely used to measure global perceptions of stress, the PSS-10 has been employed in trials testing psychological factors such as stress, anxiety, and depression in adults treated for cancer [87, 88]. PSS-10 scores have shown adequate reliability and validity [89].

The Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue; [90]) was used to assess self-reported levels of fatigue in the past week. The FACIT-Fatigue is a 13-item measure which asks participants to report on chronic illness-related fatigue and its impact upon daily activities and function. Responses are indicated using a 5-point likert scale that spans from 0 (*not at all*) to 4 (*very much*). Ranging from 0 to 52, FACIT-Fatigue scores are obtained by reverse-scoring negatively-worded items and then summing all items; higher scores reflect less fatigue. Of note, item 8 (i.e., “I am able to do my usual activities”) was not included in the

survey due to human error; thus, the upper score limit is 48 (instead of 52) for the purpose of this study. Scores on the FACIT-Fatigue have been shown to be a valid and reliable measure of fatigue in cancer survivors [90, 91]. Taken together, the three aforementioned measures pertaining to psychological factors (i.e., the CES-D-10, the PSS-10, and the FACIT-Fatigue) were used to address objective 3.

QoL. The Functional Assessment of Cancer Therapy—General (FACT-G; [92]) was used to assess self-reported QoL in the past week. The FACT-G is a 27-item measure that comprises five subscales (i.e., physical well-being, social/family well-being, emotional well-being, functional well-being, and fatigue). Participants are asked to report their health-related QoL using a 5-point likert scale that spans from 0 (*not at all*) to 4 (*very much*). Ranging from 0 to 108, FACT-G scores are obtained by reverse-scoring negatively-worded items, summing all items, and then summing scores for all subscales; higher scores indicate better QoL. There is substantial evidence for the reliability and validity of the FACT-G in a range of cancer cohorts [93]. Global FACT-G scores were used to address objective 1.

PA. The Leisure-Time Exercise Questionnaire (LTEQ; [94]) was used to assess PA levels. The first item probes the number of times participants engaged in light/mild, moderate, or strenuous/vigorous intensity PA for a minimum of 15 minutes during their leisure time in a typical week. Although different PA recommendations exist, most are consistent with each other and recommend that cancer survivors accumulate at least 150 minutes of moderate-to-vigorous intensity aerobic training per week for health benefits (e.g., www.cancer.org/healthy/eat-healthy-get-active/get-active/fitting-in-fitness.html). Accordingly, this study was focused on moderate and strenuous/vigorous PA. For analysis, the frequency scores for moderate and vigorous PA were multiplied by a corresponding metabolic equivalent for task (MET) value (i.e., moderate

*5; vigorous *9), and summed to obtain a moderate-to-vigorous intensity PA (MVPA) Leisure Score Index (LSI). Cut-off points can be created using the LSI; a MVPA LSI ≥ 24 indicates that an individual is *active*, whereas a MVPA LSI < 24 indicates that they are *insufficiently active* [95]. Thus, participants scoring ≥ 24 are likely to meet most PA guidelines [96]. The LTEQ has demonstrated reliability and validity with accelerometer data [97] and this measure has been widely-used in studies with adult cancer survivors [96]. Both continuous MVPA LSI scores and derived MVPA LSI classifications (i.e., *active* and *insufficiently active*) were used to address objective 4.

Interview Guide. An interview guide was developed, pilot-tested, and revised based on feedback to explore participants' lived experiences with CRCI and the role of PA in their lives. Open-ended questions centered on: (1) participants' views of predisposing factors to their cognitive impairments, (2) how they felt these impairments have impacted their QoL, as well as (3) any strategies they used to manage these impairments. Probes were used when responses lacked sufficient detail, depth, or clarity [98]. Finally, follow-up questions were used to further pursue central themes, elaborate on the context of answers, and explore the implications of what was said. This tool was used to collect the data necessary to address objective 2.

Quantitative Data Analysis

Quantitative data were managed in Microsoft Excel (Version 2203) and analyzed using IBM SPSS Statistics (Version 28). Descriptive statistics (i.e., means, standard deviations (SD), frequencies, ranges) were computed for all study variables to describe the sample (and subsample interviewed) and address objective 1a. For the latter, means and standard deviations (and corresponding confidence intervals) were computed for self-reported cognitive function (based on the FACT-Cog PCI subscale) and each objective cognitive function test used (i.e., M-

WCST, A-LNST, TMT). To address objective 1b, the association between cognitive function and QoL was estimated using Pearson correlations. To address objective 3, bivariate correlations (i.e., Pearson for correlations involving two continuous variables [i.e., time since diagnosis, depressive symptoms, perceived stress, fatigue, self-reported cognitive function, each of the three objective cognitive function tests] and Spearman for correlations involving a categorical variable [i.e., cancer stage, chemotherapy exposure]) were computed to describe the associations between medical/psychological variables and cognitive function (self-report and objective). Finally, to address objective 4, bivariate correlations were computed to describe the associations between cognitive function (self-report and objective) and MVPA (i.e., Pearson for continuous MVPA LSI and Spearman for derived MVPA classifications). Effect sizes (r) were computed to describe the magnitude of associations; effect sizes of $r=\pm.10$, $r=\pm.30$, $r=\pm.50$ were interpreted as small, moderate, and large correlations, respectively [99].

Qualitative Data Analysis

Qualitative data were managed and analyzed using Microsoft Word (Version 2203). Each interview was transcribed verbatim by SS within one week of the interview. Coding and theme development was done inductively by SS following Braun and Clarke's [100] six-step guidelines for conducting thematic analysis. First, SS immersed herself within the data by reviewing each transcript several times. Second, once familiar with the transcripts, initial codes were generated for each participant. This involved systematically coding salient features of the raw data across all interviews; salient features were determined based on their relevance to the research purpose. Third, sub-themes were developed by grouping similar codes within each interview. Fourth, similar sub-themes were reviewed and grouped together into main themes. SS then compared results and created a master table to represent main themes and sub-themes. Fifth, themes were

defined and named to capture their essence. Following this, JB reviewed the themes in relation to the raw data and relevance to the research objective. Finally, SS refined themes and sub-themes, selected compelling quotes from transcripts to illustrate each, and prepared this written report to relay the data and communicate participants' experiences.

Qualitative Rigor

To enhance the rigor and trustworthiness of qualitative data, several steps were undertaken. First, the interview guide was pilot-tested. For this, an AYA cancer survivor was selected purposively to garner her opinions on the guide's structure, questions/probes, and feasibility to be conducted within the allotted time (to avoid increasing participant burden). Based on her feedback, the interview guide was revised prior to interviewing participants. In addition, open-ended questions were asked to allow participants to express what they felt was important and expand upon/alter responses as they wished. By being empathetic and attentive throughout, SS developed rapport with participants, which is key to a constructive qualitative interview [101]. Further, a thorough analysis of interviews was conducted by SS, and she engaged in critical discussions with JB while developing and reporting themes/subthemes. Also, SS took time to acknowledge and reflect upon any preconceptions, personal experiences, and prior knowledge of the literature while interpreting data. Finally, detailed descriptions of the research process and analyses have been provided above to ensure transparency.

Chapter 4: Results

Quantitative Results

Sample

In total, 49 AYAs were enrolled and consented to the study, but three did not provide any data. Thus, the analytic sample was comprised of 46 survivors of AYA cancer between 23 to 39 years of age (M_{age}=31.4±5.4) at the time of data collection (see Table 2 for characteristics). Regarding sociodemographic information, most participants were born female (91.3%; n=42), self-identified as White (69.6%; n=32), were married or living with a partner (52.2%; n=24), had completed post-secondary education (89.1%; n=41), were either working or transitioning into work (73.9%; n=34), and had an annual household income below $100,000 CAD (67.4%; n=31). In terms of medical characteristics, participants were between 15 to 38 years of age at diagnosis (M_{age}=28.3±6.2) and their time since diagnosis ranged from 0 to 10 years (M_{age}=3.2±2.9). There was diversity in cancer stage, type, and treatments reported, but most were diagnosed with stage II cancer (37.0%; n=17), a blood cancer (30.4%; n=14) and received surgery as primary treatment (76.1%; n=35). Participants largely perceived their overall health as "Good to very good" (73.9%; n=34). Further, 13.0% (n=6) reported previous concussion(s) and 26.1% (n=12) reported cannabis use in the past month. The sub-sample who participated in the semi-structured interview was comprised of 16 AYAs who were between 23 to 39 years of age (M_{age}=30.8±6.0) at the time of data collection and followed similar sociodemographic and medical trends as the total sample.

Table 2. *Participants' Sociodemographic and Medical Characteristics*

	Total Sample Values (n=46)	**Sub-Sample[a] Values (n=16)**
Sociodemographic Characteristics		
Current age (M years ± SD; range)	31.4 ± 5.4; 23-39	30.8 ± 6.0; 23-39
Sex, *n* (% female)	42 (91.3)	14 (87.5)

Gender identity, *n* (% woman)	41 (89.1)	14 (87.5)
Ethnicity, *n* (% White)	32 (69.6)	12 (75.0)
Civil status, *n* (% married or common law)	24 (52.2)	7 (43.8)
Highest level of completed education, *n* (% post-secondary)	41 (89.1)	15 (93.8)
Vocational status, *n* (% working or transitioning to work)	34 (73.9)	10 (62.5)
Annual household income, *n* (% < $100,000 CAD)	31 (67.4)	12 (75.0)
Medical Characteristics		
Age at diagnosis (M years ± SD; range)	28.3 ± 6.2; 15-38	27.6 ± 7.9; 15-38
Time since diagnosis (M years ± SD; range)	3.2 ± 2.9; 0-10	3.2 ± 3.0; 0-10
Cancer stage, *n* (%)		
I	6 (13.0)	1 (6.3)
II	17 (37.0)	7 (43.8)
III	15 (32.6)	3 (18.8)
N/A or do not know	8 (17.4)	5 (31.3)
Cancer type, *n* (%)		
Blood	14 (30.4)	4 (25.5)
Breast	13 (28.3)	3 (18.8)
Sarcoma	4 (8.7)	3 (18.8)
Brain	4 (8.7)	2 (12.5)
Carcinoma	4 (8.7)	1 (6.3)
Gynecologic	3 (6.5)	2 (12.5)
Colorectal	2 (4.3)	0 (0)
Melanoma	1 (2.2)	1 (6.3)
Testicular	1 (2.2)	0 (0)
Treatments received, *n* (%)		
Surgery	35 (76.1)	13 (81.3)
Chemotherapy	34 (73.9)	11 (68.8)
Radiation	26 (56.5)	9 (56.3)
Hormonal	13 (28.3)	3 (18.8)
Other	8 (17.4)	3 (18.8)
Perceived overall health, *n* (%)		
Poor to fair	9 (19.6)	6 (37.5)
Good to very good	34 (73.9)	10 (62.5)
Excellent	3 (6.5)	0 (0)
Previous concussion(s), *n* (%)	6 (13.0)	2 (12.5)
Cannabis use in the past month, *n* (%)	12 (26.1)	7 (43.8)

Notes. SD=standard deviation.
[a]Sub-sample refers to participants interviewed.

Descriptive Statistics

As seen in Table 3, relative to scale ranges, participants reported moderate levels of depressive symptoms (M=12.1±5.5; scale range=0-30), perceived stress (M=21.1±7.2; scale range=0-40), fatigue (M=25.2±11.5; scale range=0-48), and QoL (M=68.8±18.3; scale range=0-108). On average, participants were physically active based on their self-reported MVPA (M=27.3±20.6), and 24 (52.2%) had a MVPA LSI ≥24 (i.e., the established cut-point [95] for

being classified as "active"). The mean PCI subscale score[2] (M=44.7±17.4; range=0-72) fell within the clinically meaningful CRCI range [76], with 28 participants (60.9%) scoring below the 54/72 cut-point used to discriminate CRCI cases from non-cases. In terms of objective cognitive functioning, participants' average M-WCST score (measured via % perseverative errors; M=33.7±27.8) placed them in the 20th percentile rank as compared to norms from a heterogenous sample of healthy individuals aged 16-75 years [102][3], indicating poor EF performance. Participants' average A-LNST score (measured via total points received in reordering digits/letters; M=12.7±2.4) was above the normative value (M=8.7±2.9) for healthy adults aged 19-60 years [103][3]; this *may* suggest that working memory was not as affected as EF in this sample. Finally, participants' average TMT score (measured via time taken to complete TMT-B in seconds; M=54.5±17.6) placed them in the 40th percentile rank as compared to age-stratified norms for healthy individuals aged 25-34 years [104][3] (i.e., the age bracket corresponding to this sample's average age of 31.4±5.4 years); this indicates poor EF and processing speed performance. Of note, due to scant published norms for computer-based neuropsychological tests, results were compared to norms from non-computerized tests (see **Chapter 5: Discussion**).

Table 3. *Descriptive Statistics for Psychological, PA, and Cognitive Function Variables*

Variables	Values (Mean ± SD; Score Range)	95% CI
Psychological Factors		
Depressive symptoms	12.1 ± 5.5; 3-25	[10.4, 13.7]
Perceived Stress	21.1 ± 7.2; 6-38	[18.9, 23.3]
Fatigue	25.2 ± 11.5; 7-44	[21.7, 28.7]
QoL	68.8 ± 18.3; 30-97	[63.3, 74.3]
PA		
MVPA (continuous)	27.3 ± 20.6; 0-70	[21.0, 33.7]

[2] PCI subscale scores were used in analyses for this study, but descriptive statistics for all other FACT-Cog subscales can be found in **Supplemental File 1**.
[3] Efforts were made to locate age-matched percentiles norms validated from computer-based testing, but none were found; comparison of descriptive statistics should be made with this caveat in mind.

Cognitive Function		
Self-reported cognitive function	44.7 ± 17.4; 4-69	[39.5, 49.9]
Objective cognitive function		
M-WCST (EF)	33.7 ± 27.8; 0-100	[25.0, 42.4]
A-LNST (working memory)	12.7 ± 2.4; 8-19	[12.0, 13.5]
TMT (EF/processing speed)[a]	54.5 ± 17.6; 26.7-98.8	[48.9, 60.2]

Notes. SD=standard deviation; CI=confidence interval; QoL=quality of life; PA=physical activity; MVPA=moderate-to-vigorous intensity physical activity; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking Test; Depressive symptoms (scale range: 0-30); Perceived stress (scale range: 0-40); Fatigue (scale range: 0-48); QoL (scale range: 0-108); MVPA (LSI scores≥24="active"; LSI scores<24="insufficiently active"); Self-reported cognitive function (PCI subscale range: 0-72; scores <54/72 indicate clinically meaningful impairment); M-WCST values represent % perseverative error; A-LNST values represent total points reordered; TMT values represent TMT-B scores in seconds.

[a]TMT data from one participant was excluded from analyses because she experienced tumour-related loss of function in her dominant hand and thus completed the test with her non-dominant hand.

Correlations

As shown in Table 4, correlations between time since diagnosis and cognitive function (self-report and objective) were small and negative (apart from the A-LNST test, which was small and positive), implying that those who reported greater time since diagnosis self-reported lower cognitive function and scored worse on the M-WCST, but better on the A-LNST and TMT. Cancer stage had small positive correlations with self-reported cognitive function and the M-WCST, but small negative associations with the A-LNST and TMT; this suggests that participants with more advanced cancer stages at diagnosis self-reported greater cognitive function and scored better on the M-WCST and TMT, but worse on the A-LNST. Last, there were small negative correlations between chemotherapy exposure and both self-reported cognitive function and the A-LNST, and moderate associations between chemotherapy exposure and both the M-WCST and TMT (positive and negative, respectively); this implies that participants who underwent chemotherapy self-reported lower cognitive function and scored worse on the A-LNST, but better on the M-WCST and TMT.

Table 4. *Bivariate Correlations Between Cognitive Function and Select Medical Characteristics*

Variables	Self-Report Cognitive Function	Objective Cognitive Function		
	PCI	M-WCST (EF)	A-LNST (working memory)	TMT (EF/processing speed)
Time since diagnosis	-.131	-.003	.083	-.077
Cancer stage *(1=stage I; 2=stage II; 3=stage III)*[a]	.055	.159	-.259	-.199
Chemotherapy *(0=no; 1=yes)*[a]	-.060	.314*	-.104	-.316

Notes. PCI=Perceived Cognitive Impairment; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking Test.
Higher TMT scores indicate worse outcomes.
Higher PCI, M-WCST, and A-LNST scores indicate better outcomes.
[a]Spearman rho correlation coefficients; elsewhere, Pearson correlation coefficients.
*p<.05; **p<.01. We note that *p*-values are reported, but effect sizes are interpreted as per APA guidelines.

Table 5 presents correlations between cognitive function, psychological factors, and PA (i.e., continuous MVPA LSI and derived MVPA LSI classifications). There were moderate-to-large negative correlations between self-reported cognitive function and both depressive symptoms and perceived stress, whereby participants who self-reported lower cognitive function reported higher levels of depressive symptoms and perceived stress. There were large positive correlations between self-reported cognitive function and both fatigue and QoL, whereby participants who self-reported lower cognitive function reported greater fatigue and poorer QoL. Relative to correlations observed for self-reported cognitive function, smaller correlations were noted between all three objective tests of cognitive function and each psychological factor. Specifically, there were small negative correlations between the M-WCST and A-LNST and both depressive symptoms and perceived stress and there were small positive correlations between the TMT and the same psychological factors; this implies that those scoring worse on each test reported more depressive symptoms and perceived stress. Correlations between all three objective tests of cognitive function and both fatigue and QoL were also small; their direction implies that those who scored worse on each test reported greater fatigue (apart from

the M-WCST which showed less fatigue with worse performance) and poorer QoL. Finally, correlations between MVPA (continuous and classified) and both self-reported and objective cognitive function (all three tests) were small and their direction implies that participants who were more active self-reported better cognitive function and scored better on the M-WCST and TMT, but worse on the A-LNST.

Table 5. *Bivariate Correlations Between Cognitive Function, Psychological Factors, and PA*

Variables	1	2	3	4	5	6[a]	7	8	9	10
1. Depressive symptoms	-									
2. Perceived stress	.708**	-								
3. Fatigue	-.793**	-.532**	-							
4. QoL	-.831**	-.674**	.819**	-						
5. MVPA LSI (continuous)	-.296	-.154	.380*	.328*	-					
6. MVPA *(0=insufficiently active; 1=active)*[a]	-.342*	-.282	-.351*	-.419*	.863**	-				
7. PCI subscale	-.632**	-.465**	.507**	.594**	.138	.174	-			
8. M-WCST (EF)	-.186	-.137	-.113	.046	.038	.020	.199	-		
9. A-LNST (working memory)	-.189	-.133	.184	.180	-.043	-.112	.308*	.406**	-	
10. TMT (EF/processing speed)	.111	.134	-.241	-.228	-.026	-.027	-.016	-.422**	-.425**	-

Notes. QoL=quality of life; PA=physical activity; MVPA=moderate-to-vigorous intensity physical activity; LSI-Leisure Score Index; PCI=Perceived Cognitive Impairment; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking test.
Higher depression, perceived stress, and TMT scores indicate worse outcomes.
Higher fatigue, quality of life, MVPA, PCI, M-WCST, and A-LNST scores indicate better outcomes.
[a]Spearman rho correlation coefficients; elsewhere, Pearson correlation coefficients.
*p<.05; **p<.01. We note that *p*-values are reported, but effect sizes are interpreted as per APA guidelines.

Of note, although the aim of this study was to explore CRCI in AYA cancer survivors *broadly*, **Supplemental File 2** presents the same tables as above but excludes brain cancer survivors' (n=4; 8.7%) data in acknowledgment that this group's specific tumour locations and/or cancer treatments may confound results. Based on visual comparison of descriptive statistics and correlations, results are very similar to those reported herein and lead to the same interpretations.

Qualitative Results

The average interview length was 69 minutes (range=42-91). Profiles of participants who were interviewed are noted in Table 6. As displayed in Figure 2, four themes comprising 13 subthemes emerged from the data: (1) descriptions and interpretations of the CRCI phenomenon, (2) effects of CRCI on day-to-day and QoL, (3) cognitive-behavioural self-management strategies, and (4) recommendations for improving care. In the following sections, each theme is accompanied by brief representative quotations from individuals identified by pseudonyms; longer excerpts of participants' accounts are provided in **Appendix I**. Of note, in the quotations, […] indicates that text was omitted to enhance clarity.

Table 6. *Profiles of Interview Participants (n=16)*

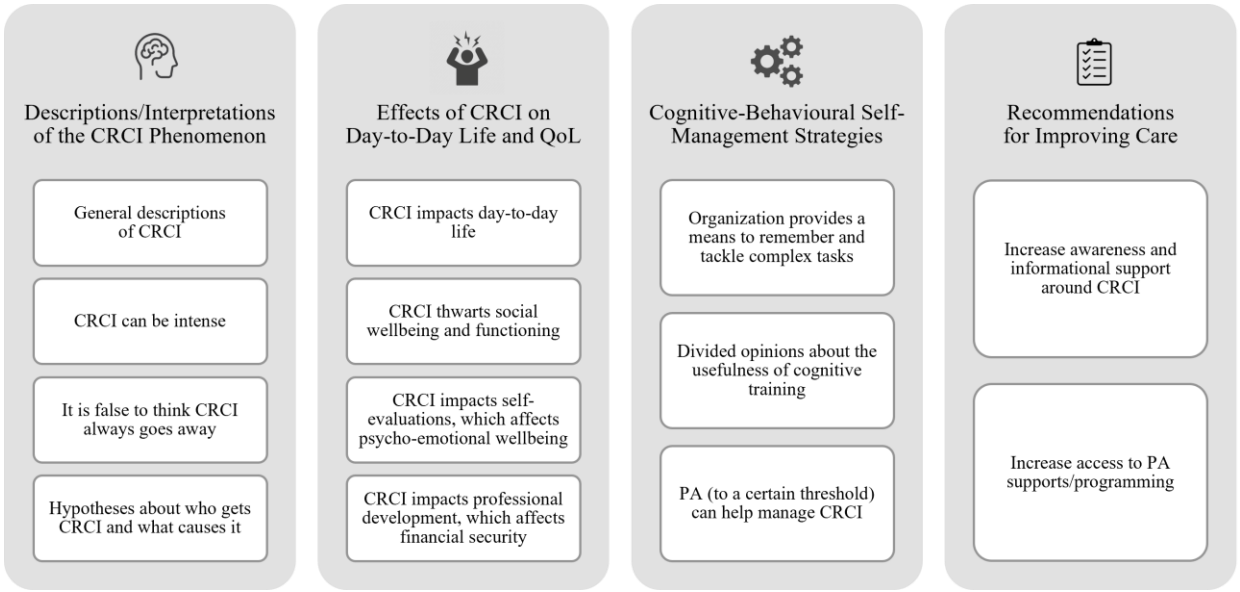
Participant Pseudonym	Sex	Age	Cancer Stage	Cancer Type	Cancer Treatment	PCI Score	MVPA LSI Score/ Classification
Sarah	Female	39	III	Breast	S + C + R	33	NR
Mia	Female	38	II	Carcinoma	S	35	25 / Insufficiently active
Sydney	Female	37	II	Breast	S + C + R	34	46 / Active
Jaime	Female	25	-[a]	Blood	S + C	31	15 / Insufficiently active
Jack	Male	26	II	Sarcoma	C + R	54[b]	24 / Active
Emma	Female	39	-[a]	Breast	S + C + R	17	10 / Insufficiently active
Priya	Female	38	III	Gynecologic	S + C	44	10 / Active
Erica	Female	28	II	Brain	S + C + R	48	25 / Active
Layla	Female	29	II	Blood	C + R	41	24 / Active
Nina	Female	36	I	Gynecologic	S	37	5 / Insufficiently active
Lauren	Female	25	-[a]	Sarcoma	S + C	51	33 / Active
Eva	Female	26	-[a]	Sarcoma	S + C + R	38	0 / Insufficiently active
Taylor	Female	23	II	Blood	S + C	37	10 / Insufficiently active
Cole	Male	25	II	Blood	C + R	8	10 / Insufficiently active
Peyton	Female	27	III	Melanoma	S	29	12.5 / Insufficiently active
Ivy	Female	32	-[a]	Brain	S	39	35 / Active

Notes. S=surgery; C=chemotherapy; R=radiation therapy; NR=not reported; PCI=perceived cognitive impairment (subscale range: 0-72; scores <54/72 indicate clinically meaningful impairment); MVPA=moderate-to-vigorous intensity physical activity (LSI scores≥24="active"; LSI scores<24="insufficiently active"); LSI=Leisure Score Index.

[a]Reported as "not applicable" or "do not know."

[b]Participant scored on the upper edge of the PCI cut-off value but was invited for an interview to gain male perspective.

Figure 2. *Themes and Subthemes Encompassing AYAs' Lived Experiences with CRCI*



Notes. CRCI=Cancer-related cognitive impairment; QoL=Quality of life; PA=Physical activity.

Theme 1: Descriptions and Interpretations of the CRCI Phenomenon

The first theme captures participants' thoughts about the origins, evolution, and meaning of CRCI following cancer treatment. These were organized into four subthemes: *general descriptions of CRCI*, *CRCI can be intense*, *it is false to think CRCI always goes away*, and *hypotheses about who gets CRCI and what causes it*.

The *general descriptions of CRCI* subtheme illustrates the meanings that participants ascribed to their cognitive impairment, which was painted out to be "fog"-like (Nina), a "constant cloud" (Jaime), and a "black hole" (Priya). According to Sydney, CRCI makes "everything [feel] like it's been muted a bit… like… when you're sick and your brain's just not moving quite at [the right] speed." She went on to say, "I feel like that all the time, but I'm not sick anymore." Participants illuminated troubles with their memory, word recollection, concentration, and ability to both process and learn information. For Jack and Mia respectively,

these deficits added “a layer of difficulty” to everything and made it feel as if she “can’t trust [her] brain.”

As reflected within the *CRCI can be intense* subtheme, participants’ cognitive impairment often presented frequently and with considerable severity. Lauren remarked “It’s hard to say how frequently I have *actual* issues, but… it comes to my attention that I am having this problem… at least once or twice a week.” Others affirmed struggling with cognitive impairment even more often; that is, either “multiple times a week” (Peyton) or “pretty much every day” (Nina). CRCI was such a constant for Jack that he explained, “I basically build like, the way that I interact around [CRCI].” When asked to describe their CRCI severity on a scale from 0 to 10, ratings ranged from “two” (Erica) to “severely… 10” (Ivy), although most felt it landed right in the middle of the scale. On average, as Peyton explained, “it bothers me, obviously, but… I can still live my life around it.” Further, CRCI severity was described to be fluid, such that “some days might be less [severe] than others” (Layla), and that “it’s definitely worse [on] the days that [they] do more” (Sarah).

The *it is false to think CRCI always goes away* subtheme encompasses an unfortunate reality. Cognitive impairment was most pronounced during primary treatment and immediately after it had ended. Participants described a “rapid drop” (Jack) in their cognitive function during treatment that was “consuming” (Layla). Indeed, in recalling her experience during this time, Emma said “I don’t think I was functioning at all cognitively.” Although CRCI was typically worse during/immediately after treatment for participants, many continued to struggle post-treatment and felt their CRCI got “progressively worse” (Cole). In looking for a way to describe the dynamic nature of her cognitive impairment, Mia explained that her cognitive function changed “in waves” wherein it vacillated between improving and worsening depending on

adjustments to medication. Others also noted that their cognitive function continuously changed and that "it's been better than during treatment… but it's definitely not a huge improvement" (Emma). Importantly, while slight-to-moderate improvements in cognitive function were discussed, participants largely credited these to "work[ing] really hard" (Layla) to adjust to and self-manage their CRCI because they accepted cognitive impairment as a permanent side effect that they needed to get used to. As Peyton exemplified, "I don't know… if [my cognitive function is] getting better, or if I'm just getting… used to living with how my brain works."

Finally, the *hypotheses about who gets CRCI and what causes it* subtheme reflects that participants largely attributed CRCI to either their cancer treatment(s) or medication(s). Importantly, since most individuals diagnosed with cancer receive one or more forms of treatment/medication, participants felt that CRCI could affect anybody, regardless of their cancer type, stage, or treatment regimens. For instance, when speaking to the causes, Emma said, "I think treatment…" and added, "I feel like its [affected] everybody that I've talked to." Likewise, Lauren said, "My guess is that people experience [CRCI] with cancer treatment in general. I don't know if that has to do with the fact that you're given like, so many drugs…and all that just messes with your brain… I feel like in general, cancer patients… have some sort of cognitive issues related to treatment."

Theme 2: Effects of CRCI on Day-to-Day Life and QoL

The second theme demonstrates that participants explicitly linked CRCI to QoL and reveals its tremendous, multidimensional burden. Specifically, participants noted that when cognitive troubles manifested, their physical, social, psycho-emotional, and professional wellbeing and function were adversely impacted. Consequences were grouped into four subthemes: *CRCI impedes day-to-day life*, *CRCI thwarts social wellbeing and function*, *CRCI*

impacts self-evaluations which affects psycho-emotional wellbeing, and *CRCI obstructs professional development which affects financial security*.

The *CRCI impedes day-to-day life* subtheme captures how CRCI can thwart one's ability to undertake instrumental activities of daily living (IADL); that is, key life tasks needed to live independently and maintain health. Participants described basic tasks like cooking and housekeeping as challenging because "everything takes more focus, more work" (Sarah) and because they would get easily distracted. For instance, Peyton said, "baking… cooking… laundry… it just takes longer to do stuff and [requires] being more thorough because I have to like, go back and make sure, or like, re-read or that kind of stuff." Due to the extra time and effort required to complete such tasks, participants appeared to neglect self-care (e.g., brushing their teeth, eating, engaging in PA). Erica remarked, "This sounds so gross, but I'd forget to brush my teeth or I would forget to eat breakfast or something like that," while Taylor conveyed, "Stuff takes longer for me… [so] I don't leave enough time for my walks." Participants also mentioned difficulties with upholding personal values such as being punctual. Sarah said, "I was never late for anything before… Now I'm late for everything and I hate it. It's like there's not enough time in a day for me to get through anything. I just seem like I'm failing a lot." Moreover, driving was discussed as another common IADL affected by CRCI. Particularly, due to difficulties with focusing and processing situations, many participants limited or stopped driving out of apprehension for threatening the physical safety of oneself and others. Priya remarked, "I've been really nervous about… driving just because I feel like my reaction time is kind of slow… like if someone ran out in front of my car or turned suddenly, would I be able to react as fast as I could before?" Mirroring this hesitation, Sarah said, "There has been a couple times driving where… I just have come home because I know that I shouldn't be out there

because I can't focus enough. Or I've had a close call or something, right? Where I'm like, 'Hey… I'm not here.' So there ha[ve] been those days where I just shut it down."

The *CRCI thwarts social wellbeing and functioning* subtheme reflects that CRCI strained relationships with others (e.g., romantic, familial, friendships) as it often caused communication struggles and left individuals feeling misunderstood. For example, Sydney said, "I do need more time to process… [than my] very quick-thinking partner… that alone is frustrating. I mean, that's basically the crux of like all of our communication problems." Further, Mia mentioned that she "ha[s] a father who… doesn't understand being forgetful. He doesn't understand that [CRCI] is something that I'm dealing with so he'll get upset, saying that I don't remember something because I don't want to do it." Lack of understanding and negative comments from others was also discussed by Lauren who explained, "I would get very hurt when people would tell me… 'Oh, you don't remember this?'… my memory is not as great… it's hard for the people in my life to understand that." Moreover, participants described feeling like a "bad friend" (Taylor) because CRCI made it difficult for them to be as thoughtful or to recall memories and details about loved ones' lives. Collectively, cognitive difficulties seemed to create "an internal barrier" (Emma) that inhibited social engagement and led to self-isolation for participants. For instance, Sarah said, "Because I can't articulate how I feel, I just avoid… some of my family…. They don't understand." Similarly, Nina expressed, "Sometimes when I can't put a sentence together, I feel really ridiculous and then it kind of makes you not want to talk to people because you feel like… they're probably thinking, 'Oh my gosh, what's going on with her?' So… maybe I am a little bit more isolating myself."

The *CRCI impacts self-evaluations which affects psycho-emotional wellbeing* subtheme captures the heavy inward struggles and distress that CRCI can cause. Participants expressed

feeling like “a failure” (Emma), a “damaged version” of themselves (Taylor), and “like a shell of… what [they] once thought [they were]” (Peyton) due to their cognitive impairment. This loss of self-worth and identity often stemmed from feeling less intelligent than prior to their cancer experience and gave rise to many negative emotions and thoughts. Sarah shared, “It makes you insecure… You don’t recognize your brain, right? All the things that you grew up learning how to study and knowing how to do… they don’t work anymore… It’s very unnerving… not being who you were and not being as smart as you were.” Correspondingly, Layla expressed, “My memory was quite sharp… I always got high grades. So, it was really, really disappointing. I think [CRCI] took a lot of my identity. I lost a lot of my confidence in myself and developed a lot of imposter syndrome… Initially, [CRCI] was really, really upsetting… I went home and cried every day… it was just so hard and frustrating.” On the other hand, negative emotions were also thought to fuel cognitive troubles, suggesting that the connection between CRCI and psychological distress is bidirectional, or as Taylor put it, a “vicious cycle.” Jack illustrated, “I think it happens in both directions. I think if I’m having issues with my cognition, I feel depressed and slow and low. And conversely if I’m having anxiety… I’m so hyper-focused on those things that I can’t pay attention well, I get distracted, I can’t remember what's going on… I think they feed all on each other like writhing massive snakes.”

Finally, the *CRCI obstructs professional development which affects financial security* subtheme encapsulates the toll CRCI takes on work/school performance and motivations to pursue professional opportunities. Nina exemplified this when she said, “I did decide to step back a little bit from work because I felt like I…couldn’t function [cognitively]… I can’t make mistakes in my work… I’ve cut down my hours. So yeah, it affected me financially… And it’s frustrating because, like, if I was in my 50s or 60s, I’d probably be retired and I wouldn’t have to

work. It wouldn't matter, you know? But it matters right now for me because I'm so young… I probably have to work another twenty years." As Nina alluded to (and others mentioned), AYAs bear many financial responsibilities, making this consequence of CRCI especially taxing for them. Moreover, those currently unemployed or on medical leave described CRCI as a barrier to finding/returning to work or pursuing further schooling. Cole explained, "It's been very hard to be able to consistently stay with like a full-time job… There's so much to learn… There's so many mistakes that you can make in a day… It just seems that every attempt has been futile for me." Others prolonged returning to work or ceased their job searches altogether out of fear or discouragement that it would "take [them] longer to finish tasks" (Eva) and ultimately, that they would not "bring value to the team" (Peyton). As Mia said, "It's not fair to a new employer for me to go there and have all of this confusion and everything until I'm all sorted out."

Theme 3: Cognitive-Behavioural Self-Management Strategies

The third theme reflects the cognitive-behavioural self-management strategies that participants used to self-manage their CRCI. The strategies described herein were used to help participants feel better able to remember, focus, and tackle complex tasks. Strategies are captured within three subthemes: *organization provides a means to remember and tackle complex tasks*, *divided opinions about the usefulness of cognitive training*, and *PA (to a certain threshold) can help manage CRCI*.

The *organization provides a means to remember and tackle complex tasks* subtheme captures the various organizational methods and tools that participants used to help them self-manage their CRCI (in some cases), specifically by helping to jog their memory and reserve their cognitive energy. To help manage troubles with memory, participants described "stick[ing] to a routine" (Mia), scheduling "everything in a calendar" with constant reminder alerts (Sarah),

"writ[ing] everything down" (Emma), and essentially, as Jaime explained, "putting [stuff] somewhere that's not inside my head." However, for others, "calendars and all that stuff… just doesn't work" (Cole) because ironically, they were often forgotten or misplaced. For instance, Jack said, "I try and make lists and then a few days later, I forget that I made a list. And then a few months later, I'm going through, like erasing iPhone notes and going, 'Oh, I was supposed to do this or that'… So, I do make lists, but I'm not successful at using them." Beyond routines, scheduling, and notes/lists, participants mentioned organizing their days intentionally to undertake certain tasks when their cognitive function was at its best. For example, Layla mentioned, "I know that I have better [cognitive] function in the morning. So, [I try] putting more complex things in the beginning of my day versus trying to do them in the afternoon because I'm exhausted and I… don't have the capacity as much."

The *divided opinions about the usefulness of cognitive training* subtheme captures that some participants found exercising their brains through cognitively-demanding games/activities beneficial, while others preferred to engage in activities that calmed their brain (e.g., mindfulness activities). In terms of exercising the brain, Erica remarked that "listening to podcasts and that kind of thing... keep[s] my brain working. One thing that I got really into during treatment… is sudoku puzzles… just remembering those little things I thought was really good practice… It made me focus and… utilize my short-term memory." Similarly, Taylor said, "I started to play a lot of solitaire on my phone… sometimes I feel like it helps me to like, get my brain working." Other examples Taylor gave included not "turn[ing] on [TV] subtitles so that [she had] to focus more" and "try[ing] to use… scientific papers that are in English [when conducting research for university] so that it's harder" (as English is not her first language). In contrast, others discussed the cognitive benefits of calming the brain through mindfulness activities. Erica cited,

"Meditation is like my number one [strategy]… it is amazing. It has all these benefits… I find my memory is better," and Ivy described that a simple five-minute guided meditation session helped her go "from being, like, very frazzled and fe[eling] like [her] head [is] being pulled in a million different directions to… just like, all of a sudden [feeling that things were] manageable… it helps put the pieces in order."

Finally, the *PA (to a certain threshold) can help manage CRCI* subtheme captures that many participants engaged in PA as an explicit self-management strategy for CRCI; however, proper dosing was important as overexertion could lead to cognitive fatigue. Indeed, participants discussed that engaging in PA (regardless of PA type; e.g., aerobic, resistance, yoga) helped them better concentrate, remember, and "not be stuck in that… weird foggy state as much" (Priya). As shared by Jack and Erica respectively, "I can [focus] whenever I come back from exercise, I get so much done… I'm just more successful," and "I find that the days that I've gone to the gym the day before… I feel like my memory is better… I feel more alert." Emma found that PA "definitely helped [her] brain" and made it easier for her to tackle tasks that were otherwise difficult. Further, Ivy found that PA (specifically, lane swimming) helped calm her brain and thus provide some relief from her cognitive struggles, tying into the above sub-theme. She said, "For me, [when I swim laps] … the counting of strokes and breath… it's just so meditative… [I feel] mental effects and benefits." Critically, participants mentioned that engaging in "too much" PA could cause mental fatigue, and thus decrease their cognitive function. For instance, Emma mentioned, "If I push myself too hard [during PA], I'm just done. Like everything—physically, emotionally, cognitively, it's just like total body shutdown… I am trying to learn the window where it feels good, when it's not too much." Similarly, Layla explained, "I started working out with a personal trainer in the summer… if I worked out too

many days… the physical fatigue contribute[d] to increased brain fog… I tried working out… 3-4 times a week, and I had to cut it back to twice a week because… it was too much physically and it really impacted my brain." However, Layla went on to say, "I think other than the overexertion and getting to the fatigue point… I feel good in myself… [PA] helps with… your mental health, and then that translates into having better cognitive function." Furthermore, of those *not* explicitly using PA as a strategy, many felt it *could* be useful in self-managing their CRCI, yet they were unsure how best to reap its benefits. As Sydney conveyed, "PA clears your mind, so I can certainly… see the link [between PA and cognitive function] … I don't know exactly… which type of PA… or if there's kind of a strategy of 'you should be doing *these* five things' and 'you work them in *this* order' or whatever… But… I can see the reason that they would be linked for sure."

Theme 4: Recommendations for Improving Care

As AYA cancer survivors, participants expressed that their concerns were often neglected, they had to advocate for themselves, and they seldom felt represented within the healthcare system. Participants unanimously described feeling ill-informed about CRCI and as if they "didn't have the tools necessary in place that would have helped" (Cole) navigate this challenging side effect. As such, they provided recommendations for improving care, which are captured within this final theme. Suggestions for successful survivorship were grouped into two subthemes: *increased informational support around CRCI* and *greater access to PA supports/programming.*

The *increased informational support around CRCI* subtheme captures participants' desires for more systematic awareness and information around CRCI. Sarah expressed, "I think the more awareness we have that this is a real thing that all cancer patients go through, then we

won't feel so alienated by it." Likewise, Eva said, "Difficulty focusing… memory issues… [health professionals] don't tell you about these things and you don't expect it, and then it actually happens to you. You feel like something's wrong with you when it's not. So, I think it's important to discuss that with you." Nearly every participant echoed feeling uninformed about CRCI as a potential side effect of cancer treatment and discussed being left to understand and deal with cognitive impairment via "trial and error" (Peyton). Thus, Mia remarked, "It would have been better if [health professionals] said, '*These* are some of the symptoms that you may have. If you run into these, *these* are some of the coping strategies you can deal with,' instead of leaving it up to me to go onto these Facebook groups." By the same token, Layla remarked "I think preparing people in advance for [CRCI] would be helpful… Medical professionals need… to help with cognitive strategies… To be like, 'Yeah, so you may just have to write things down more.' Like I know…it should be intuitive, but it wasn't in that moment. So, like… 'Write things down more,' 'chunk things up in your day'… 'have [complex] things in the morning.' Like those things would have been really really helpful tips because you're dealing with something that you've never thought about or you never had to do."

The *greater access to PA supports/programming* subtheme reflects participants' overwhelming desire for PA supports during and following cancer treatment (both for CRCI self-management purposes and general health reasons) as it was often not presented as an option or was inaccessible to them. In relation to CRCI, Taylor explained, "[My friend] was prescribed physiotherapy during her treatment… Her cognitive function, I would say, is better than mine… She always had to do workouts during treatment, but when I was in treatment, they were like, 'Just stay in bed and just rest.' And they told her, like, 'You should move. You should go out of the house at least once every day.' I feel like if my doctors would have told me the same… that I

would definitely have increased my cognitive function or made it less worse." More broadly, participants mentioned that they would have liked more dialogue and information around the benefits of PA and how to engage in it appropriately. For instance, Priya said, "It would have been really helpful if the doctor had more of a conversation about PA… Like providing some kind of tips or even directing people to some resources." In parallel, Layla said, "Some sort of… graphic info sheet that had either organizations you could access… as well as information on PA, the importance of it, how much PA cancer patients should be doing, or what activities they should be partaking in versus what's contraindicated… would be helpful… I think… when people are [doing] really, really poorly and they're trying to incorporate exercise, they need to know distance and frequency and timing and that kind of stuff to help." Furthermore, participants believed that help from PA professionals (e.g., kinesiologists) in creating detailed, individualized PA plans would be beneficial in setting them (and future AYAs) up for success following cancer treatment. As Sydney mentioned, "An actual recommendation to say, 'We'd like to have you work with somebody to set up what would be a good physical exercise plan for you,'…would go pretty far."

Chapter 5: Discussion

As the disease survival rate rises for cancer, AYAs are increasingly burdened with CRCI, a source of significant distress [10], diminished QoL [3], and various social and recreational repercussions [15]. Nevertheless, CRCI remains understudied and untreated in AYAs [17]. Key knowledge gaps hinder the development of CRCI-related supportive care services that address AYAs' unique needs. Thus, the purpose of this observational study was to better understand CRCI and how it may relate to QoL as well as select medical (i.e., time since diagnosis, cancer type, chemotherapy exposure) and psychological factors (i.e., depressive symptoms, perceived stress, fatigue) in AYA cancer survivors through use of quantitative and qualitative methods. In addition, based on emerging evidence that PA may enhance cognitive function in other populations, PA was explored as a behavioural strategy that AYAs may use to manage their CRCI. The following chapter summarizes and contextualizes key results within previous literature, delves into the meanings and relevance of findings, acknowledges the limitations of this study, and provides recommendations for future research and practice.

Summary and Contextualization of Findings

Quantitative data from 46 participants were analyzed to describe patterns of cognitive function amongst AYA cancer survivors (objective 1a). To do so, self-report and performance-based methods were used following recommendations to employ both and capitalize on their respective advantages whenever possible [19]. In accordance with limited previous literature conducted within this age cohort [10, 33, 44] and hypothesis 1a, impaired levels of self-reported cognitive function were observed. Indeed, the average score ($M=44.7\pm17.4$) on the PCI subscale of the FACT-Cog fell below the mark denoting clinically meaningful CRCI (i.e., 54/72), with 60.9% of participants meeting criteria. Correspondingly, performance on neuropsychological

tests assessing different dimensions of cognitive function was generally impaired in this sample. Echoing findings from a recent study with 139 AYA cancer survivors [105], average performance on two neuropsychological tests (i.e., M-WCST and the TMT) suggests weak EF and processing speed in this sample as compared to available normative data from healthy individuals [102, 104]. Conversely, average performance on the A-LNST was above healthy norms [103], indicating that working memory was perhaps not as affected as EF and processing speed; however, these results must be interpreted cautiously given the normative values used for comparison and the use of online testing (as discussed below). Nonetheless, because this finding is incongruent with previous literature demonstrating weak working memory performance in children and adolescent survivors of non-CNS cancer [106], more studies aiming to describe patterns of cognitive function amongst AYA cancer survivors will help determine if the observed levels herein are sample-specific or in fact representative of this population. To this end, the development of appropriate norms and values is needed to better contextualize these results and others moving forward.

Furthermore, research over the years has shown that AYA cancer survivors are disproportionally burdened by cancer [1] and recent data show that they experience cognitive difficulties [10, 33, 44, 45]. Yet, there is a lack of studies that employ both quantitative and qualitative methods to gain an in-depth understanding of the associations between cognitive function and QoL in this group. As predicted in hypothesis 1b, large and small respective associations show that QoL decreased as both self-reported and objective cognitive function decreased in this sample. This finding is in line with previous research [107], yet there is more evidence to support the relationship between self-reported cognitive function and QoL (both present and long-term) in cancer survivors than that between objective cognitive function and

QoL [108, 109]. Qualitative data also support this relationship and suggest paying particular attention to certain dimensions of QoL, at least for those reporting clinically meaningful cognitive impairment. Specifically, while no hypotheses were formed for objective 2 (i.e., to understand the lived experiences of AYA cancer survivors who reported clinically meaningful CRCI) due to its exploratory nature, results revealed the multidimensional consequences CRCI has for AYAs' overall QoL (regardless of their cancer type, disease stage, or form(s) of treatment received). In agreement with previous research predominantly conducted with breast cancer survivors, qualitative findings illuminate that AYAs also experience significant negative impacts of CRCI on their daily life (including diminished independence) [16], social life [16, 110], psycho-emotional well-being [111-113], and professional capabilities [16, 113-116]. Moreover, the accounts of interviewed AYAs–who self-reported clinically meaningful levels of CRCI—suggests there may be bidirectional relationship between CRCI and psychological distress (e.g., depressive symptoms, perceived stress, anxiety), corroborating results from a comprehensive population-based study comprising 2,646 AYA cancer survivors [10]. Accordingly, the design of relevant CRCI programs may require specific attention to QoL—a potential determinant of AYAs' participation and adherence in such programs. In other words, improving CRCI may very well enhance QoL, but those with lower psycho-emotional wellbeing (for instance) might be harder to recruit or less adherent to interventions.

Analysis of qualitative data to address objective 2 revealed novel insight into the *effects of CRCI on day-to-day life and on QoL* that have not been well explored. Many of the interviewed AYAs described feeling less intelligent than they did prior to their cancer experience, often leading to a loss of sense of self, and thus, significant emotional turbulence. Previous research has shown that AYA cancer survivors face various obstacles as they navigate

professional workplace settings [117]; CRCI may exacerbate this by impeding re-integration into work, reducing capability to work, and causing job loss, all of which may be reasons for feeling "less intelligent." However, this feeling may also be related to AYA cancer survivors having to continually explain, defend, and/or validate their 'slower' task completion or mistakes that stem from struggles with CRCI. Having to constantly explain or justify work output (or lack thereof) to well-intentioned coworkers who lack sensitivity and/or awareness of CRCI represents a larger societal issue and an important factor to consider when designing return-to-work support services for AYA cancer survivors, especially for those who have clinically meaningful levels of cognitive impairment.

Another finding of this study was that AYA cancer survivors spoke in favour of certain care strategies. Supporting conclusions from a qualitative meta-synthesis of research conducted with breast cancer survivors [48], results highlight that AYAs also make use of compensatory strategies to cope with CRCI in their daily lives. Specifically, congruent with previous findings [16, 118], organizational strategies (e.g., writing lists, scheduling, setting alerts) were commonly discussed as a self-management technique. As well, mirroring existing evidence [16, 112, 119, 120], some participants described engaging in cognitive training (i.e., cognitively-demanding games/tasks) to manage their cognitive troubles; indeed, results from a recent feasibility trial [121] suggest this may be an effective way to mitigate CRCI in AYAs. In contrast, others discussed cognitive benefits from more mindful activities, in line with research supporting mind-body interventions such as meditation [122], mindfulness-based stress-reduction [123, 124], biofeedback [125], and imagery [126] for improving CRCI. Collectively, these findings underscore that no single strategy may work or be desirable for AYA cancer survivors to manage (or eradicate) this phenomenon.

Moreover, results emphasize the intersectionality that exists amongst AYAs' CRCI experiences, their cancer experiences, and their psychological states. In addition to making specific reference to medical characteristics and psychological factors when discussing their cognitive impairments during interviews, the quantitative results generally support hypothesis 3a stipulating that inverse associations between cognitive function and cancer stage, chemotherapy exposure, depressive symptoms, perceived stress, and fatigue would be observed. Similar to previous research ([53] and [11-14], respectively), those exposed to chemotherapy and those reporting higher levels of fatigue self-reported worse cognitive function and performed worse on two tests of objective cognitive function (i.e., the A-LNST and TMT, but not the M-WCST). Further, depressive symptoms and perceived stress were inversely associated with self-reported and objective cognitive function, congruent with extant research linking cognitive impairment with both depression [11, 13, 18, 39-41] and stress [12]. Therefore, these results represent important factors for researchers to consider when designing CRCI programs for AYA cancer survivors as they appear to influence (or be influenced by) CRCI. However, it is important to note that contrary to hypothesis 3a, those with more advanced cancer stages at diagnosis self-reported better cognitive function and scored better on objective tests of EF and processing speed (i.e., the M-WCST and TMT), but worse on the A-LNST for working memory. This finding contradicts previous research with older breast cancer survivors (albeit, pre-systemic treatment) [51] that showed poorer performance on tests of EF in those with more advanced (as opposed to early stage) cancer and emphasizes possible heterogeneity in outcomes across populations. In addition, contrary to hypothesis 3b, the observed direction of associations implies that as time since diagnosis increased, both self-reported and objective cognitive function largely (i.e., except for performance on the A-LNST) decreased. Mirroring a recent review of longitudinal studies

focused on CRCI in breast cancer survivors that suggested many decline cognitively over the course of disease [127], this finding is concerning given the societal pressures for AYA (and older) cancer survivors to 'return to normal' following treatment.

Last, both qualitative and quantitative data emphasize that interventions promoting PA to mitigate CRCI should be developed and evaluated. As predicted in hypothesis 4, MVPA analyzed as both a continuous variable (i.e., MVPA LSI) and divided into categories (i.e., *active* and *insufficiently active*) was linked with better self-reported and objective cognitive function (on all tests except the A-LNST). As well, similar to a qualitative study conducted with breast cancer survivors [118], the accounts of interviewed AYAs highlight the promise of PA as a behavioural strategy to self-manage CRCI; many discussed cognitive benefits following PA, others felt that it could be beneficial despite not explicitly using it as a strategy, and overall, most desired for greater access to PA supports and programming during cancer care. These combined results fit within the context of previous literature synthesized by Campbell and colleagues [25] that reported significant positive effects of PA (delivered through heterogenous interventions) on both self-reported [69, 128-138] and objective cognitive function [68, 69, 139] in cancer survivors of varying diagnoses. They are also in line with findings from a recent proof-of-concept study conducted with AYA cancer survivors [140, 141] that suggested PA may improve neural activity underlying their EF. However, participants mentioned that engaging in "too much" PA caused mental fatigue and in turn reduced their cognitive function; this highlights the heterogeneity in opinions on PA and suggests that researchers should investigate how PA interventions may be developed to minimize adverse effects since the concept of 'overload' is not currently well-documented.

Interpretations

Above, the results of this study were summarized and key points were made while contextualizing them within previous literature. The following section delves into the meanings and relevance of findings and offers potential reasons for unexpected results.

CRCI and Associated Factors in AYAs

There is substantial evidence to support that CRCI is an issue for many cancer survivors, although most research to date has confirmed this in breast cancer survivors who are typically older in age. When considering the high levels of self-reported CRCI (both in questionnaires and interviews) in conjunction with relatively poor objective cognitive performance in this sample, results provide evidence that AYAs *also* struggle significantly with CRCI. As expected, many reported clinically meaningful CRCI, and both EF and processing speed were weak in this sample as compared to the norms used. Regardless of the underlying mechanisms for AYA cancer survivors experiencing CRCI, it represents an important issue for researchers and practitioners to prioritize. However, participants' working memory performance (as assessed using the A-LNST) was above average norms; this suggests it was not as affected as the other two cognitive domains and emphasizes the heterogeneity in results within this study and across others [106]. Although it is difficult to speculate on reasons for these findings, it is possible that the A-LNST norms used [103] were not appropriate for comparison. Indeed, they were developed from demographically-adjusted in-person testing conducted in Spanish (not English), and norms were taken from healthy individuals aged 19-60 years (not AYAs). Also, since both age and education can influence A-LNST performance such that older age and lower education relate to worse test performance [142], it is possible that completing the A-LNST favoured participants of this study (who were younger and on average, completed more education than

those from which norms were developed). Thus, given the emerging trend to use online neuropsychological testing, there is a need to develop norms across different computerized platforms to allow for more accurate comparison of results in the future.

Moreover, findings from this study and others suggest that psychological distress may be an important contributor to AYAs' CRCI (or vice versa). Specifically, results show that several psychological factors are related to CRCI in AYAs wherein those reporting poorer QoL and greater depressive symptoms, perceived stress, and levels of fatigue may also report greater cognitive impairment. While conclusions regarding direction of association cannot be made due to the cross-sectional analysis of quantitative data, analysis of qualitative data calls attention to a potential bidirectional relationship between CRCI and psychological distress. These data suggest that interventional strategies aimed at overcoming psychological issues may also help mitigate CRCI (or vice versa). Also, AYAs with depression, stress, and fatigue may need to be specifically targeted in such research because reasons for these associations warrant further attention. For instance, depression and stress may stem from the financial hardships that CRCI causes by impeding AYAs' professional capabilities. Similarly, such distress may be the result of perceived stigma from others when AYAs struggle with CRCI in social situations. Since both cognitive and affective dysfunction share similar neurologic underpinnings (see [143] for review), future studies involving more robust cognitive measures like neuroimaging are needed to identify which specific associated psychological factors may predispose AYAs to a higher risk of CRCI, as well as to evaluate potential confounding variables or moderators between cognitive function and QoL.

Further, results showed that cognitive function relates to cancer stage and time since diagnosis, although associations were in unexpected directions. Results imply that for the most

part, those with more advanced cancer stages at diagnosis both self-reported and objectively showed better cognitive function. The lack of current research on this topic makes speculation difficult but suggests that disease stage may play a role in severity of CRCI and that researchers should evaluate this link moving forward. As well, the negative correlations between time since diagnosis and cognitive function is this study were not anticipated, but somewhat supported by the qualitative data. That is, cognitive function was predicted to increase with time, yet a handful of AYAs discussed that their cognitive impairment felt dynamic or continued to worsen post-treatment. Moving forward, longitudinal studies will be pivotal for tracking AYAs' cognitive function over time to confirm these observed patterns.

PA as Self-Management for CRCI

Overall, findings from this study emphasize that PA may be an effective behavioural strategy to manage/mitigate CRCI. Quantitative data showed that PA was positively associated with both self-reported and objective cognitive function, although associations had small effect sizes. Qualitative findings also support the notion that PA may be a helpful self-management tool for CRCI. Indeed, many participants reported feeling more focused, alert, and able to remember following bouts of PA, and interestingly, even those who did *not* discuss use of PA as an explicit strategy believed that it *could* help manage CRCI. This suggests that AYAs may be willing engage in PA for their cognitive and mental well-being; thus, researchers should consider PA when studying factors associated with CRCI in AYA cancer survivors. However, it is important to note that while emerging research (observational and experimental) is showing promise for PA, some studies have reported that PA did *not* positively influence cognitive outcomes (e.g., [144, 145]), and participants in this study made comments to suggest that not all PA is 'good.' To inform future PA intervention design, researchers will need to answer several questions,

namely how much/often PA is needed to induce cognitive benefits, what type (or combination of types) are most beneficial, and how long the effects of PA last on cognitive function. As well, to minimize the risk of social desirability and/or recall bias, researchers should employ objective measures to quantify PA (alongside self-report to gather contextual PA data); this may help overcome limitations of this study and others and to provide evidence for which aspects of PA are most influential on cognitive function. Additionally, as suggested in recent work with breast cancer survivors [146], it is plausible that the potential cognitive benefits of PA are more acute than long-lasting (as measured in this study) in AYAs. Therefore, researchers may wish to investigate more regular PA in AYAs' daily environments through use of *Ecological Momentary Assessment* methodology [147] which has been gaining traction in PA research for its application in understanding time-varying effects of PA correlates [148]. Repeated, real-time observations and use of objective PA measures may help yield greater insights into whether cognitive benefits from PA are indeed acute or may be sustained.

Of note, certain barriers may stand in the way of AYAs' participation in PA. In this study, the unfavorable links between CRCI and depressive symptoms, perceived stress, fatigue and QoL suggest that some may have a hard time motivating themselves to engage in PA. AYAs may also have occupational or social commitments that should be considered when designing PA programming. Also, not all participants referenced PA participation during their interview; as evidence grows in support of the positive effect(s) of PA on cognitive function, more messaging is needed to inform AYAs about its benefits as a potential way to help them build self-efficacy and overcome barriers. Relatedly, drawing on the *Health Belief Model* [149] for predicting and explaining health behaviours, researchers should aim to identify and understand AYA cancer survivors' perceived benefits, barriers, and self-efficacy in regards to engaging in PA for their

brain health. Doing so may help guide the creation of preliminary PA-based CRCI self-management programming for this population.

Further, analogous to findings indicating that some participants felt benefits from cognitive training while others preferred mindfulness/meditation as self-management for CRCI, results suggest that individuals may experience differential benefits from engaging in *mindful* versus *mindless* PA. For instance, in her interview, Ivy mentioned that the act of counting strokes and focusing on her breath while swimming was meditative for her and elicited mental benefits; this could be considered a *mindful* form of PA (i.e., during which one is present and has a heightened sense of attention; other examples: yoga, qigong). On the other hand, Erica described benefits following sessions at the gym; resistance training (if practiced) could be considered a *mindless* form of PA (i.e., during which movement is more autonomous and does not require attention; other example: walking). Diamond and Ling [150] proposed that PA involving a cognitive load (i.e., mental effort) may lead to "better" cognitive effects than mindless PA; however, this has been criticized [151] due to the lack of empirical evidence (see [152] for exception) and findings from this study suggest that a) individuals may prefer one type over the other, and b) there could be benefits to both. Thus, future research should aim to test the potential cognitive benefits of both mindful *and* mindless PA in AYA cancer survivors and include more qualitative research to determine whether self-selection of PA may be important when aiming to manage CRCI.

Critically, while the relationship between cognitive function and PA was generally encouraging throughout results, and while PA is typically viewed as a positive behaviour, qualitative findings suggest that some caution may be required around this potential self-management strategy for CRCI. That is, many indicated a downside whereby engaging in "too

much" PA caused mental fatigue and thus reduced their cognitive function. This may be explained by considering the *Individual Zones for Optimal Functioning Model* [153, 154] which posits a relationship between arousal levels and optimal athletic performance; in line with this, it is possible that there may be an individualized threshold for which PA induces optimal cognitive effects based on one's level of mental fatigue prior to engaging in PA. Building off the emerging practice of "personalized/precision medicine" which aims to tailor care based on individual differences (e.g., genes, environments, lifestyle), future research should seek to identify how to match the right PA frequency, intensity, and duration to each AYA cancer survivor so they may feel cognitive benefits and avoid mental fatigue.

Limitations

It is important to consider results in light of the following limitations. First, the cross-sectional nature of this study precludes conclusions about directionality and causality of relationships. A second limitation is that the analytic sample size and composition (i.e., mostly those born female, self-identifying as White, and between the ages of 23-39 years) did not allow for exploration of differences in estimates or experience based on age or other possible moderators (e.g., sex, ethnicity, education, PA level). The generalizability of results is also limited because participants all fell within the young adult age range (despite recruitment efforts also targeting adolescents). Given that the brain undergoes structural and functional maturation during the shift from adolescence to adulthood [155, 156], the cognitive function of a 16-year-old likely differs notably from that of a 39-year-old (i.e., the upper and lower cut-offs for the recruited AYA sample); consequently, results may not be comparable to younger AYAs' experiences with CRCI. Further, most participants (73.9%) perceived their overall health as "Good to very good" and the sample was generally classified as "active" based on their self-

reported PA (as is the case with many PA studies). It is therefore possible that the qualitative themes reported herein may differ from those with AYAs who do *not* view themselves as healthy nor active, perhaps indicating that future studies should purposively recruit those in worse perceived health to understand their specific experiences with CRCI and thoughts around PA. There are also inherent limitations to using self-report measures (e.g., social desirability, recall bias) whereby participants may have under- or over-estimated their PA levels and thus influenced results. Moreover, participants were recruited using convenience sampling and as such, it is possible that the sample was biased towards those with greater computer literacy and/or ability to spend time online; those who struggle with this due to cognitive issues may have articulated different experiences. Importantly, since methodological choices were constrained for this master's degree, there was no control group in this study, hindering the ability to directly compare this sample's cognitive performance with that of age- and education-matched controls. As such, objective cognitive function data (obtained through computer-based means in consideration of the COVID-19 pandemic) were compared to the most appropriate normative values that could be found; yet, despite researchers' best attempts, norms were taken from studies that involved in-person testing with healthy populations [102-104] and are not all age- nor education-matched. Hence, it is acknowledged that there was suboptimal comparison of objective cognitive data. Relatedly, although being able to collect data from a distance and to recruit widely was certainly a strength of this study, it did not allow for supervision of participants during neuropsychological testing. Therefore, despite providing clear instructions and requesting that tests be completed in a quiet, distraction-free environment and at a time that participants felt most cognitively alert, it is possible that external disturbances were present and/or instructions were not precisely followed, which may have affected test performance and

skewed results. Finally, there is inherent subjectivity in thematic analysis wherein the researchers' own biases and assumptions could have affected identification and interpretation of themes/subthemes presented herein, although several steps were undertaken to mitigate this risk (see **Qualitative Rigor** above).

Implications and Future Recommendations

Notwithstanding the limitations, the current findings complement previous research and provide methodological, conceptual, and practical contributions to the literature. To corroborate and further expand on the current results, these implications are highlighted below, along with areas where future research is needed.

Methodological

To the author's knowledge, this is among only two other studies ([140, 141]) to explore how CRCI relates to PA in AYA cancer survivors and represents the first attempt to do so using both quantitative and qualitative methods. Employing multiple methods helped gather complimentary information, more so than one method alone would have provided [72]. That is, the quantitative data provided the information necessary to: (1) describe the extent to which AYAs struggle with CRCI following primary treatment through both self-report and objective neuropsychological data, and (2) determine the strength of associations between cognitive function and both QoL and certain medical/psychological factors that are often discussed in the literature as potential risk factors for CRCI (i.e., time since diagnosis, cancer stage, treatment type, depression, perceived stress, fatigue; see [5, 23]). On the other hand, the qualitative data helped furnish a better understanding of how AYAs describe, experience, and cope with CRCI, along with their own recommendations for improving care moving forward. Taken together, not only do results confirm that AYAs (like other cancer cohorts) struggle with CRCI, but they

provide valuable information that may help design research methods to map the specific burden of CRCI for AYAs (e.g., questionnaires containing items that ask about concerns AYAs have indicated herein) and guide the development of interventions based on strategies they already use (e.g., organization, cognitive training, mindfulness, PA).

Further, efforts were made to recruit a more diverse sample of AYAs than in previous studies by not placing restrictions on cancer type, stage, or treatment(s) received within the inclusion criteria. Additionally, the virtual nature of this study enabled widespread recruitment and thus, the collection of diverse experiences, particularly during interviews. As a result of these methodological choices, the recruited sample was also comprised of males (unlike most published CRCI research which focuses solely on females diagnosed with breast cancer; see [5] for review). Although they represented only a small percentage (i.e., 8.7%) of the total sample, this study shows that males are also affected by CRCI. Coupled with evidence suggesting that sex-specific differences may underlie cognitive function in healthy youth [157] and pediatric cancer survivors [158] (and brain structure more broadly [159]), findings highlight a need for researchers to embrace recruitment strategies that specifically target males in such research and involve them early in the research process to develop male-informed strategies. In relation to the former, researchers should consider advertising their studies through male-oriented social media channels, using active recruitment strategies (e.g., reaching out to males from hospital registries that agreed to be contacted for future research), and circulating informational resources with relevant information to them. Doing so may help recruit more males and in turn provide greater insight into how male AYAs experience CRCI as compared to their female counterparts.

Moreover, recruited participants had undergone several forms of cancer treatment, but given the small sample size, analyses were focused on chemotherapy exposure. This was

justified based on ample evidence associating CRCI with chemotherapy [5, 53] and because there would have been too much heterogeneity if all forms of treatment were analyzed. Nonetheless, results suggest that AYAs who underwent other forms of primary treatment (e.g., surgery, radiation therapy, hormone therapy) also struggle with CRCI. Based on these findings, future longitudinal research is needed to investigate how various anti-cancer therapies may relate to CRCI (e.g., the extent to which individuals experience CRCI with each treatment type, whether there are compounding effects of undergoing multiple forms of treatment, how long deficits persist after each treatment type). This may help better understand whether certain forms of cancer treatment present a greater risk for cognitive impairment.

Conceptual

Results from this study support the descriptions and multidimensional consequences of CRCI previously described in the literature but also suggest there may be specific implications for AYAs. Current operational definitions of CRCI are quite simplistic (especially when considering the magnitude of qualitative data reported herein) and either researcher-developed or based on the accounts of older populations (namely, middle-aged and older breast cancer survivors). However, this study sheds light on the meanings that AYAs ascribe to their cognitive impairment (including thick descriptions of the phenomenon, along with their thoughts on its origin, progression, and severity) and indicates that there may be specific consequences of CRCI that are especially detrimental to this group given their life stage and responsibilities. For instance, as captured in the qualitative findings, AYAs seemed especially distressed about the toll CRCI took on their daily life (i.e., by impacting their independence) and on their professional development and capabilities (and thus, their finances) given expectations to contribute to society and provide for themselves and their families; these consequences may not be as

applicable to pediatric nor older retired cancer survivors. As such, it is important to develop a more comprehensive and representative definition of CRCI for AYAs, perhaps through use of a *grounded theory* approach [160]. Indeed, as CRCI research has largely been atheoretical, there is a critical need to build a theoretical framework from the ground up to: a) facilitate a greater understanding of AYAs' experiences with CRCI to create a more age-appropriate definition, and b) guide investigation into determinants and outcomes of this phenomenon. In contribution, the current results provide preliminary data on what could be discussed further with participants during interviews or focus groups. Ultimately, as research continues to grow in this field, it would be helpful to have a theory to guide future predictions, design, and interpretation of similar studies in AYAs.

Practical

While practical implications are limited given the cross-sectional nature of this study, findings do suggest that PA guidelines need to be better tailored for AYAs struggling with their cognitive function. Popular media disseminates that for optimal health benefits, adults should engage in 150 minutes of MVPA and two bouts of resistance training per week [161], but these flagship guidelines fail to provide context around effective PA engagement. PA guidelines/recommendations for cancer survivors do exist (i.e., [70, 162]), but their uptake is quite poor and they also lack description. Consequently, as Sydney mentioned in her interview, many cancer survivors are unsure about *how* to appropriately engage in PA (e.g., how much to do, where/when to engage in it, what type/intensity is best) and reap its potential benefits. This may be another reason for overexertion (i.e., the recurring concept of "too much" PA) causing mental fatigue, as previously discussed. Current cancer guidelines prescribe specific doses of PA to improve cancer-related health outcomes such as depressive symptoms, anxiety, fatigue,

physical functioning, and health-related QoL [70], but they have yet to provide dosage and context (e.g., frequency, duration, intensity, timing, environment) around recommended PA for cognitive function. Experimental research is needed to fill this gap and eventually update PA guidelines for cancer survivors. Recognizing that creating practical change is challenging and takes time, in the meantime, it would be beneficial for health promotion materials and popular infographics like "Moving through cancer: Exercise for people living with and beyond cancer" [163] to add CRCI as something PA can potentially help with (alongside cancer-related fatigue, health-related QoL, physical function, anxiety, etc.), but to also discuss the risks of overexertion.

In addition, qualitative data suggest that participants felt unequipped to handle CRCI and emphasize a critical need for greater awareness and informational support around this phenomenon. It may be helpful to partner with health professionals in the cancer care sphere when conducting such research so that they may relay information and potential coping strategies to survivors during treatment. Further, results provide a starting point for creating informational resources (e.g., brochures, infographics) that provide background on this potential side effect of cancer, common strategies to cope, as well as links to age-appropriate support groups; disseminating such materials during cancer treatment (perhaps through established relationships with health professionals) and making them available to survivors via popular survivorship platforms may help increase both awareness and information around CRCI.

Conclusion

Overall, findings from this thesis contribute to the sparse literature on CRCI in AYA cancer survivors and demonstrate that this group faces many cognitive struggles, particularly concerning their memory, EF, and processing speed. These struggles correlate with psychological factors like depressive symptoms, stress, and fatigue, and have deleterious

consequences for AYAs' daily and overall QoL. Moreover, among revealing other cognitive-behavioural strategies, findings collectively illuminate the potential of PA in helping AYAs self-manage CRCI. This provides support for continuing to investigate links between cognitive function and PA, specifically through high-quality experimental research (i.e., involving multiple cognitive and PA measures, pre/post testing, and long-term follow-up) that tests the putative mechanisms underlying potential benefits of PA as well as optimal PA dosages/contexts. As well, this study lays important groundwork for creating future CRCI-self-management programming and supports for this underrepresented population and highlights that AYAs would benefit from more systematic awareness, assessment, and monitoring of CRCI in healthcare.

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Appendix A: Research Board Ethics Approval Notice

03/08/2021

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-05-21-6889
Titre du projet / Project Title	Physical activity, cognitive function, psychological well-being, and quality of life in young persons treated for cancer
Type de projet / Project Type	Thèse de maîtrise / Master's thesis
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	03/08/2021
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	02/08/2022

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Sitara SHARMA	École des sciences de l'activité physique / School of Human Kinetics	Chercheur Principal / Principal Investigator
Jennifer BRUNET	École des sciences de l'activité physique / School of Human Kinetics	Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments

550, rue Cumberland, pièce 154 Ottawa (Ontario) K1N 6N5 Canada
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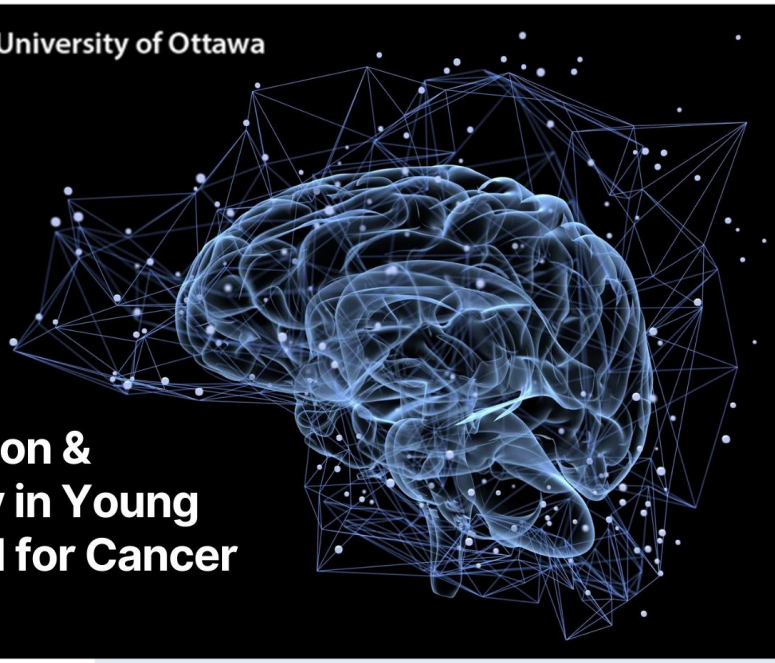
613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

Appendix B: Recruitment Flyer

Université d'Ottawa | University of Ottawa



Cognitive Function & Physical Activity in Young Persons Treated for Cancer

Are you a young (16–39 years), English-speaking cancer survivor who was 15–39 years at diagnosis?

Have you completed primary cancer treatment?

Do you have computer, Internet & audio/visual device access?

If so, this study may be of interest to you!

For more info, contact:

Sitara Sharma (MA Student),
University of Ottawa

T: [redacted]
E: [redacted]

Many cancer survivors experience **cognitive difficulties** and **psychological distress** during and/or after cancer treatments.

This study will explore associations between cognitive function, psychological factors, and quality of life in young persons treated for cancer, as well as the potential use of physical activity as a behavioural intervention.

Taking part in this online study involves:

- Completing a survey
- Completing short neuropsychological tests assessing different cognitive domains
- Possibly participating in an interview to explore how cancer has impacted your cognitive function

You will be entered into a draw to win a $100 CAD Visa gift card for your time!

The ethical aspects of this study have been reviewed and approved by the University of Ottawa Research Ethics Board.

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Appendix C: Recruitment Email Script

Hello *[insert potential participant's name here],*

Thank you for your interest in our study. The following is some background, followed by some screening questions.

The purpose of this study is to explore possible links between physical activity, cognitive function, psychological factors, and quality of life in adolescents and young adults treated for cancer. As a participant, you would be asked to complete two tasks. The first is a 30-minute online survey. The second is to complete three short neuropsychological tests, which should take approximately 10 to 15minutes. These tests are designed to assess different cognitive domains, meaning memory, attention, executive functioning, and processing speed. For each task that you begin (i.e., the survey and the neuropsychological tests), you will be entered into a draw to win a $100 CAD Visa gift card!

Additionally, depending on your survey results, you *may* be invited to participate in a 1-hour interview (using an online platform) to further explore how you feel you have been impacted by cancer in terms of your cognitive functioning, and what you do to manage this. Interviews will only be conducted with a small number of participants. If you do participate in the interview, you will receive another entry for the draw.

If this study interests you, we must determine if you are eligible to participate. To do so, I have nine questions below that I would like you to read through and respond with either "yes" or "no." If you are uncomfortable at any point, you may choose not to answer.

Screening Questions:

1. Were you between 15-39 years of age when you were diagnosed with cancer? (yes/no)
2. Are you currently between 16-39 years of age? (yes/no)
3. Were you diagnosed with nonmetastatic cancer (i.e., stage I-III, if applicable to your cancer)? (yes/no)
4. Have you completed primary cancer treatment? (yes/no)
5. Do you have access to a computer, the Internet, and audio-visual devices (e.g., webcam)? (yes/no)
6. Are you comfortable reading and answering questions in English? (yes/no)
7. Are you currently experiencing any residual symptoms (e.g., dizziness, headaches, loss of concentration) of traumatic brain injury or concussion? (yes/no)
8. Are you currently taking any selective serotonin reuptake inhibitor (SSRI) medication for treatment of depression, anxiety, or any other psychological condition? (yes/no)
9. Have you received a diagnosis of a substance use disorder (e.g., alcohol, narcotics) by a medical professional within the past year? (yes/no)

After emailing back your responses, if you are eligible to participate, you will be emailed a "Participant Protocol Document" containing detailed instructions on how to complete this

study. If you are no longer interested, I would appreciate it if you responded to this email to let me know.

Thank you again for your interest in this study! Please let me know if you have any questions. I look forward to hearing back from you.

Best,

Sitara Sharma, MA Student
University of Ottawa, Faculty of Health Sciences
125 University Private, Ottawa, ON, K1N 6N5

[If the individual responds and meets eligibility, email them back with their Participant ID and the "Participant Protocol Document" which contains detailed instructions and links for completing all steps of the study]

[If the individual responds and does NOT meet eligibility, thank them for their interest and let them know they are not eligible to take part in the study.]

[If the individual responds that they are no longer interested, thank them for their time.]

Appendix D: Participant Protocol Document

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Study Protocol

Cognitive Function & Physical Activity in Young Persons Treated for Cancer

Thank you for choosing to participate in our research! The following document will walk you through the step-by-step protocol of our study. We ask that you ***read all instructions carefully*** and follow them in the order that they are written. ***Please complete both steps within one week of receiving this protocol document (or let us know if you need more time).***

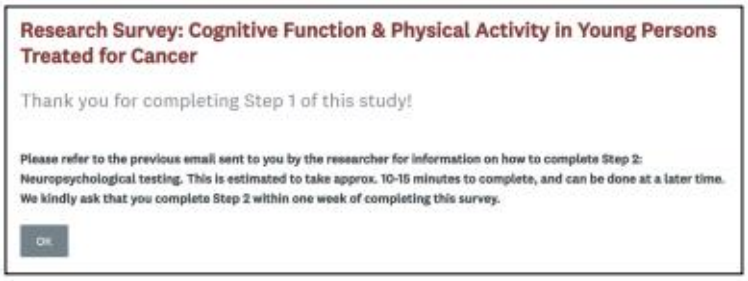
Note: If at any point, you wish to withdraw from the study and have your data removed, please email [redacted]

Step 1: Survey

The first portion of this study consists of an online survey, which you can access through this link: https://www.surveymonkey.ca/r/3CKMTJT. This link will first lead you to a participant consent form that provides detailed information on the study and the researchers. After reading through, if you choose to participate (i.e., click "Yes" at the bottom of the page), you will be able to begin the survey.

Please use the Participant ID you were provided with by the researcher to identify yourself, when asked in Question #2. This survey will take approximately 30 minutes to complete. It will ask you questions about your sociodemographic and medical information, cognitive function, mental health, stress, fatigue, quality of life, and physical activity levels. ***Please note, none of the questions in this survey are mandatory.*** If, for whatever reason, you do not want to answer a question, you may select "Prefer not to answer" or just leave the question blank.

Once the survey is complete, you will be asked to refer back to the researcher's recruitment email (or this protocol document) for a link to Step 2 to complete within the week. There will also be resources available in case you feel any psychological/emotional discomfort when completing the survey.



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Step 2: Neuropsychological Testing

The next step (and final step for most participants) involves neuropsychological testing, which you can access through this link: https://mili2nd.co/3g3b. This link will lead you to a landing page hosted by Inquisit (shown below). Prior to beginning the tests, you will need to download the app installer (IQWebPlayerSetup) which takes approx. 1 minute. Once you click "Start" you will need to ***enter the Participant ID you were provided with by the researcher to identify yourself.***

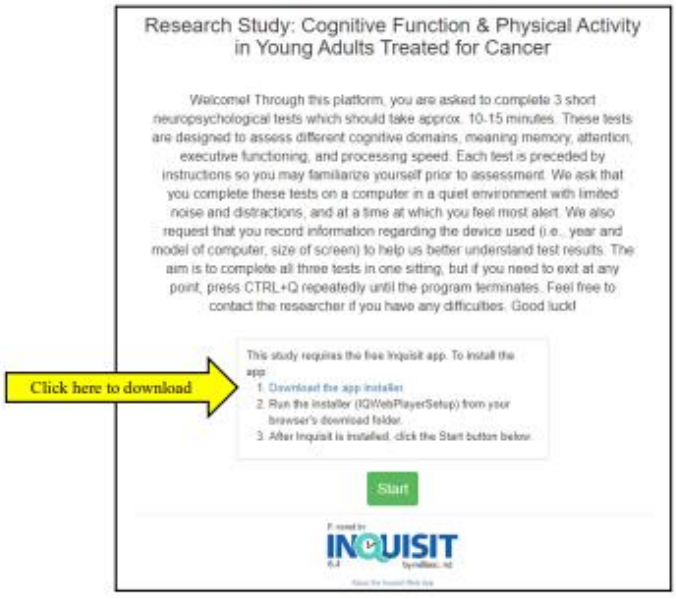
There will be 3 tests to complete which will take approx. 10-15 minutes. These tests are designed to assess different cognitive domains (i.e., memory, attention, executive functioning, processing speed) and are all preceded by clear instructions.

We ask that you please:

- Complete these tests ***on a computer*** in a quiet environment with limited noise and distractions
- Complete these tests at a time ***you feel most alert***
- ***Record information regarding the device used*** (i.e., year and model of computer, size of screen) to help us better understand test results
- Please refrain from writing information down or checking your phone during the tests (as tempting as it may be!)

The aim is to complete all tests in one sitting, but ***if you need to exit the platform at any time, press CTRL+Q repeatedly until it terminates the program.*** Also, feel free to take short mental breaks between the three tests (but please try not to remove yourself from the quiet, distraction-free environment or use your phone during this time).

You are welcome to reach out to the researcher if you have any questions or difficulties.



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After completion of all three neuropsychological tests, you will receive the following message. At this point, you can exit the program and/or uninstall Inquisit Web.

You're Done!

Thank you so much for your participation! Your responses are very valuable to us as we try to better understand the relationship between cognitive function, mental health, and physical activity in young persons treated for cancer in order to create appropriate future trials and psychosocial supports.

As a reminder, ***a small subset of participants will be asked to participate in an interview with the researcher*** based on survey responses. Otherwise, you have successfully completed this research study!

For each step (i.e., survey, neuropsychological tests, interview) that you participate in, you will receive an entry into a draw for a $100 CAD VISA gift card.

At this point, please email [redacted] to inform her that you have completed this study. In this email, please include the information you recorded regarding the device used (i.e., year and model of computer, size of screen) when completing the neuropsychological tests.

Thank you!

Appendix E: Informed Consent Form

Study Title: Physical activity, cognitive function, psychological well-being, and quality of life in adolescents and young adults treated for cancer

Principal Investigator: Sitara Sharma, MA Student
University of Ottawa, Faculty of Health Sciences
125 University Private, Ottawa, ON, K1N 6N5

Supervisor: Jennifer Brunet, PhD
University of Ottawa, Faculty of Health Sciences
125 University Private, Ottawa, ON, K1N 6N5

Thank you for taking the time to learn about this research study. This form will explain the study and what will happen in the study if you decide to participate. When we say "you" in this form, we mean you (the participant), and when we say "we," we are referring to the researchers.

Your consent (agreement) is required to participate in this study. If you would like to participate in this study, please read this form and click "AGREE" where indicated at the end of this form.

Why are you being invited to take part in this study? Cancer survivors report reduced quality of life due to difficulties with cognitive function and psychological distress during and/or after cancer treatments. We are conducting a study to explore associations between cognitive function, psychological factors, and quality of life in adolescent and young adult cancer survivors, a distinct but largely understudied population in the oncology literature. We are also interested in exploring the potential use of physical activity as a behavioural intervention to mitigate cancer-related cognitive impairment.

Why is this study being done? The purpose of this study is to better understand cancer-related cognitive impairment in adolescent and young adult cancer survivors, as well as the potential role of physical activity as a moderator between cognitive function and quality of life. This study is Ms. Sitara Sharma's MA thesis, which is being conducted under the supervision of Dr. Jennifer Brunet at University of Ottawa.

How many people will take part in this study? We are aiming to recruit 120 adolescents and young adults treated for cancer to participate in this study.

What will I be asked to do if I participate in this study? If you agree, you will be asked to:

1. Complete an online survey (approximately 30-40 minutes) with questionnaires that inquire about demographic/medical characteristics, cognitive function, mood, stress, fatigue, quality of life, and physical activity levels.
2. Complete three neuropsychological tests online (approximately 10 to 15 minutes) to assess cognitive function.
3. Potentially participate in an interview online (approximately 1 hour) to discuss your cancer experience, with particular focus on your cognitive function and the role of

physical activity in your life. Please note, only a small group of participants will be asked to complete this task.

Are there any benefits to taking part in this study? There are no direct benefits of this research to you; however, this project will make a contribution to the oncology literature because findings derived from this study will help to better understand how adolescent and young adult cancer survivors are affected by cancer-related cognitive impairments, and whether physical activity may play a moderating role in improving quality of life. This is important as it can inform the development of appropriately-targeted and effective interventions that are appropriate for increasing adolescent and young adult cancer survivors' cognitive function, as well as their overall physical, psychological, and psychosocial well-being.

For your time as a participant, you will be entered into a draw to win a $100 CAD Visa gift card. You will receive one entry into the draw for each study component that you begin (i.e., survey, neuropsychological tests, interview, if applicable), for up to three entries.

What are the risks of this study? Your participation in this online study will entail that you volunteer personal information, and this may cause you to feel psychological and/or emotional discomfort. If you feel that you need support, you can register for the University Health Network (UHN) Cancer Chat Canada program at https://cancerchat.desouzainstitute.com/users/register or call The Ottawa Hospital Cancer Center (TOHCC) Social Work Support Groups (Coping with Cancer Stress) at 613-737-7700 ext. 70516. For immediate support on a 24/7 basis, you can call the Distress Centre at 613-238-3311 or Crisis Services Canada at 1-833-456-4566.

What about privacy? The information that we collect from you will remain strictly confidential and will be used solely for research purposes. Only members of the research team will have access to any data that you provide. All of your data will be kept confidential and will not contain information that may lead to your identification. However, this is an online study; therefore, in order to minimize the risk of security breaches and to help ensure your confidentiality, we recommend that you use standard safety measures such as signing out of your account, closing your browser, and locking your screen or device when you are no longer using them/when you have completed each component of the study.

Please note, we will make every effort possible to keep your personal information confidential, but we cannot guarantee complete confidentiality. On rare occasions the Research Ethics Board at the University of Ottawa may access the study data as required by law, to ensure proper data management and to verify the ethical conduct of the study.

How will your information be stored? All of your data will be stored in a secure manner. Files will be kept for a period of 5 years after the research is completed on Ms. Sharma and Dr. Brunet's password-protected computers which are kept at their respective homes or locked offices at the University of Ottawa. The data will not be stored on a memory stick or any other easily lost/accessed media, nor will it be e-mailed.

What are my rights as a participant? You are under no obligation to participate in this study. You can choose whether or not you would like to take part and may exit the survey, neuropsychological testing session, or interview (if applicable) at any time. If you choose to participate, you are not waiving any of your legal rights and you can skip any procedure(s) without consequences. If you choose to withdraw from the study at any point, you will be given the option of withdrawing your data.

Who can answer questions I might have about this study? If you have questions about taking part in this study, you can talk to the principal investigator or supervisor of this study at the University of Ottawa:

Principal Investigator:
Sitara Sharma, MA Student
School of Human Kinetics
University of Ottawa

Supervisor
Dr. Jennifer Brunet, PhD
School of Human Kinetics
University of Ottawa

If you have any questions regarding the ethical conduct of this study, you may contact the Protocol Officer for Ethics in Research at the University of Ottawa:
Address: Tabaret Hall, 550 Cumberland Street, Room 154, Ottawa, ON K1N 6N5
Tel: (613)-562-5387
Email: ethics@uottawa.ca

If you would like a copy of this consent form, please save or print this page.

Do you consent to participate in this study?

☐ Click here if you **AGREE** to take part in this study.

☐ Click here if you do **NOT** agree to take part in this study.

Appendix F: Survey

Sociodemographic and Medical Questionnaire

This portion of the survey is needed to help understand the characteristics of participants in the study. For this reason, it is very important information and will be held in strict confidence.

General Background

1. What is your current age (in years)? _____

2. What is your biological sex?
    a. Female
    b. Male
    c. Prefer not to answer

3. What option best describes your current gender identity?
    a. Gender-fluid
    b. Man
    c. Non-binary
    d. Transgender man
    e. Transgender woman
    f. Two-spirit
    g. Woman
    h. Other (Please specify, if comfortable) _____
    i. Prefer not to answer

4. Which cultural and racial background(s) do you identify with? Please select all that apply
    a. Arab (e.g., Egyptian, Kuwaiti, Libyan)
    b. Black (e.g., African, Nigerian, Somali)
    c. Chinese
    d. Filipino
    e. Indigenous (Inuit, Métis, North American Indian)
    f. Japanese
    g. Korean
    h. Latin American (e.g., Chilean, Costa Rican, Mexican)
    i. South Asian (e.g., East Indian, Pakistani, Bangladeshi, Sri Lankan, etc.)
    j. South East Asian (e.g., Vietnamese, Cambodian, Malaysian, Laotian, Thai, etc.)
    k. West Asian (e.g., Afghan, Assyrian, Iranian, etc.)
    l. White (Caucasian)
    m. Other (Please specify, if comfortable) _____
    n. Prefer not to answer

5. What is your civil (relationship) status?
    a. Single
    b. Married or living with a life partner
    c. Separated

d. Divorced
e. Widowed
f. Prefer not to answer

6. What is your highest completed level of education?
    a. Primary/Elementary School
    b. Middle School
    c. High School Diploma
    d. College Diploma
    e. University Degree
    f. Prefer not to answer

7. What is your current employment status?
    a. Student
    b. Full-time work
    c. Part-time work
    d. Homemaker
    e. Paid sick leave
    f. Unemployed
    g. Other (Please specify) _____
    h. Prefer not to answer

8. What is your annual household income in Canadian dollars?
    a. Less than $20,000
    b. Between $20,000 and $39,999
    c. Between $40,000 and $59,999
    d. Between $60,000 and $79,000
    e. Between $80,000 and $99,999
    f. Over $100,000
    g. Prefer not to answer

9. In general, would you say your overall health is:
    a. Excellent
    b. Very good
    c. Good
    d. Fair
    e. Poor

10. Have you ever had a concussion?
    a. Yes
    b. No
    c. Prefer not to answer

11. If you answered “yes” to having had a concussion:
    a. How many concussions have you had? _____

   b. Did you lose consciousness (for any of the concussions, if multiple)? _____
   c. If applicable, how many minutes did you lose consciousness for (if multiple times, indicate the longest period of time)? _____

12. Have you consumed cannabis in the past month?
    a. Yes
    b. No
    c. Prefer not to answer

13. Do you <u>currently</u> consume cannabis?
    a. Yes
    b. No
    c. Prefer not to answer

14. If you answered "yes" to consuming cannabis:
    a. How often do you consume cannabis per week? _____
    b. What quantity of cannabis do you consume? _____
    c. How long have you been using cannabis for? _____
    d. What mode(s) of consumption (e.g., edibles, oils, smoking, vaping) do you use? _____
    e. If you know the THC:CBD or the potency, please specify (otherwise, write '999') _____

15. Are you currently participating in any research trial(s)?
    a. Yes
    b. No

16. If you answered "yes" to currently participating in any research trial(s), what is the nature of the trial?
    a. Physical activity trial
    b. Psychosocial trial
    c. Clinical trial
    d. Other (Please specify) _____

Cancer-related Questions

1. What was your age at cancer diagnosis (in years)? _____

2. What type of cancer(s) were you diagnosed with? _____

3. What stage of cancer were you diagnosed with?
    a. Stage 0
    b. Stage I
    c. Stage II
    d. Stage III
    e. Not applicable

f. Do not know

4. When did you complete active treatment for your cancer (MM/YYYY)?
_____

5. Please indicate which medical treatments you received for cancer and the date (MM/YYYY) of the last treatment, if applicable.

a. Surgery ☐ Yes ☐ No
If you received surgery, please indicate the date of your last surgery.
Date (month/year): _____ ☐ Do not remember

b. Chemotherapy ☐ Yes ☐ No
If you received chemotherapy, please indicate the date of your last treatment.
Date (month/year): _____ ☐ Do not remember

c. Radiation Therapy ☐ Yes ☐ No
If you received surgery, please indicate the date of your last treatment.
Date (month/year): _____ ☐ Do not remember

d. Hormonal Therapy ☐ Yes ☐ No
If you received hormonal therapy (or are still receiving hormonal therapy), please indicate the date of your last treatment.
Date (month/year): _____ ☐ Do not remember

e. Other treatment ☐ Yes ☐ No
If you received “other treatment”, please indicate the date of your last treatment.
Date (month/year): _____ ☐ Do not remember

Functional Assessment of Cancer Therapy—Cognition (FACT-Cog) Version 3

Below is a list of statements that other people with your condition have said are important. Please click one number per line to indicate your response as it applies to the past 7 days.

PERCEIVED COGNITIVE IMPAIRMENTS

1. I have trouble forming thoughts.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

2. My thinking has been slow.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

3. I have had trouble concentrating.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

4. I have had trouble finding my way to a familiar place.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

5. I have had trouble remembering where I put things, like my keys or my wallet.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

6. I have had trouble remembering new information, like phone numbers or simple instructions.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

7. I have had trouble recalling the name of an object while talking to someone.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

8. I have had trouble finding the right word(s) to express myself.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

9. I have used the wrong word when I referred to an object.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

10. I have had trouble saying what I mean in conversations with others.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

11. I have walked into a room and forgotten what I meant to get or do there.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

12. I have had to work really hard to pay attention or I would make a mistake.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

13. I have forgotten names of people soon after being introduced.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

14. My reactions in everyday situations have been slow.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

15. I have had to work harder than usual to keep track of what I was doing.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

16. My thinking has been slower than usual.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

17. I have had to work harder than usual to express myself clearly.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

18. I have had to use written lists more often than usual so I would not forget things.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

19. I have trouble keeping track of what I am doing if I am interrupted.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

20. I have trouble shifting back and forth between different activities that require thinking.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

COMMENTS FROM OTHERS

1. Other people have told me I seemed to have trouble remembering information.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

2. Other people have told me I seemed to have trouble speaking clearly.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

3. Other people have told me I seemed to have trouble thinking clearly.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

4. Other people have told me I seemed confused.

0	1	2	3	4
Never	About once a week	Two to three times a week	Nearly every day	Several times a day

PERCEIVED COGNITIVE ABILITIES

1. I have been able to concentrate.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. I have been able to bring to mind words that I wanted to use while talking to someone.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. I have been able to remember things, like where I left my keys or wallet.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. I have been able to remember to do things, like take medicine or buy something I needed.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I am able to pay attention and keep track of what I am doing without extra effort.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. My mind is as sharp as it has always been.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. My memory is as good as it has always been.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

8. I am able to shift back and forth between two activities that require thinking.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

9. I am able to keep track of what I am doing, even if I am interrupted.

0	1	2	3	4

Not at all	A little bit	Somewhat	Quite a bit	Very much

IMPACT ON QUALITY OF LIFE

1. I have been upset about these problems.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. These problems have interfered with my ability to work.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. These problems have interfered with my ability to do things I enjoy.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. These problems have interfered with the quality of my life.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

10-Item Center for Epidemiologic Studies Depression Scale (CES-D-10)

Below is a list of some of the ways you may have felt or behaved. Please indicate how often you have felt this way during the past 7 days by selecting the appropriate box for each question.

1. I was bothered by things that usually don't bother me.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

2. I had trouble keeping my mind on what I was doing.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

3. I felt depressed.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

4. I felt that everything I did was an effort.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

5. I felt hopeful about the future.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (1-7 days)

6. I felt fearful.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

7. My sleep was restless.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

8. I was happy.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

9. I felt lonely.

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

10. I could not “get going.”

0	1	2	3
Rarely or none of the time (less than 1 day)	Some or a little of the time (1-2 days)	Occasionally or a moderate amount of time (3-4 days)	All of the time (5-7 days)

Perceived Stress Scale (PSS)

For each question choose from the following alternatives:
0 – Never, 1 – Almost Never, 2 – Sometimes, 3 – Fairly Often, 4 – Very Often

1. In the last month, how often have you been upset because of something that happened unexpectedly?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

2. In the last month, how often have you felt that you were unable to control the important things in your life?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

3. In the last month, how often have you felt nervous and stressed?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

4. In the last month, how often have you felt confident about your ability to handle your personal problems?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

5. In the last month, how often have you felt that things were going your way?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

6. In the last month, how often have you found that you could not cope with all the things that you had to do?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

7. In the last month, how often have you been able to control irritations in your life?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

8. In the last month, how often have you felt that you were on top of things?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

9. In the last month, how often have you been angered because of things that happened that were outside of your control?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

Functional Assessment of Chronic Illness Therapy–Fatigue (FACT-F) Version 4

Below is a list of statements that other people with your illness have said are important. Please click one number per line to indicate your response as it applies to the past 7 days.

1. I feel fatigued.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. I feel weak all over.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. I feel listless ("washed out").

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. I feel tired.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I have trouble starting things because I am tired.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. I have trouble finishing things because I am tired.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. I have energy.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

8. I am able to do my usual activities.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

9. I need to sleep during the day.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

10. I am too tired to eat.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

11. I need help doing my usual activities.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

12. I am frustrated by being too tired to do the things I want to do.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

13. I have to limit my social activity because I am tired.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

Functional Assessment of Cancer Therapy—General (FACT-G) Version 4

Below is a list of statements that other people with your illness have said are important. Please click one number per line to indicate your response as it applies to the past 7 days.

PHYSICAL WELL-BEING

1. I have a lack of energy.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. I have nausea.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. Because of my physical condition, I have trouble meeting the needs of my family.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. I have pain.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I am bothered by side effects of treatment.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. I feel ill.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. I am forced to spend time in bed.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

SOCIAL/FAMILY WELL-BEING

1. I feel close to my friends.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. I get emotional support from my family.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. I get support from my friends.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. My family has accepted my illness.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I am satisfied with family communication about my illness.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. I feel close to my partner (or the person who is my main support).

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. *Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box* ☐ *and go to the next section.*

   I am satisfied with my sex life.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

EMOTIONAL WELL-BEING

1. I feel sad.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. I am satisfied with how I am coping with my illness.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. I am losing hope in the fight against my illness.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. I feel nervous.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I worry about dying.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. I worry that my condition will get worse.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

FUNCTIONAL WELL-BEING

1. I am able to work (including work at home).

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. My work (including work at home) is fulfilling.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. I am able to enjoy life.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. I have accepted my illness.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. I am sleeping well.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. I am enjoying the things I usually do for fun.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. I am content with the quality of my life right now.

0	1	2	3	4
Not at all	A little bit	Somewhat	Quite a bit	Very much

Leisure-Time Exercise Questionnaire (LTEQ)

1. During a typical 7-day period (a week), how many times on average do you do the following kinds of exercise for more than 15 minutes during your free time? Please write your answer in the appropriate box.

    a. **STRENUOUS EXERCISE (HEART BEATS RAPIDLY)** (e.g., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long-distance bicycling).

    _____

    b. **MODERATE EXERCISE (NOT EXHAUSTING)** (e.g., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing).

    _____

    c. **MILD EXERCISE (MINIMAL EFFORT)** (e.g., yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking).

    _____

2. During a typical 7-day period (a week), in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

    a. Often
    b. Sometimes
    c. Never/rarely

3. During a typical 7-day period (a week), when you engage in physical activity:

    a. Who do you engage in physical activity with *most often* with? Please select only one answer.
        i. Partner(s)
        ii. Friend(s)
        iii. Colleague(s)
        iv. Sibling(s)
        v. Parent(s)
        vi. Child(ren)
        vii. Alone

    b. Where do you engage in physical activity *most* often? Please select only one answer.
        i. At home
        ii. At a fitness studio/centre/club/gym
        iii. Hospital gym
        iv. At work
        v. Other, please specify: _____

c. In what environment do you *most often* engage in physical activity? Please select only one answer.
    i. Indoors
    ii. Outdoors

d. What time of day do you *most often* engage in physical activity? Please select only one answer.
    i. Morning
    ii. Afternoon
    iii. Evening
    iv. Night

e. What types of physical activity do you do? Please select ALL that apply.
    i. Strengthening (i.e., activities that help you build muscle mass like body weight exercises [e.g., squats, push-ups and lunges], exercise involving resistance from a weight, a band, or a weight machine)
    ii. Aerobic/endurance (i.e., activities that speed up your heart rate and breathing like brisk walking, swimming, jogging, cycling, dancing)
    iii. Stretching/balance (i.e., activities to maintain flexibility and increase your range of motion like static stretching [holding a stretch position for up to 60 seconds], as well as to help you feel steadier on your feet and prevent falls such as tai chi or yoga)

Thank you for your participation!

If you felt any psychological and/or emotional discomfort from completing this survey and feel that you need support, the following are some resources you can access:

- University Health Network (UHN) Cancer Chat Canada program (https://cancerchat.desouzainstitute.com/)
- The Ottawa Hospital Cancer Center (TOHCC) Social Work Support Groups (Coping with Cancer Stress) at 613-737-7700 ext. 70516
- The Distress Centre (24/7 support) at 613-238-3311
- Crisis Services Canada (24/7 support) at 1-833-456-4566.

If you would like to be considered for future research projects, please email us and include your name, contact information, age, and cancer diagnosis in the body of the email.

Appendix G: Recruitment Telephone Script

[Potential participant calls to express interest]

Hello *[insert potential participant's name here]*, thank you for your interest in participating in our study! My name is Sitara and I am the Principal Investigator for this study. Do you have a few minutes right now for me to speak to you about the study?

[If the potential participant says 'yes', proceed. If the potential participant says 'no, not now', determine a better time to contact them.]

The purpose of this study is to explore possible links between physical activity, cognitive function, psychological factors, and quality of life in adolescents and young adults treated for cancer. As a participant, you would be asked to complete two tasks. The first is a 30- minute online survey. The second is to complete three short neuropsychological tests, which should take approximately 10 to 15 minutes. These tests are designed to assess different cognitive domains, meaning memory, attention, executive functioning, and processing speed. For each task that you begin (i.e., the survey and the neuropsychological tests), you will be entered into a draw to win a $100 CAD Visa gift card!

Additionally, depending on your survey results, you *may* be invited to participate in a 1-hour interview (using an online platform) to further explore how you feel you have been impacted by cancer in terms of your cognitive functioning, and what you do to manage this. Interviews will only be conducted with a small number of participants. If you do participate in the interview, you will receive another entry for the draw.

Does this study sound like something you would be interested in doing?

[If the potential participant says 'yes', proceed to the questions. If the potential participant says 'no, not now', determine a better time to contact them. If the potential participant says 'no, I do not want to participate at all,' they will be thanked for their time and no further contact will be made.]

The first thing we need to do is determine if you are eligible to participate. To do this, I will need to ask you some questions about yourself and your medical history. If you are uncomfortable at any point, you may choose not to answer. Is it okay if I ask you the eligibility questions now?

[If the potential participant says 'yes', proceed to the questions. If the potential participant says 'no, not now', determine a better time to contact them. If the potential participant says 'no, I do not want to participate at all', they will be thanked for their time and no further contact will be made.]

Great, I have 9 questions for you, and I'd like you to answer with a simple "yes" or "no" response.

1. Were you between 15-39 years of age <u>when you were diagnosed</u> with cancer? (yes/no) *[must answer yes]*
2. Are you <u>currently</u> between 16-39 years of age? (yes/no) *[must answer yes]*

3. Were you diagnosed with nonmetastatic cancer (i.e., stage I-III, if applicable to your cancer)? (yes/no) *[must answer yes]*
4. Have you completed primary cancer treatment? (yes/no) *[must answer yes]*
5. Do you have access to a computer, the Internet, and audio-visual devices (e.g., webcam)? (yes/no) *[must answer yes]*
6. Are you comfortable reading and answering questions in English? (yes/no) *[must answer yes]*
7. Are you currently experiencing any residual symptoms (e.g., dizziness, headaches, loss of concentration) of traumatic brain injury or concussion? (yes/no) *[must answer no]*
8. Are you currently taking any selective serotonin reuptake inhibitor (SSRI) medication for treatment of depression, anxiety, or any other psychological condition? (yes/no) *[must answer no]*
9. Have you received a diagnosis of a substance use disorder (e.g., alcohol, narcotics) by a medical professional within the past year? (yes/no) *[must answer no]*

[If at any point (i.e., while answering questions 1 through 9) potential participants are not eligible, research personnel will say the following.]

Thank you for your response and interest, you are not eligible to participate in this study.

[If potential participants are eligible, research personnel will say the following.]

Thank you for your responses, you are eligible to participate in this study! I will email you the "Participant Protocol Document" containing detailed instructions on how to complete this study. If you are no longer interested, I would appreciate it if you respond to that email to let me know.

[Confirm participant's name and email address]

Great, thank you for your time and interest, I will be in touch via email shortly.

Appendix H: Interview Guide

Introduction

Welcome! Thank you for agreeing to participate in this interview. My name is Sitara and I am a Master's student at the University of Ottawa. The reason I invited you to take part in this interview is because you indicated that you are experiencing cancer-related cognitive impairments. My goal is to better understand your perceptions of these impairments by gathering your thoughts, feelings, and opinions about your experiences with cancer, and how it has impacted your cognitive function and overall quality of life. This interview will last approximately one hour.

Before we begin, I'd like to review a few things that are useful to know about this interview:

1. I am audio recording the session so to ensure that I get all the information and exactly as you said it.
2. Your name as well as other names used during this interview will be kept confidential and will be removed once the interview is over. In this way, your confidentiality will be assured.
3. There are no right or wrong answers. Feel free to say whatever you want. Anything you're thinking is important and interesting. I want to hear your thoughts and opinions.
4. Please do not feel pressured to answer any of the questions, if you choose you may skip over any questions.

Do you have any questions or concerns before we begin?

Interview Questions

1. Can you tell me what was it like being diagnosed with cancer when you were ____ years old?
    a. Can you describe any specific challenges you faced by being diagnosed at this age?
        i. Emotional/psychological, physical, social, financial.
2. Can you describe your current cognitive function?
    a. What specific cognitive difficulties or impairments (e.g., impaired memory, attention, etc.) do you experience?
        i. Could you elaborate on the frequency and severity of these difficulties or impairments?
        ii. When would you say these difficulties or impairments began?
            a. How did you come to notice them?
        iii. Do you think that the cognitive difficulties or impairments you are experiencing are due to your specific cancer (i.e., _____) and the treatments you received, namely _____? Why or why not?
3. Can you tell me how the cognitive difficulties or impairments you just mentioned have affected your:
    a. Day-to-day life?
    b. Schooling and/or work?

    c. Social/family relationships?
        i. *[Probe] Have your cognitive difficulties or impairments ever been a barrier in your relationships with family, friends, and/or romantic partners? How so?*
    d. Emotional/psychological wellbeing?
        i. *[Probe] Can you tell me about any accompanying psychological distress (e.g., stress, anxiety, depression, fatigue) you feel because of your cognitive difficulties or impairments?*
        ii. *[Probe] Which adverse emotional effects are the most/least bothersome to you? Why?*
        iii. *[Probe] Do you think your cognitive difficulties or impairments stem from treatment or from associated psychological distress? Why?*
        iv. *[Probe] Has this affected the way you see yourself? How?*
    e. Physical wellbeing?
    f. Financial situation?
    g. Overall quality of life?
    h. Have your cognitive difficulties or impairments affected you in any other way? If so, could you please describe how?
4. Do you think that being diagnosed when you were _____ years and now being where you are in life influence how you experience your cognitive difficulties or impairments? How so?
5. Do your family/friends/peers ever comment on your cognitive function or act in a way that makes you feel they are aware of your cognitive difficulties/impairments? If so, could you give me examples of what they say or do?
6. Compared to before you were diagnosed, how do you think your cognitive function has changed over the course of your cancer journey?
    a. After diagnosis?
    b. During treatment?
    c. Immediately after treatment? What about as time went on after treatment?
7. What strategies do you use to manage your cognitive difficulties or impairments?
    a. Why these?
    b. Was/is physical activity one of such strategies? Why so? Why not?
8. Do you believe physical activity can improve your cognitive function? Why/why not?
9. Has anyone ever recommended that you engage in physical activity to improve your cognitive function? If so, who? What did they say?
    a. How does it feel when you engage in physical activity?
    b. Do you feel that physical activity helps improve your memory? Attention? Processing speed? Any other cognitive domains? Why or why not?
    c. Do you feel that physical activity helps to reduce the negative thoughts and feelings you have about your cognitive difficulties or impairments? Why so?
10. What barriers to engaging in physical activity have your cognitive difficulties or impairments presented?
    a. What strategies do you use to continue engaging in physical activity despite these barriers? For example, do you schedule it at a specific time? Do you plan it in a certain way?
11. What do you think health professionals could or should do to help promote physical activity in those who are suffering from cognitive difficulties and impairments after being diagnosed with cancer?

Ending Questions/Remarks

12. Is there anything else that you feel that we did not get a chance to discuss?
13. Do you have anything else to add surrounding cancer, cognitive function or physical activity?

Thank you so much for your time, I really appreciate you providing me with your experiences.

At this point in time, I would like to remind you that my contact information can be found in the consent form you were provided, alongside a number of resources, should you require support.

Appendix I: Qualitative Themes Table

Objective: Describe young adults' lived experiences with CRCI, the meanings that they ascribe to their cognitive function in the aftermath of cancer, as well as understand how they self-manage it.

Main themes	Sub-themes	Quotations
Participants' descriptions and interpretations of the CRCI phenomenon *This theme captures participants' thoughts about the origins, evolution, and meaning of CRCI.*	*General descriptions of CRCI:* When participants described their cognitive impairment, these descriptions illuminated troubles with memory, concentration, information processing, finding words.	Mia: I can't trust my brain. Like, I can't trust my brain that I'm going to remember something. Sydney: Everything feels like it's been muted a bit… you know, like … when you're sick and your brain's just not moving quite at [the right] speed? I feel like that all the time, but I'm not sick anymore. Jaime: There's the spacing out, there's the… [lack of] concentration at work… The general like fog over my head is like… this constant cloud of, like, [being] unable to really, clearly, crisply process things. Jack: It's a layer of difficulty to what I'm doing… that's how I would describe most of my cognition… it's a video game and I turn the difficulty level up one. Priya: It's almost like the synapses in your brain like stop firing and I just have, like, a gap where I just can't talk… nothing is connecting. And… I don't know what to say… you know, how sometimes things are on the tip of your tongue and then you just can't remember? It's not like that. There actually feels like there's like a black hole in between where the messages are being connected or transferred in your brain. Nina: Everything feels like it's in a fog…day-to-day conversation is difficult. Like finding words and putting a sentence together. I'm feel like some days I'm like stumbling over words or I have to work really hard to come up with a sentence. It's really…it's really weird.
	CRCI can be intense: Descriptions of participants' CRCI indicated that their cognitive difficulties presented both frequently and with considerable severity.	*Frequency: Several times per week if not daily; worse when fatigued* Sarah: [Brain fog] probably happens every day, for sure. It's definitely worse the days that I do more. So, if I have kind of a day where I'm not like puttering around the house and stuff, then it's not as bad… but the days where I am really physical… I'm just fatigued really quickly. So, then it's worse. Sydney: Daily, definitely daily. Jaime: I guess pretty much daily. Jack: The [difficulty with] switching of tasks, info processing, that's a constant. I basically build like, the way that I interact around that… But every now and then I have days…I have really thick chemo brain and I am retaining nothing…and those days, I'd say they happen maybe once or twice a month… those days I almost should start taking sick days. I'm pretty much lost. And then I come into work the next day and go, what did I do? Like, what is this thing that you wrote? Like, I don't understand me. Priya: I would say [cognitive impairments] happen like at least five times a week. Nina: The memory is bad most days and like that feeling of being in a fog, that's there pretty much every day. Lauren: It's hard to say how frequently I have *actual* issues, but how frequently it comes to my attention that I am having this problem is

		maybe like…at least once or twice a week. Something will come up where I'm like, 'Okay, we have an issue.'" Peyton: Definitely, like, multiple times a week for sure. *Severity: Ranges from minimal to severe, with most participants feeling like it's "right in the middle" of the scale; severity is fluid depending on the day and how tired one is* Erica: Like a two [out of 10]. It's just like little things. Layla: I would say, like, [CRCI severity] averages like a five [out of 10], but like some days might be less than others kind of thing. Eva: I'd say I'm at a six [out of 10] right now. Taylor: For me, [CRCI is] like super strong. So, I would say like an eight because… I'm I always comparing myself to my pre-cancer self. Cole: [Severity] varies daily…I'd say like six or seven [out of 10] overall. Peyton: I don't know… like a five… kind of like, right in the middle. Five, six, like, it bothers me, obviously, but… I can still live my life around it. Ivy: I would say [CRCI affects me] severely…10.
	It is false to think CRCI always goes away: Additional descriptions indicated that CRCI could worsen over time or fluctuate and that participants could continue to struggle post-treatment. However, in most cases, cognitive troubles were most pronounced during and immediately after treatment ended. Although slight-to-moderate improvements were mentioned over time, participants attributed these to becoming more skilled at living with CRCI and/or taking actions to support their cognitive function (as described below).	*Worsened over time or fluctuates* Sydney: It feels worse to me. It does NOT feel like it's gotten better…it feels worse, but it's not dramatic. Nina: [Cognitive function] got worse after the surgery…I think my memory and concentration really…like you would think it's gotten…I would have…I kind of hoped it would get better after the surgery because the cancer's gone, but it's got a bit worse. Cole: It definitely got progressively worse. Mia: [Brain fog has] gone in waves. It's gone in waves. At times, it's gotten better. And then, just like I said, with this last adjustment [of medication], it's gone back down. *Has gotten somewhat better over time* Jack: It was a rapid drop [in cognitive function]. I don't remember that beginning phase, all I remember is kind of being at the bottom. And I'd say [I've] slowly been recovering and… plateaued in a lot of ways in terms of cognition. So, like, my stutter was really thick before and what would happen pretty regularly, and I would get caught in those loops. And now I kind of just pause and my sentences and say the same syllable every few, few times, every now and then. So, it's gotten a little better on that front. The same thing with the memory. It's gotten a little bit better. And now I pretty much feel like I've been at the same place for the past two or so years. Emma: Before [cancer], I felt like cognitive function was a strength. I was very much a "do it all, get it all done" person… manage many things and be totally fine, don't have to write anything down, don't have to stumble on my words, you know… I don't think I was functioning at all cognitively [during treatment]… And after…I think it's been better than during treatment…but it's definitely not a huge improvement.

		Priya: I think I have like, less of like the kind of like "brain fog," foggy stuff now…I'm able to, like, function fairly normally…So, some of the fog has lifted, I guess. Layla: I think [my CRCI is] improving. I had a lot of brain fog… I did chemo until last November and then I did radiation in March/April of this year… after the radiation, the fatigue and brain fog was just…so consuming… some of that… theory knowledge is coming back, but I've had to work really hard over the last few months in order to do that. Peyton: I think I've like kind of plateaued. Like, when I started, it was like, a steady decline [in cognitive function]. And then like I would say, the past like 6-8 months, it's like, plateaued… I don't know if… [my cognitive function is] getting better, or if I'm just getting, like, used to living with how my brain works.
	Hypotheses about who gets CRCI and what causes it: Participants attributed the origin of CRCI to either their cancer treatment(s) or the medication(s) that they took. They also felt that CRCI affects survivors regardless of their diagnosis type, stage, or form of primary treatment.	Mia: I think [brain fog] comes from the medication… from the getting the right balance of medication. Jaime: I definitely think that the treatment was a big cause of it. Like, all the chemicals… Emma: I don't think it has anything to do with my cancer… I think treatment… I have quite a few friends that have been through this, too, and I feel like it's [affected] everybody that I've talked to. Layla: I think it has to do with the drugs…like I have heard from other survivors…through chemo…the brain fog and…cognitive function really kind of was impacted. Lauren: My guess is that people experience [CRCI] with cancer treatment in general. I don't know if that has to do with the fact that you're given like so many drugs…and all that just messes with your brain…I feel like in general, cancer patients…have some sort of cognitive issues related to treatment. Eva: I think [CRCI happens] because of the treatment.
Effects of CRCI on day-to-day life and quality of life *This theme demonstrates that participants explicitly linked CRCI to QoL. They noted that when cognitive troubles manifest, their physical, social, psycho-emotional and professional wellbeing and function is adversely impacted.*	*CRCI impedes day-to-day life:* Participants made several remarks about how CRCI thwarts their ability to undertake instrumental activities of daily living. They gave examples that it made cooking and housework hard because everything takes longer and requires more effort or because they would easily get distracted. They also appeared to neglect self-care (e.g., brushing their teeth, engaging in PA) and had difficulties upholding values (e.g., being punctual).	*Everything takes longer and requires more effortful attention* Sarah: Everything is more work. Everything takes more focus, more work… So, then you get more tired from all the efforts, so then it's like, "I don't want to do that because it's too much work," …I can only do one thing at a time…and then I see something else and think "Oh, I got to do that too." And then I get overwhelmed because the list gets longer, and then I get tired and can't do them…it's brutal. Priya: I have had, like, a lot of…really dumb things happen, I flooded my kitchen one day because I left the water running on my dish and washing machine was also on and so I couldn't hear a noise…So things like that…when I'm like cooking…I need to be like just focusing on that activity…I can't walk away and like be like, 'Oh, I'll just quickly check my email' because then I'll like start doing something [else] and a half an hour later I'm like, 'Oh my goodness, I was cooking.' Taylor: Definitely things take longer for me because… sometimes I lose track of what I was going to do or what I was going to say. So, like, for example, when I'm cooking, sometimes like [I] prepare everything and then I just forget what I was going to do. And obviously it will take me longer to get my cooking done. And that's an impact in my day-to-day life because like, sometimes I have to plan in extra time… like with just daily activities like getting ready, cooking, going out, I would say it just takes longer.

	Further, some limited or stopped driving out of apprehension for threatening physical safety of oneself and others.	Peyton: I just need to go a lot slower doing things… just like taking the time to like, think things through and… mak[e] sure I… remembered everything… like baking or like cooking, just like making sure that I've like, done all the steps or like, even when I do like laundry… double checking that I like, put the laundry soap in the laundry, like compartment type thing. So, it just takes longer to do stuff and [requires] being more thorough because I have to like, go back and make sure, or like re-read or that kind of stuff. *Since necessary daily tasks take longer, participants often neglect self-care (e.g., brushing their teeth, engaging in PA)* Sarah: I was never late for anything before… Now I'm late for everything and I hate it. It's like there's not enough time in a day for me to get through anything. I just seem like I'm failing a lot. Um, so…and I yeah, and then I get so tired sometimes that I can't do what I planned, right? So, the workouts…like I said, I used to do yoga tons in the morning, but now I get…I'm just really tired. Sydney: I often think I can do more than I can… because I work out in the morning, I might be like, "Ah, I can sleep a little bit longer…like I'm tired, I'm going to just sleep a little bit longer." And then all of a sudden you get up and you're like "Well, now I really don't have time to do this," even though I know that I like…if I really thought about it, I would know that I would need to get up a little bit earlier to do something. I think when it only impacts myself, I am worse at that planning. Erica: This sounds so gross, but like I sometimes… I'd forget to brush my teeth, or I would forget to eat breakfast or something like that. Taylor: Stuff takes longer for me…[so] I don't leave enough time for my walks. So, I'm like, I want to go for a walk at 10 am until 12:00 pm, right?... And then I only get out of bed at 9:30, and then I have to cook breakfast and do this and do that. And then I'm like, "oh yeah, I wanted to go for a walk, but now I only have like one hour left, so I'm not going." *Threatens/causes fear for physical safety (usually with driving)* Sarah: There has been a couple times driving where I've just said—I just have come home because I know that I shouldn't be out there because I can't focus enough. Or I've had a close call or something, right? Where I'm like, "hey, I'm not, I'm not here." So there, there has been those days where I just shut it down. Sydney: I definitely feel like I have to work at driving. That is one of those things where you're kind of like, 'bring it in, this is really important. You're driving a vehicle that could kill someone. Please, like think.' But it is harder, you know, and that part's really terrifying. Priya: I've been really nervous about like…more nervous about driving just because I feel like my reaction time is kind of slow… I live in a space where it's like a spot where there's no traffic and we just have a highway, but like, I had to go to the city and I avoided going downtown or where there was traffic. I was just kind of afraid I wasn't going to be able to, like, react as fast as I needed to in that situation. Just kind of like slow processing, feeling like if I ran out in front of my car, turned suddenly, would I be able to react as fast as I could before?
	CRCI thwarts social wellbeing and functioning:	*Source of strain for relationships*

	CRCI was a source of strain in participants' relationships with others because it caused communication struggles and left them feeling poorly understood by others. They also wrestled with their role as a friend as they felt less thoughtful and able to remember details about loved ones' lives. Moreover, cognitive difficulties inhibited social engagement and led to self-isolation.	Sydney: I do need more time to process. Like, even in things where it's like, I guess, no decision, I may not even hear the question until a second or two after it's been asked, where my brain finally registers what it was. And unfortunately, I have a very quick-thinking partner. And that's…and that alone is frustrating. I mean, that's basically the crux of like all of our communication problems. Mia: I have a father who's very…he's a difficult person to deal with. And he doesn't understand being forgetful. He doesn't understand that [cognitive impairment] is something that I'm dealing with so he'll get upset, saying that I don't remember something because I don't want to do it. Not just because I forget. Lauren: I would get very hurt when people would tell me…you know, like, 'Oh, you don't remember this?' Like, my memory is not as great [and] I'm reminded of it by like certain people. Like, I just get very offended at it…Sometimes I'll randomly forget something that…was important in a conversation that I had. And then the person who I had it with will bring it up and be like, 'Why don't you remember that specifically?' Like, 'Are you selectively remembering?' And I'm like, 'No, I promise this thing just happens like at random, like I don't remember certain … it's hard for the people in my life to understand that. *Not feeling understood – not feeling a sense of belonging* Sarah: I remember how I felt. I just remember feeling like nobody understood that piece, right? Like everybody felt sorry for me because my hair was gone and, and…you know, that kind of stuff, but it was the not being able to talk and not being able to articulate what even was happening. But nobody—so you just feel really alone through all of that part, right? Because they don't—nobody really understands that part. Like until you're in the chemo, like the "cancer world," then *those* people talk about brain fog, but people in your circle… they don't. So, they just kind of stare at you like you're…as you're trying to figure out what to say they just kind of look at you with those sad eyes. Taylor: My friend…we've known each other for 11 years now, and she tells me stories, and I was like, "I'm not sure if I was there" because… it's completely erased from my memory…Sometimes I even feel like a bad friend because I can't remember anymore. Sarah: I am more forgetful so I'm not as thoughtful as I used to be because I can't remember milestones and stuff unless they're on my phone… that just makes me feel like I'm a shitty person. *Avoiding others/isolating due to difficulties with communicating* Sarah: I find that I'm avoiding hard things now because they're too much. So, I can't…because I can't articulate how it feel, I just avoid [people]… Some of my family, especially if it's hard, I just—they don't understand and I'm never gonna make them so… Jack: [CRCI] probably affected my relationships with others because I couldn't open up, I couldn't engage, and I was just missing for a lot of it. I know with my sister, at the very least, it wasn't until this year that I, like, sat down and talked to my sister and she could hear where I was at that time and I could hear how much like resentment she'd slowly built up over the years just because I was absent from her world and she didn't want that.

		Emma: It makes me nervous because I don't want to ask them again or make them see that I didn't remember something really important. So, I'm kind of hesitant with how I approach conversations… I definitely avoid [people]…I guess I feel like…maybe they're annoyed with the things that they have to put up with from me, and I feel like they are like, you know, "do I have to hang out with her?" I don't know if it's true… But I feel… just like an internal barrier. Nina: Sometimes when I can't put a sentence together, I feel really ridiculous and then it kind of makes you not want to talk to people because you feel like you can't even put a sentence together and if they don't know what's going on, they're probably thinking, "oh my gosh, what's going on with her?" So, I guess it kind of makes it… maybe I am a little bit more isolating myself.
	CRCI impacts self-evaluations, which affects psycho-emotional wellbeing: CRCI negatively impacted participants self-worth and sense of identity; since these facets of the self were considered to be central, it gave rise to negative emotions and thoughts. However, as participants explained it, negative emotions and thoughts could also generate cognitive troubles, suggesting that the connection between CRCI and psychological distress is bi-directional.	*Loss of identity/decreased self-worth evoking negative emotions* Sarah: It makes you insecure…you don't recognize who you are. You don't recognize your brain…All the things that you grew up learning how to study and knowing how to do, for you, they don't work anymore…It's very unnerving not being able to do what you did… and not being as smart as you were. Sydney: There's certainly more stress, um, stress and anxiety over not getting enough done…and I think part of it comes back to the cognitive stuff, because a lot of it is just like triaging tasks, like "how do I take everything I need to do and organize it in a way that I can get at everything, or at least have a plan for how I'm going to?" and that planning ability has decreased. And because of that, then I feel like, part of it is kind of a loss of a sense of self, or who I used to know, and not seeing that line up with who I am now. Layla: My memory was quite sharp…I always got high grades. So, it was really, really disappointing. I think [CRCI] took a lot of my identity. I lost a lot of my confidence in myself and developed a lot of imposter syndrome…I've learned to manage [CRCI], but initially it was really, really upsetting because it was frustrating and it wasn't who I was … I went home and cried every day. Sarah: [CRCI] messes with…I guess it would be self-esteem, kind of? I don't know, self-confidence?... like you feel like… "I don't know who I am anymore." And nobody gets that… Everyone just thinks cancer is over and "Oh, you're back to where you were!" Well, you're not even an eighth of who you were before. Like it's totally different. Jaime: My husband will hear me say it all the time where I'm just like, you know, "I wish I wasn't…I wish I didn't feel so slow." Like I don't…I'm not the way I used to be, and it makes me feel bad. Like I used to, like, I don't know…it just feels bad. Jack: A lot of it is pride and a little bit of ego, but I do like to view myself as a pretty capable person. I achieve like, not mastery, but adequate function in almost anything I try pretty quickly, and so to like lose the capability to do things [due to CRCI] I think was really challenging for me. Emma: I feel like a failure sometimes, you know? I'm just very down on myself that I should be able to function. And why am I not functioning? It's hard because it's compared to before.

		Taylor: I feel like I'm super hard on myself and sometimes like I feel like I'm now like a damaged version of me, so like I'm worth less than I was before I had cancer. Peyton: I feel like I'm just like a shell of like, what I once thought I was… just not quite feeling the same mentally as before cancer. *Feeling less intelligent* Sarah: [Intelligence] has taken a beating for sure. Like, I'm scared to study anything new because I'm not sure I can retain it. I'm not sure that I can even have the energy to focus that hard on something. So, then it makes me feel like I shouldn't, which isn't a great feeling, right? Mia: I feel like I'm not as smart as before, because I feel like I'd be able to do so many other things before. I'd be able to come up with better words for some of the…my confusion and stuff like that. Like the words were there. It's harder. Jaime: I should have been that career-woman-manager, whatever go-getter. And now I'm just like, ugh, I just want to enter data or something, you know? I don't even care about money. I don't care, but then at the same time, I'm like, I should have been, you know, like I *was* smart… Taylor: It has gotten better, but there's still like times when I'm trying to say something and I will just sit there with my mouth open and I can't figure out what I want to say… I feel really stupid. *CRCI and distress: A "vicious cycle"* Sarah: The cognitive stuff kind of builds up, you know, like you don't feel the same. But then as it builds up and happens more often, then it's way more stressful. Um, but then now, you get stressed because you know that's going to happen, and so it's like two circles. Jack: I think it happens in both directions. I think I if I'm having issues with my cognition, I feel depressed and slow and low. And conversely, if I'm having anxiety, um, I think I'm so hyper-focused on those things that I can't pay attention well, I get distracted, I can't remember what's going on…And then when I can't remember what's going on, I start to feel like an idiot and that starts to trigger the depression, and then the depression starts to trigger like lack of energy. And I think they feed all on each other like writhing massive snakes. Layla: I think [brain fog and distress] both feed into each other and think they're super multifactorial. I feel like the brain fog probably plays into the depression. Like it probably leads into it because of the emotional toll that it takes. Taylor: I also feel it's kind of like a vicious cycle because yeah, when you get anxious, of course your concentration or whatever decreases and when you notice that your concentration decreases, of course you get more anxious…
	CRCI obstructs professional development, which affects their financial security. In discussing the impacts of CRCI, participants felt that it	*Difficult to perform well or at the same level as before* Emma: My job [as a Mental Health Counsellor] is…you have to be on the ball and I just didn't feel like it would be fair to my clients to have to try to have a conversation with me…like I didn't feel like I could give them what they needed. I was worried that I wouldn't be able to come up with, you know, things you have to come up with during counseling sessions and to be able to respond in an appropriate manner. You know, like you have to think about all the things—your body language, what

	impeded their professional development by making it difficult to perform in school/work; as a result, it was a deterrent to finding new work/pursuing further schooling. Participants discussed that this was especially challenging for them due to the impact on their financial security.	you say, how you say it, and I just didn't feel confident that I could make that a good experience. And I didn't even get there to even try. When I can't even do the desk duties in an efficient manner, I thought I shouldn't even be with people. Priya: Just going slower…I do a lot of consulting work that's like I only get paid when I do the work, not like a salary job. So that makes me nervous about taking on big projects, like I just don't know if I'll have the ability to produce as much in the same time span as I could have before… Layla: I couldn't remember things for school, I was trying to do placement, and it was just…it was a lot. I couldn't remember information. Like, everything that I learned about anatomy over the past 15 years, I couldn't remember. Taylor: Oh my God, [school's] really hard because my…my mind, it just wanders all the time. Like when I read something, I am thinking about something that doesn't have anything to do with this topic, and I will read 2-3 pages and then I'm like, "I don't even know what it said." Like, I read it, but like the information never entered my brain, I would say. *Barrier to finding/returning to work or pursuing further schooling* Mia: I was in the process of going through interviews and applying and all that fun jazz. But … it's not fair to a new employer for me to go there and have all of this confusion and everything until I'm all sorted out…So really, I stopped looking. Cole: … it's been very hard to be able to consistently stay with like a full-time job just because I…there's so much to learn or like, there's so many mistakes that you can make in a day, but it just seems that every attempt has been futile for me. Peyton: I'm like, starting to like, think about returning to work [as an Emergency Nurse], but like, fatigue and like my cognitive function are like the two, kind of like biggest things like holding me back…it's not like I'm going back to a desk job where like, I can just like sit on a computer and like, take a break. Like, I could kill somebody if I make mess up…So yeah, like, that's, like the number one like fear around returning to work… [and] I definitely feel like I'm not as… productive, I guess. So, like… returning to work, like, am I going to be able to like, bring value to the team? Eva: I don't know what I'll do if I would be asked to work… I do get afraid that, you know, maybe it'll take me longer to finish tasks. *Affects finances* Sarah: [Return to work was] very difficult. Like, trying to wrap your head around what that person needs, what's happening. What are their symptoms? Like the actual, you know, my job [as a Massage Therapist] of figuring out what's wrong…And then the pressure of feeling like I need to do more financially, just business-wise too, right? You need to be more and more. And just the stress of that of not knowing if I can, right? Emma: I'm back on medical leave because I couldn't do my job, so that's huge, obviously. Nina: I did decide to step back a little bit from work because I felt like… I couldn't function, like I couldn't work the hours I was working… if I'm going to be at work, I need to be 100%. I can't make mistakes in my

		work… I've cut down my hours, so yeah, it affected me financially.... And it's frustrating because, like, if I was in my 50s or 60s, I'd probably be retired, and I wouldn't have to work. It wouldn't matter, you know, but it matters right now for me because I'm so young. Like… I probably have to work another 20 years… Peyton: If I feel like if I can never go back to my full my full-time job like I used to [due to cognitive impairment] …I will get a different job somewhere else that's like, a desk job or something like that. But then like, that also is like kind of stressful too because like then that has like financial constraints, because like going from 12 hours to 8 hours [of work].
Cognitive-behavioural strategies to self-manage CRCI *This theme captures how participants engaged in several strategies to help themselves cope with their CRCI, including using organizational tools, engaging in cognitively demanding or calming tasks, and PA.*	*Organization provides a means to remember and tackle complex tasks:* Using organizational tools, creating routine, and planning days strategically helped participants keep on top of things that are difficult due to CRCI.	*Routines, scheduling, lists, writing things down* Sarah: Everything is in a calendar. Lots of things have alerts, but for the most part, because of my job, I look at my calendar between every person. So, it's a constant every hour reminder of what's going to happen. Mia: I try to stick to a routine. That way I don't forget. I write things down…everything [is] in the calendar. Sydney: I tend to write notes in places that I can see them and reference them again. So, whenever I'm in a meeting, I'm taking down notes…I'm pretty good at still being like, "Okay, the information that I need happened around this date, around this time, with these people," and I just can't get that last piece of information which has been really helpful to go back into my notes to find them…so I would say like, you know, keeping really comprehensive calendars, taking notes. Jaime: Writing is the big thing or just like putting [stuff] somewhere that's not inside my head. Emma: I have a booklet that I put everything in, and if it's not in there, then I'm in trouble. I also have lists for my kids of the things that they have to do because I can't remember to tell them all the things that they need to remember. And I have a calendar that has the times that…so I have a kids' calendar of where they need to be and when and what they need to do to get ready for that. And I have my own calendar in my phone…that…before I get out of bed, I have finally…I've been working really hard on routines to try to remember things, so I try to use routines to help with my memory. My routine in the morning is that the first thing I do, before I even get out of bed, is check my calendar. Otherwise, I won't remember that I have anything that day… it's taken me a long time to even remember to write those things, like it's been a long time coming to even get to where I am with these things now. Peyton: I realized you can't just tell me to get something. Like, I have to write everything down. Notes and stuff like that. Eva: I make a list of all of the things that I need to do… that helps me, you know, be able to remember things and get things done… I think that's what's helped me the most. *Contrary opinion: Organization doesn't always work* Jack: I try and make lists and then a few days later, I forget that I made a list. And then a few months later, I'm going through, like erasing iPhone notes and going, 'Oh, I was supposed to do this or that and this." So, I do make lists, but I'm not successful at using them. Cole: I tried calendars and all that stuff, and it just doesn't work.

		Planning days intentionally Emma: I think I try plan my days now so that I have time…so I only really feel good in the morning and the afternoons are really rough, so I try to plan the most important things that I need with [cognitive function] in the morning and allow myself time to rest in the afternoon. Layla: I know that I have better [cognitive] function in the morning. So, putting more complex things in the beginning of my day versus trying to do them in the afternoon because I'm exhausted and I…and I just don't have the capacity as much.
	Divided opinions about the usefulness of cognitive training: There was division amongst participants about the effectiveness of cognitive training. Some believed that engaging in cognitively demanding activities helped exercise their brain by activating their short-term memory and requiring greater focus. However, others preferred to engage in activities that calmed their brain (e.g., mindfulness) as they found increases in their memory.	*Exercising the brain* Erica: Listening to podcasts and that kind of thing [helps]—like keeping my brain working. One thing that I got really into during treatment… is sudoku puzzles. And I just found that they are so great to help with, like, memory, and, you know, I never, like, tried to beat time or anything like that, but I thought it was really good because…just remembering those little things I thought was really good practice and stuff like that…it made me focus and it made you know, utilize my short-term memory and that kind of thing. Taylor: I started to play a lot of solitaire on my phone… I feel like it helps me to like get my brain working. And with the deficit in language, I mean, I have always watched my shows in English with subtitles. But now I'm trying…sometimes I've tried to say, "don't turn on the subtitles" so that I have to focus more on what the people say in those movies or in the shows. And when I have to do research for university, I try to use articles or like scientific papers that are in English, so that it's harder for me and that I have to focus more. So, I feel like I sometimes like challenge myself, even if I know it's super hard, like I just want to challenge myself. *Calming the brain* Erica: Meditation is like my number one [strategy]… I find my memory is better… Ivy: There's like a five minute structured morning guided meditation that I sometimes like to do… I [go] from being, like, very frazzled and fe[eling] like my head [is] being pulled in a million different directions to… just like, all of a sudden [feeling that things are] manageable… it helps put the pieces in order.
	PA may help manage CRCI up to a certain threshold: Some participants shared that engaging in PA helped them to improve their cognitive function by helping them feel more focused, alert, and able to remember. Building on this notion, even those who were not engaging in PA as an explicit strategy to manage their CRCI believed that it could	*PA increases cognitive function* Jack: I can [focus] whenever I come back from exercise, I get so much done… Cooking, cleaning, art, writing, whatever it is, post-exercise, I'm just more successful. Emma: Before COVID, I was going to exercise therapy… it definitely helped my brain… then when COVID shut everything down, it was hard… I managed to find some online stuff… and it always makes me feel… overall, everything functions better…In the online classes, we do circuits and I think it's helpful with the circuits because I seem to remember what it is I need to do the 2nd or 3rd time around and that's big because when I started, it would be like every time we did the circuit over, "Oh, yeah, that's what we were doing," but I've noticed the last few weeks that I can just…as soon as she says next thing is cardio or whatever, and I'll be like, "Oh yeah, we were doing this," and that is huge. I was like, "Oh, I'm actually ready to do the next thing!"

	potentially improve cognitive function. Importantly though, when talking about PA, participants' accounts illuminated that could also be detrimental, wherein "too much" PA could increase mental fatigue, and thus decreases their cognitive function.	Priya: I just think [PA] helps everything, like work better…like movement patterns, making sure that the connectivity is happening. Like… 'if you're not using it, you're losing it' kind of mentality. So, like, the more kind of novel things I could [physically] engage my body in…I trust that that means that… it's helping my brain fire better and…not be stuck in that like weird foggy state as much. Erica: I love going to the gym… I find that the days that I've gone to the gym the day before, I feel better the next day. And I feel like my memory is better…I feel like I'm not as tired…I feel more alert. Ivy: For me, [when I swim laps]… the counting of strokes and breath, like it's just so meditative… [I feel] mental effects and benefits. Layla: I just tried to do what I could in terms of walking, and then there is an organization called Wellspring and they offer virtual exercise classes. So, I signed up with them and started doing some [exercise] with them, and… I definitely think it helped in terms of cognitive function but then their timing just didn't work well. So that's why I switched into a personal trainer. But, you know, I think other than the overexertion and getting to the fatigue point, I think there is a really good balance and finding I feel good in myself. So, then it helps with all those cognitive emotions and depression, anxiety, your mental health. And then that translates into having better cognitive function, less brain fog… *Contrary opinion: "Too much PA" increases mental fatigue and thus reduces cognitive function* Sarah: [Physical activity is] good and bad, actually. Good in the sense that… it just generally makes you feel better…but if you overdo it, then I get stupid tired and I'm [cognitively] worse. Emma: If I push myself too hard [during PA], I'm just done, like everything—physically, emotionally, cognitively, it's just like total body shutdown. But I am trying to learn the window where it feels good, when it's not too much. Layla: I started working out with a personal trainer in the summer… and what I would find is that if I worked out too many days… physical fatigue contributes to increased brain fog and increased like cognitive dysfunction. So, when I'm more tired physically… I don't necessarily have the cognitive capacity that I normally would…. I think it's more from increased exertion as well as frequency. So, I tried working out 3 times a week or a few more, 3-4 times a week, and I had to cut it back to twice a week because… I couldn't function… it was too much physically and it really impacted my brain. *Belief in PA as a strategy (despite not explicitly using it to manage CRCI)* Sydney: Physical activity clears your mind, so I can certainly see…I can see the link [between PA and cognition]. Um, I don't know exactly, you know, which type of PA and if there are particular types, or if there's kind of a strategy of "you should be doing these 5 things and work them in this order" or whatever…that I don't…I don't know. But I mean yes, [I] can see the reason that they would be linked for sure. Jaime: I feel like yes…[it] probably wasn't my main goal when going, but I always was convinced that [PA] would help in that sense as well. Nina: I would think [PA] would be a good strategy.

Recommendations for improving care *This theme captures, that in many cases, participants felt ill-informed about CRCI and unequipped to deal with it. They offered that treatment plans that give patients information regarding cognitive impairment and strategies to cope could help. Additionally, participants desired for increased access to PA supports and programming.*	*Increase awareness and information around CRCI:* Participants discussed that they were uninformed about CRCI, felt alienated by it, and had to learn to manage it via trial and error; thus, they desired for increased awareness/information around this potential side effect.	Sarah: I think the more awareness we have that this is a real thing that all cancer patients go through, then we won't feel so alienated by it. Mia: All of these things that I've dealt with, with the whole cognitive thing, it's more me finding out on my own. It would have been better if they said, "these are some of the symptoms that you may have. If you run into these, these are some of the coping strategies you can deal with," instead of leaving it up to me to go onto these Facebook groups… Layla: I think preparing people in advance for [CRCI] would be helpful…medical professionals needed to be able to help with cognitive strategies…I ended up being so depressed and things weren't working that it would have been helpful for them to be like, 'Yeah, so you may just have to write things down more.' Like I know…it should be intuitive, but it wasn't in that moment. So, like…just write things down more, like chunk things up in your day…have things in the morning. Like those things would have been really really helpful tips because you're dealing with something that you've never thought about or you never had to do. Cole: I didn't have the tools necessary in place that would have helped. Peyton: [I would like] more discussion around like, brain fog and how that can impact your life. I feel like it's very brushed over, like, "Yeah, you might get brain fog" and you're kind of like, "Oh, okay." And then it just happens… I found it quite distressing when it happened, but…there's not a lot of discussion about what that might look like for you and like how to, like, adjust in that kind of stuff. I feel like for myself it was very much like trial and error. Eva: I would definitely have liked somebody talking to me and explaining that, you know, these are some things that can happen in addition to like physical symptoms… Like, they talk to you about fatigue, but they don't talk to you about, like… difficulty focusing,… memory issues,… they don't tell you about these things and you don't even expect it, and then it actually happens to you. You feel like something's wrong with you when it's not. So I think it's important to discuss that with you.
	Increase access to PA programs and support: PA was often not presented as an option to participants during treatment or was inaccessible. This, participants desired for more dialogue, information, and tailored recommendations around/in regards to engaging in PA.	Taylor: [My friend] was prescribed physiotherapy during her treatment… her cognitive function, I would say, is better than mine… she always had to do workouts during treatment, but when I was in treatment, they were like, "Just stay in bed and just rest." And they told her, like, "You should move. You should go out of the house at least once every day." I feel like if my doctors would have told me the same… that I would definitely have increased my cognitive function or made it less worse. Sarah: I do think that the PA is very important. It's also a lot of it is very financially hard to do. So, I think there probably needs to be more access for cancer patients to have either free or minimal fees required to do it. Sydney: I mean, if they could then recommend you go and see, you know, a kinesiologist, that would be helpful or at least something where like if that was an actual recommendation to say, "we'd like to have you work with somebody to kind of set up what would be a good physical exercise plan for you," I think that that would go pretty far because I still remember, like all the exercises my PT gave me right after I finished and I integrate them into a lot of what I do still. Emma: I live in a rural, like a small community, and there's no services here for me except the exercise program that I was doing before COVID, but… there's not enough spots, there needs to be more funding for that…

		The program that I'm in now I'm paying for, but I don't have an income, right? So, it's kind of like, "Oh, I'm taking a big chunk out of our budget to pay for this" … I'd happily pay for it if I had an income, but it's kind of stressful to have to pay for it. So definitely, if there could be some sort of programs that people can access. Priya: It would have been really helpful if the doctor had had more of a conversation about PA…like providing some kind of tips or even directing people to some resources…[or] even just asking the question, like 'How can you be supported to have PA?' Would be helpful to sort of have some dialogue. [And] if someone was interested, being able to direct them to a couple of really simple resources websites. Layla: Some sort of… graphic info sheet that had either organizations you could access for that kind of thing, as well as information on PA, the importance of it, how much PA cancer patients should be doing or what activities they should be partaking in versus what's contraindicated… even just giving tips and tricks on how to exercise during different phases, whether it's during chemo, whether it's doing during radiation would be helpful…I think, you know, when people are [doing] really, really poorly and they're trying to incorporate exercise, they need to know distance and frequency and timing and that kind of stuff to help.

Supplemental File 1: All Self-Reported Cognitive Function Scores

Table 7. *Descriptive Statistics for All FACT-Cog Subscales*

FACT-Cog Scores	Values (Mean ± SD; Score Range)	95% CI
PCI Subscale	44.7 ± 17.4; 4-69	[39.5, 49.9]
Oth Subscale	14.0 ± 3.4; 1-16	[13.0, 15.0]
PCA Subscale	14.9 ± 5.9; 1-27	[13.1, 16.7]
QoL Subscale	9.4 ± 4.6; 0-16	[8.0, 10.8]
Total FACT-Cog	83.1 ± 28.7; 12-128	[74.4, 91.7]

Notes. FACT-Cog= Functional Assessment of Cancer Therapy—Cognition; SD=standard deviation; CI=confidence interval; PCI=Perceived Cognitive Impairment (18 items; subscale range: 0-72; scores <54/72 indicate clinically meaningful impairment); Oth=Comments from Others (4 items; subscale range: 0-16); PCA=Perceived Cognitive Abilities (7 items; subscale range: 0-28); QoL=Impact on Quality of Life (4 items; subscale range: 0-16); Total FACT-Cog (33 items; range: 0-132)

Supplemental File 2: Quantitative Data Tables Excluding Brain Cancer Survivors

Table 8. *Participants' Sociodemographic and Medical Characteristics (Excluding Brain Cancer Survivors)*

	Total Sample Values (n=42)	Sub-Sample Values (n=14)
Sociodemographic Characteristics		
Current age (M years ± SD; range)	31.6 ± 5.5; 23-39	30.9 ± 6.4; 23-39
Sex, *n* (% female)	38 (90.5)	12 (85.7)
Gender identity, *n* (% woman)	38 (90.5)	12 (85.7)
Ethnicity, *n* (% White)	29 (69.0)	10 (71.4)
Civil status, *n* (% married or common law)	22 (52.4)	6 (42.9)
Highest level of completed education, *n* (% post-secondary)	38 (90.5)	13 (92.9)
Vocational status, *n* (% working or transitioning into work)	31 (73.8)	9 (64.3)
Annual household income, *n* (% > $100,000 CAD)	13 (31.0)	3 (21.4)
Medical Characteristics		
Age at diagnosis (M years ± SD; range)	28.4 ± 6.2; 15-38	27.5 ± 8.5; 15-38
Time since diagnosis (M years ± SD; range)	3.2 ± 2.9; 0-10	3.4 ± 3.2; 0-10
Cancer stage, *n* (%)		
I	6 (14.3)	1 (7.1)
II	14 (33.3)	6 (42.9)
III	15 (35.7)	3 (21.4)
N/A or do not know	7 (16.7)	4 (28.6)
Cancer type, *n* (%)		
Blood	14 (33.3)	4 (28.6)
Breast	13 (31.0)	3 (21.4)
Sarcoma	4 (9.5)	3 (21.4)
Carcinoma	4 (9.5)	1 (7.1)
Gynecologic	3 (7.1)	2 (14.3)
Colorectal	2 (4.8)	0 (0)
Melanoma	1 (2.4)	1 (7.1)
Testicular	1 (2.4)	0 (0)
Treatments received, *n* (%)		
Surgery	33 (78.6)	11 (78.6)
Chemotherapy	34 (81.0)	11 (78.6)
Radiation	23 (54.8)	8 (57.1)
Hormonal	13 (31.0)	3 (21.4)
Other	8 (19.0)	3 (21.4)
Perceived overall health, *n* (%)		
Poor to fair	9 (21.4)	6 (42.9)
Good to very good	31 (73.8)	8 (57.1)
Excellent	2 (4.8)	0 (0)
Previous concussion(s), *n* (%)	4 (9.5)	1 (7.1)
Cannabis use in the past month, *n* (%)	10 (23.8)	6 (42.9)

Notes. SD=standard deviation.

[a]Sub-sample refers to participants interviewed.

Table 9. *Descriptive Statistics for Psychological, PA, and Cognitive Function Variables (Excluding Brain Cancer Survivors)*

Variables	Values (Mean ± SD; Score Range)	95% CI
Psychological Factors		
Depressive symptoms	12.3 ± 5.5; 3-25	[10.5, 14.0]
Perceived tress	21.4 ± 7.4; 6-38	[19.1, 23.7]
Fatigue	24.8 ± 11.6; 7-44	[21.1, 28.5]
QoL	68.6 ± 18.3; 30-97	[62.8, 74.4]
PA		
MVPA (continuous)	27.3 ± 21.6; 0-70	[20.3, 34.3]
Cognitive Function		
Self-reported cognitive function	44.8 ± 17.4; 4-69	[39.3, 50.2]
Objective cognitive function		
M-WCST (EF)	36.7 ± 27.6; 0-100	[27.6, 45.7]
A-LNST (working memory)	12.9 ± 2.5; 8-19	[12.1, 13.7]
TMT (EF/processing speed)	52.0 ± 16.1; 26.7-94.3	[46.5, 57.4]

Notes. SD=standard deviation; CI=confidence interval; QoL=quality of life; PA=physical activity; MVPA=moderate-to-vigorous intensity physical activity; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking Test; Depressive symptoms (scale range: 0-30); Perceived stress (scale range: 0-40); Fatigue (scale range: 0-48); QoL (scale range: 0-108); MVPA (LSI scores≥24="active"; LSI scores<24="insufficiently active"); Self-reported cognitive function (PCI subscale range: 0-72; scores <54/72 indicate clinically meaningful impairment); M-WCST values represent % perseverative error; A-LNST values represent total points reordered; TMT values represent TMT-B scores in seconds.

Table 10. *Bivariate Correlations Between Cognitive Function and Select Medical Characteristics (Excluding Brain Cancer Survivors)*

Variables	Self-Report Cognitive Function	Objective Cognitive Function		
	PCI	M-WCST (EF)	A-LNST (working memory)	TMT (EF/processing speed)
Time since diagnosis	-.073	-.021	.081	-.022
Cancer stage *(1=Stage 1; 2=Stage 2; 3=Stage 3)*[a]	.059	.123	-.340	-.121
Chemotherapy *(0=no; 1=yes)*[a]	-.040	.290	-.149	-.267

Notes. PCI=Perceived Cognitive Impairment; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking Test.
Higher TMT scores indicate worse outcomes.
Higher PCI, M-WCST, and A-LNST scores indicate better outcomes.
[a]Spearman rho correlation coefficients; elsewhere, Pearson correlation coefficients.
*p<.05; **p<.01. We note that *p*-values are reported, but effect sizes are interpreted as per APA guidelines.

Table 11. *Bivariate Correlations Between Cognitive Function, Psychological Factors, and PA (Excluding Brain Cancer Survivors)*

Variables	1	2	3	4	5	6[a]	7	8	9	10
1. Depressive symptoms	-									
2. Perceived stress	.697**	-								
3. Fatigue	-.780**	-.507**	-							
4. QoL	-.819**	-.665**	.807**	-						
5. MVPA LSI (continuous)	-.304	-.159	.397*	.340*	-					
6. MVPA *(0=insufficiently active; 1=active)*[a]	-.352*	-.259	-.381*	-.416**	.862**	-				
7. PCI subscale	-.626**	-.473**	.506**	.585**	.124	.144	-			
8. M-WCST (EF)	-.236	-.194	-.103	.051	.042	.019	.211	-		
9. A-LNST (working memory)	-.232	-.181	.224	.203	-.046	-.117	.323*	.417**	-	
10. TMT (EF/processing speed)	.169	.200	-.241	-.261	-.052	-.177	-.047	-.320	-.370*	-

Notes. QoL=quality of life; PA=physical activity; MVPA=moderate-to-vigorous intensity physical activity; LSI-Leisure Score Index; PCI=Perceived Cognitive Impairment; M-WCST=Modified Wisconsin Card Sorting Test; EF=executive functioning; A-LNST=Auditory Letter-Number Sequencing Test; TMT=Trailmaking test.
Higher depression, perceived stress, and TMT scores indicate worse outcomes.
Higher fatigue, quality of life, MVPA, PCI, M-WCST, and A-LNST scores indicate better outcomes.
[a]Spearman rho correlation coefficients; elsewhere, Pearson correlation coefficients.
*p<.05; **p<.01. We note that *p*-values are reported, but effect sizes are interpreted as per APA guidelines.