PreCog: An Investigation of the Manifestation and Development of Cancer Related Cognitive Impairment from Pretreatment for Patients Preparing for CRS-HIPEC Surgery

Study Submitted in partial fulfilment for the requirement of the award of Doctor of Philosophy (PhD)

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Appendix G: List of Publications and Conference Attendance Related to the Thesis .....

List of Abbreviations

6MWD	6 Minute Walk Distance
6MWT	6 Minute Walk Test
A&E	Accident and Emergency
ASA	American Society of Anaesthesiologists
BDNF	Brain Derived Neurotropic Factor
CBEP	Community Based Exercise Programme
CC	Cytoreduction Completeness
CFO	Comments From Others
CFQ	Cognitive Failures Questionnaire (Broadbent et al., 1982)
CG	Control Group
CNS	Central Nervous System
COWAT-FAS	Controlled Oral Word Association Test -Letters F, A, S
CRCI	Cancer-related Cognitive Impairment
CRS-HIPEC	Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy
DT	Distress Thermometer (NCCN, 1999)
E-health	Electronic health
ERAS	Enhanced Recovery After Surgery
Euro-Qol-EQ-5D-5L	European Quality of Life 5 Dimensions 5 Levels (EuroQoL Group, 1990)
EWB	Emotional Wellbeing
FACT-Cog	Functional Assessment of Cancer Therapy-Cognition (Wagner et al., 2009)
FACT-G	Functional Assessment of Cancer Therapy-General (Cella et al., 1993)
FITT	Frequency, Intensity, Time, Type
FWB	Functional Wellbeing
GSE	Generalised Self-Efficacy (Schwarzer & Jerusalem, 1995)
HBEP	Home Based Exercise Programme
HC	Healthy Control
HDU	High Dependency Unit
HPA-axis	Hypothalamic-pituitary-adrenal- axis
HrQoL	Health-related Quality of Life
ICCTF	International Cancer and Cognition Task Force
IES-r	Impact of Events Scale-revised (Horowitz et al., 1979)
ImpactQoL	Impact of Perceived Cognitive Impairments on Quality of Life
MoCA	Montreal Cognitive Assessment
NCCN	National Comprehensive Cancer Network
NCCP	National Cancer Control Programme
NCT	National Clinical Trials
NIH	National Institute of Health
Ob	Objective

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PANO	Physical Activity and Nutrition Optimisation
PCA	Perceived Cognitive Abilities
PCI	Perceived Cognitive Impairment
PG	Patient Group
PM	Peritoneal Malignancy
PMP	Pseudomyxoma peritonei
PPI	Public and Patient Involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
PWB	Physical Wellbeing
QoL	Quality of Life
Q-Q plot	Quantile- Quantile plot
Sub	Subjective
SWB	Social Wellbeing
TMT	Trail Making Test
UK	United Kingdom
US	United States
WHO	World Health Organisation

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Abstract

Thesis Title: PreCog: An Investigation of the Manifestation and Development of Cancer Related Cognitive Impairment from Pretreatment for Patients Preparing for CRS-HIPEC Surgery.

PhD Candidate: Aideen Scriney

Background Cancer related cognitive impairment (CRCI) refers to challenges with memory, attention and executive function during and post treatment(s). Recent work shows it may be present at diagnosis, but little is known about how it is experienced, manifests, continues through treatment or is influenced by psychological wellbeing, or prehabilitation intervention before treatment.
Aims Understand prevalence, expression and experience of CRCI pre- and post-surgery for patients undergoing Cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC), and the impact of bimodal prehabilitation exercise and nutrition intervention on patient experience, CRCI and psychological wellbeing.
Methods Systematic reviews synthesised findings for Pretreatment CRCI prevalence and measurement, and prehabilitation intervention impact on fitness and psychological wellbeing. PreCOG followed n=29 patients undergoing HIPEC in a nested RCT PANO trial at baseline, pre-, post- and one year post-surgery for those engaging in bimodal structured exercise and nutrition prehabilitation support compared to usual care. Outcomes included CRCI prevalence and influences of exercise and nutrition pre- and rehabilitation, and psychological wellbeing. Patients were administered self-report questionnaires across all time points, neuropsychological tests at one year follow up, and completed semi-structured interviews pre- and post-surgery.
Results Findings from systematic reviews highlighted variation in the CRCI measurement landscape and an association between self-reported CRCI and psychological wellbeing. The prehabilitation review highlighted the lack of current research exploring the potential for exercise and nutrition support to positively impact psychological outcomes and health-related quality of life (HrQoL). Within empirical studies, CRCI prevalence ranged across assessment timepoints from 13%-27% and was associated with emotional wellbeing as measured by the FACT-G (baseline). Intervention patients showed increased cognitive quality of life compared to controls preoperatively, and higher emotional wellbeing one-year post-surgery. Self-report (subjective) CRCI did not correlate with neuropsychological tests (objective impairment) at one year follow-up, but prevalence was 16% employing both measures. Thematic analysis identified themes of anxiety, awareness of cognitive concern and enrichment, and need for physical and mental preparation pre-surgery (n=29). Postoperatively, interviews highlighted cognitive fluctuations, need for psychological support and challenges adjusting to physical and psychological challenges as a result of complex surgery and recovery (n=18).
Conclusion: The relationship between cognitive experience, psychological wellbeing and quality of life is complex during the pretreatment period and may be supported by cognitive enrichment and prehabilitation. CRCI trajectory is variable and individual screening and targeted intervention would benefit patients. Development of sensitive and ecologically valid testing, as well as neuroimaging, could help to identify the conceptual underpinnings of subjective and objective CRCI.

Chapter 1. Introduction

1.1 Introduction

1.1.1: State of Cancer research and survivorship:

1.1.1.1 The State of Cancer Research

In 2025 it is projected that there will be over two million new cases of cancer diagnosed, as well as over 600,000 deaths within the United States alone (Siegel et al., 2025). On a global scale, incidence rates are also of great concern, with over 19 million new cases across the world in 2022 according to the World Health Organisation (Ferlay et al., 2024). Europe accounted for over 4.47 million cancer cases worldwide (Ferlay et al., 2024). Without intervention, this number is also expected to increase by 25% by 2035 (European Commission. Directorate General for Research and Innovation., 2020). With an increased incidence of cancer diagnoses, there will also be an increased incidence of mortality. As of 2024, it is estimated that 1.27 million cancer deaths occurred within Europe (Santucci et al., 2024). In 2025, it is estimated that there will be 1.3 million cancer related deaths within the European Union (Santucci et al., 2025). Ireland reported the highest cancer incidence rate in Europe in 2020 for both sexes combined (Dyba et al., 2021), with a more recent incidence rate of approximately 718.2 per 100,000 people as of 2022 (European Union, 2025). According to the Irish cancer society, cancer accounts for 30% of national mortality rates each year, with over 9000 deaths each year as of 2019 (Irish Cancer Society, 2025). It is clear that cancer incidence and mortality represent a clear burden on an individual, national and international level.

1.1.1.2 Survivorship and Symptoms

Despite the concerning cancer incidence and mortality rates globally, there also exists promising survivorship rates for patients. In the US, there were 18.6 million individuals alive with a history of cancer, and this figure is expected to exceed 22 million by 2035 (Wagle et al., 2025). As of 2022, approximately 200,000 survivors were alive in Ireland, however rates of cancer survivorship tend to vary largely across cancer types (Irish Cancer Society, 2025). In Italy, rates of cancer survivorship are

projected to increase approximately 3% per year (Guzzinati et al., 2018), however this increasing survivorship also requires increased support for comorbidities (Sarfati et al., 2016) and for patients as they return to work, schooling and family life (Lagergren et al., 2019). Positive trends are also predicted in terms of survivorship, with projections estimating that within the EU, cancer mortality will decrease by 3.5% for men and 1.2% for women between 2020-2025 (Santucci et al., 2025). With increasing survivorship comes the additional challenges associated with an aging population. The prevalence of dementia within cancer is poorly understood, and the number of people with co-morbid cancer and dementia is likely to rise (McWilliams et al., 2017). As such, the need to understand the experience of long-term survivorship and aging is important to address the needs of an aging population as it relates to patient experience of symptoms, wellbeing, quality of life and cognition.

With increasing survivorship comes the need to understand the trajectory of patient symptomology from diagnosis to survivorship. Cancer survivorship includes many phases, including but not limited to acute survivorship, transitional survivorship to posttreatment, extended survivorship under observation and surveillance, chronic survivorship and finally permanent survivorship (Gosain & Miller, 2013). Gosain and Miller (2013, p.405) described the fluctuations in symptomatology and experience during these phases as “Seasons of Survivorship”. It's clear that patients face a myriad of challenges in survivorship that can be impacted by continued treatments like pain, fatigue, cognitive impacts and psychological effects like depression (Gosain & Miller, 2013). As survivorship increases it is important to understand and respond to the challenges of long-term survivorship.

1.1.1.3 Research and Policy

Cancer represents a high patient burden from diagnosis through survivorship both within Ireland and the wider world. It poses a larger physical, psychological and economic burden for patients as well as increased burden on health care services as age of populations increase (Popat et al., 2013). The continuum of cancer care is associated with out-of-pocket costs and psychosocial costs relating to quality of life (Essue et al., 2020). Due to the high rates of incidence and mortality, as well as varied survivorship rates, research and policy on both national and international levels has focused on effective strategies to decrease cancer burden from diagnosis to survivorship. The European Commission in 2020 launched their report *Conquering Cancer: mission*

possible. The goal of the board of the mission statement is that *"by 2030 there will be 3 million lives saved from cancer, living longer and better"* (European Commission. Directorate General for Research and Innovation., 2020, p. 43). The framework outlines key pillars to guide future research and policy. The framework is built across three key areas requiring increased understanding: prevent what is preventable, optimise diagnostics and treatment, and support quality of life. Practical guidelines include developing novel approaches for screening and detection, advancing personalised medicine approaches across Europe and to develop an EU wide research programme focusing on improving quality of life for cancer patients and survivors. The European Cancer Organisation also highlights the need for multidisciplinary and patient-centred care and the promotion of policy recommendations (European Cancer Organisation, 2025). Prominent UK organisations are also at the forefront of cancer policy and research such as Macmillan cancer support and Cancer Research UK.

On an Irish level, research and policy has also started to focus on combating the increased levels of incidence and its negative impacts on quality of life. The *National Cancer Strategy 2017-2026* was developed as a result of strategic consultation with public and organisational consultation to refine further specific needs for patients from diagnosis towards survivorship. Key areas for improvement highlighted include the need for increased psychosocial services across the cancer care continuum, local links with centres and support services, service development for rare cancers and communication and integration of services. The report outlines four key areas of action: 1. Reduce cancer burden, 2. Provide optimal care, 3. Maximise patient involvement and quality of life, and 4. Enable and Assure Change (Department of Health, 2017). In 2024, the Department of Health published their most recent report on the implementation of their national strategy, outlining key performance indicators and current progress as of December 2023 (Department of Health, 2024). The Irish Cancer Society has also outlined a strategic plan for 2020-2025 outlining their commitments to increasing prevention and detection, world-class treatments with equal access and living well with and after cancer (Irish Cancer Society, 2020). Irish research organisations such as Breakthrough Cancer Research also aim to fund innovative research fast in order to achieve their mission statement for an eventual 100% cancer survival rate for all cancer types.

It is clear that research and policy on national and international levels are currently focused at combating this increased incidence of cancer. However, policy and

research appear to primarily focus on detection and prevention or quality of life into survivorship. This indicates a potential gap in research and policy pertaining to innovative treatments *before* and *during* that can be effective in increasing quality of life.

1.1.1.4 Rare and Common Cancers

Thus far, the majority of statistics mentioned have focused on aggregate and combined data that is overwhelmingly based on the data from common cancers. Common cancer types include those which occur in large portions of the population. In terms of incidence, in 2025 it is estimated that in the US the leading sites for males will be prostate, lung, colon and rectum, urinary bladder and melanoma, and for females will be breast, lung, colon and rectum, uterine and melanoma (Siegel et al., 2024). The EU presents a similar landscape, with the most commonly occurring cancers being lung, colorectal, pancreas, breast and prostate cancers (Eurostat, 2025).

More recently, the research landscape has been changing to acknowledge the gap in literature and research for more rare cancer types (Alvi et al., 2017; DeSantis et al., 2017; Gatta et al., 2011; Mathoulin-Pélissier & Pritchard-Jones, 2019; Sandler et al., 2021). Rare cancer prevalence can be difficult to define but is often understood as cancers that occur in less than 6 people per 100,000 (Gatta et al., 2011). The slow progression of treatment approaches and other improvements for rare cancers is a result of gaps in the literature and research, which is often due to geographical constraints and small sample sizes (Sandler et al., 2021). This lack of available research is concerning, as in 2022, rare cancers accounted for 26.7% of all cancer diagnoses and 30% of all cancer related deaths worldwide (Elmadani et al., 2025). These cancers also are often associated with complicated treatment pathways, increased burden, and lower five-year survival rates compared to more common cancers (Gatta et al., 2017). Although research is currently increasing, low numbers for evidence-based randomised controlled trials are still barriers to efficacious treatments (Mathoulin-Pélissier & Pritchard-Jones, 2019). European policy has acknowledged the need to address this knowledge gap, and the *Rare Cancer Agenda 2030* highlights key recommendations related to individualised supportive care needs and the fostering of new research thorough support and networking within healthcare systems (Joint Action on Rare Cancers, 2020).

Due to the gaps described, the present study focuses on rare cancer types, in particular peritoneal malignancy. Peritoneal Malignancy is a rare and aggressive cancer

that develops within the tissues of the peritoneum or from organs that are adjacent to the peritoneal lining (Anwar & Kasi, 2024). The treatment pathway is highly invasive including both cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC), which involves removing tumours from the affected sites and then heated chemotherapy is poured into the surgical site over a period of several hours (Mayo Clinic, 2025). It occurs in approximately 6.78 per million people in the United States (Anwar & Kasi, 2024). Peritoneal malignancy represents a risk of morbidity as well as multiple post-operative stressors during recovery (Loughney et al., 2020). These patients represent a cohort that would greatly benefit from a research and policy focus on efficacious treatment at all stages of their cancer journey. Although peritoneal malignancy is considered a rare cancer due to its prevalence (Anwar & Kasi, 2024), research findings and experiences of patients preparing for CRS-HIPEC may be applicable to other cancer types for a number of reasons. CRS-HIPEC patients may take part in a range of neoadjuvant and adjuvant treatments like chemotherapy as part of their treatment pathway as well as surgery (Chen et al., 2020, Schneider et al., 2017) as well as the nature of the different cancer types including appendix, urachus, pancreas, biliary tract and cervix (Carr, 2021). Therefore, patients with peritoneal malignancy provide a unique opportunity to investigate a wide patient group with varied tumour presentation, but at the same time a consistent surgical treatment experience in CRS-HIPEC.

1.1.2: The Burden of Treatment: Cancer Related Cognitive Impairments (CRCI)

1.1.2.1 Defining CRCI and Prevalence

Cancer represents a time of multi-dimensional stress and burden for patients. This burden can also endure for long periods after the patient is cancer free within phases of survivorship (Gosain et al., 2013). Psychological distress is widely reported for patients for a number of reasons including but not limited to fertility related psychological distress (Logan et al., 2019), diagnosis related anxiety and depression (Linden et al., 2012; Schumacher et al., 2013) and an overall decrease in quality of life both during treatment and into survivorship (Shim et al., 2006, 2021; Torvinen et al., 2013). Health-related quality of life (HrQoL) is frequently applied within cancer research and is highly relevant for patients, with research suggesting that perceived levels in certain HrQoL domains can help aid in survival prognosis (Efficace et al., 2006). HrQoL generally refers to: 1. Perceived ability to function in daily life in

physical, psychological and social domains; 2. As a subdomain of overall quality of life; 3. Perceived wellbeing of the aspects of quality of life that are directly impacted by health; or 4. The self-perceived values assigned to different health states (Karimi & Brazier, 2016). HrQoL is also important when attempting to understand patient wellbeing in cancer. Wellbeing for cancer patients can encompass a wide range of factors and has been described by patients both as the absence of challenges that threaten quality of life, and the presence of normal activities and routine (Skaczkowski et al., 2023).

Cognition impacts many domains of quality of life, as research into cognitively vulnerable populations such as people with dementia indicates that improved cognitive performance is associated with higher health related quality of life across multiple subdomains (Ezzati et al., 2019). Within cancer research, the term "chemobrain" was traditionally used to describe the associated effects of treatment on cognitive function (Ahles & Saykin, 2007, Argyriou et al., 2011). Treatment approaches can vary greatly across cancer types including but not limited to surgeries, chemotherapy, hormonal therapies, immunotherapies and radiotherapies (National Cancer Institute, 2017). However, as research developed, the prevalence of cognitive impairment prior to treatment caused researchers to expand their focus of CRCI to the cancer continuum from diagnosis to survivorship, leading to the development of conceptual models that explore CRCI across the cancer continuum, including both the experience of perceived self-reported CRCI, and objective cognitive domains explored through neuropsychological tests (Hutterer & Oberndorfer, 2021). CRCI generally refers to impairments or dysfunction relating to issues with short term and working memory, attention, executive functions and/or processing speed (Hutchinson et al., 2012). A study by Oerlemans and colleagues (2022) assessed self-perceived cognitive function and HrQoL from a registry of cancer survivors who completed quality of life questionnaires with cognitive subscales. They found that perceived impaired cognitive function was directly related to poorer emotional functioning and levels of fatigue. Research with patients diagnosed with low-grade glioma found that poorer cognitive function as assessed by objective tests was negatively associated with HrQoL, both globally and for disease specific scales. In particular, across cognitive domains including executive function, processing speed, working memory and information processing were all associated with levels of mental health (Boele et al., 2014). Research has also indicated that cognitive function is associated with quality of life and

other psychosocial variables, in particular, results indicating that delayed recall impairment is associated with lower overall QoL as well as emotional and functional wellbeing (Williams et al., 2017).

It is evident that cognitive impairments can impact upon HrQoL and as such should be addressed within patient care from diagnosis to survivorship. However, defining cognitive impairments related to cancer, or CRCI, has proven difficult in terms of defining the nature of impairment, aetiology and even measurement challenges. CRCI is a prevalent issue for patients that can greatly restrict quality of life (Hutterer & Oberndorfer, 2021). However, as CRCI refers to a wide range of cognitive issues, determining the prevalence of CRCI can prove challenging (Ahles & Hurria, 2018), as the cognitive impairments reported can vary widely in terms of onset, severity, duration of the impairment and also the cognitive domains affected (Hutterer & Oberndorfer, 2021). CRCI can also be elusive in presentation as it is traditionally mild to moderate in presentation and may be misunderstood by patients (Boykoff et al., 2009).

In 2021, Hutterer and Oberndorfer outlined the current clinical prevalence of CRCI from diagnosis to survivorship in their narrative review. They reported that between 10-30% of cancer patients exhibit detectable cognitive deficits prior to treatment. Thirty percent of patients reported that cognitive issues increased during the course of their chemotherapy cycles. Seventy-five percent of patients report impairments 6-12 months post chemotherapy. Post-treatment long term, approximately 15-35% of cancer patients report changes in cognitive performance. Janelsins and colleagues (2011, 2014), have also reported 75% prevalence for cognitive issues during or after chemotherapy.

Despite its prevalence throughout the cancer journey, the understanding of CRCI requires further research to understand its causes and mechanisms in order to provide effective treatment from the point of diagnosis.

1.1.2.2 Current Conceptual Issues

Certain conceptual issues in CRCI need to be better understood in order to apply findings to interventions that can provide support to patients. The International Cognition and Cancer Task Force (ICCTF) was founded in 2006 to allow for collaboration on an international level for CRCI. The goals of the ICCTF include the homogenisation of study methods, improved estimates of incidence and severity, and a better understanding of the instances of cognitive changes and individual risk factors

(Deprez et al., 2018). Recent research has also highlighted multiple recommendations for future CRCI research, including increased identification of CRCI and development of appropriate treatment approaches (Yang & Von Ah, 2024). As well as increased investigation into the association between CRCI and psychological wellbeing (Haywood et al., 2024).

To provide effective treatment for CRCI, it is important that we understand its various possible causes. It is currently unknown whether CRCI is as a result of the cancer itself, low baseline reserves, acute or chronic physiological stress responses or psychosociological symptoms (Hutterer & Oberndorfer, 2021). Initially, researchers explored how CRCI could result from exposure to neurotoxins during chemotherapy, thereby experiencing negative impacts on cognition during treatment (Ahles & Saykin, 2007; Olson & Marks, 2019). From a mechanistic and biological perspective, CRCI may occur as a result of a number of factors including neuro or systemic inflammation, disruption to the blood brain barrier, impaired neurogenesis, loss of certain cells or cellular senescence. There is also evidence to suggest that certain biomarkers can be predictive of chemotherapy induced cognitive impairments such as brain derived neurotrophic factor (BDNF) (Kuil et al., 2025). It is clear that treatment can affect cognition in cancer patients, however the impacts of treatments as well as other factors across the cancer continuum are areas requiring further research.

Some research has also challenged the idea of CRCI occurring only as a result of treatments; up to 30% of patients report experiences of CRCI before any treatment even occurs (Hutterer & Oberndorfer, 2021). A conceptual review by Lange and colleagues in 2019 highlighted how CRCI complaints were highly prevalent in the literature for breast cancer patients undergoing chemotherapy, but also for those undergoing alternative treatments including hormone therapy. Reported issues included memory, processing speed, attention and executive function. Olson and Marks in 2019 reviewed the literature pertaining specifically to non-central nervous system cancers as research indicates that these patients experience cognitive decline prior to treatment, which suggests the impairment could be as a result of tumour derived factors. They suggest that cognitive impairment is as a result of complex interplay between the immune system, genetic factors, host behaviour and psychosocial state.

It is clear that the effects of various invasive treatment approaches can exacerbate the cognitive impairment experienced by patients. However, psychosocial factors can also negatively impact this experience and potentially further impact

cognition. Indeed, current conceptual models of CRCI highlight the role of psychosocial factors (Ahles & Hurria, 2018; Janelsins et al., 2014; Lange et al., 2019, Oppegaard et al., 2023a). In particular, Haywood and colleagues' (2024) recent model of CRCI explored CRCI as a contributing factor towards psychopathology (such as anxiety and depression) in cancer survivors. The authors also suggest that the relationship between psychopathology could be bi-directional, that CRCI may not only contribute to psychopathology but that psychological factors could also contribute to the development of CRCI. Yang and Hendrix in 2018 reviewed how psychological factors may impact CRCI in breast cancer patients. Overall, they found large variance in the types of tests used and also across the psychological determinants predictive of CRCI. Psychological factors encompassed many terms including "worry" and mental fatigue, as well as anxiety, stress and depression. However, psychological distress was still associated with lower performance on cognitive function tests. Andreotti and colleagues in 2015 proposed a stress reactivity model of cognitive decline in non-central nervous system (CNS) cancer patients. They proposed that chronic stressful experiences pre-diagnosis may cause dysregulation to stress reactivity systems, resulting in increased allostatic load which may induce prefrontal changes and cognitive deficits. Chronic psychological diseases such as anxiety and depression can also result in a chronic stress condition which can also heighten inflammatory states, contributing to cognitive impairment.

As global cancer survivorship increases, it is also pertinent to understand the interplay between CRCI and the aging process. Within healthy aging, considerable individual variability can exist, with factors such as physical activity and engaging in intellectual activities as important in the cognitive aging trajectory (Sánchez-Izquierdo et al., 2021). Systematic review evidence has also suggested that cancer and treatment related factors such as chemotherapy could contribute to the incidence of dementia which is of particular concern given the aging population (Kao et al., 2023). For elderly patients, cognitive decline as a result of treatment is of great concern and in a study of patients over 65 years, over half stated they would rather reduce their lifespan than lose the ability to take care of their daily needs and themselves (Soto Perez De Celis et al., 2018). Some research suggests that chemotherapy can affect biomarkers of ageing (Abraham et al., 2025). Currently it is unknown whether these potential changes accelerate ageing compared to the otherwise healthy population, or whether the levels

of dysfunction are parallel to those of a similarly aged population (Ahles & Hurria, 2018).

Another factor associated with age is levels of cognitive reserve which is highly associated with a decline during the ageing process (Mandelblatt et al., 2014). Cognitive reserve is the term given to explain and measure the protective effect of enrichment factors on the expression of cognitive decline where pathology or other factors are at play. Originating in the ageing cognitive decline and dementia literature, it has more recently been modelled in cancer cognition (Liesto et al., 2022). Factors such as years of education and psychological resilience can be associated with better cognitive performance and protect against cognitive decline post cancer treatment (Liesto et al., 2022). Associations have also been reported in literature between common underlying processes involved in cancer, aging, and low cognitive reserve (Mandelblatt et al., 2013). Lifestyle factors such as taking part in exercise and physical activity posttreatment have also been shown to improve cognitive function after cancer treatment (Myers et al., 2018).

1.1.2.3. Categories of Impairment

In order to develop meaningful standardised interventions, the cognitive domains that underpin CRCI must be fully understood and categorised. CRCI assessment involves the exploration of multiple cognitive domains. Capetti and colleagues (2025) recently reviewed the literature regarding neuropsychological assessment in non-CNS cancer. They determined that common domains of interest include executive function, memory, attention and information processing.

1.1.2.3.1 Executive Function There exists a large body of evidence to support that cancer patients experience issues with executive function. Executive function encompasses domains mediated by prefrontal regions of the brain, including working memory, inhibitory control, cognitive flexibility, planning, reasoning and problem solving (Cristofori et al., 2019). Hodgson and colleagues in 2013 analysed 13 studies to assess the effects of chemotherapy on cognition. They found that the strongest evidence was established for executive function and memory problems related to treatment. Continued problems after treatment are also a persistent challenge for cancer patients. For example, Wefel et al. (2010) demonstrated an acute decline in executive function which moderately persisted long term across 42 patients who underwent

neuropsychological testing. Interestingly, fMRI research has indicated that irrespective of the history of chemotherapy, breast cancer survivors can exhibit reduced activation in the prefrontal regions of the brain (Kesler et al., 2011). More recent literature identifies functional, vascular and metabolic features of interest when imaging cancer patients post treatment, paving the way for future studies to uncover the mechanisms behind CRCI such as oxidative stress, neuroinflammatory factors and others to be identified (Silverman et al., 2025).

1.1.2.3.2 Memory. Memory deficits as a result of cancer can occur across several perceptual domains. Janelsins and colleagues in 2018 longitudinally assessed the trajectory of CRCI within a nationwide cohort study from pre to post treatment. Their primary outcome was visual memory as measured by the delayed match to sample test. Results indicated that between pre- to 6 months post- chemotherapy, patients significantly declined on the task, whilst the control group did not. Patients also exhibited a time effect as a significant decline was evident from pre to 6 months post chemotherapy. These same patients also exhibited significant decline in other neuropsychological memory tests including immediate recall, delayed recall and single-item memory tests. In a related study, Williams and colleagues in 2020 cross-sectionally assessed cognitive function in patients with chronic lymphocytic leukaemia. They found that across 150 patients, those in the higher risk category recalled 2 fewer words on Hopkins verbal learning test than low risk patients.

1.1.2.3.3 Attention. Attention is another core cognitive domain that allows patients to maintain high quality of life. Within cognitive psychology, attention can be defined as the ability to focus on one set of stimuli within an environment whilst ignoring other irrelevant stimuli (Callahan & Terry, 2015, p. 161). Approximately 75% of breast cancer patients report changes in attentional function, despite little being known about its causes or trajectory (Kohler et al., 2020). A meta-analysis assessed the prevalence of depression and cognitive impairment for breast cancer survivors who underwent taxane-based chemotherapy. Meta-analysis was conducted on 11 studies containing neuropsychological tests of cognition. Results supported that attentional deficits were significant in patients even 6 months or more after their treatment concluded (Ibrahim et al., 2021). The trajectory of attention from pre to post surgery is less well understood. Kohler and colleagues (2020) assessed the trajectory of attentional processes from pre surgery to 12 months post-surgery among breast cancer

patients. Pre-surgery scores on the attentional function index indicated that patients exhibited attentional deficits. The sample's overall attentional function improved across the 12 months span but remained in the moderate range. Anxiety and fatigue and receiving adjuvant chemotherapy predicted lower attentional function.

1.1.2.4 Limitations of current CRCI research

It is evident that there is a body of research supporting the presence and impact of CRCI for patients and survivors across multiple cognitive domains. However, in order to design effective interventions, the limitations of the current research must first be considered.

To date, the vast majority of research on CRCI across non-CNS cancer pertains to breast cancer patients (Yang & Von Ah, 2024). Although this is largely due to commonality and suitability for longitudinal assessment, it also means that results may not be generalisable to over 200 other cancer types (Cancer Research UK, 2014). There is a need to expand the scope of CRCI research to include other common and rare cancer types. Patients with peritoneal malignancy undergoing CRS-HIPEC represent a suitable cohort for further research due to the rarity of the cancer itself, as well as the complex treatment pathway of combined cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (Loughney et al., 2020). By conducting high quality randomised control trials across both common and rare cancer types and various treatment pathways, it will allow for increased comparison which will ultimately aid in understanding the causes of CRCI.

Arguably the greatest current limitation in CRCI research currently is the discordant relationship between subjective and objective measures of CRCI. Subjective measures refer to those self-report measures that offer an experiential account of the patient's feelings, while objective measures refer to the common neuropsychological tests used to determine a level of cognitive function through scoring on a task. Common subjective measures of CRCI can include the FACT-Cognition (Wagner et al., 2009), Cognitive Failures Questionnaire (Broadbent et al., 1982) and the cognitive items of the EORTC QLQ-C30 (Aaronson et al., 1993). Subjective assessments focus on the patient’s own perception of the extent of their cognitive impairment, and that also includes considering if this change has also been noticed by friends and family members (Pullens et al., 2010). The second category of measurement is the use of

objective neuropsychological tests. These are mainly traditional neuropsychological tests that were developed for use with lesion impairments with moderate to severe dysfunction (Ahles & Hurria, 2018). Objective testing allows for the testing of various cognitive domains including memory, verbal fluency, speed of processing and attention (Capetti et al., 2025).

In theory, objective and subjective measures of cognitive function should be concordant and complement each other in order to provide a detailed overview of both neuropsychological deficits and patient experience, however in reality this is not the case. It is well documented that there exists a disparity between patients reporting of CRCI on subjective tests, and objective impairments measured (Hutchinson et al., 2012; Hutterer & Oberndorfer, 2021; O'Farrell et al., 2017). In general, patients tend to report subjective impairment, but objective performance shows that they actually fall within the normal range on neuropsychological tests (Ahles & Hurria, 2018). Biglia and colleagues in 2012 assessed both objective and subjective cognitive function in a group of breast cancer patients undergoing chemotherapy. They were assessed before and then 1, 3 and 6 months after treatment. They found that across timepoints, self-perception of cognitive deficits was unrelated to objective cognitive decline. Similarly, and in a longitudinal study, O'Farrell and colleagues in 2017 assessed breast cancer patients using repeated cognitive assessment batteries as well as the FACT-Cognition. The researchers employed multi-level modelling to assess the co-variation between subjective and objective measures across timepoints. They also assessed clinical change metrics. In both cases, they found no association between objective and subjective cognitive decline. Whilst subjective cognitive function is an important predictor of both objective cognitive decline and higher risk of decline in other pathologies such as dementia, it remains unclear why co-association at the same timepoint typically reveals little or no relationship. More research is needed to understand when both co-associate along the cancer treatment pathway and what factors may contribute to this.

As the discrepancy between objective and subjective cognitive impairment becomes more evident, research has begun to explore the potential reasons for these differences. Research has indicated that associations exist between psychological states, fatigue, and subjective cognitive impairment in cancer (Yang & Hendrix, 2018). In both of the studies above (Biglia et al., 2012; O'Farrell et al., 2017), associations were found between emotional states including anxiety and fatigue, and subjective cognitive impairment. Hutchinson and colleagues (2012) suggest that perceived cognitive

impairment is commonly associated with fatigue, anxiety and depression; however, the causal relationship between self-report and actual manifestation of impaired performance on cognitive tests remains unclear. Other research with ovarian cancer patients reported observed objective impairment was high, however this was not associated with perceived cognitive impairments (Wang et al., 2024). It has been suggested that subjective CRCI may be functionally separate to objective cognitive function and may be more closely related to other subjective cancer experiences such as psychological wellbeing (Bray et al., 2018, Areklett et al., 2024).

The discrepancy could also be attributed to validity issues of traditional neuropsychological tests themselves to assess CRCI. CRCI clinically presents as subtle in nature (Brewster et al., 2017; Wefel et al., 2015), and as previously mentioned, neuropsychological tests were designed to assess moderate to severe impairments (Ahles & Hurria, 2018). This calls into question the suitability of traditional neuropsychological tests, which may not be sensitive to capture such subtle deficits. In fact, the use of neuropsychological tests may be to either over- or under-estimation of the extent of CRCI in non-CNS cancer (Sleurs et al., 2022); and this may be due to the fact that they are not cancer-specific or sensitive to the particular challenge associated with treatment or disease burden factors associated with CRCI (Capetti et al., 2025). Neuropsychological tests are also conducted in strict laboratory settings, with an aim of obtaining the patient's best possible performance. This means that they may not be valid for detecting impairment across time in everyday situations, with some researchers suggesting that more ecologically based cognitive tests may be more applicable to CRCI (Hutchinson et al., 2012).

A third possibility could be that patients report aspects of subjective impairment that are actually a result of deficits in other areas - *referred cognitive impairment.* Ahles & Hurria (2018) used the example of a patient self-reporting forgetfulness which they may perceive as memory issues, when in reality forgetfulness could result from issues with information retention, information retrieval, or learning. This distinction between actual domains affected is crucial for our understanding of CRCI.

Finally, another limitation of current CRCI research is the lack of pre-treatment assessment. As research primarily pertains to chemotherapy in breast cancer, assessment usually occurs from the beginning of treatment and not from initial diagnosis. It would be beneficial for researchers to assess the diagnosis to treatment time point, as both objective and subjective testing indicates that pretreatment

impairment is a prevalent issue, the cause of which is still currently unknown (Hutterer & Oberndorfer, 2021). Some preclinical animal research has also highlighted the potential for cancer itself to impact cognitive impairment pretreatment, which presents avenues for further research (Joly et al., 2015).

1.1.2.5 Future CRCI research and the present study:

It is clear that there needs to be a deeper understanding of both subjective and objective CRCI in terms of prevalence, clinical presentation, aetiology and associated factors. As a parallel consideration within another chronic illness, dementia research reports similar issues with measurement, such as heterogeneity across studies, and the need to explore relationships between subjective impairment and psychological issues such as depression (Burmester et al., 2016). The issue of measurement in dementia research has largely focused on attempting to understand how to accurately measure subjective concern (Wion et al., 2022). The importance of ecological validity and how everyday function and task performance may elucidate cognitive experience has also been a source of research interest in determining the true perceived impact of cognitive difficulties within dementia research (Schmitter-Edgecombe et al., 2014). Qualitative research with patients experiencing CRCI has indicated that CRCI results in decreased overall quality of life, including difficulties returning to work, engaging in social activities and negative psychological experiences (Haywood et al., 2023, Sharma & Brunet, 2023). Quality of life and the negative impacts of cognition on health-related quality of life should be considered when understanding the everyday impact of CRCI.

When assessing CRCI, it must be considered that traditional neuropsychological tests may not be sufficient to detect the subtle and ecological nature of CRCI (Hutterer & Oberndorfer, 2021). Subjective or perceived CRCI may reflect patients' experiences of anxiety, depression, fatigue and overall quality of life. They provide valuable insight into patient experiences and therefore can be considered important for quantifying symptomatic treatment effects (Wagner et al., 2020). As such, when assessing an under researched cancer type such as peritoneal malignancy for CRCI, it is important to first understand the subjective cognitive domains reported by patients themselves, as these experiences are directly affecting their quality of life.

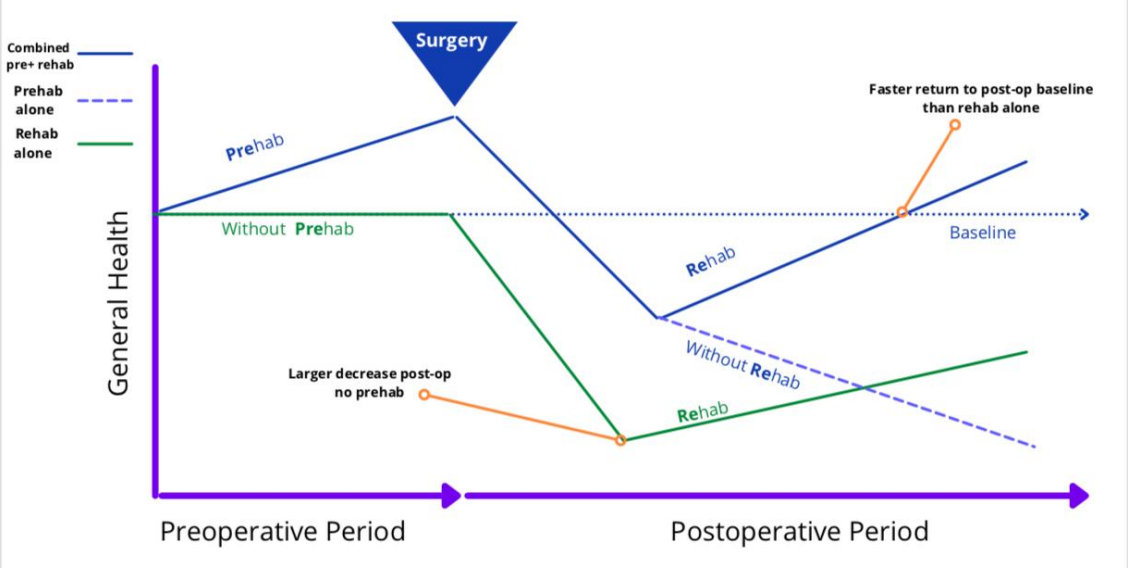
1.1.3: Prehabilitation

1.1.3.1 What is Prehabilitation

Traditionally, when a cancer patient was met with a diagnosis of invasive treatment or surgery, the prescription prior to these physically stressful and traumatic events would have been to rest (Carli et al., 2017). However, more recently, a wealth of research has supported the use of targeted interventions before any treatment occurs, in order to prepare patients for the stresses associated with recovery (Macmillan Cancer Support, 2020, 2025). Research supports that postoperative morbidity can be related to the pre-operative condition of patients combined with the level of surgical stress experienced (Gillis et al., 2022b). Evidence from prehabilitation literature indicates that prehabilitation allows for a greater level of health pre-treatment or surgery compared to care as usual, allowing patients preparation for the stress of surgery and treatment (Coca-Martinez & Carli, 2024). A combined prehabilitation and rehabilitation pathway also allows for a faster return to baseline levels of general health, compared to prehabilitation or rehabilitation alone (Faithfull et al., 2019). Figure 1 below depicts a comparison between the patient trajectory of patients undergoing, prehabilitation, rehabilitation, or both in relation to general health (Banugo & Amoako, 2017; Carli et al., 2017; Macmillan Cancer Support, 2020). As indicated by the blue line, when a patient undertakes both prehabilitation before surgery, their overall levels of general health increase. After surgery when they then engage in rehabilitation, they are starting the process with increased levels of post-surgical general health, and this allows patients to return to baseline levels of general health much faster than with rehabilitation alone or with no intervention.

Figure 1.1

Patient Trajectory from Pre to Post-op when Engaging in Combined Pre and Rehabilitation Versus Prehabilitation/Rehabilitation Alone



Note: Patient Trajectory from Pre to Post-op when Engaging in Combined Pre and Rehabilitation Versus Prehabilitation/Rehabilitation Alone in Relation to Baseline General Health. Based on Macmillan, 2020, Carli et al., 2017 and Banugo & Amoako, 2017.

1.1.3.2 Current Prehabilitation Approaches:

Prehabilitation can encompass many different interventions and combinations. Macmillan Cancer Support (2020) defines the key pillars of lifestyle prehabilitation interventions to be exercise, nutrition, and psychological support. Clinical guidelines were updated by Macmillan Cancer Support in 2025, highlighting the need for multimodal prehabilitation as well as other recommendations including the provision of educational surgery schools on the benefits of prehabilitation and individualised screening approaches. These can be implemented at universal, specialised, or targeted levels, depending on the level of support required by the patient.

1.1.3.2.1 Exercise. Exercise prehabilitation is arguably the most commonly researched area of prehabilitation. The American College of Sports Medicine suggests that patients should engage in exercise throughout their cancer journey. They suggest that patients engage in 150 minutes of aerobic exercise weekly, combined with two sessions of resistance training (Campbell et al., 2019). Exercise organisations also advocate for the use of individualised exercise supports as an additional therapy that can help provide support against the negative effects of treatment (Cormie et al., 2018).

A typical exercise prehabilitation programme will generally consist of a warm up, followed by cardiovascular and resistance training, while some programmes will also include elements of flexibility training and functional tasks (Kuthia, 2021).

In terms of efficacy, there is a wealth of evidence to support exercise prehabilitation. This is true for both physical and psychological benefits. Improvements in functional capacity are frequently reported as a result of exercise interventions. Waterland and colleagues in 2021 reviewed multimodal prehabilitation interventions for patients with abdominal cancer that included exercise on postoperative outcomes. They found that across 22 studies, significant support was found for interventions improving functional capacity as measured by the 6-minute walk test. A review of exercise prehabilitation for pancreatic cancer found similar results, with support being found for improvements in muscle mass and function (Bundred et al., 2020). Exercise prehabilitation can also have benefits for health-related quality of life (HrQoL) and other psychological metrics. Mishra and colleagues (2012, 2015) have explored the effects of exercise interventions on HrQoL. In 2012 they assessed over 40 clinical exercise prehabilitation trials across cancer types on HrQoL. Across trials, exercise resulted in increases in HrQoL which included cancer specific concerns, emotional wellbeing and social functioning. Exercise prehabilitation can also result in positive effects on psychological symptoms such as anxiety and stress (Knoerl et al., 2022).

1.1.3.2.2 Nutrition. Another common prehabilitation intervention is nutritional support or optimization. The aim of nutrition support before treatment and surgery is to optimise nutrient stores and metabolic reserves in order to then compensate against the catabolic responses to surgery (West et al., 2017). The European Society for Clinical Nutrition and Metabolism (ESPEN) outlines how patients should undergo nutritional screening as early as possible in care due to the associations between malnutrition and poor prognostic outcomes (Bargetzi et al., 2021). Nutritional support is highly relevant for cancer patients across cancer types, as the malnutrition evident can be as a result of reduced food intake and metabolic stress can be as a result of the cancer itself, and then be compounded by the effects of treatment (Arends et al., 2017). Macmillan Cancer Support (2020, 2025) outlines how nutrition prehabilitation can improve nutritional status before cancer surgery. Within research, current evidence suggests that nutritional prehabilitation could benefit from increased standardisation, as studies vary in treatments and use of validated nutritional assessments (Gillis et al., 2021).

Nutritional prehabilitation has been found to be most effective at improving postoperative and clinical outcomes. Several reviews have reported on the use of nutritional prehabilitation interventions such as carbohydrate loading interventions improving postoperative wellbeing (Pillinger et al., 2018). Gillis and colleagues in 2018 reviewed the effects of nutritional prehabilitation both with and without combined exercise programmes on patients who underwent colorectal surgery. They found that across nine studies, nutritional prehabilitation both with or without combined exercise prehabilitation significantly reduced length of hospital stay. They also found moderate evidence to support increases in functional capacity for combined exercise and nutritional prehabilitation.

1.1.3.2.3. Psychological Prehabilitation. The third pillar of prehabilitation is psychological prehabilitation. The aim of psychological prehabilitation is to target the psychological burden of cancer treatment and surgery such as anxiety and distress (Fradelos et al., 2017) by increasing resilience (Macmillan Cancer Support, 2020, 2025). It is well documented that cancer surgery and treatment can result in psychological issues in survivorship including fatigue affecting health related quality of life (Fortmann et al., 2018), as well as anxiety and depression, which even at low levels can impact quality of life (Yi & Syrjala, 2017). Evidence suggests that psychological factors such as anxiety, depression and low self-efficacy can result in negative post-surgical outcomes (Levett & Grimmett, 2019). Macmillan Cancer Support (2020) outlines psychological prehabilitation as providing wellbeing support in the form of information and guidance at a universal level. At a targeted level, psychological prehabilitation should be more individualised, including anxiety management and solution focused therapy combined by psychological problem-solving techniques. At a specialised level, psychological prehabilitation can consist of more in-depth interventions tailored to patients' individual psychological needs provided by licensed professionals providing interventions such as psychotherapy, counselling and cognitive behavioural therapy.

Psychological prehabilitation interventions have been reported to have positive effects on both physiological and psychological outcomes. Levett and Grimmett in 2019 reviewed the evidence for psychological factors, prehabilitation and surgical outcomes. They found that pre-operative outcomes such as anxiety, depression and low self-efficacy consistently are associated with worse physiological surgical outcomes as well as postoperative quality of life. Tsimopoulou and colleagues in 2015 conducted a

systematic review of psychological prehabilitation interventions. Interestingly, they found that psychological interventions did not impact upon post-operative outcomes but did impact positively on patient reported outcomes including psychological, symptomatic and health related quality of life outcomes. In 2022, Grimmett and colleagues conducted an umbrella review of existing systematic reviews and meta-analyses that pertain to psychological prehabilitation. Across twenty reviews, findings indicated that there exists a lack of consistency and standardisation across both psychological prehabilitation prescription and outcome measures. Interventions were also generalised across all patients and did not specifically target those with high distress. Psychological prehabilitation represents an emerging prehabilitation treatment that has the potential to positively impact on post-surgical outcomes and can potentially reverse the negative impacts of psychological distress on patients which can include lower functional capacity, higher levels of pain, and non-compliance with medical treatment (Scheede-Bergdahl et al., 2019).

1.1.3.3 Emerging approaches

Within the current prehabilitation literature, lifestyle prehabilitation interventions are largely dominated by exercise, nutrition and psychological based interventions (Macmillan Cancer Support, 2020). However, as evidence grows for the efficacy of these more traditional approaches, the opportunity to explore newer emerging approaches has also presented itself. This includes not only the exploration of new interventions but also how these interventions are delivered, and in what combinations. Emerging approaches in prehabilitation at present include the application of multimodal prehabilitation, the use of tele and e-medicine (Tay et al., 2024) and increased research into the potential benefits of cognitive prehabilitation to support cognitive function for cancer patients (Sheppard et al., 2025).

1.1.3.3.1 Multimodal Prehabilitation. As the evidence for high quality unimodal interventions increases, research has turned to assess the efficacy of multimodal interventions. Multimodal interventions can be defined as “two or more intervention components specifically selected for their potential cumulative or synergistic effects on health outcomes”, with these combinations usually consisting of exercise, nutrition and psychological interventions (Santa Mina et al., 2021, p. 3). The

use of multimodal prehabilitation has been supported by both expert consensus and patients themselves through exploration of feasibility (Brahmbhatt et al., 2020). Brahmbhatt and colleagues (2022) reviewed the literature regarding multimodal prehabilitation interventions. The studies included for review largely focused on improvements in functional capacity, length of hospital stay and pulmonary complications. Van Rooijen and colleagues in 2019b employed a four pillar prehabilitation model consisting of an exercise intervention, nutritional support, psychological support and smoking cessation support with 50 colorectal cancer patients scheduled for surgery. They found that the programme was safe and feasible with a high programme attendance of 90%. Eighty six percent of patients in the intervention group reported returning to baseline levels of functional capacity after 4 weeks. Minnella and colleagues in 2019 found similar results for patients undergoing radical cystectomies. They found that as a result of a multimodal prehabilitation intervention, patients reported a return to baseline functional capacity after 4 weeks. In 2024, Zhou and colleagues reported in their meta-analysis of prehabilitation in colorectal surgery that multimodal prehabilitation can improve functional capacity for patients undergoing surgery. With regards to CRS-HIPEC and peritoneal malignancy, in 2021 Cortés-Guiral and colleagues reported on recommendations made regarding prehabilitation and peritoneal malignancy from the 2018 10th peritoneal malignancy workshop (Cortés-Guiral et al., 2021). It was recommended that patients with peritoneal malignancy be included in multimodal prehabilitation intervention as part of care, including psychological, physical, nutritional and perioperative elements (Cortés-Guiral et al., 2021). In the Irish context, observational research also suggests that patients who undergo CRS-HIPEC treatment are subject to postoperative decreases in physical fitness and may be appropriate candidates for prehabilitation intervention (Loughney et al., 2020).

Due to the complex interaction between psychological state, nutritional status and physical performance, a targeted multimodal approach can optimize a patient's ability to partake in interventions by improving motivation and adherence to prehabilitation programmes. Recent evidence has also supported that malnutrition moderates the response to multimodal prehabilitation (Gillis et al., 2022a). If patients are malnourished or have low motivation due to depression or anxiety, they may be less likely to adhere to exercise-based interventions and so not optimise fitness for surgery or treatment (Scheede-Bergdahl et al., 2019). Macmillan Cancer Support's 2025

clinical guidelines highlight the continued research and clinical exploration of the provision of multimodal prehabilitation for cancer patients. Including the provision of integrated prehabilitation screening tools and progressing the prehabilitation research agenda.

1.1.3.3.2 E-Health and Medicine. E-health can aid in the delivery of person-centred care that is individualised, cost effective and easier for patients to integrate into their daily lives (Tebeje & Klein, 2021). The use of tele-medicine has been most evident with the transition to home-based exercise programmes (HBEP) for patients partaking in exercise prehabilitation. Remote prehabilitation interventions could potentially mitigate the issues faced by traditional prehabilitation interventions including access, programme adherence, economic sustainability and personalisation (Barberan-Garcia et al., 2021). Ngo-Huang and colleagues in 2019 assessed the impact of a home-based exercise programme for patients with pancreatic cancer. The home-based programme was based on the exercise recommendations by the American College of Sports Medicine and participants were called by research staff once every two weeks in order to monitor patient adherence and experience. Exercise activity was monitored via accelerometers as well as self-report. They found that the programme was effective in improving functional capacity as measured by the 6-minute walk test and physical activity was also associated with increased HrQoL. Al-Naime and colleagues (2021) have developed a multimodal monitoring tool for prehabilitation interventions that allows for personalisation and to allow patients to receive individualised support and options for exercise based on the FIIT (Frequency, Intensity, Interval, Time) principles.

Organisations that traditionally provided hospital-based exercise programmes are now also transitioning towards hybrid models to cater for patients who may not otherwise be able to access services including ExWell medical in Ireland (Tully et al., 2020). The development of nutritional dietary recall tools such as Foodbook 24 has also allowed for increased monitoring and recall of dietary adherence through an online platform (Timon et al., 2017).

It is clear that the further development of e-health paradigms for use with prehabilitation can aid in mitigating geographical barriers that prevent patients from accessing prehabilitation services that they could benefit from.

1.1.3.3.3 Cognitive Prehabilitation. Psychological prehabilitation is a key pillar of multimodal prehabilitative care. However, current approaches primarily focus

on goal setting and motivation, anxiety reduction and at a specialised level specific psychological support such as cognitive behavioural therapy (Macmillan Cancer Support, 2020). Despite the clear prevalence of cancer related cognitive impairment, its long term persistence and its relationship with both cancer and treatment related effects, cognitive prehabilitation is in its infancy.

Despite the lack of current prehabilitation evidence, support for the use of cognitive training prehabilitation can be found within related research, in particular evidence from cognitive rehabilitation programmes for cancer survivors. Cherrier and colleagues in 2013 conducted a randomised trial of cognitive rehabilitation across various cancer types. Patients took part in a screening session which included a neurocognitive assessment battery and self-perception questionnaires. Participants in the treatment condition took part in 7 workshops which included memory aids, development of memory skills and mindfulness meditation. They found that the treatment condition showed improvements in perceived cognitive impairment as well as increased HrQoL and also in objective measures of attention and a trend towards improved verbal memory. In 2019, Fernandes and colleagues conducted a systematic review of cognitive rehabilitation for cancer related cognitive dysfunction. Nineteen studies met the inclusion criteria and included the data of over 1000 participants. Results were very promising with all studies reporting improvements on at least one cognitive measure. The most commonly reported improvements were found in improvements in memory. This was followed by executive function and processing speed. Another review looked at cognitive rehabilitation programmes for breast cancer survivors treated with chemotherapy. Of the 10 included studies, cognitive training and compensatory strategies either alone or in combination showed improvements in executive function, working and verbal memory, processing speed and attention (Syed Alwi et al., 2021).

In terms of cognitive prehabilitation, to date a handful of studies have been conducted to assess the feasibility and efficiency of different programmes. Vlisides and colleagues in 2019 assessed the feasibility of a home-based cognitive prehabilitation programme for older adults awaiting major non-cancer related surgery. The cognitive training was a computer-based battery that targeted executive function, attention, working memory and visuospatial processing using games like *Divided Attention, Card Shark* and *Eye for Detail*. Their primary aim was postoperative delirium and perioperative cognitive function assessed by the NIH Toolbox, which consisted of tests

including flanker inhibitory control and attention test, the list-sorting working memory test and the pattern comparison control and attention test. Results were mixed, reporting no significant differences between the intervention and control conditions, and low adherence due to technological barriers. Rengel and colleagues 2021 also explored the use of combined cognitive and exercise prehabilitation for patients awaiting major non cardiac surgery. Patients were assessed using the NIH cognitive battery. Participants in the intervention group received a tablet with preloaded cognitive training games as well as a resistance based prescribed home-based exercise plan. Overall, results indicated a trend towards improvement of cognitive performance compared to the control condition. Volz in 2021 reviewed the evidence to support cognitive training prior to surgery for gynaecological patients. This review included a wide range of cognitive dysfunction that also included affective dysfunction like anxiety. They found that for programmes employing electronic cognitive training, results were promising when accounting for non-compliance. They suggest that patients could benefit from validated screening tools to personalise cognitive patient care. Recently, Sheppard and colleagues (2025) conducted the first extensive literature review to explore prehabilitation to support cognitive outcomes in cancer. The review proposed a model of prehabilitation to support cognition through targeted compensatory strategies before and after treatment. The review also proposed supporting a range of modifiable risk factors to support cognitive resilience including physical activity, nutrition, emotional wellbeing and social support. Based on an extensive literature review, the authors propose a model of cognitive prehabilitation that employs pre-treatment multimodal prehabilitation interventions with the addition of external compensatory cognitive strategies (Sheppard, 2025).

Overall, the current landscape of cognitive prehabilitation is mixed. While evidence from rehabilitation studies is promising, there is a clear need for the development of more cognitive prehabilitation trials to assess the efficacy of training interventions. Cancer patients with CRCI represent a very specific cohort with impairments in subjective and objective cognitive function that impacts on their quality of life. There is currently not enough evidence in this emerging field to assess adequately the efficacy of cognitive training interventions. Patients can benefit from screening for cognitive issues and targeted interventions that are delivered in a personalised manner to best suit them. At present, there is a need for increased research on cognitive prehabilitation as a treatment option for patients suffering from CRCI.

1.1.4: The Present Study: Exploring CRCI Through the Lens of Prehabilitation.

Cancer related cognitive impairment (CRCI) and cancer prehabilitation represent two emerging research areas within the scope of cancer research. The present research aims to combine these two novel research areas and explore a bimodal exercise and nutrition prehabilitation programme and its potential effects on CRCI and psychological wellbeing. Throughout the intervention, the incidence and expression of CRCI among a rare cancer cohort will also be monitored and assessed.

1.1.4.1 Exercise and Nutrition Prehabilitation to Support Cognitive Function

Currently, there are no theoretical frameworks that can determine the aetiology or mechanisms of CRCI as research is currently limited. Multifactorial frameworks also highlight the complexity of the CRCI landscape (Oppegaard et al., 2023a). Existing conceptual frameworks aim to identify potential causes and/or moderators of CRCI, such as biological and genetic predispositions, whilst also understanding how behavioural and psychological factors impact CRCI at pre, peri and postoperative phases (Haywood et al., 2024, Hutterer & Oberndorfer et al., 2021, Lange et al., 2019, Oppegaard et al., 2023a).

Lange and colleague's 2019 conceptual schema highlights both factors that may contribute towards the development, as well as potential treatment approaches including behavioural interventions like physical activity. Similarly, Ahles and Hurria (2018) conceptual model of CRCI highlights diet and exercise as potential lifestyle predictors of cognitive function and aging. Physical activity was also discussed as a potential strategy for the management and treatment of CRCI as part of Hutterer and Oberndorfer (2021) conceptual schema of CRCI. The authors also highlighted the importance of health-related quality of life and CRCI from pretreatment to survivorship. In particular, it was observed that CRCI can negatively impact overall quality of life. Similarly, this same relationship has also been observed within qualitative CRCI research, with particular impact of CRCI on social functioning (Haywood et al., 2023).

Oppegaard and colleagues (2023a) developed a multifactorial model of CRCI based on a literature search of over 100 studies. They categorised factors as patient specific factors, social determinants of health, co-occurring symptoms and treatment related factors. The authors highlight the associations between physical activity and

expression of neurotropic and neuroprotective factors that potentially affect hippocampal neurogenesis (Zimmer et al., 2016). They also identified the need for more research in the area of physical activity and CRCI. Clearly physical activity has potential in the treatment of CRCI, but research warrants further investigation (Yang & Von Ah, 2024). In older patients, physical activity can aid in reducing neuroinflammation and associated inflammatory responses after surgery in the central nervous system, which can potentially impact cognitive function (Culley & Crosby, 2015). Reflective of CRCI research at large, much of the evidence for physical activity pertains to breast cancer patients and survivors. Hartman and colleagues in 2018 randomised 87 sedentary breast cancer survivors to a physical activity exercise arm for 12 weeks to assess neurocognitive function. Primary outcomes included objective and subjective measures of cognitive function. Results indicated an improvement in processing speed in the exercise group compared to controls. Interestingly, results were most pronounced for patients who were less than two years into survivorship, identifying the need for early intervention. Bernal and colleagues (2023) also conducted a systematic review of physical activity and exercise approaches for CRCI amongst childhood cancer survivors. Across 22 studies, moderate quality evidence was found to support the benefit of physical activity to improve cognitive performance in both objective and subjective measures of CRCI.

With regards to behavioural interventions, the evidence that nutritional support improves cognition is less clear. It has however been identified as a means of supporting cognitive resilience (Sheppard et al., 2025). There is also evidence supporting a possible link between nutrition status and cognitive function. Cognition has been shown to be possibly affected by diet across non-cancer disease populations, such as dementia (Petersson & Philippou, 2016). In terms of cancer survivorship, one study (Coro et al., 2020) interviewed 15 cancer survivors about how their diet may potentially impact their cognitive complaints. Results indicate a largely bidirectional relationship between diet and cognitive function. Some participants reported that they felt their dietary choices may be impacting their energy levels and mental fatigue. Whilst some participants noticed an inverse effect whereby cognitive issues experienced, such as issues with memory and sustaining attention, may have caused them to experience challenges choosing healthy meals and with meal planning. A systematic review also conducted by this research group investigated diet and cognitive function in cancer survivors with CRCI. Twelve studies were included for final review.

Across studies, the majority explored relationships between subjective cognitive function and diet. Fruit and vegetable intake was the most common dietary variable to support the relationship between diet and cognitive function, but further research is required (Coro et al., 2019). The research team in 2022 conducted an online feasibility study to assess the effects of dietary intake on both objective and subjective cognitive function. Results were non-significant, and authors highlighted the increased need for research in this domain (Coro et al., 2022).

Although research is currently limited, there exists associations between physical activity levels, diet and cognitive function. Cognitive complaints also can inversely affect health behaviour choices (Coro et al., 2020). Due to the growing feasibility and acceptability of prehabilitation interventions for cancer patients, it presents a unique opportunity to explore the potential positive impacts of prehabilitation on CRCI.

As the adoption of exercise and nutrition prehabilitation approaches for cancer patients increases, there also exists an opportunity to expand research across cancer types and to rare cancer types such as peritoneal malignancy. The potential positive impacts on cognitive function and effect on CRCI in this rare cancer type should also be considered. A prehabilitation intervention offers a great opportunity to explore the impacts of this emerging treatment approach, and the cognitive function of patients during this experience in tandem.

1.1.4.2 The Exploration of Psychological Factors and Cognitive Function

In addition to exercise and nutrition, psychological factors potentially play a role in the aetiology of CRCI. Many current CRCI conceptual frameworks also highlight psychological factors such as anxiety, depression, fatigue and stress (Lange et al., 2019, Ahles & Hurria, 2018, Andreotti et al., 2015, Hutterer & Oberndorfer, 2021, Haywood et al., 2024). Cancer patients frequently exhibit affective issues like anxiety and depression. The risk of developing clinical levels of depression in the first year after a diagnosis across cancer types is approximately 15-20% (Riedl & Schuessler, 2022). In terms of anxiety, meta-analysis indicates that the proportion of patients exhibiting anxiety symptoms or disorders is approximately 23% (Amiri, 2024). Patients also report that cancer related fatigue is also a prevalent issue, with 56% of patients in one study reporting that cancer related fatigue has a significant impact on quality of

life. This high prevalence of psychological issues can potentially negatively impact cognitive function among cancer patients (Bai & Yu, 2021).

A previous systematic review has explored the influence of psychological variables and CRCI amongst breast cancer patients (Yang & Hendrix, 2018). Results were largely inconsistent with regards to the measurement of various psychological constructs and their associations with cognitive impairment, with depression and stress most frequently explored within research. The authors identify the need for further research into confounding variables and the need for the expansion of studies beyond breast cancer research. Krolak and colleagues in 2017 assessed the relationship between cognitive function and psychosocial factors among 262 lymphoma survivors. Results indicated that compared to healthy controls, lymphoma survivors scored significantly lower on both objective and subjective cognitive function. With regards to psychological variables, fatigue and anxiety were related to cognitive function. More recently, Haywood and colleagues in 2024 explored the potential for psychological distress to both be worsened by CRCI and contribute to the development of CRCI through their proposed transdiagnostic psychopathology model, suggesting that the relationship between psychological factors and CRCI could be bi-directional.

At present, the psychological influences on CRCI requires further research before targeted approaches such as psychological prehabilitation can develop to support patients with specific psychosocial issues that could contribute to CRCI development.

1.4.3 Aims and Objectives

Throughout this introductory chapter, three primary areas have been discussed. The first area addressed the growing incidence of cancer across the globe. Cancer research and policy were also explored, in particular how these are now placing an increased emphasis on treatment approaches that support quality of life. The need to focus on rare cancer types was also highlighted as there is a lack of current research in these areas in favour of common cancer types.

The concept of cancer-related cognitive impairment was critically introduced and explored in the second section. CRCI was defined and highlighted as a prevalent but under researched issue for cancer patients that has a significant impact on quality of life. Current CRCI theoretical issues were also explored, including overarching questions such as the incidence, affected domains, aetiology and point of manifestation. Current CRCI conceptual issues were also explored such as the apparent dissonance

between objective and subjective assessment measures. Recommendations for future research were explored including an increased focus on non-breast cancer, assessment from the point of diagnosis and future standardisation of assessment metrics.

Section three focused on a relatively new treatment approach; prehabilitation. The concept of prehabilitation was explained including the pillars of lifestyle prehabilitation, exercise, nutrition and psychological support. Emerging prehabilitation approaches were also explored with a focus on multimodal approaches that can be administered remotely and new interventions that address the current gap in the literature for effective cognitive prehabilitation to support CRCI.

The final section provides an overview and rationale for the basis of the present research through an exploration of the potential applications of exercise and nutrition pre-and rehabilitation interventions to address cognitive concerns, and how increased research into the relationship between psychological wellbeing and cognitive function could provide a framework for understanding CRCI across the cancer continuum, in particular at the point of diagnosis, and before treatment toxicity effects..

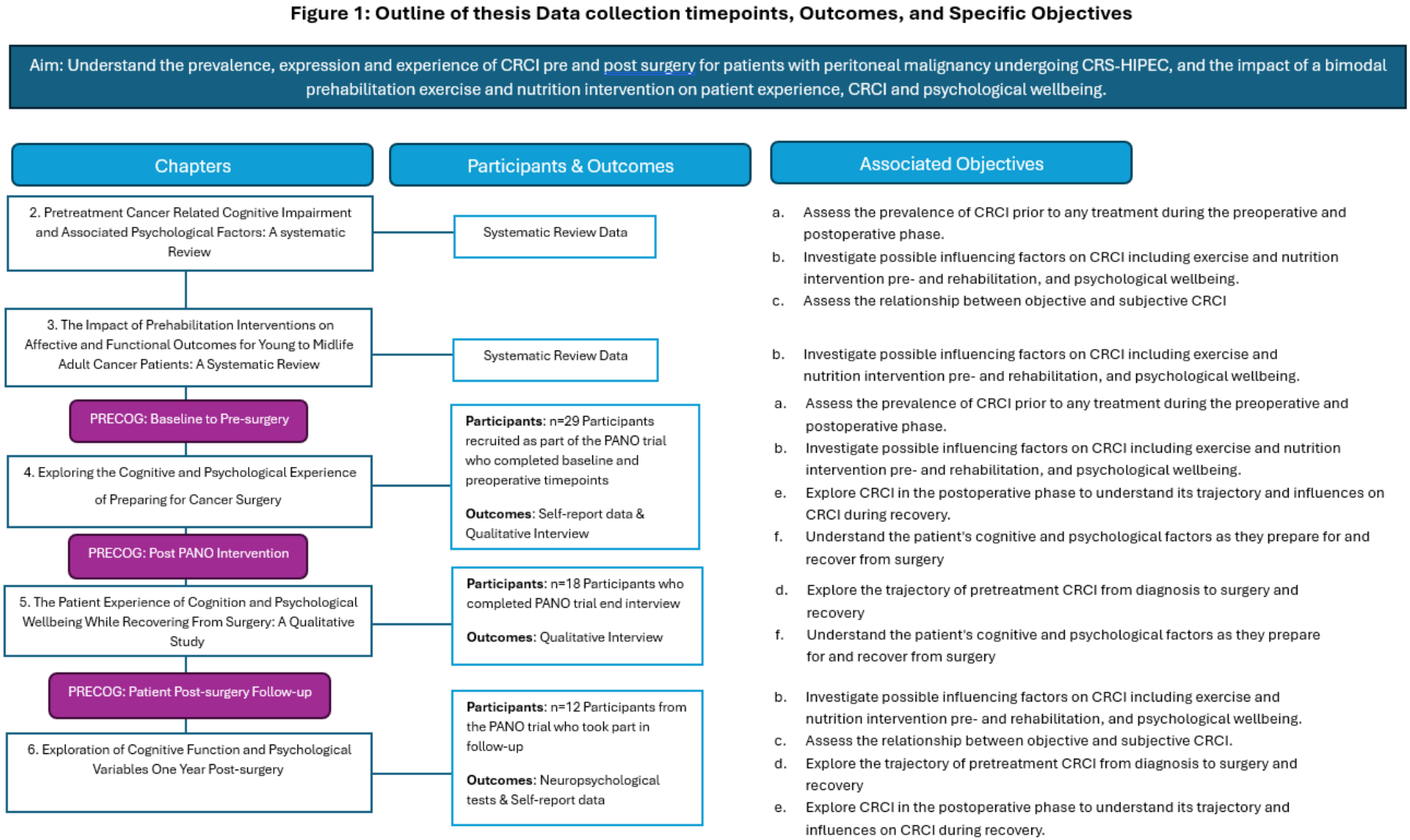
The overall aim of this thesis is to understand the prevalence, expression and experience of CRCI pre- and post-surgery for patients with peritoneal malignancy undergoing CRS-HIPEC, and the impact of a bimodal prehabilitation exercise and nutrition intervention on patient experience of preparation and recovery from surgery, CRCI and psychological wellbeing. This thesis will address multiple gaps in our current understanding by 1. investigating a rare cancer cohort, 2. implementing interventions in the pre-treatment phase, and 3. exploring the impact of a combined pre and rehabilitation approach on CRCI before, during and after treatment. Additionally, systematic evidence will also be investigated to explore evidence across both prehabilitation approaches and cancer related cognitive impairment from a psychological perspective.

Both qualitative and quantitative methods will be employed in a multi-method study to understand the prevalence and trajectory of CRCI among patients with peritoneal malignancy (PM) undergoing CRS-HIPEC, and their lived experiences of the intervention and usual care, and CRCI. Data will be collected at baseline to pre-surgery (pre-surgery phase), postintervention (postoperative phase) and approximately one-year post-surgery (postoperative follow-up). This research project is nested within a parent prehabilitation feasibility trial. The PANO trial (Physical Activity and Nutrition Optimisation) trial assesses the feasibility of exercise and nutrition combined pre- and

rehabilitation for patients scheduled for CRS-HIPEC treatment. A flow chart of thesis data collection timepoints and associated data collection methods and objectives are outlined below in figure 1.2. Specific thesis objectives include:

a. Assess the prevalence of CRCI prior to any treatment during the preoperative and postoperative phase.
b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.
c. Assess the relationship between objective and subjective CRCI.
d. Explore the trajectory of pretreatment CRCI from diagnosis to surgery and recovery.
e. Explore CRCI in the postoperative phase to understand its trajectory and influences on CRCI during recovery.
f. Understand the patient's cognitive and psychological factors as they prepare for and recover from surgery.

Figure 1.2 *Outline of Thesis Data Collection Timepoints, Outcomes and Specific Objectives*



1.1.5 Background to the PANO Trial and Context for The Nested Research Project

1.1.5.1 Background

This PhD research project is nested within a larger national research trial. The PANO (Physical Activity and Nutrition Optimisation) trial is a single-site feasibility study based in the Mater Hospital, Dublin Ireland in partnership with Dublin City University, The Royal College of Surgeons in Ireland and ExWell Medical. The aim of the PANO trial is to assess the feasibility of a combined pre and post prehabilitation and rehabilitation program for patients with Peritoneal Malignancies (PM), scheduled to undergo CRS-HIPEC surgery at the National Centre for PM based in the Mater Hospital, Dublin. The intervention is bimodal, consisting of structured exercise and nutrition support pre- and post-surgery. The project was funded by The Irish Research Council (Research Ireland) COALESE grant and was developed based on previous observational research on this patient cohort, indicating that patients would benefit from a physical and nutrition based prehabilitation programme. Prior national research among other cancer patient cohorts has also demonstrated the feasibility of exercise prehabilitation and rehabilitation in community and home-based settings provided by ExWell Medical (ExWell Medical, n.d).

1.1.5.2 Methods

The full details of methods for the PANO trial can be found on ClinicalTrials.gov ID NCT05305820.

1.1.5.2.1 Participants. Inclusion Criteria: age ≥18 years, multidisciplinary team referral for CRS-HIPEC for colorectal/appendix/ovarian peritoneal disease or pseudomyxoma peritonei (+/- completed neoadjuvant cancer treatment), WHO performance status ≤2. Exclusion Criteria: inability to provide informed consent, impaired cognitive function with a reduced ability to either understand advice /instructions from or communicate with the research team, declined surgery, surgery in less than 2 weeks, pregnancy or breastfeeding, inability to participate in the exercise training (unable to perform the 6 Minute Walk Test), absolute contraindications to exercise testing, veganism.

1.1.5.2.2 Procedure. Thirty-six participants were recruited as part of the PANO trial. Patients were recruited when presenting for the first time at the National Institute

for Peritoneal Malignancy at the Mater Hospital, Dublin. Patients were approached with information about the trial if deemed eligible by the clinical team. They were then given time to consider their participation and were contacted by a member of the research team to confirm participation. Once patients consented, they were randomised to be part of either an intervention or care as usual group.

Intervention group patients were contacted weekly by a member of the research team to monitor adherence and provide additional support. Patients were assessed across four timepoints as part of the PANO trial 1) Baseline, 2) Preoperatively 3) Postoperatively (when deemed fit to participate in the intervention or control equivalent by the clinical team) and 4) Six weeks from postoperative assessment. Assessments were hybrid and administered either in person at the Mater, an ExWell Centre or another community location, or over the phone and using postage pack assessments. This was to facilitate the national sample as patients were based across Ireland. The outcomes for the PANO Trial are listed in Table 1.1.

Table 1.1

List of Outcomes for The PANO trial

Outcome	Measures
Primary	
Feasibility	Adherence, Engagement, Retention
Cardiorespiratory Fitness	6-minute Walk Test
Secondary	
Strength	Handgrip Test Sit to Stand Test
Activity Levels	Use of activpal monitor
Psychological Well Being	Impact of Events Scale NCCN Distress Thermometer Cancer Relevant Self Efficacy Scale General Self Efficacy Scale Cognitive Reserve Index
Health Related Quality of Life	FACT-G Euro-Qol-eq-5D-5L
Nutritional Status	Foodbook 24 dietary recall tool Malnutrition Screening
Cognitive Function	FACT-Cognition

Outcome	Measures
Exploratory	
Health Economics	Cost Analysis
Serology Markers	Analysis of serology biomarkers
Postoperative Outcomes	Postoperative Morbidity Score Clavien Dindo Index
Smoking Status	Smoking Status
Patient Experience	Semi- structured Interview

1.1.5.3 The Intervention Programme:

The intervention programme consisted of combined exercise and nutrition pre and rehabilitation from the period up to surgery, and for six weeks following surgery when deemed clinically fit to participate. Intervention details are as follows:

1.1.5.3.1 Exercise ExWell Medical, a community-based exercise rehabilitation specialist programme led the exercise component of the intervention. The intervention started once patients were enrolled and continued to the point of surgery. Post surgery, when deemed clinically fit to participate, they resumed the exercise intervention for six weeks. The programme was hybrid whereby patients could participate in person in a number of ExWell Medical classes based across Ireland or a hybrid model. The hybrid approach involves access to a series of online classes and phone-based support from ExWell exercise professionals. In addition, participants were provided with an at home exercise booklet, exercise diary and a Fitbit so that they could monitor their activity. The exercise programme consists of a combination of aerobic and resistance-based exercises. A sample exercise class would include the following based on prior work (Tully et al., 2020, Loughney et al., 2024). The exercise intervention is described using the frequency, intensity, time, type (FITT) principle. Frequency: Participants were instructed to take part in exercise 3-5 times a week before surgery and 3 times a week post-surgery. Intensity: Based on individual ability, sessions were either interval based or continuous. Continuous involves moderate intensity exercise for the duration of the exercise session. Interval training is a series of moderate intensity to high exercises repeated throughout the session. Time: Interval sessions involved a first session consisting of 30 minutes of

moderate to high intensity exercise including 5-minute warm up and four repeated intervals exercises of 2-3 minutes follow-up by a 5-minute cool down. Subsequent sessions are similar but of a longer duration (40 minutes). For continuous sessions, session one is also 30 minutes consisting of 5-minute warm up, 20 minutes continuous moderate intensity exercise, and a 5-minute cool down. After surgery, participants begin exercises in 20-minute sessions with an aim of increasing duration by 10 minutes weekly until pre-surgery durations are achieved. Type: Type of exercises was dependent on the location of the participant as community or home based, and their access to gym equipment. This can include upright cycle ergometer, recumbent cycle ergometer, treadmill, elliptical ergometer, and rowing ergometer. Home based participants also had access to the ExWell at home exercise booklet detailing a range of appropriate home-based exercises, as well as the use of walking, jogging and cycling. Resistance training uses a circuit of 6-10 exercises alternating upper and lower body workouts based on guidance from the exercise booklet.

1.1.5.3.2 Nutrition Participants met a member of the dietetic team at study baseline assessment for nutrition screening. Patients were screened based on nutritional risk and provided with nutritional optimization information. Patients identified as being at nutritional risk were advised to follow a high calorie and high protein diet. Patients who had a lower nutritional risk were advised to increase their intake of protein by approximately 25g per day. If needed, the team also advised the patient on symptom specific information and symptom management.

1.1.5.4 The Nested PhD Project

This nested PhD project is embedded within the PANO trial. The project extends the trial aims by focusing on cognitive function, psychological wellbeing and the patient experience. In addition to the timepoints included within the trial, the PhD project explores patient experience and cognitive function 12-months post-surgery. The PhD Project focuses on three time periods to explore the cognitive experience and associated experience of patient wellbeing from PM diagnosis to survivorship: The baseline to preoperative timepoints of patients enrolled in the trial (Chapter 4); the postintervention timepoint within the trial through qualitative interview (Chapter 5); and approximately one year post surgery (Chapter 6). Within the nested research, the PhD student was responsible for data collection, analysis and interpretation for all

chapters. The sections below will explore key overarching methodological and design considerations related to the nested PhD project.

1.1.5.4.1 Multiple-methods Investigation. A number of assessment and methodological considerations were explored when deciding on the most appropriate methods for this nested project within a single-site feasibility research design. Given the clinical complexity of patients with PM preparing for CRS-HIPEC (See 1.1.4), and the design complexity of the research project, a pragmatist paradigm was deemed the most appropriate epistemological approach for the research project. A pragmatist approach considers the most appropriate methods to ask specific research questions, within the context of complex research settings and designs (Morgan, 2014, p.29). Pragmatism is highly relevant in patient orientated research including identifying research priorities and most appropriate research methods, by valuing the patient voice in the creation of knowledge through interaction with experience (Allemang et al., 2021). Furthermore, the following considerations had to be made in relation to the larger PANO trial: 1) Patient burden and the number of outcome assessments at each timepoint; 2) The nature of assessments and the requirement for participant in-person versus at home or virtual engagement; and 3) The possibility of attrition throughout the trial.

This nested PhD project adopts a multiple-methods study design. The use of terminology regarding multimethod and mixed-methods research has been the source of methodological confusion (Anguera et al., 2018) and it is important to distinguish between them. Mixed methods research is the use of both qualitative and quantitative forms of data collection whereby deliberate integration occurs between datasets or findings (Bazeley & Kemp, 2012). In contrast, multimethod research deliberately uses multiple research methods including quantitative and qualitative, but do not specifically integrate during data collection or analysis (Plano Clark & Ivankova, 2016, p.55). In the context of this research project, multiple methods of data collection were employed at different study timepoints to address distinctive study objectives. It was not the intent and nor was it appropriate to integrate the datasets or the analysis. Instead, multiple methods are employed across the studies (see figure 1.3) to provide distinctive perspectives on specific research questions related to CRCI, prehabilitation and psychological wellbeing. The use of multiple qualitative and quantitative research methods also helped to mitigate the potential risk of attrition across datasets and risk of

overinterpretation of the small quantitative data set when drawing findings (ranging from n=29-12 across studies).

1.1.5.4.2 Reflexivity. It was important during the research process to consider how my personal role as a PhD researcher may influence or impact upon my understanding and interpretation of the objectives of this research. On a personal level, as a female psychology PhD student, I am aware that my interview style and approach may be influenced by my psychological background. In addition to this, my role as a cognitive and psychological health researcher may pre-determine my perception of the importance of psychological wellbeing and physical health as it relates to cognitive impairment. On an interpersonal level, it was important to be aware of my own role within the larger PANO trial. I was responsible for the data collection and patient engagement for some patients. This may have inadvertently affected levels of self-disclosure for patients that I had more contact with as part of the trial. In particular those as part of the intervention who were aware we are exploring intervention efficacy. The patient semi-structured topic guide was developed with appropriate prompts to promote consistency across interview topics explored. The wider PANO research team also highlighted these observations, and the decision was made to debrief with a member of the research team and take a break after emotionally taxing interviews.

Throughout my PhD research project, I engaged in many forms of reflexive practice. During data collection, I recorded reflections on each interview experience, I also met with my research mentor in Breakthrough Cancer Research, to explore my experience as an interviewer and how best to ethically and safely explore the topics of cancer treatment and recovery with patients. During data analysis, I met frequently with my supervision team to discuss preliminary analysis and emerging themes, potential sources of bias, and if emerging themes are reflective of patient experiences. Once preliminary themes were generated, the research team met again to discuss findings and reflect on how these represented the patient experience.

1.1.5.4.3 The Role of Public and Patient Involvement. Public and Patient Involvement was central to the trial and PhD due to its patient-centred focus. The PPI panel was specifically developed for the project and consisted of members of the public (n=1), patient representatives with a CRS-HIPEC experience (n=6) and patient family members (n=2). Some of the PPI members were part of the steering group and all PPI played an important role across a number of key phases within the research project. For my PhD, I worked closely with the PPI panel who took part in a number of zoom online

sessions throughout the project. The format included a short presentation from myself followed by discussion on the specific topic with the panel. Members were then provided with relevant information and documents to review following each session and provided feedback to me by phone or email. The PPI group were integral in the following project activities:

1. Development and reviewing patient documentation- Including patient recruitment materials, plain language statements and consent forms.

2. Topic guides for patient interviews- Feedback on patient topic guides for pre and post operative patient interviews and development of appropriate prompts for interview.

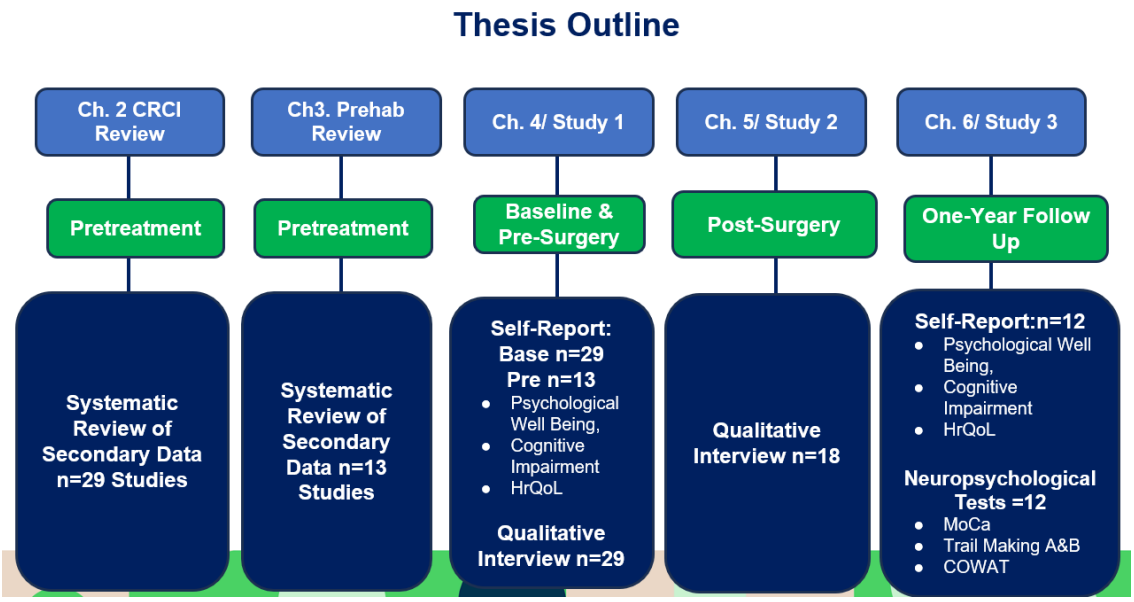
3. Review of patient self-report materials- Reviewed patient assessment packs to ensure patient understanding, clarity and time to complete self-report measures.

4, Dissemination activities- The PPI group were consulted about the most appropriate lay dissemination activities for the project including podcasts and other media.

1.1.6 Thesis Conspectus

The outline of each study as well as methods applied at each timepoint is outlined below in figure 1.3.

Figure 1.3*: Thesis Outline*



1.1.6.1 Chapter 1: Literature Review

Chapter one explores the literature as it relates to 1) Cancer incidence and rare cancer 2) Cancer Related Cognitive Impairment 3) Prehabilitation 4) Exploring cognition through the lens of prehabilitation. This chapter highlights the current conceptual models and considerations regarding CRCI research. The primary mechanisms of CRCI are explored and the primary cognitive domains of interest are identified. Methodological considerations in CRCI research are highlighted, including both subjective and objective modes of assessment. Prehabilitation is then explored as an intervention outlining the concept of multimodal prehabilitation including physical and psychological benefits. Exercise, Nutrition and Psychological prehabilitation are explained and the state of art in current prehabilitation research is illustrated. The chapter concludes by integrating CRCI research with prehabilitation to explore the conceptual associations between the two constructs, and how prehabilitation interventions may impact upon cognitive function.

1.1.6.2 Chapter 2: Pretreatment Cancer Related Cognitive Impairment and Associated Psychological Factors: A systematic Review

This systematic review explores the literature pertaining to CRCI prevalence prior to surgery or treatment. In order to better understand the experience of CRCI and its relationship with psychological factors, this review assesses CRCI prior to initiation of treatment or surgery to help elucidate how psychological factors like anxiety and depression may impact CRCI prior to treatment related effects. In addition, this review also highlights the issue of measurement and reports on the range of self-report measures and neuropsychological tests used. Associations between objective and subjective measurement are explored as well the long-term CRCI trajectory. To our knowledge, this is the first review to assess the prevalence of pretreatment CRCI across cancer types and associations with psychological factors.

1.1.6.3 Chapter 3: The Impact of Prehabilitation Interventions on Affective and Functional Outcomes for Young to Midlife Adult Cancer Patients: A Systematic Review

This review aims to explore how prehabilitation can impact both psychological and physical outcomes and as a result contribute to our understanding of how prehabilitation intervention may be applied to promote patient wellbeing. This review

explores physical, psychological and nutrition prehabilitation interventions and how they impact functional outcomes and psychological outcomes including anxiety, depression, stress and HrQoL. The review is focused on young to midlife adult cancer patients (18-55), due to a lack of literature exploring this age group as it relates to prehabilitation.

1.1.6.4 Chapter 4: Exploring the Cognitive and Psychological Experience of Preparing for Cancer Surgery

Chapter 4 explores the patient experience of cognition and psychological factors from baseline to CRS-HIPEC treatment within the context of a bi-modal exercise and nutrition prehabilitation trial. Twenty-nine patients are assessed at baseline and pretreatment timepoints on a range of self-report measures with an aim to explore subjective CRCI and potential associated factors including psychological wellbeing and health-related quality of life to assess CRCI prevalence and baseline to pretreatment changes. Furthermore, between-group differences are also assessed between those taking part in the intervention and the control group, allowing for the exploration of the potential impacts of exercise and nutrition. In addition, qualitative exploration of pretreatment experience through semi-structured interviews provides in-depth insight into the pretreatment patient experience explored through thematic analysis.

1.1.6.5 Chapter 5: The Patient Experience of Cognition and Psychological Wellbeing While Recovering From Surgery: A Qualitative Study

This chapter contributes to our understanding of postoperative patient experience by qualitatively investigating the experiences of patients (n=18) upon completion of either the bimodal exercise and nutrition pre and rehabilitation, or care as usual. Semi-structured interviews are analysed using thematic analysis with an emphasis on how patients experience cognition and psychological wellbeing post-surgery with the goal of increasing our understanding of CRCI trajectory in recovery, psychological and physical wellbeing and quality of life.

1.1.6.6 Chapter 6: Exploration of Cognitive Function and Psychological Variables One Year Post-surgery

Chapter 6 reports on both the subjective and objective experience of CRCI for patients approximately one year post surgery through use of both self-report measures

of cognitive impairment, and a neuropsychological test battery assessing mild cognitive impairment, verbal fluency, attention, processing speed and executive function. The prevalence of CRCI is explored as well as levels of impairment across norms and scoring criteria. This chapter assesses associations between subjective and objective measures of CRCI to aid in our understanding of CRCI conceptualisation and postoperative experience. In addition, associations are also assessed between CRCI and emotional wellbeing to provide an overview of patient experience and CRCI trajectory one year post surgery.

1.1.6.7 Chapter 7: General Discussion

Chapter 7 synthesises the evidence from our three empirical studies to provide an overview of findings and situate findings within the wider research landscape. Results are discussed in reference to methodological and theoretical considerations, and a conceptual understanding of the relationship between pretreatment CRCI, psychological wellbeing and quality of life is proposed. The strengths and limitations of the research project are considered and opportunities for further research are discussed. The role and contribution of public and patient involvement within the research project is highlighted and finally a number of conclusions are illustrated.

Chapter 2: Pretreatment Cancer Related Cognitive Impairment and Associated Psychological Factors: A systematic Review

This work has been accepted for publication as of December 2025.

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Scriney A, Gurren L, Gallagher P, Loughney L and Boran L (2026) Pretreatment cancer related cognitive impairment and associated psychological factors: a systematic review. Front. Psychol. 16:1682455. doi: 10.3389/fpsyg.2025.1682455

2:1 Introduction

Cancer related cognitive impairment (CRCI) describes general deficits that some cancer patients may experience in domains including but not limited to memory, attention, processing speed and other executive functions (Lange et al., 2019). It has garnered attention due to its prevalence before, during and after treatment occurs (Hutterer and Oberndorfer, 2021), and due to its association and interaction with overall health related quality of life (Shim et al., 2021), and psychological variables such as anxiety and depression (Brandenbarg et al., 2019, Hashemi et al., 2020, Hutterer & Oberndorfer, 2021, Lange et al., 2019). Indeed, psychological factors have been a particular focus in recent CRCI research, with Haywood and colleagues (Haywood et al., 2024) calling for increased research into the potential transdiagnostic nature of psychopathology and CRCI, and how each concept may functionally contribute and interact with the other into survivorship. Finally, research has focused on the development of guidelines and standardization of CRCI tools and measures, since the establishment of the International Cancer and Cognition Task Force (ICCTF) (Deprez et al., 2018).

Standardization and sensitivity of CRCI measurement has proven challenging. Firstly, traditional neuropsychological tests may not provide adequate sensitivity to measure the mild to moderate impairment experienced by patients with CRCI (Ahles and Hurria, 2018). Secondly, there is a lack of correlation between subjective/self-report of cognitive issues and objective CRCI measurement (Henneghan et al., 2021). CRCI subjective measurement usually involves validated measures like the FACT-cognition (Wagner et al., 2009) or the Cognitive Failures Questionnaire (Broadbent et

al., 1982). However, it is also sometimes measured in cancer patients using larger scale quality of life assessments such as the EORTC QLQ-C30 (Aaronson et al., 1993). This can be problematic as the EORTC QLQ-C30 only contains two items that load to the symptom subscale of cognition (Sharma and Brunet, 2023). More work is required to both understand and standardize the process of CRCI measurement (Deprez et al., 2018; Henneghan et al., 2021; Sharma and Brunet, 2023; Wefel et al., 2011), to improve the rigor and reliability of research findings to further our knowledge of CRCI, and to increase the clinical applicability of findings (Henneghan et al., 2021).

Traditionally cognitive impairments related to cancer diagnosis were largely attributed to treatment related factors with terms such as "chemobrain" used to describe the association between the treatment and resulting cognitive deficits (Janelsins et al., 2014; Onzi et al., 2022). Although treatment effects are evident, research has also highlighted the presence of pretreatment CRCI across a wide range of cancer types including breast, leukaemia, colorectal cancer and testicular cancers (Olson and Marks, 2019). Notwithstanding difficulties in measuring CRCI, some evidence suggests that pretreatment CRCI can occur in approximately 30% of patients (Janelsins et al., 2014) and is evident from both self-report (11–33%) and neuropsychological (5–11%) tests prior to chemotherapy (Hutterer and Oberndorfer, 2021). The existence and increased evidence of pretreatment CRCI has led researchers to present possible causes of and contributing factors to CRCI beyond treatment related factors, including genetics (Lange et al., 2019; Ahles and Hurria, 2018; Janelsins et al., 2014), inflammatory biomarkers (Lange et al., 2019; Ahles and Hurria, 2018; Janelsins et al., 2014; Andreotti et al., 2015), and tumour derived factors (Ahles and Hurria, 2018; Olson and Marks, 2019; Oppegaard, 2023a). Additionally, many models also highlight the role of psychological factors including anxiety, depression, stress and fatigue, as experiencing psychological distress such as anxiety and depression may result in cognitive complaints, as well as the multifaceted nature of fatigue (Lange et al., 2019; Hutterer and Oberndorfer, 2021; Ahles and Hurria, 2018; Andreotti et al., 2015; Oppegaard, 2023a). More recently, a report on the National Cancer Institute's meeting on CRCI research design acknowledged the multiple factors at play including cancer, disease burden and treatment, biological mechanisms, patient factors and concurrent symptoms like anxiety and depression (Janelsins et al., 2025). Current clinical guidelines also highlight the potential role of psychological factors, particularly in relation to subjective cognitive function (Zhang et al., 2025), and it is well documented that

psychological distress caused by anxiety and depression can impact cognitive function even in clinically healthy populations (Snyder, 2013).

To date, there have been a number of systematic reviews focusing on the interplay between psychological variables and cancer related cognitive impairment in cancer cohorts undergoing surgery or treatment. Yang and Hendrix (2018) explored psychological factors as they related to CRCI with breast cancer patients. They concluded that depression was most associated with CRCI, followed by anxiety. Oliva et al. (2024) conducted an umbrella review exploring cognitive impairment following breast cancer surgery. Eighteen systematic reviews were included, and they found that while objective and subjective tests were weakly or not correlated, overall CRCI was associated with psychological variables including distress and fatigue. No systematic review has looked at pretreatment CRCI across cancer types or its association with psychological factors. Synthesizing existing evidence would help to elucidate the presence of pretreatment CRCI, and further our understanding of the potential interplay between cognitive function prior to treatment, and baseline anxiety and depression. To understand pretreatment CRCI and its possible association with anxiety and depression, the aim of this systematic review is to synthesize existing evidence of: (1) Prevalence of pretreatment objective and subjective CRCI , (2) Any associations between subjective and objective measures of cognitive function either pretreatment or across time, (3) Any associations between pretreatment subjective and objective measures of CRCI and anxiety and/or depression; and (4) Longitudinal changes in CRCI

These research questions will address the following research questions:

a. Assess the prevalence of CRCI prior to any treatment during the preoperative and postoperative phase.
b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.
c. Assess the relationship between objective and subjective CRCI.

2.2. Methods

This review was conducted and reported in line with the preferred reporting for systematic reviews and meta-analyses (PRISMA) statements (Page et al., 2021). The

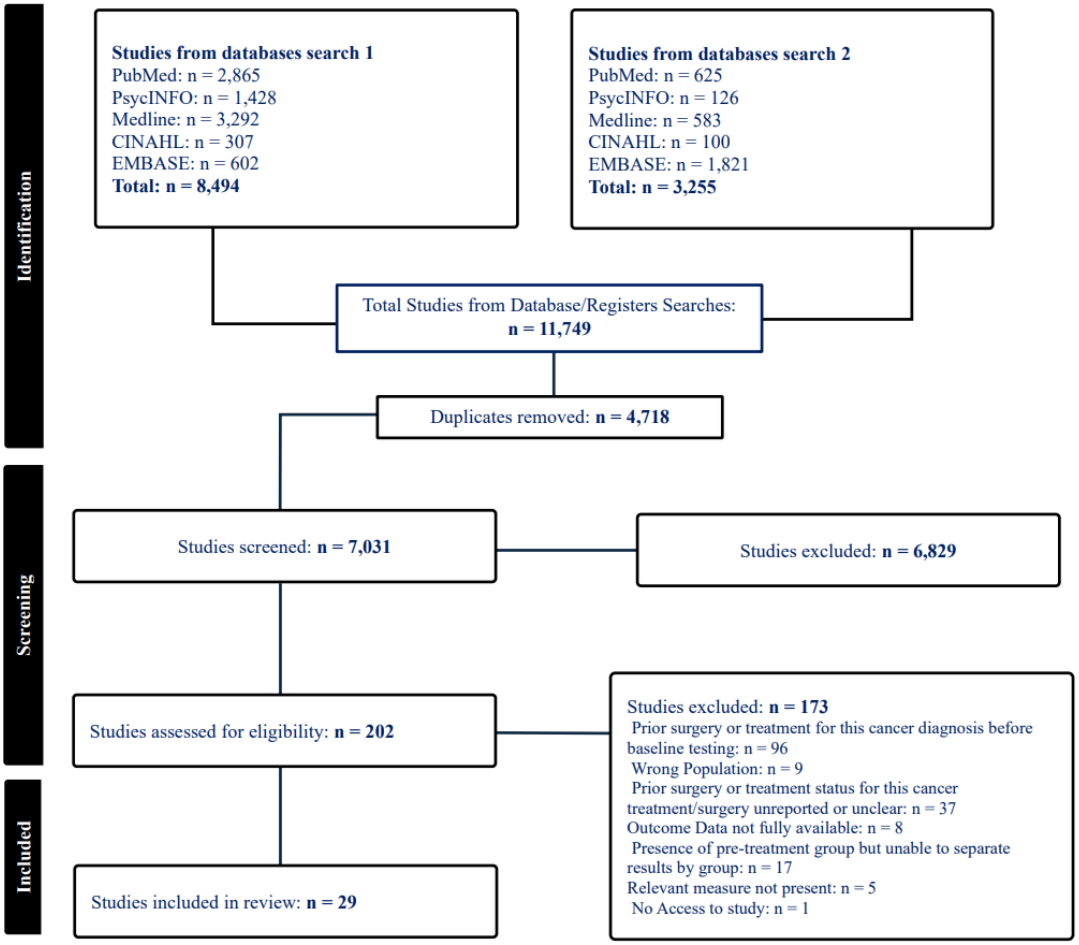
review protocol was registered on the PROSPERO protocol database (No. CRD42023392837).

2.2.1 Search strategy

A systematic literature search of articles relating to CRCI and psychological variables was conducted. Five databases were identified and included based on relevance to the research question: PsycINFO, MEDLINE, CINAHL, EMBASE, and PubMed. Search terms were collated based on relevance to the research question and from previous literature. Search terms were organized into three categories: (1) Cancer Related Terms, (2) Cognition Related Terms, and (3) Psychological Factor Related Terms. Searches were limited to peer reviewed articles published in English with human participants only. Wild card expanders were applied to free text search terms as appropriate for each of the databases. Figure 2.1 represents the PRISMA screening strategy for each stage of screening. Searches were initially conducted (Search 1) In February 2023 and updated inclusive of January 2025 (Search 2).

Figure 2.1

PRISMA Flowchart of Screening and Review Process for Included Studies n=29



2.2.2 Inclusion criteria

Studies were included if they explored CRCI, and anxiety and/ or depression. As the review is focused on the pretreatment time point, data had to be available before any cancer surgery or treatment had occurred. Studies were excluded if participants were <18 years old or were being treated for Central Nervous System (CNS) cancer types, due to the potential associations with cognitive function due to specific cancer type site or tumour location. Full exclusion and inclusion criteria are outlined below in Table 2.1.

2.2.3 Quality assessment

Studies included for data extraction were assessed for quality by two reviewers independently (AS and LG) using the Joanna Briggs Institute Critical Appraisal Checklists. Checklists were applied depending on appropriate study methodology with checklists ranging from eight to nine items. These included cohort studies, analytical cross-sectional, case control studies (Moola et al., 2020), randomized control trials (Munn et al., 2020) and prevalence study checklists (Barker et al., 2023). Raters responded to each item using responses “yes,” “no,” “unclear” and “not applicable,” with final assessments categorized as “include,” “exclude” or “seek further information.” The critical appraisal aimed to inform the results of the review by assessing study methodology and the extent to which efforts were made to address potential sources of bias in design. As the purpose of the review was to provide a comprehensive overview of all the available evidence and the quality assessment was undertaken to aid critical evaluation of the findings, the decision was made to not exclude studies on the basis of the quality assessment. After separate quality assessment, the first and second reviewer consulted on any disagreements to reach a consensus. Consensus was reached for all disagreements, so a moderator was not required.

Table 2.1

Exclusion and Inclusion Criteria

Inclusion Criteria	Exclusion Criteria
Explores CRCI	Central Nervous System Cancers
Explores anxiety and/or depression	
>18 years of age	Childhood or Young Adult Population
Outcome measurement of cognitive function	Not related to CRCI, anxiety & depression
Pretreatment and/or any surgery time point	No pretreatment time point data
Peer reviewed journal articles	No empirical data
Published in English	Not available in English
Outcome Measurement of Anxiety and/or Depression	No measure of cognitive function (subjective or objective) and anxiety and/or depression
Any Study Design	

2.2.3 Screening process

Screening was conducted in two stages using systematic review software Covidence. Title and abstract and full text screening was conducted alongside a second reviewer (LG). All texts were exported from referencing software Zotero to Covidence where duplicates were then identified and removed. During title and abstract screening, any texts deemed irrelevant by the two reviewers were discarded. This process was repeated for full text screening, where texts were read in full by both reviewers to determine relevance to the research question. Studies were then excluded or included based on specific criteria (see Table 2.1). If any conflicts or disagreements arose, these were discussed and resolved between the first and second reviewer.

2.2.4 Data extraction

Data extraction was conducted on eligible studies by the first reviewer. Extracted data included (1) Authors, (2) Study Design, (3) Cancer type and stage, (4) demographic and medical information, (5) Outcomes of interest, (6) Data analysis conducted, (7) Description of Results, and (8) Country. Anxiety and Depression outcome measures were coded as any tool type and associated measurement scale used to measure the construct of anxiety or depression, including also measures with specific subscale scores related to anxiety or depression. Cognitive measures were defined as any objective or subjective measures with the aim of measuring any cognitive construct related to cognitive impairment, performance, function or decline, not screening. This could include cognitive self-report questionnaires or questionnaires containing a distinct cognitive subscale, objective tests of cognitive performance in any domain, or a cognitive screening multidimensional tool.

2.2.5 Data synthesis

Due to the exploratory nature of this review, included data varied across study designs, measurement tools and cancer types. Due to this, a narrative synthesis was employed to best capture the heterogeneity and variance of studies, whilst also synthesizing results narratively across four main outcomes of interest: (1) Levels of pretreatment objective and subjective CRCI (2) Relationship between objective and subjective CRCI, (3) Relationship between objective and subjective CRCI, and anxiety and depression, (4) Change in cognition over time.

2.3 Results

2.3.1 Search results

Figure 2.1 represents the data screening and inclusion process for the current review. Eleven thousand seven hundred forty-nine papers were included for abstract screening. After duplicate removal, 7,031 papers remained. Six thousand eight hundred twenty-nine papers were excluded at the title and abstract screening stage, with 202 papers included at full text screening. After full text screening, 29 papers were included (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich, 1999; Cimprich and Ronis, 2001; Cimprich et al., 2005; Chun et al., 2023; De Rosa et al., 2021; Fayette et al.,

2023; François et al., 2024; Gates et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Jung et al., 2022; Juríčková et al., 2023; Kathpalia et al., 2024; Knoerl et al., 2024; Lange et al., 2020; Lehto, 2013; Patel et al., 2015; Patel et al., 2023; Savard et al., 2023; Scheibel, 2004; Tulk et al., 2021; Zhuang et al., 2023). Study characteristics for all papers are included in Table 2.2 below.

Table 2.2 *Characteristics of Included Papers n=29*

Author, Year	Country	Cancer Type	Study timepoints	Healthy Control Group	Total n, (total, Patients n)	Gender	Average Age Patients	Cancer Related Inclusion/Exclusion Criteria
Aspelund et al., 2024	Iceland	Breast	1	Yes	179 (n=112)	F=179	PG:61.8, CG: 60.9	
Bernstein et al., 2018	Canada	Head and neck	1	Yes	120 (n=80)	M=103, F= 17	PG: 58.3, CG: 54.6	Excluded: Metastatic
Chun et al., 2023	South Korea	Small Cell Lung	1	No	21 (n=21)	M=20, F=1	Total: 75	
Cimprich et al., 1999	United States	Breast	1	No	74 (n=74)	F=74	Total: 56	Included: Stage I-II
Cimprich et al., 2001	United States	Breast	3	Yes	95 (n=47)	F=95	PG: 64, CG: 61	
Cimprich et al., 2004	United States	Breast	1	No	184 (n=184)	F=184	Total 54.6	Included: Stage 0-II
De Rosa et al., 2021	Italy	Gynaecological	2	No	73 (n=73)	F=73	Total 50.2	Included: FIGO stage I-III, Excluded: CNS Pathologies
Fayette et al., 2023	Czech Republic	Hodgkin's Lymphoma	3	Yes	81(n=36)	F=49, M=32	PG: 38.63 CG: 41.57	
François et al., 2024	France	Locally Advanced Rectal	5	No	101(n=101)	M=59, F=42	Median = 80	Included: Tumour Stage II, III, IV Excluded: Metastatic
Gates et al., 2024	Australia	Aggressive Lymphoma	2	Yes	102 (n=30)	F=55, M=47	PG:57, CG:56	Excluded: Lymphomatous CNS Involvement
Hardy-Leger et al., 2020*	France	Breast	1	No	264	F=264 (263 in analysis)	Total: 54.0	Included: cT0-cT3, cN0-3 Tumour
Hermelink et al., 2007**	Germany	Breast	2	No	109 (n=109)	F=109, (101 in analysis)	Total: 48.6	Included: Stage 0-IIIc Excluded Metastasis
Hermelink et al., 2010**	Germany	Breast	3	No	101 (n=101)	F=101	Total: 48.5	Included: Stage 0-IIIc Excluded Metastasis
Hermelink et al., 2015†	Germany	Breast	1	Yes	226 (n=60)	F=226	PG: 50.4, CG: 52.6	Included: Stage 0-IIIc Excluded: Metastasis
Hermelink et al., 2017†	Germany	Breast	3	Yes	206 (n= 150)	F=206	Patient Chemotherapy: m=47.7 Patient Non-Chemotherapy: m=53.4, Controls: m=52.3	Included Stage 0-IIIc Excluded: Metastasis
Hu et al., 2023	China	Breast	3	Yes	74 (n=36)	F=74	PG:47.9, CG 1: 52.9, CG 2: 44.94	Excluded: Presence of Brain Tumour
Janelsins et al., 2022	United States	Lymphoma	3	Yes	460 (n=248)	F=180, M=280	PG: 55.40, CG: 53.96	Excluded: CNS Disease

Author, Year	Country	Cancer Type	Study timepoints	Healthy Control Group	Total n, (total, Patients n)	Gender	Average Age Patients	Cancer Related Inclusion/Exclusion Criteria
Jung et al., 2022	South Korea	Thyroid	1	No	130 (n = 130)	F=130 (124 in analysis)	Total: 43.99	Excluded: Metastasis
Juríčková et al., 2023	Czech Republic	Hodgkin Lymphoma	1	Yes	80 (n=40)	F=44, M=36	PG: 39.14, CG: 38.41	
Kathpalia et al., 2024	India	Non-Hodgkin Lymphoma	1	Yes	62 (n=31)	F=27, M=35	PG: 51.9, CG: 50	Excluded: Presence of secondary cancer
Knoerl et al., 2024	United States	Breast	2	No	49 (n=49)	F=49 (47 in analysis)	Total: 52.8	Included: Stage I-III
Lange et al., 2020*	France	Breast	1	Yes	396 (n=264)	F=396	PG: 54.1, CG: 53.2	Included: cT0-cT3, cN0-3 Tumour
Lehto et al., 2013	United States	Lung Malignancy	2	Yes	23 (n=15)	F=8, M=15	Total: 61.4	
Patel et al., 2015 † †	United States	Breast	1	Yes	262 (n=174)	F= 262	PG:61.82, CG: 60.48	Excluded: Metastasis
Patel et al., 2023 † †	United States	Breast	4	Yes	250 (n=173)	F=250	PG: 60, CG: 61	Excluded: Metastasis
Savard et al., 2023	Canada	Prostate	4	No	130 (n=130)	M=130	Total: 63.39	
Scheibel et al., 2004	United States	Myelogenous Leukaemia	2	No	30 (n=30)	F=10, M=20	PG: 46.0	
Tulk et al., 2021	Canada	Prostate	2	No	24 (n=24)	M=24	Total 69.63	Included: T2,3,4
Zhuang et al., 2023	China	Breast	2	Yes	41(n=21)	F=41	PG 44 CG 40.3	Included: Stage I-III Excluded Metastasis

Note: * = Papers contained data from the same patient cohort, **= Papers contained data from the same patient cohort,† = Papers contained data from the same patient cohort

,† † = Papers contained data from the same patient cohort, PG = Patient Group, CG= Control Group

2.3.2 Quality assessment

Although studies were not dependent on quality assessment for inclusion, study quality was generally high, and all included studies were deemed adequate for inclusion by both reviewers. The full quality assessment is included in Appendix A.

2.3.3 Characteristics of Included Papers

Study characteristics of included papers are presented below (Table 2.2). Papers included the data of 2,920 patients. Patient sample size ranged from 15 (Lehto, 2013) to 264 (Lange et al., 2020) patients. The average patient age was 55.09 years. Sixteen papers had female only participants (Cimprich, 1999; Cimprich and Ronis, 2001; Cimprich et al., 2005; De Rosa et al., 2021; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Jung et al., 2022; Knoerl et al., 2024; Lange et al., 2020; Patel et al., 2015; Patel et al., 2023; Zhuang et al., 2023) (Table 2.2). Publication dates ranged from 1999 to 2024, with 18 papers published within the last 5 years (See Table 2.2). Eleven papers were cross sectional in design (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich, 1999; Cimprich et al., 2005; Hardy-Leger et al., 2021; Hermelink et al., 2015; Jung et al., 2022; Juríčková et al., 2023; Kathpalia et al., 2024; Lange et al., 2020; Patel et al., 2015), one was retrospective (Chun et al., 2023) while 17 papers had prospective and/ or longitudinal designs with multiple assessment timepoints (Cimprich and Ronis, 2001; Cimprich et al., 2005; Chun et al., 2023; De Rosa et al., 2021; Fayette et al., 2023; François et al., 2024; Gates et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Knoerl et al., 2024; Lehto, 2013; Patel et al., 2023; Savard et al., 2023; Scheibel, 2004; Tulk et al., 2021; Zhuang et al., 2023). Sixteen papers included a healthy control group for analysis (Table 2.2) (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich and Ronis, 2001; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Juríčková et al., 2023; Kathpalia et al., 2024; Lange et al., 2020; Lehto, 2013; Patel et al., 2015; Patel et al., 2023; Zhuang et al., 2023).

Cancer type varied across papers, but included 15 breast cancer papers (Aspelund et al., 2024; Cimprich, 1999; Cimprich and Ronis, 2001; Cimprich et al., 2005; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010;

Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Knoerl et al., 2024; Lange et al., 2020; Patel et al., 2015; Patel et al., 2023; Zhuang et al., 2023). As shown in Table 2, Thirteen papers applied inclusion criteria based on cancer/ tumour stage (Cimprich, 1999; Cimprich et al., 2005; De Rosa et al., 2021; François et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Knoerl et al., 2024; Lange et al., 2020; Tulk et al., 2021; Zhuang et al., 2023). Fifteen papers excluded participants based on presence of metastasis or CNS disease (Bernstein et al., 2018; De Rosa et al., 2021; François et al., 2024; Gates et al., 2024; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Jung et al., 2022; Kathpalia et al., 2024; Patel et al., 2015; Patel et al., 2023; Zhuang et al., 2023). With regard to treatment type, eight papers explored surgery (Aspelund et al., 2024; Cimprich, 1999; Cimprich and Ronis, 2001; Cimprich et al., 2005; Jung et al., 2022; Knoerl et al., 2024; Lehto, 2013; Savard et al., 2023), eight chemotherapy only (Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2007; Hermelink et al., 2010; Hu et al., 2023; Janelsins et al., 2022; Scheibel, 2004; Zhuang et al., 2023), and the remaining 13 papers explored combinations of treatment types (Bernstein et al., 2018; Chun et al., 2023; De Rosa et al., 2021; François et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2015; Hermelink et al., 2017; Juríčková et al., 2024; Lange et al., 2020; Patel et al., 2015; Patel et al., 2023; Tulk et al., 2021).

2.3.4 Included Measures

Measures included in each paper are outlined below in Table 2.3. Fifteen papers measured both objective and subjective cognitive function (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich et al., 2005; François et al., 2024; Gates et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Lange et al., 2020; Patel et al., 2023; Tulk et al., 2021). Nine papers measured objective impairment only (Cimprich and Ronis, 2001; Chun et al., 2023; Fayette et al., 2023; Jung et al., 2022; Juríčková et al., 2023; Kathpalia et al., 2024; Patel et al., 2015; Scheibel, 2004; Zhuang et al., 2023). Five papers measured subjective impairment only (Cimprich, 1999; De Rosa et al., 2021; Knoerl et al., 2024; Lehto, 2013; Savard et al., 2023).

Twenty-four papers explored cognitive impairment using objective cognitive

neuropsychological assessments (see Table 2.3). The most frequent tests included were the trail making test (n = 16), Digit span (n = 16) and the Stroop color-word test (n = 8), followed by the Hopkins verbal learning test-revised (n = 7), the digit symbols test (n = 7), and the controlled oral word association test (n = 6). The most common domains measured across papers were attention (n = 20), memory (n = 20), and executive functions (n = 18) (see Table 3). Twenty papers explored CRCI using subjective measures including The Functional Assessment of Cancer Therapy (FACT) Cognition scale (n = 9), The Attentional Function Index (n = 3), the cognitive function subscale of the European Organization for Research and Treatment of Cancer questionnaire (EORTC) (n = 6), the cognitive function subscale of the Patient-Reported Outcomes Measurement Information System (PROMIS) (n = 1), The Questionnaire of Experienced Attention Deficits (FEDA) (n = 4) and the Brief Rating Inventory of Executive Function-Adult (BRIEF-A) (n = 1) (see Table 2.3).

For psychological outcomes, eight papers included measures of depression only (Cimprich and Ronis, 2001; Chun et al., 2023; De Rosa et al., 2021; François et al., 2024; Jung et al., 2022; Kathpalia et al., 2024; Patel et al., 2023; Scheibel, 2004), two papers included measures of anxiety only (Lehto, 2013; Patel et al., 2015), The remaining 19 papers included a measure of both anxiety and depression (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich, 1999; Cimprich et al., 2005; Fayette et al., 2023; Gates et al., 2024; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Juríčková et al., 2023; Knoerl et al., 2024; Lange et al., 2020; Savard et al., 2023; Tulk et al., 2021; Zhuang et al., 2023) (See Table 2.3).

Table 2.3 *Characteristics of Included Measures for n=29 Studies*

Author	Ob.	Sub.	Objective Cognitive measures	Reported Cognitive Domains	Sub. measures	Anxiety	Depression
Aspelund et al., 2024	X	X	5 second psychomotor visual test, TMT A&B, digit span, RVALT, COWA test.	Attention, executive function, processing speed, working and verbal memory, verbal fluency	PROMIS CF 8a	GAD-7	CES-D
Bernstein et al., 2018	X	X	Vocabulary and matrix reasoning, digit span, spatial span, HVLT-R, brief visuospatial memory test -R, the D-KEFS Stroop test, TMT A&B, grooved pegboard	Concentration/ attention, executive function, memory, motor dexterity processing speed	Fact Cog V3	HADS	HADS
Chun et al., 2023	X		MMSE	Cognitive function			GDSSF-K
Cimprich et al., 1999		X			AFI	POMS	POMS
Cimprich et al., 2001	X		Digit span, digit symbol, the Necker cube pattern control test	Capacity to direct attention			POMS
Cimprich et al., 2004	X	X	Digit span, TMT A&B, three shapes three words test	Capacity to direct attention, short-term memory	AFI	POMS-SF	POMS-SF
De Rosa et al., 2021		X			Fact Cog V3		BDI
Fayette et al., 2023	X		Auditory verbal learning test, complex figure test (ROCFT), TMT A&B, verbal fluency test, logical memory test, continuous performance test 3, digit span, similarities, digit symbol, letter number sequencing, the Stroop test.	Abstraction/executive functions, attention/vigilance, verbal memory and learning, working memory/flexibility, processing speed/psychomotor speed		HAM-A BAI	HAM-D BDI
François et al., 2024	X	X	MMSE	Attention and calculation, language, memory recall, orientation, registration, visuospatial ability	EORTC-CF		GDS
Gates et al., 2024	X	X	TMT A&B, HVLT-R, digit span, the Stroop test, COWA test	Attention, executive function, learning and memory, processing speed, verbal fluency, working memory	FACT-Cog V3	PROMIS-7a	PROMIS-8b SF
Hardy-Leger et al., 2020	X	X	HVLT, digit span, letter-number sequencing, spatial span, TMT A&B, symbol search, the Stroop test, D2 test, Fluency score	Attention, executive function, episodic memory, processing speed, working memory	FACT-Cog V3	HADS	HADS

Author	Ob.	Sub.	Objective Cognitive measures	Reported Cognitive Domains	Sub. measures	Anxiety	Depression
Hermelink et al., 2007	X	X	Logical memory I,II, D2 test, digit symbol, TMT A&B, Regensburg word fluency test, digit span	Attention, concentration, cognitive flexibility, divided attention, executive function, processing speed, psychomotor function, selective attention, verbal memory, verbal working memory	EORTC-CF, FEDA	HADS	HADS
Hermelink et al., 2010	X	X	Logical memory I,II, D2 test, digit symbol test, TMT A&B, Regensburg word fluency test, digit span	Attention, concentration, cognitive flexibility, divided attention, executive function, processing speed, psychomotor function, selective attention, verbal memory, verbal working memory	EORTC-CF, FEDA	HADS	HADS
Hermelink et al., 2015	X	X	Go/Nogo, TMT A&B, test of attentional performance, digit span, verbal learning and memory test, R-Word fluency test,	Attention, executive function, memory, processing speed, verbal memory	EORTC-CF, FEDA		PHQ-D
Hermelink et al., 2017	X	X	Go/Nogo, TMT A&B, test of attentional performance, digit span, verbal learning and memory test, R-Word fluency test,	Attention, executive function, memory, processing speed, verbal memory	EORTC-CF, FEDA		PHQ-D
Hu et al., 2023	X	X	TMT A, VFT, digit span	Attention, executive function, motor skills, processing speed, working memory, semantic memory, verbal fluency, visual search	FACT-Cog	SAS	SDS
Janelsins et al., 2022	X	X	CANTAB, Hopkins verbal learning & memory test, TMT A&B, COWA	Attention, executive function, memory	FACT-Cog	STAI	MFSI
Jung et al., 2022	X		Digit span, COWA, TMT A&B, the Stroop test	Attention, cognitive control (Executive Function)			PHQ-8
Juríčková et al., 2023	X		Auditory verbal learning Test, Rey-Osterrieth complex figure test, TMT A&B, VFT, Continuous performance test, WAIS-III: Digits span, similarities, digit symbols- coding, letter number sequencing. Logical memory from Wechsler memory (WMS-IIIa) subtest and the Stroop test.	Abstraction/ executive functions, attention/vigilance, memory and learning, processing speed /psychomotor speed, verbal memory and learning, working memory/flexibility		HAM-A, BAI	HAM-D, BDI
Kathpalia et al., 2024	X		MoCA	Attention and concentration, executive function, calculations and orientation, conceptual thinking, language, memory, visuo-constructional skills			PHQ-9
Knoerl et al., 2024		X			EORTC-CF	HADS	HADS
Lange et al., 2020	X	X	HVLT, digit span, letter-number sequencing, spatial span, TMT A&B, symbol search, the Stroop test, D2 test, fluency score	Attention and executive function, episodic memory, processing speed, verbal fluency, working memory	FACT-Cog	HADS	HADS

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Author	Ob.	Sub.	Objective Cognitive measures	Reported Cognitive Domains	Sub. measures	Anxiety	Depression
Lehto et al., 2013		X			AFI	PSWQ	
Patel et al., 2015	X		Trials 4, colour-word inhibition, inhibition switching from the D-KEFS, HVLT (Total and delayed recall, verbal mem), processing speed index -WAIS-IV	Executive function, memory, processing speed		BSI	
Patel et al., 2023	X	X	Wechsler digit span scale	Attention/concentration (working memory)	BRIEF-A		BSI 18
Savard et al., 2023		X			Fact-Cog	HADS	HADS-PHQ-9
Scheibel et al., 2004	X		Digit symbol, Consistent long-term retrieval and 30 min delayed recall from VSRT, TMT A&B, COWA test	Graph-motor speed, verbal learning, verbal memory, verbal fluency, visual-motor and sequencing skills			MMPI
Tulk et al., 2021	X	X	HVLT-R, COWA test, letter number sequencing	Lexical fluency, verbal learning and memory, working memory	FACT-Cog	HADS	HADS
Zhuang et al., 2023	X		MMSE, number connection test, digit symbol, line tracing test, serial dot test, the Stroop test, auditory verbal learning test,	Attention, executive function, fine motor skills, long-term memory, processing speed, short-term memory, visual ability, reaction capability		SAS	SDS

Note: TMT= Trail Making Test*, RVALT*=Rey Auditory Verbal Learning Fluency Test *, COWA*= Controlled Oral Word Association*, HVLT-(R)*=Hopkins Verbal Learning Test-(Revised)*, D-KEFS*= Delis-Kaplan Executive Function System, *MMSE*= Mini Mental State Examination*, VFT*=Verbal Fluency Test*, DST*=Digit Span Test*, CANTAB*= Cambridge Neuropsychological Test Automated Battery*, WMS*=Wechsler Memory Scale*, MoCA*= Montreal Cognitive Assessment*, WAIS*= Wechsler Adult Intelligence Scale*, VSRT*= Verbal Selective Reminding Test, PROMIS CF-8a= Patient-Reported Outcomes Measurement Information System 8a, FACT-Cog= Functional Assessment of Cancer Therapy, EORTC-CF= European Organisation for Research and Treatment of Cancer- Cognitive Function scale , FEDA= Fragebogenerlebter Defizite der Aufmerksamkeit (The Questionnaire of Experienced Deficits of Attention), BRIEF-A = Behavior Rating Inventory of Executive Function-Adult Version.*GAD-7*= Generalized Anxiety Disorder-7*, CES-D* = Centre for Epidemiological Studies Depression Scale, *GDS SF-K* = Geriatric Depression Scale Short Form -Korean, *GDS*=Geriatric Depression Scale, *HADS* = Hospital Anxiety & Depression Scale, *POMS*=Profile of Mood States, *POMS-SF*= Profile of Mood States- Short Form, *BDI*= Beck Depression Inventory, *BAI* =Beck Anxiety Inventory, *HAM-A*=Hamilton Anxiety, *HAM-D*=Hamilton Depression, *PHQ-D*=Patient Health Questionnaire- Depression, *STAI* = Spielberger Trait Anxiety Inventory, *MFSI*= Multidimensional Fatigue Symptom Inventory, *PHQ-8*= Patient Health Questionnaire -8, *PHQ-9*= Patient Health Questionnaire-9, *PSWQ*= Penn State Worry Questionnaire, *PROMIS* =Patient-Reported Outcomes Measurement Information System, *PROMIS 8b SF*= Patient-Reported Outcomes Measurement Information System, 8b Short Form, *BDI-II*= Beck Depression Inventory-II, *BSI*= Brief Symptom Inventory, *BSI-18*= Brief Symptom Inventory-18, *MMPI*= Minnesota Multiphasic Personality Inventory, *SAS*= Self-rating Anxiety Scale, *SDS*= Self-rating Depression Scale,

2.3.5 Level of Pretreatment Cognitive Impairment Measured by Objective and Subjective Assessments

Within the 29 papers included in analysis, the data of 25 discrete studies was reported. Three papers (Hermelink et al., 2010; Hermelink et al., 2017; Patel et al., 2023) reported on follow-up timepoints for the same patient cohort (Hermelink et al., 2007; Hermelink et al., 2015; Patel et al., 2015) Later papers included additional information about timepoints that was extracted where relevant. One study, Hardy-Leger et al. (2021) conducted additional analyses on the same patient cohort as Lange et al. (2020). Studies varied in the ways they chose to measure levels of objective or subjective cognitive impairment. This can be distilled into two main measurement approaches: (1) Comparison with healthy control group, (2) Predefined test criteria. A common predefined criteria was use of the International Cancer and Cognition Taskforce criteria for objective cognitive impairment. This was defined as a global deficit score criteria of a z score >1.5 standard deviations below healthy controls on at least two tests or one test with a z score standard deviation of ≥ 2.0 (Wefel et al., 2011). Other common approaches included standardized tests, population or age adjusted norms for a given test, or standard cut-offs for a given subjective cognitive measure.

2.3.5.1 Objective Cognitive Impairment Pretreatment

Pretreatment Twenty studies explored objective cognitive impairment at the pretreatment timepoint. Results are summarized below in Table 2.4. Impairment was recorded either by test, as a global cognitive function score, or by cognitive domain. Impairment was defined as both relative to healthy control groups and using predefined test norms. Fourteen studies included a healthy control group (HCs) alongside patient groups (PGs) (Table 2.4). Ten of these 14 studies reported significant results on at least one test compared to HCs (Aspelund et al., 2024; Cimprich and Ronis, 2001; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2015; Hu et al., 2023; Juríčková et al., 2023; Kathpalia et al., 2024; Lange et al., 2020; Patel et al., 2015). For most studies, this was in the direction of reduced performance compared to HCs. One study reported better performance on one test for PGs compared to HCs (Hu et al., 2023), while two studies reported increased performance compared to norms for PGs compared to norms on some test indices (Hermelink et al., 2007; Hermelink et al., 2015). The most common reported domains were processing speed and executive functions. Eleven studies reported levels of cognitive impairment within patient groups applying

population norms or predefined test criteria. Within these, reported observed impairment in at least one domain ranged from 13.8% (Aspelund et al., 2024) to 78.2% (Jung et al., 2022).

Table 2.4 *Summary of Findings for Pretreatment Objective Cognitive Impairment*

Study	Patient Group (PG) Comparisons to Healthy Control (HC) Groups Findings			Patient Groups (PG) based on Impairment Criteria or Norms	
	HC Group Y/N	Differences PGs & HCs Y/N	Findings	PGs Test Norms Y/N	Findings
Aspelund et al., 2024	Y	Y	PG Sig. worse processing speed (p=.01) PG Sig. worse verbal memory (p<.001) Overall prevalence of CI non sig	Y	13.8% prevalence of CI
Bernstein et al., 2018	Y	N	No Sig. Differences	Y	11.3% impaired in 2 or more domains 33.8% impaired in one domain
Chun et al., 2023	N			Y	Scores within test norms
Cimprich et al., 2001	Y	Y	PG sig. worse scores compared to HCs (p<.05)	Y	Scores fell within test norms
Cimprich et al., 2004	N			Y	Scores fell within test norms
Fayette et al., 2023	Y	Y	PG Sig. Worse verbal memory and learning, speed of processing/psychomotor speed and abstraction/executive functions	N	
François et al., 2024	N			Y	Scores fell within test norms
Gates et al., 024	Y	Y	PG Sig. worse on average for all neuropsychological tests. (all p≤0.033).)	N	
Hermelink et al., 2007, 2010	N			Y	5 tests showed sig. worse scores than norms 1 test showed sig. better (digit symbol) 31% patients ≥ 2 tests in the lower 5% range. 32% patients had moderate CI
Hermelink et al., 2015, 2017	Y	Y	PGs sig worse behavioural control indices go/no commission and omission errors. All other indices non sig.	Y	PGs Sig. worse on seven indices PGs Better score on three indices All case patients 41.3% prevalence based on the least stringent definition of impairment. 8% based on most stringent.
Hu et al., 2023	Y	Y	PGs Sig. worse verbal fluency PGs Sig worse digit span PGs Sig better Trail making Test (A)	N	
Janelsins et al., 2022	Y	N	No Sig Differences	N	

Study	Patient Group (PG) Comparisons to Healthy Control (HC) Groups Findings			Patient Groups (PG) based on Impairment Criteria or Norms	
	HC Group Y/N	Differences PGs & HCs Y/N	Findings	PGs Test Norms Y/N	Findings
Jung et al., 2022	N			Y	78.2% of patients impaired based on applied criteria. Working memory domain most common.
Juríčková et al., 2023	Y	Y	PGs Sig. worse Auditory Verbal Learning Test PGs Sig. worse Verbal Fluency Test PGs Sig. worse Trail Making Test (A&B)	N	
Kathpalia et al., 2024	Y	Y	PGs Sig worse cognitive function (MoCA) (p<.001) PGs Sig worse MoCA subdomains attention, concentration & calculation, language, memory, conceptual thinking (p=0.001-p<.05)	N	
Lange et al., 2020, Hardy-Leger et al., 2020	Y	Y	PGs Sig worse overall cog impairment and all subdomains attention, EF, WM, Processing speed (p<.001)	Y	CI observed in 28% of patients
Patel et al., 2023, 2015	Y	Y	PGs Sig. worse Executive function, processing speed, verbal memory (p=.02-p<.001) PGs worse attention/concentration p<.05	N	
Scheibel et al., 2004	N			Y	Digit symbol scores fell within norms
Tulk et al., 2021	N			Y	CI observed in 29% of patients
Zhuang et al., 2023	Y	N	No difference between PGs and HCs	N	Scores fell within test cut off

2.3.5.2 Subjective Cognitive Impairment Pretreatment

Seventeen studies explored subjective cognitive impairment at the pretreatment timepoint. Results are summarized below in Table 2.5. For the given subjective measures, a higher score indicates better perceived cognitive function. Impairment was defined as both relative to healthy control groups and using measure scoring criteria. Nine of the 17 studies included a healthy control group (HCs) alongside patient groups (PGs) (Table 2.5). With regards to healthy control groups, 7 of the 9 studies reported worse performance of patient groups compared to healthy controls (Aspelund et al., 2024; Bernstein et al., 2018; Gates et al., 2024; Hermelink et al., 2015; Janelsins et al., 2022; Lange et al., 2020; Lehto, 2013). Nine studies reported scores or levels of perceived impairment for patient groups using predefined criteria or norms. Across these studies reported prevalence for subjective measures ranged from 17.55% (Savard et al., 2023) to 29% (Tulk et al., 2021) (see Table 2.5).

Table 2.5 *Summary of Findings for Pretreatment Subjective Cognitive Impairment*

Study	HC findings			PGs based	
	HC Group Y/N	Differences Y/N	Findings	PG Measure Scores Y/N	Findings
Aspelund et al., 2024	Y	Y	PG Sig. Worse Cog Complaints on PROMIS-CF p<.001	N	
Berstein et al., 2018	Y	Y	PG Sig. Worse FACT-Cog Subscales (unadjusted p<.001-.012)	N	
Cimprich et al., 1999	N			Y	Only 27% of patients in highest interquartile range of AFI
Cimprich et al., 2004	N			Y	25% of PG effective cognitive functioning on AFI 50% moderate cognitive function on AFI 25% lowest level of cognitive function on AFI
De Rosa et al., 2021	N			Y	PGs FACT-Cog Perceived Cog Impairment Subscale High score (61.35/72)
Francois et al, 2024	N			Y	PGs EORTC-CF 86.43/100
Gates et al., 2024	Y	Y	Sig. Effect of Group on FACT-Cog Perceived Cognitive Impairments Impact on QoL	N	
Hardy-Leger et al., 2020, Lange et al., 2020	Y	Y	PGs sig worse scores on FACT-Cog p<0.01	Y	15% of patients reported significant complaints in both Perceived cognitive impairment (PCI)and cognitive abilities domains. 2% in all domains. 24.3% PCI domain only.
Hermelink et al., 2007, 2010	N			Y	PGs EORTC-CF Score 84/100 PGs FEDA Score 89.9/108
Hermelink et al., 2015, 2017	Y	Y	PGs Sig Worse score on FEDA and EORTC-CF PGs Sig Worse score on EORTC-CF Case Matched	N	
Hu et al., 2023	Y	N	No Sig. Differences	N	
Janelsins et al., 2022	Y	Y	PGs sig worse scores on FACT-Cog (p=.01) PGs sig worse scores on self-rated attention (p=01)	N	
Knoerl et al., 2024	N			Y	PGs EORTC-CF Score high (77/100)
Lehto et al., 2013	Y	Y	PGs Worse scores on AFI	N	
Patel et al., 2023	Y	N	No. Sig Differences	N	
Savard et al., 2023	N			Y	PGs 17.55% FACT-Cog Perceived Cognitive Impairment Subscale (<54)
Tulk et al., 2021	N			Y	PGs 29% Prevalence FACT-Cog

2.3.6 Relationships Between Objective and Subjective Cognitive Impairment

Twelve studies included a measure of both objective and subjective cognitive function (see Table 3). Of these, five studies did not directly explore the relationship between objective and subjective measurement (Aspelund et al., 2024; François et al., 2024; Hu et al., 2023; Janelsins et al., 2022; Patel et al., 2023). Objective measures included associations between subjective cognitive impairment and individual tests, specific domains, or composite general cognitive function scores. Overall, seven of the 12 studies reported on associations between objective and subjective measures of cognitive function across nine individual papers (Bernstein et al., 2018; Cimprich et al., 2005; Hardy-Leger et al., 2021; Hermelink et al., 2007; Hermelink et al., 2010; Hermelink et al., 2015; Hermelink et al., 2017; Gates et al., 2024; Tulk et al., 2021).

Two studies found some associations between subjective and objective cognitive function. Bernstein and colleagues (Bernstein et al., 2018) reported that all objective tests other than motor dexterity correlated with "comments from others" and "perceived cognitive abilities" subscales of the Fact-Cog in Supplementary material. Similarly, Hermelink et al. (2015) reported a significant correlation between omission errors in the go/no go cognitive test and scores on self-reported cognitive function measured by the FEDA and EORTC. At one year post chemotherapy, Hermelink et al. (2017), reported in their follow up paper that scores on the FEDA measure of subjective cognitive function correlated significantly with the composite score of cognitive performance.

The remaining five studies reported no associations between objective and subjective measures of cognitive function, either as correlations (Cimprich et al., 2005; Hermelink et al., 2007; Gates et al., 2024), as a function of change across time (Hermelink et al., 2010; Tulk et al., 2021), or in multivariate analysis (Lange et al., 2020). Interestingly, a paper by Hardy-Leger et al. (2021), conducted a sub analysis on the same data set as Lange et al. (2020) by grouping patients based on degree of subjective cognitive complaints, ranging from "no complaints" to "consistent complaints" across five groups. They found that the no complaints group performed significantly better in executive function tasks than the significant complaints groups.

2.3.7 Relationship between cognition and psychological variables

Nineteen studies explored the relationship between anxiety and/ or depression and cognitive function (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich, 1999; Cimprich and Ronis, 2001; Cimprich et al., 2005; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2007; Hermelink et al., 2015; Janelsins et al., 2022; Jung et al., 2022; Juríčková et al., 2023; Knoerl et al., 2024; Lange et al., 2020; Lehto, 2013; Patel et al., 2015; Savard et al., 2023; Scheibel, 2004; Tulk et al., 2021). Thirteen studies included both anxiety and depression (Aspelund et al., 2024; Bernstein et al., 2018; Cimprich, 1999; Cimprich et al., 2005; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2007; Janelsins et al., 2022; Juríčková et al., 2023; Knoerl et al., 2024; Lange et al., 2020; Savard et al., 2023; Tulk et al., 2021).

2.3.7.1 Anxiety

Eleven studies reported on the relationship between objective cognitive function and anxiety (Table 2.6). Of these, eight studies reported no relationship between anxiety and objective cognitive function (Aspelund et al., 2024; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2015; Juríčková et al., 2023; Lange et al., 2020; Patel et al., 2015; Tulk et al., 2021). Three studies reported significant associations between at least one objective cognitive test and measures of anxiety (Bernstein et al., 2018; Cimprich et al., 2005; Janelsins et al., 2022). Based on reported domains (Table 2.3), represented domains included capacity to direct attention (Cimprich et al., 2005), attention and concentration, processing speed, motor dexterity (Bernstein et al., 2018), memory, and executive function (Janelsins et al., 2022). In most cases, the relationships indicated that increased anxiety was associated with increased subjective cognitive impairment and decreased objective cognitive performance, except for one objective (Cimprich et al., 2005) report. Ten studies reported on the relationship between anxiety and subjective cognitive function (Table 2.6). Of these, two studies (Aspelund et al., 2024; Lange et al., 2020) reported a non-significant relationship between self-reported cognitive impairment and anxiety, with eight of ten studies reporting a significant relationship. Relationships are summarized in Table 2.6 below.

Table 2.6 *Summary of Relationships Between Anxiety and Cognitive Impairment*

	Objective Cognitive Impairment			Subjective Cognitive Impairment	
Study	**Analysis**	**Significant Relationship Y/N**	**Findings**	**Significant Relationship Y/N**	**Findings**
Aspelund et al., 2024	Regression	N	No relationship between objective tests and Anxiety	N	No Sig. relationship between subjective cognitive impairment and Anxiety
Bernstein et al., 2018	Correlations	Y	Sig. Inverse correlation between motor dexterity, processing speed and concentration with HADS Anxiety Scores	Y	Sig. Inverse correlation between FACT-Cog Subscales and HADS Anxiety *. Sig correlation with overall FACT Total score.
Cimprich et al., 1999	Correlation			Y	Sig. Inverse correlation between AFI scores and Anxiety (Total Mood Disturbance)
Cimprich et al., 2004	Correlations &Regression	Y	Sig. small inverse correlations between digit span backwards test and trail making test B and POMS-SF. Increased scores on anxiety subscale were correlated with increased test performance.	Y	Anxiety sig predictor of level of perceived cognitive effectiveness. Sig strong relationship between POMS-SF scores and AFI subscales.
Fayette et al., 2023	Regression	N	No relationship between objective tests and Anxiety		
Gates et al., 2024		N	No relationship between objective tests and Anxiety		
Lange et al., 2020	Multivariate Logistic Regression	N	No relationship between objective tests and Anxiety	N	No Sig. relationship between subjective cognitive impairment and Anxiety
Lehto et al., 2013	Correlations (non-parametric)			Y	Preoperatively Sig. association between increased worry and subjective CI.
Hermelink et al., 2007, 2010	Correlations	N	No relationship between objective tests and Anxiety	Y	Pre and Post treatment, inverse Sig. correlations between subjective CI and Anxiety.
Janelsins et al., 2022	Mixed Linear Models	Y	Baseline anxiety is associated with worse performance on some cognitive tests. Including rapid visual processing, category fluency and immediate recall*.	Y	Higher Baseline anxiety sig. associated with PCI *
Juríčková et al., 2023	Correlation	N	No relationship between objective tests and Anxiety		
Knoerl et al., 2024	Correlations & Regression			Y	At diagnosis sig. inverse correlation between baseline cognitive function and Anxiety.

	Objective Cognitive Impairment			Subjective Cognitive Impairment	
Study	**Analysis**	**Significant Relationship Y/N**	**Findings**	**Significant Relationship Y/N**	**Findings**
Patel et al., 2015	Multivariable Linear Regression	N	No relationship between objective measures and Anxiety		
Tulk et al., 2021	Correlation & HMR	N	No relationship between objective measures and Anxiety	Y	Deterioration of PCI during 12m follow-up sig. associated with increased Anxiety.

Note *=Included in paper as Supplementary Information

2.3.7.2 Depression

Fourteen studies measured the relationship between levels of depression and objective cognitive impairment (Table 2.7). Of these, nine studies reported no relationship between depression and objective cognitive function (Aspelund et al., 2024; Cimprich and Ronis, 2001; Cimprich et al., 2005; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2007; Hermelink et al., 2015; Lange et al., 2020; Tulk et al., 2021). Five studies reported a relationship between at least one objective cognitive test and levels of depression (Bernstein et al., 2018; Janelsins et al., 2022; Jung et al., 2022; Juríčková et al., 2023; Scheibel, 2004). Within these, based on reported domains (Table 2.3), affected cognitive domains included motor dexterity, verbal memory, visual memory, concentration (Bernstein et al., 2018), executive function (Bernstein et al., 2018; Janelsins et al., 2022), memory (Janelsins et al., 2022), processing speed (Janelsins et al., 2022; Juríčková et al., 2023) and visual motor and sequencing skills (Scheibel, 2004). In all cases, depression was inversely related to cognitive performance. Eleven studies measured the relationship between depression and subjective cognitive impairment. Four studies reported no significant relationship (Knoerl et al., 2024; Lange et al., 2020; Savard et al., 2023; Tulk et al., 2021). The remaining seven studies reported some associations between depression and subjective cognitive impairment, relationships were inverse except for Bernstein and colleagues (Bernstein et al., 2018), who found a positive relationship between depression and two FACT-Cog subscales (Table 2.7). Results are summarized below in Table 2.7.

Table 2.7 *Summary of Relationships Between Depression and Cognitive Impairment*

	Objective Cognitive Impairment			Subjective Cognitive Impairment	
Study	**Analysis**	**Significant Relationship Y/N**	**Findings**	**Significant Relationship Y/N**	**Findings**
Aspelund et al., 2024	Regression	N	No relationship between objective tests and Depression	Y	Depression was a Sig. predictor of cognitive complaints (p=0.01)
Bernstein et al., 2018	Correlations	Y	Sig. Inverse correlation between motor dexterity, verbal memory, Visual memory, processing speed, concentration, executive function,	Y	Depression mixed correlations with FACT-Cog subscales. Positive correlation with PCI subscale and overall score. Negative PCA, CFO and IQL subscales.*
Cimprich et al., 1999	Correlation			Y	Sig. Inverse correlation between AFI scores and (Total Mood Disturbance)
Cimprich et al., 2001	Correlation & Multiple Regression	N	No relationship between objective tests and Depression		
Cimprich et al., 2004	Correlations &Regression	N	No relationship between objective tests and Depression	Y	Depression sig predictor of level of perceived cognitive effectiveness. Sig strong relationship between POMS-SF scores and AFI subscales.
Fayette et al., 2023	Regression	N	No relationship between objective tests and Depression		
Gates et al., 2024		N	No relationship between objective tests and Depression		
Lange et al., 2020	Multivariate Logistic Regression	N	No relationship between objective tests and Depression.	N	No Sig. relationship between subjective cognitive impairment and Depression
Hermelink et al., 2007, 2010	Correlations	N	No relationship between objective tests and Depression	Y	Sig. Inverse relationship between Depression and FEDA and EORTC-CF. Depression sig. predictor of subjective cognition (FEDA & EORTC-CF).
Hermelink et al., 2015, 2017	Multivariable linear regression	N	No relationship between objective tests and Depression	Y	Sig. Association of Depression on scores on self-report measures (EORTC-CF, FEDA)
Janelsins et al., 2022	Mixed Linear Models	Y	Baseline depression associated with worse performance on some cognitive tests. Including Hopkins verbal learning test and Trail making test*.	Y	Higher Baseline depression sig. associated with PCI*

	Objective Cognitive Impairment			Subjective Cognitive Impairment	
Study	**Analysis**	**Significant Relationship Y/N**	**Findings**	**Significant Relationship Y/N**	**Findings**
Jung et al., 2022	Regression	Y	Sig. association between lower total cognitive function and Depression.		
Juríčková et al., 2023	Correlation	Y	Depression sig. inverse correlation with speed of processing/psychomotor speed.		
Knoerl et al., 2024	Correlations & Regression			N	No/Weak relationship between depression and EORTC-CF scores.
Savard et al., 2023	Repeated Measures LMM			N	No relationship between depression and FACT-Cog scores.
Scheibel et al., 2004	Correlations and Analysis of Variance	Y	Changes on the MMPI-D scale were related to change in scores from the TMT-B. But other correlations were not sig.		
Tulk et al., 2021	Correlation & HMR	N	No relationship between objective measures and Depression	N	No relationship between Depression and Subjective cognitive impairment. (FACT-Cog)

Note *=Included in paper as Supplementary Information

2.3.8 Changes in Cognitive Impairment Across Time

Sixteen studies included multiple timepoints (Table 2.8). Seven studies had two assessment timepoints (De Rosa et al., 2021; Gates et al., 2024; Knoerl et al., 2024; Lehto, 2013; Scheibel, 2004; Tulk et al., 2021; Zhuang et al., 2023). Nine studies had 3 or more assessment time points (Cimprich and Ronis, 2001; Fayette et al., 2023; François et al., 2024; Hermelink et al., 2010; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Patel et al., 2023; Savard et al., 2023). For most studies, assessments included a baseline pretreatment assessment followed by a one or more post or during treatment follow up. One study (Knoerl et al., 2024) conducted two assessments one prior to study randomization and the final prior to surgery and did not explore changes in cognitive function over time. Nine studies assessed changes in cognitive impairment or function over time in relation to healthy control groups (Cimprich and Ronis, 2001; Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2017; Hu et al., 2023; Janelsins et al., 2022; Lehto, 2013; Patel et al., 2023; Zhuang et al., 2023). Eight studies reported that between first and final assessments, changes were observed in objective cognitive function (Fayette et al., 2023; Gates et al., 2024; Hermelink et al., 2007; Hermelink et al., 2017; Janelsins et al., 2022; Scheibel, 2004; Tulk et al., 2021; Zhuang et al., 2023). Eleven studies assessed changes in subjective cognitive function over time (Table 8). Of these, seven studies reported changes in subjective cognitive function overtime (De Rosa et al., 2021; Gates et al., 2024; Hermelink et al., 2010; Hu et al., 2023; Janelsins et al., 2022; Savard et al., 2023; Tulk et al., 2021). The majority of studies reported declines in subjective cognition across timepoints or in some cases no changes. For objective cognitive function, results were mixed, given the variation in timepoints and assessment measures. Results are summarized below in Table 2.8.

Table 2.8 *Summary of Changes in Cognition*

Study Details				Objective Cognitive Impairment		Subjective Cognitive Impairment	
Study	**HCs Y/N**	**Timepoints**	**Timepoint Details**	**Change in Cognition Overtime**	**Findings**	**Change in Cognition Overtime**	**Findings**
Cimprich et al., 2001	Y	3	1. Before Surgery 2. Approx. 2 Weeks post-surgery 3. Approx. 3 months post-surgery	N	Non. Sig trend of change over time for total attention scores. The mean TAS score at T3 was sig. improved compared to T1 (p=0.16) For the patient group, there was a significant group x time interaction (p=.005) breast cancer group gradual gain in Total Attention Score cognitive function overtime.		
De Rosa et al., 2021	N	2	1. Before starting surgical and or medical treatment 2. 6 months from the end of therapy			Y	Sig. reduction in PCI scores from T1-T2 (p<.0.05).
Fayette et al., 2023	Y	3	1. Prior to treatment 2. Promptly after treatment 3. 12 months after baseline assessment	Y	Sig. Group differences pre and post chemotherapy. Deficits also persisted at third assessment verbal memory and learning, and abstraction/executive function. Sig improvement across both groups between 1-3 timepoints across some cognitive domains but still remained less than HCs.		
François et al., 2024	N	5	1. Inclusion 2. Prior to surgery 3. 3 months post 4. 6 months post 5 .12 months post	N	No. sig differences in MMSE scores across any timepoints.	N	No sig improvements at a patient level overtime. Some between group differences sig. at 3M Overall gradual EORTC non. Sig improvement.
Gates et al., 2024	Y	2	1. Treatment naive baseline assessment 2. 6-8 weeks post treatment assessment	Y	Fixed effect for time for HVLT-R (p<.001) and Delayed recall (p=0.046) with sig. improvements post treatment for patients.	Y	Patients perceived cognitive impairment and perceived cognitive abilities were worse at follow up compared to baseline (p=0.004).

Hermelink et al., 2007, 2010	N	3	1. Before the start of preoperative chemotherapy (T1) 2. Before the last chemotherapy cycle (approx. 5m later) (T2) 3. Approx 1 year after baseline (T3)	Y	At T2 MANOVA sig. overall improvement in tests (p<.001). Cognitive decline observed in 27% of patients and improvement in 28% of patients.	Y	Significant increase in cog problems from T1-T2, significant increase in cognitive problems for both FEDA and EORTC-CF (Both p<.001), partial recovery at T3.
Hermelink et al., 2017	Y	3	1. Prior to primary surgery or neoadjuvant chemotherapy 2. A min of one week after completion of chemotherapy 3. One year after T1	Y	Decline in total cognitive indices scores in both patient groups relative to controls (p=.04). Steady improvement was observed in the sample as a whole.		
Hu et al., 2023	Y	3	1. Before neoadjuvant chemotherapy 2. Before the second cycle of neoadjuvant chemotherapy 3. Completion of neoadjuvant chemotherapy	N	No sig changes in neuropsychological test scores.	Y	Compared with prior to neoadjuvant chemotherapy, the scores on the FACT-Cog declined significantly at assessment 1 and 2, and scores on the PCA subscale declined at assessment 2 (p<.05).
Janelsins et al., 2022	Y	3	1. T1 Prechemotherapy -within 7 days prior to the first chemo 2.A2 post chemotherapy within 1 month of the last chemo administration 3.A3 6-month follow-up from A2	Y	Between the first and third assessment, patients' performance was worse than controls and showed less improvement over time. Across multiple tests.	Y	Across time patients reported more cognitive complaints compared with controls including attention difficulty (P=.01) and perceived cognitive impairment (p<.05).
Knoerl et al., 2024	N	2	1. Prior to randomization 2.Prior to Surgery			N/A	Secondary analysis, did not explore change in cognition, only in relation to anxiety levels.
Letho et al., 2013	Y	2	1. Time of treatment planning following diagnosis 2. 3-4 weeks after surgical resection			N	Between timepoints, malignancy group did not drop significantly in cognitive effectiveness on the AFI.
Patel et al., 2023	Y	4	1. Baseline before any systemic or local treatment 2. Approx one month after completion of their primary cancer treatment. 3. 1 year after treatment completion	N	Objective test scores were unchanged from baseline in patients but showed modest improvement in controls.	N	Levels of subjective cognitive function from baseline were unchanged for patient groups. Controls showed modest improvement.

			4. 2 years after treatment completion				
Scheibel et al., 2004	N	2	1. Baseline 2. On - treatment	Y	Main effect of time for digit symbol ($p<0.027$) (although will within normative) CLTR effect of time $p<0.021$) TMT-B effect of time ($p<0.009$), Declines on treatment.		
Savard et al., 2023	N	5	1. Baseline 2. 3 months post 3. 6m post 4. 9 months 5. 12 months			Y	Sig, reductions in Fact-Cog Impact scores overtime ($p<.001$)
Tulk et al., 2021	N	2	1. Before beginning prostate cancer treatment (baseline) 2. 12 months following first evaluation	Y	Patients had sig. declines over first year of treatment when compared with group with no cognitive function issues at baseline.	Y	29% of patients demonstrated sig. declines in subjective cognition during first year of treatment.
Zhuang et al., 2023	Y	2	1. T0 before neoadjuvant treatment or surgery 2. T1 one week after completing chemotherapy (approx. 5-6 months post)	Y	Sig. lower performance in the LTT and WDT tests post chemotherapy ($p=.002$, $p=.003$) for patients.		

2.4 Discussion

To our knowledge, this is the first review to synthesize levels of pretreatment subjective and objective cancer related cognitive impairment, across multiple cancer types and treatments and its relationship with both anxiety and depression. Secondary objectives included investigating associations between objectively measured and subjectively reported cognitive issues. Finally, longitudinal changes across time into the postoperative period were explored. Pretreatment CRCI was evident across studies, particularly subjective CRCI, and inclusion of healthy control groups allowed for better interpretation of CRCI levels. Objective pretreatment CRCI ranged from 13.8% (Aspelund et al., 2024) to 78.2% (Jung et al., 2022) within studies, while subjective CRCI ranged from 17.55% (Savard et al., 2023) to 29% (Tulk et al., 2021). Support was also found for a relationship between psychological variables and subjective cognitive function, particularly with regards to anxiety. Heterogeneity across study designs prevented further analysis of the trajectory of change in cognition across time from pre to post treatment.

2.4.1 Heterogeneity and Variance

Heterogeneity and variance were aspects of both study characteristics and outcomes of interest within this review. The heterogeneity in subjective measures of cognitive impairment used presents some difficulty in interpretation given the differences between common assessment tools. As reviewed by the Cancer Neuroscience Initiative Working group in 2021 (Henneghan et al., 2021), the EORTC-CF, which was used in 6 papers, consists of only 2 items, and may not be adequate to fully capture the complex nature of CRCI assessment, as opposed to the FACT-Cog which consists of 37 items and 4 subscales, and was used in 9 papers. Although single item measures can report cognitive change among cancer patients during chemotherapy (Onyedibe et al., 2025), levels of subjective CRCI may be over or underreported when relying on a shorter measure. Variance was also noted in the objective cognitive assessments used, but in general, studies were consistent in investigating common domains such as attention, memory and executive function. This is possibly a consequence of the International Cancer and Cognition Task Force, which recommended in 2011 specific cognitive tests and domains of interest to standardize

objective CRCI research (Wefel et al., 2011). Notably, the three primary tests they recommended were all represented in the most commonly used tests within the current review, including the most used test, the trail-making test. This indicates that objective CRCI research is largely adhering to a standardized approach to assessing recommended domains which will allow for increased comparison across studies as the evidence base grows.

2.4.2 Pretreatment CRCI

The review findings indicate that levels of pretreatment CRCI remain a complex topic, and that more targeted research at the pretreatment timepoint is required to fully understand levels of CRCI pretreatment. Research is needed to further establish pretreatment CRCI causes and associations within research, across cancer types beyond breast, to understand why it can occur. Compared to Hutterer and Oberndorfer's (2021) review paper exploring CRCI prevalence across timepoints, levels of subjective CRCI pretreatment observed in this review were comparable to that observed prechemotherapy only. In contrast, levels of objective CRCI observed were higher. As this review focused on pre any treatment or surgery, these comparisons shed light on the possible existence of pretreatment CRCI from diagnosis or prior any surgery or treatment. This review further builds on this research by observing largely similar levels of CRCI prior to both chemotherapy and surgery. It also highlights the importance of understanding pretreatment CRCI at a cancer specific level and identifying potentially at-risk cohorts. The study that recorded the highest level of pretreatment objective impairment (Jung et al., 2022), pertained to newly diagnosed patients with thyroid cancer. As we know that hormonal treatment effects have been explored in CRCI modelling as impacting on function (Hutterer and Oberndorfer, 2021), there is an increased need to investigate pretreatment CRCI in cancers that may be more susceptible to pretreatment CRCI.

Compared to healthy control groups, increased subjective and objective impairment was evident pretreatment. Objective function was more varied, including instances of increased performance of patient groups relative to healthy controls in some cases. These findings speak to the importance of including a healthy control

group for test comparison as they can provide insight beyond standardized test or population norms, which may not capture the mild to moderate CRCI experience.

2.4.3 Relationship Between Objective and Subjective CRCI

With regard to the relationships between objective and subjective cognitive impairment, only seven studies directly reported on this relationship. Of these, only two reported any association between objective test performance and self-reported subjective cognitive function. This lack of research was notable, as the relationship between self-reported cognitive impairment, and objective cognitive performance is a keen area of interest within CRCI research (Ahles and Hurria, 2018). A lack of association between objective and subjective CRCI has been previously noted within the literature (Fardell et al., 2022; Hutchinson et al., 2012), potentially due to insufficient sensitivity of neuropsychological tests for CRCI, or associations between subjective CRCI and other psychological factors (Ahles and Hurria, 2018; Zhang et al., 2025). Differences in assessment administration, assessment timeframes and the misattribution of cognitive difficulties when applying self-report tools could help further explain these discrepancies (Hutchinson et al., 2012). As patients with cancer can have high indices of anxiety and depression, emotional state during test or self-report administration may also be impacting both test scores and perceived impairment (Hutchinson et al., 2012; Zhang et al., 2025). More research investigating the relationships between objective and subjective CRCI will aid in our understanding of CRCI experiences, its association with other variables like psychological wellbeing, and how to help patients experiencing these issues. Other areas of research such as cognitive aging could give us more insight into the temporal relationships between objective and subjective cognitive function (Snitz et al., 2015) and inform future research.

2.4.4 CRCI and Psychological Variables

It was clear from results that anxiety and depression had some association with CRCI, suggesting that CRCI could be associated with increased anxiety and depression, however the nature of these relationships varied across both psychological and cognitive variables. Little support was found for a relationship between anxiety and

objective cognitive function. In contrast, only two of ten studies that assessed anxiety and subjective cognitive function reported no relationship. These findings speak to the complex nature of CRCI, and the potential psychological underpinnings. Pretreatment subjective cognitive experience may better align conceptually with the overall psychological burden of cancer diagnosis, as factors like pretreatment worry and anxiety could possibly influence perception of cognition, as both experience of anxiety and perception of cognition are recorded using self-report measures and as such are influenced by the patient's own perceptual experiences. This idea has previously been explored in recent models like Oppegaard and colleagues (Oppegaard, 2023a) multifactorial model of CRCI. When this model was evaluated within cancer patients during treatment, they found that co-occurring symptoms like state anxiety produced the largest variance in subjective cognitive function (Oppegaard et al., 2023b). Results also reflect other conceptual CRCI frameworks, by highlighting associations between CRCI and psychological variables. Some models suggest that sociodemographic and psychological factors may act alongside treatment related factors to increase likelihood of post treatment cognitive impairment (Ahles and Hurria, 2018). The present review provides further insight into the complexity of these interactions, observing the presence of relationships between psychological variables and CRCI, prior to an interaction with treatment related effects. Results related to depression were more mixed. Compared to anxiety, more support was found for relationships between subjective cognitive impairment and depression compared to objective cognitive function with seven of 11 studies reporting a significant association. Findings indicate overall that subjective cognitive impairments are associated with psychological factors like anxiety and depression more than objective measures. This review extends prior work exploring psychological variables and CRCI through breast cancer (Yang and Hendrix, 2018), by expanding across cancer types, also suggesting an influence of psychological variables on CRCI. Understanding these relationships is critical for the future of CRCI treatment intervention providing individualized patient psychological support.

2.4.5 Changes Across Time

Changes in cognition across time were explored in studies with multiple assessment timepoints. However, conclusions that could be drawn were limited due to

heterogeneity across both number of assessment timepoints and duration of assessment periods. Results of objective change were varied and included both improvements and declines in performance across timepoints. For subjective CRCI, results were more consistent and indicated overall increases in subjective cognitive impairment over time. Standardization of assessment timepoints and inclusion of a core set of patient reported outcomes like psychological wellbeing when investigating CRCI could help to elucidate the long-term relationships between cognitive change and associated variables. This will in turn aid in the creation of appropriate long-term treatment and support for survivors.

2.4.6 Limitations and Future Directions

There are some limitations of the present review. Searches were limited to those only published in English. Many of the studies also employed convenience sampling through specific clinics and hospitals, limiting generalizability. Furthermore, the majority of papers excluded patients based on presence of metastasis, CNS involvement, prior history of cancer or treatment, or included specific cancer/tumour stages. This was important to ascertain given the focus of the present review on pretreatment cognitive impairment, as presence of a historical cancer diagnosis or treatment makes it difficult to fully extrapolate whether baseline CRCI levels reported are a true reflection of pretreatment CRCI. Although inclusion criteria were not based on cancer type, 40% of included studies pertained to breast cancer cohorts, where the age at diagnosis is typically around the fifties (Hendrick et al., 2021). The representation of breast cancer within this review is reflective of the current state of CRCI literature, which traditionally focused on breast cancer patients and chemotherapy induced changes (Ahles and Hurria, 2018; Ahles and Saykin, 2007).

Insights from this review can help to inform future CRCI research. CRCI research would benefit from increased rigor when applying objective and subjective cognitive measures and patient reported outcomes to allow for more nuanced comparisons and analysis within this research landscape. By increasing standardization of measures this will allow for increased comparison across studies. Although patterns and common neuropsychological tests emerged, there was still a large volume of different tests applied across studies (Table 3). Also of note was the marked contrast in

terms of item count between longer measures like the FACT-Cog, and shorter measures such as the EORTC-CF scale (Henneghan et al., 2021). By standardizing common objective and subjective tools, as well as recording psychological wellbeing as standard, this will allow for a fuller picture of the relationship between CRCI and psychological variables. Insight can also be gained from work conducted around cognitive perception during aging (Snitz et al., 2015). On multiple occasions, the presence of a healthy control group allowed for a richer interpretation of research findings and shed light on the complexity of CRCI research. Where possible, including healthy control groups will provide increased insight and the opportunity to elucidate how CRCI may present. Inclusion of both baseline testing timepoints, and detail of prior and current treatment history will allow for increased rigor when investigating pretreatment CRCI. Increasing standardization across time points within longitudinal research will also provide the opportunity for generalizability, comparison across studies, and a holistic interpretation of CRCI from diagnosis to survivorship. By assessing cognitive impairment as early as possible, we can learn more about its trajectory and the interaction with treatment effects, including not only chemotherapy or radiotherapy, but also surgical effects like anaesthesia exposure, particularly in elderly populations (Sun et al., 2019). We can also learn more about potential prehabilitative or rehabilitative interventions to target CRCI and psychological wellbeing (Levett and Grimmett, 2019; Scriney et al., 2022). Review findings suggested that there may be a relationship between psychological variables and subjective cognitive impairment so efforts should be made to assess both in future CRCI research. Potential future research could also focus on addressing both subjective CRCI experience, and psychological difficulties through targeted interventions.

2.5 Conclusion

This review explored pretreatment CRCI and its association with psychological variables across cancer types and treatments. Pretreatment CRCI ranges indicated 13.8% (Aspelund et al., 2024) to 78.2% (Jung et al., 2022) within objective studies, while subjective CRCI ranged from 17.55% (Savard et al., 2023) to 29% (Tulk et al., 2021). Some support was found for associations between subjective cognitive function and psychological variables, in particular anxiety. Associations between psychological

variables and objective CRCI were largely inconsistent. Findings indicated weak associations between objective and subjective measures of cognitive function at diagnosis. Variation in study design prevented further analysis of trajectory of change, but some declines in subjective cognitive function were observed. This review highlighted the heterogeneity that currently exists in the CRCI landscape, and that increased standardization would benefit future research. Understanding more about pretreatment CRCI, and its relationship with psychological variables will benefit clinicians and other allied health professionals when caring for patients and will also provide further insights for the application of pre and rehabilitation care. This review highlights the complex relationship between cognitive function and psychological wellbeing and the need to further understand this relationship to ultimately enhance patient wellbeing and pre and postoperative cognitive care.

Chapter 3 The Impact of Prehabilitation Interventions on Affective and Functional Outcomes for Young to Midlife Adult Cancer Patients: A Systematic Review

An edited version of the review has been previously published in the Wiley Journal of Psycho-oncology.

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3.1 Introduction

Cancer is one of the most prevalent global health crises, with 19 million new cases reported in 2022 (Ferlay et al., 2024). Improvements to cancer prevention preventative treatment are at the forefront of policy and research on national (Department of Health, 2017) and international (Cormie et al., 2018, European Commission, 2020) levels. Experience of cancer can also result in many physical and psychological burdens for patients, including persistent psychological distress like anxiety and depression (Stein et al., 2008). Within cancer, specific treatment related factors and stress can also contribute to psychological distress during recovery (Ikhile et al., 2024). Prehabilitation is based on the principle of pre-emptive preparation of patients to reduce treatment related side effects and enhance recovery by optimizing physical and psychological status. It occurs during the period between diagnosis and acute treatment, and includes interventions such as exercise, nutrition and psychological intervention (Coca-Martinez & Carli, 2024). Prehabilitation interventions can be unimodal, whereby one intervention is employed or bi- or multi-modal which uses combinations of interventions (Bausys et al., 2022). For the purpose of this review, we have categorised lifestyle prehabilitation as proposed by the Macmillan Cancer Support model (Macmillan Cancer Support, 2020), including exercise, nutrition and psychological support/interventions as key pillars of treatment (Macmillan Cancer Support, 2020, 2025).

Exercise prehabilitation is the use of exercise to increase cardiorespiratory strength and reduces postoperative complications and optimises recovery by supporting physiological reserves and reducing loss of muscle (Coca-Martinez & Carli, 2024). A combination of aerobic and resistance training can potentially positively impact a wide range of cancer-related side effects such as physical function, anxiety, depression, as well as psychological outcomes and overall health-related quality of life (HrQoL) (Campbell et al., 2019). Patients who exercise frequently post-diagnosis have lower mortality rates, fewer rates of recurrence and less severe side effects (Cormie et al., 2017). Qualitative evidence suggests that patients support aerobic exercise prehabilitation as a means of preparation both physically and emotionally for surgery (Banerjee et al., 2021).

Nutritional prehabilitation, the optimization of nutrient and metabolic stores to compensate for malnutrition and deficiencies is common during invasive cancer treatment or surgery (West et al., 2017). Malnutrition for cancer patients can be as a result of reduced food intake and metabolic derangements that can be induced by the cancer or tumour itself (Arends et al., 2017). The use of nutritional support improves nutritional status before cancer surgery (Macmillan et al., 2020) decreases mortality and increases functional outcomes across cancer types (Bargetzi et al., 2021). Currently, more work is required regarding this intervention due to heterogeneity across studies that report nutritional prehabilitation interventions and associated nutritional assessment (Gillis et al., 2021).

Psychological prehabilitation includes counselling, psychotherapies or other therapeutic approaches (Hall et al., 2025). This intervention is used to counter the adverse affective impacts of treatment which are common for patients which can include anxiety and depression (Fradelos et al., 2017), issues self-efficacy to manage psychological symptoms (Marinelli et al., 2022) and the experiencing fatigue (Fortmann et al., 2018). Evidence suggests that even short forms of psychological interventions are effective at reducing depression and fatigue post-surgery, compared to care as usual (Grassen et al., 2013). Evidence suggests that the combination of two or more interventions, either bimodal or multimodal prehabilitation, increases efficacy (Luther et al., 2018). The psychological benefits of prehabilitation are a keen area of emerging research and how they may increase quality of life (Silver et al., 2013). Reported benefits of psychological prehabilitation can include increased resilience

against anxiety and depression (Li et al., 2017, Tsimopoulou et al., 2015). Exercise prehabilitation can also improve psychological outcomes like HrQoL (Ngo-Huang et al., 2019). The psychological impact of prehabilitation is important to ascertain further. For example, research with colorectal cancer patients has shown that depression can be associated with functional status, and that these patients may benefit most from prehabilitation approaches (Barrett-Berstein et al., 2019). In addition to research showing how psychological prehabilitation improves psychological outcomes (Tsimopoulou et al., 2015), there is also a body of research demonstrating the potential positive impacts exercise and nutrition prehabilitation also has on psychological wellbeing. Research by Mishra and colleagues (2012,2015), suggested that exercise prehabilitation can improve emotional wellbeing and HrQoL. Other prehabilitation research highlights the impact of exercise prehabilitation on symptoms like anxiety and depression and potential interactions with other patient reported outcomes like cognitive function (Knoerl et al., 2022). With regards to psychological prehabilitation, more research is required to further standardise and understand the efficacy of preoperative psychological approaches including type of intervention, and the direct effects of psychological interventions when multimodal approaches are applied (Levett & Grimmett, 2019).

The aim of this systematic review is to assess the impact of prehabilitation interventions on functional and psychological outcomes in young to midlife adult age range. To date, reviews include either older (Bruns et al., 2016, Daniels et al., 2021, Looijaard et al., 2018) or younger age groups (Ospina et al., 2022, Zhi et al., 2019). In addition, a recent umbrella review of 55 systematic reviews of prehabilitation for surgery including cancer reported a mean age of 61 years (McIsaac et al., 2022). Similarly, a more recent review of prehabilitation intervention efficacy also reported a mean age of 62 years across 186 unique randomised control trials (McIsaac et al., 2024). The present review will specifically address age- related gaps in the existing evidence by focussing on the young to midlife adult age range of 18–55 years. Young adult cancer patients have been defined as up to the age of 39 (National Cancer Institute, 2015). However, research indicates that midlife is a period where the prevalence of multiple risk factors is high, and it is at this point when the prevalence of cancer increases for many cancer types (White et al., 2014). The present review also builds on the existing literature by focussing on both functional and affective outcomes.

Functional outcomes are those which measure a patient's functional capacity or ability to take part in daily activity. Affective outcomes, defined in the present review as those that include a measure of anxiety, depression, stress or HrQoL, have been explored within prehabilitation literature when referring to psychological interventions, (Tsimopoulou et al., 2015). However, for other types of prehabilitation they are rarely the focus in favour of post-operative and functional outcomes such as walk tests (Campbell et al., 2019, Waterland et al., 2021). This currently leads to a lack of evidence currently to support psychological based interventions due to mixed efficacy and heterogeneity (Levett et al., 2019).

The aim of this review is to provide an overview of the literature regarding prehabilitation interventions for young to midlife adults (18-55 years). The review will also assess the degree to which they have both direct and indirect effects on functional and affective outcomes that are important for quality of life. This will address the following question within the PhD research project:

b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.

3.2 Methods

The present systematic review was reported and conducted in line with the preferred reporting for systematic reviews and meta- analyses (PRISMA) statements.

3.2.1. Search Strategy

A systematic review of literature relating to prehabilitation for cancer treatment was conducted between 31 January 2021 and October 2021. Five relevant databases were identified for inclusion: Psychological Information database (PsychINFO), Medical Literature Analysis and Retrieval System Online (MEDLINE), Cumulated Index to Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE) and Public MEDLINE (PubMed). Search terms were chosen based on relevance and previous literature: 1. Cancer related terms 2. Prehabilitation related

terms 3. Intervention related terms and 4. Lifestyle related terms. Searches were limited to peer reviewed articles, published in English and conducted on human participants. Figure 3.1 below represents the PRISMA screening strategy.

3.2.2. Inclusion Criteria

Studies were included if they involved a prehabilitation intervention that began any time before the patient's treatment occurred, and the mean age of participants was ≤55 years. Full inclusion and exclusion criteria are displayed in Table 3.1 below.

Table 3.1

Exclusion and Inclusion Criteria

Inclusion Criteria	Exclusion Criteria
Cancer of any type or stage	Wrong Disease Type
The mean age of total participants within a study of between 18-55 years	Child, adolescent or Geriatric Focus
Peer reviewed journal articles	Not current research- Study Protocol or Review Article
Prehabilitation	Not prehabilitation – no pre-treatment or surgery intervention
	Artificial Nutritional Support
Affective and/or Functional outcome measures	No relevant outcome measures
Published in English	Not available in English

3.2.3 Screening Process

A two-stage screening process was employed using Covidence. Abstract and full text screening included a secondary reviewer. All conflicts were addressed in partnership with the second reviewer.

3.2.4 Quality Assessment

Articles were assessed for quality using a checklist based on previous literature (Dunne et al., 2015, Jefferies et al., 2012). The checklist contained 12 items relating to the quality of methodological, statistical and clarity of design and reporting of results.

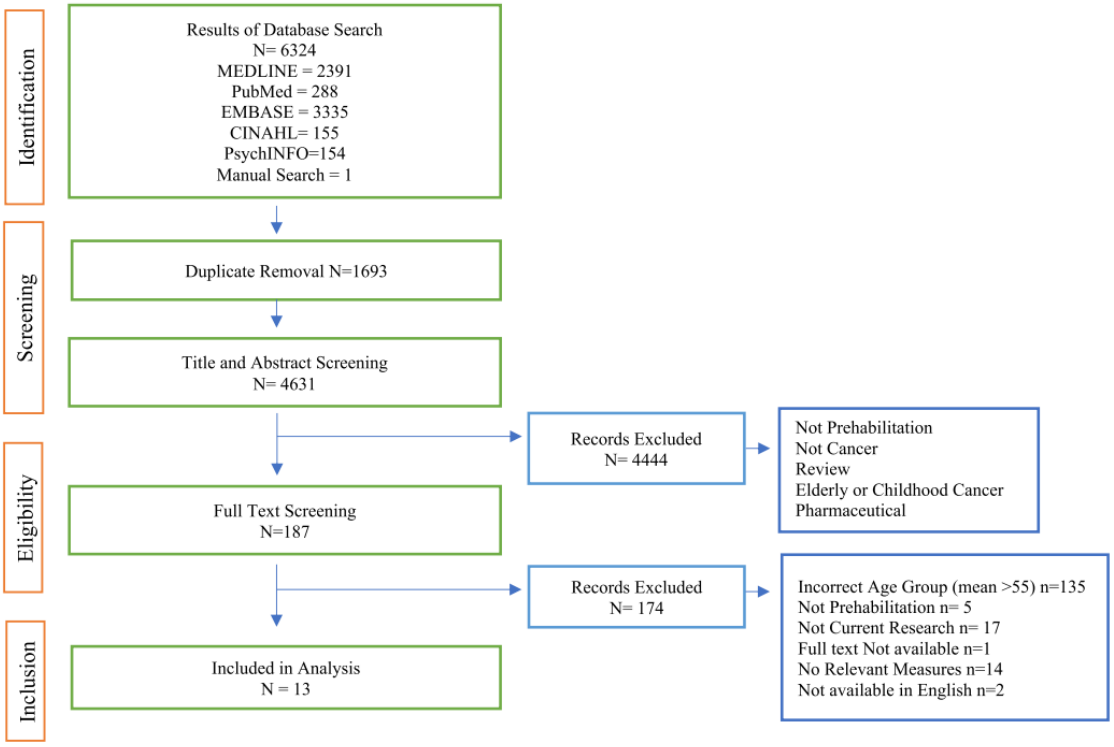
The Checklist scores articles in a range of 0–2. Scores of two indicated a “yes” response, scores of one indicated a “partial” response and scores of 0 indicated a “no” or “don't know” response. A higher score indicates a higher quality article, with 17–24 representing good quality research, a score of 9–16 is acceptable quality and a score of 0–8 represents low quality research (See Table 3.2) (See Appendix B for full quality assessment). Figure 3.1 below outlines the screening and review process for included studies.

3.2.5 Data Extraction

Eligible articles were screened for inclusion based on the criteria outlined in Table 1 above. Extracted data included: (1) Reference, (2) Study design, (3) Prehabilitation type, (4) Participant demographics, (5) Intervention design and description, (6) Points of data collection and follow up, (7) Outcomes of interest, (8) Relevant measures, (9) Description of results, (10) Effect sizes where applicable. Prehabilitation was coded as either psychological, nutritional or exercise based and whether it was unimodal or multimodal. Study design was also coded. If available, the pooled effect size of interventions on relevant outcome measures were calculated. Depending on study design these may be between or within-group. Due to the heterogeneity of outcome measures resulting from full-text data extraction, and to increase clarity, a narrative synthesis approach was employed (Popay et al., 2006).As studies varied in design, significance was coded based on the guidelines outlined within each study and included both statistical significance and clinical significance as defined within each study where applicable.

Figure 3.1

PRISMA Flowchart of Screening and Reviewing Process for Included Studies n=13



3.3 Results

Figure 3.1 above represents data screening and inclusion. 6324 studies were included for abstract screening and after duplicate removal, 4631 studies remained. Of those, 4444 studies were deemed ineligible for full text inclusion, and 187 studies were included for full text screening. One study within this was added by manual search (Galantino et al., 2012). In total, 13 were eligible for inclusion based on the criteria (See Table 3.1). Study characteristics are outlined below in Table 3.2.

3.3.1 Study Characteristics

Eight of the 13 studies were randomised control trials RCTs (Belleau et al., 2001, Can et al., 2009, de Moor et al., 2008, Foley et al., 2010, Garssen et al., 2013, Li et al., 2017, Millstine et al., 2019, Zaman et al., 2021). Year of publication ranged from 1999 to 2021. All studies used unimodal interventions. Eight studies employed various psychological interventions. These included psychological counselling (Ambler et al., 1999, Garssen et al., 2013, Li et al., 2017) psychoeducation (Belleau et al., 2001) mindfulness-based interventions (de Moor et al., 2008, Foley et al., 2010, Millstine et al., 2019) and psychosocial return to work support (Zaman et al., 2021). Only one study employed a nutrition-based intervention (Can et al., 2009) and four studies employed exercise- based interventions (Brahmbhatt et al., 2020, de Paleville et al., 2007, Galantino et al., 2012, Singh et al., 2017). The mean age of participants was 53 years. A total of 797 participants were included. Participants were largely female. Eight studies included all female participants (Ambler et al., 1999, Belleau et al., 2001, Brahmbhatt et al., 2020, de Moor et al., 2008, de Paleville et al., 2007, Galantino et al., 2012, Garssen et al., 2013, Millstine et al., 2019). Across the other studies, male participation accounted for 22.6% (Foley et al., 2010), 50% (Singh et al., 2017), 57.6% (Li et al., 2017) 65% (Can et al., 2009) and 64% (Zaman et al., 2021) of the recruited participants. Cancer type predominantly consisted of breast cancer (n = 8) (Ambler et al., 1999, Belleau et al., 2001, Brahmbhatt et al., 2020, de Moor et al., de Paleville et al., 2007 ,2008, Galantino et al., 2012, Garssen et al., 2013, Millstine et al., 2019) other cancer types represented included laryngeal (Li et al., 2017) rectal (Can et al., 2009, Singh et al., 2017), and multiple cancer types (Foley et al., 2010, Zaman et al., 2021). A breakdown of study characteristics is presented in Table 3.2 below.

Table 3.2

Characteristics of Included Studies n=13

Author	Design	Country	Gender Breakdown	Patients (n)	Age (mean)	Primary Outcome	Type of Treatment	Follow up	Quality Appraisal
Ambler et al., 1999	Controlled Trial	England	100% Female	110	49.5	Anxiety	Breast Cancer Surgery	2 weeks, 6 months	Acceptable
Belleau et al., 2001	Randomised Control Trial	Canada	100% Female	60	51.82	Anxiety	Mastectomy, Segmentectomy, modified radical mastectomy	N/A	Good
Brahmbhatt et al., 2020	Feasibility Trial	Canada	100% Female	22	54.18	Feasibility	Mastectomy or Lumpectomy	6 weeks, 12 weeks	Good
Can et al., 2009	Randomised Control Trial	Turkey	65% Male, 35% Female	40	54.32	Quality of Life (Qol) and reduction in Gastrointestinal complaints	Chemotherapy	6 weeks in treatment	Good
de Moor et al., 2008	Randomised Control Trial	United States	100% Female	49	53.60	Distress and Perceived stress management	Breast cancer Surgery	2 weeks	Good
de Paleville et al., 2007	Case Study	United States	100% Female	1	42	Functional tasks	Chemotherapy	Intervention end (week 9)	Acceptable
Foley et al., 2010	Randomised Control Trial	Australia	77% Female, 23% Male	115	55.17	Depression, Anxiety and Health-related QoL	Varied	Post treatment, 3 months	Good
Garssen et al., 2013	Randomised Control Trial	Netherlands	100% Female	70	53	Psychological Effects	Mastectomy or Lumpectomy	Day 2, 5, 1 month, 3 months	Good
Li et al., 2017	Randomised Control Trial	China	57.6% Male, 42.4% Female	210	55.3	QoL	Non-specific therapy	3 months	Good
Millstine et al., 2019	Randomised Control Trial	United States	100% Female	28	55.6	Fatigue, Stress, QoL	Breast Cancer Surgery	2 weeks, 3 months	Good
Singh et al., 2017	Feasibility Trial	Australia	50% Male, 50% Female	10	54.4	Muscle performance	Curative Resection	2 months	Good
Zaman et al., 2021	Randomised Control Trial	Netherlands	64% Male, 36% Female	88	55	Number of days on sick leave	Gastrointestinal	3,6,9,12 months	Good
Galantino et al., 2012	Case Study Series	United States	100% Female	4	54.75	Cognition, Perceived Cognition, QoL, Mood	Breast Cancer	1 month, 3month post	Acceptable

3.3.2 Measures

Large heterogeneity existed between measures. For measures such as HrQoL, affective subscales of interest were extracted and assessed where available. Affective measures of interest were chosen based on ability to measure psychological wellbeing including anxiety, depression, stress and HrQoL due to the presence of emotional and social functional components. Functional measures included variations of the 6 min walk test, the sit to stand test, and other tasks such as ascending and descending stairs. Affective outcome measures are summarised in Table 3.3 below.

Table 3.3

Summary of Affective Outcome Assessment Measures of Final Studies

Construct	Measures	Description	Studies
Health Related Quality of Life	European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORT-QLQ-C30)	**Subscales:** physical, role, cognitive, *emotional, *social & *total global health score	Garssen et al., 2013, Li et al., 2017, Singh et al., 2017, Zaman et al., 2021
	Short Form Health (Survey -SF-36 (V2))	**Subscales:** Eight subdomains, two composites; physical component summary & *mental component summary	Can et al., 2009, Singh et al.,2017, Zaman et al., 2021
	Functional Assessment of Cancer Therapy-General (FACT-G)	**Subscales:** physical wellbeing, *social/family wellbeing, *emotional wellbeing, functional wellbeing	Can et al., 2009, Foley et al., 2010, Millstein et al., 2019
	Functional Assessment of Cancer Therapy- Breast (FACT-B)	**Subscales:** physical wellbeing, social/family wellbeing, emotional wellbeing, functional wellbeing	Galantino et al., 2012
Depression	Hospital Anxiety and Depression Scale (HADS)	**Subscales:** anxiety, *depression	Ambler et al., 1999
	Hamilton Rating Scale for Depression HAM-D	**Subscales:** one 17 item scale, higher score indicating symptom severity	Foley et al., 2010, Li et al., 2017
	Profile of Mood States	**Subscales:** depression subscale	Garssen et al., 2013
	Profile of Mood States	**Subscales:** tension-anxiety, anger-hostility, vigour-activity, fatigue-inertia, depression-dejection, confusion-bewilderment	Galantino et al., 2012
Anxiety	Hospital Anxiety and Depression Scale (HADS)	**Subscales:** *anxiety, depression	Ambler et al., 1999
	Hamilton Rating Scale for Anxiety (HAM-A)	**Subscales:** one 14 item scale, higher score indicating symptom severity	Foley et al., 2010, Li et al., 2017
	The Situational Anxiety Inventory	**Subscales:** Adapted from the State-Trait Anxiety Inventory, 20 items, 10 to decent absence of and 10 to detect presence of unpleasant emotional states	Belleau et al., 2001
	The State Trait Anxiety Inventory	**Subscales:** Dutch edition, state anxiety 20 item scale	Garssen et al., 2013
Stress	Rotterdam Symptom Checklist (RCSL)	**Subscales:** *psychological scale, physical scale	Ambler et al., 1999
	Perceived Stress Scale (PSS)	**Subscales:** one scale 14 items apprising stress within one's life	de Moor et al., 2008, Millstein et al., 2019
	Depression Anxiety Stress Scale (DASS)	**Subscales:** depression, anxiety and *stress	Foley et al., 2010

3.3.3 Prehabilitation Exercise Interventions

Four studies involved exercise interventions (Galantino et al., 2012, Singh et al., 2017, de Paleville et al., 2007, Brahmbhatt et al., 2020). Variation existed between type and mode of delivery. Two studies employed both aerobic exercise and resistance training (Singh et al., 2017, Brahmbhatt et al., 2020). Intervention length varied from one to three months. One study used aerobic exercise only (de Paleville et al., 2007). One study employed Iyengar Yoga exercises (Galantino et al., 2012) and duration and frequency of interventions varied from 2 to 5 times weekly and 15–70 min per session. In some cases, qualitative components and feasibility analysis were also introduced at follow-up assessments (Brahmbhatt et al., 2020). Two studies increased exercise intensity as participants progressed based on a gradually increasing duration by 5 min (de Paleville et al., 2007) and using rates of perceived exertion (Brahmbhatt et al., 2020). A breakdown of exercise study characteristics is presented below in Table 3.4.

Table 3.4

Characteristics of Exercise Intervention Studies

Author	Exercise Type	Duration (Max)	Frequency	Mode of Delivery	Exercises	Equipment
Brahmbhatt et al., 2020	Aerobic & Resistance	40 minutes	3-5 times weekly	Remote Supervision	*Aerobic:* Brisk walking *Resistance:* Standing rows, shoulder external rotation, front raise, lateral raise, bicep curls, tricep extensions, wall push ups and chest press *Mobility and stretching*	Resistance bands and exercise manual
de Paleville et al., 2007	Aerobic Only	35 minutes	5 time weekly	Supervised and home based	*Aerobic:* Walking *Warm up and stretching*	Pedometer, training log
Galantino et al., 2012	Iyengar-inspired Yoga Program	70 minutes	2 times weekly	Small group sessions and home-based	*Aerobic:* Iyengar Yoga Class with 14 poses	A mat, two bolsters, two chairs, two blankets, one eye bandage, belt, two blocks and a 1-lb. weight.
Singh et al., 2017	Aerobic & Resistance	60 minutes	2 times weekly (supervised)	Supervised	*Aerobic:* Walking or jogging, cycling, rowing *Resistance:* Chest press, seated row, latissimus pull down, leg extension, leg curl, leg press	Treadmill, exercise bike, rowing machine, standard resistance training gym machinery

3.3.3.1 Outcomes

3.3.3.1.1 Affective Measures. Measures of HrQoL were employed across three studies. These included European organisation for research and treatment of cancer quality-of-life questionnaire core 30 (EORTC-QLQ-C30) (Singh et al., 2017) and the Short form health survey (SF- 36) (Singh et al., 2017, Brahmbhatt) the Functional Assessment of Cancer Therapy- Breast (FACT-B) (Galantino et al., 2012) (Table 3). Results of the EORTC-QLQ-C30 indicated that exercise interventions had a modest non-significant effect on global health (d baseline-pre = 0.55) but returned to baseline levels post-surgery. Scores on the social and emotional subscales of the EORTC-QLQ-C30 also showed a minimal effect of exercise (d = 0.09–0.10) (Singh et al., 2017). Results of the short form health survey indicated a small non-significant decline post-surgery in mental composite scores (d = baseline to pre = 0.08, baseline to post = 0.07). For Brahmbhatt and colleagues (2020) single arm feasibility study, the SF-36 mental composite score worsened from baseline to pre-op but increased by 4.36 points post-op representing a clinically significant improvement. In terms of effect, the baseline to preoperative effect on the mental composite score was low. Galantino et al., 2012 reported improvements in quality of life (QoL) across participants in their case study series but did not provide sufficient data for further interpretation. Qualitatively, improvements were reported at 3 months follow-up across all participants. This study also reported decreases in mood disturbances across participants during the intervention, but that these decreases were not maintained at follow-up.

3.3.3.1.2. Functional Measures. Primary outcomes included muscle strength (Singh et al., 2017), functional ability, Galantino et al., 2012, de Paleville et al., 2007) and feasibility (Brahmbhatt et al., 2020). Walk tests measured functional capacity across three studies (Singh et al., 2017, de Paleville et al., 2007, Brahmbhatt et al., 2020). Other measures of functional capacity included The Disabilities of Arm Shoulder and Hand measure (DASH) (Brahmbhatt et al., 2020), stair climbs, chair raises, arm curls, sit and reach and related reach tasks (Galantino et al., 2012, Singh et al., 2017, de Paleville et al., 2007). Results indicated promising improvements in functional capacity as a result of exercise prehabilitation. The 6-min walk backward test (d baseline-pre = 0.55) showed statistically significant improvements ($p < 0.035$) (Galantino et al., 2012) and results of the 6 -min walk test distance were of clinical significance in another study, 37 m over the clinically significant distance (Brahmbhatt

et al., 2020). Results of the 400 m walk test were statistically significant (d baseline - pre = 0.68) (Galantino et al., 2012). Case study data also indicated an over 40% improvement in 12 -min walk distance from baseline to post (de Paleville et al., 2007). Results of the other measures varied. Ability to ascend stairs improved (de Paleville et al., 2007). Overall, results of other measures were non -significant but moderate in effect (d = 0.39–0.68) (Galantino et al., 2012) and represented case study improvements of 5%–41% (de Paleville et al., 2007). The DASH was employed in one study (Brahmbhatt et al., 2020) and found a non -statistically significant increase in DASH scores but reported a clinically meaningful increase in DASH scores pre -post -op of over 15 points. Qualitative case series data from the yoga intervention also indicated increases in flexibility and balance across all participants from measures of functional arm reach (Galantino et al., 2012).

3.3.4 Prehabilitation Nutrition Interventions

Only one study used a nutrition-based intervention (Can et al., 2009). This involved the use of probiotic kefir to supplement patients as they underwent chemotherapy for colorectal cancer. Kefir is a natural probiotic that mimics the beneficial bacteria found in dairy products. Forty participants were randomised to either the control or intervention condition. Intervention participants ingested 500 ml of weekly kefir before and during chemotherapy in two 250 ml rounds. Data was collected at baseline, week three and week six of treatment cycles.

3.3.4.1 Outcomes

3.3.4.1.1. Affective Measures. HrQoL was assessed at the three time points using the Functional assessment of cancer therapy -general (FACT -G) questionnaire. The effect of kefir on HrQoL was non-significant. With regards to the affective subscales, all between group differences were non-significant at all time points.

3.3.5. Prehabilitation Psychological Interventions

Eight studies employed psychological interventions (Ambler et al., 1999, Belleau et al., 2001, de Moor et al., 2008, Foley et al., 2010, Garssen et al., 2013, Li et al., 2017, Millstine et al., 2019, Zaman et al., 2021,). Intervention duration varied from

days to weeks pre -surgery (Grassen et al., 2013, Millstine et al., 2019). Follow -ups ranged from 2 weeks to 12 months (Zaman et al., 2021). Follow -up assessments generally included repeated administration of study outcome measures. One study did not assess patients post intervention (Belleau et al., 2021). Treatments focused on the pre -surgical/treatment and surgical consultation phases. One study continued the intervention into the perioperative phase (Foley et al., 2010) and another study continued support up to 9 months post-surgery (Zaman et al., 2021). Anxiety reduction was the primary outcome in five studies (Ambler et al., 1999, Belleau et al., 2001, Foley et al., 2010, Garssen et al., 2013, Li et al., 2017). As with the physical interventions, modes of intervention varied across studies. Two studies employed the use of tailored nurse advocacy. These included counselling from diagnosis to surgery and offering psychoeducational support (Li et al., 2017, Ambler et al., 1999). Mindfulness - based practice and meditation were commonly used, including mindfulness-based training with cognitive elements (Foley et al., 2010) and mindfulness-based home neurofeedback (Millstine et al., 2019). Many interventions used multidisciplinary approaches combining education, counselling and cognition (Li et al., 2007, Belleau et al., 2001). Other interventions included expressive writing (de Moor et al., 2008) and stress management (Garssen et al., 2013). One study employed a tailored psychosocial return-to-work support intervention (Zaman et al., 2021). Three interventions took place onsite (Ambler et al., 1999, Belleau et al., 2001, Garssen et al., 2013), two were offsite (de Moor et al., 2008, Millstine et al., 2019) and three used a combination (Foley et al., 2010, Li et al., 2017, Zaman et al., 2021).

3.3.5.1 Outcomes

3.3.5.1.1 Affective Measures. Anxiety was assessed across five studies (Ambler et al., 1999, Belleau et al., 2001, Foley et al., 2010, Garssen et al., 2013, Li et al., 2017). Anxiety measures varied widely and included the Hospital anxiety and depression Scale (HADS) Scale, The Situational Anxiety Inventory, The Hamilton rating Scale for anxiety and The State Trait Anxiety Inventory (See Table 3). Overall, psychological interventions were moderately successful for anxiety. Four of seven interventions showed significant anxiety improvements (Ambler et al., 1999, Belleau et al., 2001, Foley et al., 2010, Li et al., 2017). Another study produced a clinically significant result pre-surgery, but with no intervention effects (Garssen et al., 2013).

Foley and colleagues (2010) reported large effects of their mindfulness-based intervention from baseline to 3 months follow-up ($p < 0.002$, $d = 0.59$). Ambler and colleagues (1999) reported a significant reduction in anxiety pre-treatment to 2-week follow-up ($P < 0.003$) ($d = 0.45$). Other studies had small to moderate effects of interventions on anxiety scores ranging from $d = 0.26$- 0.4 (Belleau et al., 2001, Li et al., 2017). However, these effects were not always maintained at 6-month follow-up (Ambler et al., 1999). Less successful interventions included expressive writing (de Moor et al., 2008), and stress management training (Garssen et al., 2013).

Depression was assessed in five studies (Ambler et al., 1999, de Moor et al., 2008, Foley et al., 2010, Garssen et al., 2013, Li et al., 2017) and assessed as primary outcome in one study (Foley et al., 2010). Measures included The Brief Symptom Inventory, The HAM-D, The HADS and The Profile of Mood States: Depression (See Table 3). Three studies found significant moderate- large effects on depression (Foley et al., 2010, Garssen et al., 2013, Li et al., 2017). Foley and colleagues (2010) reported clinically significant decreases in symptoms over time ($p < 0.001$, $d = 0.83$). Li and colleagues (2017) reported a significant ($p < 0.05$) effect on depression ($d = 0.33$). Significant effects were also found between groups day-5 post treatment as a result of the stress management intervention, but these were not significant after day 5 (Garssen et al., 2013). The nurse advocacy counselling intervention (Ambler et al., 1999) and the expressive writing intervention (de Moor et al., 2008) reported no effect.

Finally, stress and distress were assessed within four studies (Ambler et al., 1999, Belleau et al., 2001, Foley et al., 2010, Millstine et al., 2019). Measures employed included The Perceived Stress Scale, The Depression Anxiety Stress Scale and The Rotterdam Symptom Checklist (See Table 3.3). Only one study (Foley et al., 2010) found a significant reduction in symptoms as a result of mindfulness-based CBT ($p < 0.001$, $d = 0.53$). Other studies reported non-significant trends relating to stress and distress. Millstine and colleagues (2019) reported a small decrease in perceived stress as a result of EEG mindfulness- based meditation. Ambler and colleagues (1999) found a decrease in psychological distress pre-post treatment for the nurse advocacy counselling intervention. HrQoL was measured by Grassen and colleagues (2013) and reported increased scores on the EORTC at days 2 and 30 post intervention but with no significant between group effects.

3.3.6 Risk of bias

All included studies were of acceptable quality-based criteria outlined (Dunne et al., 2017). There was no evidence of reporting bias. Risk of selection bias was low as many studies employed a RCT design. However, some studies did not include a control group and did not adequately outline recruitment strategy and eligibility. For full quality assessment scoring see Appendix B.

3.4 Discussion

To our knowledge, this is the first review of its kind assessing the effects of prehabilitation interventions on affective and functional outcomes for young to midlife adult (18–55 years) participants. Evidence was found to support the alleviation of anxiety as a result of prehabilitation interventions, with support for health-related QoL, stress and depression being less-robust and underrepresented. Findings moderately supported the therapeutic validity of exercise prehabilitation to improve functional capacity both in terms of clinical and experimental improvements. All studies included in this review were unimodal, involving only one prehabilitation intervention as opposed to multimodal, where multiple interventions are employed in combination (Bolshinsky et al., 2018, Gillis et al., 2018). This is not in line with previous systematic evidence, in which multimodal interventions are usually represented (Bolshinsky et al., 2018, Gillis et al., 2018, Hijazi et al.,2017, Jain et al., 2022). The majority of studies retained were psychological interventions, indicating that exercise prehabilitation is not the primary focus of prehabilitation interventions within the 18–55 age range, despite younger patients being reported to be in favour of exercise prehabilitation (Banerjee et al., 2021). Only one study employed a nutritional intervention. This could relate to the age of diagnosis for cancers that required the most nutritional support such as colon or gastrointestinal. Regardless of cancer type, general nutritional support is highlighted as a key pillar of prehabilitation treatment.

Studies were largely heterogeneous in design. The majority of studies applied a randomised control trial design. Feasibility as a construct appeared to be assessed in exercise studies that occurred more recently, within the past 5 years (Brahmbhatt et al.,

2021, Singh et al., 2017). Despite large variance in psychological techniques and the development of novel interventions, no psychological intervention identified feasibility as a primary outcome. These data could provide a context for interpreting non-significant results observed, as some of the psychological interventions, particularly mindfulness and meditation- focused, require high levels of commitment (Foley et al., 2010, Millstine et al., 2019). Assessments included a high battery of measures, with the majority of studies reporting over five outcome assessments. Both the time commitment of interventions and assessments could be contributing to the mixed efficacy of results, particularly for psychological interventions as patient distress could be affecting adherence (Brebach et al., 2016). For exercise, levels of adherence can also relate to baseline level of fitness, which could also impact upon the results of smaller exercise intervention studies (Halliday et al., 2021).

The majority of studies focused on breast cancer. This could be due to a number of factors including the age range of interest, the relatively quick timeline from diagnosis to treatment or the distressing nature of breast cancer surgery for women requiring increased psychological support (Perez-Tejada et al., 2019). The studies represented in this review focus on psychological intervention; however, these results are heavily confounded by the treatment pathways related to cancer subtypes.

There was an over-representation of female participants. This could have had implications for the prevalence of anxiety-related research, as women report increased levels of cancer treatment- related anxiety compared to men (Jimenez-Fonseca et al., 2018, Pitman et al., 2018). Variation existed across treatment, surgery types and heterogeneity between follow-up assessments (See Table 3.2) also made it difficult to ascertain any distinct differences between treatment or surgery with regards to outcomes. Two studies (de Paleville et al., 2007, Galantino et al., 2012) also employed a case study and case series design, such that results for relevant outcomes were largely descriptive in nature and difficult to generalise to functional and affective outcomes for prehabilitation interventions at large.

Assessment of affective outcomes resulted in thought-provoking findings. Study measures varied with some studies employing a combined measure to assess affective outcomes (See Table 3.3). Interventions produced a moderate effect on anxiety. This is in line with research trends, which indicate a positive effect of prehabilitation on

anxiety (Silver et al., 2013, Tsimopoulou et al., 2015). Similar to functional capacity and exercise, anxiety measures were only represented within the unimodal psychological interventions. It is interesting to note that only one exercise intervention (Galantino et al., 2012), employed a measure of anxiety, as that previous literature indicates that exercise can aid in alleviating preoperative anxiety (Quist et al., 2015) and therefore would be expected as an included outcome. This could be due to the nature of the yoga-based intervention, which is known to aid in anxiety reduction (Saeed et al., 2019).

The evidence for depression was less definitive and not statistically supported, as only seven studies included assessments. The positive reported effects on depression are surprising, as it was not the primary outcome for many interventions. Measures of depression were included mainly within the psychological interventions, and not alongside measures of functional capacity within exercise interventions, apart from Galantino and colleagues 2012 yoga-based intervention. This was unanticipated, due to literature supporting the link between exercise and treatment for even moderate depression (Netz et al., 2017). The lack of affective measures assessed within the nutritional intervention was unanticipated, due to trends exploring the positive impact of nutrition on affective outcomes (Duarte-Silva et al., 2021).

Stress and distress were under-represented, appearing in four psychological interventions. Of those, two shared a common measure, the Perceived Stress Scale. Low numbers and large heterogeneity made it difficult to ascertain the effect of the interventions on stress and distress, with clinical significance only found in one study.

HrQoL was the only affective measure to be assessed across the three modes of prehabilitation. Results did not support a statistically significant increase in HrQoL as a result of any intervention. However, clinically significant increases were found for both exercise and psychological intervention types within studies, where non-statistically significant results were included but results were compared against clinically significant improvements based on prior research or clinical standards. These mixed results for the mental components of HrQoL across studies was surprising due to the relatively consistent effects of the interventions on outcomes, like anxiety.

Overall, the functional outcomes assessed indicated moderate to large effects of exercise prehabilitation for improving functional capacity. Only studies employing

exercise prehabilitation assessed functional outcomes. The overall effect of exercise prehabilitation was large, indicating particular improvements across functional walking tasks. Some measures focused on time taken to travel certain distances, whilst others focused on distance travelled within certain timeframes as well as other markers of function such as flexibility and balance. This variation amongst measures made it difficult to directly compare efficacy. Three studies did not have sufficient power to report significance (Brahmbhatt et al., 2020, de Paleville et al., 2007, Galantino et al., 2012). The results of the present review provides moderate support for the clinical efficacy of exercise prehabilitation. The present review also found a low number of eligible studies to provide evidence for the efficacy of nutritional or psychological support on functional outcomes.

The main strength of this review is that it explored the effectiveness of prehabilitation focusing on functional and affective outcomes for young-to midlife adult cancer patients between 18-55 years. The review was conducted in a rigorous manner using pre-selected search terms over several databases. Two independent assessors screened candidate articles using pre-defined search terms which minimised bias. The quality of each study was evaluated using a validated checklist. Large heterogeneity across all prehabilitation outcome measures prevented assessment via a meta-analysis, limiting generalisability. The age range of 18–55 years possibly confounded study findings by over representing certain cancer types and female gender. This age range was also selected using mean values as it was not possible to obtain the range for all studies, this may have skewed the representation of ages. This was interesting as this unintentionally resulted in a narrow focus of cancer type which further highlights the need for increased focus of young to midlife adults across cancer types. The large representation across female cancer types would be generalisable to the population at large, as research from cancer research UK suggests that for adults in the 24–59 age bracket, rates of female cancer increase more compared to male indicine rates (Cancer Research UK, 2015), the large representation of breast cancer was also representative, as breast cancer was the most common cancer type reported by the National Cancer Institute (National Cancer Institute, 2015). Due to the relatively new development of prehabilitation within cancer treatment, no restrictions in publication date were placed on studies. As a result of study design and participant count, some studies lacked sufficient power to report statistical significance, (Galantino et al., 2012,

de Paleville et al., 2007, Brahmbhatt et al., 2020) but did find clinically significant results, which may have resulted in an underestimation of the true effectiveness of interventions. Some studies failed to report the relevant affective scores for each subscale, which also created data extraction issues for some HrQoL subscales. Heterogeneity of study design also meant that follow up assessments were not consistent (See Table 3.2).

In terms of functional capacity, studies also reported large improvements within their populations despite lacking power to report statistical significance (Galantino et al., 2012, de Paleville et al., 2007, Brahmbhatt et al., 2020). This was also the case for anxiety, where clinical improvements were also observed (Garssen et al., 2013). It would appear that the results of the present review moderately supports the clinical efficacy of exercise prehabilitation. The use of clinical change metrics and change scores is common in health-related intervention research. This allows for an increasingly patient-centred approach as patient feedback can drive improvements in quality (Berger et al., 2020). From a clinical perspective, the results of the present review provide increasing evidence for the use of prehabilitation among cancer patients between the ages of 18–55 to improve anxiety and functional capacity.

3.5 Conclusion

This evidence synthesis indicates that cancer patients gain psychological and functional effects from psychological and exercise prehabilitation, respectively. Included studies illustrated that there is a wide variance across modes of prehabilitation, study design as well as assessment measures. Interestingly, uni-modal interventions were reported only in this review. Given the direct benefit from each uni-modal intervention, the efficacy of multi-modal prehabilitation is warranted. The present study adds to the literature by assessing the impact of prehabilitation on affective outcomes, and by focussing on the young to midlife age range of cancer patients.

A review by Sheppard and colleagues (2025) explored the application of prehabilitation to address cognitive outcomes within urologic cancers. They noted the dearth of research exploring prehabilitation approaches for cognitive outcomes and

proposed that cognitive resilience could be supported through physical activity, nutrition and wellbeing strategies. Understanding the psychological and physical benefits of prehabilitation approaches may aid in developing future prehabilitation programmes addressing optimising cognitive function. The results of this review highlight the complexity of providing effective prehabilitation intervention to target functional and affective outcomes,

Chapters 4,5, and 6 explore the experiences of patients engaged in a bimodal exercise and nutrition intervention pre and post CRS-HIPEC treatment. Research has advocated for the application of prehabilitation within the scope of CRS-HIPEC treatment (Cortés-Gurial et al., 2021). Furthermore, recent qualitative research with CRS-HIPEC survivors indicates that there exists unmet quality of life needs for patients post CRS-HIPEC (Falla-Zuniga et al., 2024). Observational research by Loughney and colleagues in 2020 also highlighted patients preparing for CRS-HIPEC treatment as patients that could benefit from prehabilitation. The studies in chapters 4, 5 and 6 will allow for the observation of the potential psychological and cognitive benefits of prehabilitation, when exercise and nutrition support are provided in tandem.

Chapter 4: Exploring the Cognitive and Psychological Experience of Preparing for Cancer Surgery

4.1 Introduction:

The systematic review in Chapter 2 highlighted the prevalence of pretreatment CRCI and the association between self-report CRCI and psychological variables. The systematic review in chapter 3 highlighted the physical and psychological impacts of prehabilitation in cancer. To date, little is known about the prevalence of pretreatment cancer-related cognitive impairment for patients preparing for CRS-HIPEC treatment. This chapter assesses the baseline and pre-surgery self-report cognitive, psychological and quality of life data for patients preparing for CRS-HIPEC surgery who are enrolled in a combined pre-and rehabilitative exercise and nutrition intervention as part of the PANO trial (Chapter 1, section 1.1.5). In addition, patients were interviewed at the pre-surgery timepoint in order to provide an in-depth analysis and context for the cognitive and psychological experience of patients with peritoneal malignancy in the period prior to surgery.

Preparation for cancer surgery represents a time of inordinate stress for patients as they navigate the potential for postoperative morbidity and complications (Bates et al., 2024). However, more recently, CRCI is now emerging as an area of concern with methodological and theoretical questions and considerations regarding its aetiology, influences and measurement (Ahles & Hurria, 2018). The existence of cognitive impairment prior to cancer treatment requires further considerations of the causes and influencing factors of pretreatment CRCI including the cancer itself, cognitive reserve, stress or psychological symptoms (Hutterer & Oberndorfer, 2021).

Chapter 1 highlighted the current state of cancer research and CRCI, as well as the evidence base for prehabilitation to increase patient psychological wellbeing and health related quality of life. One third of cancer patients experience perioperative anxiety related to fear of anaesthesia alone (Walker et al., 2016). For cancer patients, in the period between diagnosis and surgery, psychological distress can be exacerbated by the additional stress of neoadjuvant treatment, as well as the physical and psychological burden of diagnosis (Walker et al., 2016). Anxiety and depression during the preoperative period have also been observed within gastric cancer patients awaiting

surgery, with a prevalence of 20.75% (Xu et al., 2016). Within colorectal cancer, preoperative anxiety has previously been found in 16.8% of patients, and depression in 12.9% of patients awaiting surgery (Gülmez et al., 2022). Therefore, psychological wellbeing for patients preparing for cancer surgery is central to understanding postoperative recovery and quality of life (Lee et al., 2018). Both anxiety and depression can impact quality of life, and despite this, patients often do not change their coping styles to address this psychological distress (Gil et al., 2012).

Chapter 2 (2.3.7) highlighted that anxiety and depression can be related to experiences of CRCI. While much of the research focuses on the mechanisms and prevalence of CRCI (Lange et al., 2019, Ahles & Hurria et al., 2018), less is known about the psychosocial and quality of life impacts for patients experiencing CRCI. A recent narrative review by Yang and Von Ah (2024) explored the interplay between CRCI and quality of life for cancer survivors. They identified practical disruptions including a diminished ability to either return to work or complete work-related tasks, as well as psychosocial challenges and a general withdrawal from social life to avoid embarrassment in cognitively demanding environments. Self-confidence can also be impacted, with other research suggesting that levels of self-efficacy, alongside perceived cognitive impairment and sustained attention are predictive of overall quality of life for individuals who report CRCI (Maeir et al., 2023). In recent years, efforts have also been made to understand the qualitative experience of CRCI and its implications for psychosocial wellbeing and quality of life in cancer (Haywood et al., 2023, Sharma & Brunet, 2023, Coro et al., 2020). Themes generally encompassed difficulties experienced in work and social life, the negative psychological impacts on wellbeing, and the need for increased knowledge and intervention for CRCI. One study (Coro et al., 2020), investigated the cognitive impact on health behaviours related to diet and nutrition through qualitative investigation, and reported that cognitive issues impacted on meal planning and ability to maintain a healthy diet. To date there is a dearth of qualitative literature exploring the cognitive experience of cancer patients awaiting surgery. Given that subjective and objective CRCI was observed across a range of cancer types prior to treatment or surgery in the systematic review CRCI and psychological factors in Chapter 2, it is important to ascertain the qualitative cognitive experience of patients to allow for increased understanding of how CRCI issues may manifest for patients and its interaction with psychological wellbeing and quality of life. Understanding the cognitive and psychological experience of patients prior to

surgery can aid in our understanding of the potential impacts of prehabilitation intervention approaches to help support patients prior to surgery. As illustrated in Chapter 3's review of prehabilitation approaches, prehabilitation can support both functional and affective outcomes (Section 3.3), but more research is required to assess the combined impact of multimodal approaches, and the role of prehabilitation in cognitive function.

Lifestyle prehabilitation can also support psychological wellbeing by reducing anxiety and stress (Knorel et al., 2022). When faced with psychological distress pre-surgery, many patients choose not to engage in structured psychological support, potentially out of a desire to maintain normalcy, or to avoid the additional burden of psychological intervention (Yigitbas & Bulut, 2024). Due to the immediate physical needs of patients preparing for cancer surgery, a bimodal exercise and nutrition-based approach could potentially address psychological and cognitive needs, whilst also addressing the direct need for preoperative physical fitness to support post operative recovery (Gillis et al., 2022b).

The combined burden of diagnosis and treatment presents unique challenges for patients preparing for cancer surgery. As previously mentioned, (Chapter 1,1.4), peritoneal malignancy (PM) is a rare cancer, affecting approximately 6.78 per million people in the United States alone (Anwar & Kasi, 2024). Evidence from Ireland suggests that incidence is increasing, in the range of 400 per 4.5 million across all forms of PM (Solon et al., 2017). The advent of new treatments for PM like cytoreductive surgery with heated intraperitoneal chemotherapy (CRS-HIPEC), has improved patient prognosis and outcomes (Kelly et al., 2021). However, CRS-HIPEC represents a highly invasive and physically demanding surgery with considerable postoperative insult (Loughney et al., 2020). CRS-HIPEC treatment involves the removal of tumours from the affected site followed by the abdominal cavity being bathed by heated chemotherapy. Due to the nature of the treatment, CRS-HIPEC carries dual risks associated with both surgery and chemotherapy (Mayo Clinic, 2025). Prior research has explored patient reported outcomes for CRS-HIPEC after surgery, with impacts on patient health related quality of life (Bakkers et al., 2023, Loughney et al., 2020). Research has also found that patients undergoing CRS-HIPEC can be susceptible to postoperative cognitive dysfunction as measured by objective cognitive testing (Yu et al., 2016, 2017). Prehabilitation has previously been established as appropriate for these patients, due to the physical morbidity prior to treatment, and the

psychological stress (Cortés-Gurial et al., 2021). Due to the invasive nature of treatment, and the psychological impact of a rare cancer diagnosis, more research is required focusing on the preoperative experience of patients awaiting CRS-HIPEC treatment, to help understand the trajectory of patient reported outcomes and cognitive function.

Traditionally, CRCI is assessed with subjective self-report questionnaires or objective neuropsychological assessment. Methodologically, this has proven challenging as there is often a lack of correlation between subjective and objective reports (Ahles & Hurria, 2018). Interviews have been previously applied within CRCI research alongside self-report data to provide further insight into the range of cognitive issues experienced, and the impacts that these issues may have on other constructs like quality of life (Shilling & Jenkins, 2007). Qualitative investigations are also important within the emerging field of prehabilitation research to help understand psychological and physical barriers to prehabilitation engagement (van der Velde et al., 2023). Using a multi methods approach including both self-report and qualitative data will help us to interrogate fully, for the first time, the preoperative subjective CRCI experience, and the potential impact of prehabilitation engagement for PM patients preparing for CRS-HIPEC treatment.

To date, there is a dearth of research exploring the pretreatment cognitive and psychological experience of patients preparing for CRS-HIPEC treatment.

The aim of the present study is to understand the prevalence and cognitive experience of patients preparing for CRS HIPEC treatment as well as influencing factors including psychological wellbeing and prehabilitative intervention compared to a control group. The following study objectives are explored:

a. Assess the prevalence of CRCI prior to any treatment during the preoperative and postoperative phase.
b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.
e. Explore CRCI in the postoperative phase to understand its trajectory and influences on CRCI during recovery.
f. Understand the patient's cognitive and psychological factors as they prepare for and recover from surgery through qualitative investigation.

4.2 Methods

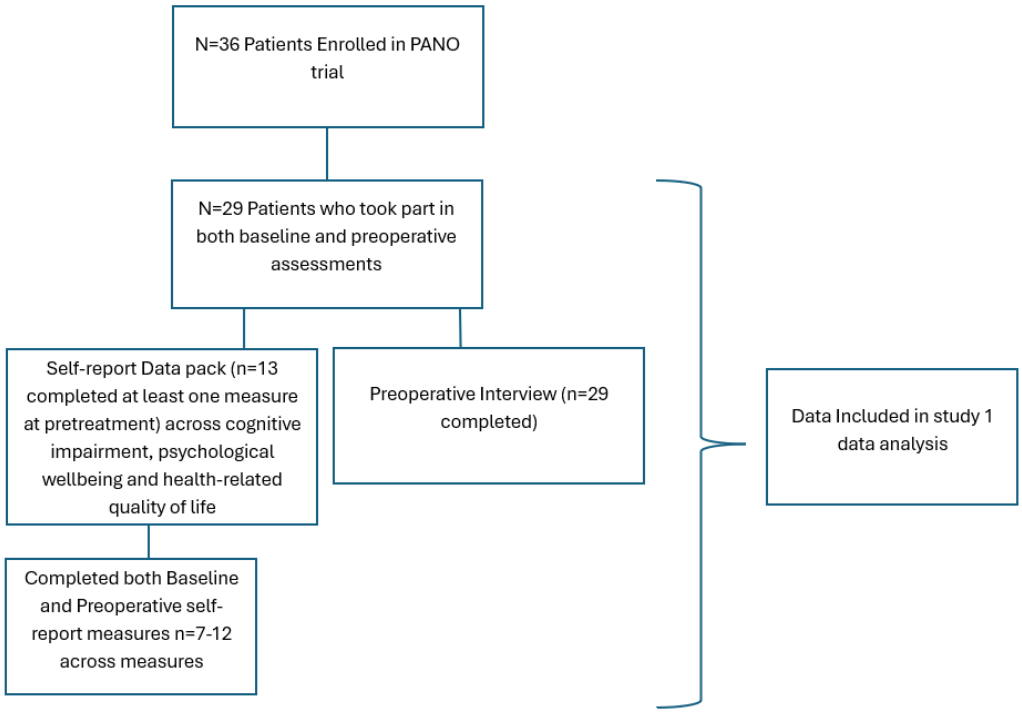
4.2.1 Study design

The PANO trial (Perioperative Exercise and Nutrition Optimisation NCT05305820) is a single-site feasibility trial assessing the effects of a combined pre- and rehabilitation intervention for patients with peritoneal malignancy (PM) preparing for CRS-HIPEC treatment compared to a control group receiving usual care (n=36). The bimodal intervention consists of structured exercise and nutrition support. The full intervention and outcome details for the PANO trial have been described elsewhere (Chapter 1 section 1.1.5). This study is a nested study within the PANO trial study.

The nested study is an observational multi-methods investigation of the self-report and qualitative experience of PM patients preparing for CRS-HIPEC treatment, whilst engaged in a prehabilitation intervention or care as usual. The multi-methods approach collects both quantitative subjective self-reported patient data as well as qualitative investigation of patient experience in order to provide an in-depth overview of patient experience preparing for CRS-HIPEC treatment. For the purpose of this study, analysis is focused on the cognitive, psychological wellbeing and quality of life data related to the baseline and preoperative trial timepoints. Figure 4.1 below provides an outline of study assessment timepoints.

Figure 4.1

Flow Diagram of Participants and Assessments



Note: n=25 participants completed baseline questionnaire data, n=29 participants included baseline demographic and clinical data

4.2.2 Quantitative Data Methods

4.2.2.1 Participants

Participants were n=29 cancer patients enrolled in the PANO trial (NCT05305820). Participants with CRS-HIPEC for colorectal/appendix/ovarian peritoneal disease or pseudomyxoma peritonei (+/- completed neoadjuvant cancer treatment) were recruited, as referred via the multidisciplinary team. Inclusion criteria were being aged 18 years of age or over and having a WHO performance status ≤2. Exclusion criteria were an inability to provide informed consent, impaired cognitive function with a reduced ability to either understand advice /instructions from or communicate with the research team, had declined surgery, had surgery in less than 2 weeks, pregnancy or breastfeeding, inability to participate in the exercise training (unable to perform the 6 Minute Walk Test) or absolute contraindications to exercise testing and veganism.

4.2.2.2 Procedure

Participants who were enrolled in the PANO trial and were assessed at baseline and preoperatively (n=29) were included in the current analysis. All eligible participants were recruited from the National Centre for Peritoneal Malignancy at the Mater Misericordiae University Hospital, Dublin, Ireland, between August 2022 to March 2024. Eligible patients were approached upon presentation at the clinic by a member of the clinical research team with information about the trial (Appendix C.1). After 72 hours, patients were contacted by a member of the research team to confirm their participation in the PANO trial. Participants were consented (Appendix C.2) and randomly assigned to the intervention (exercise and nutrition), or a control group at baseline. Participants were assessed upon enrolment (Baseline assessment) and prior to surgery (Preoperative assessment). At baseline and preoperative assessment, patients completed a number of self-report questionnaires which were completed either at a clinic in the hospital with a member of the research team or posted to patients to complete independently. As outlined in Figure 4.1 above, the data of n=29 participants were included in the current analysis based on their completion of both baseline and pre-surgery timepoints including presurgical interview.

4.2.2.3 Self-Report Measures

As part of the prehabilitation trial, participants were assessed on a range of physical and nutritional outcomes (see Table 1.1 in Chapter 1). Psychological and cognitive wellbeing assessments relevant to this nested study are outlined below. Due to potential licensing limitations self-report questionnaires are not included as appendices.

4.2.2.3.1 Functional Assessment of Cancer Therapy- Cognition. The Functional Assessment of Cancer Therapy Version 3- Cognition (Wagner et al., 2009) is a self-report measure designed to assess cancer related cognitive problems. The measure is a self-report 37 item questionnaire and scales are scored using Likert scale of 0-4 ratings, with a higher overall score per subscale indicating higher perceived overall cognitive function. For this assessment all scales ranged from 0 (not at all) to 4 (very much). The measure is scored using four subscales including perceived cognitive

impairments (PCI) (18 items, range 0-72), impact of perceived cognitive impairments on QoL (ImpactQoL) (4 Items, range 0-16), comments from others (CFO) (4 items, range, 0-16) and perceived cognitive abilities (PCA) (7 items, range 0-28). It is recommended from the FACT Group that PCI and PCA subscales should be used to interpret levels of perceived impairments. This measure has been shown to be valid across a range of cancer populations (Van-Dyk et al., 2020, Wagner et al., 2009). Raw scores on each measure are totalled for each subscale and reverse scoring is applied as required. A higher score is indicative of better perceived cognitive performance. The FACT-Cognition has shown high internal consistency ranging from Cronbach's alpha of 0.92-0.97 across subscales (Oliveira et al., 2022). Research has identified a PCI subscale score of less than or equal to 54 as having the ability to discriminate between CRCI and non CRCI cases among cancer survivors (Van-Dyk et al., 2020).

4.2.2.3.2 Years of Education. Years of education and vocational training was recorded as a proxy for cognitive reserve based on total years of education and vocational training item of the Cognitive Reserve Index (Nucci et al., 2012). Years of education and the vocational training is recorded as the number of years of education and vocational training attained, with a higher number of years indicative of increased cognitive reserve capacity. Years of education is a commonly applied proxy of cognitive reserve capacity, due partly to the associations between educational attainment and cognitive decline in non-cancer populations (Pinto et al., 2024), and links between higher education as a protective factor against cognitive decline in cancer populations (Liesto et al., 2022).

4.2.2.3.3 General Self Efficacy. The Generalised Self Efficacy Scale (Schwarzer & Jerusalem, 1995) is used to measure how people respond to life events. The measure consists of 10 items and is scored using a Likert scale ranging from 1 (not true at all) to 4 (exactly true). Items are positively scored with a possible low score of 10 and high score of 40, and higher scores indicate better self-efficacy. General self-efficacy has been previously explored within cancer populations preparing for cancer treatment in the Irish context (Loughney et al., 2024). Evaluation of the measure has indicated high validity and internal consistency across studies (Cronbach's alpha .91) (Zeng et al., 2022).

4.2.2.3.4 The NCCN Distress Thermometer. The NCCN Distress Thermometer (NCCN, 1999) was used to detect levels of psychosocial distress as patients prepare for surgery. The distress thermometer is presented as a visual analogue scale whereby patients are instructed to rate their level of stress on a scale from 0 to 10, with 0 representing “no distress” and a score of 10 representing “extreme distress”. Prior work has suggested a cut off score of three on the distress thermometer is indicative of distress across a large cancer population (Cutillo et al., 2013). Research has indicated that the item has high sensitivity (77.1%) and specificity (66.1%) to detect cancer related distress (Hughes et al., 2011).

4.2.2.3.5 The Impact of Events Scale-Revised. The Impact of Events Scale-Revised (IES-r) is a 22-item self-report measure of traumatic stress symptoms focused on intrusive thoughts and avoidant behaviours (Horowitz et al., 1979). Frequency of symptoms are self-reported from during the previous week using a five-point scale from 0 (not at all) to 4 (Extremely). Total scores range from 0 to 88 with higher scores indicative of greater cancer-related stress. Scores in the range of > 24 are reflective of clinically significant stress while higher scores of >37 can be related to decreased immune function in breast cancer patients (Kawarmura et al., 2001). The measure has high internal consistency with Cronbach's alpha > .9 (Creamer et al., 2003).

4.2.2.3.6 The Functional Assessment of Cancer Therapy - General. The Functional Assessment of Cancer Therapy- General (FACT-G) Version 4 (Cella et al., 1993) is a 27 item self-report survey that measures quality of life. Patients respond on a five-point Likert scale ranging from 0 (not at all) to 4 (very much). The measure includes four subscales measuring physical well-being (PWB, range 0-28), functional wellbeing (FWB, range 0-28), social/family wellbeing (SWB, range 0-28), and emotional wellbeing (EWB, range 0-24) which create a total score. The total score is derived from the total of the four subscales, and scores are reverse scored as required. The total ranges from 0-108, with a higher total score reflecting a higher perceived health related quality of life (Cella et al., 1993). The FACT-G reports good internal consistency (Cronbach’s alpha =.88) (Yusufov et al., 2024). The measure has shown reliability and validity amongst older populations with cancer (Overcash et al., 2001), and both total and subscales have indicated generalised reliability across cancer populations (Victorson et al., 2008).

4.2.2.3.7 Euro-QoL-EQ-5D-5L. The EQ-5D is a standardised and validated self-report measure describing health status (non-specific disease but applicable to cancer). The global health status rating was used within this study to assess global health status. Patients were asked to report using a visual analogue scale with a measure of "Your Health Today" ranging from 0-100. A higher global health score indicates good health related quality of life (The EuroQoL group, 1990).

4.2.3 Quantitative Data Analysis

Quantitative self-report data was analysed by the PhD researcher using IBM Statistics Software SPSS version 30. To assess the prevalence of CRCI at baseline, a one sample Wilcoxon signed rank test and analysis of frequency data were used to assess perceived cognitive impairment in relation to a predefined cut off score of ≤54 (Van-Dyk et al., 2020). To observe influences on CRCI including psychological wellbeing, exercise and nutrition, descriptive statistics were reported and analysed at baseline according to study arm (Intervention or Control). Independent sample t-tests were used to assess group difference at baseline of continuous variables age, years of education and peritoneal complications index score. Tests of normality (Shapiro-Wilks, Levene's Test), indicated that for continuous variables age and peritoneal cancer index, normality was violated, so the Mann-Whitney U test was used. Chi squared tests were applied for categorical variables Gender, Cancer Type, ASA grade and neoadjuvant treatment. In all cases raw data was analysed without transformation and all available observations were retained, and missing values were not substituted. Tests of normality including Shapiro-Wilks, Kolmogorov-Smirnov and evaluation of Q-Q plots and histograms per variable were used to assess normality. In all cases, non-parametric analysis including Mann-Whiney U and Wilcoxon Signed Rank tests were applied. For non-parametric analysis, Mann-Whitney U tests were used to evaluate the between group effect of group and baseline and preoperative assessment timepoints. Wilcoxon signed rank tests were used to assess the within-group effect of time on self-report data both at population and group level. To assess the influence of psychological factors on cognition, Spearman rank correlation coefficients were applied to evaluate relationships between perceived cognitive impairment and selected self-report measures. Across all tests, a p value of $p<.05$ two tailed was considered significant, and exact significance applied.

4.2.4 Qualitative Data Methods

4.2.4.1 Participants and Procedure

Twenty-nine participants took part in semi-structured interviews between September 2022 and May 2024 as part of their preoperative assessment. Interviews were conducted either by the PhD researcher or a member of the research team. Interviews took place either over the phone or in person (dependent on participant preference) and were recorded using a Dictaphone. Semi structured interviews followed a topic guide which was developed specifically for this research project (See Table 4.1 below). For phone interviews, participants were asked to be in a quiet location free from distractions. Patients were informed that any identifying information would be removed during analysis, and that any disclosure during the interview would not affect their care in any way. After the recording was completed, patients were debriefed and offered a follow-up support call, if required.

4.2.4.2 Semi-structured Interview Protocol Development

An interview topic guide was co-created by the PhD researcher with a Public Patient Involvement (PPI) panel. Interview topic guides were developed to address the following questions:

1. How do patients prepare for CRS-HIPEC treatment?

2. How do patients cope emotionally with their upcoming major complex surgery and what are their hopes for recovery?

3. How do patients experience cognitive function from diagnosis to pre-surgery?

4. How do patients perceive their own health, as well as perceptions of current and future health behaviours?

In addition, the specifics of the prehabilitation intervention were explored for those in the intervention condition. The draft interview topic guide was reviewed and amended by the PPI panel consisting of members of the public, and patients who had previously undergone the CRS-HIPEC procedure. The interview topics for both the intervention and control groups are outlined below in Table 4.1. Full topic guides for preoperative interviews are included in Appendix C.3.

Table 4.1

Topic Guide for Preoperative Interview

Topics	Intervention Group	Control Group
1. a	Feelings about Exercise Preparation	Preparation for surgery
b	Feelings about dietary preparation	
2.	Perception of surgery	Perception of surgery
3.	Cognitive health	Cognitive health
4.	Attitude towards own health and behaviour change	Attitude towards own health and behaviour change

4.2.4.3 Ethics

Ethical Approval for the study was obtained from Dublin City University Research Ethics Committee (DCU/2022/258) (See Appendix F.1). This research required a high degree of ethical consideration. For the qualitative investigations, particular care was given to the development of a public patient involvement (PPI) supported topic guide that aimed to address relevant research questions whilst also being aware of patient sensitivities regarding diagnosis, treatment and recovery. A short practice interview was also conducted with a member of the research team for training purposes. For all interviews, participants were made aware that their responses would not affect their medical care in any way, and that the use of the interviews was for research purposes. After interviews were completed, participants were asked if they required a follow-up check in call, due to the potentially emotional nature of interviews. To ensure research safety, an in-person research protocol was developed alongside project supervisors, along with appropriate escalations procedures as required.

4.2.4.4 Qualitative Data Analysis

Interviews were transcribed by either the PhD researcher, or a research assistant and any patient identifiers were removed. All of the analysis was undertaken by the PhD researcher. Interview data was coded using NVivo 14 qualitative research software (Lumivero, 2023). Codes were then organised topically and thematic maps generated

used Miro collaboration software. Reflexive Thematic analysis was applied to analyse the interviews (Braun and Clarke, 2022) to allow for the natural emergence of patient experiences. The aim of thematic analysis is to provide insight by identifying patterns and themes through focusing on the meaning across a given dataset (Braun & Clarke, 2012). Reflexive thematic analysis has been widely applied within healthcare research due to its flexibility for applied research settings and ability to compliment or provide further insight to quantitative self-report data (Braun & Clarke, 2014). Braun and Clarke's (2022, p 35-36) six step thematic analysis approach was applied, consisting of: 1) Data Familiarisation: This involved listening and reading the interview transcripts to become broadly familiar with the content of the interview set. Written notes and annotations were used to mark points of interest within the data familiarisation process. 2) Generating Initial Codes: Initial codes were highlighted using NVivo 14 software (Lumivero, 2023). Codes at this level acted as labels for features within the data set. Codes were generated at both a semantic and latent level. Relevant codes from the dataset were then collated and organised. 3) Generating Initial Themes: This involved examining the collated codes from step 2, and identifying areas of similarity to find potential themes, and collapsing codes that share identified features or patterns. Potential relationships between codes and themes are also considered. 4) Developing and Reviewing Themes: Potential themes were organised and assessed in relation to the dataset to ensure that themes and subthemes are representative of the dataset. This included identifying themes and codes and whether they were meaningful in the context of the dataset. Themes were organised in collaboration software Miro. 5) Refining, Defining and Naming Themes: Themes were refined and organised based on unique contribution and relevance to the research question. A hierarchical theme and subtheme map were generated in Miro by conceptually organising subthemes to a corresponding main theme. (See Appendix C.4). Theme names were generated and each theme and subtheme was defined. 6)Writing Up: Themes and subthemes were organised as a cohesive analytics narrative.

4.3 Results

4.3.1 Participant Demographic and Clinical Characteristics

Patient demographics and clinical factors for n= 29 patients are outlined below in Table 4.2. Of 29 patients, one did not proceed to surgery, therefore clinical data was not collected, however they completed both assessment timepoints, so data was retained. Of the 29, 15 were randomised to the control group and 14 to the intervention group, and 55% (n=16) were female. The average age was 58 (SD 11) years, and the age ranged from 30-73 years. Fifty percent of patients had pseudomyxoma peritonei (PMP) as primary cancer diagnosis. Twelve patients were given neoadjuvant treatment prior to surgery. For those in the intervention group, average time between baseline and preoperative interview assessment was 25.5 days, and average duration of intervention was 28.8 days. For the control group, average time between baseline and preoperative assessment was 25.45 days.

Group differences at baseline were non-significant except for peritoneal cancer index scores, an indicator of extent of tumour spread (p=<.05), which indicated that the intervention group had a significantly lower cancer index and tumour spread (Median=3.5), compared to the control group (Median= 14) (See Table 4.2).

Table 4.2

Participant Demographic and Clinical Characteristics (n=29)

Variable	Intervention (n=15)	Control (n=14)	Total (n=29)	Group Difference (p)
Age: **Mdn, IQR,** m, sd (n)	**55, 21,** 55.5, 12.99 (15)	**63, 10**, 61.1, 8.1(14)	**63, 13,** 58.2, 11.1, (29)	p=.377
Gender: Female, % (n)	8, 53.3% (15)	8, 57.1% (14)	16, 55.2% (29)	P=.837
Years of Education & Vocational Training **Mdn, IQR,** m, sd (n)	**17.3, 4.0,** 17.4, 3.1 (10)	**17.0, 5.5**,15.1, 4.6 (9)	**17, 5.0**,16.3, 3.9 (19)	p=.356
Cancer Type				
(n)	(14)	(14)	(28)	p=.774
Colorectal n	5	4	9	
Ovarian n	2	2	4	
PMP n	7	7	14	
Other n	0	1	1	
ASA Grade				
(n)	(14)	(14)	(28)	p=.587
Normal Healthy	1	0	1	
Mild Systemic Disease	6	6	12	
Severe Systemic Disease	7	8	15	
Peritoneal Cancer Index **Mdn, IQR**, m, sd (n)	**3.5, 16.0,** 9.6, 9.9 (14)	**14.0,12.5,** 16.6, 8.6 (14)	**11.5, 18.25,** 13.14, 9.78 (28)	p=.021*
Neoadjuvant Treatment				
(n)	(15)	(14)	(29)	p=.876
Yes	6	6	12	
No	9	8	17	

Note: *Significant at p<.05 non-parametric, two tailed exact test statistic, m=mean, sd=standard deviation, Mdn=median, IQR=Interquartile range ASA=American Society of Anaesthesiologists Grade, PMP= pseudomyxoma peritonei

4.3.1 Quantitative Results

4.3.1.2 CRCI Prevalence

In order to determine CRCI prevalence, the FACT-Cog Perceived Cognitive Impairment (FACT-Cog PCI) subscale was used to determine the proportion of patients exhibiting impairment based on a predefined cut off score of ≤54. Results of a one sample Wilcoxon signed rank test at baseline and pre-surgery determined that median PCI scores differed significantly from a test value threshold of 54 indicating that impairment was not observed at a group level at baseline (Mdn= 68, z= 261.5, n=23,

p<.001), or pre-surgery (Mdn = 66, z=55.5, n=11,P=.045). Analysis of frequency reported that of n=23 included cases who completed the baseline PCI, n=3 (13.04%) of participants scored on or below this threshold on the FACT-Cog PCI subscale, indicative of perceived cognitive impairment (Van-Dyk et al., 2020). Pre-surgery, of n=11 available PCI scores, n=3 (27.3%) of participants scored on or below this threshold, indicating perceived cognitive impairment based on a predefined cut-off score (Van-Dyk et al.2020).

4.3.1.3 Relationship between CRCI and Psychological Wellbeing

A Spearman rank correlation coefficient was calculated in order to evaluate the relationship between CRCI as measured by the Fact-Cog PCI subscale at baseline, and variables associated with psychological wellbeing such as distress and general emotional function (NCCN Distress Thermometer, The Emotional Wellbeing Subscale (EWB) of the FACT General, and the Impact of Events Scale-revised (IES-r). There was a significant moderate positive correlation between the FACT-Cog PCI and FACT-G EWB subscales, *r*s (20) =.481, p=.023. Correlations with the other self-report measures were non-significant: IES-r, *r*s (19) =-.274, p=.229, NCCN, *r*s (21) =-.289, p=.181.

4.3.1.4 Between-Group Effects Differences Between Control and Intervention Groups Across Self-Report Data

Tests of normality indicated that in all cases self-report data was not normally distributed. Due to participant attrition and the challenge of data collection with a patient cohort about to undergo complex major surgery, n=13 participants completed preoperative self-report data. The matched sample between baseline and preoperative assessments includes the data ranging from 7 to 12 participants across each of the self-report measures across measures of cognitive impairment (Table 4.5), psychological wellbeing and health related quality of life (Table 4.7). For clarity, samples for each measure, and matched samples across baseline to preoperative timepoints are included across tables. A Mann-Whitney U test was performed to evaluate whether self-report cognition data differed by control or intervention group (Table 4.3). There was no significant difference between groups at baseline or pre-surgery on Fact-Cognition scores.

Table 4.3

Mann-Whitney U Test- Baseline and Preoperative Difference Between Control and Intervention Groups on FACT-Cognition Scores

Variable	Intervention Mean Rank Score	Control Mean Rank Score	z	p	n
FACT COG Total Baseline	10.45	13.42	83	0.32	23
FACT COG Total Preoperative	6.43	5.25	11	0.65	11
Perceived Cog Impairment Baseline	11.18	12.75	75	0.61	23
Perceived Cog Impairment Preoperative	6.43	5.25	11	0.65	11
Comments from Others Baseline	10.9	12	66	0.72	22
Comments from Others Preoperative	6.29	5.5	12	0.79	11
Perceived Cog abilities Baseline	10.36	13.5	84	0.29	23
Perceived Cog abilities Preoperative	6.93	4.38	7.5	0.23	11
Impact on QoL Baseline	10.73	13.17	80	0.41	23
Impact on QoL Preoperative	5.93	6.13	14.5	1.00	11

Note: *p<.05, Exact Significance Applied

Similarly, results on the Mann-Whitney U tests assessing differences on baseline and preoperative psychological wellbeing scores were also non-significant for baseline (base) and pre-surgery (pre) timepoints. IES-R (base z=52, p=0.606; pre z=10, p=0.762), GSE (base z=71.5, p=0.74; pre z=11. p=0.648). Scores between groups on the NCCN distress thermometer at baseline approached significance at p=0.068 but were non-significant at preoperative assessment (base z=40.5, p=0.068; pre z=9.5, p=0.61).

With regards to health-related quality of life, tests indicated that there were no significant differences between group scores at baseline or pre-surgery assessments. Scores for all other patient reported outcomes are outlined below in Table 4.4.

Table 4.4

Mann-Whitney U Test- Baseline and Preoperative Difference Between Control and Intervention Groups on Other Patient Reported Outcomes

Variable	Intervention Mean Rank	Control Mean Rank	z	p	n
FACT-General					
FACT G Total Baseline	11.5	12.55	72	0.74	23
FACT G Total Preoperative	5.93	6.13	14.5	1.00	11
Physical Wellbeing Baseline	13.04	10.86	53.5	0.45	23
Physical Wellbeing Preoperative	6.93	4.38	7.5	0.23	11
Social Wellbeing Baseline	11.29	12.77	74.5	0.61	23
Social Wellbeing Preoperative	5.14	7.5	20	0.32	11
Emotional Wellbeing Baseline	11.92	12.09	67	1.00	23
Emotional Wellbeing Preoperative	5.93	6.13	14.5	1.00	11
Functional Wellbeing Baseline	10.55	12.45	71	0.52	23
Functional Wellbeing Preoperative	5.86	6.25	15	1.00	11
Self-Efficacy Baseline	11.54	12.5	71.5	0.74	23
Self-Efficacy Preoperative	6.36	5.38	11	0.65	11
NCCN Distress Baseline	15.13	9.88	40.5	0.07	24
NCCN Distress Preoperative	5.92	4.88	9.5	0.61	10
Impact of Events Baseline	12.27	10.73	52	0.61	22
Impact of Events Preoperative	5.83	5	10	0.76	10
EuroQol Global Score Baseline	12.19	13.88	88.5	0.57	25
EuroQol Global Score Preoperative	9.1	5.89	9.5	0.13	13

Note: *p<.05, Exact Significance Applied

4.3.1.5 Within Group Effects

To assess change across time on patient reported outcomes, a Wilcoxon signed rank test was conducted to evaluate the effect of time across self-report data from baseline to preoperative assessments. The results of the Wilcoxon signed rank test, medians (Mdn) and population (n) are reported below in table 4.6. For cognitive function, the Wilcoxon test indicated that there was a significant difference of time on the impact on quality of life (Impact on QoL) FACT-Cognition subscale, with

significantly higher scores reported at preoperative assessment (Mdn=15), compared to baseline assessment (Mdn=12). Results for the FACT-Cognition are displayed below in table 4.5.

Table 4.5

Wilcoxon Signed Rank Test-Baseline to Preoperative Assessment for FACT-Cognition

Variable	Baseline	Preoperative			
	Mdn	Mdn	z	p	Matched n
FACT COG Total	117	114	-,415	.678	9
Perceived Cog Impairment	68	66	-1.602	.109	9
Comments from Others	16	16	-1.00	.317	8
Perceived Cog abilities	27	19	-.422	.673	9
Impact on QoL	12	15	-2.380	.017*	9

Note: *Assumption, two tailed p <.05, Mdn= Median

A Wilcoxon-Signed Rank Test was conducted on control and intervention groups separately to determine differences across time between group conditions. The test indicated that there was a significant difference between baseline and pre-surgery (z=-1.992, p=.046) for the FACT Cog impact on quality of life (Impact QoL) subscale for the intervention group only. The median score for the intervention group was Mdn=7 at baseline compared to Mdn= 15 at pre-surgery. All other scales reported a non-significant difference for either intervention or control groups. Results are reported below in table 4.6.

Table 4.6

Wilcoxon-Signed Rank Test by Intervention and Control Groups for FACT-Cognition Scores

Variable	Baseline Intervention	Preoperative				Baseline Control	Preoperative			
	Mdn	Mdn	z	p	Matched n	Mdn	Mdn	z	p	Matched n
FACT COG Total	114	125	-.736	.462	6	126	98.5	.00	1.00	3
Perceived Cog Impairment	66	67	-.526	.599	6	69.44	62.0	-1.604	.109	3
Comments from Others	16	16	.00	1.00	5	16	16	-1.000	.317	3
Perceived Cog abilities	25	26	-.674	.500	6	27.5	15	-1.604	.109	3
Impact on QoL	7	15	-1.992	.046*	6	14	15.5	-1.342	.180	3

Note: *Assumption, two tailed p <.05, Mdn= Median

With regards to psychological wellbeing, the Wilcoxon signed rank test found no significant differences between baseline and pre-surgery scores on the NCCN Distress Thermometer, The Impact of Events Scale-Revised and The Generalised Self Efficacy Scale. Similarly, for health-related quality of life, the Wilcoxon signed rank test found no significant differences between baseline and preoperative assessment time points, including EuroQoL Global Health score, Fact-General and Fact General subscales (PWB, SWB, EWB, FWB). For a full breakdown of scores for psychological wellbeing and health-related quality of life, please see Table 4.7.

Table 4.7

Wilcoxon Signed Rank Test from Baseline to Preoperative Assessment for Other Patient Reported Outcomes

Variable	Baseline Mdn	Preoperative Mdn	z	p	Matched n
FACT General					
FACT General Total	86.5	88.42	.491	.623	8
Physical Wellbeing	25	26	-1.362	.173	8
Social Wellbeing	27.5	26.92	-0.254	.799	8
Emotional Wellbeing	14	16.5	-0.315	.752	8
Functional Wellbeing	20.5	22.5	-0.949	.343	8
General Self Efficacy	34	32	-.422	.673	8
NCCN Distress Thermometer	3.5	3	-1.153	.249	9
Impact of Events Scale	20.5	21.5	-.845	.398	7
EuroQoL Global Score	77.5	70	.120	.905	12

Note: *Assumption, two tailed p <.05, Mdn= Median

4.3.2 Qualitative Results

4.3.2.1 Interview Information

Twenty-nine patients completed the preoperative interviews (Table 2). The average days before surgery was m= 3.27 (1.15). Average interview duration was 24.04 minutes (range 09.42- 1.00.36, Mdn 22.51). Intervention and control groups were not analysed separately, as the objective of the interviews was to gain in depth understanding of the patient experience of cognitive and psychological factors as they prepare for surgery, and not solely factors related to intervention experience. Participant quotes are labelled as follows: (Gender, Age, Intervention/Control group). Interview responses were coded as either AS or SM.

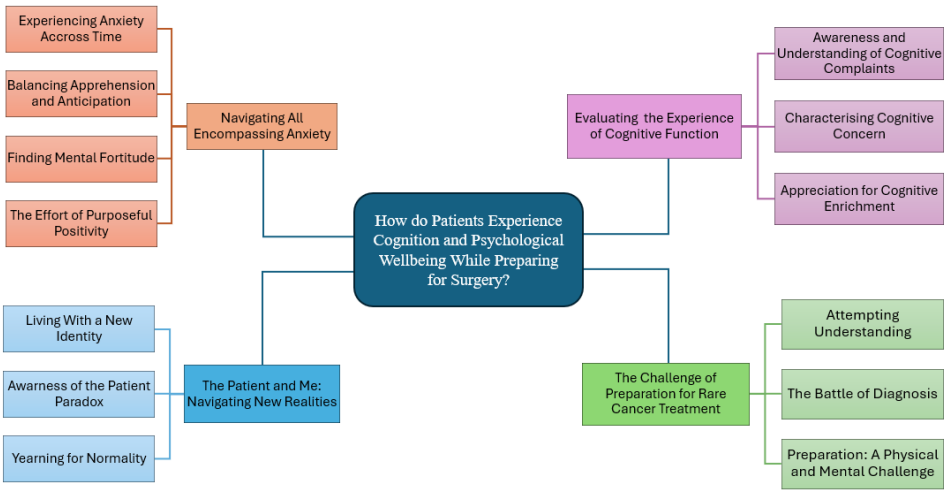
4.3.3 Thematic Analysis

In understanding (1) how patients experience their cognition while preparing for surgery and (2) how patients experience psychological factors that can relate to cognition, four central themes were identified through the analysis. The first theme

Navigating All Encompassing Anxiety explores the efforts made by patients to mentally combat the inevitable anxiety felt as they approach their surgery, and how this anxiety is rooted in past, present and future experiences. The second theme, *The Patient and Me: Navigating New Realities,* illustrates the new role and realities adopted by patients upon diagnosis, as well as the apparent contradictions between how they themselves may feel, and the severity of their forthcoming treatment. The third theme, *Evaluating the Experience of Cognitive Function,* illustrates cognitive dynamics including areas like awareness, the interplay between cognition and psychological factors, and also cognitive domains of interest. Finally, *The Challenge of Preparation for Rare Cancer Treatment* highlights the nature of preparing for CRS-HIPEC treatment, coming to terms with their rare cancer diagnosis through reflection, and the mental and physical preparation involved. Main themes and subthemes are outlined below in figure 4.2.

Figure 4.2

Preoperative Thematic Map



4.3.3.1 Theme 1: Navigating All Encompassing Anxiety

This theme captures the nature of the anxiety experienced by patients preoperatively, and efforts they made to combat these feelings which are explored across four subthemes. Many patients experienced an overwhelming sense of anxiety about their upcoming surgery, and it constantly occupied their thoughts. "*It's all of the*

stuff em, that's going on in my life altogether, it's too much and there are days where you wish you could hide in your bedroom and close the door and do something mindless" (Female,42 Intervention). Anxiety was represented both in the context of the past, as well as projected on to their future experience of recovery. This theme explores how patients navigated their anxiety. For many, a sense of positivity and optimism was evident and there was an acknowledgement that although at times difficult, optimism was the best way to maintain a positive perspective of surgery. Patients leaned on sources of optimism to nurture the necessary psychological strength and ultimately expressed a sense of anticipation about surgery and their future recovery. These experiences are encapsulated across four subthemes: *1. Experiencing Anxiety Across Time, 2. Balancing Apprehension and Anticipation, 3. Finding Mental Fortitude, 4. The Effort of Purposeful Positivity.*

4.3.3.1.1 Subtheme 1: Experiencing Anxiety Across Time. For patients, anxiety was experienced and expressed in a non-linear, all-encompassing manner, with patients often exploring multiple sources of anxiety across timepoints. Some anxiety was rooted in patients' own perceptions of their preoperative health and health before diagnosis. Wellbeing was a source of concern, and how it could potentially negatively impact on their recovery. Possible physical and psychological reasons to help explain their diagnosis were explored, both as a way to reflect on their diagnosis and act as a source of clarity, and to perhaps grapple with the shocking nature of an unexpected cancer diagnosis. *"So, I'm kind of wondering., is all that is all that worry and stress probably ...might have affected my immune system or something?* (Female, 66 Control).

They also reflected on their lifestyle to date, and worried that potentially their poor current physical health could hinder recovery.

> " *I would eat vegetables, but I really want to be- you know I've got this cancer for a reason - so I'm thinking you know why did it appear? You know, was it anything- was it linked to my diet?"* (Male, 61, Control).

Another common source of concern was the more immediate future and recovery. Patients explored the various psychological and physical difficulties that they may encounter during their immediate postoperative recovery. The severity and length

of the surgery itself was a source of worry for patients as well as a fear of possible postoperative complications, such as a colostomy bag.

> *"There's anxiety there- it's a big, it's a big serious operation, it's eh you know 7 hours 8 hours on the table, that's a long time. And it's, it's an unfortunate sort of diagnosis that I have. It seems to be a particularly tricky and rare"* (Male, 63, Control).

This surgical anxiety was overwhelming, and interacted with their daily lives, occupying thoughts and manifesting in physical ways, such as difficulty sleeping.

> "*I was in the hospital yesterday and I walked out with the idea "I don't want to do this". (AS okay) It's so excessive, it's so extensive, it's extraordinary life changing, my life in essence is over- that's how I see it".* (Male, 53, Intervention).

Anxiety was also projected onto long-term recovery and future quality of life. This anxiety was rooted in uncertainty and a sense of the unknown. It was expressed more as what patients wished or intended for their future recovery and life, but acknowledgment that at present it is not possible to provide themselves with any reassurance. This anxiety included self-doubt about the ability to cope with life after surgery, in particular changes to day-to-day lifestyle.

> "*It's just that the initial thing of "how will I cope?" and like food wise and you know it's just changing...I-I-suppose it's – it's the fear of like all the things that are going to change in my life you know that kind of way like?*" (F, 66, Control).

Existential anxiety was also evident, whereby patients pondered their own mortality and spirituality, and how this may have changed as they approached surgery.

> *"I suppose I kind of… people aren't really too aware of the morality until it's kind of put in front of them like I think when you get cancer diagnosis it kind of puts a bit of an hourglass in front of you and you kind of realise that… life's very finite"* (Male, 30, Intervention).

4.3.3.1.2 Subtheme 2: Balancing Apprehension and Anticipation. This subtheme highlights the contradictions in patients' emotions regarding surgery. Patients

navigated contrasting emotions and were aware of these apparent contradictions acknowledging feeling, "*delighted to be having it, but I'm terrified at the same time"* (Female, 68, Control). They explored their reasons for these feelings, namely their hopes for their future that at times eclipsed current anxiety. "*I'm kind of., I can't wait to kind of get it over and done with [..] and the other part I suppose there's a little bit of anxiety knowing that it's quite eh major surgery"* (Female, 53, Control).

Patients expressed feelings of both frustration and anticipation. Despite feelings of apprehension about the surgery itself and recovery, there was a sense of impatience and a longing for the surgery to be over with. Patients were*:*

> *"at a point where I just want it done now. I feel like I just need to get past it. I know the lead up to any of these types of things is often - it's a different type of worry but it's a little bit worse because you're just thinking - it occupies your head* (Female, 42, Intervention).

Despite experiencing anticipation for surgery, patients also felt anxiety and trepidation at the thought of the severity of surgery itself and the possibility of postoperative complications. As surgery approached, patients were forced to face the reality of their situation. Time both allowed patients to forget about their surgery day to day but as time drew closer, the reality of surgery was a source of anxiety. *"Now that it's, now that it's coming close, I suppose I am concerned about the em…any possible complications when the surgery is happening or whatever [..] the aftermath more the…more how I'll be physically"* (Female, 57, Control).

4.3.3.1.3 Subtheme 3: Finding Mental Fortitude. Finding the mental fortitude to combat anxiety and distress was important for patients. Patients found mental fortitude in a number of ways. In terms of physical reassurance, patients with a high degree of physical fitness and health believed that their physical state would be of benefit to them in the postoperative phase. *"Well, I know probably from exercising that should help by my muscles- that should help my body recover, I know the protein I'm taking should help my body recover."* (Female, 64, Intervention). This was regardless of intervention or control condition, but patients taking part in the exercise intervention were also aware of the potential physical benefits of exercise and nutrition supports to promote postoperative recovery.

Patients also found prior medical history, including previous cancer treatments, or unrelated surgeries helpful when predicting how they will recover. For patients who were receiving neoadjuvant treatments or other surgeries prior to their CRS-HIPEC, their response to these treatments were further reassurance that they may also tolerate surgery well.

> *"I just have to remind myself that I recovered strongly after my first operation [..] that hopefully that I -I might have nearly you know obviously not the same strength but near enough hopefully to it and that I coped with chemotherapy…you know made me feel more optimistic about the future."* (Female, 66, Control).

They acknowledged that although this surgery is linked to increased postoperative complications and may be more intensive than their prior experiences, if they recovered well from prior experiences, this could reduce the risk of a long hospital stay, or postoperative complications. Trust in the medical team itself was also a source of fortitude for patients. They expressed appreciation for the expertise of the surgical team, as well as the care and information provided by the wider medical team in the run up to surgery.

> *"I've great confidence in the surgery team that I've been talking to and they kind of give this feeling of you know they know what they're doing and they've done this before and em you know they've seen many [patients name], before me like sort of thing *laughs* and, eh I've great confidence with them"* (Female, 66, Intervention).

Family was another source of mental fortitude and external motivation for patients while preparing for surgery. Family members motivated patients to strive to recover well, and in the preoperative phase motivated them to make the lifestyle changes necessary to optimize recovery, either directly through the intervention program or without it. *Now if my husband hadn't of kept at me, I possibly would have been lazy and wouldn't have done them. You know? But yeah. No, I enjoyed [the exercises].* (Female, 66, Intervention). Patients expressed gratitude for the support, in particular practical support, received by family members, and felt a sense of responsibility in ensuring a positive recovery so as not to further disrupt family life. *"So their lives haven't changed that was, that was really important to me, that their*

routine and their lives aren't affected by this you know?" (Male, 38, Intervention). Important family milestones and events were also used as goals for patients to strive to attend and be a part of post-surgery. Patients drew on these future milestones for determination and motivation.

> *"It's literally a couple of hours I presume sitting in a hall, em watching everybody who's in med school get their certificates. But just to be there with him and with the family you know? And em as I say it's the 1st of [Month] so obviously if I can't get there it's not the end of the world, but it's kind of a little - a little goal that I think I should aim for, even to be there briefly you know?"* (Female,65, Control)

4.3.3.1.4 Subtheme 4: The Effort of Purposeful Positivity. Feelings of optimism and positivity were expressed alongside or in response to feelings of worry and concern. However, positivity involves effort and purpose to maintain, as it can be directly challenged by periods of low mood. Some patients acknowledged the range of medical challenges they have faced to date, and the upcoming challenge of surgery, but above all maintained a sense of optimism and awareness that surgery is a necessity. "*So I view the surgery as something necessary but positive to, you know to take it out, you know whatever has to come out and give me a chance to keep fighting"* (Female, 67, Intervention).

Some patients also defined their positive mindset as a part of their personality, and the natural way that they approached any prior life challenges.

> *"I would say generally good. I mean you know I live on the mantra that the glass is half full so, eh positivity is where I go with it you know I try to kind of turn you know whatever the negative into a positive eh wherever possible*" (Male, 55, Intervention).

For these patients they felt that the natural response to surgery was a positive mindset. Their positive personalities helped them navigate their challenges to date.

Other patients described positivity as a psychological state that had to be maintained in order to mentally face the challenge of CRS-HIPEC, and to come to terms with their diagnosis. It was a purposeful state, adopted and maintained actively by patients as they felt it was necessary for their psychological wellbeing and as a way

to cope with future uncertainties including postoperative complications. *"God I am positive, I have to be positive like you know?"* (Male,40, Control). Patients also expressed feelings of depression and anxiety but acknowledged that a positive mindset could aid in alleviating periods of psychological distress.

> "*I think for them to dive straight in like this is a good thing. So yeah, I know it could come back but I'm trying not to think about that. And eh, you know I'm trying to stay positive for my family as well because it's very easy to slip over to the dark side."* (Male, 61, Control).

Despite largely maintaining positivity, periods of low mood were unavoidable. Negative emotion for most patients was periodical, with times of *"sort of stepping...from-into the shadow and out"* (Female, 54 Intervention). Depressive states and negative emotion were associated with acknowledging that surgery is approaching, or reminders of their illness. Patients ultimately were very aware of the mental and physical challenges that faced them but chose to either find comfort in their naturally positive mindset, or to actively foster this mindset. In the face of the medical challenge of surgery, a positive mindset was understood as necessary to deal with the challenges of surgery.

> *"Yeah, I think like that mentally really helps me and I think like it puts me in the healthy mindset in terms of like...yeah I have this thing to deal with and like...yeah it can be overcome like and regardless of it …being there and being present, I feel good"* (Male, 30, Intervention)

4.3.3.2 Theme 2: The Patient and Me: Navigating New Realities

This theme encapsulates the notion that for many patients, diagnosis is not only accompanied by psychological stress, but also the creation of a new identity and a new way of navigating reality. Patients take on many new roles and responsibilities. "*It's hard to be, it's hard to keep up the diligence all the time but then you are concerned about- are you meeting the right kind of criteria? Are you doing the right thing?"* (Male,30, Intervention). They engage in information seeking about their condition, advocating for their own wellbeing and navigating the complexities of treatment options. They also act as a support and science communicators for family and friends, sharing information about their condition and disease progression. This sense of

identity is explored in the subtheme *Living With a New Identity.* The second subtheme, *Awareness of the Patient Paradox,* explores coming to terms with the patient experience and new identity, but having relatively few symptoms and how this creates internal conflicts. Finally, *Yearning for Normality* illustrates how in response to this new sense of identity, patients yearned to return to a state of normality, and spent time exploring the possibilities of their future post-surgical quality of life. Whilst trying to maintain a sense of normalcy, patients were sometimes affronted by reminders of their condition, such as the realities of physical recovery and dealing with postoperative complications.

4.3.3.2.1 Subtheme 1: Living with A New Identity. With diagnosis comes the acceptance of a new role of patient, which takes up not only physical time, but also psychological space in day to day life. Patients have to learn to navigate their old life and responsibilities with the added complexity of treatments and surgeries. They also have to learn to live with an increased awareness of mortality as a result of their diagnosis.

Physical manifestations and reminders of the patient's status were met with anxiety and stress. The possibility of having a stoma bag due to postoperative complications was a large source of stress. The stoma would act as both a possible longer term physical change, but also a physical manifestation of patient status and a new reality for patients to navigate in daily life.

> *"I'm dearly hoping that wherever the cancer is in the colon, he'll be able to em, take it out and put it back together again. I say it's my ignorance about the bag but- I just, any alien body, em I would find, I think very difficult to cope with, you know?"* (Female, 65, Control).

Some patients were very aware of how they navigated their illness when dealing with friends and family. They did not want their illness to change how they were perceived amongst those close to them, or for it to place artificial limitations on them when taking part in activities with others. "*That highlights your disease when that happens. [...]just makes it more dramatic, it makes it more dramatic so people say "(Name) can't do it because she has to have surgery". Then you become...you become that person with cancer* (Female, 59, Control).

Patients struggled to come to terms with an increased sense of vulnerability and awareness of mortality that they carry in daily life pre-surgery as well as the knowledge that this new awareness will possibly persist into postoperative life.

> *"I thought I'd live into my 80s sort of thing you know, I supposed we all do (SM Yeah) but em ehh…you know, and I didn't expect…at this stage of my life feeling ... these big worries do you know what I mean?"* (Female, 66, Control)

This new awareness of mortality was difficult to navigate in daily life, and coloured mundane experiences like travel.

> *"not kind of emotional about it but it is it's hard to describe like do you know even leaving my house in Dublin today was kind of a bit like… yeah you be reminiscing about things as though you're not going to come back like- and I know that's a very- that's a very strange and a bit dramatic but… yeah that's kind of the way you are and you kind of have to snap yourself out of it" (*Male, 30, Intervention)

4.3.3.2.2 Subtheme 2: Awareness of the Patient Paradox. Although there was a strong awareness of the severity and intensity of the upcoming surgery, an apparent paradox existed between degree of illness, and a lack of physical symptoms, or current high levels of patient quality of life. For many, life continued as normal and included high levels of physical activity. For patients participating in the intervention program, it did not present a major difficulty for them and was easily adapted into day to day life. This paradox created a sense of confusion. *Do you know it sounds crazy? I feel quite good!* (Female, 55, Control). Their health status as a cancer patient was at odds with their physical ability as for many patients, they were able to maintain a level of fitness that they were satisfied with. *"Yeah so, I'm like I'd consider myself apart from needing to have this surgery I'm fit and well. You know Im- I haven't been this last week and a half, but I had been walking about 5k a day"* (Female, 66, Control).

Patients were also aware that this lack of physical symptoms may be at odds with what is expected by others, and that they may present as physically well in public despite their illness.

> "*No, I feel really good honestly like I think I'm not in pain, I'm not like- unable to do things, like and that's…I think such a strange thing for me to kind of cope*

to come to terms with that and just like, I've never really had any… deficits or impact. Apart from like being in chemo where obviously there's a change to my appearance, but most people are almost like in disbelief when I tell them" (Male, 30, Intervention).

The exercise and nutrition intervention further added to this disparity, as for some, their current levels of physical fitness exceed the scope of the program.

"*They just appeared em -that's very judgemental of me- appeared much more em sick and em just I suppose the level of exercise that was going to be happening at the class would have been way below what I'm currently capable of* "(Female, 42, Intervention).

This was encouraging for them as it provided validation about their physical preparation for surgery, but further exemplified the disparity between apparent physical fitness, and the reality of having a cancer diagnosis. *"So, my concern was that the program would be designed for, like a sick person, and in my head I'm not sick, there's nothing wrong with me do you know what I mean"* (Male, 38, Intervention).

The juxtaposition between illness and absence of symptoms was a disorientating experience, whereby patients maintained a functional quality of life, but could not avoid the fact that they were in preparation for major complex cancer surgery.

"You know, like I haven't lost my hair. I haven't lost weight. You know I haven't done any of that, you know what I mean? So, em…I'm not, yeah...I suppose that's my biggest fear of this surgery now will that change" (Female, 59, Control).

4.3.3.2.3 Subtheme 3: Yearning for Normality. Regardless of present physical health status, patients longed to return to a sense of normality. The concept of normality was represented as a past state that once was, a state that can be recovered in the postoperative period, and also as a new normal fraught with uncertainty. Changes in normal day to day life were largely based on patients' individual life experiences and comparing this to changes from diagnosis or discussing what may change post-surgery.

The concept of returning to normality was explored primarily through what was physically and practically possible for patients at that time, and how this may change into the future. Even for patients who did not feel physically unwell, this period in their

lives still represented a period of intense stress and physical uncertainty. Those with lower quality of life expressed a longing to return to a previous standard of health. *"I'm not really able to engage in everyday life I used to do just basic- like I'd just love to be able to get back to my kind of normal life where I did the shopping and the cooking and the minding of everybody"* (Female, 65, Control). Patients discussed various possibilities for the future that involved returning to activities that they were about to take part in prior to their diagnosis. *"I hope I will be able to do things I've been doing like up until now- well not so much gardening- but a bit of gardening"* (Female, 68, Control). Patients longed for the time before their diagnosis, or to move beyond the point of surgery and experience life after recovery.

For others, there was an acute belief that what was once normal will no longer be possible once surgery is completed. Diagnosis represents the end of current reality as understood by patients. Future possibilities were discussed with a sense of uncertainty, and awareness of potential future physical and mental limitations.

> *"You recover from the surgery, but you don't recover really. Your body changes forever. Anyway, but if you've your ovaries out you just catapult 10/15 years forward in terms of your …. Menopause and perimenopause. So… there's a lot of unknowns*" (Female, 42, Intervention).

Patients expressed hope that future quality of life would be positive, but this notion was marred by acknowledgment that life as they knew it, would never be the same. This was evident in patients who had multiple surgeries and treatments prior to CRS-HIPEC, as what is now a normal quality of life for them had been coloured by their past medical recovery experiences.

> "*Yeah well, I don't think normally where is, I've a new norm now sort of when I was diagnosed my erm thinking was you know do everything I can to get back to normal but I, I'll never reach that"* (Female, 67, Intervention)

Normalcy was an illuminating concept and provided insight into patients' self-perceptions of their own capacity to not only recover physically, but also to mentally recover from the trauma of surgery. Patients expressed uncertainty about their future realities, but also certainty about the fact that regardless, the concept of normal was redefined.

"Life has obviously changed quite a bit like but...I still held on to a lot of aspects of it like and even if it dramatically changed overnight, as long as I'm still alive and I can chat to my family and enjoy their company, that's really all I care about" (Male, 30, Intervention)

4.3.3.3 Theme 3: Evaluating the Experience of Cognitive Function

This theme elucidates how patients make sense of their own perceived cognitive function and how that is ultimately expressed. *"I feel like the world is moving faster than I am, if you know what I mean (SM Okay), I can't keep up, do you know that kind of way?"* (Female, 66, Control). Whilst reflecting on cognition, participants acknowledged both cognitively taxing activities and psychological states, as well as potentially enriching activities and lifestyles that could contribute towards healthy cognitive function. Subtheme 1, Awareness *and Understanding of Cognitive Complaints,* illustrates the degree to which patients reflected on the existence of cognitive problems, and the various factors that they attributed issues in cognition to. It also highlights those for whom cognition was not a concern. In subtheme 2, *Characterising Cognitive Concern,* particular domains of cognitive concern are illustrated, as patients reflected on instances when they perceived impairment and how these were represented in daily life. Subtheme 3, *Appreciation for Cognitive Enrichment,* describes the process of introspection and reflection whereby patients discuss cognitively demanding and enriching activities that they believe may have contributed to their overall level of cognitive reserve, and in turn potentially protect them from cancer related cognitive impairment.

4.3.3.3.1 Subtheme 1: Awareness and Understanding of Cognitive Complaints. Patients displayed high levels of introspection and an ability to examine their cognitive function. Patients described observing issues with their cognitive function and were able to reflect on these across time and across situations. In some cases, cognitive issues were pronounced with patients observing marked differences in everyday life, illustrating how these struggles impeded on everyday tasks and negatively impacted wellbeing. *We don't have to drive all the time, but I do sometimes go ok when I am driving "really focus, really focus!" because otherwise I may miss*

something" (Female, 55, Control). Others oscillated between periods of high and low cognitive function as they navigated diagnosis, preparing for treatment and in some cases neoadjuvant treatments like chemotherapy. *"And, you know I'm – I'm I feel after- but during chemo I-I would have found a little bit you know, my head a little bit fuzzy. But other than that, now that has gone"* (Female, 65, intervention). The use of prompts or other cognitive strategies was also discussed as a way to combat or cope with any noticed cognitive concerns, indicating a habitual awareness of impaired function. *"It just is and you just kind of accept it. Um I write down lists, I… use a calendar a lot because I find… it's stressful if I don't know"* (Female, 45, Intervention). For others, preparing for surgery was not associated with any deficits in cognitive function. These patients observed that their cognitive function did not deviate largely from its pre diagnosis state. *"I said with regards to health my memory is the same as it always has been and that nothing has changed there"* (Male, 66 control).

Some patients posited that cognitive impairment may have been present either prior to diagnosis, or during the pretreatment period.

> *"Before I "got sick" but like I had stuff I had pains in my stomach for a year, year and a half...I just never...they'd come and go, and I just put it off and just keep working. But I'd notice from back then it would have even been a year before the just little things little things like that as I said like the tv, not major things now just little things"* (Male, 45, Intervention).

Others attempted to explain or excuse experiences by attributing them to possible personal and treatment related factors. For example, age was highlighted as a potential contributing factor to any described cognitive concerns, with patients often referencing their age when discussing issues with memory. *"See that's a hard one- well it's not a hard one but as a person matures, one's memory and one's cognitive behaviour kind of slightly changes anyway"* (Female, 66, Intervention). Patients also posited that cognitive concerns were common across either patients, or the general public. Medical and treatment related factors, particularly chemotherapy were also discussed as potential causes of cognitive concerns. It was assumed that any issues are *"down to me and probably chemobrain"* (Female, 63, Control) and that chemotherapy possibly impacted cognition.

Patients were acutely aware that preparation for surgery is a time of immense stress and uncertainty, and that this may undoubtedly impact on their cognition. For many, the concept of wellbeing was understood as both influenced by and an influencing factor on cognitive function. *"I was also very anxious and very stressed, and my mind was very consumed with the diagnosis at the time as well"* (Female, 45, Intervention). Stress and a sense of being overwhelmed contributed to cognitive experience by exacerbating feelings of distraction, overthinking and preoccupation.

> *"My head is very full. Em it was full before this anyway- in terms of my day to day life at the moment- where I'm at, there's a lot going on anyway. Em, so this added in has led to absentmindedness, zoning out at times*" (Female, 42, Intervention).

Patients acknowledge that between their diagnosis and surgery, they find it arduous to focus on daily responsibilities, and that this would naturally impact on ability to focus and attend to daily life.

In contrast to negative perceptions and feelings about cognitive state, there was also a sense of resignation in the face of the cognitive issues described. This resignation was illustrated as accepting their current level of cognitive function *"I just kind of get on with it..."* (Male, 73, Control). Patients avoid worrying or examining their described concerns, often accepting them as a reasonable side effect of the overall cancer experience, whether this be due to medical treatments or the stress and anxiety associated with diagnosis. *"I don't know, I don't know if it changes the way I feel you just kind of go "argh" you know it wouldn't bother me too much to be honest with you. Not a dramatic thing."* (Male, 55, Intervention). Distraction was also seen as a positive sensation, an aid to avoid becoming overwhelmed by the prospect of surgery.

> *"The area I work in I understand as well that some of those are protective factors like your brain will zone you out and those - you almost go into that em trance like state at times. So, my work has helped me in some ways it's been a distraction"* (Female, 42, Intervention)

Patients had an awareness and understanding of their cognition. Cognition was understood as fluid, with patients reflecting on periods of changing function, as well as contributing factors that may influence the cognitive experience.

4.3.3.3.2 Subtheme 2: Characterising Cognitive Concern. This subtheme characterises the primary areas of cognitive concerns that were discussed by patients. For patients experiencing cognitive issues, either presently or in the past, patterns emerged in terms of the nature of cognitive deficits experienced, with these issues manifesting primarily across two areas of cognitive function: memory and concentration. Short term memory or recall were highlighted, whilst concentration issues were noticed when attempting daily tasks or leisure activities.

> *"I do know I'm distracted, it sounds so stupid, but you know I have noticed I'm running my eyes- a bit like what I was saying about reading dense books- I run my eyes across the list and actually not read it"* (Female ,55, Control).

Short term memory and generalised memory issues were a strong focus of cognitive concern. Patients frequently described experiences of forgetfulness, in particular, forgetting the names of people or the location of objects. "*Yeah, words coming to me and going into the room and forgetting what I went in for, and that's basically yeah or forgetting where you put something"* (Female, 66, Intervention). This sensation was perceived as peculiar and acknowledged as a deviation from normal cognitive expectations. *"Maybe I was in a rush or something like that and I'm like I can't believe that. I mean I was doing that beforehand, but I think it's definitely worse now. Definitely"* (Male ,61, Control). Patients referenced specific sensations of forgetfulness experienced in daily life like "*You know you go into a room and forgot why you're there"* (Female, 42, Intervention) or:

> "*You would be sitting having a conversation and the word would just not come to me. You know? If you were trying to think of somebody's name or the name of and you can see the person in your head, but the name would just not come"* (Female, 66, Intervention)

This lapse in memory represents a common cognitive experience. It seemed that this example was at the forefront of patients' minds, potentially as cause for concern or at the least cause for introspection about their current cognitive function.

> *"It's a peculiar thing yeah it's-it's it's kind of like short term it's down to stupid stuff like "where did I put that?" or you just-just sort of you know misplacing things or just sort of you know sort of forgetting things which I didn't have before"* (Male, 63, Control)

Whilst reflecting on cognitive experience, attention and concentration represented another domain of emerging concern across patients. Focus was often discussed in relation to the ability to take part in daily tasks and activities. Patients reflected across time on their abilities and compared their prior cognitive state to that of today. Mundane activities like reading and general discussion with individuals was a common catalyst for issues with focus to be highlighted.

> "*I've just got a good a few books since then and I have chosen lighter books because of the concentration factor - books that I might have turned my nose up at a few months ago - I now just find anything light- a good story it doesn't matter what it's like give it to me and I'll read it. So, I suppose concentration in that area- just concentrating on something heavier I would find a bit harder at the moment"* (Female, 64, Intervention).

Issues with focus and attention were understood as a real-world concern as they often translated to feelings of absentmindedness or distraction and when interacting with others. *"If there's a bit of pressure on me to do something or pressure to answer a certain question or something like that, I wouldn't … I needed more time … to process it"* (Female, 66, Control).

When reflecting upon cognition and cognitive concerns, patients often expanded their understanding of cognitive experience to encompass mental and physical fatigue. They illustrated experiences of lacking the mental energy to maintain focus on tasks. This was understood as independent of physical understanding of fatigue or tiredness and expressed a deeper sense of mental or cognitive fatigue that prevented completion or participation in tasks such as reading, consuming media or engaging in conversation. Patients highlighted that this sensation was abstract and was largely illustrated as a general sense of activities that were once easy becoming taxing or requiring increased effort.

> "*Just the thoughts of sometimes going on to the computer I find everything is taking me a huge effort to kind of to get myself up and to do the letter I'm putting things off a lot more than I would"* (Female, 65, Control).

4.3.3.3.3 Subtheme 3: Appreciation for Cognitive Enrichment. For patients that did not express cognitive concern, there existed an awareness that this potentially could be attributed to a history of cognitively demanding or enriching activities. When

reflecting on good cognitive functioning and their lives to date, they posited that factors like their employment or hobbies could have positively impacted their cognition and protected against diagnosis or treatment related cognitive stress. *"No, no I lecture (AS Oh Okay), so I don't really have a problem with anything like that, because I'm active."* (Male, 53, Intervention).

Enriching activities were understood as activities or interests that required a level of focus and concentration. Some were task-based, such as playing a musical instrument or conducting general administrative tasks.

> "*My office work like it might just be like paying your visa bill or planning some-some party you know birthday gifts for the grandkids, something like that and I enjoy that it's like a light bulb switches on and I'm feeling productive"* (Female, 67, Intervention).

But enriching activities were also passive and interest based, such as reading for leisure or keeping *"up with current affairs, news etcetera"* (Female, 66, Control). Patients linked these factors to the maintenance of their current levels of attention and memory. Cognitive demanding activities, such as current or past employment, were also discussed. Patients reflected on how their work contributed positively towards their cognitive function by having to keep organised, and multitasking.

> *"I do think my work - although it's not madly important I we were down a lot of staff so I was working very intensely sort of filling in on a lot of stuff so you'd never have a minute so I developed very good systems of sort of writing various forms of sort of to do lists"* (Female, 55, Control).

There was an enduring sense of appreciation for cognitive demanding activities. For some they provided a source of distraction and a sense of productivity. Patients acknowledge that in order to maintain healthy cognition, they must keep "active" and engage in activities *"that keeps my head ticking over"* (Male, 72, Intervention), promoting cognitive capacity.

4.3.3.4 Theme 4: The Challenge of Preparation for Rare Cancer Treatment

This theme encapsulates the novel challenges faced by patients with peritoneal malignancies preparing for CRS-HIPEC. Patients faced a myriad of challenges whilst

preparing for surgery which compounded feelings of stress and uncertainty. *"It is strange yeah um but then I suppose it's just such a strange, rare situation"* (Female, 54, Intervention). This concept is explored across three subthemes. Subtheme 1, *Attempting Understanding* illustrates the complex mental process of coming to terms with a rare cancer diagnosis, and navigating feelings of shock, confusion and ultimately acceptance about the need for surgery. Subtheme 2, *The Battle of Diagnosis* highlights the challenges and associated stress that came with obtaining an accurate diagnosis to commence treatment. Patients reflect on the burden and oftentimes traumatic experiences and health crises they had to endure before receiving their diagnosis. Finally, subtheme 3, *Preparation: A Physical and Mental Challenge,* outlines how patients approached preparation for surgery from a physical and psychological perspective.

4.3.3.4.1 Subtheme 1: Attempting Understanding. Patients struggled to come to terms with the nature of both their rare cancer diagnosis, and preparation for extensive surgery. Emotions were all-encompassing, with shock and uncertainty at the forefront. Patients felt overwhelmed by the severity of their diagnosis, and confusion about why they are now in this position. The diagnosis was described as *"a bolt from the blue"*, and at complete odds with self-perceptions of their health *"I mean, it was a shock to me (laughter) and a shock to family and friends as I said because it was the last thing they would have expected to hear"* (Female, 53, Control). Others approached surgery with a sense of resignation and stoicism. They did not dwell on diagnosis or surgery, instead accepting surgery as necessary, and accepting the prospect of post operative complications.

> *"Would I prefer not to be doing a big operation on Monday? Yes, I would. Would I prefer to have not gotten cancer in the first place? Yes, obviously I would. But-but they're realities now the cancer is a reality, and the operation is a reality and the best way to deal with it and I-, I'm just trying to keep my head in that, that space"* (Male, 63, Control).

Some relied on comparisons with other patients to find comfort and reassurance about their diagnosis and positive prospects for recovery. These included their current

levels of fitness and general health, a lack of symptoms, or how well they tolerated neoadjuvant treatment.

> *"The chemo did knock me a bit as well. And I'm really pleased with the outcome because I know there's a lot worse off than me- put it like that. So…and considering my age I'm, I'm hoping that I'm doing alright"* (Male, 62, Control).

Diagnosis often resulted in a sense of uncertainty. Patients often questioned themselves and this at times resulted in them feeling untethered, and not in control. *"But yeah so… And when, when you kind of see it this way like you do… you have to relinquish control, you have no control, so you just sort of submit to what comes"* (Female, 54, Intervention).

Information seeking was seen as a source of comfort and means of control for patients. Due to the rarity of the cancer itself and the complexity of major surgery, many patients were largely unaware of their cancer type prior to diagnosis. Patients struggled to relate to other cancer patients due to the rarity of their diagnosis. Information seeking and knowing what to ask and when was also a struggle.

> *"There's some questions I have and I asked them in the early days, I can't even remember it now and -and my attitude now is kind of em I do want information and that but there comes a point you know where eh it's good to know the information but it's mentally about sort of being prepared for what's- what's going to happen"* (Male, 63, Control).

Patients were uncertain about the diagnosis, possible complications and how they would cope with recovery. Uncertainty was partly attributed to the fact that oftentimes patients and even the medical team were unaware of how extensive the procedure would be until the surgery itself is over.

> *"Yeah, it's a lot of unknown. Yep, exactly there's a lot of unknowns. There is a possibility. There is a possibility I may have to have my ovaries out. And that … you know that would be a completely different recovery."* (Female, 42, Intervention).

Patients often reflected on their own health status in relation to others as a means of reassurance. Patients used prior treatments and surgeries as a means to comfort themselves. These experiences acted as an anchor to refer back to in periods of

doubt about recovery. *"Like I've done it a few times before so like I'm - I'm confident in like the medical staff and like I'm confident in, like my ability to recover from it.*" (Male, 30, Intervention). Current health and symptoms were also pivotal when speculating about the experience of recovery. For patients, being aware of their health in relation to others was a positive source of comfort; they felt that this was indicative of how they would recover post-surgery.

> *"I just say bring it on- let it happen and it will be fine. The doctors know what they're doing and all that sort of thing and I'm strong, physically strong and you know I'll be making the best effort to recover"* (Female, 64, Intervention).

Feelings of appreciation and gratitude were also palpable. Patients moved through the shock of diagnosis towards gratitude for the surgical team, and appreciation for their current health and an appreciation overall for the fact that a viable treatment option is available to them and that the cancer was discovered.

> *"I'm not angry at or resentful about any of this look, if anything I'm glad it happened, because it was found and it can be treated, and I said look in not so long away I'll just have a few scars on my stomach, and this will be a memory type of thing you know?"* (Male, 38, Intervention).

4.3.3.4.2. Subtheme 2: The Battle of Diagnosis. Diagnosis of rare cancer can be challenging, and for some patients the process of getting a diagnosis was a harrowing experience including misdiagnosis, multiple hospital visits and various treatments before a diagnosis was obtained.

> *"So, I, I just (laughter) basically at that point cos I'd been sent home a few times I just said that I wasn't going home because I knew that there was something else, you know what I mean going on so. Eventually yeah, they told me that my blood markers were very high for infection and so they did admit me"* (Female, 66, Control)

Getting a diagnosis sometimes took a period of weeks or even months for some patients. Some patients presented with symptoms at Accident and Emergency (A&E) and were misdiagnosed and sent home. These experiences intensified frustrations and meant that by the time diagnosis was obtained, they had already faced a myriad of medical hardships.

"On the Monday, they tried to put a stent into my bowel, and that failed. So, on the Tuesday, I went for emergency surgery and then straight into surgery and got fitted with a stoma as well (AS Okay). And they did biopsies., they took my appendix out. I was in a sort of induced coma for three days after that." (Male, 38, Intervention)

For many, surgery and treatment were a familiar experience as patients recounted multiple prior extensive surgeries and treatments. In some cases, this was for a recurrence. For these patients' surgery wasn't necessarily a shock, but it represented the manifestation of fears when living with a cancer diagnosis. Patients struggled with this notion, as despite prior treatments and surgeries, that their cancer had returned and dampened potential feelings of hope or optimism for recovery.

"The first time round the surgeon kept saying "you might not need chemotherapy" so I thought maybe I won't need chemotherapy and then sure enough I did and I actually realised I got very cross and I realised it was because I got very disappointed because I sort of thought "oh maybe I won't have chemo and the op will be enough" (Female, 55, Control).

It is evident that for some patients the rarity of their cancer diagnosis and symptomatology resulted in challenges during diagnosis. These challenges heightened feelings of stress and anxiety. Patients had to undergo feeling dismissed and misunderstood by medical professionals before eventually receiving their diagnosis. Diagnosis represented the end of uncertainty, but the beginning of a new process of the preparation for treatment.

"I think once I heard there was a mass there, I just felt, look I know this is something that's not right and at that stage I just wanted someone to tell me what I was (AS Yeah) and how we could sort it. Like so, I was so tired of being sent home all the time that when I actually got the diagnosis it was...in a strange way a kind of a relief?" (Female, 66, Control).

4.3.3.4.3 Subtheme 3: Preparation: A Physical and Mental Challenge*:* This subtheme encapsulates the various ways patients prepare for surgery. In terms of physical preparation, this was expressed both as the structured support provided by the prehabilitation intervention (exercise and nutrition), as well as unstructured, general physical activities. By being part of the intervention, patients felt *"that I'm not just a*

number going, I'm more. I'm more important than that, you know what I mean?" (Female, 66, Intervention). Psychological preparation was also evident, and a sense that patients were aware that maintaining psychological wellbeing prior to surgery was necessary to promote recovery. Psychological and physical wellbeing were also understood as intertwined constructs, both contributing to overall wellbeing and in turn, recovery.

Patients struggled with psychological preparation. There existed an awareness that psychological preparation would be arduous. *"Em I'm not ok every day. There's days I get very upset and very nervous. I do find it hard to talk about without getting emotional"* (Female, 42, Intervention). Patients struggle to come to terms with diagnosis and preparation for surgery, feeling insecure about their psychological state, wondering *"how will I cope"* (Female, 66, Control). Psychological preparation was seen as a necessary challenge that would benefit them in the postoperative period. Some patients engaged in external psychological support in the form of counselling to come to terms with the diagnosis. *"You can't measure what they do for you cos it's nice to have a conversation every two weeks with someone who's very objective (AS Yes) ...em…and just kind of helped you...yeah focus your attention so like that"* (Male, 30, Intervention).

Physical preparation was an important factor when preparing for surgery. For patients taking part in the prehabilitation intervention, structured physical activity acted as an additional form of support. They were thankful for the intervention requirements as it acted as a tangible source of preparation that patients could engage in with confidence.

> *"I was always a very active person so the exercise part of the programme really appealed to me and I was delighted to actually be doing it cos I think I was explaining down where we were the weather conditions it was kind of dangerous to be getting out where I was so I wasn't really getting the opportunity to get out so I was delighted to be able to do the exercises and it was a focus and a task for me every day"* (Female, 67, Intervention)

Patients not taking part in the intervention program were also aware of the need for physical preparation. This manifested primarily as unstructured physical activities like walking. *"Em yeah, I suppose, just try and stay as physically fit...as I possibly*

could. Emm just try and eat healthy as I could and emm and also to keep good mental positive attitude." (Female, 66, Control).

Patients were acutely aware that there was a symbiotic relationship between mental and physical preparation, understanding that *"if you're not in a mental state it's very hard to be in a good physical state"* (Male, 30, Intervention). The concepts were frequently intertwined, and how taking care of themselves physically had a positive impact on overall wellbeing and psychological health. Green space and leaving the home for exercise was important for patients illustrating how it promoted positive emotion and prevented fatigue in preparation for treatment. *"Like there's some days I don't, if I don't prioritise a walk early in the morning or by the end of the day, I'm just mentally too tired to get up and do it"* (Female, 42, Intervention).

4.4 Discussion

This is the first study to explore the cognitive and psychological experiences of patients preparing for CRS-HIPEC surgery. The objectives of this research were to 1) Assess the prevalence of CRCI prior to any treatment during the preoperative phase; 2) Investigate possible influencing factors on CRCI including exercise and nutrition intervention and psychological wellbeing; 3) Observe the trajectory of pretreatment CRCI from diagnosis to surgery; and 4) Understand the patient experience of cognitive and psychological factors as they prepared for surgery. Through analysis of patient reported outcomes and semi-structured interviews, findings from this chapter help to elucidate the complex experience of preparation for major complex surgery and its impact on cognitive function. Quantitative findings indicated variability in perceived cognition during the pre-surgery period, and that factors like emotional wellbeing may interact with perceived cognition pre-surgery. Perceived cognition varied from diagnosis to pre-surgery. Prehabilitation findings also indicated that exercise and nutrition support improvements on the impact of cognition on quality of life. Qualitative findings provided in depth nuance and understanding of the complex intersection of cognitive function, psychological wellbeing and quality of life in the preparation for surgery and how these factors related to the experience of a PM diagnosis and CRS-HIPEC treatment.

Patient reported outcomes were used to investigate perceived CRCI and the trajectory of perceived cognitive impairment from diagnosis to pre-surgery and associated variables of distress and health-related quality of life. Findings indicated that although Fact-Cognition PCI scores did not change significantly from baseline to pre-surgery, levels of perceived cognitive impairment based on predefined cut-off criteria (Van Dyk et al., 2020) increased from baseline (13%) to pre-surgery (27%). Interestingly, analysis of individual scores indicates that only one patient reported scores on or below the PCI cut off at both baseline and pre-surgery assessment. Within the presurgical assessment cohort, neoadjuvant treatment did not appear to impact prevalence scores at pretreatment, as of the three patients reporting PCI, only one received neoadjuvant treatment. As a context factor, the majority of patients (n=17) did not receive neoadjuvant treatment prior to surgery. Rates of presurgical subjective CRCI prevalence in this rare cancer cohort preparing for complex major cancer surgery are similar to that reported within literature (11-33%) (Hutterer & Oberdorfer, 2021). Indeed, results are also representative of levels of subjective CRCI reported within the CRCI systematic review, which reported a range of 17.6-29% across included studies (Chapter 2 2.3.5.2). With regards to a healthy population, data from the Korea Community Health Survey reported that 17.4% of middle aged and 29.4% of older adults reported cognitive impairment (Roh et al., 2021). Given that the mean age of the present cohort was 58 years, results speak to potential pretreatment CRCI but also highlights the importance of a healthy control group for future research into the CRS-HIPEC and cognitive impairment. To date, CRCI research has primarily focused on either exploring the potential aetiology of pretreatment impairment (Hutterer & Oberndorfer, 2021, Olson & Marks, 2019) or exploring variability as it relates to postoperative chemotherapy and long-term effects (Hutterer & Oberndorfer, 2021, Yang & Von-Ah, 2024, Lange et al., 2019). However, the present findings suggest that variability could also exist within the diagnosis to presurgical timeframe. Further research is required within this time period to interrogate associations with non-treatment related factors such as psychological wellbeing. A focus on subjective cognitive screening at the pretreatment timepoint could help to identify further individual variability as it relates to pretreatment CRCI and associated psychological factors. In terms of changes in cognition over time across FACT-Cognition subscales, results indicated that scores on the Impact of Cognition on Quality of Life (ImpactQoL) subscale increased significantly from baseline to preoperative assessment indicating

decreased impact of cognition on quality of life. Further investigation revealed that this effect was significant within the intervention group only. Although it is difficult to compare against other studies given at present, these findings suggest that prehabilitation effects could be driving increases in cognitive quality of life pre-surgery. Indeed, a previous systematic review of 19 trials including both animal and human models highlights the potential benefits of movement and exercise support on CRCI (Zimmer et al., 2016). Overall, the findings of this present study highlight the interplay between cognitive function and quality of life, and that prehabilitation may have the potential to positively impact perceived cognitive function.

Within the present study, psychological wellbeing was explored using the NCCN Distress Thermometer, the Impacts of Events Scale-Revised, the Generalised Self-Efficacy Scale, and the Emotional Wellbeing subscale (EWB) of the FACT-General measure. EWB was significantly associated with PCI at baseline. This adds further support to similar findings between psychological wellbeing as measured by anxiety and depression and self-reported subjective prior to surgery or treatment CRCI within Chapter 2's systematic review (Chapter 2, 2.3.7). It has been suggested within CRCI research that subjective CRCI may share theoretical underpinnings with other psychological constructs (Bray et al., 2018, Areklett et al., 2024). These findings suggest that this relationship may also be evident in patients with peritoneal malignancy before the influence of treatment related factors.

The use of semi-structured interviews to qualitatively investigate patient experience provided invaluable insight into the pretreatment experiences of cognitive function and psychological wellbeing, which to date have not been explored through qualitative research. The theme *Evaluating the Experience of Cognitive Concern* highlights variability within cognitive experiences and offers not only an opportunity to understand first-hand experiences of impairment or fluctuation, but also to shed light on possible supportive or enriching activities that may aid in the maintenance of high levels of perceived cognitive function whilst preparing for surgery. The subtheme *Characterising Cognitive Concern* illustrated commonalities among experience of impairments or changes within domains of memory and attention or concentration. These domains have been highlighted in CRCI research as areas of common concern within breast cancer research (Wefel et al., 2015). This research highlights, for the first time, the impact on these domains at the pretreatment timepoint. Participants exhibited

an acute awareness of any cognitive concerns and were also able to articulate periods of good cognitive function. Activities that are known to promote cognitive reserve such as working (Vance et al., 2016) or playing music (Wolff et al., 2023) were discussed as they related to protecting or enriching cognitive function. Investigating cognitive enrichment and reserve as it relates to predicting risk of CRCI and/or protective effects against CRCI progression could help to unravel relationships between cognitive enrichment and maintaining cognitive quality of life before and during cancer treatment, which is a keen area of research in the CRCI landscape (Duan et al., 2025).

Patients also discussed cognitive function as it related to overall emotional wellbeing, which is interesting to note given the correlation observed between EWB and PCI scores at baseline in the quantitative analysis. Interview data further elucidated this relationship, by exploring the nuance of the seemingly bi-directional relationship between psychological factors such as stress and cognition and how both may interact with each other. This bi-directional relationship between psychopathology and CRCI has been previously explored theoretically by Haywood and colleagues (2024). However, the qualitative investigation allowed not only for investigation about this relationship to be further explored, but also how this relationship manifests and its consequences in daily life.

Psychological wellbeing was further explored through the theme *Navigating All Encompassing Anxiety.* It was evident within the qualitative findings that anxiety was a common experience for patients prior to surgery. Sources of anxiety included concerns for future quality of life and postoperative complications as well as concerns about how their past lifestyle may have contributed to their diagnosis, or if they had prepared sufficiently for surgery. The degree of observed anxiety and range of sources highlight the specific nature of cancer-related anxiety and how this may deviate from generalised anxiety. Whilst generalised anxiety can manifest across a range of environments and situations (Mortazavi et al., 2014), cancer-related anxiety may be representative of a unique set of psychological responses to the threat of morbidity. In 2017, Curran and colleagues proposed a model of cancer-related anxiety. The model highlights the threatening nature of a cancer diagnosis, and how prior schemas relating to mortality, experiences with cancer, psychological vulnerability and cognitive processes will all determine level of cancer-related anxiety. The model also highlights how coming to terms with one's mortality and adjustment to living with cancer and cancer related

threats are central to the experience of cancer related anxiety. It appears that some aspects of this model are echoed within the experiences of PM patients preparing for CRS-HIPEC surgery. However, for patients preparing for CRS-HIPEC treatment, it seemed that in addition to adjustment and mortality related anxieties as explored in Curran and colleagues (2017) model, the physical intensity of the CRS-HIPEC treatment itself was an additional source of concern as illustrated in the subtheme *Experiencing Anxiety Across Time*. These qualitative findings support the need to acknowledge cancer related anxiety as a nuanced separate construct to generalised anxiety in cancer research, which has implications for future anxiety measurement for cancer patients.

Apart from experiences of anxiety, patients described additional psychological shifts in perspective and psychological adjustment required as a result of diagnosis. *The Patient & Me: Navigating New Realities*, illustrated how some patients maintained a high quality of life prior to surgery and in some cases did not exhibit any notable symptoms. This high level of quality of life was also evident in self-report measures and may have also impacted upon cognitive quality of life from baseline to pretreatment. An association between health-related quality of life and cognitive impairment has been reported in non-cancer (Pan et al., 2015) and breast cancer populations previously (Von Ah et al., 2024). Patients also described the challenges associated with identifying as a cancer patient and adjusting to a new definition of normalcy or normal day to day life. Adjustment to identity as a cancer patient has challenges, as patients may struggle to identify as a “cancer survivor” before completion of primary treatment, a term which in of itself has been a source of debate within literature (Cheung & Delfabbro, 2016). Pretreatment in this case may create uncertainty related to self-identity. Even in the pretreatment time period, uncertainty regarding postoperative normality was evident with concerns regarding future quality of life and returning to prior levels of function. Interestingly, qualitative explorations of survivors' perspectives of postoperative adjustment highlight similarities, including returning to previous lifestyles, acceptance of a new normalcy and adjusting to physical changes including living with an ostomy bag (Fitch, 2021). It appears that concerns regarding future quality of life manifest in the pretreatment period and may maintain postoperatively. Clinicians should be aware of these early manifestations of quality of

life concerns, in particular when discussing complex treatment pathways such as CRS-HIPEC, in order to provide realistic guidance.

The final theme *The Challenge of Preparation for Rare Cancer Treatment* described the additional challenges of obtaining a rare cancer diagnosis and preparing for an invasive surgical procedure like CRS-HIPEC. Patients highlighted how the difficulties associated with obtaining their diagnosis increased distress and uncertainty. Prior research has identified unmet care needs of patients with rare gastric cancer during treatment and postoperatively including information needs and physical and daily living (de Heus et al., 2021). However, this qualitative analysis identified the period of diagnosis as a distressing event. Immediate psychological support tailored to rare cancer diagnosis, and the pathway of diagnosis and treatment may represent an additional unmet care need for patients diagnosed with Peritoneal Malignancy. The uncertainty associated with a rare cancer diagnosis was also evident in the subtheme *Attempting Understanding.* Cancer rarity contributed to feelings of uncertainty, and the severity of diagnosis often conflicted with attempts to understand their illness, as at times it was in contrast to current levels of quality of life. These experiences can be common when faced with a cancer diagnosis. Some aspects including understanding the diagnosis and comparisons with others are evident within adjustment theories such as Taylor's (1983) theory of adjustment to life threatening events. It appears that patients are making efforts to adapt to their diagnosis and the challenge of surgery.

In the face of diagnosis, patients attempted to prepare for their surgery through physical and psychological means. It was here that effects of prehabilitation were discussed as they related to overall psychological wellbeing. Patients exhibited an awareness of the need for physical prehabilitation, irrespective of intervention condition. Patients were also aware of the relationship between physical activity and psychological health. In quantitative analysis, the intervention group exhibited significant improvements in cognitive quality of life from baseline to pretreatment assessment. As part of the intervention, patients were called weekly to monitor adherence and report any concerns related to exercise and nutrition. As part of the intervention patients were also guided by professionals regarding exercise and nutrition advice. However, all patients were pooled together for the purpose of my qualitative research and not by study arm. Therefore, further research is required to examine the

relationships between prehabilitation intervention, quality of life and perceived cognitive impairment.

There are some limitations associated with the present study. Due to challenges with data collection and patient attrition, the final matched sample from baseline to pre-surgery was lower than anticipated. Although non-parametric tests were applied to report conservative findings, the small population makes it difficult to generalise findings. As this research is nested within a larger prehabilitation trial, convenience sampling was applied and as previously mentioned this meant that patients were subject to inclusion and exclusion criteria based on trial participation. This includes exclusion criteria on minimum levels of physical fitness and cognitive capacity to take part which may exclude those with severe cognitive concerns. However, this did mean that intervention effects as they related to cognition and psychological wellbeing could be interrogated. While focusing on psychological distress, anxiety and depression could not be directly measured using the selected patient reported outcomes. However, the EWB subscale of the FACT-G allowed for exploration of psychological wellbeing within the scope of HrQoL. In addition, measures of stress and general distress including the NCCN Distress Thermometer and the Impact of Events Scale-Revised, provided an overview of the experience of psychological wellbeing while preparing for CRS-HIPEC. As explored in Chapter 1, CRCI measurement can be both subjective and objective through neuropsychological testing. Due to the focus on psychological and physical preparation for surgery and qualitative patient experience self-report cognitive impairment was chosen as the most appropriate measurement tool. This was further supported by the findings in Chapter 2 illustrating a relationship between psychological wellbeing and self-reported cognitive impairment. This study's strengths include the novel assessment of pretreatment CRCI as it relates to 1) CRCI and 2) Prehabilitation. Use of multiple methods allowed for an in-depth analysis of research findings and increased contextual nuance that would not have been possible through quantitative investigation alone. The inclusion of a public and patient involvement group to further validate topic guide development also increases the validity of the qualitative investigation.

Findings from the current study will provide opportunities for clinical application and future research. Results highlight the need to further investigate the relationship between pretreatment and perceived cognitive impairment and

psychological wellbeing. As indicated by patient interviews, preoperative anxiety was a strong theme for patients. Further investigation of anxiety and preoperative PCI among CRS-HIPEC patients would further our understanding of any direct links between pretreatment anxiety and perceived cognition. The present prehabilitation intervention focused on modifiable lifestyle factors such as exercise and nutrition, however, qualitative results indicated patient awareness of psychological distress and the importance of mental and physical preparation for surgery. Qualitative analysis also highlighted additional unmet care needs for CRS-HIPEC patients including experience of cancer-related anxiety and the need for additional support during the period of diagnosis. The addition of psychological prehabilitation could help alleviate preoperative anxiety and further bolster the resilience and optimism expressed prior to surgery, as evident from results in Chapter 3, (3.3). Finally, as the current study focused on the relationship between self-reported cognition and psychological wellbeing, future research should include objective cognitive assessment at the pretreatment timepoint to further explore CRCI experience before CRS-HIPEC.

4.5 Conclusion

This study explored experience of cognition and overall psychological wellbeing for patients preparing for CRS-HIPEC treatment. Patients were also engaged in a prehabilitation trial consisting of exercise and nutrition support. Results found low levels of perceived cognitive impairment through PROs, but perceived cognitive impairment was associated with emotional wellbeing. Impact of cognition on quality of life also decreased pre-surgery for the intervention group. Emotional wellbeing and HrQoL was maintained from baseline to pre-surgery. Patient interviews reflect PROs in terms of quality of life and the interaction between cognition and psychological wellbeing. In addition, interviews highlighted multiple sources of anxiety, the benefits of physical and psychological preparation for surgery and patient challenges associated with PM diagnosis and CRS-HIPEC. This study highlights the complex relationship between preoperative cognitive function, quality of life and psychological wellbeing while preparing for cancer surgery. Further research should focus on further exploration

of the relationship between these variables pre-surgery, and the addition of neuropsychological testing.

Chapter 5: The Patient Experience of Cognition and Psychological Wellbeing While Recovering From Surgery: A Qualitative Study

5.1 Introduction

The relationship between possible effects of cancer treatment on postoperative cognitive function have been well established (Ahles et al., 2018, Lange et al., 2019, Oppegaard et al., 2023a). Early CRCI research focused on cancer treatment, chemotherapy related effects (Ahles & Saykin, 2007), and chemotherapy induced cognitive impairment also known as "chemobrain" (Argyriou et al., 2011). Although the exact mechanisms require further research, it has been suggested that pro-inflammatory cytokine pathways may lead to possible neurotoxicity effects, affecting cognitive function and overall quality of life (Vitali et al., 2017). Thus, the term "chemobrain" may not adequately encompass the range of factors that could contribute to cognitive experience in cancer (Bender & Thelen, 2013). As models move towards this view of multifaceted co-occurring factors, understanding the experience of psychological, physical, and recovery factors post-surgery from the perspective of the patient, as it relates to CRCI and psychological wellbeing, is necessary.

However, little is known about factors beyond chemotherapy and other treatments, such as psychological wellbeing, and how this may affect CRCI experience postoperatively. Evidence suggests that postoperative CRCI can have detrimental effects on overall quality of life, impacting social function, ability to take part in daily activities and returning to work (Yang & Von Ah, 2024) if untreated. Existing conceptual models of CRCI have also highlighted how multiple factors may contribute to CRCI across the cancer continuum and interact dynamically across pretreatment to long-term recovery such as patient related factors, co-occurring symptoms and social determinants of health (Oppegaard et al., 2023a).

Evidence suggests that cancer survivorship has specific risk factors for anxiety and depression that include psychological stress and treatment related factors (Ikhile et al., 2024). Research about postoperative experience of cancer patients indicates that they can be vulnerable to a range of long-term persistent effects of psychological distress that can remain from diagnosis into recovery, as well as "late-effects" that may

also appear post-treatment (American Cancer Society, 2025, Stein, 2008). It is well reported that breast cancer patients experience varying levels of psychological distress during recovery which can be aggravated by the continuation of treatments, fear of recurrence and uncertainty (Tao et al., 2024). Rates of anxiety and depression among patients treated for cancer far exceed that of the general population with two thirds of cancer patients also exhibit clinical levels of anxiety (Pitman et al., 2018). Evidence suggests that cancer survivorship has specific risk factors for anxiety and depression that include psychological stress and treatment related factors (Ikhile et al., 2024). Similarly, variability and transience have been highlighted within experience of CRCI six to twelve months post treatment (Hutterer & Oberndorfer, 2021). Understanding the dynamics between these fluctuations in cognitive function will further progress the development of appropriate and targeted interventions in future research.

Furthermore, the physical stress of CRS-HIPEC treatment may pose additional challenges for patients given the nature of the complex and rare cancer. In 2024, it was reported that patients undergoing CRS-HIPEC experienced physical and psychological challenges including feelings of uncertainty, issues adapting to current quality of life, emotional struggles and challenges related to physical aspects of recovery (Falla-Zuniga et al., 2024). Postoperative research among cancer patients across a range of cancer types has identified similar concerns regarding issues with daily social functioning and returning to the workplace (Haywood et al., 2023). Understanding how these experiences conceptually may interact with each other to impact quality of life will aid in identifying postoperative factors associated with psychological wellbeing and cognitive function.

Chapter 4 (4.3.3) reported on the qualitative experience of patients prior to CRS-HIPEC treatment and illustrated experiences of anxiety and uncertainty of future quality of life. Research has highlighted potential moderators of postoperative CRS-HIPEC quality of life including preoperative age and performance status (Wang et al., 2022). Abelson and colleagues in 2018 interviewed 24 colorectal cancer patients about sources of pre and postoperative distress. They identified specific sources of psychological stress in the preoperative and postoperative phases. Postoperative psychological distress related to immediate distress in hospital due to fatigue and physical complications. Distress was also evident when assessing quality of recovery compared to preoperative expectations. Experiences with social support were also a

cause for distress, as patients worried about becoming a burden to friends and family. We know from research that interventions like exercise support preoperatively can support postoperative health-related quality of life via increases in physical wellbeing in colorectal cancer (Van Rooijen et al., 2019a). Combined pre and rehabilitation programs have also been recommended as part of the Enhance Recovery After Surgery (ERAS) guidelines for colorectal cancers to improve postoperative clinical outcomes (Gonella et al., 2024). The relationship between exercise and cognitive function requires further research due to study heterogeneity, but there is preliminary evidence to support exercise intervention supporting cognitive function (Myers et al., 2018). Qualitative evidence also highlights how CRCI can interact with nutrition postoperatively for cancer patients, making it more difficult to adapt to the new quality of life changes associated with nutrition (Coro et al., 2020). It is clear that increased research is required to understand how the combination of psychological, cognitive and lifestyle factors can interact and contribute to quality of life postoperatively.

Conceptual models of CRCI indicate that there exists a wealth of postoperative research on patient reported outcomes and measurement of CRCI and associated factors, in particular the effects of treatment related factors on CRCI long term (Hutterer & Oberndorfer, 2021, Lange et al., 2019). Quality of life post CRS-HIPEC surgery has been a keen area of research, primarily due to the physical insult of surgery and risk of postoperative complications (Hamilton et al., 2016, Schneider et al., 2017). However, to date, research has not explored how cognitive function may interact with the experience of CRS-HIPEC recovery and impact quality of life.

It is clear that there exists gaps in literature exploring the effects of pre and rehabilitation approaches on cognitive and psychological outcomes. CRS-HIPEC as a treatment also requires increased investigation due to its physical burden for patients during recovery. Qualitative investigation will allow for an in-depth nuanced understanding of the physical and psychological experience of recovery can help to elucidate the complex relationships between treatment related factors, cognition and psychological wellbeing. More research is required to understand the nuance of psychological wellbeing post CRS-HIPEC treatment.

The present study aims to explore postoperative patient experience through qualitative analysis. Specific objectives include understanding the patient experience

post-surgery through qualitative investigation and investigating possible influencing factors on CRCI including exercise and nutrition intervention and psychological wellbeing. This study will directly address the following research objectives:

d. Explore the trajectory of pretreatment CRCI from diagnosis to surgery and recovery.
f. Understand the patient's cognitive and psychological factors as they prepare for and recover from surgery through qualitative investigation.

5.2 Methods

5.2.1 Design

This exploratory nested qualitative study reports on a subgroup of patients enrolled in the PANO trial. The trial as previously outlined in Chapter 1 section 1.1.5 is a combined bimodal pre and rehabilitation feasibility intervention trial. This study reports on the postoperative patient experience from semi-structured interviews conducted upon completion of the PANO trial (NCT05305820).

5.2.2 Participants

The details of the patient group including trial inclusion and exclusion criteria have been previously described in Chapter 4, section 4.2. Patients who participated in the postoperative semi-structured interview upon completion of the PANO trial were included in the current analyses. and of the n=36 patients enrolled in the trial; this study includes the interviews of n=18 patients who completed the final postoperative data collection point.

5.2.3 Procedure

Participants were interviewed from both the intervention and control group condition using a semi structured interview guide that was developed in conjunction with a public patient involvement panel (Chapter 4 section 4.2). Semi-structured interviews took place either over the phone or in person, due to the geographical spread of patients across Ireland. Interviews were recorded via a Dictaphone. Prior to recording, patients were made aware of the anonymisation process and that they were free to pause the interview at any time or to skip questions they were not comfortable answering. Post interview, the interviewer debriefed the patient and offered a subsequent check in call if required due to the emotional nature of content discussed.

5.2.4 Interview Topic Guide

Topic guides encompassed experiences of recovery, reflections on the intervention experience and explorations of quality of life, cognition and psychological wellbeing. Topic Guides for patient interviews were developed based on prior work observing the postoperative wellbeing of patients who engaged in pre and rehabilitation for cancer treatment (Loughney et al., 2024, Tully et al., 2020), as well as observational research exploring postoperative physical wellbeing and overall health related quality of life for patients recovering from CRS-HIPEC treatment (Loughney et al., 2020). In addition, research of CRCI modelling (Ahles & Hurria, 2018, Hutterer & Oberndorfer, 2021, Lange et al., 2019), guided the formulation of topic guide questions related to CRCI by highlighting potential lifestyle factors associated with CRCI such as physical and psychological wellbeing, as well as current cognitive domains of interest in the literature. Topic guides for both intervention and control groups are shown below in Table 5.1. For full topic guide questions for both groups please refer to appendix D.1.

Table 5.1

Topic Guides for Postoperative Interview

Topics	Intervention Group	Control Group
1	Feelings about recovery	Feelings about recovery
2	Impact on health-related quality of life	Impact on health-related quality of life
3	Reflection on intervention experience	Reflection on Intervention experience
4	Reflection on the experience of cognition from pre to post surgery	Reflection on the experience of cognition from pre to post surgery
5	Support during the cancer experience	Support during the cancer experience

5.2.5 Ethics

This Study received approval from Dublin City University DCU/2022/158 (for approval please see Appendix F.1).

5.2.6 Data Analysis

Interviews were transcribed by the PhD researcher and members of the PANO research team, and any patient identifiers removed. Interviews were coded and analysed

by the PhD researcher using qualitative research software NVivo 14 (Lumivero, 2025). Organization and creation of themes and subthemes were illustrated using online collaboration software Miro. Inductive reflexive thematic analysis (Braun & Clarke, 2022), was applied to the study interview data. Thematic analysis is widely applied within psychology literature to explore both psychological phenomena and lifestyle behaviours for cancer survivors (Kim et al., 2020), and to help understand pre- and rehabilitative lifestyle exercise and nutritional needs and barriers (Swan et al., 2021). The process of thematic analysis has been previously described (Chapter 4, 4.2.4.4). To summarise, thematic analysis consisted of six phases based on Braun and Clarke's (2022) reflexive thematic analysis method: 1) Data Familiarisation, 2) Generating Initial Codes, 3) Generating Initial Themes, 4) Developing and Reviewing Themes, 5) Refining, Defining and Naming Themes and 6) Writing Up. A hierarchical map of themes and subthemes was generated in Miro (See Appendix D.2).

5.3 Results

5.3.1 Participant Demographics

Eighteen patients completed postoperative interviews. The average age of participants at time of enrolment was 57.89 years (SD 10.98, Range 30-70) . Eleven patients were intervention and seven in the control group. Of the 18, 61% were female (female n=11, male n=7). The average time since surgery was 289 days, or 41 weeks. Patients in the intervention group (n=11), continued a six-week combined exercise and nutrition rehabilitation program post-surgery as soon as they were deemed physically fit by the clinical team as part of their participation in the PANO trial (Chapter 1 section 1.1.5). The control patients had significantly higher tumour spread compared to the intervention group based on peritoneal cancer index scores with significant differences observed across peritoneal cancer index scores (p=.03), ASA grade (p=.04) and Cytoreduction Completeness (CC) Scores (p=<.001). Participant demographics are outlined below in Table 5.2.

Table 5.2

Participant Demographics and Clinical Characteristics (n=18)

Variable	Intervention (11)	Control (7)	Total (18)	Group Difference (p)
Age: **Mdn, IQR** m, sd	**59,21,**55.91,13.16	**63,11**,61,5.86	**61,12**,57.89,10.98	p=.346
Gender: Female, %	6, 54.5%	5, 71.4%	11, 61.1%	P=.121
Years of Education (n=17) **Mdn, IQR,** m, sd	**16,4,**16.8,2.81(9)	**17.5,6**,16.52.81(6)	**17,5,**16.7,2.71(15)	p=.955
Days from Surgery **Mdn, IQR**, m, sd	**218,255**,253.64,125.10	**284,299**,344,183	**237,237.75**,288.78,151.90	p=.246
Cancer Type				
Colorectal	5	1	6	p=.223
Ovarian	1	2	3	
PMP	5	4	9	
ASA Grade				
Normal Healthy	1		1	p=.0.04*
Mild Systemic Disease	4	5	9	
Severe Systemic Disease	6	2	8	
Peritoneal Cancer Index **Mdn, IQR, m, sd**	**4,8,**7.73,7.36	**14,9,**15,5.13	**10, 15,**10.56,7.38	p=0.03*
Cytoreduction Completeness Score				
No Disease	10	5	15	p=<.001*
Present >.25cm	0	2	2	
Present >2.5 cm	1		1	
Adjuvant Chemotherapy				
Yes	8	3	11	p=.346
No	3	4	7	

Note: *Significant at p<.05 non-parametric, two tailed exact test statistic, m=mean, sd=standard deviation, Mdn=median, IQR=Interquartile range, ASA=American Society of Anaesthesiologists Grade, PMP= pseudomyxoma peritonei

5.3.2 Interview Characteristics

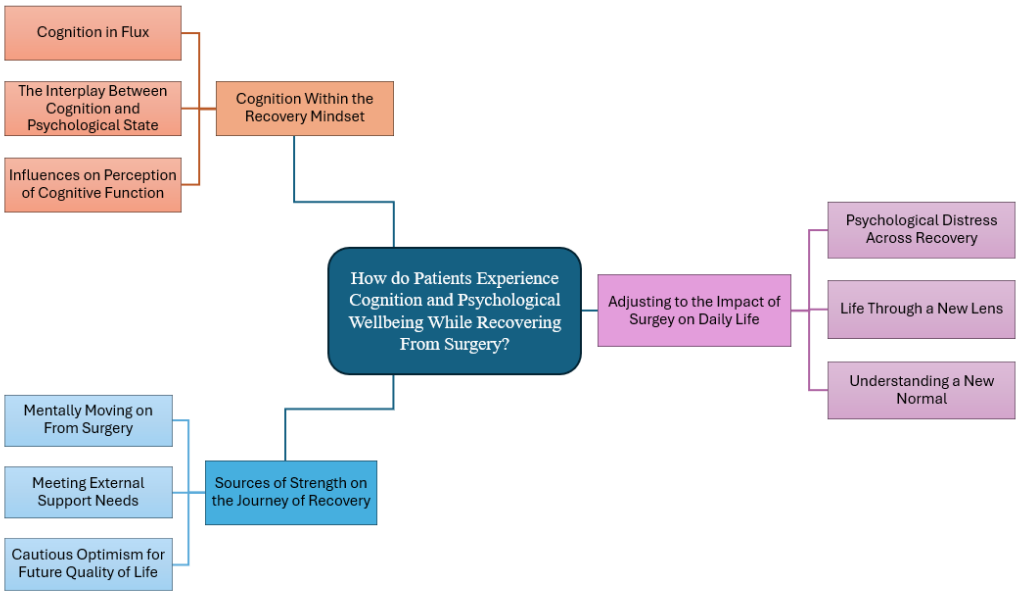
Interviews occurred between March 2023 and January 2025. Average interview duration was 36.63 minutes (SD:12.56, median 36.15, range 19:42-57:18). Interviews took place either via phone call or in person. Included quotes are presented as follows: (gender, age, control/intervention group). Interviewer responses are coded as either AS or SM.

5.3.3. Thematic Analysis

In analysing patient interviews to understand how patients experience their cognition while recovering from major complex surgery and how patients experience psychological factors that can relate to cognition, three central themes with subthemes were identified (see Figure 5.1). The first theme, *Cognition Within the Recovery Mindset*, explores how patients relate to their cognitive experiences during recovery. Cognition was expressed as being in a constant state of change and this theme highlighted the immediate cognitive burden of recovery. The second theme, *Sources of Strength on the Journey of Recovery,* outlines both internal and external sources of strength and support that patients relied upon during their recovery experience, as well as gaps in supportive care. Finally, theme 3: *Adjusting to the Impact of Surgery on Daily Life encompasses* the psychological and physical alterations as a result of diagnosis and surgery and how these interact with each other to contribute to overall quality of life in recovery. Aspects of this include a psychological shift in perspective and adjustment to new challenges, and the scope and breadth of psychological distress across the recovery period.

Figure 5.1

Postoperative Thematic Map



5.3.3.1 Theme 1: Cognition Within the Recovery Mindset

This theme captures how patients reflect on their perceived cognition within the context of recovery. Many patients felt that cognition was not a static construct but rather it fluctuated greatly and was impacted by both psychological wellbeing and treatment related factors. Patients highlighted common cognitive domains like memory, attention and concentration when discussing cognitive concerns post-surgery. Patients were aware of changes in cognition throughout the post-operative recovery journey, with a marked contrast between immediate inpatient recovery, and reflection on current cognitive states, months after treatment. *"I was a bit- trying to think of the names of the stuff. And I thought, oh god, will I ever get my mind back again, you know, I'd be fine,"* (Female, 65, Intervention). Not only did psychological wellbeing impact perception of cognition, but poor cognitive function also negatively impacted psychological wellbeing and self-perception, leading to a perceived increase in a sense of uncertainty during recovery. Patients highlighted possible treatment related causes of impairment and explored cognitively enriching activities and cognitive support strategies that supported their cognitive function and aided recovery. This theme reflects these areas by encompassing three subthemes *1. Cognition in Flux, 2. The Interplay Between Cognition and Psychological State* and *3. Influences on Perception of Cognitive Function.*

5.3.3.1.1 Subtheme 1: Cognition in flux. When discussing cognitive concerns, patients were acutely aware of the trajectory of recovery and changes in cognitive function from immediately postoperatively in hospital, compared to long term recovery, and how some cognitive issues may have also persisted through recovery.

> *"I'm doing -this one thing actually that I noticed now em, and I've noticed over the past few months. It hasn't happened too much recently, but. Things just go out of my head, and I totally forget about them"* (Female, 67, Control).

Immediate recovery represented a time of immense physical stress for patients. This physical burden included the physical insult of surgery, the compounding impact of neoadjuvant or adjuvant treatments, as well as residual effects of anaesthesia and any postoperative complications. These physical effects compounded feelings of psychological distress, fatigue and cognitive complications. Patients also reported

residual cognitive concern beyond the period of immediate recovery or treatment, including everyday experiences of forgetfulness, or an overall decline in concentration.

During their time in hospital, patients were under considerable psychological stress. Intense fatigue resulted in lapses in concentration and memory which at times was a distressing experience for patients, as they struggled to recall postoperative conversations with medical professionals.

> *"Yeah well, it's just, it's scary for me to be like, Jesus like that you know, I woke up so early from the surgery I was like this must have gone wrong, like horrifically bad. And eh do you know I think I was just- I just wasn't aware of the conversation that I had"* (Male,30, Intervention).

Generally, patients struggled to maintain an accurate perception of time during the immediate postoperative phase due to cognitive fatigue. Cognitively demanding tasks such as reading were also a challenge. Immediate recovery was intertwined with physical and psychological burden and a general lack of control and autonomy whilst recovering in wards. This combined load seemed to make patients susceptible and sensitive to a general experience of cognitive lapse.

> *"I suppose immediately after my surgery. There would have been I suppose as I mentioned you know a bit of tiredness or you might have lapses in concentration, or you wouldn't, -You know, things that you might have done even say like reading you mightn't have read as much, you know, in the same quantity because, you know, you just get tired"*(Female, 53,Control).

Reflecting on the trajectory of recovery, some patients were able to report either improvements in cognition over time, or that they did not experience any changes in cognition from the pre to postoperative phase. This was a source of comfort for patients, acting as a reflection overall of their recovery and general wellbeing.

> *"I know the first time I mentioned that I was having a bit of fogginess em sometimes em. But I, I can't say that that actually at this moment in time that I'm experiencing anything like that"* (Male,55, Intervention).

Patients also pondered whether any cognitive concern they expressed currently was a true reflection of a new postoperative state, or whether they were just more aware of cognitive issues that were present prior to diagnosis or surgery. *"I wouldn't say my*

attention or focus is particularly good. But I think it, I don't know if it ever was?" (Female,54, Intervention).

For those who reported cognitive issues, common domains affected included general memory and concentration. Rather than acute experiences, issues with concentration and focus were more generalised and not limited to demanding tasks or environments. *"I actually would have, probably before the operation. I don't know maybe I certainly would have em, would have em id notice now that my eh…I had a lot of kind of brain fog for a long time?"* (F,66, Control).

There was an awareness of decline in everyday environments and situations, in particular in relation to lapses in memory.

> "*I forgot to pick it up (AS okay) because it was from my daughter in law's house, and we all met up and as soon as I saw my daughter, never even occurred to me about the jumper you know? Whereas before, that would have been a trigger I would have gone oh my god I forgot the Jumper, I (AS yes) totally, forgot. It's like some stuff just goes totally out of my head"* (Female ,67, Control)

Adjuvant treatments also impacted on long term cognitive recovery, manifesting as problems with general concentration. In some cases, issues associated with adjuvant treatment eventually subsided and patients returned to normal perceived cognition.

> "*My memory wasn't great. Yeah, I was a bit- trying to think of the names of the stuff. And I thought, oh god, will I ever get my mind back again, you know, I'd be fine, probably you wouldn't have noticed it or anything but notice it myself. But em No, I'm back now to being grand, not a bother you know"* (Female, 65, Intervention).

In general, patients' experiences of cognition fluctuated and were most heightened in the immediate postoperative phase of recovery. Persistent issues with memory and concentration interfered with some patients' daily lives, even during long term recovery, while for others cognitive issues were not a factor during the postoperative period.

5.3.3.1.2: Subtheme 2: The Interplay Between Cognition and Psychological State. This subtheme highlights the interplay between psychological state and cognitive

function. Psychological wellbeing seemed to both impact on and be affected by perception of cognitive changes. Emotions were also thought of as intertwined with cognitive experience, and at times impacted negatively on patients, resulting in overall decreased cognitive function in day to day life. Patients displayed an overall awareness of the interaction between psychological and cognitive wellbeing. Some patients struggled with negative emotions as a result of increases in perception of cognitive issues.

> "*I try not to beat myself up about it, but at the time I'm thinking, oh, my God, that's really stupid. Now you know what I mean. Why am I doing this? And I'm all, you know, come on, you know, pull yourself together, those things"* (Female, 67, Control)

Patients were aware of their cognitive state and how this either was impacted negatively as a result of cancer and treatments, or how they had retained or returned to a normal level of perceived cognitive function postoperatively. In some instances, increased perception of cognition changes impacted self-confidence, causing patients to withdraw from social life *"Even in conversation, eh …like eh...I wouldn't be giving my opinion as much or I would be unsure if I've done you know not enough research (laughter) but just a little more unsure of my, of my opinions"* (Female,67,Control). For others, positive feelings about cognition improved psychological wellbeing, increasing resilience and positive emotion. *"Well, the funny thing is, that I actually have more clarity now than I ever had (laughter). Eh em and eh I've, ...I feel mentally strong like"* (Female,66, Control).

The memory of the traumatic period of surgery, and status as a patient is ever present, and some patients believe that this results in feelings of absentmindedness and lapses in concentration. These overwhelming thoughts sometimes result in increased anxiety, which could further fuel negative perception of cognitive function.

> *"It's never off your mind with this week and coming now, and next week coming, it's permanently there what's going to be told to you next week. (AS yeah). You know so ehh...a kind of a stress. Theres's nights I can't sleep, you know (AS yep) or I wake up, and I wake up in a panic. You know you're kind of... get panicky"* (Female,59, Intervention).

Patients' psychological wellbeing and perception of cognition interacted throughout the course of recovery. At times, the trauma of surgery was overwhelming and impacted on focus, by occupying day to day thoughts. There existed an awareness of how psychological tools and cognitive prompts could be used to promote healthy cognitive function. These experiences illustrate how cognitive and psychological distress interfere and impact upon each other in the cancer journey, and how these effects may manifest in daily life.

5.3.3.1.3 Subtheme 3: Influences on Perception of Cognitive Function. This subtheme illustrates how both positive and negative influences on cognition were understood by patients. Patients highlighted aspects of their recovery that they felt were integral to supporting cognition. These included cognitively demanding tasks and enrichment activities, like return to hobbies or the working environment.

Tasks and activities that required a level of focus and cognitive demand were viewed as a positive force in recovery and increasing self-confidence. The ability to return to work was a central tenet of cognitive recovery and viewed as a return to normal cognitive ability. An active work environment helped patients to regain a sense of control and allowed them to detach from the experience of treatment. *"I mean, in the [workplace], there's no time[..]There used to be a time when you get a bit of a lull, but now there's always something happening. So it's always busy"* (Female,53, Control). Tasks like administration and working with figures help to confirm for patients that their cognitive function had recovered or remained intact *"But everything else is fine, you know my work, I do- I do my work there as well paperwork, administration a lot of physical work to do. And em you know it's fine you know?"* (Female ,66, Intervention). Apart from work, some patients discussed engaging with leisure activities like brain teasers and puzzles, as a way to monitor and support cognitive ability. *"But well, what I did was I started doing the sudoku (AS okay yeah) yeah and I do it every single day and I find it really helpful, it's fantastic you know it makes your brain work"* (Female,65, Intervention). In terms of structured cognitive support, patients were in support of offering individualised support with cognitive function as required, in the event that resources are made available.

Treatment related effects were highlighted as potential negative influences on cognition. Chemotherapy resulted in periods of decreased concentration and memory.

"We used to call it "chemobrain", you know? Which I wouldn't probably have thought existed, but it actually does, I think" (Female,65, Intervention). Patients attributed issues with maintaining focus and lapses in memory as a side effect of chemotherapy treatment and were not surprised or alarmed by their cognitive experiences. *"You know em, I call it, I call it "chemobrain" (AS yeah). You just, you just don't think."* (Female,59, Intervention). Surgery related effects, such as residual effects from anaesthesia were also explored as possible contributing factors towards post operative cognitive fatigue.

> "*It was a long surgery that I had, and I knew it would be kind of with the anaesthesia you know in your system. And I had been told by people that oh you know kind of takes a while for all of that to kind of get out of your system you know so...It didn't it didn't bother me you know it didn't really bother me I kind of , as I say I kind of half expected it you know?*" (Female,53, Control).

Patients also believed that the general cognitive effects of aging could also help to explain their periods of cognitive concerns *"I wouldn't have as good a memory as I would have had 40 years ago. But I mean I think you get a bit older, you're and it's I think it's not mixing as well you know"* (Male,70, Intervention).

Patients also showed an awareness and understanding that perceived cognition function could be improved or protected by psychological support or tools. Psychological counselling post treatment was a source of cognitive focus and clarity, allowing them a space to process and make sense of their cancer experience. Mindfulness and engaging with mindfulness techniques was also explored as a cognitive tool to allow patients to remain present in daily life, and to aid memory and concentration during daily tasks, like gardening.

> *"I actually think the, the mindfulness as I'm very mindful. Like say for example, since you know, I leave my trowel in the garden, maybe the trowel could be anywhere. But last night I stuck it in a pot, and I said to myself, remember this is where you put the trowel. So, when you come out tomorrow, you know where it is. I'm always mindful like that. Yeah, which is a great, great benefit to me."* (Female,67, Intervention).

The use of cognitive prompts like note taking, also gave patients a sense of control over their memory *"I've learned over the years, I, I write things down. So, if I*

ever go to the doctors or talk to the dietitian, or talk to whoever the physio, I will be taking notes. So, I have my own records" (Female,55, Control).

Patients were aware and cognisant of activities that promote cognitive wellbeing, and factors that may hinder cognitive ability. The ability to work and take part in daily life was comforting for patients and acted as further reassurance that they had recovered well thus far and would continue to maintain cognitive function.

5.3.3.2 Theme 2: Sources of Strength on the Journey of Recovery

This theme explores the various sources of psychological, practical and physical support that patients leaned on within the recovery journey. These were both internal, as patients expressed psychological resilience and optimism as well as external, including the structured support of the exercise and nutrition intervention, psychological counselling or support from others such as friends and family. Subtheme 1, *Mentally Moving on From Surgery,* illustrates how patients dealt with the toll of surgery and the various approaches they used to move on from the experience of surgery towards long term recovery, and how this was challenged by further treatments. Subtheme 2, *Meeting External Support Needs*, explores how various supportive care needs were met during recovery, either through structured or unstructured supports. It also highlights gaps in supportive care experienced, such as the need for increased psychological support. Many patients also highlighted a sense of optimism, and a determination to recover well to promote quality of life, and this is explored in Subtheme 3, *Cautious Optimism for Future Quality of Life.*

5.3.3.2.1 Subtheme 1: Mentally Moving on From Surgery. The combined trauma of surgery and diagnosis for many patients was both mentally and physically overwhelming in the postoperative period. In order to reintegrate into daily life, patients engaged in compartmentalisation with regards to their surgical experience. For some, this was an intentional act or seen as a positive adaptation to cope with recovery. Without engaging in psychological avoidance, patients pondered whether they would have been able to regain their current quality of life or engage in work or social life. For patients who recovered well, there was a sense of separation from surgery, that it and any physical and psychological impacts were in the past, and did not impact current

quality of life. "*I just kind of felt OK, this is behind me now and it's kind of onwards and hopefully upwards, you know, but that was that was the attitude that I would have had "* (Female,53, Control).For some, reflecting and opening up about the experience of diagnosis was stressful, and difficult to recall "*and it's not that I haven't thought about it since but actually verbalising it I suppose"*(Female ,67,C).

There existed a sense of disbelief regarding the physical impact of surgery and rare cancer diagnosis. With this came a sense of isolation, as patients felt they were expected to continue with daily life, despite the life changing experience they had endured not long ago.

> *"But actually, experiencing it was different, you sort of felt like you've been through cancer, massive ordeal and all of a sudden, I'm back home, looking after- not looking after myself but getting on with my life as before. And my life, wasn't, isn't really like before"* (Female, 67, Control)

For some, having to continue with adjuvant treatment postoperatively made it difficult to mentally move on from the surgical experience. Patients wanted to be perceived as physically well even as they were undergoing additional treatment.

> *"I have been for a long time trying to protect my family and friends from thinking that I was really sick, if you know what I mean. Ah and maybe it's just now it's time to you know and I'm- I'm not really sick I, I mean I'm going through treatment and I am sick, but em I'm not em, I suppose I want them to look at me in the same way as they would look at anyone else."* (Female, 66, Control).

In the wake of surgery and recovery, resignation was employed as a psychological mechanism to make sense of diagnosis and protect against further psychological trauma. Rather than engage in anxiety or blame, patients learned to accept their diagnosis and the prospect of further surgery or treatments. The surgical experience was sometimes minimised as patients separated themselves from surgery and recovery. Although attempts are made to avoid the surgical experience, patients acknowledge that this is not always possible as they engage in daily life, such as watching television.

"It's impossible to avoid it like, every TV show or every movie like it's just an easy thing to write into a script, (AS Yes), if you want to kill off a character so it's impossible to – to avoid it" (Male ,30, Intervention).

5.3.3.2.2 Subtheme 2: Meeting External Support Needs. In the postoperative period, a lack of psychological support was highlighted as a potential gap in postoperative care. This lack of support hindered recovery, increasing feelings of isolation or ignoring psychological support needs. Patients struggled to integrate with local or community level support, with the challenge of HIPEC adding increased complexity to the recovery experience. Psychological support was viewed as a potentially positive addition to postoperative care that could be adapted to suit individual psychological needs and stages of recovery.

Patients that did engage with structured support like counselling felt it positively contributed to recovery, helping them to probe underlying emotions and work through the trauma of surgery. *"Yeah, yeah, like that has actually cleared yeah. I have been getting counselling so, that has really -really helped me to sort of break through a lot of those sorts of things"* (Female, 66, Control). However, it was acknowledged that the decision to seek and engage with psychological support was an individual choice and would depend on patients own psychological response to surgery and recovery

"I suppose there's a bit of a balance to be stuck really, and I mean – and I suppose it's very hard – it's very hard to know different people will react, you know will react to surgery and medications and things in different ways. Do you know what I mean?" (Female ,53, Control).

Even though some patients felt that they had sufficient support through family and friends, there was a strong sense of needing psychological support available, particularly for those who may be isolated in the postoperative period. Patients were very appreciative of social support and wondered how they could have faced recovery without it.

"I think people who maybe did not have the support? Like I was lucky, I had support from everyone all around me, my neighbours, everybody. It was actually fabulous. I couldn't believe it. I couldn't believe that I was that important that they'd actually- they'd actually do that you know?" (Female,66, Intervention).

Although patients were aware of support groups, they didn't always meet the needs or expectations of patients recovering from HIPEC, since some groups were *"completely geared towards people who weren't working who were getting chemotherapy. No one had heard of the type of cancer that I'd had but wasn't even listed I don't think"* (Female,54, Intervention). Some patients also avoided seeking out additional psychological support groups or services as they felt this would be an additional source of stress or burden during their recovery. Such as the burden of having to seek an alternative therapist if you don't feel comfortable, or that participation in support groups would increase stress and anxiety.

Mental and physical hardship during recovery was highlighted as an issue whereby patients would benefit from psychological support. The mental monotony and fatigue of physical recovery can take a psychological toll on patients, compounded by the ongoing anxiety of subsequent treatment or surveillance scans. The burden of experiences like fatigue could be alleviated by support and counselling.

> *"You know, for mental health and all sorts of areas like that. And actually, mental health is a thing as well as part of this whole situation. You know you do., like I've been in bed, for days on end em eh you know out of recovery. I can kind of get you down a little bit"* (Male,55, Intervention).

This post surgery period was emphasised as a time of significant psychological uncertainty and upheaval. It was clear that patients believed that intervention during this period would reduce feelings of isolation and allow them to process both their past traumatic experiences, and future concerns. *"My mind is changed you know, you've gone through something, and it's really affected you and you're just there isn't much there's no help"* (Female, 67,Control).

There exists a need to improve the availability of psychological support for patients recovering from CRS-HIPEC surgery. The physical and mental recovery of HIPEC presents psychological challenges, but patients currently feel unsupported psychologically in their transition to postoperative recovery. Psychological support was understood as a delicate individual process whereby the support provided needed to match patients' unique needs based on their own journey from surgery towards recovery.

To aid recovery, structured and unstructured sources of support were used by patients to promote quality of life. Sources of structured support included psychological counselling, nutrition advice and exercise classes. The intervention components were also an additional source of structured support. Patients also relied on friends and family for emotional and practical support during recovery. Medical reassurance was also important for patients as they dealt with the uncertainty of postoperative complications. The combination of physical and mental support supported overall quality of life and wellbeing.

> *"It's all linked. I mean everything is linked, it's, it's, you know it's from diet, exercise to kind of backup services...everything is wrapped around as I said earlier a holistic approach. Em I think people em have a much better outcome from these things"* (Male ,55, Intervention).

There existed an awareness of the psychological benefits of structured intervention support, and that supporting exercise and nutrition would inadvertently promote psychological recovery.

> *"And that comes into the mental thing as well you know you're, you know you're mentally I-I could see myself getting better, kind of see myself, looking healthier and it was just all...do you know the whole lot together was just a great experience to tell you the truth."* (Male, 45, Intervention).

Patients also relied on family and friends for emotional and practical support during immediate recovery. Immediate recovery was marred with anxiety and uncertainty, and patients relied heavily on close family and friends during times of mental and physical vulnerability.

> *"My family were fantastic, my husband was brilliant, my job was, I couldn't fault- I got support from everywhere. And what happened was then because of that when I had the support then I knew that you that I can-I can get better"* (Female ,66, Intervention).

Medical reassurance was also important during this time. During their time in hospital, the opinions and attitude of the medical team towards recovery and surgery were a great source of comfort for patients. *"It is attitude, and I think the attitude of*

everyone in the hospital, was always very positive, so that kind of leads back again to make you feel more comfortable" (Male,63, Control). After leaving the hospital, anxiety and uncertainty increased as patients no longer had the immediate comfort of medical guidance when navigating postoperative complications. Patients leaned on friends and family members in medical fields at times to provide this assurance in the absence of the direct medical team. "*And then I have my daughter, is a medic. So she was, she was a support to me (AS Yeah), And she resigned her job for two months to stay at home with me. So, I had that support"* (Female ,65, Intervention). Patients also noted that the calls they received as part of their participation in the trial aided recovery by acting as a further source of comfort for any questions, or as a source of general support when they did not want to contact the medical team. *"I feel that even though this isn't what would you call it, help related to the actual surgery, I felt I was in being kept the loop or something like that"* (Female,57, Control).

Support was paramount to the journey of recovery and took many forms. Structured support provided confidence and motivation to strive and continue to recover well in a supported environment. Lifestyle structural changes like diet and exercise further promote recovery by positively impacting psychological wellbeing. Support from close family and friends increased wellbeing during a time of psychological and physical frailty, allowing patients to focus on recovery, and lean on them though periods of distress.

5.3.3.2.3 Subtheme 3: Cautious Optimism for Future Quality of Life. For patients, a positive surgical experience allowed them to be optimistic for their futures and future quality of life. Physically, how they coped with surgery and recovery was a source of reassurance and allowed for a reduction in anxiety whereby they could now focus their attention on their futures. Patients were cautiously optimistic but were aware that recovery would be a long process.

Many patients described positive recovery experiences, that in turn increased optimism about their current health status and future health prospects. These included a lack of postoperative complications, need for further treatments or a reduced hospital stay. *"I think it was just like, we were better prepped in general like myself and obviously the support from yourselves and I think yeah, everything kind of culminated together to give me a, a, a good surgery"* (Male,30, Intervention).

This lack of physical impact allowed patients to detach from the trauma of surgery itself and focus on the future. Reflecting on their surgical experience and treatments also promoted optimism. *"Compared to other people like I met in the oncology day oncology who were very-very ill. And in fact, the immunotherapy is fine. The most tiring thing is kind of traveling up to get my immunotherapy and travelling home"* (Female,53, Control).

Regardless of current physical condition, patients were aware that recovery was a long and arduous process.

> *"Mentally, again my, my approach to it is, is very much em, I take it step by step. I'm not looking to jump forward too far, because I know that that's not a viable way to look at it. Em so, so I take it step by step* (Male,55, Intervention).

Patients acknowledged that they experienced increased anxiety preoperatively, and that thankfully anxiety had lessened during the postoperative phase. This contrast was stark, with anxiety decreasing significantly after completion of CRS-HIPEC

A reduction in psychological distress supported emotional wellbeing postoperatively. Patients could appreciate that compared to their preoperative psychological state, their levels of anxiety had largely improved.

> "*I'd say the last, from the 20th of [Month] to and say the two or three weeks after that was probably the most emotional, I've been in my whole life (AS ok) em so but after the operation I was ok"* (Male ,38, Intervention).

Preoperative anxiety was largely related to feelings of uncertainty, and now that patients were in the postoperative phase they could finally feel a sense of relief from presurgical fears. *"It's better not to be looking up too much because you don't know what's going to happen. So, I'd say I'd massive anxiety before it (AS mhm), but ...not about it afterwards if that makes sense."* (Female ,54, Intervention). The unknown had been realised, and they were now about to focus on long term recovery and future quality of life.

Striking a balance between optimism and realism was important, as patients learned when to push themselves during physical activities, and when to allow their bodies more time for adjustment and healing.

"I would have always pushed myself and you know been really pushing myself to do, whatever, but I have to now realise that it's not possible. So, I just have to work within the limits that I can, you know?" (Female,67, Intervention).

Surgery despite the physical and psychological challenge was a positive experience. A positive postoperative phase further encouraged patients to increase physical activity and quality of life. "*Keep positive that we're going to be here hopefully for another while away. You know, no, I keep that, I keep positive. It doesn't really stop doing anything"* (Female ,66, Intervention). Determination and optimism in recovery was cushioned by a firm sense of realism and ability to evaluate the physical boundaries of current activity and ultimately increase quality of life.

5.3.3.3 Theme 3: Adjusting to the Impact of Surgery on Daily Life

This theme highlights the psychological changes and shifts in perspective experienced by patients as a result of their diagnosis and surgery. Psychologically, surgery represented a traumatic event that patients were still coming to terms with during their physical recovery. Changes in psychological distress throughout the recovery period are explored in subtheme 1, *Psychological Distress Across Recovery.* Subtheme 2, *Life Through a New Lens* illustrates various ways that patients have changed their perspectives or outlook on life as a result of diagnosis and surgery, focusing on time, mortality and appreciation for health. Finally, subtheme 3, *Understanding a New Normal* highlights the challenges patients faced when coming to terms with their new levels of physical wellbeing and quality of life, and how patients navigated these changes internally.

5.3.3.3.1 Subtheme 1: Psychological Distress Across Recovery. Surgery was understood as a physically and mentally traumatising event, that patients are still experiencing the lingering effects of today. Distress fluctuated across time, concentrating largely during immediate and inpatient recovery.

"*Mentally I think that was just...That was probably the worst experience I'd ever had, in hospital was the last time I was in like. And I think that after I came out, like I visibly looked like, fairly bad like"* (Male 30, Intervention).

Changes and declines in physical wellbeing were another source of distress, as it prevented patients from reengaging in normal life, or returning to pretreatment levels of functioning. Patients recounted past periods of mental distress and how they struggled to cope with the challenges associated with recovery and subsequent treatments.

Hospital recovery was a strange and isolating experience for patients. Regardless of the high standard of postoperative care from staff, patients could not avoid feelings of loss of autonomy and vulnerability while recovering in hospital.

> *"You're too wrecked to stand, and you know, it's that kind of extra stuff where like. And you don't want to be bothering a nurse like, oh can you check the toilets is someone there so then I can go down, do you know. You like having your own independence and I definitely think, that was a big thing for me was like. I was nervous when I was being moved from the HDU [high dependency unit] to a ward like, cos I just know how it is before in terms of like…you're pretty much in worse shape than everyone else in the ward I think."* (Male, 30, Intervention)

Physical and practical factors contributed to these feelings, like issues with assigned meals, accessing bathrooms and common spaces while physically frail, and experiencing a general lack of privacy during a mentally and physically arduous experience. "*But you know my, I felt my senses were very heightened in terms of self-preservation."* (Female, 67, Control).

Physical recovery in hospital was mentally and physically draining. Coupled with residual effects of anaesthesia and general fatigue, patients described periods of physical trauma including dramatic weight loss or physical complications as well as pains related to scarring and internal recovery.

> *"Yeah, I was very- I was upset on the phone, my throat was unbelievably sore. I suppose that was because they had the tube down my throat for such a long time. Wasn't like the last time where it was just a little bit. The last surgery was like a walk in the park ...um...compared to this one"* (Female,54, Intervention).

The continuation of treatments and remnants of illness were ongoing sources of psychological distress. Recurrence of illness and adjuvant treatments acted as retraumatising events, mirroring the shock of diagnosis and trepidation of invasive

treatment or the prospect of further surgery. Patients reflected on prior experiences of treatments and how more recent treatments were more physically taxing.

> "*Physically like it was really hard, em... You know until everything healed up, and then I got about a month or so yeah, I think every month or so before I started the new treatment (AS okay). But it's since the new treatment now like this, this new treatment is the worst treatment I've ever been on"* (Female,59, Intervention).

Adapting to physical lifestyle challenges was also a source of distress and low mood, such as having to adapt to a new diet, which is common given the physical implications of CRS-HIPEC. Patients acknowledge the direct link between issues with treatments and lifestyle, and current low mood.

> *"It's quite important to sort of settle your guts. And I found that quite depressing. Because it would be very different than my normal diet. And I do think there's a big link between what you eat and your mood"* (Female,55, Control).

Since patients had now been engaged in recovery long term, they were able to reflect on prior experiences of distress that they may not have acknowledged initially.

> *"I've a few pictures of like myself that I look at, and I don't think I realized how bad I was at the time but yeah...it- it definitely took a mental toll on me a lot bigger than I think I was aware of"* (Male,30, Intervention).

For those facing additional treatments or where surgery was not completely successful, daily life was now interspersed with panic and anxiety about the future. *"There're nights I can't sleep, you know (AS yep) or I wake up, and I wake up in a panic. You know you're kind of get panicky."* (Female,59, Intervention). The experience of cancer diagnoses also increased general anxiety in daily life.

> *"You know do you feel your stomach is turning all the time, and it would be over everything. If (name) was going out in the car, and all I'd be worried about would she get back alright and the same with the daughter and son and I'm*

sitting there thinking things that can't happen do you know what I mean silly things like," (Male,70, Intervention).

5.3.3.3.2 Subtheme 2: Life Through a New Lens. This subtheme illustrates how the combined experience of diagnosis, surgery and recovery caused patients to shift their perspectives regarding health, mortality and appreciation for life, largely focused on the concept of time and mortality. Patients no longer have the luxury of feeling removed from mortality.

"*If you go oh, isn't it awful you know if they said that to me, you know you'd just collapse in self-pity when in fact you know you know you just went well okay this is and I'm lucky to be alive really"* (Female,55, Control).

Similarly, patients expressed feeling that their relationship with time both past and present has been altered as a result of their experiences. Changes in perception of mortality were cause for anxiety, however, not all shifts in perspective were inherently negative. *"If they hadn't found it...I could have gone on for a year, two years maybe before it would become a problem and then it would be too late."* (Male,66, Control). Patients reported a strong sense of appreciation and gratitude for surgery and their ability to recover well, particularly how this process allowed them to reevaluate what was important in their lives.

Patients were acutely aware that their successful surgery did not mean that their cancer experience was behind them. They expressed a sense of continued uncertainty and living "in limbo". Although immediate recovery has passed, the future will be determined by surveillance scans and the constant monitoring of symptoms, which at any point could result in traumatising events like further treatment or surgery. "*And it's never off your mind with this week and coming now, and next week coming, it's permanently there what's going to be told to you next week"* (Female,59, Intervention). This constant awareness of mortality is mentally taxing for patients, as thoughts of mortality and further cancer diagnoses are overwhelming. *"It is, it's horrible like you know like you're looking at your kids and thinking I'm I going I'm I going to get to see these grow up like and its- that's horrible thoughts like you know*" (Female,66, Intervention). Adjuvant treatment and surveillance scans were stark reminders or mortality for patients, and that recurrence could be a possibility in the future.

"*So yeah, I feel like time's going by quickly, and I feel like that's the case for everyone. I think just sometimes I'm a bit more aware of it in terms of like...I'm happy about getting closer to scans*" (Male,30, Intervention).

In contrast to feelings of anxiety and uncertainty, the patient experience offered some participants a new perspective on life. Illness was an opportunity for patients to pause and reevaluate what was truly important. "*When people say God look what you've come through, look it, there's people worse off than me, you know I'm doing what I have to do, I'm still here that's the main thing. You know?*" (Female,66, Intervention). There was a sense of relief associated with this new perspective, as patients could let go of issues or concerns that prior to their experience would have become all encompassing. Appreciation and gratitude for health was also evident. Patients were aware that they faced a rare diagnosis and complex treatment pathway.

"*It was always just called "the C word" like people were even afraid to mention the word! You know now, like every third person is getting cancer in some form or another so like it's not the big thing and treatment is an awful lot better and stuff like that and people need to eh kind of understand that?*" (Male,66, Control).

They were grateful for the expertise of the medical team, and for their ability to recover well. For intervention patients, support in the rehabilitative phase changed the perspective of exercise as wellness and how it positively contributed to quality of life.

"The exercise and it's just kind of getting yourself right, you know in that frame of mind you know getting yourself up in the morning you know, getting yourself a little bit of a drive you know that you probably wouldn't have had before." (Male, 45, Intervention)

Despite their arduous journey, patients were overall grateful for their journey of recovery, and the positive aspects of recovery such as an increased appreciation for and a new perspective on life.

"*I suppose it gets kind of a, a reality you know kind of when, you just -I kind of feel really like you just try to, to make the most of what you can when you can you know that's the way I – I would think on it*" (Female,53,Control).

The experience of cancer marked a fundamental physical and psychological shift for patients. This paradigm shift resulted in increased fear and anxiety of mortality and time, but also feelings of appreciation and gratitude. The cancer experience has altered their view of life and offered a new lens by which patients will understand and contend with future life challenges.

5.3.3.3.3 Subtheme 3: Understanding a New Normal. Now that patients are well into recovery, the once uncertain future of recovery has become a very real physical and mental challenge that patients grapple with as part of daily life. *"It's a new normal. The old normal is gone- this is the new normal"* (Female,67, Intervention). This process involved adapting to new physical lifestyle challenges and quality of life constraints. These periods were interjected with feelings of isolation and resignation about quality of life changes.

Prioritising and protecting a good quality of life was important for patients. For many, returning to preoperative quality of life was not possible due to physical complications in recovery, or diminished energy levels from adjuvant treatment or fatigue. During immediate recovery physical limitations in hospital heightened feelings of unease and a need for self-preservation. *"I have to look after myself you know it was a really strong feeling of, look you've now just to make sure everything is okay"* (Female,67, Control).

Experience of postoperative quality of life varied, and patients acknowledged that similar to psychological recovery, physical quality of life was an individual concept that varied widely across individual contexts, and that no one factor was *"a silver bullet to save you"* (Female ,55, Control). This was further heightened by the diverse range of postoperative complications, tumour sites and treatment options associated with peritoneal malignancy. Patients described periods of adaptation and assimilation to their new quality of life and physical challenges. Adapting to the use of a colostomy or stoma bag was a large physical and psychological challenge. *".. but the stoma, I still think about it all the time going into the bathroom and checking it and do you know what I mean"* (Male,70, Intervention). When highlighting quality of life issues, diet and adjusting to the demands of the stoma bag were present, as was the issue of diet more generally, due to the physical consequences of surgery. Patients

described changing both the quantity and types of foods they ate and worried about potential effects.

> *"I mean I've never eaten as much toasted cheese sandwiches in my life (laughter), em because it's obviously the only thing you can eat, on, when you're out. So yeah, my diet has changed radically, and it does slightly concern me somewhat"* (Female,55, Control).

In terms of physical adaptation, patients were concerned about lifting heavy items or young children, out of fear of tearing stitches during recovery or causing further bowel discomfort. Despite challenges, patients expected to recover well and were aware that recovery was a slow process, measured by small improvements like walking *"I just was walking more or less that's you know and I built up my steps and I had little routes around the area to walk"* (Female,67, Control).

5.4 Discussion

The postoperative period is a time of physical and emotional upheaval for many patients. The objectives of this study were to understand the patient experience post-surgery through qualitative investigation and investigate possible influencing factors on CRCI including exercise and nutrition intervention and psychological wellbeing. This is to our knowledge, the first qualitative exploration of cognitive function and psychological wellbeing for patients recovering from CRS-HIPEC engaged in combined pre-and rehabilitation. Findings shed light on the complex cognitive and psychological variability that patients face during recovery. Thematic analysis highlighted three primary themes to illustrate the complexity of the patient experience: *Cognition Within the Recovery Mindset, Sources of Strength on the Journey of Recovery* and *Adjustment to the Impact of Surgery on Daily Life*. Findings illustrate the psychological and cognitive experiences of CRS-HIPEC patients after combined pre-and rehabilitation.

Cognitive experiences and their relationship to psychological constructs were illustrated within the theme *Cognition Within the Recovery Mindset.* When reflecting on cognitive experiences patients were aware of a distinction between immediate

postoperative recovery and the present day. As interviews were conducted on average 41 weeks/10months post-surgery, this allowed patients to wholly reflect on the experience of postoperative recovery. Prior CRCI qualitative research has explored patients' experiences on average three to five years post treatment (Haywood et al., 2023, Sharma & Brunet, 2023). These findings illustrate the variability in patient experience from the immediate postoperative period and longer-term recovery. Compared to patients further in their recovery journey (Haywood et al., 2023, Sharma & Brunet, 2023), patients in the present study reported similar difficulties and barriers as those living with CRCI in long-term survivorship, including difficulty in social situations, self-confidence in cognitive function and issues with returning to work (Haywood et al., 2023). Patients also used similar descriptive terms to describe their daily cognitive experiences as outlined by Sharma & Brunet (2023), including the idea of "fog". However, compared to prior work which focused on those who have self-reported CRCI (Haywood et al., 2023, Sharma & Brunet, 2023), findings of the present research also allowed for increased insight into CRCI fluctuations within this cancer population, and how for some, postoperative cognitive experience improved. Patients also in this group made efforts to attribute their CRCI to various causes such as treatment, which was also noted in the experiences of long-term survivors (Sharma & Brunet, 2023). Variability was represented cognitively as fluctuations in cognitive experience, primarily memory and cognitive fatigue, and how these problems were exacerbated in hospital, which could be possibly explained as a result of the invasive nature of the complex CRS-HIPEC procedure (Karimi et al., 2024). In some cases, cognitive concerns had subsided as recovery progressed, while for others cognitive concerns were persistent, further highlighting the importance of understanding what contributes to individual variability of cognitive experience. Previous conceptual schemas of CRCI emphasise the transient nature of CRCI within the 6–12-month period post treatment across studies (Hutterer & Oberndorfer, 2021). The results of this research highlight that this transience within the postoperative period, as evidenced through the theme *"Cognition in Flux"*, is an issue for patients recovering from CRS-HIPEC. Research has also highlighted a dose dependent relationship between chemotherapy and cognitive symptoms, but more work is required to understand the long-term effects of it and other treatments on CRCI (Bai & Yu, 2021). In addition, the present findings expand on prior CRCI qualitative literature (Haywood et al., 2023, Sharma & Brunet, 2023) by exploring cognitive experience for all patients post

treatment within a patient cohort as opposed to only those who self-report cognitive problems in recovery. This aspect of the research provided valuable insight into factors that can potentially contribute positively to cognitive health and wellbeing like physical and cognitive activities. It provided insight into the importance of returning to work and cognitively demanding activities to promote cognitive and psychological wellbeing. The present findings in this chapter contribute to the research landscape by aiding our understanding of how patients experience fluctuations in perceived cognition, and how other factors may contribute to this experience. It also contributes by providing an insight into healthy cognitive function post CRS-HIPEC, and the potential positive impacts of combined exercise and nutrition pre- and rehabilitation.

Consistent with prior conceptual research (Hutterer & Oberndorfer, 2021, Lange et al., 2019), patients noted that adjuvant treatments like chemotherapy may have negatively impacted their cognition. However, patients were also able to highlight factors that supported cognitive perception, such as returning to work and taking part in cognitively demanding tasks. Returning to work has previously been highlighted by patients as a challenge postoperatively due to cognitive impairments (Haywood et al., 2023). These findings highlight the importance of supporting patients postoperatively in their return to work or other cognitively enriching activities, as they can contribute to feelings of self-confidence and normality in recovery. As prior qualitative research explores the experience of survivors who experience persistent cognitive impairment across a range of cancer types (Haywood et al., 2023, Sharma & Brunet, 2023), the present findings contribute to the literature by highlighting the positive cognitive experience postoperatively which helps us learn more about the continuum of cognitive health to CRCI.

Findings also illustrated an in-depth insight into the psychological experience of patients recovering from CRS-HIPEC. Interestingly, the interaction between psychological wellbeing and cognitive function postoperatively was bi-directional, with patients describing instances whereby cognition influenced and was influenced by psychological wellbeing. In terms of psychological impact, cognitive lapses created issues with self-confidence and navigating social situations. Concentration was impacted by the experience of surgery and cancer occupying thoughts. Rumination after even successful cancer treatments is a common experience. Across cancer types, patients describe intrusive all encompassing thoughts even through periods of remission

that impact on daily life (Öcalan & Üzar-Özçetin, 2023). The concept of a bi-directional association between psychological wellbeing and CRCI has been previously proposed within conceptual models (Haywood et al., 2024). It appears there is a risk of psychological distress as a result of cognitive status, and future research should address this supportive care gap.

The main theme *Sources of Strength on the Journey of Recovery* further highlighted additional supportive care needs for CRS-HIPEC patients in recovery. In particular a need for increased psychological support was highlighted. Prior research has attempted to distinguish between long-term persistent psychological distress among cancer survivors, and late effects of treatment (Stein et al., 2008). There exist variability and challenges in determining the prevalence of psychological distress as well as acknowledging that the cancer experience in of itself is dynamic and as such psychological distress may also fluctuate (Stein et al., 2008). Immediate recovery has previously been described as a psychologically taxing experience (Abelson et al., 2018). Furthermore, fluctuations in mental state are a common experience post CRS-HIPEC surgery (Eriksson et al., 2013), as patients grapple with the completion of surgery and transition to long term physical recovery. The present research supports this as patients noted fluctuations in both psychological and mental state post-surgery, in particular, during immediate postoperative recovery in hospital. How psychological distress manifests through qualitative investigation furthers our understanding of psychological distress in cancer survivorship. A lack of support post peritoneal treatment also increases feelings of isolation and difficulty accessing subsequent support (Lond et al., 2025). Feelings of distress were evident during the postoperative period and recovery and present findings supported prior phenomenological explorations of the experiences of patients with peritoneal mesothelioma. In particular, physical experiences marked by changes and a struggle adjusting to new realities such as scarring and ostomy bags. Coping with malnutrition due to limited postoperative diet was another factor that contributed to negative wellbeing in recovery in this cohort, which has previously been observed in patients with peritoneal mesothelioma (Lond et al., 2025). Distress management from diagnosis has been previously recommended by the National Comprehensive Cancer Network (NCCN) within standard care, as well as the provision of appropriate signposting of psychosocial services to patients and families (Riba et al., 2019). In Ireland, the proposed model of psychosocial and psycho-

oncology care recommends group based psychosocial education even for persistent mild levels of distress (Greally, 2020). The combination of living with a rare cancer diagnosis and CRS-HIPEC treatments makes patients vulnerable to psychological distress post-surgery, and patients advocate for increased provision of psychological intervention to complement existing family support.

As part of trial participation, eleven out of eighteen of these patients were assigned and participated in combined pre and rehabilitation that included structured exercise and nutrition support. Trial participation supported physical wellbeing but also contributed positively towards experience of psychological and social support through engagement both with the intervention and intervention team members. Recent meta-analytic evidence across over 80 studies supports the effect of physical activity on people diagnosed with cancer on psychological health outcomes (Calder et al., 2025). The link between exercise and factors that are known to moderate stress via the HPA axis like dopamine and serotonin have been well established (Mikkelsen et al., 2017). Given the influence of stress on cognitive function (Andreotti et al., 2015), exercise could promote both psychological wellbeing and cognitive function. The experience of patients within the current trial highlights the potential for engagement in exercise and nutrition structured support to also support overall patient wellbeing.

Adjustment to life post-surgery also represents another area where increased support may be required. Patients highlighted challenges associated with CRS-HIPEC treatment including adapting to nutritional requirements and physical challenges like adapting to life with a colostomy bag. Psychological nursing intervention within a comprehensive care model has been shown to be effective on psychological and postoperative outcomes for patients with a colostomy bag (Yu & Tang, 2021). Early postoperative intervention may help to mitigate physical and psychological adjustment post-surgery for those struggling with quality of life challenges. Findings also illustrated the psychological shift in perspective experienced by patients post diagnosis and surgery. CRS-HIPEC patients were both fearful and optimistic about future quality of life, and balanced uncertainty about future treatments with an enduring sense of resilience and optimism. Time was now inextricably linked to an increased awareness of mortality and measured by distance from surgery and surveillance scans. This concept of “scanxiety” has been previously noted as a common issue for patients into survivorship (Patel et al., 2024). Awareness of fear of recurrence is important for

psycho-oncology researchers as it has the potential to share commonalities with generalised health anxiety (Maheu et al., 2021). Understanding the sources of both psychological distresses, and conversely optimism and determination for patients post-surgery can help to develop appropriate future supports.

This study has some limitations. Given that participants were recruited from a preexisting combined prehabilitation and rehabilitation trial, they were subject to the inclusion and exclusion criteria associated with participation including a minimum functional capacity to engage in exercise. This may have increased perceptions of quality of life and positive perceptions of recovery as patients would have had acceptable levels of fitness prior to surgery, and physical fitness can be associated with quality of life in cancer survivors (Bettariga et al., 2025). Similarly, only patients still participating in the trial took part, as some patients may have withdrawn from the trial due to being no longer well enough to engage, and as such do not have patient characteristics for those who were unable to engage. This meant that only patients who were physically fit to engage in the intervention post-surgery were interviewed. Due to the nature of applied clinical research, the range of time between surgery and patient interviews was variable, ranging from 15-96 weeks. Given that the trajectory of change during recovery was highlighted across themes, future research could benefit from a focus on either immediate or long-term recovery in isolation.

The results of the present study have implications for clinical research and practice. It is clear that patients required additional signposting and access to psychological support postoperatively. As national and international guidelines are already in place, the provision of psychological services or information about services should be provided as part of standard care. Fluctuations in cognition had a negative impact on quality of life, and increased psychoeducation for patients about CRCI would help to navigate feelings of uncertainty and isolation in recovery. Finally, results of this study highlighted the importance of psychological and physical wellbeing as it relates to perceived cognitive function in the postoperative period. Future research should focus on exploring the physical and psychological pre and postoperative correlates of perceived cognitive function in order to further our conceptual understanding of CRCI.

5.5 Conclusion

This study for the first time explored the cognitive and psychological experiences of patients engaged in a combined pre- and rehabilitation programme after CRS-HIPEC treatment. Findings illustrate considerable individual variability across cognitive experiences postoperatively, as well as fluctuations in psychological distress. Adjustment to life post-surgery was explored as patients adapted to new challenges and psychologically came to terms with their new perspective on life. Supportive care needs were also highlighted, in particular gaps in psychological care. This work illustrates the importance of understanding the postoperative CRS-HIPEC experience, and the trajectory of perceived cognition and psychological wellbeing for this cohort.

Chapter 6: Exploration of Cognitive Function and Psychological Variables One Year Post-surgery

6.1 Introduction

Cancer related cognitive impairment can have detrimental effects on patients postoperatively, including contributing to a reduction in psychological wellbeing (Haywood et al., 2024) and negative impacts on quality of life (Haywood et al., 2023). Multifactorial models of CRCI illustrate the dynamic interplay of how both person related and quality of life factors can interact with CRCI from pretreatment to recovery, including psychological wellbeing (Oppegaard et al., 2023a). Model conceptualization and aetiology have remained the focus of research exploring a range of treatment, sociodemographic and psychological related factors (Ahles & Hurria, 2018, Oppegaard et al., 2023a). Neuropsychological tests have been traditionally applied alongside self-report measures of cognitive complaints to determine risk within Alzheimer's disease (Rabin et al., 2012). As outlined in chapter 2, a lack of correlation can exist between objective and subjective CRCI measurement. However, recent pretreatment evidence also exists that illustrates high objective impairment amongst patients newly diagnosed with Ovarian cancer, with no associations with subjective measurement (Wang et al., 2024). The co-associations between the two constructs seems to be variable, as recent evidence suggests that perceived impairment can predict objective performance on some executive function related tasks (Goodhew & Edwards, 2025).

The lack of correlation between objective and subjective cognitive function is evident during adjuvant treatment as well, and across time in prospective studies (Biglia et al., 2012, O'Farrell et al., 2017). Indeed, a recent umbrella review by Oliva and colleagues (2024) found that self-report measures of cognitive function were weakly or not associated with neuropsychological tests. These correlational issues are not only present posttreatment, but also in chemotherapy naive patients (Onyedibe et al., 2025). Furthermore, the findings of our systematic review of subjective and objective cognitive impairment prior to any surgery or treatment (Chapter 2, 2.3.6) also reported that of a possible 12 papers only two reported any relationship between objective and subjective cognitive impairment.

In 2011, the International Cancer and Cognition Taskforce (ICCTF), provided guidelines for the use of neuropsychological tests in cancer research (Wefel et al., 2011). Recommendations included the use of neuropsychological testing alongside self-report measures, as these remain the "gold standard" of cognitive testing. Recommended domains of interest included learning and memory, processing speed and executive function. The taskforce (Wefel et al., 2011), also proposed a number of relevant tests with adequate psychometric properties. These included The Hopkins Verbal Learning Test-Revised, The Trail Making Test (A&B) and the Controlled Oral Word Association Test (COWAT). Our systematic review of cancer pretreatment subjective and objective cognitive impairment (Chapter 2, 2.3.4) reported these same three tests among the most commonly used assessments. Furthermore, Capetti and colleagues (2025) recently conducted a systematic review of cognitive screening and assessment within oncology practice. Across 178 studies, 151 different cognitive tests were applied and across relevant domains: The Hopkins Verbal Learning Test Revised was most used to assess memory, the COWAT to assess language, and the Trail Making Test for attention and executive function.

Despite standardisation efforts, questions remain regarding the cause of differences between perceived cognitive experience through subjective measures, and objective neuropsychological test performance. One possible explanation suggested in the literature is the sensitivity of traditional neuropsychological tests to measure CRCI, which primarily presents as mild to moderate levels of cognitive impairment which can be subtle compared to the moderate to severe levels of impairment that traditional neuropsychological tests may have been created to detect (Ahles & Hurria, 2018). The aforementioned cognitive domains recommended for testing by the ICCTF were selected based on prior research suggesting a frontal subcortical impairment profile encompassing learning and memory, processing speed and executive function, and tests chosen based on strong psychometric properties (Wefel et al., 2011). Further methodological issues pertain to the nature of subjective assessments, which usually ask patients to recall cognitive function over a period of time, compared to neuropsychological tests which collect a more limited timeframe of cognitive activity (O'Farrell et al., 2017). In addition, fluctuations in CRCI from diagnosis to survivorship may pose difficulties for objective testing (Oliva et al., 2024). In 2018, the ICCTF also provided guidelines for and suggested the application of neuroimaging techniques alongside cognitive testing to expand the scope of CRCI research (Deprez et

al., 2018). The use of neuroimaging approaches to assess CRCI in patients has economical and practical challenges, however, recently efforts are being made to incorporate and assess the feasibility of novel neurocognitive measurement like functional near-infrared spectroscopy in order to apply neurocognitive testing within the scope of CRCI measurement (Saita et al., 2025).

The nature and underlying constructs related to perceived cognitive impairment have also been highlighted as a potential explanation for the disparity in objective and subjective CRCI measurement, namely commonalities between experiences of perceived CRCI and other psychological issues (Oliva et al., 2024). Some review research has suggested that subjective cognitive impairment could be representative of different underlying constructs compared to objecting testing, which may explain the differences in reported results (Bray et al., 2018, Areklett et al., 2024) Recent evidence has also found that subjective impairment may be predictive of some objective constructs, but not others (Goodhew & Ewards, 2025). Within theory and conceptualisation, it has also been suggested that psychological factors could contribute to CRCI development prior to treatment (Hutterer & Oberndorfer, 2021, Haywood et al., 2024). Haywood and colleagues (2024) proposed a transdiagnostic model whereby CRCI can be both influenced by psychopathology, and a contributing factor of psychopathology in cancer survivorship. Understanding more about this relationship will inform CRCI conceptualisation from diagnosis to survivorship, as well as underlying constructs that could contribute to perceived cognitive impairment. Indeed, our systematic review found an association between self-reported cognitive impairment and psychological factors, in particular anxiety (Chapter 2, 2.3.7.1), whereas results for associations between objective CRCI and anxiety and depression varied across studies. Results from Chapter 4 (4.3.1.3) also supported an association between emotional wellbeing and perceived cognitive impairment among patients with peritoneal malignancy preparing for CRS-HIPEC treatment. A relationship between subjective or perceived CRCI and psychological variables has been reported across a range of psychological variables including self-efficacy (Maeir et al., 2023), distress (Lycke et al., 2019), anxiety (Yang & Hendrix, 2018) and depression (Yang et al., 2024). Regardless of objective cognitive test performance, perceived cognitive impairment is important to ascertain due to its relationship to patient quality of life, which can include psychosocial and functional daily challenges (Von Ah et al., 2024).

Treatment-related factors can also contribute to the development of CRCI into survivorship (Ahles & Hurria, 2018, Lange et al., 2019, Oppegaard et al., 2023a). Chapter 5 explored the qualitative experiences of CRCI, psychological wellbeing and quality of life among a cohort of patients recovering from CRS-HIPEC treatment. The psychological and quality of life impacts of long term CRCI warrant further investigation (Von Ah et al., 2024), and in order to understand this experience, both subjective and objective factors should be considered (Országhová et al., 2021), and also within the first year post surgery, particularly as the effects of treatments like chemotherapy on CRCI may be dose related, and more research is required to understand the effects of treatments on CRCI (Bai & Yu, 2021). Review papers highlight this variance, noting that across some studies up to 75% of patients had cognitive decline after chemotherapy treatments persisting to 6-12 months post-surgery, whilst up to 35% of patients experience cognitive changes posttreatment (Hutterer & Oberdorfer et al., 2021). Patients highlighted postoperative recovery as a physical and mental challenge, as well as the stress of initiation of further treatments. Physical activity rehabilitation has been identified as beneficial across the cancer care continuum from prehabilitative to rehabilitative phases, and can improve psychological, physical and cognitive-behavioural outcomes (Silver et al., 2013). There is also preliminary support for exercise rehabilitation to reduce CRCI (Zimmer et al., 2016). Understanding how the effects of treatment and psychological factors interact with each other will aid our understanding of CRCI manifestation into survivorship.

Chapters 4 and 5 explored the impact and prevalence of subjective CRCI through self -report measures and qualitative experience from baseline to pre-surgery (Chapter 4), and qualitatively post-surgery (Chapter 5) for patients with Peritoneal Malignancy undergoing CRS-HIPEC surgery who took part in a combined bimodal pre and rehabilitation program.

This chapter examines the self-reported CRCI and objective CRCI at approximately one-year post surgery to:1) identify the prevalence of and relationship between subjective and objective CRCI one-year post surgery; 2) explore the associations between emotional wellbeing and subjective and objective CRCI and 3) explore differences between patients who took part in combined pre and rehabilitation post treatment and control care as usual on CRCI, psychological wellbeing and quality of life. This study will directly explore the following research project objectives:

b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.
c. Assess the relationship between objective and subjective CRCI.
d. Explore the trajectory of pretreatment CRCI from diagnosis to surgery and recovery.
e. Explore CRCI in the postoperative phase to understand its trajectory and influences on CRCI during recovery.

6.2 Methods

6.2.1 Design

This follow-up exploratory nested study reports on patient reported outcomes and neuropsychological test scores of patients who participated in the PANO trial approximately one year post surgery, which explored the feasibility of a bimodal exercise and nutrition pre and rehabilitation program for CRS-HIPEC patients against a control care as usual group.

6.2.2 Participants

Participants were 12 patients that consented to follow-up assessment from the PANO trial (PANO NCT05305820). For a patient flow diagram please see figure 1.2. The details of the PANO trial have been previously described (Chapter 1, section 1.1.5). Of the 12 participants in this nested study, 6 patients took part in the bimodal combined pre and rehabilitation feasibility intervention. The intervention consisted of structured exercise and nutrition support from diagnosis to surgery (prehabilitation), and for six weeks post-surgery (rehabilitation). Exercise support was provided by ExWell Medical, an organisation specialising in chronic illness exercise rehabilitation. Nutrition support was provided by the dietetic clinical team at Mater Misericordiae University Hospital. The control group received care as usual. The exclusion and inclusion criteria for patients has been previously described (Chapter 4, Section 4.2).

6.2.3 Procedure

All participants were contacted to confirm consent to follow-up participation (appendix E.2). Assessments were in-person, and the location was arranged to suit the

geographical needs of the participants. Assessments took place between August 2022-November 2024. Participants were provided with the plain language statement before participation (appendix E.1). All assessment measures were completed in-person using paper-based format. Neuropsychological test administration was approximately 15 minutes. After neuropsychological tests were complete, patients completed the self-report measures. Neuropsychological tests were administered by the PhD researcher, who received appropriate training. After test completion, participants were debriefed (appendix E.3).

6.2.4 Ethics

Ethical approval for this study was granted by Dublin City University Research Ethics Committee (DCUREC/2023/047) (Appendix F.2).

6.2.5 Materials

The following patient reported self-report measures and neuropsychological tests are included, some descriptions from Chapter 4 (4.2) as rereported here for clarity. Due to potential licensing limitations self-report questionnaires and neuropsychological tests are not included as appendices.

6.2.5.1 Self-Report Measures

6.2.5.1.1 Functional Assessment of Cancer Therapy- Cognition. The Functional Assessment of Cancer Therapy Version 3- Cognition (Wagner et al., 2009) is a self-report measure designed to assess cancer related cognitive problems. The measure is a self-report 37 item questionnaire and scales are scored using Likert scale of 0-4 ratings, with a higher overall score per subscale indicating higher perceived overall cognitive function. For this assessment Perceived Cognitive Abilities and Impact on Quality of Life subscales ranged from 0 (not at all) to 4 (very much) while the Perceived Cognitive Impairment Subscale and Comments from Others subscale ranged from 0 (Never) to 4 (Several times a day).The measure is scored using four subscales including perceived cognitive impairments (PCI) (18 items, range 0-72), impact of perceived cognitive impairments on QoL (ImpactQoL) (4 Items, range 0-16) , comments from others (CFO) (4 items, range, 0-16) and perceived cognitive abilities (PCA) (7 items, range 0-28). It is recommended from the FACT Group that PCI and PCA subscales should be used to interpret levels of perceived impairments. This

measure has been shown to be valid across a range of cancer populations (Van-Dyk et al., 2020, Wagner et al., 2009). Raw scores on each measure are totalled for each subscale and reverse scoring is applied as required. A higher score is indicative of better perceived cognitive performance. The FACT-Cognition has shown high internal consistency ranging from Cronbach's alpha of 0.92-0.97 across subscales (Oliveira et al., 2022). Research has identified a PCI subscale score of less than or equal to 54 as having the ability to discriminate between CRCI and non CRCI cases among cancer survivors (Van-Dyk et al., 2020).

6.2.5.1.2 Years of Education. Years of education and vocational training was recorded as a proxy for cognitive reserve based on total years of education and vocational training item of the Cognitive Reserve Index (Nucci et al., 2012). Years of education and vocational training is recorded as the number of years of education and vocational training attained, with a higher number of years indicative of increased cognitive reserve capacity. Years of education is a commonly applied proxy of cognitive reserve capacity, due partly to the associations between educational attainment and cognitive decline in non-cancer populations (Pinto et al., 2024), and links between higher education as a protective factor against cognitive decline in cancer populations (Liesto et al., 2022).

6.2.5.1.3 General Self Efficacy. The Generalised Self Efficacy Scale (Schwarzer & Jerusalem, 1995) is used to measure how people respond to life events. The measure consists of 10 items and is scored using a Likert scale ranging from 1 (not true at all) to 4 (exactly true). Items are positively scored with a possible low score of 10 and high score of 40, and higher scores indicate better self-efficacy. General self-efficacy has been previously explored within cancer populations preparing for cancer treatment in the Irish context (Loughney et al., 2024). Evaluation of the measure has indicated high validity and internal consistency across studies (Cronbach's alpha .91) (Zeng et al., 2022).

6.2.5.1.4 Cognitive Failures Questionnaire. The Cognitive Failures Questionnaire (Broadbent et al., 1982) is a 25 item self-report questionnaire designed to assess lapses in attention, memory and cognition in daily life within the past 6 months. Participants are asked to respond to items with a Likert scale response ranging from 0 “Never” to 4 “Very much”. A higher score indicates a higher degree of perceived cognitive impairment. Patients are scored on a range of 0-25 representing low frequency of cognitive complaints, 26-50 moderate cognitive complaints, 51-75 high

cognitive complaints and 75+ Very high frequency of cognitive complaints. The CFQ has demonstrated high internal consistency and validity (Cronbach's alpha .80-.90) (Ekici et al., 2016).

6.2.5.1.5 The Functional Assessment of Cancer Therapy -General. The Functional Assessment of Cancer Therapy- General (FACT-G) Version 4 (Cella et al., 1993) is a 27 item self-report survey that measures quality of life. Patients respond on a five-point Likert scale ranging from 0 (not at all) to 4 (very much). The measure includes four subscales measuring physical well-being (PWB, range 0-28), functional wellbeing (FWB, range 0-28), social/family wellbeing (SWB, range 0-28), and emotional wellbeing (EWB, range 0-24) which create a total score. The total score is derived from the total of the four subscales, and scores are reverse scored as required. The total ranges from 0-108, with a higher total score reflecting a higher perceived health related quality of life (Cella et al., 1993). The FACT-G reports good internal consistency (Cronbach's alpha =.88) (Yusufov et al., 2024). The measure has shown reliability and validity amongst older populations with cancer (Overcash et al., 2001), and both total and subscales have indicated generalised reliability across cancer populations (Victorson et al., 2008). For the purpose of this analysis, the Emotional Wellbeing (EWB) subscale of the FACT-General was used as a measure of emotional wellbeing. The subscale has shown good internal consistency for cancer populations (Cronbach's alpha =0.77) (Costet et al., 2005).

6.2.5.1.6 Euro-QoL-EQ-5D-5L. The EQ-5D is a standardised and validated self-report measure describing health status (non-specific disease but applicable to cancer). The global health status rating was used within this study to assess global health status. Patients were asked to report using a visual analogue scale a measure of "Your Health Today" ranging from 0-100. A higher global health score indicates good health related quality of life (The EuroQOL group, 1990).

6.2.5.2 Neuropsychological Tests

6.2.5.2.1 The Montreal Cognitive Assessment Tool (MoCA). The MoCA Version 8.1 (Nasreddine et al., 2005) is a brief screening tool to assess mild cognitive impairment. The tool consists of questions and tasks relating to six cognitive domains: Short-term memory, Visuospatial abilities, Executive functions, Attention, concentration, working memory, Language and orientation to time and place. The test uses a paper-based administration and takes approximately 10 minutes to complete. The

test is scored out of a possible 30 points, with a total score of <26 indicating possibility of mild cognitive impairment. Conventional guidelines for administration and scoring were applied, including an additional point added for <12 years educational attainment. The MoCA has demonstrated high reliability and validity across general populations (Suchy-Dicey et al., 2025). For training certifications please see Appendix E.4.

6.2.5.2.2 Trail Making Test. The trail making test (Retain et al., 1958) is a two-part paper-based neuropsychological assessment consisting of two parts. Part A instructs participants to draw a line connecting circles numbered 1-25 that are distributed randomly on paper. Part B asks participants to repeat this process, but with a sequence of alternating letters A-L and numbers 1-13. For both trials, patients are instructed to complete the task in the shortest time possible. Scores are recorded as time taken to complete each trial. Errors are also recorded. Participants were provided with instructions and sample demonstrations. Time to completion was recorded and participant errors were noted. Part A assesses visuoperceptual abilities while Part B assesses working memory, secondary task switching and executive function (Sánchez-Cubillo et al., 2009). Patients are scored as the number of seconds taken to complete part A and B, with shorter time indicating better performance. Age and education stratified norms have been reported for both Part A and B in healthy populations (Tombaugh et al., 2004). The trail making test has shown acceptable validity and reliability in research for use with cancer patients (Matuoka et al., 2020)

6.2.5.2.3 Controlled Oral Word Association Test. The Controlled Oral Word Association Test (COWAT) is a neuropsychological test of verbal fluency (Benton et al., 1983). Participants are instructed to name as many individual words as possible beginning with a certain letter in one minute excluding proper nouns and repetitions and pluralisms. For this study the letter battery F-A-S was used. Scores are derived by adding up the number of individual words for each letter category to derive a total score as the number of words across the three letters combined. For the COWAT-FAS participants were instructed to name as many individual words as possible in one minute beginning with the relevant letter, excluding proper nouns, repetitions and plurals. Errors were discounted during scoring. Age stratified norms are available for the COWAT (Tombaugh et al., 1999). The test shows high reliability and validity among healthy adult populations (Suchy-Dicey et al., 2024).

6.2.6 Data Analysis

Data analysis was conducted using IBM SPSS Statistics software version 30. Due to small sample size, non-parametric analysis was applied across the dataset. Descriptive statistics were analysed by condition (control and intervention) and for the overall group. Between group differences for continuous demographic and clinical variables (Age, Years of Education, Days from Surgery, Peritoneal Cancer Index) were analysed using a Mann-Whitney U test, with exact significance applied at 95% confidence interval. Categorical variables (Gender, Cancer Type, ASA Grade, Cytoreduction Completeness Score, Adjuvant Chemotherapy) were analysed with Chi^2 tests with monte Carlo correction applied. One sample Wilcoxon Signed Rank tests were applied to analyse the prevalence of objective and subjective impairment against standardised neuropsychological test norms for the MoCA (Nasreddine et al., 2005), Trail Making Test A and B (Tombaugh et al., 2004) and the COWAT-FAS (Tombaugh et al., 1999), and against the Fact-Cognition Perceived Cognitive Impairment cut-off score (Van-Dyk et al., 2020).

Individual test performance scores were analysed against available age stratified norms for the COWAT-FAS and Trail Making Test A and B scores. In addition, the International Cancer and Cognition Task Force (Wefel et al., 2011) proposed scoring criteria was applied to explore objective cognitive impairment within neuropsychological tests (COWAT FAS & Trail Making Test A&B). Impairment is classed as -1.5 standard deviations on or below a given normative mean across two or more tests, or -2.0 standard deviations on or below a given normative mean on one test. Prevalence levels were assessed at both group and individual levels Patient reported outcomes were scored based on relevant measure guidelines.

Between group differences for all measures were assessed with the Mann-Whitney U test, with exact significance applied. Spearman rank tests were computed to assess the relationship between 1) Objective and subjective cognitive function and 2) Relationship between emotional wellbeing and objective and subjective cognitive function.

6.3 Results

6.3.1 Participant Demographics

Participant demographic and clinical characteristics by group and totals are shown below in table 6.1.The average time since surgery was 350 days, or 50 weeks. Of the n=12 participant group, six patients were in the intervention group and six in the control condition. With regards to gender, n=10 patients were female, and n=2 were male. The average age of participants at time of assessment was 60.42 years. Surgical completeness scores indicated that for the majority of patients (n=10), no disease remained post-surgery. For the remaining patients (n=2), >.25 cm of mass remained. In terms of group differences, only peritoneal cancer index scores were significantly different between groups ($p < .05$); the intervention group had significantly lower peritoneal cancer spread compared to the control group pre-surgery.

Table 6.1

Participant Demographic and Clinical Characteristics (n=12)

Variable	Intervention (6)	Control (6)	Total (12)	Group Difference (p)
Age: **Mdn, IQR** m, sd	**65.50,23** 58.67, 13.06	**61.50, 13,**62.17, 6.88	**65.50, 13**,60.42, 10.12	p=.485
Gender: Female, %	4, 33.3%	6, 100%	10, 80%	P=.121
Years of Education (10) **Mdn, IQR**, m, sd	**16, 4,** 16.8, 2.17 (5)	**18, 5.50,** 16.6, 2.88 (5)	**17, 5**,16.7, 2.41(10)	p=.841
Days from Surgery **Mdn IQR**, m, sd	**338.50, 189**, 348.17, 101.36	**339.50, 108,** 350.50,72.97	**339.50,176.5**,349.33, 84.21	p=.699
Cancer Type Colorectal Ovarian PMP	 3 1 2	 1 2 3	 4 3 5	p=.465
ASA Grade Mild Systemic Disease Severe Systemic Disease	 2 4	 5 1	 7 5	p=.079
Peritoneal Cancer Index **Mdn, IQR,** m, sd	**3.50, 5.50,** 4.83, 3.60	**15.50, 8.75,** 16.00, 4.60	**11, 13.50,**13.14, 9.78	p=.002*
Cytoreduction Completeness Score No Disease Present >.25cm	 6 0	 4 2	 10 2	p=.121
Adjuvant Chemotherapy Yes No	 5 1	 2 4	 7 5	p=.079

Note: *Significant at p<.05 non-parametric, two tailed exact test statistic, m=mean, sd=standard deviation, Mdn=median, IQR=Interquartile range, ASA=American Society of Anaesthesiologists Grade, PMP= pseudomyxoma peritonei

6.3.2 Participant Characteristics for Self-Reported Cognitive Impairment and Neuropsychological Test Performance and Patient Reported Outcomes

The descriptive statistics by group (Mdn, IQR, m, sd) for all patient reported outcomes and neuropsychological test scores are displayed below in table 6.2.

Table 6.2

Descriptive Statistics for Patient Reported Outcomes and Neuropsychological Test Scores

Variable	Intervention (n=6)	Control (n=6)	Total (n=12)
Self-Reported Cognitive Function, Mdn, IQR (m, sd)			
FACT Cog Total	**126.5, 23.75** (121.33, 12.24)	**125.5, 29.75** (116.67,16.88)	**126, 25.5** (119.00, 14.27)
Perceived Cognitive Impairment	**70,10.75** (67.17, 5.64)	**67.5,17.75** (62.33, 10.33)	**68, 11.25** (64.75, 8.32)
Comments From Others	**16, .00** (16, 0.00)	**16, .00** (16, 0.00)	**16, .00** (16, 0.00)
Perceived Cognitive Abilities	**26, 9.5** (23.67, 5.72)	**26, 4.75** (25.17, 2.64)	**26, 6.50** (24.42, 4.32)
Impact on Quality of Life	**15, 3.25** (14.5, 1.76)	**15.5, 6.5** (13.17, 4.45)	**15.5, 3.75** (13.83, 3.30)
Cognitive Failures Questionnaire	**19, 23.5** (23.67, 11.98)	**17, 28.5** (21.67, 18.78)	**17.5, 22** (22.67, 15.05)
Neuropsychological Tests (Mdn, IQR m, sd**)**			
MoCA Total Score	**28.5, 3.25** (27.67, 2.51)	**28, 2.0** (27.67, 1.63)	**28, 2** (27.67, 2.02)
COWAT FAS Total	**41.5, 5.50** (43.17, 6.55)	**40.5, 11.75** (41.67, 8.64)	**41.5, 6.0** (42.41, 7.35)
Trail Making Test A (m seconds, SD)	**29.57, 11.34** (30.28, 8.32)	**34.93, 10.54** (34.14, 7.33)	**32.69, 11.18** (32.21, 7.74)
Trail Making Test B (m seconds, SD)	**71.5, 31.41** (78.22, 28.24)	**67, 35.33** (69.47, 22.62)	**69, 23.04** (73.84, 24.82)
Other Patient Reported Outcomes (Mdn IQR, m, sd**)**			
FACT- General Total	**97, 10.42** (97.72, 5.52)	**96, 14** (93.22, 7.94)	**96.5, 10.5** (95.47, 6.93)
Physical Wellbeing	**26.5, 5.5** (24.83, 3.76)	**26, 4.75** (24.83, 3.60)	**26, 3.75** (24.83, 3.51)
Social Wellbeing	**28, 4.17** (26.56, 2.25)	**27.5, 3.42** (26.56, 1.96)	**28, 3.75** (26.55, 2.01)
Emotional Wellbeing	**22, 2** (21.67, 1.63)	**18, 8.25** (17.5, 3.83)	**21, 4.0** (19.53, 3.56)
Functional Wellbeing	**25.5, 4.25** (24.67, 2.16)	**25, 5.50** (24.33, 3.56)	**25, 4.50** (24.5, 2.81)
Generalised Self-Efficacy	**37.5, 3.5** (36.17, 3.13)	**36.5, 5.75** (34.67, 3.39)	**37, 4.75** (35.42, 3.20)
EuroQoL Global Score	**82.5, 25** (85.53, 11.58)	**85, 28.75** (82.5, 15.41)	**82.5, 23.75** (84.17, 13.11)

Note: m=mean, sd=standard deviation, Mdn=median, IQR=Interquartile range

6.3.3 Cognitive Impairment Prevalence

6.3.3.1 Neuropsychological Test results & Test Norms

Based on the cut off guidelines scores for the MoCA, n=2 participants scored below <26 points indicating mild impaired objective cognitive function. Scores on the Trail Making Test A and B did not differ at a group level from age and education stratified test norms of the group mean (62 years) (Tombaugh et al., 2004). Similarly,

age-stratified scores on COWAT FAS total scores for the group mean fell within normal range (Tombaugh et al., 1998). However, at an individual level, differences were observed between patient scores and test norms, in particular scores for the Trail Making Test A and B where 66.67% of patients exhibited lower performance on the Trail Making Test B compared to age and education stratified norms. Chi² tests were used to assess differences between groups on the number of patients scoring below test cut offs or norms, revealing no significant difference between the intervention and control groups across all tests. Table 6.3 below outlines the number of patients in each group who performed worse than these cut offs and norms.

In addition to individual scores above or below the age-stratified average, the International Cancer and Cognition Taskforce (ICCTF) impairment criteria were also applied to cognitive tests. Scores indicated that objective cognitive impairment was observed in n=1 participant in the control group and n=1 intervention group based on ICCTF scoring guidelines. Results are displayed below in Table 6.4.

Table 6.3

Number of Participants Scoring Below Test Cut Off/Norms and Between Group Differences

Measure	Intervention (n), %	Control (n), %	Total (n), %	Group Difference (p)
MoCA	1, 16.67	1, 16.67	2, 16.67%	.100
TMT A	3, 50	4, 66.67	7, 58.33	.545
TMT B	4, 66.67	4, 66.67	8, 66.7	1.00
COWAT FAS	1, 16.67	3, 50	4, 33.33	.545
FACT-Cognition PCI	0,0	2,33.33	2,16.67%	.455

Table 6.4

Number of Participants Who Met Criteria for Impairment Based on ICCTF Scoring*

Measure	Intervention (n), %	Control (n), %	Total (n), %
TMT A	0, 0	0,0	0,0
TMT B	1, 16.67	1, 16.67	2, 16.67
COWAT FAS	0. 0	0.0	0.0

Note: *International Cancer and Cognition Task Force criteria of scores -1.5 SDs on or below normative values, or one score -2.0 SDs on or below normative value on one test

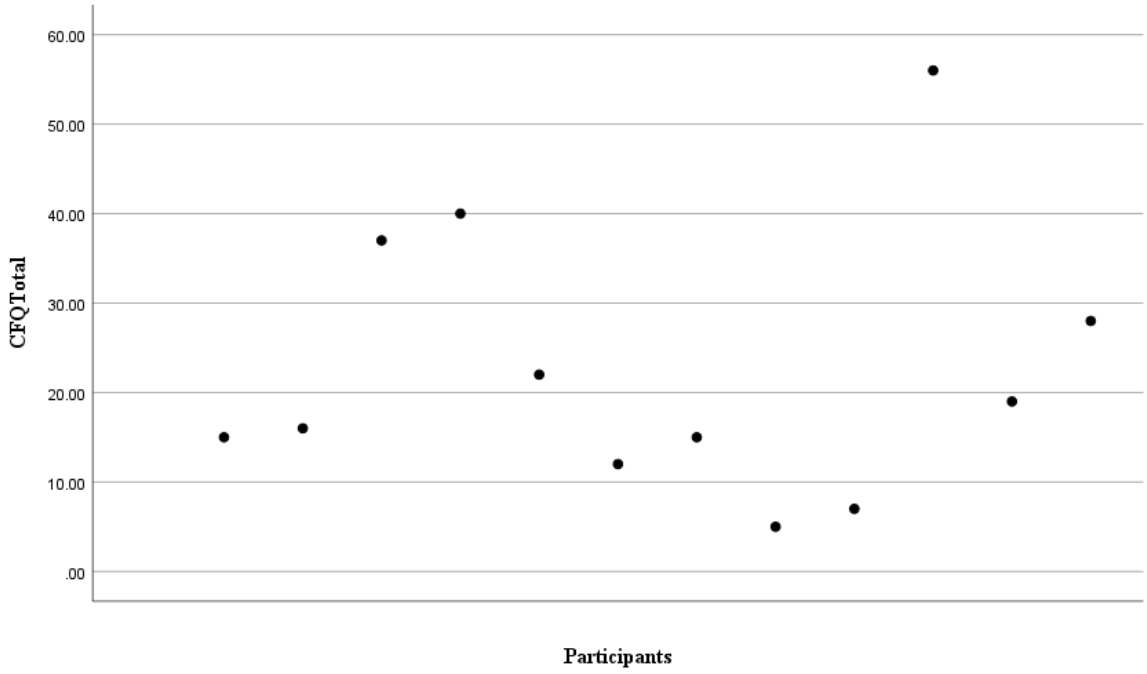
6.3.3.2 Self-Reported Cognitive Function

A one sample Wilcoxon Signed rank test showed that the median score on the FACT-Cognitive PCI did not differ significantly from the PCI cut off score of 54, indicating non-significant levels of perceived cognitive impairment. Results indicated

that n=2 (16.67%) patients scored below the Perceived Cognitive Impairment cut off (See Table 6.3). Analysis of scores on the Cognitive Failures Questionnaire indicated that n=8 patients reported low frequency of cognitive concerns (0-25), n=3 reported moderate frequency of cognitive concerns (26-50) and n=1 patient reported high frequency of cognitive concerns (51-75). Individual Scores for the Cognitive Failures Questionnaire are displayed below in figure 6.1.

Figure 6.1

Scatter plot of Individual Scores on The Cognitive Failures Questionnaire (CFQ) Total Scores



Note: X axis depicts individual scores (n=12) per participant, Y axis is the total score on the Cognitive Failures Questionnaire

6.3.4 Between Group Differences

A Mann Whitney U test was conducted to assess the differences between the control and intervention groups on patient reported outcomes and neuropsychological test scores. The results of all patient reported outcomes and neuropsychological tests results are shown in table 6.5 below. Results indicated that there was a significant difference between intervention (mean rank =6.67) and control groups (mean rank=4.33) on the Emotional Wellbeing scores from the FACT-General measure,

indicating the intervention group had significantly higher emotional wellbeing compared to the control group. Results between groups on all other measures were non-significant. Results are displayed below in table 6.5.

Table 6.5

Mann-Whitney U Test for Cognitive Function and Patient Reported Outcomes

Variable	Intervention Mean Rank	Control Mean Rank	z	p
Self-Reported Cognitive Function				
FACT COG Total	7.42	5.58	12.5	0.394
Perceived Cog Impairment	7.58	5.42	11.5	0.310
Comments from Others	6.50	6.50	18	1.00
Perceived Cog abilities	6.58	6.42	17.5	0.937
Impact on QoL	6.57	6.25	16.5	.818
Cognitive Failures Questionnaire	7.08	5.92	14.5	.589
Neuropsychological Tests				
MoCA Total Score	6.92	6.08	15.5	.699
COWAT FAS Total	6.75	6.25	16.5	.818
Trail Making Test A (m seconds, SD)	5.33	7.67	25.0	.310
Trail Making Test A Errors (n)				
Trail Making Test B (m seconds, SD)	7.08	5.92	14.5	.589
Trial Making Test B Errors (n)				
Patient Reported Outcomes				
FACT-General Total	7.42	5.58	12.5	.394
Physical Wellbeing	6.67	6.33	17	.937
Social Wellbeing	6.75	6.25	16.5	.818
Emotional Wellbeing	6.67	4.33	5.0	.041*
Functional Wellbeing	6.42	6.58	18.5	1.00
Generalised Self Efficacy	7.83	5.17	10	.240
EuroQoL Global Score	6.92	6.08	15.5	.699

Note: *p<.05, Exact Significance Applied

6.3.5 Relationship between Objective and Subjective CRCI

Spearman rank correlations were conducted to assess the relationship between subjective cognitive impairment (Cognitive Failures Questionnaire Total, Fact-

Cognition Perceived Cognitive Impairment subscale) and objective global cognitive function as measured by the MoCA. In terms of the FACT-Cognition PCI, there was no significant relationship between scores on the MoCA (r=.254, p=.426), COWAT FAS Total Scores (r=-.067, p=.835), TMT A (r=.257, p=.421) or TMT B (r=.197, p= .539**).** Similarly, there were no significant associations between scores on the Cognitive Failures Questionnaire and objective measures: MoCA (r=-.136, p=.673), COWAT FAS (r=-.092, p=.776), TMT A (r=-.144, p=656), TMT B (r=.000, p=1.00).

6.3.6 Relationship between Cognitive function and Emotional Wellbeing

Spearman rank correlations were conducted to assess the relationship between subjective and objective cognitive function, and emotional wellbeing as measured by the FACT-General Emotional Wellbeing subscale, and measures of objective and subjective cognitive impairment. For subjective impairment, there was no significant correlation between emotional wellbeing and FACT-Cognition PCI scores (r=.435, p=.157), or total scores on the Cognitive Failures Questionnaire (r=.039, p=.903). Similarly, for objective impairment, there were no significant associations between emotional wellbeing and scores on the MoCA (r=.363, p=.247), COWAT FAS total scores (-.089, p=806), TMT A (-.175, p=.586) and TMT B (r=.007, p=.982) scores.

6.4 Discussion

This is the first study to assess both the subjective and objective cognitive experience of patients recovering from CRS-HIPEC treatment, and associations with emotional wellbeing. This research aimed to further our knowledge of CRCI through investigation of a number of factors including: 1) The prevalence of subjective and objective CRCI one-year post surgery and the relationship between subjective and objective measures; 2) Associations between emotional wellbeing and subjective and objective CRCI; and 3) differences between patients who took part in combined pre- and rehabilitation post treatment and control care as usual

In terms of prevalence, results indicate considerable variability of study findings both between subjective and objective measurement, and between objective test scores. Variability was also observed across perceived CRCI trajectory compared to

pretreatment scores (Chapter 4, 4.3.1.2). Prevalence of perceived impairment reduced from 27.3% preoperatively, to 16.67%. Dynamic fluctuation across CRCI postoperatively has been observed within theoretical modelling, particularly during the first 6-12 months after treatment (Hutterer & Oberndorfer, 2021). The application of ICCTF criteria also provided increased insight into the prevalence of objective impairment based on individual tests. Within CRS-HIPEC research, postoperative cognitive dysfunction has largely been explored within the immediate postoperative period. Yu and colleagues (2016, 2017), reported that one-week post-surgery, postoperative objective cognitive dysfunction was reported in 39.2% of CRS-HIPEC patients. Research into colorectal cancer also has reported 33% of patients exhibiting objective cognitive dysfunction at 6 month follow up after completion of adjuvant chemotherapy (Cruzado et al., 2014). However, Vardy and colleagues (2022) reported that long-term, there were no statistically significant differences between colorectal cancer survivors 6-12 years post treatment compared with healthy controls. Beyond colorectal cancer, review evidence also suggests that up to 75% of patients can experience persistent cognitive impairment up to 12 months posttreatment (Hutterer & Oberndorfer, 2021). The present results suggest that objective impairment one year post treatment is prevalent to a degree within CRS-HIPEC treatment patients. With regards to other cancer types, research in the first year following a breast cancer diagnosis using the MoCA reported an objective cognitive impairment prevalence rate of 8.1% (Ramalho et al., 2017). Other systematic review evidence for breast cancer survivors reports an estimated prevalence of 21-34% longitudinally based on meta-analysis (Whittaker et al., 2022). In comparison with this literature results of the present research indicate that CRCI is evident for CRS-HIPEC patients post treatment. However, given the small sample size of the current study, further large scale investigation would be required to confirm and generalise current findings.

An additional complicating factor is that postoperative treatment such as neoadjuvant treatment can have CRCI impacts. In the present research, 58.3% of patients had adjuvant chemotherapy (n=7). Both neoadjuvant and adjuvant treatments could have contributed to perceived prevalence, as some research suggests that neoadjuvant treatments can be associated with attentional difficulties based on cerebral blood flow changes (Chen et al., 2017). The trail making test B indicated the highest levels of cognitive impairment based on comparisons with age stratified norms. Prior

research with older breast cancer survivors exploring long-term cognitive decline and comparing TMT-B test scores to norms have reported much lower prevalence rates in the 3% range (Luo et al., 2023). Given this, the results of the present research are high, however it must be noted that the small sample size of the present research limits comparison or generalisability of individual test results.

Findings from this present research highlight the importance of understanding individual variability across both subjective and objective measurement, but also within objective test performance across multiple objective performance measures. Based on group averages, scores did not deviate from age stratified norms for cognitive tests. However, at an individual level results provided interesting insight regarding subjective and objective CRCI prevalence one year post treatment. With regards to subjective tests, 16.67% (n=2) patients, both in the control group, self-reported scores lower than the cut-off for the FACT-Cognition perceived cognitive impairment scale. In terms of the Cognitive Failures Questionnaire, n=4 patients reported moderate to high frequency of cognitive concerns (moderate, n=2 intervention n=1 control, high n=1 control). Objective tests results further highlighted variability within cognitive measurement. Based on International Cancer and Cognition Task Force (ICCTF) neuropsychological test performance criteria, objective impairment was observed within n=2 (16.67%) patients, both based on performance on the Trail Making Test Part B, and n=2 patients (16.67%) scored below the recommended cut-off for the MoCA. The future inclusion of alternative testing methods such as neuroimaging would aid in understanding the neural underpinnings of objective test performance. Research indicates that approximately 30% (ranging from 13-48%) of cancer patients report deterioration in cognition with each chemotherapy cycle (Hutterer & Oberndorfer, 2021). In addition, more research is currently required to understand the dose repose relationship between CRCI and chemotherapy, as well as the manifestation or trajectory of CRCI from treatments beyond chemotherapy (Bai & Yu, 2021). This research contributes to the literature as within this cohort patients underwent combined CRS-HIPEC and in some cases adjuvant or neoadjuvant treatments. With regards to CRS-HIPEC specifically, research has indicated that patients recovering from CRS-HIPEC may be susceptible to postoperative objective cognitive dysfunction a week post-surgery, possibly driven by increases in some inflammatory markers (Yu et al., 2017). This present research

contributes to the literature by providing further evidence for prevalence and trajectory of cognitive impairment after CRS-HIPEC one year post surgery.

These findings validate prior literature reporting on the lack of correlation between objective and subjective measures (Hutchinson et al., 2012). This finding is consistent with previous research which frequently reports a lack of correlation between the two constructs across studies (Oliva et al., 2024, Ahles & Hurria, 2018, Bray et al., 2018). Results from Chapter 2's systematic review of pretreatment CRCI did not find strong evidence for correlations between subjective and objective CRCI across a range of cross-sectional and prospective research designs. Findings from this chapter extend this lack of correlation between subjective and objective measures of CRCI to the post-operative period. Despite a similar prevalence across both subjective and objective measures based on scoring guidelines and criteria (16.67%), no correlations between objective and subjective measures were observed. These findings further support the need to extrapolate the differences between objective and subjective cognitive experience, and whether results could be due to a fundamental difference in the underlying constructs of perceived cognitive impairment, as posited by prior research (Areklett et al., 2024).

In terms of objective tests, the test that indicated a presence of objective CRCI based on population norms was the Trail-Making Test. Part B is largely indicative of working memory and secondary task switching ability among healthy older adults, while part A measures visuoperceptual abilities (Sánchez-Cubillo et al., 2009). Although subjective measures of cognitive impairment did not correlate with the Trail Making Test, qualitative insights of patients postoperatively speak to the existence of working memory difficulties in day to day life postoperatively, including task execution, or an overall lapse in attentiveness (Chapter 5, 5.3.3.1). These findings suggest that decreased cognitive function is maintained for some beyond the immediate postoperative period. Recent research with colorectal cancer patients has also reported significantly longer Trail Making Test times within four weeks of completing chemotherapy compared to controls (Aydin et al., 2025). Prior research suggests that classic neuropsychological tests may lack sensitivity to observe objective impairment, and that the trajectory of CRCI is variable 6-12 months post treatment (Ahles & Hurria, 2018, Hutterer & Oberndorfer, 2021). Within the observed sample, n=1 participant who scored below the cut-off score on the MoCA also had observed cognitive impairment

based on the TMT B scores. The trail-making test B may, as previously suggested (Wefel et al., 2011), possess adequate sensitivity to observe objective impairment within CRCI, but more large-scale research will be required with a healthy control group to further validate findings.

At the time of testing, the intervention group had completed a combined pre- and rehabilitation program. Findings indicated that across all subjective and objective test measures, no group differences were observed. More research is required to understand the acute and long-term effects of exercise on cognitive function for cancer patients. Within health populations, long-term exercise has shown small positive effects on cognitive function, however effects were not specific to any cognitive domains and studies, with effects also evident based on dose duration and type of exercise indicating that at present, the intricacies of the effects of exercise on cognitive function long term require more investigation (Sebastian et al., 2020).

In terms of groups differences at one-year post-surgery, group differences were evident only in the emotional wellbeing subscale of the FACT-General scale. The physical effects of exercise have been shown to increase psychological wellbeing, including anxiety and depression within a breast cancer cohort (Mehnert et al., 2011). A recent systematic review and meta-analysis of 27 intervention studies across cancer types found that exercise interventions for patients undergoing a range of cancer treatments resulted in reduced anxiety and depression severity, and an increase in HrQoL (Soong et al., 2025). Exercise across a range of modes have been shown to increase HrQoL among healthy adults, with motivating factors including group support from classes, increasing physical fitness and emotional stability (McGrath et al., 2011). In addition, exercise has been shown to improve HrQoL in cancer survivors, including emotional wellbeing (Mishra et al., 2014). Results of Chapter 5's post intervention interviews indicated that participants viewed the intervention program as an additional source of support during the postoperative period (Chapter 5). Increased support during the postoperative period could have contributed to overall emotional wellbeing in long-term recovery, or the positive physical benefits of exercise could have contributed to overall quality of life and emotional wellbeing. The disparity also highlights potential gaps in supportive care needs for patients, as evident by the lower levels of emotional wellbeing in the control group. This theme was also highlighted in post intervention

interviews, as patients advocated for increased psychological support as standard within the post-surgery care pathway.

This study also aimed to assess any relationship between emotional wellbeing, and measures of either objective or subjective impairment. Correlation analysis found no significant associations between any cognitive measures and emotional wellbeing. This is in contrast to findings in Chapter 4, which found a correlation between emotional wellbeing and subjective cognitive impairment at baseline. As prior research indicates that subjective cognitive impairment aligns more closely with psychological wellbeing than objective measures (Oliva et al., 2024, Pace et al., 2024), this lack of correlation suggests this relationship may change in the course of treatment. The concept of factors related to CRCI being dynamic and changing across CRCI experience has been suggested previously within CRCI theory (Oppegaard et al., 2023a). As postoperative CRCI has the potential to be further impacted by adjuvant treatments (Oppegaard et al., 2023a). Evidence from patient lived experience also indicates that cognitive issues are highlighted in specific citations including returning to work or interactions with others. As these experiences are variable across individuals it may be difficult to capture the nature of individual impairment based on current measures (Haywood et al., 2023). Fluctuations in psychological wellbeing across stages of recovery have been previously established in systematic research with breast cancer, acknowledging that across the recovery continuum, different factors can be associated with psychological wellbeing such as physical recovery, further treatments and uncertainty about the future (Tao et al., 2024). However, the qualitative findings delved into the psychological experience of participants pre (Chapter 4), and post (Chapter 5) surgery. While anxiety and psychological distress was evident at both time points within both interview sets, postoperative distress was largely retrospective, as patients spoke about previous experiences of distress post-surgery which for most had decreased as patients progressed to long-term recovery, while preoperative anxiety included current levels of psychological distress (Chapter 4). Further investigation of the temporal distinctions between heightened experience of psychological distress or anxiety, heightened periods of cognitive concern, and then individual experience of immediate and long-term recovery could help us to understand potential periods of psychological and cognitive vulnerability for patients.

There are some limitations within the present research. Due to patient attrition, twelve participants took part in the follow-up study, limiting generalisability of findings. Cognitive testing also took place across a variety of testing locations in order to cater to the geographical needs of participants across private locations, community centres and meeting rooms, however, in all cases noise and distractions were avoided. As patients who consented to follow-up were part of the intervention trial (Chapter 1, section 1.1.5), those who participated in follow-up were those who volunteered to participate at this timepoint, which means that they may have had high physical fitness and quality of life. As part of the intervention trial, participants resumed intervention activities when deemed clinically fit to participate. This meant that for some patients the intervention may have resumed soon after surgery, but for others with postoperative complications or a lengthy hospital stay, the return to exercise and nutrition support was delayed due to the physical capacity of the participant. This inadvertently created variability in the long-term survivorship patient pathway.

The results of the present study highlight avenues and opportunities for future research. It is clear that more research is required to interrogate the psychological and cognitive changes from immediate to long-term recovery. In particular, the nuances that exist with regards to determinants of cognitive and psychological distress during recovery. Further research as well as the integration of additional testing such as neuroimaging is required to understand the neuropsychological underpinnings of objective test performance, including the influences of biological factors such as cerebral blood flow fluctuations and inflammation which have also been reported in literature associated with objective test performance (Chen et al., 2017, Yu et al., 2017). Finally, as general emotional wellbeing was highlighted as impacted in post-surgery recovery, further research should expand on postoperative CRS-HIPEC psychological wellbeing through investigation of anxiety, depression and distress.

6.5 Conclusion

This research highlights the objective and subjective cognition of patients at one-year post-surgery. Results further supported a lack of correlation between objective and subjective CRCI but also highlighted considerable variability across test scores and

modes of impairment. Perceived CRCI reduced compared to pretreatment levels. Patients who took part in combined pre and rehabilitation post-surgery also reported significantly higher emotional wellbeing one year post surgery. Results further reveal the complexity of psychological wellbeing and cognitive impairment along the cancer care continuum and the need to understand determinants of psychological and cognitive wellbeing from post-surgery to long-term survivorship. They also illustrate the need to consolidate and further investigate measurement approaches within CRCI research to address individual variability, across not only objective and subjective impairment, but also across tests and self-report measures. Further research should investigate the various psychological factors that could impact cognition and quality of life at each stage of the recovery journey.

7.1 General Discussion

The aim of this thesis was threefold: To critically uncover the prevalence, manifestation and lived experience of CRCI as a function of psychological wellbeing in a rare cancer cohort, some of whom engaged with a bimodal exercise and nutrition optimisation program before and after surgery. The thesis approached this aim in a multipronged way: (1) critical and systematic review of two distinct literatures in cancer research: CRCI present at time of cancer diagnosis, as distinct to emerging as a toxicity effect of treatment; and Prehabilitation impacts on physical, nutrition and cognitive outcomes for patients; (2) implementation of validated self-report measures of CRCI alongside lived experience patient interviews from diagnosis, through to Post-Prehabilitation before surgery, and Post surgery; and (3) exploration of the relationship between self-reported and objective measures of CRCI, as well as psychological wellbeing and quality of life at follow up in recovery

This chapter will consolidate thesis findings and situate them within the wider research landscape. In light of thesis findings recommendations for future research and CRCI conceptualisation will be outlined and considered. Discussion of research findings will be explored through summary of main research findings (7.2). Methodological considerations will be outlined (7.3), followed by a theoretical overview of findings and how these either validate or contribute towards existing schemas or models of CRCI (7.4). Based on findings and associated theories, a conceptual schema of the relationship between pretreatment CRCI, psychological wellbeing and Health-related quality of life (HrQoL) is then proposed. The unique empirical contribution of the research study is outlined including unique contributions to the prehabilitation landscape (7.5) as well as recommendations for future research (7.6). Strengths and weaknesses are considered (7.7) as well as the role of public and patient involvement in the research project. Finally, conclusions are made regarding the contribution of the research project to this research landscape (7.8).

7.1.2 Summary of main research findings

This research explored for the first time the cognitive, psychological and patient experience of people with peritoneal malignancy (PM) preparing for CRS-HIPEC

treatment. Systematic reviews synthesised the evidence for both pretreatment CRCI and its interaction with psychological variables, and affective and functional outcomes as they related to prehabilitation interventions for young to midlife adults. The findings of three empirical research chapters elucidated the cognitive experience of patients preparing and recovering from CRS-HIPEC treatment using self-report measures, qualitative investigations and neuropsychological testing. Findings also highlighted the role of exercise and nutrition pre- and rehabilitation for patients from diagnosis to a 1-year follow-up, both through quantitative investigation and exploration of intervention experience through qualitative interview. This thesis adds a unique contribution to both the CRCI and prehabilitation research landscape by investigating CRCI and prehabilitation effects for patients preparing for CRS-HIPEC treatment. The use of multiple assessment approaches including self-report, neuropsychological testing and qualitative interview data provided the opportunity to explore this phenomenon across multiple research modalities. The research project aimed to address the following specific research questions:

a. Assess the prevalence of CRCI prior to any treatment during the preoperative and postoperative phase.
b. Investigate possible influencing factors on CRCI including exercise and nutrition intervention pre- and rehabilitation, and psychological wellbeing.
c. Assess the relationship between objective and subjective CRCI.
d. Explore the trajectory of pretreatment CRCI from diagnosis to surgery and recovery.
e. Explore CRCI in the postoperative phase to understand its trajectory and influences on CRCI during recovery.
f. Understand the patient's cognitive and psychological factors as they prepare for and recover from surgery through qualitative investigation

7.1.2.1 Chapter 2: Pretreatment Cancer Related Cognitive Impairment and Associated Psychological Factors: A systematic Review

This systematic review was the first review to explore objective and subjective CRCI prior to any surgery or treatment and its association with psychological variables across cancer types. Results of this review supported the presence of pretreatment CRCI with an emphasis on self-report measures. Objective and subjective pretreatment cognitive impairment ranged from 13.8% (Aspelund et al., 2024) to 78.2% (Jung et al., 2022), and 17.55% (Savard et al., 2023) to 29% (Tulk et al., 2021) respectively. Not only do these findings confirm the CRCI is not just a toxicity effect of cancer treatment, but that it can be present from the time of diagnosis. The relationship between anxiety, depression and CRCI is also informative as both co-occurring when symptom burden has reached threshold levels for diagnosis suggest one that is bidirectional: increased anxiety and depression may have negative cognitive consequences for the patient, but also, worsening cognition may reduce psychological health. The associations between anxiety, depression and CRCI at the pretreatment time point deepen our understanding of CRCI, in particular the potential relationship between subjective or perceived CRCI and psychological wellbeing.

7.1.2.2 Chapter 3: The Impact of Prehabilitation Interventions on Affective and Functional Outcomes for Young to Midlife Adult Cancer Patients: A Systematic Review

The purpose of this systematic review was to explore the evidence base exercise, nutrition and psychological prehabilitation impacts on affective and functional outcomes in young to midlife (18-55) cancer patients - a cohort overlooked in traditional ageing cancers (childhood or senior adult).The extent to which established bi-modal prehabilitation programs (without extended or continued intervention after surgery or treatment) have specific or generalised outcome impacts was unclear within the literature, and the review confirmed a domain specific impact - the majority of physical exercise programs show functional improvement, but this does not typically extend to psychological outcomes. Additionally, typical prehabilitation programs do not include cognitive interventions or cognitive outcome measures, despite an appreciation within the wider cancer literature of the role of psychological health in cancer care. Given that patients in the current thesis

were taking part in a combined exercise and nutrition prehabilitation program, and their age profile overlapped with the age window of interest in the review, understanding the potential for affective and functional impacts as a result of prehabilitation is essential. The most relevant and informative result was that psychological prehabilitation can reduce anxiety, whilst exercise prehabilitation positively impacts functional outcomes only. Results increase knowledge of the effects of exercise prehabilitation and functional outcomes which provides context and support for the expected effects of the exercise component of the prehabilitation intervention among CRS-HIPEC patients.

7.1.2.3 Chapter 4: Exploring the Cognitive and Psychological, and Patient Experience of Preparing for Cancer Surgery

This Chapter explored the cognitive and psychological experience of patients preparing for CRS-HIPEC treatment from baseline to pre-surgery. This is the first study to explore the pretreatment cognitive experience of patients preparing for CRS-HIPEC treatment. It makes an important contribution to the literature by investigating pretreatment CRCI prevalence as well as the trajectory of change from baseline to pre-surgery timepoints. Furthermore, this is also the first research to our knowledge to qualitatively investigate the experience of cognition and psychological wellbeing during preparation for CRS-HIPEC treatment, providing much needed insight into the patient voice and perspective. Results indicated that approximately 13% of patients exhibited subjective cognitive impairment at baseline which increased to 27.3% pre-surgery indicating cognitive variability in the presurgical time period. Subjective cognitive impairment was significantly associated with emotional wellbeing at baseline, confirming findings from the systematic review in Chapter 2 which reported an association between subjective cognitive impairment and psychological factors prior to treatment or surgery. Analysis of baseline to pretreatment CRCI also indicated that the impact of cognitive issues on quality of life decreased significantly for the prehabilitation intervention group across time. The use of both self-report data and patient interviews allowed for an in-depth analysis of patient experience pretreatment. Qualitative findings contextualised cognitive and patient reported outcome data and further highlighted the impact of psychological factors like anxiety and health-related quality of life on perceived cognition for CRS-HIPEC patients. Qualitative themes of all-encompassing anxiety highlighted the multiple facets of pretreatment patient anxiety and how it relates to future quality of life. Subthemes of preparation highlighted

the unique physical and psychological preparation for CRS-HIPEC treatment, and how the prehabilitation intervention aids not only physical, but also psychological preparation. Finally, cognitive themes explored not only impairment and its relationship to psychological wellbeing, but also general awareness of cognitive function and reserve activities.

7.1.2.4 Chapter 5: The Patient Experience of Cognition and Psychological Wellbeing While Recovering from Surgery: A Qualitative Study

Chapter 5 explores the patient experience post CRS-HIPEC upon completion of the intervention trial (PANO NCT05305820). This chapter provides a unique contribution by exploring for the first time the cognitive and psychological experience of CRS-HIPEC patients post-surgery, and the potential impacts of combined pre- and rehabilitation. Findings highlight the transition from immediate recovery and long-term recovery noting fluctuations in perceived cognitive function and psychological distress across the postoperative recovery experience. The importance of psychological wellbeing and quality of life as influences on cognition are also highlighted. In particular, aspects of quality of life that promote cognitive health and wellbeing. The experience of cancer treatment altered perspectives of time, mortality and normal functioning for patients. Chapter 5 provided a unique opportunity to understand the trajectory of recovery as it related to cognitive function from the patient perspective. Postoperative themes highlight the trajectory of cognitive fluctuations and the bi-directional relationship between postoperative cognition and psychological wellbeing. These findings illustrate the complexity of CRS-HIPEC recovery, and aid in the identification of supportive care needs.

7.1.2.5 Chapter 6: An Investigation of Subjective and Objective Cognitive Function and influencing factors one year post CRS-HIPEC surgery

Chapter 6 makes an original contribution to the research landscape by assessing both objective and subjective cognition at one-year post-surgery for CRS-HIPEC patients. Between group analysis also explored any long-term maintained changes as a result of a combined pre- and rehabilitation intervention, manifestation and prevalence of CRCI. The relationship between emotional wellbeing and cognitive outcomes was also explored.

Findings supported prior literature reporting a lack of correlation between objective and subjective measures of cognitive function. Similarly, there were no correlations between emotional wellbeing and either subjective or objective cognitive function. At a group level, significant differences were observed in levels of emotional wellbeing, with the intervention group reporting higher emotional wellbeing. These findings highlight the complexity of recovery for CRS-HIPEC patients and substantiate the findings from Chapter 5's qualitative investigation illustrating recovering from CRS-HIPEC as a continuum, with changes in cognition, psychological wellbeing and quality of life evident throughout the recovery process.

7.1.3 Methodological Considerations

This research project was novel in its use of multi-methods and research design approaches to holistically assess both CRCI experience and prehabilitation effects as they related to cognition and psychological wellbeing. In order to achieve this central aim, this study used a combination of patients lived experiences, self-report data, associations and change trajectories and neuropsychological test performance. This research also benefited from being a nested study in a parent intervention pre- and rehabilitation research trial (PANO NCT05305820) as this not only allowed for further observation of the cognitive trajectory and its associations but also allowed for the potential impacts of lifestyle modifications on cognitive function to be explored. The concept of exercise or physical activity to promote CRCI recovery in survivorship has been previously highlighted as an area where increased research is required (Yang & Von Ah, 2024). Being a nested study in the prehabilitation intervention allowed for the observation of prehabilitation effects on CRCI from diagnosis among patients preparing for CRS-HIPEC which has previously not been explored.

It is important to note, however, that despite the benefits of being able to observe prehabilitation effects, the intervention component increased complexity of interpretation for the observation and trajectory of CRCI, given that at each stage of assessment from diagnosis to pretreatment (Chapter 4), postoperative lived experience (Chapter 5) and one year follow-up (Chapter 6), a portion of the patient cohort engaged in supported exercise and nutrition. The effects of pre and rehabilitation were evident with improvements in the impact of cognitive function on quality of life from diagnosis to pre-surgery (Chapter 4),

and increased emotional wellbeing at one year follow up (Chapter 6). Although illuminating, the prehabilitation intervention may have acted as an additional confounding variable when aiming to unpack the relationships between cognitive function, psychological wellbeing and quality of life. We know, for example, that exercise may positively impact cognitive function (Zimmer et al., 2016), and that exercise interventions during active cancer treatment can result in improvements in health-related quality of life (Mishra et al., 2012). Thus, the inclusion of the effects of a prehabilitation trial increases complexity when interpreting the thesis findings. Nonetheless, a recent narrative review by Sheppard and colleagues (2025), considered the potential role of prehabilitation to support cognitive function within urological cancer research. They acknowledge the dearth of research currently available with regards to prehabilitation and cognitive function compared to the rehabilitation research landscape. Furthermore, the need to further investigate factors pertaining to pretreatment CRCI is well recognised (Hutterer & Oberndorfer, 2021). Consequently, irrespective of increased interpretive complexity, the addition of information about the impacts of prehabilitative exercise and nutrition as it relates to peritoneal malignancy and CRS-HIPEC treatment provides relevant and pertinent information regarding the interplay of prehabilitation and cognitive function that is currently lacking within cancer research.

Multiple methods of data collection were employed across multiple timepoints to provide complementary exploratory in-depth analysis of the two constructs that required increased investigation 1) CRCI and 2) Prehabilitation. This use of multi-methods within this thesis increased the depth of interpretation of findings. In study one, the use of both self-report data and qualitative semi-structured interviews increased knowledge regarding the pretreatment experience of CRCI. While patient reported outcomes investigated prevalence of CRCI trajectory and associations with other variables, thematic analysis of patient interviews allowed for increased investigation of how exactly CRCI may manifest in daily life and the relationship it has to constructs that can increase impairment such as psychological distress but also support cognitive health like reserve activities. The qualitative perspective ensured that the patient voice and perspective was foregrounded. The use of multiple assessment approaches pretreatment allowed for the investigation of a novel timepoint from diagnosis to surgery which included quantitative information regarding prevalence and between group difference, and interview themes providing context to the challenges of treatment and how they may relate to an awareness of changes

in cognitive function, and preoperative anxiety. Multi-methods across chapter 5 and 6 allowed a more nuanced understanding of the postoperative/post-intervention experience. In chapter 5, the qualitative patient experience was explored from the point of intervention completion, approximately 42 weeks post-surgery. In Chapter 6, multiple approaches to quantitative data were applied to assess the relationship between objective CRCI as measured by neuropsychological tests, and self-reported cognition. In this case, multiple methods provided increased evidence for the lack of correlation between objective and subjective methods of cognitive measurement which would not have been possible through subjective or objective investigation alone. It is clear that a multi-methods approach increased the quality and novelty of research findings, and was appropriate for the construct of CRCI, by increasing knowledge of variability and trajectory, how CRCI manifests in daily life, and relationships between objective and subjective impairment.

As part of the one-year follow up assessment, patients took part in neuropsychological assessments. Specific neuropsychological tests included the Trail Making Test and The Controlled Oral Word Association Test (COWAT) due to their popularity within CRCI literature (Capetti et al., 2025) and recommendations put forward by the International Cancer and Cognition Task Force (Wefel et al., 2011) for their ability to capture important domains thought to be related to CRCI including attention, processing speed, verbal fluency and executive function. It must be noted that within literature and guidelines (Capetti et al., 2025, Wefel et al., 2011), the Hopkins Verbal Learning Test-Revised (Benedict et al., 1991) has also been highlighted as a possible test of memory within CRCI research. The test was considered for inclusion within the research project, however due to practical considerations including time for administration and clinical supervision requirements, the decision was made to not include the test. Alternatively, the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) was included as an overall global screening test of mild cognitive impairment. As the test includes multiple assessment domains including short term memory, the inclusion of the MoCA in addition to the COWAT and the Trail Making Test, provided a comprehensive overview of objective cognitive function within the research cohort.

The present research study was nested within a larger feasibility RCT design which recruited n=36 participants with peritoneal malignancy scheduled for CRS-HIPEC treatment. Study 1 (Chapter 4) included the data of n=29 patients who took part in both baseline testing and presurgical interview. Due to attrition and practical challenges related

to data collection before and during cancer treatments, participant numbers were lower than previously anticipated across all timepoints. The decision was made to apply non-parametric analysis across the data set. Non-parametric methods of analysis are appropriate for use with small sample sizes as they require limited assumptions about the data to be made (Whitley & Ball, 2002). One disadvantage of non-parametric testing is the reduced power (Siegel, 1957) and this should be taken into consideration when observing significant findings. Alternative approaches including difference in difference analysis and regressions were considered when creating a data analysis plan. Ultimately, non-parametric tests without missing case substitutions were deemed most appropriate when considering the overall aims of the thesis, which was to further knowledge of CRCI, including prevalence, expression and influencing factors from pretreatment to one year post surgery for patients undergoing CRS-HIPEC treatment. As qualitative interviews took place alongside quantitative data collection from pre-surgery to postintervention, quantitative analysis of raw scores was deemed most appropriate to complement qualitative research findings. The novelty of the research design for this project increased complexity of interpretation but ultimately provided increased knowledge and understanding of the experiences of CRCI and potential influences such as psychological wellbeing and pre and rehabilitation.

7.1.4 Theoretical Considerations

The present research presents a number of theoretical considerations for both the confirmation and expansion of current schemas and models of CRCI. In particular, this research provides increased knowledge about the CRCI experience from the diagnosis to pre-surgery timeframe. Three recent models and schemas of CRCI attempt to understand potential influencing factors (Hutterer & Oberndorfer, 2021), the multifactorial nature of CRCI development across the cancer continuum (Oppegaard et al., 2023a) and the possible transdiagnostic relationship between CRCI and psychopathology (Haywood et al., 2024). Whilst other research has attempted to review the literature pertaining to the potential biological, tumour and inflammation determinants of pretreatment CRCI (Olson & Marks, 2019), the findings of this research project focus on the experience of CRCI as it relates to psychological factors, quality of life and lifestyle modification in the form of exercise and nutrition.

7.1.4.1 Schema Depicting the Complexity of CRCI- Hutterer and Oberndorfer, 2021

This schema of CRCI complexity was developed by Hutterer and Oberndorfer (2021) based on extensive literature review focusing on the clinical presentation, pathophysiology, diagnosis and management of CRCI. Through exploration of the literature, the authors conclude that CRCI is a common occurrence for patients and is not limited to the impact of neurotoxicity. In addition, simultaneous and co-occurring factors including psychological and treatment related factors may co-occur and culminate to exacerbate cognitive impairment.

This schema highlights the potential contributing factors to CRCI across five key areas: 1) central nervous system brain related factors 2) pre-morbid factors 3) cancer related treatment factors 4) systemic inflammation associated cognitive dysfunction and 5) psychological factors. Within the construct of CRCI, the schema acknowledges the existence of pretreatment CRCI, transient "early" CRCI and persistent "long-term" CRCI. Importantly, this model emphasises the interrelationship between CRCI and health-related quality of life, including negative impacts on quality of life, acknowledging the impact of CRCI on autonomy, self-confidence, everyday activities, social relationships and return to work.

7.1.4.1.1 Theoretical Contribution of the Present Research. Findings from the present study further validate the CRCI complexity schema (Hutterer and Oberndorfer, 2021) through identification of fluctuations in CRCI from pre surgery or treatment to one year follow up, and evidence supporting the contribution of psychological factors and quality of life implications on CRCI. In particular, findings highlighted the interplay between CRCI and quality of life.

This research extends this schema in two key ways. The first is by identifying transience in the pre-surgery timeframe. In Chapter 4, results indicated that the proportion of participants experiencing perceived cognitive impairments increased from 13% at baseline to 27.3% pre-surgery. As the schema depicts variability within the treatment phase, our results further inform the experience of variability within earlier phases of CRCI than previously depicted. Secondly, our research furthers the interrelationship between health-related quality of life (HrQoL) and CRCI. Findings from Chapter 4 illustrated a relationship at diagnosis between perceived cognitive impairment scores and

scores on the emotional wellbeing (EWB) subscale of the FACT-General measure of HrQoL. These findings are interesting as not only does EWB represent psychological wellbeing, but it is also understood as a facet of overall health-related quality of life. Our research furthered our understanding of HrQoL and cognition as qualitative themes both pre and post-surgery highlighted the need for cognitive enrichment activities and how these positively promoted overall cognitive health. This was illustrated in the subthemes *"Appreciation for Cognitive Enrichment"* (Chapter 4) and *"Influences on Perception of Cognitive Function"* (Chapter 5). Indeed, the potential positive effects of prehabilitation may also have contributed to both overall quality of life, and cognitive quality of life pre and postoperatively. Scores on the "Impact of cognition on quality of life" FACT-Cognition subscale increased significantly from baseline to pre-surgery timepoints indicating improvement. Furthermore, significant differences were found in terms of increased EWB for the intervention group at one year follow-up compared to care as usual. These findings culminate to infer that health-related quality of life is integral to the experience of CRCI, both in terms of negative impacts from, and positive quality of life to increase cognitive wellbeing.

7.1.4.2 The Multifactorial Model of CRCI- Oppegaard et al., 2023a

The Multifactorial Model of CRCI (Oppegaard et al., 2023a) was developed from a comprehensive literature review to identify risk factors and mechanisms associated with CRCI. The model attempts to operationally define CRCI as "a temporary or persistent subjective or objective change in higher-order mental processes that occurs with cancer or its treatments" (Oppegaard et al., 2023, p.137). The model illustrates the experience of CRCI as occurring across the cancer continuum and that each identified factor is dynamic and can interact with CRCI at various points across this continuum. Identified factors include: 1) Social determinants of health 2) Patient-specific factors 3) Co-occurring symptoms 4) Treatment factors and 5) Biologic mechanisms. As the model depicts CRCI from prior to diagnosis into survivorship, it is acknowledged that along this continuum, the relationships between factors and their potential effects on CRCI may change.

7.1.4.2.1 Theoretical Contribution of the Present Research. Findings from the current research project validate facets of the Multifactorial model through multiple

observations. Firstly, results validate the concept of CRCI as a continuum that can occur from prior to cancer diagnosis into survivorship. This concept was illustrated from pre to post treatment as evidenced by fluctuations in experience of perceived cognitive impairment. Furthermore, qualitative experiences both pre and post treatment illustrated an awareness of cognitive fluctuations across the themes *"Awareness and Understanding of Cognitive Complaints"* (Chapter 4) and *"Cognition in Flux"* (Chapter 5). During the postsurgical phase, variability was also experienced between psychological experience of immediate and long-term recovery within the themes *"Cognition in Flux"* and *"Psychological Distress Across Recovery"*. These findings may also speak to how this variability could interact with CRCI across the cancer continuum. The multifactorial model highlighted the contribution of patient related factors and co-occurring symptoms as contributing factors to CRCI across the continuum. Our findings support the contribution of patient related factors such as anxiety and lifestyle modification to CRCI experience pre and post treatment. Systematic review evidence from Chapter 2 also supported a relationship between anxiety and self-reported cognitive function prior to treatment or surgery. The impact of exercise and nutrition intervention before and after surgery also illustrates the importance of patient-specific factors in supporting CRCI and psychological wellbeing across the continuum. The use of multiple methods allowed for the exploration of a range of social determinants of health, co-occurring symptoms and patient specific factors both pre- and post-surgery, further highlighting

The results of the present study also provided some insights that can potentially give increased context to and complement the Multifactorial model. At present, the model acknowledges the dynamic interaction of factors across the CRCI continuum, and the results of our research further contextualise dynamic interactions between CRCI, psychological wellbeing and quality of life at the pretreatment timepoint through findings from chapter 2's systematic review, and Chapter 4's investigation of CRCI from baseline to pre-surgery. The model also notes that currently, how social determinants of health such as economic status, education and working activity may contribute to CRCI is currently not fully understood. The exploration of reserve and work activities, as highlighted in this thesis, may contribute positively to cognitive function and overall quality of life pre and postoperatively increasing knowledge about the positive impacts of social determinants of health on cognition. Finally, our research provides additional context about how the factors outlined in the model may interact with the construct of HrQoL.

7.1.4.3 Proposed Model of Functional Associations -Haywood et al., 2024

Haywood and colleagues (2024) explored the potential etiological mechanisms that contribute to CRCI, with a particular focus on psychopathology. The authors proposed that not only can poor psychological health functionally contribute to the development of CRCI in survivorship, but that CRCI may also contribute towards the development of psychological distress, representing a transdiagnostic psychopathology across these constructs in cancer survivors. They propose that CRCI, in combination with other factors, contributes towards the development of psychological illness or distress during survivorship. The model does not focus on a particular timepoint and recognises the potential for CRCI to develop across the cancer trajectory.

7.1.4.3.1 Theoretical Contribution of the Present Research. The present research findings provide some support for transdiagnostic psychopathology across CRCI and emotional factors. The results of Chapter 2's systematic review of pretreatment CRCI highlighted associations between self-reported CRCI and anxiety and depression prior to any surgery or treatments. At baseline assessment, perceived cognitive impairment was also significantly associated with emotional wellbeing (Chapter 4, 4.3.1.3). Furthermore, within qualitative analysis, anxiety was highlighted as a central theme in the presurgical patient experience, illustrated across the main theme *"Navigating All Encompassing Anxiety".* The interplay between cognitive function and psychological wellbeing was also explored pretreatment across the main theme "*Evaluating the Experience of Cognitive Concern"* (Chapter 4). These concepts were further illustrated postoperatively, through the theme *"The Interplay Between Cognition and Psychological State"* (Chapter 5).

Results from the present research provide further insight to relationships between psychological factors and CRCI that extend and contribute to the model. The results of our investigations during the pretreatment timepoint provide particular context to the interplay between psychological factors and CRCI prior to surgery. Furthermore, while the Haywood et al model focuses on the possibility for psychopathology, the exploratory nature of this research meant that the experiences of patients with high levels of psychological wellbeing and cognitive function were also investigated. As Haywood and colleagues (2024) highlighted the relationship between CRCI and psychopathology, this

research also illustrates the potential for a strengths-based approach between increases in psychological wellbeing and cognitive health that highlights cognitive health and strength for patients where evident and promotes efforts to maintain and promote cognitive health. These findings allowed for an understanding of potential factors that positively impact cognition and contribute to overall cognitive health and in turn promote overall health related quality of life.

7.1.4.4 A Conceptual Schema of Pretreatment Cognitive Experience, Psychological Wellbeing and Health-related Quality of Life

Considering the results of the present research in light of the current theoretical models presents the opportunity to further our understanding of pretreatment CRCI as it relates to psychological wellbeing and health-related quality of life. These findings culminate across three central tenets: 1) Pretreatment CRCI is evident within empirical research, systematic reviews and prior modelling; 2) CRCI is related to psychological wellbeing and health-related quality of life, and at pretreatment these associations would not have been confounded by treatment-related effects; and 3) Exploratory investigation of patient experiences allows for an increased understanding of the continuum from CRCI to cognitive health and factors that can positively and negatively contribute to cognitive experience.

One central theoretical finding from this research is the conceptualisation of cognitive health within the continuum of CRCI and cognitive experience. Upon diagnosis, each patient has the capacity to develop CRCI, or conversely the capacity to maintain their cognitive function as evident through our research. The factors that contribute to CRCI development have been previously described within theory (Hutterer & Oberndorfer, 2021, Oppegaard et al., 2023a), as has the ability for CRCI to occur across the continuum from diagnosis to survivorship (Hutterer & Oberndorfer, 2021, Oppegaard et al., 2023a, Haywood et al., 2024). However, our findings contribute to theory by portraying cognitive experience as a continuum of cognitive health whereby CRCI at the pretreatment timepoint can develop, or cognitive health can maintain. While other theoretical approaches consider the continuum by which cognitive impairment can occur within a cancer journey, and that degree of cognitive concern can vary across time, continuum in the context of the current research highlights a need to understand both the lived experience of cognitive health and

CRCI within a cancer journey in order to fully understand how and when to help support patients. A second theoretical contribution is the acknowledgment of pre or rehabilitation approaches from the point of diagnosis and pretreatment as a potential contributing factor to transition from experiencing CRCI towards cognitive health. Finally, our theoretical findings demonstrate the role of both psychological wellbeing and health-related quality of life within the pretreatment timepoint. We know that these factors interact with CRCI through both empirical and theoretical research. Research into healthy cognitive aging also supports associations between cognitive health and psychological wellbeing (Llewellyn et al., 2008), and an interplay between health-related quality of life and cognition was evident within our empirical research. Figure 7.1 below depicts a conceptual model of the potential interactions between cognitive experience, psychological wellbeing and health-related quality of life.

Figure 7.1

A Preliminary Conceptual Schema of the Relationship Between Cognitive Experience, Psychological Wellbeing and Health-Related Quality of Life

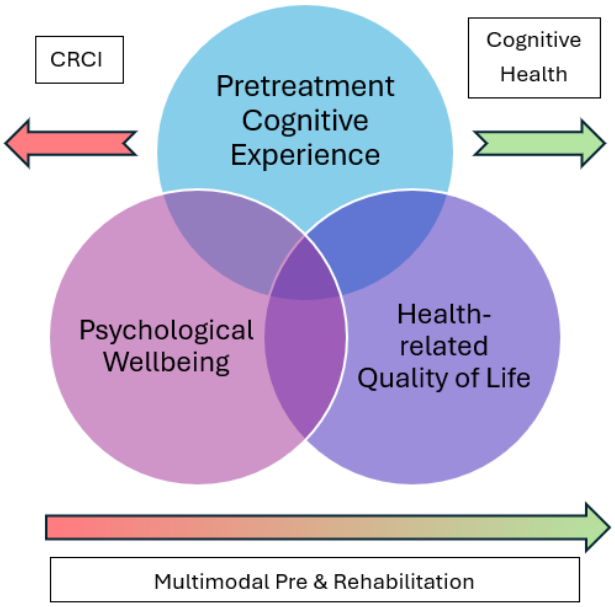


Figure one above depicts the potential manifestation of pretreatment CRCI experience, and how psychological factors and health-related quality can be associated with both CRCI and cognitive health prior to treatment or surgery. The centre circle depicts the concept of cognitive experience and how it can be negatively impacted by

cancer resulting in experience of CRCI, or when patients are unaffected by cognitive impairment, healthy cognition is maintained at the pretreatment timepoint. Psychological Wellbeing and HrQoL are illustrated as central to the experience of both CRCI and healthy cognition. In addition, the opportunity for intervention through prehabilitation is highlighted as a potential driver from a state of CRCI to healthy cognition within the pretreatment timepoint as previously explored by Sheppard and colleagues (2025).

7.1.5 Unique Empirical Contributions of the Research Project

This research project contributes novel empirical findings that help to advance knowledge across the three key areas of CRCI, Pre- and rehabilitation and CRS-HIPEC patient experience. This is the first research project to investigate CRCI in patients with peritoneal malignancy from pretreatment to one year follow-up. It is also the first empirical investigation of CRS-HIPEC and cognitive function whilst patients engage in a bimodal exercise and nutrition prehabilitation trial. Furthermore, the inclusion of multiple timepoints allows for novel investigation across the CRCI continuum from baseline to one year follow-up.

7.1.5.1 Contributions to Pretreatment CRCI Research

This research contributes empirically to the pretreatment CRCI research landscape through a number of fundamental observations. Firstly, empirical findings from Chapter 4's investigation from baseline to pretreatment illustrated that 13% of patients exhibited self-reported CRCI at baseline testing, which increased to 27.3% pre-surgery based on perceived cognitive impairment cut off scores. This is further validated by findings from Chapter 2's Systematic review, which indicated that CRCI was evident prior to surgery or treatment for both objective and subjective impairment compared to healthy control groups and within standardised scoring or cut-offs. Our results extended previous literature by observing a small perceived cognitive impairment (PCI) effect prior to any surgery or treatment within CRS-HIPEC patients, and review evidence extended knowledge of pretreatment CRCI beyond the traditional scope of breast cancer research, which has been previously highlighted as an area requiring further investigation (Yang & Von Ah, 2024). Review results were observed across a number of other cancer types, including but not limited to head and neck (Bernstein et al., 2018), Lymphoma (Juríčková et al., 2023, Kathpalia et al., 2024) and prostate (Tulk et al., 2021). Furthermore, results from both the

systematic review findings and empirical pretreatment evidence supported an association between psychological variables and self-reported CRCI prior to treatment or surgery. The systematic review highlighted that in 10 relevant studies, eight reported associations between anxiety and subjective cognitive function (Chapter 2, 2.3.7.1). Similarly, among CRS-HIPEC patients, there was a significant association between emotional wellbeing and perceived cognitive impairment at baseline testing prior to treatment or surgery (Chapter 4, 4.3.1.3). Results also speak to variability across the diagnosis to pretreatment continuum, which contributes further to CRCI theory and modelling, as variability has previously been only highlighted in the posttreatment period (Hutterer & Oberndorfer, 2021). For the first time, this study allowed for explorations of cognitive health and its factors through qualitative investigation across the theme *"Appreciation for Cognitive Enrichment"* (Chapter 4), as well as the potential positive impacts of prehabilitation at the pretreatment timepoint. The culmination of these findings speak to the potential interplay between pretreatment CRCI, cognitive health, psychological wellbeing and health-related quality of life (Figure 7.1).

7.1.5.2 CRCI Across the Survivorship Continuum

Thus far, theoretical and empirical considerations of this study have largely focused on the pretreatment timepoint, due to its novelty and need for increased research during this time period. However, the present research also highlights novel contributions about CRCI across the survivorship continuum from diagnosis to approximately one year post-surgery. In particular, it provides novel information on the experience of patients with peritoneal malignancy and CRS-HIPEC treatment. In line with prior research (Biglia et al., 2012, O'Farrell et al., 2017), a lack of correlation was found between objective and subjective measurement at one year follow-up post CRS-HIPEC surgery (Chapter 6, 6.3.5). These results contribute to the wider cognitive measurement literature, as subjective and objective cognitive function has been the source of investigation within dementia research (Burmester et al., 2016) and traumatic brain injury (Gardner et al., 2017). In addition, results speak to the variability of the CRCI trajectory, as the proportion of patients who exhibited perceived cognitive impairment at one-year follow-up was 16.67%, indicative of variability and a reduction from pre to post surgery. Transience within the first-year post treatment has been previously identified within conceptual schemas of CRCI (Hutterer & Oberndorfer et al., 2021) and these results further highlight CRCI

trajectory within peritoneal malignancy specifically and the cognitive impact of potential treatment related effects.

7.1.5.3 Qualitative Understanding of CRS-HIPEC Treatment Experience

In addition to novel insights gained from quantitative investigation, the inclusion of semi-structured interviews pre and post-surgery provided nuance, context and in-depth insights into the patient experience that would not have been possible with quantitative investigation alone. In addition to the cognitive insights discussed in relation to theoretical considerations (7.4), qualitative findings increased knowledge of important factors that contribute to wellbeing, quality of life and psychological distress for patients with peritoneal malignancy during preparation for and recovery from CRS-HIPEC treatment. To our knowledge, this was the first qualitative investigation of the experience of patients preparing for CRS-HIPEC treatment. This means that for the first time, we were able to explore the psychological experiences of patients prior to surgery. Feelings of anxiety were evident within patient experience, and in addition to traditional examples of cancer-related anxiety (Curran et al., 2017), patient interviews also highlighted additional contextual sources of emotional distress for patients, including the severity of surgery and the possibility of adapting to life with a colostomy bag. Findings also illustrated positive aspects of preparation, including experiencing physical and cognitive wellbeing, optimism and resilience. Given the complexity of CRS-HIPEC and recovery, the qualitative experience of recovery has been the subject of increased research interest (Falla-Zuniga et al., 2024, Ward & Greenbaum, 2024). Post-surgery results emphasise the considerable variability of patient experience, as patients indicated high levels of quality of life within interviews, but acknowledged a distinct period of transition from immediate to long-term recovery. Immediate recovery was a time of considerable psychological distress and distinct cognitive complaints. Similar to the preoperative experience, the observation of patients who returned to high levels of quality of life and did not report persistent cognitive issues allowed for an increased awareness of the factors that contribute to a positive recovery experience such as social support, exercise and returning to work. Patients highlighted supportive care needs currently lacking within follow up care, in particular the need for increased general interaction post-surgery with the clinical team, and the need for increased provision of psychological support. The addition of qualitative insights to this

research project was central in understanding the patient experience and contributed greatly to the novelty and empirical findings of the research project.

Qualitative research within this project also contributed to a greater understanding of the lived experience of CRCI for patients. As explored by prior qualitative research of CRCI (Haywood et al., 2023, Sharma & Brunet, 2023), qualitative approaches provide an increased understanding of lived experience beyond the scope of neuropsychological testing or questionnaires, such as areas of improvement in education and knowledge, as well as psychosocial impacts. The current research increases knowledge of lived experience at the pretreatment timepoint for CRCI allowing for a novel understanding of this issue. Within the context of this project, qualitative approaches allowed for the interrogation of aspects of cognitive function not accessible through objective testing or self-report scales alone, in particular the perception of cognitive fluctuations and the relationship between cognition and psychological wellbeing throughout the recovery process. Interviews also allowed for the exploration of potential future interventions to promote cognition and wellbeing, as patients were given the opportunity to explore in depth how they fostered physical and psychological wellbeing through their experience of cancer.

7.1.5.4 Prehabilitation in the Cognition Context

Findings from the present research further highlighted the positive impacts of pre- and rehabilitation within the novel context of both CRCI and CRS-HIPEC treatment. The parent study (PANO NCT05305820) is to our knowledge, the first high quality bimodal exercise and nutrition prehabilitation randomised controlled trial for patients scheduled for CRS-HIPEC treatment. Findings from this thesis has furthered our understanding and knowledge of prehabilitation within this under-researched cohort from the perspective of cognition function, patient experience, and psychological wellbeing. Preoperatively, results indicated a significant improvement in impact of cognition on quality of life for the group engaged in prehabilitation compared to care as usual. These findings demonstrate a potential association between cognition, quality of life and exercise and nutrition prehabilitation. As we know that exercise may positively impact cognitive function (Zimmer et al., 2016), results provide promising support for the use of lifestyle modification to support cognitive function via increases in quality of life. Approximately

one year post surgery, patients who took part in combined pre-and rehabilitation also exhibited significantly higher levels of emotional wellbeing compared to care as usual. These findings illustrate the potential for long-term lifestyle modification maintenance to support psychological wellbeing and health-related quality of life. In 2021, recommendations were made based on the 10th Peritoneal Malignancy Workshop in 2018 to develop standardised multimodal prehabilitation intervention for patients undergoing CRS with or without HIPEC (Cortés-Guiral et al., 2021). Recommendations included the provision of exercise, nutrition, psychological, haematological, anaesthesiology and critical care support. Specific cognitive recommendations were not made; however, our findings indicate that prehabilitation could potentially positively support cognitive function through exercise and nutrition support (Cortés-Guiral et al., 2021). Findings from our prehabilitation review highlighted the effects of exercise support on functional outcomes and psychological support for affective outcomes. Within our review all relevant papers applied unimodal intervention. The use of multimodal intervention within our research meant that observations of potential cross modal effects of prehabilitation, such as improvements in emotional wellbeing and cognitive quality of life could be made. Qualitative research suggests that barriers to prehabilitation for abdominal surgery patients can include a lack of awareness of benefits and the time and patient input required to participate (Clemons et al., 2024). Models of prehabilitation also highlight how a graded approach from universal to targeted intervention may be of most benefit when determining the degree of intervention (Macmillan, 2020). It has been demonstrated within this research that exercise and nutrition pre and rehabilitation may support emotional wellbeing and cognitive quality of life. As such, the combined positive effects of exercise and nutrition support could aid in supporting affective outcomes. However, as pre-surgical anxiety was also evident qualitatively through the main theme *"Navigating All Encompassing Anxiety"*, results highlight the need for appropriate screening as part of prehabilitation intervention, by implementing a stratified approach to identify patients who may require additional psychological support through direct psychological intervention (Levett & Grimmett, 2019).

7.1.6 Future Research and Recommendations

Results of the present research project present multiple opportunities for future research as well as recommendations for future clinical care. Findings highlighted the

unique contribution of multiple qualitative and quantitative assessment methods to the progression of pretreatment CRCI theory. As figure 7.1 illustrates, CRCI, psychological wellbeing and HrQoL interact with each other within the pretreatment cognitive experience, however some outstanding questions still remain. Firstly, as previously mentioned, this schema does not take into account the biological cancer related factors that may contribute to CRCI from diagnosis, and further research is needed to understand and integrate these factors within CRCI research. Future research is also required to infer directionality between constructs, so these have not been defined within the schema. It is important to identify the direct relationships between these constructs in order to develop target intervention approaches appropriate for degree of psychological wellbeing and CRCI. Finally, mode of prehabilitation is also undefined, as this may include multiple components of lifestyle modification including exercise, nutrition and psychological support, as well as emerging approaches like cognitive training and support. Research should focus on the development of pre and rehabilitation approaches to target CRCI and promote cognitive health, both through lifestyle modification and potentially through direct cognitive support with an overall aim of promoting quality of life.

Findings also illustrate opportunities for further methodological considerations that can positively contribute to future CRCI research. As previously mentioned, the present research was nested within a larger, feasibility RCT. Further research would benefit from a full scale RCT investigation of the benefits of prehabilitation for CRS-HIPEC patients, as the small sample size of the present research may limit generalisability of findings. Furthermore, findings from our research indicated associations between psychological wellbeing and cognitive function, as well as psychological distress evident qualitatively pre and post treatment. Findings from the systematic review of prehabilitation intervention also supported the use of psychological prehabilitation to support affective wellbeing. Future research would benefit from the integration of psychological prehabilitation to observe potential benefits as they relate to CRS-HIPEC treatment, and cognitive function. Findings from the systematic review of CRCI highlighted the importance of a healthy control group in analysis of CRCI prevalence, and future research should aim to include a healthy control group where possible, as the measurement and interpretation of CRCI remains a keen area of research. When assessing CRCI, the inclusion of measures of psychological wellbeing and screening tools to assess levels of distress, anxiety and depression so that patients can be treated appropriately from diagnosis. In addition,

assessment of health-related quality of life pretreatment across cancer types would allow for increased investigation of the associations observed within the present research and the preliminary conceptual observations illustrated in figure 7.1.

Within this research, support was found for a lack of association between subjective and objective impairment at one-year follow up. Difficulties within CRCI measurement have been the source of research interest (Hutchinson et al., 2012). Further research would benefit from increased investigation of objective test measures and their applicability to CRCI research. The application of additional testing measures such as neuroimaging techniques may aid in unpacking the neuropsychological underpinnings of CRCI in order to develop validated testing batteries that may also reflect levels of perceived cognitive impairment. Qualitative investigation of patient experience provided additional insight into how CRCI may affect daily life. Dementia research is subject to similar measurement issues regarding validity of subjective and objective measurement and heterogeneity within research (Burmester et al., 2016). Some dementia research has highlighted the importance of assessment of functional change within a naturalistic environment as important in determining the progression from healthy cognitive aging to dementia (Schmitter-Edgecombe et al., 2014). CRCI research may benefit from the inclusion of methods that increase ecological validity, as neuropsychological tests usually reflect controlled laboratory settings. The inclusion of assessment of cognitive impairment as it relates to daily activities including qualitative investigations could increase knowledge and ultimately increase assessment accuracy.

The scope of the current study did not allow for the evaluation of either cognitive pre or rehabilitation approaches to be included. Sheppard and colleagues in 2025 proposed a model of cognitive prehabilitation which emphasised the need for multimodal prehabilitation and included the integration of cognitive training to support recovery and postoperative cognitive function. Increased research of the efficacy of cognitive pre and rehabilitation approaches would help to support cognitive models of prehabilitation and their integration in multimodal prehabilitation.

Finally, findings from the present study illustrated CRCI variability from pretreatment to one-year follow up. Furthermore, individual variability was also observed within assessments of subjective cognition, and between subjective and objective cognitive function. Increased research of individual variability and its factors within CRCI would

further our understanding beyond conceptual schemas, to potential individual factor clusters of CRCI. Future research would benefit from the addition of pretreatment neuropsychological testing would aid in further exploration of variability of CRCI across the cancer continuum for CRS-HIPEC patients. Longitudinal research designs would also support the exploration of CRCI, psychological wellbeing and health-related quality of life across the cancer trajectory.

In addition to future areas for research, the present findings offer some insights that could benefit current policies and guidelines within the psych-oncology and prehabilitation landscape. In September 2020, the National Cancer Control Programme put forth guidelines for psychosocial support within Ireland and a model of care for psycho-oncology (Greally et al., 2020). Among several key recommendations, the guidelines suggest that patients should be screened for distress and a comprehensive evaluation of needs, followed by subsequent distress screenings throughout the cancer journey. Results from the present research support the need for distress screening within psycho-oncological care. In terms of comprehensive needs, recommendations do not currently integrate cognitive support or assessment of specific cognitive concerns within screening or intervention. Based on results from the present research, cognitive concerns should be taken into consideration during screening and comprehensive assessment, due to evident associations with anxiety, depression, psychological wellbeing and health-related quality of life. Members of the multidisciplinary team involved in psychological care should be aware of these impacts and efforts should be made to increase knowledge of CRCI and intervention approaches. Understanding the associations between psychological factors and CRCI, including the potential for transdiagnostic psychopathology (Haywood et al., 2024) will allow multidisciplinary teams to provide appropriate support across levels of care. Psychological wellbeing, and the presence of psychological distress or anxiety emerged as a persistent finding both pre and postoperatively. Indeed, the need for increased psychological support was identified as a supportive care need during the immediate postoperative period. The variability and transience across experience should be considered when determining the timing and duration of psychological interventions.

The present research considered guidelines adopted by the International Cancer and Cognition Taskforce (Wefel et al.. 2011) when developing the design of cognitive assessment employed within this research project. Beyond traditional subjective and objective testing, the results across this project highlighted the unique contribution of

qualitative research to understanding how CRCI may manifest and what factors either contribute to it, or work to support healthy cognition. Future CRCI should, where possible, include qualitative investigation to help unpack associations between measurement approaches, and the impact of CRCI on daily activities and quality of life. In addition, the application of specific measures of perceived cognitive function, as opposed to cognitive symptoms within larger quality of life batteries would support the accurate measurement of perceived cognitive impairment. Current research is also developing updated clinical guidelines and recommendations for the delivery of prehabilitation for cancer (Macmillan Cancer Support, 2025). The addition of cognitive screening when delivering multimodal prehabilitation interventions would increase the evidence base for the positive impact of multimodal prehabilitation on cognition during cancer.

Finally, results of the present research also support the potential impact of pre and rehabilitation intervention to support cognitive function. These findings indicate that even without direct psychological intervention, exercise and nutrition support can potentially positively impact cognitive function. Cortés-Guiral and colleagues in 2021 provided guidance on the use of prehabilitation approaches for CRS-HIPEC treatment. Within intervention guidance, cognitive function is currently not included or explored. However more recent research has advocated for the inclusion of cognitive training within multimodal prehabilitation (Sheppard et al., 2025). Future research would benefit from an increased understanding of the cognitive pre and rehabilitation within the context of CRS-HIPEC in order to integrate cognitive support into current prehabilitation guidelines. This could potentially lead to updating current CRS-HIPEC prehabilitation guidelines to include cognitive assessment and support.

7.1.7 Strengths and Limitations

Thus far, methodological and theoretical considerations have demonstrated the various strengths and limitations associated with the present research. To summarise, there are limitations that should be taken into consideration when evaluating results of the present research. Due to the nature of peritoneal malignancy as a rare cancer, the samples in this study were relatively small, and in addition to this, patients were at each time point assessed across two groups, intervention and care as usual. This may limit the generalisability of current findings and highlights the need for future large-scale or multi-

site research. Limitations must also be considered for the qualitative research component, as results are reflective of the lived experience of this particular cohort, and may not be generalisable across other cancer contexts. In addition, research bias is a consideration within qualitative research. To mitigate this a reflexivity statement has been included in section 1.1.5. Participant attrition was also challenging, due in part to the nature of assessments requiring pen and paper administration and, in some cases, in person assessments. In addition, inconsistencies within baseline to preoperative and one-year follow-up labelling for the Likert scale prevented analysis across time of perceived cognitive impairment. The context of the larger prehabilitation trial also increased variability across assessment timepoints, as patients needed to be cleared by the clinical team post-surgery to resume exercise and nutrition support, assessment timelines varied based on the degree of time taken to be physically fit. Finally, due to assessment limitations associated with the parent trial, it was not logistically possible to assess objective cognitive function at all timepoints, and future research should endeavour to include objective testing alongside subjective self-report measures of CRCI where possible.

Despite limitations, this research project also has many strengths that allow results to contribute positively to CRCI and prehabilitation literature. This research is novel both in research design, assessment and cohort of interest. The exploration of peritoneal malignancy and CRS-HIPEC as a patient group allowed for insight about this rare cancer cohort, in particular the cognitive experience and impacts of prehabilitation on cognition, which to our knowledge have not been explored previously. The integration of cognitive assessment within a prehabilitation trial despite methodological complexity, provided an opportunity to explore not only prevalence and expression of CRCI, but also potential impacts on CRCI simultaneously, providing much needed timely and novel research findings related to the potential cognitive effects of prehabilitation. From a methodological perspective, the inclusion of qualitative semi-structured interviews provided increased depth and insight into the patient experience and contributed greatly to the conceptual understanding of cognitive experience as a dynamic spectrum of cognitive health to CRCI as illustrated in figure 7.1. The use of multiple modes of CRCI assessment across this research project provided for the first time, an exploration of cognitive impairment from multiple methodological perspectives, and ultimately contributed novel and unique insights to our understanding of CRCI.

Throughout this project, the presence of a public and patient involvement panel (PPI) has provided invaluable insight and experience when developing the research methods applied across this project. In 2023, Colomer-Lahiguera conducted a scoping review of over 100 studies to understand how PPI is applied and reported within cancer research. Findings outlined four frequent purposes of PPI research including helping to determine acceptability, feasibility, relevance and appropriateness of research designs. The PPI panel involved in the current project contributed greatly in determining the acceptability and relevance of research materials like study documentation and patient questionnaires as well as the acceptability of mode of questionnaire assessments. The primary contribution of the PPI panel was to determine the relevance of the topic guides for patient interviews pre and post-surgery. Patients were presented with the draft topic guides and asked to provide suggestions or feedback to improve the relevance and applicability of the topic guide questions. Patient feedback ultimately improved the specificity and applicability of topic guide questions, in particular, the addition of appropriate prompts based on specific physical and psychological symptomatology and experiences that would not have been included if not for the insight of the PPI panel. In the past, research has explored the purpose and impact of PPI involvement, suggesting that determining exact impact of PPI is largely context dependent, but determined that regardless, PPI contributes to the project through experiential knowledge (Staley, 2015). Within this project, the experiential knowledge of CRS-HIPEC treatment and the experience of cancer in general, provided invaluable insight to the development of appropriate research methodology and topic guide interview questions.

7.1.8 Conclusions

This is to our knowledge, the first study to explore the prevalence and expression of CRCI from pre-surgery or treatment to one-year follow-up for patients with peritoneal malignancy scheduled for CRS-HIPEC. In addition, this project provided novel insights into the potential effects of combined exercise and nutrition pre- and rehabilitation on cognitive and psychological wellbeing. The inclusion of multiple assessment methods, including qualitative patient interviews provided a novel overview of CRCI across multiple methodological perspectives. Self-report assessment of CRCI provided insight into CRCI prevalence, in particular variability from the point of enrolment to approximately one year post surgery. Measurement of health-related quality of life and psychological wellbeing allowed for the exploration of associations between cognitive

function, psychological wellbeing and cognitive function. These observations combined with prior theory and systematic evidence resulted in the development of a conceptual understanding of pretreatment CRCI and the potential positive impacts of prehabilitation. Results provide insights for the development of future research and recommendations for the integration of cognitive impairment screening and support as standard as part of both psycho-oncological care and prehabilitation. The findings of this research will benefit future research and policy development through the identification of pre-surgery CRCI, avenues for cognitive support via enrichment and associations with psychological wellbeing to ultimately support patient quality of life into recovery and survivorship.

References

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., Haes, J. C. J. M. D., Kaasa, S., Klee, M., Osoba, D., Razavi, D., Rofe, P. B., Schraub, S., Sneeuw, K., Sullivan, M., & Takeda, F. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology. *JNCI Journal of the National Cancer Institute*, *85*(5), 365–376. https://doi.org/10.1093/jnci/85.5.365

Abelson, J. S., Chait, A., Shen, M. J., Charlson, M., Dickerman, A., & Yeo, H. L. (2018). Sources of distress among patients undergoing surgery for colorectal cancer: A qualitative study. *Journal of Surgical Research*, *226*, 140–149. https://doi.org/10.1016/j.jss.2018.01.017

Abraham, S., Parekh, J., Lee, S., Afrin, H., Rozenblit, M., Blenman, K. R. M., Perry, R. J., Ferrucci, L. M., Liu, J., Irwin, M. L., & Lustberg, M. (2025). Accelerated Aging in Cancer and Cancer Treatment: Current Status of Biomarkers. *Cancer Medicine*, *14*(9), e70929. https://doi.org/10.1002/cam4.70929

Ahles, T. A., & Hurria, A. (2018). New Challenges in Psycho-Oncology Research IV: Cognition and cancer: Conceptual and methodological issues and future directions. *Psycho-Oncology*, *27*(1), 3–9. https://doi.org/10.1002/pon.4564

Ahles, T. A., & Saykin, A. J. (2007). Candidate mechanisms for chemotherapy-induced cognitive changes. *Nature Reviews Cancer*, *7*(3), 192–201. https://doi.org/10.1038/nrc2073

Allemang, B., Sitter, K., & Dimitropoulos, G. (2022). Pragmatism as a paradigm for patient-oriented research. *Health Expectations : An International Journal of Public Participation in Health Care and Health Policy*, *25*(1), 38–47. https://doi.org/10.1111/hex.13384

Al-Naime, K., Al-Anbuky, A., & Mawston, G. (2021). Remote Monitoring Model for the Preoperative Prehabilitation Program of Patients Requiring Abdominal Surgery. *Future Internet*, *13*(5), Article 5. https://doi.org/10.3390/fi13050104

Alvi, M. A., Wilson, R. H., & Salto-Tellez, M. (2017). Rare cancers: The greatest inequality in cancer research and oncology treatment. *British Journal of Cancer*, *117*(9), Article 9. https://doi.org/10.1038/bjc.2017.321

Ambler, N., Rumsey, N., Harcourt, D., Khan, F., Cawthorn, S., & Barker, J. (1999). Specialist nurse counsellor interventions at the time of diagnosis of breast cancer: Comparing `advocacy' with a conventional approach. *Journal of Advanced Nursing*, *29*(2), 445–453. https://doi.org/10.1046/j.1365-2648.1999.00902.x

American Cancer Society. (2025). *Managing Cancer as a Chronic Illness*. Cancer.Org. https://www.cancer.org/cancer/survivorship/long-term-health-concerns/cancer-as-a-chronic-illness.html

Amiri, S. (2024). The prevalence of anxiety symptoms/disorders in cancer patients: A meta-analysis. *Frontiers in Psychiatry*, *15*. https://doi.org/10.3389/fpsyt.2024.1422540

Andreotti, C., Root, J. C., Ahles, T. A., McEwen, B. S., & Compas, B. E. (2015). Cancer, coping, and cognition: A model for the role of stress reactivity in cancer-related cognitive decline. *Psycho-Oncology*, *24*(6), 617–623. https://doi.org/10.1002/pon.3683

Anguera, M. T., Blanco-Villaseñor, A., Losada, J. L., Sánchez-Algarra, P., & Onwuegbuzie, A. J. (2018). Revisiting the difference between mixed methods and multimethods: Is it all in the name? *Quality & Quantity*, *52*(6), 2757–2770. https://doi.org/10.1007/s11135-018-0700-2

Anwar, A., & Kasi, A. (2024). Peritoneal Cancer. In StatPearls. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK562138/

Arain, M., Campbell, M. J., Cooper, C. L., & Lancaster, G. A. (2010). What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Medical Research Methodology*, *10*(1), 67. https://doi.org/10.1186/1471-2288-10-67

Areklett, E. W., Andersson, S., Fagereng, E., Bruheim, K., Stubberud, J., & Lindemann, K. (2024). Cognitive impairment in cervical cancer survivors—Exploring the discrepancy between subjective and objective assessment. *Psycho-Oncology*, *33*(2), e6300. https://doi.org/10.1002/pon.6300

Arends, J., Baracos, V., Bertz, H., Bozzetti, F., Calder, P. C., Deutz, N. E. P., Erickson, N., Laviano, A., Lisanti, M. P., Lobo, D. N., McMillan, D. C., Muscaritoli, M., Ockenga, J., Pirlich, M., Strasser, F., de van der Schueren, M., Van Gossum, A., Vaupel, P., & Weimann, A. (2017). ESPEN expert group recommendations for action against cancer-related malnutrition. *Clinical Nutrition*, *36*(5), 1187–1196. https://doi.org/10.1016/j.clnu.2017.06.017

Aspelund, S. G., Halldorsdottir, T., Agustsson, G., Sigurdardottir Tobin, H. R., Wu, L. M., Amidi, A., Johannsdottir, K. R., Lutgendorf, S. K., Telles, R., Daly, H. F., Sigurdardottir, K., Valdimarsdottir, H. B., & Baldursdottir, B. (2024). Biological and psychological predictors of cognitive function in breast cancer patients before surgery. *Supportive Care in Cancer*, *32*(1), 88. https://doi.org/10.1007/s00520-023-08282-5

Aydin, S., Ozguzel, B., Bayramova, B., Budak, E., Aydin, E., Aydin, A., Ustuner, M., Duran, E. N., & Aydin, F. B. (2025). Cognitive flexibility, memory, and attention in colorectal cancer: Findings from a comprehensive neuropsychological assessment. *BMC Cancer*, *25*(1), 1447. https://doi.org/10.1186/s12885-025-14732-6

Bai, L., & Yu, E. (2021). A narrative review of risk factors and interventions for cancer-related cognitive impairment. *Annals of Translational Medicine*, *9*(1), 72. https://doi.org/10.21037/atm-20-6443

Bakkers, C., van de Vlasakker, V. C. J., Rovers, K. P. B., Lurvink, R. J., Nienhuijs, S. W., Burger, J. W. A., Creemers, G.-J. M., Bonhof, C. S., Mols, F., & de Hingh, I. H. J. T. (2023). The Impact of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS-HIPEC) versus Conventional Surgery on Patient-Reported Outcomes: A Comparative Cohort Study between the CAIRO6 Trial and the PROCORE Study. *Cancers*, *15*(3), Article 3. https://doi.org/10.3390/cancers15030788

Banerjee, S., Semper, K., Skarparis, K., Naisby, J., Lewis, L., Cucato, G., Mills, R., Rochester, M., & Saxton, J. (2021). Patient perspectives of vigorous intensity aerobic interval exercise prehabilitation prior to radical cystectomy: A qualitative focus group study. *Disability and Rehabilitation*, *43*(8), 1084–1091. https://doi.org/10.1080/09638288.2019.1651907

Banugo, P., & Amoako, D. (2017). Prehabilitation. *BJA Education*, *17*(12), 401–405. https://doi.org/10.1093/bjaed/mkx032

Barberan-Garcia, A., Cano, I., Bongers, B. C., Seyfried, S., Ganslandt, T., Herrle, F., & Martínez-Pallí, G. (2021). Digital Support to Multimodal Community-Based Prehabilitation: Looking for Optimization of Health Value Generation. *Frontiers in Oncology*, *11*. https://www.frontiersin.org/article/10.3389/fonc.2021.662013

Bargetzi, L., Brack, C., Herrmann, J., Bargetzi, A., Hersberger, L., Bargetzi, M., Kaegi-Braun, N., Tribolet, P., Gomes, F., Hoess, C., Pavlicek, V., Bilz, S., Sigrist, S., Brändle, M., Henzen, C., Thomann, R., Rutishauser, J., Aujesky, D., Rodondi, N., … Schuetz, P. (2021). Nutritional support during the hospital stay reduces mortality in

patients with different types of cancers: Secondary analysis of a prospective randomized trial. *Annals of Oncology*, *32*(8), 1025–1033. https://doi.org/10.1016/j.annonc.2021.05.793

Barker, T. H., Stone, J. C., Sears, K., Klugar, M., Tufanaru, C., Leonardi-Bee, J., Aromataris, E., & Munn, Z. (2023). The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. *JBI Evidence Synthesis*, *21*(3), 494–506. https://doi.org/10.11124/JBIES-22-00430

Barrett-Bernstein, M., Carli, F., Gamsa, A., Scheede-Bergdahl, C., Minnella, E., Ramanakumar, A. V., & Tourian, L. (2019). Depression and functional status in colorectal cancer patients awaiting surgery: Impact of a multimodal prehabilitation program. *Health Psychology*, *38*(10), 900–909. https://doi.org/10.1037/hea0000781

Bates, A., West, M. A., Jack, S., & Grocott, M. P. W. (2024). Preparing for and Not Waiting for Surgery. *Current Oncology*, *31*(2), 629–648. **https://doi.org/10.3390/curroncol31020046**

Bausys, A., Mazeikaite, M., Bickaite, K., Bausys, B., Bausys, R., & Strupas, K. (2022). The Role of Prehabilitation in Modern Esophagogastric Cancer Surgery: A Comprehensive Review. *Cancers*, *14*(9), Article 9. https://doi.org/10.3390/cancers14092096

Bazeley, P., & Kemp, L. (2012). Mosaics, Triangles, and DNA: Metaphors for Integrated Analysis in Mixed Methods Research. *Journal of Mixed Methods Research*, *6*(1), 55–72. https://doi.org/10.1177/1558689811419514

Belleau, F., Hagan, L., & Mâsse, B. (2001). Effects of an educational intervention on the anxiety of women awaiting mastectomies. *Canadian Oncology Nursing Journal*, *11*(4), 177–180. https://doi.org/10.5737/1181912x114177180

Bello, C. M., Eisler, P., & Heidegger, T. (2025). Perioperative Anxiety: Current Status and Future Perspectives. *Journal of Clinical Medicine*, *14*(5), 1422. https://doi.org/10.3390/jcm14051422

Bender, C. M., & Thelen, B. D. (2013). Cancer and Cognitive Changes: The Complexity of the Problem. *Seminars in Oncology Nursing*, *29*(4), 232–237. https://doi.org/10.1016/j.soncn.2013.08.003

Benedict, R. H. B., Schretlen, D., Groninger, L., & Brandt, J. (2010). Hopkins Verbal Learning Test – Revised: Normative Data and Analysis of Inter-Form and Test-Retest Reliability. *The Clinical Neuropsychologist*. https://doi.org/10.1076/clin.12.1.43.1726

Benton, A. L., Hamsher, d. S. K., & Sivan, A. B. (1983). *Controlled Oral Word Association Test (COWAT)* [Database record]. APA PsycTests.

Berger, S., Saut, A. M., & Berssaneti, F. T. (2020). Using patient feedback to drive quality improvement in hospitals: A qualitative study. *BMJ Open*, *10*(10), e037641. https://doi.org/10.1136/bmjopen-2020-037641

Bernal, J. D. K., Recchia, F., Yu, D. J., Fong, D. Y., Wong, S. H. S., Chung, P.-K., Chan, D. K. C., Capio, C. M., Yu, C. C. W., Wong, S. W. S., Sit, C. H. P., Chen, Y.-J., Thompson, W. R., & Siu, P. M. (2023). Physical activity and exercise for cancer-related cognitive impairment among individuals affected by childhood cancer: A systematic review and meta-analysis. *The Lancet Child & Adolescent Health*, *7*(1), 47–58. https://doi.org/10.1016/S2352-4642(22)00286-3

Bernstein, L. J., Pond, G. R., Gan, H. K., Tirona, K., Chan, K. K., Hope, A., Kim, J., Chen, E. X., Siu, L. L., & Razak, A. R. A. (2018). Pretreatment neurocognitive function and self-reported symptoms in patients with newly diagnosed head and neck cancer compared with noncancer cohort. *Head & Neck*, *40*(9), 2029–2042. https://doi.org/10.1002/hed.25198

Bettariga, F., Taaffe, D. R., Crespo-Garcia, C., Clay, T. D., Galvão, D. A., & Newton, R. U. (2025). Effects of resistance training vs high intensity interval training on body composition, muscle strength, cardiorespiratory fitness, and quality of life in survivors of breast cancer: A randomized trial. *Breast Cancer Research and Treatment*, *210*(2), 261–270. https://doi.org/10.1007/s10549-024-07559-5

Biglia, B., Ve, B., A, M., D, P., Dm, T., M, D., P, S., & R, T. (2012). Objective and self-reported cognitive dysfunction in breast cancer women treated with chemotherapy: A prospective study. *European Journal of Cancer Care*, *21*(4). https://doi.org/10.1111/j.1365-2354.2011.01320.x

Boele, F. W., Zant, M., Heine, E. C. E., Aaronson, N. K., Taphoorn, M. J. B., Reijneveld, J. C., Postma, T. J., Heimans, J. J., & Klein, M. (2014). The association between cognitive functioning and health-related quality of life in low-grade glioma patients. *Neuro-Oncology Practice*, *1*(2), 40–46. https://doi.org/10.1093/nop/npu007

Bolshinsky, V., Li, M. H.-G., Ismail, H., Burbury, K., Riedel, B., & Heriot, A. (2018). Multimodal Prehabilitation Programs as a Bundle of Care in Gastrointestinal Cancer Surgery: A Systematic Review. *Diseases of the Colon & Rectum*, *61*(1), 124–138. https://doi.org/10.1097/DCR.0000000000000987

Boykoff, N., Moieni, M., & Subramanian, S. K. (2009). Confronting chemobrain: An in-depth look at survivors' reports of impact on work, social networks, and health care response. *Journal of Cancer Survivorship*, *3*(4), 223. https://doi.org/10.1007/s11764-009-0098-x

Brahmbhatt, P., Minnella, E. M., Randall, I. M., & Santa Mina, D. (2022). Multimodal Prehabilitation: A Mini Review of Contemporary Research. *Current Anesthesiology Reports*, *12*(1), 99–108. https://doi.org/10.1007/s40140-021-00490-1

Brahmbhatt, P., Sabiston, C. M., Lopez, C., Chang, E., Goodman, J., Jones, J., McCready, D., Randall, I., Rotstein, S., & Santa Mina, D. (2020). Feasibility of Prehabilitation Prior to Breast Cancer Surgery: A Mixed-Methods Study. *Frontiers in Oncology*, *10*, 571091. https://doi.org/10.3389/fonc.2020.571091

Brandenbarg, D., Maass, S. W. M. C., Geerse, O. P., Stegmann, M. E., Handberg, C., Schroevers, M. J., & Duijts, S. F. A. (2019). A systematic review on the prevalence of symptoms of depression, anxiety and distress in long-term cancer survivors: Implications for primary care. *European Journal of Cancer Care*, *28*(3). https://doi.org/10.1111/ecc.13086

Braun, V., & Clarke, V. (2012). Thematic analysis. In H. Cooper, P. M. Camic, D. L. Long, A. T. Panter, D. Rindskopf, & K. J. Sher (Eds.), *APA handbook of research methods in psychology, Vol 2: Research designs: Quantitative, qualitative, neuropsychological, and biological.* (pp. 57–71). American Psychological Association. https://doi.org/10.1037/13620-004

Braun, V., & Clarke, V. (2014). What can "thematic analysis" offer health and wellbeing researchers? *International Journal of Qualitative Studies on Health and Well-Being*, *9*(1), 26152. https://doi.org/10.3402/qhw.v9.26152

Braun, V., & Clarke, V. (2022). Thematic analysis: A practical guide. SAGE.

Bray, V. J., Dhillon, H. M., & Vardy, J. L. (2018). Systematic review of self-reported cognitive function in cancer patients following chemotherapy treatment. *Journal of Cancer Survivorship*, *12*(4), 537–559. https://doi.org/10.1007/s11764-018-0692-x

Brebach, R., Sharpe, L., Costa, D. S. J., Rhodes, P., & Butow, P. (2016). Psychological intervention targeting distress for cancer patients: A meta-analytic study investigating uptake and adherence. *Psycho-Oncology*, *25*(8), 882–890. https://doi.org/10.1002/pon.4099

Brewster, K. K., Shalev, D., & Levenson, J. A. (2017). Chemotherapy-Related Cognitive Impairment #342. *Journal of Palliative Medicine*, *20*(12), 1407–1408. https://doi.org/10.1089/jpm.2017.0524

Broadbent, D. E., Cooper, P. F., FitzGerald, P., & Parkes, K. R. (1982). The Cognitive Failures Questionnaire (CFQ) and its correlates. *The British Journal of Clinical Psychology*, *21*(1), 1–16. https://doi.org/10.1111/j.2044-8260.1982.tb01421.x

Bruns, E. R. J., Van Den Heuvel, B., Buskens, C. J., Van Duijvendijk, P., Festen, S., Wassenaar, E. B., Van Der Zaag, E. S., Bemelman, W. A., & Van Munster, B. C. (2016). The effects of physical prehabilitation in elderly patients undergoing colorectal surgery: A systematic review. *Colorectal Disease*, *18*(8). https://doi.org/10.1111/codi.13429

Bundred, J. R., Kamarajah, S. K., Hammond, J. S., Wilson, C. H., Prentis, J., & Pandanaboyana, S. (2020). Prehabilitation prior to surgery for pancreatic cancer: A systematic review. *Pancreatology*, *20*(6), 1243–1250. https://doi.org/10.1016/j.pan.2020.07.411

Burmester, B., Leathem, J., & Merrick, P. (2016). Subjective Cognitive Complaints and Objective Cognitive Function in Aging: A Systematic Review and Meta-Analysis of Recent Cross-Sectional Findings. *Neuropsychology Review*, *26*(4), 376–393. https://doi.org/10.1007/s11065-016-9332-2

Calder, J., Kavanagh, P. S., Bacon, R., Chau, M., Sidhu, D., & Toohey, K. (2025). The effects of exercise dose on psychological health outcomes in people diagnosed with cancer: A systematic review and meta-analysis. *Disability and Rehabilitation*, *47*(14), 3516–3527. https://doi.org/10.1080/09638288.2024.2432919

Campbell, K. L., Winters-Stone, K. M., Wiskemann, J., May, A. M., Schwartz, A. L., Courneya, K. S., Zucker, D. S., Matthews, C. E., Ligibel, J. A., Gerber, L. H., Morris, G. S., Patel, A. V., Hue, T. F., Perna, F. M., & Schmitz, K. H. (2019). Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. *Medicine & Science in Sports & Exercise*, *51*(11), 2375–2390. https://doi.org/10.1249/MSS.0000000000002116

Can, G., Topuz, E., Derin, D., Durna, Z., & Aydiner, A. (2009). Effect of Kefir on the Quality of Life of Patients Being Treated for Colorectal Cancer. *Oncology Nursing Forum*, *36*(6), E335–E342. https://doi.org/10.1188/09.ONF.E335-E342

Cancer Research UK. (2014, December 16). *What is cancer?* Cancer Research UK. https://www.cancerresearchuk.org/about-cancer/what-is-cancer

Cancer Research UK. (2015, May 13). *Cancer incidence by age*. Cancer Research UK. https://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age

Capetti, B., Conti, L., Ferrari, M. V., Coppini, V., Ferraris, G., Marzorati, C., Monzani, D., Grasso, R., & Pravettoni, G. (2025). Neuropsychological assessment in non-central nervous system cancer patients: A systematic review of cognitive screening and assessment within oncology practice. *Health Psychology Review*, *0*(0), 1–65. https://doi.org/10.1080/17437199.2025.2536071

Carli, F., Gillis, C., & Scheede-Bergdahl, C. (2017). Promoting a culture of prehabilitation for the surgical cancer patient. *Acta Oncologica*, *56*(2), 128–133. https://doi.org/10.1080/0284186X.2016.1266081

Carr, N. J. (2021). New insights in the pathology of peritoneal surface malignancy. *Journal of Gastrointestinal Oncology*, *12*(Suppl 1), S216–S229. https://doi.org/10.21037/jgo-2020-01

Cella, D. F., Tulsky, D. S., Gray, G., Sarafian, B., Linn, E., Bonomi, A., Silberman, M., Yellen, S. B., Winicour, P., Brannon, J., Eckberg, K., Lloyd, S., Purl, S., Blendowski, C., Goodman, M., Barnicle, M., Stewart, I., McHale, M., Bonomi, P., … Harris, J. (1993). The Functional Assessment of Cancer Therapy Scale: Development and validation of the general measure. *Journal of Clinical Oncology*, *11*(3), 570–579. https://doi.org/10.1200/JCO.1993.11.3.570

Chen, X., He, X., Tao, L., Cheng, H., Li, J., Zhang, J., Qiu, B., Yu, Y., & Wang, K. (2017). The attention network changes in breast cancer patients receiving neoadjuvant chemotherapy: Evidence from an arterial spin labeling perfusion study. *Scientific Reports*, *7*, 42684. https://doi.org/10.1038/srep42684

Cheng, S.-T. (2016). Cognitive Reserve and the Prevention of Dementia: The Role of Physical and Cognitive Activities. *Current Psychiatry Reports*, *18*(9), 85. https://doi.org/10.1007/s11920-016-0721-2

Cherrier, M. M., Anderson, K., David, D., Higano, C. S., Gray, H., Church, A., & Willis, S. L. (2013). A randomized trial of cognitive rehabilitation in cancer survivors. *Life Sciences*, *93*(17), 617–622. https://doi.org/10.1016/j.lfs.2013.08.011

Cheung, S. Y., & Delfabbro, P. (2016). Are you a cancer survivor? A review on cancer identity. *Journal of Cancer Survivorship: Research and Practice*, *10*(4), 759–771. https://doi.org/10.1007/s11764-016-0521-z

Chen, J., Beal, E. W., Hays, J., Pawlik, T. M., Abdel-Misih, S., & Cloyd, J. M. (2020). Outcomes of neoadjuvant chemotherapy before CRS-HIPEC for patients with appendiceal cancer. *Journal of Surgical Oncology*, *122*(3), 388–398. https://doi.org/10.1002/jso.25967

Chun, Y. J., Kim, K. J., Lee, J. Y., Choi, J. W., Kim, T. H., Kim, H. R., Cho, B. C., Hong, M. H., & Kim, C. O. (2023). The prognostic value of comprehensive geriatric assessment on the management of older patients with small cell lung cancer. *The Korean Journal of Internal Medicine*, *38*(2), 254–263. https://doi.org/10.3904/kjim.2022.247

Cimprich, B. (1999). Pretreatment symptom distress in women newly diagnosed with breast cancer: *Cancer Nursing*, *22*(3), 185–194. https://doi.org/10.1097/00002820-199906000-00001

Cimprich, B., & Ronis, D. L. (2001). Attention and Symptom Distress in Women With and Without Breast Cancer: *Nursing Research*, *50*(2), 86–94. https://doi.org/10.1097/00006199-200103000-00004

Cimprich, B., So, H., Ronis, D. L., & Trask, C. (2005). Pre-treatment factors related to cognitive functioning in women newly diagnosed with breast cancer. *Psycho-Oncology*, *14*(1), 70–78. https://doi.org/10.1002/pon.821

Clark, V. L. P., & Ivankova, N. V. (2016). What is Mixed Methods Research? ;Considering How Mixed Methods Research is Defined In *Mixed Methods Research: A Guide to the Field* (pp. 55–78). SAGE Publications, Inc. https://doi.org/10.4135/9781483398341

Clemons, J., Zhou, Z., Hoy, S. A., Gerber, S. Q., Nambiar, A., Kwon, A., & Kin, C. (2024). No thanks and not for me: A qualitative study of barriers to prehabilitation participation. *Surgery*, *176*(6), 1697–1702. https://doi.org/10.1016/j.surg.2024.08.014

Coca-Martinez, M., & Carli, F. (2024). Prehabilitation: Who can benefit? *European Journal of Surgical Oncology*, *50*(5), 106979. https://doi.org/10.1016/j.ejso.2023.07.005

Colomer-Lahiguera, S., Steimer, M., Ellis, U., Eicher, M., Tompson, M., Corbière, T., & Haase, K. R. (2023). Patient and public involvement in cancer research: A scoping review. *Cancer Medicine*, *12*(14), 15530–15543. https://doi.org/10.1002/cam4.6200

Cormie, P., Atkinson, M., Bucci, L., Cust, A., Eakin, E., Hayes, S., McCarthy, A. L., Murnane, A., Patchell, S., & Adams, D. (2018). Clinical Oncology Society of Australia position statement on exercise in cancer care. *Medical Journal of Australia*, *209*(4), 184–187. https://doi.org/10.5694/mja18.00199

Cormie, P., Zopf, E. M., Zhang, X., & Schmitz, K. H. (2017). The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. *Epidemiologic Reviews*, *39*(1), 71–92. https://doi.org/10.1093/epirev/mxx007

Coro, D. G., Hutchinson, A. D., Banks, S., & Coates, A. M. (2020). Diet and cognitive function in cancer survivors with cancer-related cognitive impairment: A qualitative study. *European Journal of Cancer Care*, *29*(6), e13303. https://doi.org/10.1111/ecc.13303

Coro, D., Hutchinson, A., Dahlenburg, S., Banks, S., & Coates, A. (2019). The relationship between diet and cognitive function in adult cancer survivors: A systematic review. *Journal of Cancer Survivorship*, *13*(5), 773–791. https://doi.org/10.1007/s11764-019-00796-4

Cortés-Guiral, D., Mohamed, F., Glehen, O., & Passot, G. (2021). Prehabilitation of patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal malignancy. *European Journal of Surgical Oncology : The Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, *47*(1), 60–64. https://doi.org/10.1016/j.ejso.2020.01.032

Costet, N., Lapierre, V., Benhamou, E., & Galès, C. L. (2005). Reliability and validity of the Functional Assessment of Cancer Therapy General (FACT-G) in French cancer patients. *Quality of Life Research*, *14*(5), 1427–1432. https://doi.org/10.1007/s11136-004-5531-z

Cristofori, I., Cohen-Zimerman, S., & Grafman, J. (2019). Executive functions. In *Handbook of clinical neurology* (Vol. 163, pp. 197–219). https://doi.org/10.1016/B978-0-12-804281-6.00011-2

Cruzado, J. A., López-Santiago, S., Martínez-Marín, V., José-Moreno, G., Custodio, A. B., & Feliu, J. (2014). Longitudinal study of cognitive dysfunctions induced by adjuvant chemotherapy in colon cancer patients. *Supportive Care in Cancer*, *22*(7), 1815–1823. https://doi.org/10.1007/s00520-014-2147-x

Culley, D. J., & Crosby, G. (2015). Prehabilitation for Prevention of Postoperative Cognitive Dysfunction? *Anesthesiology*, *123*(1), 7–9. https://doi.org/10.1097/ALN.0000000000000698

Curran, L., Sharpe, L., & Butow, P. (2017). Anxiety in the context of cancer: A systematic review and development of an integrated model. *Clinical Psychology Review*, *56*, 40–54. https://doi.org/10.1016/j.cpr.2017.06.003

Cutillo, A., O'Hea, E., Person, S., Lessard, D., Harralson, T., & Boudreaux, E. (2017). NCCN Distress Thermometer: Cut off Points and Clinical Utility. *Oncology Nursing Forum*, *44*(3), 329–336. https://doi.org/10.1188/17.ONF.329-336

de Heus, E., van der Zwan, J. M., Husson, O., Frissen, A.-R., van Herpen, C. M. L., Merkx, M. A. W., & Duijts, S. F. A. (2021). Unmet supportive care needs of patients with rare cancer: A systematic review. *European Journal of Cancer Care*, *30*(6), e13502. https://doi.org/10.1111/ecc.13502

de Moor, J. S., Moyé, L., Low, M. D., Rivera, E., Singletary, S. E., Fouladi, R. T., & Cohen, L. (2008). Expressive writing as a presurgical stress management intervention for breast cancer patients. *Journal of the Society for Integrative Oncology*, *6*(2), 59–66.

De Paleville, D. T., Topp, R. V., & Swank, A. M. (2007). Effects of Aerobic Training Prior to and During Chemotherapy in a Breast Cancer Patient: A Case Study. *The Journal of Strength and Conditioning Research*, *21*(2), 635. https://doi.org/10.1519/R-19735.1

De Rosa, N., Della Corte, L., Giannattasio, A., Giampaolino, P., Di Carlo, C., & Bifulco, G. (2021). Cancer-related cognitive impairment (CRCI), depression and quality of life in gynecological cancer patients: A prospective study. *Archives of Gynecology and Obstetrics*, *303*(6), 1581–1588. https://doi.org/10.1007/s00404-020-05896-6

Department of Health. (2017). *National Cancer Strategy 2017-2026*. Government of Ireland.

Department of Health. (2024). *KPI Overview NCS Implementation Report 2023*. Department of Health. https://assets.gov.ie/static/documents/kpi-overview-ncs-implementation-report-2023-368a5cc3-4dd8-462c-8312-55904d238f81.pdf

Deprez, S., Kesler, S. R., Saykin, A. J., Silverman, D. H. S., de Ruiter, M. B., & McDonald, B. C. (2018). International Cognition and Cancer Task Force Recommendations for Neuroimaging Methods in the Study of Cognitive Impairment in Non-CNS Cancer

Patients. *JNCI Journal of the National Cancer Institute*, *110*(3), 223–231. https://doi.org/10.1093/jnci/djx285

DeSantis, C. E., Kramer, J. L., & Jemal, A. (2017). The burden of rare cancers in the United States. *CA: A Cancer Journal for Clinicians*, *67*(4), 261–272. https://doi.org/10.3322/caac.21400

Duan, R., Wen, Z., Zhang, T., Liu, J., Feng, T., & Ren, T. (2025). Advances in risk prediction models for cancer-related cognitive impairment. *Clinical and Experimental Medicine*, *25*(1), 74. https://doi.org/10.1007/s10238-025-01590-6

Duarte-Silva, E., Clarke, G., Dinan, T. G., & Peixoto, C. A. (2021). Personalized Nutrition for Depression: Impact on the Unholy Trinity. *Neuroimmunomodulation*, *28*(2), 47–51. https://doi.org/10.1159/000514094

Dunne, S., Mooney, O., Coffey, L., Sharp, L., Desmond, D., Timon, C., O'Sullivan, E., & Gallagher, P. (2017). Psychological variables associated with quality of life following primary treatment for head and neck cancer: A systematic review of the literature from 2004 to 2015. *Psycho-Oncology*, *26*(2), 149–160. https://doi.org/10.1002/pon.4109

Dyba, T., Randi, G., Bray, F., Martos, C., Giusti, F., Nicholson, N., Gavin, A., Flego, M., Neamtiu, L., Dimitrova, N., Negrão Carvalho, R., Ferlay, J., & Bettio, M. (2021). The European cancer burden in 2020: Incidence and mortality estimates for 40 countries and 25 major cancers. *European Journal of Cancer*, *157*, 308–347. https://doi.org/10.1016/j.ejca.2021.07.039

Efficace, F., Bottomley, A., Coens, C., Van Steen, K., Conroy, T., Schöffski, P., Schmoll, H., Van Cutsem, E., & Köhne, C.-H. (2006). Does a patient's self-reported health-related quality of life predict survival beyond key biomedical data in advanced colorectal cancer? *European Journal of Cancer*, *42*(1), 42–49. https://doi.org/10.1016/j.ejca.2005.07.025

Ekici, G., Atasavun Uysal, S., & Altuntaş, O. (2016). The Validity And Reliability Of Cognitive Failures Questionnaire In University Students. *Türk Fizyoterapi ve Rehabilitasyon Dergisi*, *27*(2), 55–55. https://doi.org/10.21653/tfrd.272979

Eriksson, H., Haglund, K., Leo Swenne, C., & Arakelian, E. (2014). Patients' experiences of postoperative health related to cytoreductive surgery and hyperthermic intraoperative

chemotherapy. *Journal of Clinical Nursing*, *23*(1–2), 201–210. https://doi.org/10.1111/jocn.12360

Essue, B. M., Iragorri, N., Fitzgerald, N., & de Oliveira, C. (2020). The psychosocial cost burden of cancer: A systematic literature review. *Psycho-Oncology*, *29*(11), 1746–1760. https://doi.org/10.1002/pon.5516

European Cancer Organisation. (2025). *Policy—European Cancer Organisation*. https://www.europeancancer.org/policy.html

European Commission. Directorate General for Research and Innovation. (2020). *Conquering cancer: Mission possible.* Publications Office. https://data.europa.eu/doi/10.2777/045403

European Union. (2025). *European Cancer Information System*. ECIS-European Cancer Information System. https://ecis.jrc.ec.europa.eu

Eurostat. (2025). *Cancer statistics—Specific cancers*. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cancer_statistics_-_specific_cancers

ExWell Medical. (n.d.). *ExWell Medical | Medical exercise rehabilitation classes*. Www.Exwell.Ie. Retrieved November 27, 2025, from https://www.exwell.ie

Ezzati, A., Zammit, A. R., Katz, M. J., Derby, C. A., Zimmerman, M. E., & Lipton, R. B. (2019). Health-related Quality of Life, Cognitive Performance, and Incident Dementia in a Community-based Elderly Cohort. *Alzheimer Disease and Associated Disorders*, *33*(3), 240–245. https://doi.org/10.1097/WAD.0000000000000324

Faithfull, S., Turner, L., Poole, K., Joy, M., Manders, R., Weprin, J., Winters-Stone, K., & Saxton, J. (2019). Prehabilitation for adults diagnosed with cancer: A systematic review of long-term physical function, nutrition and patient-reported outcomes. *European Journal of Cancer Care*, *28*(4), e13023. https://doi.org/10.1111/ecc.13023

Falla-Zuniga, L. F., King, M. C., Pawlikowski, K., Nikiforchin, A., Lopez-Ramirez, F., Barakat, P., Iugai, S., Nieroda, C., Gushchin, V., & Sardi, A. (2024). Quality of Life After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC): Cancer Survivors' Perspective Through In-Depth Interviews. *Annals of Surgical Oncology*, *31*(10), 7122–7132. https://doi.org/10.1245/s10434-024-15719-6

Fardell, J. E., Bray, V., Bell, M. L., Rabe, B., Dhillon, H., & Vardy, J. L. (2022). Screening for cognitive symptoms among cancer patients during chemotherapy: Sensitivity and

specificity of a single item self-report cognitive change score. *Psycho-Oncology*, *31*(8), 1294–1301. https://doi.org/10.1002/pon.5928

Fayette, D., Juríčková, V., Kozák, T., Mociková, H., Gaherová, L., Fajnerová, I., & Horáček, J. (2023). Cognitive impairment associated with Hodgkin's lymphoma and chemotherapy. *Neuroscience Letters*, *797*, 137082. https://doi.org/10.1016/j.neulet.2023.137082

Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2024). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: https://gco.iarc.who.int/today, accessed [19/11/2025].

Fernandes, H. A., Richard, N. M., & Edelstein, K. (2019). Cognitive rehabilitation for cancer-related cognitive dysfunction: A systematic review. *Supportive Care in Cancer*, *27*(9), 3253–3279. https://doi.org/10.1007/s00520-019-04866-2

Fitch, M. I. (2021). Perspectives of survivors: Coping with lifestyle adjustments following cancer diagnosis and treatment. *Canadian Oncology Nursing Journal*, *31*(2), 235–238.

Foley, E., Baillie, A., Huxter, M., Price, M., & Sinclair, E. (2010). Mindfulness-based cognitive therapy for individuals whose lives have been affected by cancer: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, *78*(1), 72–79. https://doi.org/10.1037/a0017566

Fortmann, J., Fisher, A., Hough, R., Gregory, A., & Pugh, G. (2018). Sleep Quality, Fatigue, and Quality of Life Among Teenage and Young Adult Cancer Survivors. *Journal of Adolescent and Young Adult Oncology*, *7*(4), 465–471. https://doi.org/10.1089/jayao.2018.0004

Fradelos, E. C., Papathanasiou, I. V., Veneti, A., Daglas, A., Christodoulou, E., Zyga, S., & Kourakos, M. (2017). Psychological Distress and Resilience in Women Diagnosed with Breast Cancer in Greece. *Asian Pacific Journal of Cancer Prevention*, *18*(9). https://doi.org/10.22034/APJCP.2017.18.9.2545

François, E., Magné, N., Boulahssass, R., Ronchin, P., Huguenet, V., De Lavigerie, B., Nouhaud, E., Cattenoz, C., Martel-Lafay, I., Terret, C., Artru, P., Clavere, P., Tchalla, A., Vendrely, V., Duc, S., Boige, V., De Sousa Carvalho, N., Gal, J., & De Bari, B. (2024). Short course radiotherapy versus radiochemotherapy for locally advanced rectal cancers in the elderly (UNICANCER PRODIGE 42/GERICO 12 study):

Quality of life and comprehensive geriatric assessment. *Radiotherapy and Oncology*, *193*, 110144. https://doi.org/10.1016/j.radonc.2024.110144

Galantino, M. L., Greene, L., Daniels, L., Dooley, B., Muscatello, L., & O'Donnell, L. (2012). Longitudinal Impact of Yoga on Chemotherapy-Related Cognitive Impairment and Quality of Life in Women with Early Stage Breast Cancer: A Case Series. *EXPLORE*, *8*(2), 127–135. https://doi.org/10.1016/j.explore.2011.12.001

Gardner, R. C., Langa, K. M., & Yaffe, K. (2017). Subjective and objective cognitive function among older adults with a history of traumatic brain injury: A population-based cohort study. *PLOS Medicine*, *14*(3), e1002246. https://doi.org/10.1371/journal.pmed.1002246

Garssen, B., Boomsma, M. F., De Jager Meezenbroek, E., Porsild, T., Berkhof, J., Berbee, M., Visser, A., Meijer, S., & Beelen, R. H. J. (2013). Stress management training for breast cancer surgery patients. *Psycho-Oncology*, *22*(3), 572–580. https://doi.org/10.1002/pon.3034

Gates, P., Dhillon, Haryana. M., Krishnasamy, M., Wilson, C., & Gough, K. (2024). Cancer-related cognitive impairment and wellbeing in patients with newly diagnosed aggressive lymphoma compared to population norms and healthy controls: An exploratory study. *Supportive Care in Cancer*, *32*(4), 238. https://doi.org/10.1007/s00520-024-08441-2

Gatta, G., Capocaccia, R., Botta, L., Mallone, S., De Angelis, R., Ardanaz, E., Comber, H., Dimitrova, N., Leinonen, M. K., Siesling, S., van der Zwan, J. M., Van Eycken, L., Visser, O., Žakelj, M. P., Anderson, L. A., Bella, F., Kaire, I., Otter, R., Stiller, C. A., … Benhamou, E. (2017). Burden and centralised treatment in Europe of rare tumours: Results of RARECAREnet—a population-based study. *The Lancet Oncology*, *18*(8), 1022–1039. https://doi.org/10.1016/S1470-2045(17)30445-X

Gatta, G., van der Zwan, J. M., Casali, P. G., Siesling, S., Dei Tos, A. P., Kunkler, I., Otter, R., Licitra, L., Mallone, S., Tavilla, A., Trama, A., & Capocaccia, R. (2011). Rare cancers are not so rare: The rare cancer burden in Europe. *European Journal of Cancer*, *47*(17), 2493–2511. https://doi.org/10.1016/j.ejca.2011.08.008

Gil, F., Costa, G., Hilker, I., & Benito, L. (2012). First Anxiety, Afterwards Depression: Psychological Distress in Cancer Patients at Diagnosis and after Medical Treatment. *Stress and Health*, *28*(5), 362–367. https://doi.org/10.1002/smi.2445

Gillis, C., Buhler, K., Bresee, L., Carli, F., Gramlich, L., Culos-Reed, N., Sajobi, T. T., & Fenton, T. R. (2018). Effects of Nutritional Prehabilitation, With and Without Exercise, on Outcomes of Patients Who Undergo Colorectal Surgery: A Systematic Review and Meta-analysis. *Gastroenterology*, *155*(2), 391-410.e4. https://doi.org/10.1053/j.gastro.2018.05.012

Gillis, C., Davies, S. J., Carli, F., Wischmeyer, P. E., Wootton, S. A., Jackson, A. A., Riedel, B., Marino, L. V., Levett, D. Z. H., & West, M. A. (2021). Current Landscape of Nutrition Within Prehabilitation Oncology Research: A Scoping Review. *Frontiers in Nutrition*, *8*. https://www.frontiersin.org/article/10.3389/fnut.2021.644723

Gillis, C., Fenton, T. R., Gramlich, L., Keller, H., Sajobi, T. T., Culos-Reed, S. N., Richer, L., Awasthi, R., & Carli, F. (2022a). Malnutrition modifies the response to multimodal prehabilitation: A pooled analysis of prehabilitation trials. *Applied Physiology, Nutrition, and Metabolism*, *47*(2), 141–150. https://doi.org/10.1139/apnm-2021-0299

Gillis, C., Ljungqvist, O., & Carli, F. (2022b). Prehabilitation, enhanced recovery after surgery, or both? A narrative review. *British Journal of Anaesthesia*, *128*(3), 434–448. https://doi.org/10.1016/j.bja.2021.12.007

Gonella, F., Massucco, P., Perotti, S., Gianolio, S., Vassallo, D., Monasterolo, S., Laezza, A., De Zolt Ponte, B., Ricotti, A., & Ferrero, A. (2024). Prehab, ERAS, Rehab: A patient care continuum around colo-rectal surgery: Prehabilitation combined with ERAS and rehabilitation to reduce morbidity and hospital stay. *European Journal of Surgical Oncology*, *50*(12), 108688. https://doi.org/10.1016/j.ejso.2024.108688

Goodhew, S. C., & Edwards, M. (2025). A meta-analysis on the relationship between subjective cognitive failures as measured by the cognitive failures questionnaire (CFQ) and objective performance on executive function tasks. *Psychonomic Bulletin & Review*, *32*(2), 528–546. https://doi.org/10.3758/s13423-024-02573-6

Gosain, R., & Miller, K. (2013). Symptoms and Symptom Management in Long-term Cancer Survivors. *The Cancer Journal*, *19*(5), 405. https://doi.org/10.1097/01.PPO.0000434391.11187.c3

Greally, H., Love, D., & Mullen, L. (2020). *Hospital and Community-based Psychosocial Care for patients with cancer and their families: A Model of Care for Psycho-Oncology*. National Cancer Control Programme.

Grimmett, C., Bradbury, K., Dalton, S. O., Fecher-Jones, I., Hoedjes, M., Varkonyi-Sepp, J., & Short, C. E. (2021). The Role of Behavioral Science in Personalized Multimodal

Prehabilitation in Cancer. *Frontiers in Psychology*, *12*. https://www.frontiersin.org/article/10.3389/fpsyg.2021.634223

Grimmett, C., Heneka, N., & Chambers, S. (2022). Psychological Interventions Prior to Cancer Surgery: A Review of Reviews. *Current Anesthesiology Reports*, *12*(1), 78–87. https://doi.org/10.1007/s40140-021-00505-x

Gülmez, S. (2023). Impact of the Preoperative Anxiety and Depression Levels on Postoperative Outcomes in Stage II/III Gastric and Colorectal Cancer Patients. *Southern Clinics of Istanbul Eurasia*, 273–278. https://doi.org/10.14744/scie.2021.04875

Guzzinati, S., Virdone, S., De Angelis, R., Panato, C., Buzzoni, C., Capocaccia, R., Francisci, S., Gigli, A., Zorzi, M., Tagliabue, G., Serraino, D., Falcini, F., Casella, C., Russo, A. G., Stracci, F., Caruso, B., Michiara, M., Caiazzo, A. L., Castaing, M., … Dal Maso, L. (2018). Characteristics of people living in Italy after a cancer diagnosis in 2010 and projections to 2020. *BMC Cancer*, *18*(1), 169. https://doi.org/10.1186/s12885-018-4053-y

Hall, A. E., Nguyen, N. H., Cascavita, C. T., Shariati, K., Patel, A. K., Chen, W., Kang, Y., Ren, X., Tseng, C.-H., Hidalgo, M. A., & Lee, J. C. (2025). The Impact of Psychological Prehabilitation on Surgical Outcomes: A Meta-analysis and Meta-regression. *Annals of Surgery*, *281*(6), 928. https://doi.org/10.1097/SLA.0000000000006677

Halliday, L. J., Doganay, E., Wynter-Blyth, V., Osborn, H., Buckley, J., & Moorthy, K. (2021). Adherence to Pre-operative Exercise and the Response to Prehabilitation in Oesophageal Cancer Patients. *Journal of Gastrointestinal Surgery*, *25*(4), 890–899. https://doi.org/10.1007/s11605-020-04561-2

Hamilton, T. D., Taylor, E. L., Cannell, A. J., McCart, J. A., & Govindarajan, A. (2016). Impact of Major Complications on Patients' Quality of Life After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy. *Annals of Surgical Oncology*, *23*(9), 2946–2952. https://doi.org/10.1245/s10434-016-5231-2

Hardy-Leger, I., Charles, C., Lange, M., Joly, F., Roux, P., Capel, A., Petrucci, J., Rigal, O., Le Fel, J., Vanlemmens, L., Everhard, S., Martin, A.-L., Vaz Luis, I., Coutant, C., Cottu, P., Levy, C., Lerebours, F., Andre, F., Licaj, I., & Dauchy, S. (2021). Differentiation of groups of patients with cognitive complaints at breast cancer

diagnosis: Results from a sub-study of the French CANTO cohort. *Psycho-Oncology*, *30*(4), 463–470. https://doi.org/10.1002/pon.5572

Hartman, S. J., Nelson, S. H., Myers, E., Natarajan, L., Sears, D. D., Palmer, B. W., Weiner, L. S., Parker, B. A., & Patterson, R. E. (2018). Randomized controlled trial of increasing physical activity on objectively measured and self-reported cognitive functioning among breast cancer survivors: The memory & motion study. *Cancer*, *124*(1), 192–202. https://doi.org/10.1002/cncr.30987

Hashemi, S.-M., Rafiemanesh, H., Aghamohammadi, T., Badakhsh, M., Amirshahi, M., Sari, M., Behnamfar, N., & Roudini, K. (2020). Prevalence of anxiety among breast cancer patients: A systematic review and meta-analysis. *Breast Cancer*, *27*(2), 166–178. https://doi.org/10.1007/s12282-019-01031-9

Haywood, D., Dauer, E., Baughman, F. D., Lawrence, B. J., Rossell, S. L., Hart, N. H., & O'Connor, M. (2023). "Is My Brain Ever Going to Work Fully Again?": Challenges and Needs of Cancer Survivors with Persistent Cancer-Related Cognitive Impairment. *Cancers*, *15*(22), 5331. ccm. https://doi.org/10.3390/cancers15225331

Haywood, D., Henry, M., Dauer, E., Lederman, O., Farley, M., Henneghan, A. M., O'Connor, M., Jefford, M., Rossell, S. L., & Hart, N. H. (2024). Cancer-related cognitive impairment as a key contributor to psychopathology in cancer survivors: Implications for prevention, treatment and supportive care. *Supportive Care in Cancer*, *32*(7), 480. https://doi.org/10.1007/s00520-024-08696-9

Hendrick, R. E., Monticciolo, D. L., Biggs, K. W., & Malak, S. F. (2021). Age distributions of breast cancer diagnosis and mortality by race and ethnicity in US women. *Cancer*, *127*(23), 4384–4392. https://doi.org/10.1002/cncr.33846

Henneghan, A. M., Van Dyk, K., Kaufmann, T., Harrison, R., Gibbons, C., Heijnen, C., & Kesler, S. R. (2021). Measuring Self-Reported Cancer-Related Cognitive Impairment: Recommendations From the Cancer Neuroscience Initiative Working Group. *JNCI: Journal of the National Cancer Institute*, *113*(12), 1625–1633. https://doi.org/10.1093/jnci/djab027

Hermelink, K., Bühner, M., Sckopke, P., Neufeld, F., Kaste, J., Voigt, V., Münzel, K., Wuerstlein, R., Ditsch, N., Hellerhoff, K., Rjosk-Dendorfer, D., Braun, M., von Koch, F. E., Härtl, K., Hasmüller, S., Bauerfeind, I., Debus, G., Herschbach, P., Mahner, S., & Harbeck, N. (2017). Chemotherapy and Post-traumatic Stress in the Causation of Cognitive Dysfunction in Breast Cancer Patients. *JNCI: Journal of the National Cancer Institute*, *109*(10), djx057. https://doi.org/10.1093/jnci/djx057

Hermelink, K., Küchenhoff, H., Untch, M., Bauerfeind, I., Lux, M. P., Bühner, M., Manitz, J., Fensterer, V., & Münzel, K. (2010). Two different sides of 'chemobrain': Determinants and nondeterminants of self-perceived cognitive dysfunction in a prospective, randomized, multicenter study. *Psycho-Oncology*, *19*(12), 1321–1328. https://doi.org/10.1002/pon.1695

Hermelink, K., Untch, M., Lux, M. P., Kreienberg, R., Beck, T., Bauerfeind, I., & Münzel, K. (2007). Cognitive function during neoadjuvant chemotherapy for breast cancer: Results of a prospective, multicenter, longitudinal study. *Cancer*, *109*(9), 1905–1913. https://doi.org/10.1002/cncr.22610

Hermelink, K., Voigt, V., Kaste, J., Neufeld, F., Wuerstlein, R., Bühner, M., Münzel, K., Rjosk-Dendorfer, D., Grandl, S., Braun, M., von Koch, F. E., Härtl, K., Hasmüller, S., Bauerfeind, I., Debus, G., Herschbach, P., & Harbeck, N. (2015). Elucidating Pretreatment Cognitive Impairment in Breast Cancer Patients: The Impact of Cancer-Related Post-Traumatic Stress. *JNCI: Journal of the National Cancer Institute*, *107*(7), djv099. https://doi.org/10.1093/jnci/djv099

Hijazi, Y., Gondal, U., & Aziz, O. (2017). A systematic review of prehabilitation programs in abdominal cancer surgery. *International Journal of Surgery*, *39*, 156–162. https://doi.org/10.1016/j.ijsu.2017.01.111

Hodgson, K. D., Hutchinson, A. D., Wilson, C. J., & Nettelbeck, T. (2013). A meta-analysis of the effects of chemotherapy on cognition in patients with cancer. *Cancer Treatment Reviews*, *39*(3), 297–304. https://doi.org/10.1016/j.ctrv.2012.11.001

Horowitz, M., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: A Measure of Subjective Stress. *Biopsychosocial Science and Medicine*, *41*(3), 209. https://doi.org/10.1037/t10132-000

Hu, Y., Yu, H., Lai, Y., Liu, J., Tan, Y., Lei, W., Zhang, J., Zhou, X., Cao, Y., Tang, Y., Liu, D., & Zhang, J. (2024). Longitudinal trajectory of amplitude of low-frequency fluctuation changes in breast cancer patients during neoadjuvant chemotherapy–A preliminary prospective study. *Brain Research Bulletin*, *206*, 110845. https://doi.org/10.1016/j.brainresbull.2023.110845

Hutchinson, A. D., Hosking, J. R., Kichenadasse, G., Mattiske, J. K., & Wilson, C. (2012). Objective and subjective cognitive impairment following chemotherapy for cancer: A systematic review. *Cancer Treatment Reviews*, *38*(7), 926–934. https://doi.org/10.1016/j.ctrv.2012.05.002

Hutterer, M., & Oberndorfer, S. (2021). Cognitive impairment in cancer patients and survivors—Clinical presentation, pathophysiology, diagnosis and management. *Memo - Magazine of European Medical Oncology*, *14*(2), 157–167. https://doi.org/10.1007/s12254-021-00690-9

Ibrahim, E. Y., Domenicano, I., Nyhan, K., Elfil, M., Mougalian, S. S., Cartmel, B., & Ehrlich, B. E. (2021). Cognitive Effects and Depression Associated With Taxane-Based Chemotherapy in Breast Cancer Survivors: A Meta-Analysis. *Frontiers in Oncology*, *11*. https://www.frontiersin.org/article/10.3389/fonc.2021.642382

Ikhile, D., Ford, E., Glass, D., Gremesty, G., & Marwijk, H. van. (2024). A systematic review of risk factors associated with depression and anxiety in cancer patients. *PLOS ONE*, *19*(3), e0296892. https://doi.org/10.1371/journal.pone.0296892

Irish Cancer Society. (2020). *Strategic Plan 2020-2025*. https://www.cancer.ie/sites/default/files/2020-09/Our%20Strategic%20Plan%202020-2025.pdf

Irish Cancer Society. (2025, March 27). Cancer statistics | Irish Cancer Society. https://www.cancer.ie/cancer-information/about-cancer/cancer-statistics

Jain, S. R., Kandarpa, V. L., Yaow, C. Y. L., Tan, W. J., Ho, L. M. L., Sivarajah, S. S., Ng, J. L., Chong, C. X. Z., Aw, D. K. L., Foo, F. J., & Koh, F. H. X. (2023). The Role and Effect of Multimodal Prehabilitation Before Major Abdominal Surgery: A Systemic Review and Meta-Analysis. *World Journal of Surgery*, *47*(1), 1. https://doi.org/10.1007/s00268-022-06761-0

Janelsins, M. C., Heckler, C. E., Peppone, L. J., Ahles, T. A., Mohile, S. G., Mustian, K. M., Palesh, O., O'Mara, A. M., Minasian, L. M., Williams, A. M., Magnuson, A., Geer, J., Dakhil, S. R., Hopkins, J. O., & Morrow, G. R. (2018). Longitudinal Trajectory and Characterization of Cancer-Related Cognitive Impairment in a Nationwide Cohort Study. *Journal of Clinical Oncology*, *36*(32), 3231–3239. https://doi.org/10.1200/JCO.2018.78.6624

Janelsins, M. C., Kesler, S. R., Ahles, T. A., & Morrow, G. R. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. *International Review of Psychiatry*, *26*(1), 102–113. https://doi.org/10.3109/09540261.2013.864260

Janelsins, M. C., Kohli, S., Mohile, S. G., Usuki, K., Ahles, T. A., & Morrow, G. R. (2011). An Update on Cancer- and Chemotherapy-Related Cognitive Dysfunction: Current Status. *Seminars in Oncology*, *38*(3), 431–438. https://doi.org/10.1053/j.seminoncol.2011.03.014

Janelsins, M. C., Mohamed, M., Peppone, L. J., Magnuson, A., Belcher, E. K., Melnik, M., Dakhil, S., Geer, J., Kamen, C., Minasian, L., Reagan, P. M., Mohile, S. G., Morrow, G. R., Ahles, T. A., & Heckler, C. E. (2022). Longitudinal Changes in Cognitive Function in a Nationwide Cohort Study of Patients With Lymphoma Treated With Chemotherapy. *JNCI: Journal of the National Cancer Institute*, *114*(1), 47–59. https://doi.org/10.1093/jnci/djab133

Janelsins, M. C., Van Dyk, K., Hartman, S. J., Koll, T. T., Cramer, C. K., Lesser, G. J., Barton, D. L., Mustian, K. M., Wagner, L. I., Ganz, P. A., Cole, P. D., Bakos, A., Root, J. C., Hardy, K., Magnuson, A., Ferguson, R. J., McDonald, B. C., Saykin, A. J., Gonzalez, B. D., … Dorsey, S. G. (2025). The National Cancer Institute clinical trials planning meeting to address gaps in observational and intervention trials for cancer-related cognitive impairment. *JNCI: Journal of the National Cancer Institute*, *117*(2), 217–228. https://doi.org/10.1093/jnci/djae209

Jefferies, P., Gallagher, P., & Dunne, S. (2012). The Paralympic athlete: A systematic review of the psychosocial literature. *Prosthetics & Orthotics International*, *36*(3), 278–289. https://doi.org/10.1177/0309364612450184

Jimenez-Fonseca, P., Calderón, C., Hernández, R., Ramón Y Cajal, T., Mut, M., Ramchandani, A., Donnay, O., & Carmona-Bayonas, A. (2018). Factors associated with anxiety and depression in cancer patients prior to initiating adjuvant therapy. *Clinical and Translational Oncology*, *20*(11), 1408–1415. https://doi.org/10.1007/s12094-018-1873-9

Joint Action on Rare Cancers. (2020). *Rare Cancer Agenda 2030*. Youcanprint. https://dam.esmo.org/image/upload/v1738073808/Rare%20Cancer%20Agenda%202030.pdf

Joly, F., Giffard, B., Rigal, O., De Ruiter, M. B., Small, B. J., Dubois, M., LeFel, J., Schagen, S. B., Ahles, T. A., Wefel, J. S., Vardy, J. L., Pancré, V., Lange, M., & Castel, H. (2015). Impact of Cancer and Its Treatments on Cognitive Function: Advances in Research From the Paris International Cognition and Cancer Task Force Symposium

and Update Since 2012. *Journal of Pain and Symptom Management*, *50*(6), 830–841. https://doi.org/10.1016/j.jpainsymman.2015.06.019

Jung, M. S., Visovatti, M., Kim, M., Cha, K., Dlamini, N., & Cui, X. (2022). Cognitive impairment in women newly diagnosed with thyroid cancer before treatment. *Supportive Care in Cancer*, *30*(11), 8959–8967. https://doi.org/10.1007/s00520-022-07299-6

Juríčková, V., Fayette, D., Jonáš, J., Fajnerová, I., Kozák, T., & Horáček, J. (2023). Pretreatment Cancer-Related Cognitive Impairment in Hodgkin Lymphoma Patients. *Current Oncology*, *30*(10), 9028–9038. https://doi.org/10.3390/curroncol30100652

Kao, Y.-S., Yeh, C.-C., Chen, Y.-F., Kao, Y.-S., Yeh, C.-C., & Chen, Y.-F. (2023). The Relationship between Cancer and Dementia: An Updated Review. *Cancers*, *15*(3). https://doi.org/10.3390/cancers15030640

Karimi, M., & Brazier, J. (2016). Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *PharmacoEconomics*, *34*(7), 645–649. https://doi.org/10.1007/s40273-016-0389-9

Karimi, M., Shirsalimi, N., & Sedighi, E. (2024). Challenges following CRS and HIPEC surgery in cancer patients with peritoneal metastasis: A comprehensive review of clinical outcomes. *Frontiers in Surgery*, *11*, 1498529. https://doi.org/10.3389/fsurg.2024.1498529

Kathpalia, M., Mishra, P., Majid, A., Khan, Mohd. A., Sharma, A., Bhurani, D., & Nidhi. (2024). Attenuated adiponectin, omentin, increased interleukin-6 and tumor necrosis factor-alpha levels with altered cognition and depression in non-Hodgkin lymphoma patients: A case-control study. *Journal of Neuroimmunology*, *392*, 578372. https://doi.org/10.1016/j.jneuroim.2024.578372

Kawamura, N., Kim, Y., & Asukai, N. (2001). Suppression of cellular immunity in men with a past history of posttraumatic stress disorder. *The American Journal of Psychiatry*, *158*(3), 484–486. https://doi.org/10.1176/appi.ajp.158.3.484

Kelly, M. E., Murphy, E., Keyes, A. M., Khan, M. F., Bolger, J. C., Grundy, J., Conneely, J., MacHale, J., McCaffrey, J., Cahill, R., Moran, B., Shields, C., & Mulsow, J. (2021). Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases: Outcomes from a national centre in the current era. *Irish Journal of Medical Science (1971 -)*, *190*(4), 1373–1377. https://doi.org/10.1007/s11845-021-02506-5

Kesler, S. R., Kent, J. S., & O'Hara, R. (2011). Prefrontal cortex and executive function impairments in primary breast cancer. *Archives of Neurology*, *68*(11), 1447–1453. psyh. https://doi.org/10.1001/archneurol.2011.245

Kim, S., Han, J., Lee, M. Y., & Jang, M. K. (2020). The experience of cancer-related fatigue, exercise and exercise adherence among women breast cancer survivors: Insights from focus group interviews. *Journal of Clinical Nursing*, *29*(5–6), 758–769. https://doi.org/10.1111/jocn.15114

Knoerl, R., Giobbie-Hurder, A., Sannes, T. S., Chagpar, A. B., Dillon, D., Dominici, L. S., Frank, E. S., Golshan, M., McTiernan, A., Rhei, E., Tolaney, S. M., Winer, E. P., Yung, R. L., Irwin, M. L., & Ligibel, J. A. (2022). Exploring the impact of exercise and mind–body prehabilitation interventions on physical and psychological outcomes in women undergoing breast cancer surgery. *Supportive Care in Cancer*, *30*(3), 2027–2036. https://doi.org/10.1007/s00520-021-06617-8

Knoerl, R., Sannes, T. S., Giobbie-Hurder, A., Frank, E. S., McTiernan, A., Winer, E. P., Irwin, M. L., & Ligibel, J. A. (2024). Exploring anxiety as an influencing factor of the impact of exercise and mind-body prehabilitation on cognitive functioning among women undergoing breast cancer surgery. *Journal of Psychosocial Oncology*, *42*(3), 448–456. https://doi.org/10.1080/07347332.2023.2282021

Kohler, C., Chang, M., Allemann-Su, Y.-Y., Vetter, M., Jung, M., Jung, M., Conley, Y., Paul, S., Kober, K. M., Cooper, B. A., Smoot, B., Levine, J. D., Miaskowski, C., & Katapodi, M. C. (2020). Changes in Attentional Function in Patients From Before Through 12 Months After Breast Cancer Surgery. *Journal of Pain and Symptom Management*, *59*(6), 1172–1185. https://doi.org/10.1016/j.jpainsymman.2020.01.001

Kuthiah, N. (2021). Perioperative prehabilitation. *Singapore Medical Journal*, *64*(2), 127–131. https://doi.org/10.11622/smedj.2021034

Lagergren, P., Schandl, A., Aaronson, N. K., Adami, H., de Lorenzo, F., Denis, L., Faithfull, S., Liu, L., Meunier, F., & Ulrich, C. (2019). Cancer survivorship: An integral part of Europe's research agenda. *Molecular Oncology*, *13*(3), 624–635. https://doi.org/10.1002/1878-0261.12428

Lange, M., Hardy-Léger, I., Licaj, I., Pistilli, B., Rigal, O., Le Fel, J., Lévy, C., Capel, A., Coutant, C., Meyer, J., Lerebours, F., Petrucci, J., Vanlemmens, L., Brion, M., Campone, M., Soulié, P., Blain, M., Vaz-Luis, I., Giffard, B., … Joly, F. (2020). Cognitive Impairment in Patients with Breast Cancer before Surgery: Results from a

CANTO Cohort Subgroup. *Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, *29*(9), 1759–1766. https://doi.org/10.1158/1055-9965.EPI-20-0346

Lange, M., Joly, F., Vardy, J., Ahles, T., Dubois, M., Tron, L., Winocur, G., De Ruiter, M. B., & Castel, H. (2019). Cancer-related cognitive impairment: An update on state of the art, detection, and management strategies in cancer survivors. *Annals of Oncology*, *30*(12), 1925–1940. https://doi.org/10.1093/annonc/mdz410

Lee, H.-H., Chiu, C.-C., Lee, K.-T., Wang, J.-J., Lin, J.-J., Chao, C.-M., & Shi, H.-Y. (2018). Do preoperative depressive symptoms predict quality of life after laparoscopic cholecystectomy: A longitudinal prospective study. *PLOS ONE*, *13*(8), e0202266. https://doi.org/10.1371/journal.pone.0202266

Lehto, R. H. (2013). Pre- and Postoperative Self-Reported Cognitive Effectiveness and Worry in Patients With Suspected Lung Malignancy. *Oncology Nursing Forum*, *40*(3), E135–E141. https://doi.org/10.1188/13.ONF.E135-E141

Levett, D. Z. H., & Grimmett, C. (2019). Psychological factors, prehabilitation and surgical outcomes: Evidence and future directions. *Anaesthesia*, *74*(S1), 36–42. https://doi.org/10.1111/anae.14507

Li, X., Li, J., Shi, Y., Wang, T., Zhang, A., Shao, N., & Wang, Z. (2017). Psychological intervention improves life quality of patients with laryngeal cancer. *Patient Preference and Adherence*, *Volume 11*, 1723–1727. https://doi.org/10.2147/PPA.S147205

Liesto, S., Sipilä, R., Hietanen, M., & Kalso, E. (2022). Cognitive function is well preserved in a cohort of breast cancer survivors: Roles of cognitive reserve, resilience, and general health. *The Breast*, *65*, 157–163. https://doi.org/10.1016/j.breast.2022.07.013

Linden, W., Vodermaier, A., Mackenzie, R., & Greig, D. (2012). Anxiety and depression after cancer diagnosis: Prevalence rates by cancer type, gender, and age. *Journal of Affective Disorders*, *141*(2–3), 343–351. https://doi.org/10.1016/j.jad.2012.03.025

Llewellyn, D. J., Lang, I. A., Langa, K. M., & Huppert, F. A. (2008). Cognitive function and psychological well-being: Findings from a population-based cohort. *Age and Ageing*, *37*(6), 685–689. https://doi.org/10.1093/ageing/afn194

Logan, S., Perz, J., Ussher, J. M., Peate, M., & Anazodo, A. (2019). Systematic review of fertility-related psychological distress in cancer patients: Informing on an improved model of care. *Psycho-Oncology*, *28*(1), 22–30. https://doi.org/10.1002/pon.4927

Lond, B., Apps, L., Quincey, K., & Williamson, I. (2025). The psychological impact of living with peritoneal mesothelioma: An Interpretative Phenomenological Analysis. *Journal of Health Psychology*, *30*(10), 2781–2797. https://doi.org/10.1177/13591053241298932

Looijaard, S. M. L. M., Slee-Valentijn, M. S., Otten, R. H. J., & Maier, A. B. (2018). Physical and Nutritional Prehabilitation in Older Patients With Colorectal Carcinoma: A Systematic Review. *Journal of Geriatric Physical Therapy*, *41*(4), 236. https://doi.org/10.1519/JPT.0000000000000125

Loughney, L., Bolger, J., Tully, R., Sorensen, J., Bambrick, M., Carroll, P. A., Arumugasamy, M., Murphy, T. J., McCaffrey, N., Robb, W. B., & Group, on B. of the P.-O. W. (2024). The effect of a pre-operative and post-operative exercise programme versus standard care on physical fitness of patients with oesophageal and gastric cancer undergoing neoadjuvant treatment prior to surgery (the PERIOP-OG trial): A randomized controlled trial. *International Journal of Surgery*, *110*(10), 6632. https://doi.org/10.1097/JS9.0000000000001663

Loughney, L., McCaffrey, N., Timon, C. M., Grundy, J., McCarren, A., Cahill, R., Moyna, N., & Mulsow, J. (2020). Physical, psychological and nutritional outcomes in a cohort of Irish patients with metastatic peritoneal malignancy scheduled for cytoreductive surgery (CRS) and heated intrapertioneal chemotherapy (HIPEC): An exploratory pilot study. *PLoS ONE*, *15*(12), e0242816. https://doi.org/10.1371/journal.pone.0242816

Lumivero. (2025). *NVivo* (Version 14) [Computer software]. https://lumivero.com/products/nvivo/

Luo, J., Schousboe, J. T., Ensrud, K. E., & Hendryx, M. (2023). Long-term changes of cognitive impairment among older breast cancer survivors. *Journal of Cancer Survivorship*, *17*(6), 1760–1768. https://doi.org/10.1007/s11764-022-01220-0

Luther, A., Gabriel, J., Watson, R. P., & Francis, N. K. (2018). The Impact of Total Body Prehabilitation on Post-Operative Outcomes After Major Abdominal Surgery: A Systematic Review. *World Journal of Surgery*, *42*(9), 2781–2791. https://doi.org/10.1007/s00268-018-4569-y

Lycke, M., Lefebvre, T., Pottel, L., Pottel, H., Ketelaars, L., Stellamans, K., Van Eygen, K., Vergauwe, P., Werbrouck, P., Cool, L., Boterberg, T., Liefhooghe, N., Schofield, P., & Debruyne, P. R. (2019). Subjective, but not objective, cognitive complaints impact long-term quality of life in cancer patients. *Journal of Psychosocial Oncology*, *37*(4), 427–440. https://doi.org/10.1080/07347332.2018.1504154

Macmillan Cancer Support. (2020). *Principles and guidance for prehabilitation within the management and support of people with cancer* (Prehabilitation Resources for Healthcare Professionals). https://www.macmillan.org.uk/dfsmedia/1a6f23537f7f4519bb0cf14c45b2a629/13225-source/prehabilitation-for-people-with-cancer

Macmillan Cancer Support. (2025). *Prehabilitation for People With Cancer: Clinical and Implementation Guidelines* (Prehabilitation Resources for Healthcare Professionals). https://www.macmillan.org.uk/dfsmedia/1a6f23537f7f4519bb0cf14c45b2a629/22869-10061/prehabilitation-for-people-with-cancer-clinical-and-implementation-guidelines

Maeir, T., Nahum, M., Makranz, C., Tsabari, S., Peretz, T., & Gilboa, Y. (2023). Predictors of quality of life among adults with self-reported cancer related cognitive impairment. *Disability and Rehabilitation*, *45*(6), 1056–1062. https://doi.org/10.1080/09638288.2022.2050954

Maheu, C., Singh, M., Tock, W. L., Eyrenci, A., Galica, J., Hébert, M., Frati, F., & Estapé, T. (2021). Fear of Cancer Recurrence, Health Anxiety, Worry, and Uncertainty: A Scoping Review About Their Conceptualization and Measurement Within Breast Cancer Survivorship Research. *Frontiers in Psychology*, *12*. https://doi.org/10.3389/fpsyg.2021.644932

Mandelblatt, J. S., Hurria, A., McDonald, B. C., Saykin, A. J., Stern, R. A., VanMeter, J. W., McGuckin, M., Traina, T., Denduluri, N., Turner, S., Howard, D., Jacobsen, P. B., & Ahles, T. (2013). Cognitive Effects of Cancer and its Treatments at the Intersection of Aging: What do we Know; What do we Need to Know? *Seminars in Oncology*, *40*(6), 10.1053/j.seminoncol.2013.09.006. https://doi.org/10.1053/j.seminoncol.2013.09.006

Mandelblatt, J. S., Jacobsen, P. B., & Ahles, T. (2014). Cognitive Effects of Cancer Systemic Therapy: Implications for the Care of Older Patients and Survivors. *Journal of Clinical Oncology*, *32*(24), 2617–2626. https://doi.org/10.1200/JCO.2014.55.1259

Marinelli, V., Danzi, O. P., Mazzi, M. A., Secchettin, E., Tuveri, M., Bonamini, D., Rimondini, M., Salvia, R., Bassi, C., & Del Piccolo, L. (2020). PREPARE: PreoPerative Anxiety REduction. One-Year Feasibility RCT on a Brief Psychological

Intervention for Pancreatic Cancer Patients Prior to Major Surgery. *Frontiers in Psychology*, *11*, 362. cmedm. https://doi.org/10.3389/fpsyg.2020.00362

Mathoulin-Pélissier, S., & Pritchard-Jones, K. (2019). Evidence-based data and rare cancers: The need for a new methodological approach in research and investigation. *European Journal of Surgical Oncology*, *45*(1), 22–30. https://doi.org/10.1016/j.ejso.2018.02.015

Matuoka, J. Y., Kurita, G. P., Nordly, M., Sjøgren, P., & de Mattos-Pimenta, C. A. (2020). Validation of a Battery of Neuropsychological Tests for Patients With Metastatic Cancer. *Clinical Nursing Research*, *29*(8), 607–615. https://doi.org/10.1177/1054773819831210

Mayo Clinic. (2025). *Hyperthermic intraperitoneal chemotherapy (HIPEC)-Overview*. https://www.mayoclinic.org/tests-procedures/hyperthermic-intraperitoneal-chemotherapy/about/pac-20583315

McGrath, J. A., O'Malley, M., & Hendrix, T. J. (2011). Group exercise mode and health-related quality of life among healthy adults. *Journal of Advanced Nursing*, *67*(3), 491–500. https://doi.org/10.1111/j.1365-2648.2010.05456.x

McIsaac, D. I., Gill, M., Boland, L., Hutton, B., Branje, K., Shaw, J., Grudzinski, A. L., Barone, N., Gillis, C., Akhtar, S., Atkins, M., Aucoin, S., Auer, R., Basualdo-Hammond, C., Beaule, P., Brindle, M., Bittner, H., Bryson, G., Carli, F., … Wijeysundera, D. (2022). Prehabilitation in adult patients undergoing surgery: An umbrella review of systematic reviews. *British Journal of Anaesthesia*, *128*(2), 244–257. https://doi.org/10.1016/j.bja.2021.11.014

McIsaac, D. I., Kidd, G., Gillis, C., Branje, K., Al-Bayati, M., Baxi, A., Grudzinski, A. L., Boland, L., Veroniki, A.-A., Wolfe, D., & Hutton, B. (2025). Relative efficacy of prehabilitation interventions and their components: Systematic review with network and component network meta-analyses of randomised controlled trials. *BMJ*, *388*, e081164. https://doi.org/10.1136/bmj-2024-081164

McWilliams, L., Farrell, C., Grande, G., Keady, J., Swarbrick, C., & Yorke, J. (2018). A systematic review of the prevalence of comorbid cancer and dementia and its implications for cancer-related care. *Aging & Mental Health*, *22*(10), 1254–1271. https://doi.org/10.1080/13607863.2017.1348476

Mehnert, A., Veers, S., Howaldt, D., Braumann, K.-M., Koch, U., & Schulz, K.-H. (2011). Effects of a Physical Exercise Rehabilitation Group Program on Anxiety, Depression,

Body Image, and Health-Related Quality of Life among Breast Cancer Patients. *Onkologie*, *34*(5), 248–253. https://doi.org/10.1159/000327813

Meissner, H., Creswell, J., Klassen, A. C., Plano, V., & Smith, K. C. (n.d.). *Best Practices for Mixed Methods Research in the Health Sciences*.

Meng, X., & D'Arcy, C. (2012). Education and Dementia in the Context of the Cognitive Reserve Hypothesis: A Systematic Review with Meta-Analyses and Qualitative Analyses. *PLoS ONE*, *7*(6), e38268. https://doi.org/10.1371/journal.pone.0038268

Mikkelsen, K., Stojanovska, L., Polenakovic, M., Bosevski, M., & Apostolopoulos, V. (2017). Exercise and mental health. *Maturitas*, *106*, 48–56. https://doi.org/10.1016/j.maturitas.2017.09.003

Millstine, D. M., Bhagra, A., Jenkins, S. M., Croghan, I. T., Stan, D. L., Boughey, J. C., Nguyen, M.-D. T., & Pruthi, S. (2019). Use of a Wearable EEG Headband as a Meditation Device for Women With Newly Diagnosed Breast Cancer: A Randomized Controlled Trial. *Integrative Cancer Therapies*, *18*, 1534735419878770. https://doi.org/10.1177/1534735419878770

Minnella, E. M., Awasthi, R., Bousquet-Dion, G., Ferreira, V., Austin, B., Audi, C., Tanguay, S., Aprikian, A., Carli, F., & Kassouf, W. (2021). Multimodal Prehabilitation to Enhance Functional Capacity Following Radical Cystectomy: A Randomized Controlled Trial. *European Urology Focus*, *7*(1), 132–138. https://doi.org/10.1016/j.euf.2019.05.016

Mishra, S. I., Scherer, R. W., Snyder, C., Geigle, P. M., Berlanstein, D. R., & Topaloglu, O. (2012). Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database of Systematic Reviews*, *8*. https://doi.org/10.1002/14651858.CD008465.pub2

Mishra, S. I., Scherer, R. W., Snyder, C., Geigle, P., & Gotay, C. (2015). The Effectiveness of Exercise Interventions for Improving Health-Related Quality of Life From Diagnosis Through Active Cancer Treatment. *Oncology Nursing Forum*, *42*(1), E33–E53. https://doi.org/10.1188/15.ONF.E33-E53

Mishra, S. I., Scherer, R. W., Snyder, C., Geigle, P., & Gotay, C. (2014). Are Exercise Programs Effective for Improving Health-Related Quality of Life Among Cancer Survivors? A Systematic Review and Meta-Analysis. *Oncology Nursing Forum*, *41*(6), E326–E342. https://doi.org/10.1188/14.ONF.E326-E342

Molenaar, C. J., Rooijen, S. J. van, Fokkenrood, H. J., Roumen, R. M., Janssen, L., & Slooter, G. D. (2022). Prehabilitation versus no prehabilitation to improve functional capacity, reduce postoperative complications and improve quality of life in colorectal cancer surgery—Molenaar. *Cochrane Library*. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013259.pub2/full

Moola, S., Munn, Z., Tufanaru, C., Aromataris, E., Sears, K., Sfetcu, R., Currie, M., Lisy, K., Qureshi, R., Mattis, P., & Mu, P. (2020). Chapter 7: Systematic reviews of etiology and risk. In *JBI Manual for Evidence Synthesis*. JBI. https://doi.org/10.46658/JBIMES-20-08

Morgan, D. L. (2014). Pragmatism as a Paradigm for Mixed Methods Research. In *Integrating Qualitative and Quantitative Methods: A Pragmatic Approach* (pp. 25–44). SAGE Publications, Inc. https://doi.org/10.4135/9781544304533

Munn, Z., Moola, S., Lisy, K., Riitano, D., & Tufanaru, C. (2020). Chapter 5: Systematic reviews of prevalence and incidence. In *JBI Manual for Evidence Synthesis*. JBI. https://doi.org/10.46658/JBIMES-20-06

Myers, J. S., Erickson, K. I., Sereika, S. M., & Bender, C. M. (2018). Exercise as an Intervention to Mitigate Decreased Cognitive Function From Cancer and Cancer Treatment: An Integrative Review. *Cancer Nursing*, *41*(4), 327–343. https://doi.org/10.1097/NCC.0000000000000549

Mortazavi, A., Youn, S. J., Newman, M. G., Castonguay, L. G., & Molnar, C. (2014). Generalized anxiety disorder. In *Translating psychological research into practice* (pp. 183–192). Springer Publishing Company.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *Journal of the American Geriatrics Society*, *53*(4), 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x

National Cancer Institute. (2015, May 15). *Adolescents and Young Adults (AYAs) with Cancer—NCI* (nciglobal,ncienterprise) [cgvArticle]. https://www.cancer.gov/types/aya

National Cancer Institute. (2017, July 31). *Types of Cancer Treatment—NCI* (nciglobal,ncienterprise) [cgvMiniLanding]. https://www.cancer.gov/about-cancer/treatment/types

NCCN. (1999). NCCN practice guidelines for the management of psychosocial distress. National Comprehensive Cancer Network. *Oncology (Williston Park, N.Y.)*, *13*(5A), 113–147.

Netz, Y. (2017). Is the Comparison between Exercise and Pharmacologic Treatment of Depression in the Clinical Practice Guideline of the American College of Physicians Evidence-Based? *Frontiers in Pharmacology*, *8*, 257. https://doi.org/10.3389/fphar.2017.00257

Ngo-Huang, A., Parker, N. H., Bruera, E., Lee, R. E., Simpson, R., O'Connor, D. P., Petzel, M. Q. B., Fontillas, R. C., Schadler, K., Xiao, L., Wang, X., Fogelman, D., Sahai, S. K., Lee, J. E., Basen-Engquist, K., & Katz, M. H. G. (2019). Home-Based Exercise Prehabilitation During Preoperative Treatment for Pancreatic Cancer Is Associated With Improvement in Physical Function and Quality of Life: *Integrative Cancer Therapies*. https://doi.org/10.1177/1534735419894061

Nucci, M., Mapelli, D., & Mondini, S. (2012). Cognitive Reserve Index questionnaire (CRIq): A new instrument for measuring cognitive reserve. *Aging Clinical and Experimental Research*, *24*(3). https://doi.org/10.3275/7800

O'Farrell, E., Smith, A., & Collins, B. (2017). Objective–subjective disparity in cancer-related cognitive impairment: Does the use of change measures help reconcile the difference? *Psycho-Oncology*, *26*(10), 1667–1674. https://doi.org/10.1002/pon.4190

Öcalan, S., & Üzar-Özçetin, Y. S. (2023). "Cancer Never Goes Out of Your Mind Even for a Single Second". Cancer-Related Ruminations From the Perspectives of Cancer Survivors. *Seminars in Oncology Nursing*, *39*(4), 151427. https://doi.org/10.1016/j.soncn.2023.151427

Oerlemans, S., Schagen, S. B., van den Hurk, C. J., Husson, O., Schoormans, D., & van de Poll-Franse, L. V. (2022). Self-perceived cognitive functioning and quality of life among cancer survivors: Results from the PROFILES registry. *Journal of Cancer Survivorship*, *16*(2), 303–313. https://doi.org/10.1007/s11764-021-01023-9

Oliva, G., Giustiniani, A., Danesin, L., Burgio, F., Arcara, G., & Conte, P. (2024). Cognitive impairment following breast cancer treatments: An umbrella review. *The Oncologist*, *29*(7), e848–e863. https://doi.org/10.1093/oncolo/oyae090

Oliveira, A. F., Santos, I. M., Fernandes, S., Bem-Haja, P., & Torres, A. (2022). Validation study of the Functional Assessment of Cancer Therapy-Cognitive Function-Version 3

for the Portuguese population. *BMC Psychology*, *10*(1), 305. https://doi.org/10.1186/s40359-022-01018-w

Olson, B., & Marks, D. L. (2019). Pretreatment Cancer-Related Cognitive Impairment—giMechanisms and Outlook. *Cancers*, *11*(5), Article 5. https://doi.org/10.3390/cancers11050687

Onyedibe, M.-C. C., Schmidt, M. E., Bizer, P., Zimmer, P., & Steindorf, K. (2025). Subjective and Objective Cancer-Related Cognitive Impairments Among Systemic and Radiation Therapy-Naïve Female Cancer Patients. *Cancer Medicine*, *14*(8), e70908. https://doi.org/10.1002/cam4.70908

Onzi, G. R., D'Agustini, N., Garcia, S. C., Guterres, S. S., Pohlmann, P. R., Rosa, D. D., & Pohlmann, A. R. (2022). Chemobrain in Breast Cancer: Mechanisms, Clinical Manifestations, and Potential Interventions. *Drug Safety*, *45*(6), 601–621. https://doi.org/10.1007/s40264-022-01182-3

Oppegaard, K. R., Mayo, S. J., Armstrong, T. S., Anguera, J. A., Kober, K. M., & Miaskowski, C. (2023a). The Multifactorial Model of Cancer-Related Cognitive Impairment. *Oncology Nursing Forum*, *50*(2), 135–147. https://doi.org/10.1188/23.ONF.135-147

Oppegaard, K. R., Mayo, S. J., Armstrong, T. S., Kober, K. M., Anguera, J. A., Wright, F., Levine, J. D., Conley, Y. P., Paul, S., Cooper, B., & Miaskowski, C. (2023b). An Evaluation of the Multifactorial Model of Cancer-Related Cognitive Impairment. *Nursing Research*, *72*(4), 272–280. https://doi.org/10.1097/NNR.0000000000000660

Országhová, Z., Mego, M., & Chovanec, M. (2021). Long-Term Cognitive Dysfunction in Cancer Survivors. *Frontiers in Molecular Biosciences*, *8*. https://doi.org/10.3389/fmolb.2021.770413

Ospina, P. A., McComb, A., Wiart, L. E., Eisenstat, D. D., & McNeely, M. L. (2018). Physical therapy interventions, other than general physical exercise interventions, in children and adolescents before, during and following treatment for cancer. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD012924

Overcash, J., Extermann, M., Parr, J., Perry, J., & Balducci, L. (2001). Validity and Reliability of the FACT-G Scale for Use in the Older Person With Cancer. *American Journal of Clinical Oncology*, *24*(6), 591.

Pace, A., Tanzilli, A., Marchioni, E., Pellerino, A., Tralongo, A. C., Bini, P., Tralongo, P., Cappa, S. F., Pace, A., Tanzilli, A., Marchioni, E., Pellerino, A., Tralongo, A. C.,

Bini, P., Tralongo, P., & Cappa, S. F. (2024). Cancer-Related Cognitive Impairments (CRCIs) in Non-Central Nervous System Adult Patients: Outcome Measures and Methodology of Assessment: A Literature Review. *Brain Sciences*, *14*(11). https://doi.org/10.3390/brainsci14111119

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, *372*, n71. https://doi.org/10.1136/bmj.n71

Pan, C.-W., Wang, X., Ma, Q., Sun, H.-P., Xu, Y., & Wang, P. (2015). Cognitive dysfunction and health-related quality of life among older Chinese. *Scientific Reports*, *5*(1), 17301. https://doi.org/10.1038/srep17301

Patel, D. S., Webster, S. N., Dowling, E. J., Knowles, C. R., Lockwood-Taylor, G., Coutts-Bain, D., Simons, L. E., Diver, E. J., Chilcot, J., Schapira, L., & Heathcote, L. C. (2024). Scanxiety and Fear of Recurrence in Young Adult Female Breast and Gynaecological Cancer Survivors: Investigating Shared Mechanisms. *Psycho-Oncology*, *33*(12), e70050. https://doi.org/10.1002/pon.70050

Patel, S. K., Breen, E. C., Paz, I. B., Kruper, L., Mortimer, J., Wong, F. L., Bhatia, S., Irwin, M. R., & Behrendt, C. E. (2023). Inflammation-related proteins as biomarkers of treatment-related behavioral symptoms: A longitudinal study of breast cancer patients and age-matched controls. *Brain, Behavior, & Immunity - Health*, *32*, 100670. https://doi.org/10.1016/j.bbih.2023.100670

Patel, S. K., Wong, A. L., Wong, F. L., Breen, E. C., Hurria, A., Smith, M., Kinjo, C., Paz, I. B., Kruper, L., Somlo, G., Mortimer, J. E., Palomares, M. R., Irwin, M. R., & Bhatia, S. (2015). Inflammatory Biomarkers, Comorbidity, and Neurocognition in Women With Newly Diagnosed Breast Cancer. *JNCI: Journal of the National Cancer Institute*, *107*(8), djv131. https://doi.org/10.1093/jnci/djv131

Perez-Tejada, J., Labaka, A., Pascual-Sagastizabal, E., Garmendia, L., Iruretagoyena, A., & Arregi, A. (2019). Predictors of psychological distress in breast cancer survivors: A biopsychosocial approach. *European Journal of Cancer Care*, *28*(6). https://doi.org/10.1111/ecc.13166

Petersson, S. D., & Philippou, E. (2016). Mediterranean Diet, Cognitive Function, and Dementia: A Systematic Review of the Evidence. *Advances in Nutrition*, *7*(5), 889–904. https://doi.org/10.3945/an.116.012138

Pillinger, N. L., Robson, J. L., & Kam, P. C. A. (2018). Nutritional Prehabilitation: Physiological Basis and Clinical Evidence. *Anaesthesia and Intensive Care*, *46*(5), 453–462. https://doi.org/10.1177/0310057X1804600505

Pinto, J. O., Peixoto, B., Dores, A. R., & Barbosa, F. (2024). Measures of cognitive reserve: An umbrella review. *The Clinical Neuropsychologist*, *38*(1), 42–115. https://doi.org/10.1080/13854046.2023.2200978

Pitman, A., Suleman, S., Hyde, N., & Hodgkiss, A. (2018). Depression and anxiety in patients with cancer. *BMJ*, k1415. https://doi.org/10.1136/bmj.k1415

Popat, K., McQueen, K., & Feeley, T. W. (2013). The global burden of cancer. *Best Practice & Research Clinical Anaesthesiology*, *27*(4), 399–408. https://doi.org/10.1016/j.bpa.2013.10.010

Popay, J., Roberts, H., Sowden, A., Petticrew, M., Arai, L., Rodgers, M., & Britten, N. (n.d.). *Guidance on the Conduct of Narrative Synthesis in Systematic Reviews*. 92.

Pullens, M. J. J., De Vries, J., & Roukema, J. A. (2010). Subjective cognitive dysfunction in breast cancer patients: A systematic review. *Psycho-Oncology*, *19*(11), 1127–1138. https://doi.org/10.1002/pon.1673

Quist, M., Adamsen, L., Rørth, M., Laursen, J. H., Christensen, K. B., & Langer, S. W. (2015). The Impact of a Multidimensional Exercise Intervention on Physical and Functional Capacity, Anxiety, and Depression in Patients With Advanced-Stage Lung Cancer Undergoing Chemotherapy. *Integrative Cancer Therapies*, *14*(4), 341–349. https://doi.org/10.1177/1534735415572887

Rabin, L. A., Wang, C., Katz, M. J., Derby, C. A., Buschke, H., & Lipton, R. B. (2012). Predicting Alzheimer's Disease: Neuropsychological Tests, Self-Reports, and Informant Reports of Cognitive Difficulties. *Journal of the American Geriatrics Society*, *60*(6), 1128–1134. https://doi.org/10.1111/j.1532-5415.2012.03956.x

Ramalho, M., Fontes, F., Ruano, L., Pereira, S., & Lunet, N. (2017). Cognitive impairment in the first year after breast cancer diagnosis: A prospective cohort study. *The Breast*, *32*, 173–178. https://doi.org/10.1016/j.breast.2017.01.018

Reitan, R., & Wolfson, D. (1985). *The Halstead-Retian neuropsychological test battery: Theory and clinical interpretation*. Neuropsychology press.

Rengel, K. F., Mehdiratta, N., Vanston, S. W., Archer, K. R., Jackson, J. C., Thompson, J. L., Pandharipande, P. P., & Hughes, C. G. (2021). A randomised pilot trial of combined cognitive and physical exercise prehabilitation to improve outcomes in surgical patients. *British Journal of Anaesthesia*, *126*(2), e55–e57. https://doi.org/10.1016/j.bja.2020.11.004

Riba, M. B., Donovan, K. A., Andersen, B., Braun, Ii., Breitbart, W. S., Brewer, B. W., Buchmann, L. O., Clark, M. M., Collins, M., Corbett, C., Fleishman, S., Garcia, S., Greenberg, D. B., Handzo, Rev. G. F., Hoofring, L., Huang, C.-H., Lally, R., Martin, S., McGuffey, L., … Darlow, S. D. (2019). Distress Management, Version 3.2019. *Journal of the National Comprehensive Cancer Network : JNCCN*, *17*(10), 1229–1249. https://doi.org/10.6004/jnccn.2019.0048

Riedl, D., & Schuessler, G. (2022). Prevalence of Depression and Cancer – A systematic review. *Zeitschrift für Psychosomatische Medizin und Psychotherapie*, *68*(1), 74–86. https://doi.org/10.13109/zptm.2021.67.oa11

Roh, M., Dan, H., & Kim, O. (2021). Influencing Factors of Subjective Cognitive Impairment in Middle-Aged and Older Adults. *International Journal of Environmental Research and Public Health*, *18*(21), 11488. https://doi.org/10.3390/ijerph182111488

Saeed, S. A., Cunningham, K., & Bloch, R. M. (n.d.). *Depression and Anxiety Disorders: Benefits of Exercise, Yoga, and Meditation*. Retrieved November 26, 2025, from https://www.aafp.org/pubs/afp/issues/2019/0515/p620.html

Saita, K., Tanabe, K., Hamai, Y., Yamauchi, M., Kaneko, F., Mikami, Y., Okamoto, W., Okada, M., Ohdan, H., & Okamura, H. (2025). Changes in chemotherapy-induced cognitive impairment in gastrointestinal cancer survivors using multidomain assessments: A prospective cohort study. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-025-01759-8

Sánchez-Cubillo, I., Periáñez, J. A., Adrover-Roig, D., Rodríguez-Sánchez, J. M., Ríos-Lago, M., Tirapu, J., & Barceló, F. (2009). Construct validity of the Trail Making Test: Role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. *Journal of the International Neuropsychological Society*, *15*(3), 438–450. https://doi.org/10.1017/S1355617709090626

Sánchez-Izquierdo, M., Fernández-Ballesteros, R., Sánchez-Izquierdo, M., & Fernández-Ballesteros, R. (2021). Cognition in Healthy Aging. *International Journal of Environmental Research and Public Health*, *18*(3). https://doi.org/10.3390/ijerph18030962

Sandler, A., Reilly, K., & Widemann, B. (2021). Editorial: Special Issue on Rare Cancers. *Current Problems in Cancer*, *45*(4), 100774. https://doi.org/10.1016/j.currproblcancer.2021.100774

Santa Mina, D., van Rooijen, S. J., Minnella, E. M., Alibhai, S. M. H., Brahmbhatt, P., Dalton, S. O., Gillis, C., Grocott, M. P. W., Howell, D., Randall, I. M., Sabiston, C. M., Silver, J. K., Slooter, G., West, M., Jack, S., & Carli, F. (2021). Multiphasic Prehabilitation Across the Cancer Continuum: A Narrative Review and Conceptual Framework. *Frontiers in Oncology*, *10*, 598425. https://doi.org/10.3389/fonc.2020.598425

Santucci, C., Mignozzi, S., Levi, F., Malvezzi, M., Boffetta, P., Negri, E., & Vecchia, C. L. (2025). European cancer mortality predictions for the year 2025 with focus on breast cancer. *Annals of Oncology*, *36*(4), 460–468. https://doi.org/10.1016/j.annonc.2025.01.014

Santucci, C., Mignozzi, S., Malvezzi, M., Boffetta, P., Collatuzzo, G., Levi, F., Vecchia, C. L., & Negri, E. (2024). European cancer mortality predictions for the year 2024 with focus on colorectal cancer. *Annals of Oncology*, *35*(3), 308–316. https://doi.org/10.1016/j.annonc.2023.12.003

Savard, J., Moussa, H., Pelletier, J.-F., Julien, P., Lacombe, L., Tiguert, R., Caumartin, Y., Dujardin, T., Toren, P., Pouliot, F., Lodde, M., Fradet, Y., Robitaille, K., & Fradet, V. (2023). Effects of omega-3 supplementation on psychological symptoms in men with prostate cancer: Secondary analysis of a double-blind placebo-controlled randomized trial. *Cancer Medicine*, *12*(19), 20163–20176. https://doi.org/10.1002/cam4.6598

Scheede-Bergdahl, C., Minnella, E. M., & Carli, F. (2019). Multi-modal prehabilitation: Addressing the why, when, what, how, who and where next? *Anaesthesia*, *74*(S1), 20–26. https://doi.org/10.1111/anae.14505

Scheibel, R. S., Valentine, A. D., O'Brien, S., & Meyers, C. A. (2004). Cognitive Dysfunction and Depression During Treatment With Interferon-Alpha and Chemotherapy. *The Journal of Neuropsychiatry and Clinical Neurosciences*. https://doi.org/10.1176/jnp.16.2.185

Schmitter-Edgecombe, M., & Parsey, C. M. (2014). Assessment of Functional Change and Cognitive Correlates in the Progression from Healthy Cognitive Aging to Dementia. *Neuropsychology*, *28*(6), 881–893. https://doi.org/10.1037/neu0000109

Schneider, M. A., Eshmuminov, D., & Lehmann, K. (2017). Major Postoperative Complications Are a Risk Factor for Impaired Survival after CRS/HIPEC. *Annals of Surgical Oncology*, *24*(8), 2224–2232. https://doi.org/10.1245/s10434-017-5821-7

Schumacher, J. R., Palta, M., Loconte, N. K., Trentham-Dietz, A., Witt, W. P., Heidrich, S. M., & Smith, M. A. (2013). Characterizing the psychological distress response before and after a cancer diagnosis. *Journal of Behavioral Medicine*, *36*(6), 591–600. https://doi.org/10.1007/s10865-012-9453-x

Schwarzer, R., & Jerusalem, M. (1995). Generalized Self-Efficacy scale. In *Measures in health psychology: A user's portfolio. Causal and control beliefs* (pp. 35–37). Windsor UK.

Scriney, A., Russell, A., Loughney, L., Gallagher, P., & Boran, L. (2022). The impact of prehabilitation interventions on affective and functional outcomes for young to midlife adult cancer patients: A systematic review. *Psycho-Oncology*, *31*(12), 2050–2062. https://doi.org/10.1002/pon.6029

Sebastian, L., Gerber, M., Uwe, P., Looser, V. N., & Keita, K. (2020). Systematic review and meta-analysis investigating moderators of long-term effects of exercise on cognition in healthy individuals. *Nature Human Behaviour*, *4*(6), 603–612. https://doi.org/10.1038/s41562-020-0851-8

Sharma, S., Brunet, J., Sharma, S., & Brunet, J. (2023). Young Adults' Lived Experiences with Cancer-Related Cognitive Impairment: An Exploratory Qualitative Study. *Current Oncology*, *30*(6), 5593–5614. https://doi.org/10.3390/curroncol30060422

Sheppard, D. P., Psutka, S. P., & Hunter, H. (2025). Prehabilitation: Cognitive considerations. *Urologic Oncology: Seminars and Original Investigations*. https://doi.org/10.1016/j.urolonc.2025.06.017

Shilling, V., & Jenkins, V. (2007). Self-reported cognitive problems in women receiving adjuvant therapy for breast cancer. *European Journal of Oncology Nursing : The Official Journal of European Oncology Nursing Society*, *11*(1), 6–15. https://doi.org/10.1016/j.ejon.2006.02.005

Shim, E.-J., Ha, H., Suh, Y.-S., Kong, S.-H., Lee, H.-J., Yang, H.-K., & Hahm, B.-J. (2021). Network analyses of associations between cancer-related physical and psychological

symptoms and quality of life in gastric cancer patients. *Psycho-Oncology*, *30*(6), 946–953. https://doi.org/10.1002/pon.5681

Shim, E.-J., Mehnert, A., Koyama, A., Cho, S.-J., Inui, H., Paik, N.-S., & Koch, U. (2006). Health-related quality of life in breast cancer: A cross-cultural survey of German, Japanese, and South Korean patients. *Breast Cancer Research and Treatment*, *99*(3), 341–350. https://doi.org/10.1007/s10549-006-9216-x

Siegel, R. L., Kratzer, T. B., Giaquinto, A. N., Sung, H., & Jemal, A. (2025). Cancer statistics, 2025. *CA: A Cancer Journal for Clinicians*, *75*(1), 10–45. https://doi.org/10.3322/caac.21871

Siegel, S. (1957). Nonparametric Statistics. *The American Statistician*, *11*(3), 13–19. https://doi.org/10.2307/2685679

Silver, J. K., Baima, J., & Mayer, R. S. (2013). Impairment-driven cancer rehabilitation: An essential component of quality care and survivorship. *CA: A Cancer Journal for Clinicians*, *63*(5), 295–317. https://doi.org/10.3322/caac.21186

Silverman, D. H. S., Sleurs, C., Gavrila Laic, R. A., Amidi, A., Chen, B. T., Deprez, S., & McDonald, B. C. (2025). Neuroimaging studies of cognitive dysfunction following cancer and treatment. *Journal of Clinical and Experimental Neuropsychology*, 1–27. https://doi.org/10.1080/13803395.2025.2526647

Singh, F., Newton, R. U., Baker, M. K., Spry, N. A., Taaffe, D. R., & Galvão, D. A. (2017). Feasibility and Efficacy of Presurgical Exercise in Survivors of Rectal Cancer Scheduled to Receive Curative Resection. *Clinical Colorectal Cancer*, *16*(4), 358–365. https://doi.org/10.1016/j.clcc.2017.03.010

Skaczkowski, G., Orbell, S., & Wilson, C. (2024). "Life Without Symptoms" or "Being Able to Enjoy Life": What does it Mean to be "Well" After Cancer? *Journal of Cancer Education*, *39*(2), 204–210. https://doi.org/10.1007/s13187-023-02397-3

Sleurs, C., Amidi, A., Wu, L. M., Kiesl, D., Zimmer, P., Lange, M., Rogiers, A., Giffard, B., Binarelli, G., Borghgraef, C., Deprez, S., Duivon, M., De Ruiter, M., Schagen, S., Ahmed-Lecheheb, D., Castel, H., Buskbjerg, C. R., Dos Santos, M., Joly, F., & Perrier, J. (2022). Cancer-related cognitive impairment in non-CNS cancer patients: Targeted review and future action plans in Europe. *Critical Reviews in Oncology/Hematology*, *180*, 103859. https://doi.org/10.1016/j.critrevonc.2022.103859

Snitz, B. E., Small, B. J., Wang, T., Chang, C.-C. H., Hughes, T. F., & Ganguli, M. (2015). Do Subjective Memory Complaints Lead or Follow Objective Cognitive Change? A

Five-Year Population Study of Temporal Influence. *Journal of the International Neuropsychological Society*, *21*(9), 732–742. https://doi.org/10.1017/S1355617715000922

Snyder, H. R. (2013). Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review. *Psychological Bulletin*, *139*(1), 81–132. https://doi.org/10.1037/a0028727

Solon, J. G., O'Neill, M., Chang, K. H., Deady, S., Cahill, R., Moran, B., Shields, C., & Mulsow, J. (2017). An 18 year population-based study on site of origin and outcome of patients with peritoneal malignancy in Ireland. *European Journal of Surgical Oncology: The Journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, *43*(10), 1924–1931. https://doi.org/10.1016/j.ejso.2017.05.010

Soong, R. Y., Low, C. E., Ong, V., Sim, I., Lee, C., Lee, F., Chew, L., Yau, C. E., Lee, A. R. Y. B., & Chen, M. Z. (2025). Exercise Interventions for Depression, Anxiety, and Quality of Life in Older Adults With Cancer: A Systematic Review and Meta-Analysis. *JAMA Network Open*, *8*(2), e2457859. https://doi.org/10.1001/jamanetworkopen.2024.57859

Soto Perez De Celis, E., Li, D., Sun, C.-L., Kim, H., Twardowski, P., Fakih, M., Chung, V. M., Cristea, M. C., Lim, D., Yuan, Y., Dale, W., Chien, L., Charles, K., Tan, H., Roberts, E., Moreno, J., Rivera, D., Katheria, V., & Hurria, A. (2018). Patient-defined goals and preferences among older adults with cancer starting chemotherapy (CT). *Journal of Clinical Oncology*, *36*(15_suppl), 10009–10009. https://doi.org/10.1200/JCO.2018.36.15_suppl.10009

Staley, K. (2015). 'Is it worth doing?' Measuring the impact of patient and public involvement in research. *Research Involvement and Engagement*, *1*(1), 6. https://doi.org/10.1186/s40900-015-0008-5

Stein, K. D., Syrjala, K. L., & Andrykowski, M. A. (2008). Physical and psychological long-term and late effects of cancer. *Cancer*, *112*(S11), 2577–2592. https://doi.org/10.1002/cncr.23448

Suchy-Dicey, A. M., Vo, T. T., Oziel, K., Buchwald, D. S., Rhoads, K., & French, B. F. (2025). Psychometric Reliability, Validity, and Generalizability of MoCA in American Indian Adults: The Strong Heart Study. *Assessment*, *32*(4), 608–621. https://doi.org/10.1177/10731911241261436

Suchy-Dicey, A. M., Vo, T. T., Oziel, K., King, R., Barbosa-Leiker, C., Rhoads, K., Verney, S., Buchwald, D. S., & French, B. F. (2024). Psychometric Properties of Controlled Oral Word Association (COWA) Test and Associations With Education and Bilingualism in American Indian Adults: The Strong Heart Study. *Assessment*, *31*(3), 745–757. https://doi.org/10.1177/10731911231180127

Sun, H., Zhang, G., Ai, B., Zhang, H., Kong, X., Lee, W.-T., Zheng, H., Yan, T., & Sun, L. (2019). A systematic review: Comparative analysis of the effects of propofol and sevoflurane on postoperative cognitive function in elderly patients with lung cancer. *BMC Cancer*, *19*(1), 1248. https://doi.org/10.1186/s12885-019-6426-2

Swan, F., Chen, H., Forbes, C. C., Johnson, M. J., & Lind, M. (2021). CANcer BEhavioural nutrition and exercise feasibility trial (CanBenefit); phase I qualitative interview findings. *Journal of Geriatric Oncology*, *12*(4), 641–648. https://doi.org/10.1016/j.jgo.2020.09.026

Syed Alwi, S. M., Narayanan, V., Che Din, N., & Mohd Taib, N. A. (2021). Cognitive Rehabilitation Programs for Survivors of Breast Cancer Treated With Chemotherapy: A Systematic Review. *Rehabilitation Oncology*, *39*(4), 155–167. https://doi.org/10.1097/01.REO.0000000000000268

Tao, L., Xiang, Y., Zeng, X., Fu, L., Li, J., & Chen, H. (2024). Psychological-Distress Factors in Patients With Breast Cancer: A Qualitative Meta-Synthesis. *Journal of Clinical Nursing*, *33*(12), 4843–4859. https://doi.org/10.1111/jocn.17532

Tay, S. S., Zhang, F., & Neo, E. J. R. (2024). The use of technology in cancer prehabilitation: A systematic review. *Frontiers in Oncology*, *14*, 1321493. https://doi.org/10.3389/fonc.2024.1321493

Taylor, S. E. (1983). Adjustment to threatening events: A theory of cognitive adaptation. *American Psychologist*, *38*(11), 1161–1173. https://doi.org/10.1037/0003-066X.38.11.1161

Tebeje, T. H., & Klein, J. (2021). Applications of e-Health to Support Person-Centered Health Care at the Time of COVID-19 Pandemic. *Telemedicine and E-Health*, *27*(2), 150–158. https://doi.org/10.1089/tmj.2020.0201

The EuroQoL Group. (1990). EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy*, *16*(3), 199–208.

Timon, C. M., Blain, R. J., McNulty, B., Kehoe, L., Evans, K., Walton, J., Flynn, A., & Gibney, E. R. (2017). The Development, Validation, and User Evaluation of Foodbook24: A Web-Based Dietary Assessment Tool Developed for the Irish Adult

Population. *Journal of Medical Internet Research*, *19*(5), e6407. https://doi.org/10.2196/jmir.6407

Tombaugh, T. N. (2004). Trail Making Test A and B: Normative data stratified by age and education. *Archives of Clinical Neuropsychology*, *19*(2), 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8

Tombaugh, T. N., Kozak, J., & Rees, L. (1999). Normative Data Stratified by Age and Education for Two Measures of Verbal Fluency: FAS and Animal Naming. *Archives of Clinical Neuropsychology*, *14*(2), 167–177. https://doi.org/10.1016/S0887-6177(97)00095-4

Torvinen, S., Färkkilä, N., Sintonen, H., Saarto, T., Roine, R. P., & Taari, K. (2013). Health-related quality of life in prostate cancer. *Acta Oncologica (Stockholm, Sweden)*, *52*(6), 1094–1101. https://doi.org/10.3109/0284186X.2012.760848

Tsimopoulou, I., Pasquali, S., Howard, R., Desai, A., Gourevitch, D., Tolosa, I., & Vohra, R. (2015). Psychological Prehabilitation Before Cancer Surgery: A Systematic Review. *Annals of Surgical Oncology*, *22*(13), 4117–4123. https://doi.org/10.1245/s10434-015-4550-z

Tulk, J., Rash, J. A., Thoms, J., Wassersug, R., Gonzalez, B., & Garland, S. N. (2023). Androgen deprivation therapy and radiation for prostate cancer-cognitive impairment, sleep, symptom burden: A prospective study. *BMJ Supportive & Palliative Care*, *13*(e2), e454–e463. https://doi.org/10.1136/bmjspcare-2021-003098

Tully, R., Loughney, L., Bolger, J., Sorensen, J., McAnena, O., Collins, C. G., Carroll, P. A., Arumugasamy, M., Murphy, T. J., & Robb, W. B. (2020). The effect of a pre- and post-operative exercise programme versus standard care on physical fitness of patients with oesophageal and gastric cancer undergoing neoadjuvant treatment prior to surgery (The PERIOP-OG Trial): Study protocol for a randomised controlled trial. *Trials*, *21*(1), Article 1. https://doi.org/10.1186/s13063-020-04311-4

van der Velde, M., van der Leeden, M., Geleijn, E., Veenhof, C., & Valkenet, K. (2023). What moves patients to participate in prehabilitation before major surgery? A mixed methods systematic review. *International Journal of Behavioral Nutrition and Physical Activity*, *20*(1), 75. https://doi.org/10.1186/s12966-023-01474-6

Van Dyk, K., Crespi, C. M., Petersen, L., & Ganz, P. A. (2020). Identifying Cancer-Related Cognitive Impairment Using the FACT-Cog Perceived Cognitive Impairment. *JNCI Cancer Spectrum*, *4*(1). https://doi.org/10.1093/jncics/pkz099

Van Rooijen, S. J., Molenaar, C. J. L., Fokkenrood, H. J. P., Roumen, R. M. H., & Slooter, G. D. (2019a). Prehabilitation versus no prehabilitation to improve functional capacity, reduce postoperative complications and improve quality of life in colorectal cancer surgery. *Cochrane Database of Systematic Reviews*, *2019*(2). Embase. https://doi.org/10.1002/14651858.CD013259

van Rooijen, S. J., Molenaar, C. J. L., Schep, G., van Lieshout, R. H. M. A., Beijer, S., Dubbers, R., Rademakers, N., Papen-Botterhuis, N. E., van Kempen, S., Carli, F., Roumen, R. M. H., & Slooter, G. D. (2019b). Making Patients Fit for Surgery: Introducing a Four Pillar Multimodal Prehabilitation Program in Colorectal Cancer. *American Journal of Physical Medicine & Rehabilitation*, *98*(10), 888–896. https://doi.org/10.1097/PHM.0000000000001221

Vance, D. E., Bail, J., Enah, C., Palmer, J., & Hoenig, A. (2016). The impact of employment on cognition and cognitive reserve: Implications across diseases and aging. *Nursing: Research and Reviews*, *Volume 6*, 61–71. https://doi.org/10.2147/NRR.S115625

Vardy, J. L., Pond, G. R., Cysique, L. A., Gates, T. M., Lagopoulos, J., Renton, C., Waite, L. M., Tannock, I. F., & Dhillon, H. M. (2022). Lack of cognitive impairment in long-term survivors of colorectal cancer. *Supportive Care in Cancer*, *30*(7), 6123–6133. https://doi.org/10.1007/s00520-022-07008-3

Victorson, D., Barocas, J., Song, J., & Cella, D. (2008). Reliability across studies from the functional assessment of cancer therapy-general (FACT-G) and its subscales: A reliability generalization. *Quality of Life Research*, *17*(9), 1137–1146. https://doi.org/10.1007/s11136-008-9398-2

Vitali, M., Ripamonti, C. I., Roila, F., Proto, C., Signorelli, D., Imbimbo, M., Corrao, G., Brissa, A., Rosaria, G., de Braud, F., Garassino, M. C., & Lo Russo, G. (2017). Cognitive impairment and chemotherapy: A brief overview. *Critical Reviews in Oncology/Hematology*, *118*, 7–14. https://doi.org/10.1016/j.critrevonc.2017.08.001

Vlisides, P. E., Das, A. R., Thompson, A. M., Kunkler, B., Zierau, M., Cantley, M. J., McKinney, A. M., & Giordani, B. (2019). Home-Based Cognitive Prehabilitation in Older Surgical Patients: A Feasibility Study. *Journal of Neurosurgical Anesthesiology*, *31*(2), 212–217. https://doi.org/10.1097/ANA.0000000000000569

Volz, S., Koch, F., Dayan, D., Upadhyay, M., Otto, S., Schochter, F., Janni, W., & Ebner, F. (2021). Is there evidence behind pre- or perioperative cognitive training in gynaecological patients on the prevention of perioperative cognitive dysfunction? A

review. *Archives of Gynecology and Obstetrics*. https://doi.org/10.1007/s00404-021-06315-0

Von Ah, D., Rio, C. J., Carter, A., Perkins, S. M., Stevens, E., Rosko, A., Davenport, A., Kalady, M., Noonan, A. M., Crouch, A., Storey, S., Overcash, J., Han, C. J., Yang, Y., Li, H., & Saligan, L. N. (2024). Association between Cognitive Function and Physical Function, Frailty, and Quality of Life in Older Breast Cancer Survivors. *Cancers*, *16*(15), 2718. https://doi.org/10.3390/cancers16152718

Voorn, M. J. J., Driessen, E. J. M., Reinders, R. J. E. F., van Kampen-van den Boogaart, V. E. M., Bongers, B. C., & Janssen-Heijnen, M. L. G. (2023). Effects of exercise prehabilitation and/or rehabilitation on health-related quality of life and fatigue in patients with non-small cell lung cancer undergoing surgery: A systematic review. *European Journal of Surgical Oncology*, *49*(10), 106909. https://doi.org/10.1016/j.ejso.2023.04.008

Wagle, N. S., Nogueira, L., Devasia, T. P., Mariotto, A. B., Yabroff, K. R., Islami, F., Jemal, A., Alteri, R., Ganz, P. A., & Siegel, R. L. (2025). Cancer treatment and survivorship statistics, 2025. *CA: A Cancer Journal for Clinicians*, *75*(4), 308–340. https://doi.org/10.3322/caac.70011

Wagner, L. I., Gray, R. J., Sparano, J. A., Whelan, T. J., Garcia, S. F., Yanez, B., Tevaarwerk, A. J., Carlos, R. C., Albain, K. S., Olson, J. A., Goetz, M. P., Pritchard, K. I., Hayes, D. F., Geyer, C. E., Dees, E. C., McCaskill-Stevens, W. J., Minasian, L. M., Sledge, G. W., & Cella, D. (2020). Patient-Reported Cognitive Impairment Among Women With Early Breast Cancer Randomly Assigned to Endocrine Therapy Alone Versus Chemoendocrine Therapy: Results From TAILORx. *Journal of Clinical Oncology*, *38*(17), 1875–1886. https://doi.org/10.1200/JCO.19.01866

Wagner, L. I., Sweet, J., Butt, Z., Lai, J. S., & Cella, D. (2009). Measuring patient self-reported cognitive function: Development of the functional assessment of cancer therapy-cognitive function instrument. *J Support Oncol*, *7*(7), W32-W39.

Walker, E. M. K., Bell, M., Cook, T. M., Grocott, M. P. W., Moonesinghe, S. R., Central SNAP-1 Organisation, & National Study Groups. (2016). Patient reported outcome of adult perioperative anaesthesia in the United Kingdom: A cross-sectional observational study†. *BJA: British Journal of Anaesthesia*, *117*(6), 758–766. **https://doi.org/10.1093/bja/aew381**

Wang, L., Ding, Y., Zhang, Y., Chen, Y., Xue, M., & Wang, X. (2024). The association between neuropsychological impairment, self-perceived cognitive deficit, symptoms,

and health related quality of life in newly diagnosed ovarian cancer patients. *Asia-Pacific Journal of Oncology Nursing*, *11*(5), 100447. https://doi.org/10.1016/j.apjon.2024.100447

Wang, Y.-F., Wang, T.-Y., Liao, T.-T., Lin, M.-H., Huang, T.-H., Hsieh, M.-C., Chen, V. C.-H., Lee, L.-W., Huang, W.-S., & Chen, C.-Y. (2022). Quality of life and symptom distress after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *World Journal of Clinical Cases*, *10*(32), 11775–11788. https://doi.org/10.12998/wjcc.v10.i32.11775

Ward, E. P., & Greenbaum, A. (2024). Exploring the Patient Experience Through Qualitative Methods: The Missing Piece of Cytoreductive Surgery and HIPEC Research. *Annals of Surgical Oncology*, *31*(12), 7679–7681. https://doi.org/10.1245/s10434-024-15997-0

Waterland, J. L., McCourt, O., Edbrooke, L., Granger, C. L., Ismail, H., Riedel, B., & Denehy, L. (2021). Efficacy of Prehabilitation Including Exercise on Postoperative Outcomes Following Abdominal Cancer Surgery: A Systematic Review and Meta-Analysis. *Frontiers in Surgery*, *8*, 628848. https://doi.org/10.3389/fsurg.2021.628848

Wefel, J. S., Kesler, S. R., Noll, K. R., & Schagen, S. B. (2015). Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. *CA: A Cancer Journal for Clinicians*, *65*(2), 123–138. https://doi.org/10.3322/caac.21258

Wefel, J. S., Saleeba, A. K., Buzdar, A. U., & Meyers, C. A. (2010). Acute and late onset cognitive dysfunction associated with chemotherapy in women with breast cancer. *Cancer*, *116*(14), 3348–3356. https://doi.org/10.1002/cncr.25098

Wefel, J. S., Vardy, J., Ahles, T., & Schagen, S. B. (2011). International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. *The Lancet Oncology*, *12*(7), 703–708. https://doi.org/10.1016/S1470-2045(10)70294-1

West, M. A., Wischmeyer, P. E., & Grocott, M. P. W. (2017). Prehabilitation and Nutritional Support to Improve Perioperative Outcomes. *Current Anesthesiology Reports*, *7*(4), 340–349. https://doi.org/10.1007/s40140-017-0245-2

White, M. C., Holman, D. M., Boehm, J. E., Peipins, L. A., Grossman, M., & Jane Henley, S. (2014). Age and Cancer Risk. *American Journal of Preventive Medicine*, *46*(3), S7–S15. https://doi.org/10.1016/j.amepre.2013.10.029

Whitley, E., & Ball, J. (2002). Statistics review 6: Nonparametric methods. *Critical Care*, *6*(6), 509–513. https://doi.org/10.1186/cc1820

Whittaker, A. L., George, R. P., & O'Malley, L. (2022). Prevalence of cognitive impairment following chemotherapy treatment for breast cancer: A systematic review and meta-analysis. *Scientific Reports, 12*(1), 2135. https://doi.org/10.1038/s41598-022-05682-1

Williams, A. M., Lindholm, J., Cook, D., Siddiqui, F., Ghanem, T. A., & Chang, S. S. (2017). Association Between Cognitive Function and Quality of Life in Patients With Head and Neck Cancer. *JAMA Otolaryngology-- Head & Neck Surgery*, *143*(12), 1228–1235. https://doi.org/10.1001/jamaoto.2017.2014

Williams, A. M., van Wijngaarden, E., Seplaki, C. L., Heckler, C. E., Weber, M. T., Barr, P. M., Zent, C. S., & Janelsins, M. C. (2020). Cognitive function in patients with chronic lymphocytic leukemia: A cross-sectional study examining effects of disease and treatment. *Leukemia & Lymphoma*, *61*(7), 1627–1635. https://doi.org/10.1080/10428194.2020.1728748

Wion, R. K., Hill, N. L., Reed Bell, T., Mogle, J., Yates, J., & Bhang, I. (2022). The Role of Cognitive Self-Report Measure Type in Predicting Cognitive Decline Among Older Adults: A Systematic Review. *Journal of Geriatric Psychiatry and Neurology*, *35*(4), 487–511. https://doi.org/10.1177/08919887211023591

Wolff, L., Quan, Y., Perry, G., & Forde Thompson, W. (2023). Music Engagement as a Source of Cognitive Reserve. *American Journal of Alzheimer's Disease & Other Dementias®*, *38*, 15333175231214833. https://doi.org/10.1177/15333175231214833

Xu, L., Pan, Q., & Lin, R. (2016). Prevalence rate and influencing factors of preoperative anxiety and depression in gastric cancer patients in China: Preliminary study. *Journal of International Medical Research*, *44*(2), 377–388. https://doi.org/10.1177/0300060515616722

Yang, Y., & Hendrix, C. C. (2018). Cancer-Related Cognitive Impairment in Breast Cancer Patients: Influences of Psychological Variables. *Asia-Pacific Journal of Oncology Nursing*, *5*(3), 296–306. https://doi.org/10.4103/apjon.apjon_16_18

Yang, Y., & Von Ah, D. (2024). Cancer-related cognitive impairment: Updates to treatment, the need for more evidence, and impact on quality of life—a narrative review. *Annals of Palliative Medicine*, *13*(5), 1265280–1261280. https://doi.org/10.21037/apm-24-70

Yang, Y., Han, J., Monroe, T. B., & Kim, S. (2024). Pain and Cognition of Breast Cancer Survivors Treated with Chemotherapy: The Mediating Role of Depression. *Seminars in Oncology Nursing*, *40*(5), 151693. https://doi.org/10.1016/j.soncn.2024.151693

Yi, J. C., & Syrjala, K. L. (2017). Anxiety and Depression in Cancer Survivors. *The Medical Clinics of North America*, *101*(6), 1099–1113. https://doi.org/10.1016/j.mcna.2017.06.005

Yigitbas, C., & Bulut, A. (2024). Exploring psychological help-seeking behaviors and stigma perception among cancer patients: A study on their impact on psychosocial adjustment. *Supportive Care in Cancer*, *32*(10), 694. https://doi.org/10.1007/s00520-024-08870-z

Yu H., Zhang Z., Wang Y., Chen C., & Peng M. (2016). Analysis of the early postoperative cognitive function in the patients with peritoneal surface malignancies after cytoreductive surgery and hyperthermic intra-peritoneal chemotherapy(CRS-HIPEC). *The Journal of Clinical Anesthesiology*, 638–641.

Yu, H., Dong, R., Lu, Y., Yang, X., Chen, C., Zhang, Z., & Peng, M. (2017). Short-Term Postoperative Cognitive Dysfunction and Inflammatory Response in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: A Pilot Study. *Mediators of Inflammation*, *2017*(1), 3605350. https://doi.org/10.1155/2017/3605350

Yu, S., & Tang, Y. (2021). Effects of comprehensive care on psychological emotions, postoperative rehabilitation and complications of colorectal cancer patients after colostomy. *American Journal of Translational Research*, *13*(6), 6889–6896. https://pmc.ncbi.nlm.nih.gov/articles/PMC8290652/

Yusufov, M., Adeyemi, O., Flannery, M., Bouillon-Minois, J.-B., Van Allen, K., Cuthel, A. M., Goldfeld, K. S., Ouchi, K., & Grudzen, C. R. (2024). Psychometric Properties of the Functional Assessment of Cancer Therapy-General for Evaluating Quality of Life in Patients With Life-Limiting Illness in the Emergency Department. *Journal of Palliative Medicine*, *27*(1), 63–74. https://doi.org/10.1089/jpm.2022.0270

Zaman, A. C. G. N. M., Tytgat, K. M. A. J., Klinkenbijl, J. H. G., Boer, F. C. D., Brink, M. A., Brinkhuis, J. C., Bruinvels, D. J., Dol, L. C. M., Van Duijvendijk, P., Hemmer, P. H. J., Lamme, B., Loosveld, O. J. L., Mok, M. M., Rejda, T., Rutten, H.,

Schoorlemmer, A., Sonneveld, D. J., Stassen, L. P. S., Veenstra, R. P., … De Boer, A. G. E. M. (2021). Effectiveness of a Tailored Work-Related Support Intervention for Patients Diagnosed with Gastrointestinal Cancer: A Multicenter Randomized Controlled Trial. *Journal of Occupational Rehabilitation*, *31*(2), 323–338. https://doi.org/10.1007/s10926-020-09920-z

Zeng, G., Fung, S., Li, J., Hussain, N., & Yu, P. (2022). Evaluating the psychometric properties and factor structure of the General Self-Efficacy scale in China. *Current Psychology: A Journal for Diverse Perspectives on Diverse Psychological Issues*, *41*(6), 3970–3980. https://doi.org/10.1007/s12144-020-00924-9

Zhang, Y., Kesler, S. R., Dietrich, J., & Chao, H. H. (2025). Cancer-Related Cognitive Impairment: A Practical Guide for Oncologists. *JCO Oncology Practice*, *21*(10), 1377–1381. https://doi.org/10.1200/OP-24-00953

Zhi, X., Xie, M., Zeng, Y., Liu, J., & Cheng, A. S. K. (2019). Effects of Exercise Intervention on Quality of Life in Adolescent and Young Adult Cancer Patients and Survivors: A Meta-Analysis. *Integrative Cancer Therapies*, *18*, 1534735419895590. https://doi.org/10.1177/1534735419895590

Zhou, L., Li, H., Zhang, Z., & Wang, L. (n.d.). Effects of multimodal prehabilitation and exercise prehabilitation on patients undergoing colorectal surgery: A systematic review and meta-analysis of randomised controlled trials. *Journal of Global Health*, *14*, 04239. https://doi.org/10.7189/jogh.14.04239

Zhuang, Y., Guo, L., Huang, W., Bo, G., Zhang, J., Zhu, Z., & Feng, Y. (2023). Altered resting-state hippocampal functional connectivity in breast cancer survivors with chemotherapy-induced amenorrhea. *Brain and Behavior*, *13*(6), e3039. https://doi.org/10.1002/brb3.3039

Zimmer, P., Baumann, F. T., Oberste, M., Wright, P., Garthe, A., Schenk, A., Elter, T., Galvao, D. A., Bloch, W., Hübner, S. T., & Wolf, F. (2016). Effects of Exercise Interventions and Physical Activity Behavior on Cancer Related Cognitive Impairments: A Systematic Review. *BioMed Research International*, *2016*(1), 1820954. https://doi.org/10.1155/2016/1820954

Appendix A: Quality Appraisal for Systematic Review Chapter 2

Cohort Studies

Study (ref)	1. Were the two groups similar and recruited from the same population?	2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	3. Was the exposure measured in a valid and reliable way?	4. Were confounding factors identified?	5. Were strategies to deal with confounding factors stated?	6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	7. Were the outcomes measured in a valid and reliable way?	8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	10.Were strategies to address incomplete follow up utilized?	11. Was appropriate statistical analysis used?	Overall Appraisal
Cimprich (2001)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Hermelink (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Janelsins (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Letho (2013)	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Not Applicable	Yes	No	Yes	Include
Fayette 2023	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes	Yes	Unclear	Yes	Include
Gates 2024	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes	Yes	Not Applicable	Yes	Include
Hermelink 2017	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes	Yes	Not Applicable	Yes	Include
Hu 2023	Unclear	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes	Yes	Not Applicable	Yes	Include
Patel 2023	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Yes	Unclear	Unclear	Yes	Include
Zhuang 2023	Yes	Yes	Unclear	Yes	Yes	Not Applicable	Yes	Yes	Yes	Not Applicable	Yes	Include

Prevalence Studies

Study (Ref)	1. Was the sample frame appropriate to address the target population?	2. Were study participants sampled in an appropriate way?	3. Was the sample size adequate?	4. Were the study subjects and the setting described in detail?	5. Was the data analysis conducted with sufficient coverage of the identified sample?	6. Were valid methods used for the identification of the condition?	7. Was the condition measured in a standard, reliable way for all participants?	8. Was there appropriate statistical analysis?	9.Was the response rate adequate, and if not, was the low response rate managed appropriately?	Overall Appraisal
Cimprich (1999)	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	Unclear	Include
Cimprich (2005)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Include
DeRosa (2021)	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	Unclear	Include
Hardy-Leger (2021)	Yes	Yes	Yes	Not Applicable	Yes	Yes	Yes	Yes	Not Applicable	Include
Hermelink (2010)	Yes	Yes	Unclear	Not Applicable	Yes	Yes	Unclear	Yes	Yes	Include
Hermelink (2007)	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Include
Jung (2022)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Scheibel (2004)	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Include
Chun 2023	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Include
Knoerl 2024	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Include
Tulk 2021	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Include

Analytical Cross sectional

Study (ref)	1.Were the criteria for inclusion in the sample clearly defined?	2.Were the study subjects and the setting described in detail?	3.Was the exposure measured in a valid and reliable way?	4.Were objective, standard criteria used for measurement of the condition?	5.Were confounding factors identified?	6.Were strategies to deal with confounding factors stated?	7.Were the outcomes measured in a valid and reliable way?	8.Was appropriate statistical analysis used?	Overall Appraisal (Include/Exclude/Seek Further Info)
Bernstein (2018)	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Include
Lange (2020)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Patel (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Aspenlund 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include
Jurickova 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include

Case Control Study

Study (ref)	1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	2. Were cases and controls matched appropriately?	3. Were the same criteria used for identification of cases and controls?	4. Was exposure measured in a standard, valid and reliable way?	5. Was exposure measured in the same way for cases and controls?	6.Were confounding factors identified?	7. Were strategies to deal with confounding factors stated?	8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	9. Was the exposure period of interest long enough to be meaningful?	10. Was appropriate statistical analysis used?	Overall Appraisal
Kathpalia 2024	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not Applicable	Yes	Include

Randomised Control Trials

Assessor: Aideen Scriney	Date of Appraisal: 22/4/25	Record Number:
Study Author: Savard	Study Title:	Study Year: 2023

	Internal Validity	Choice - Comments/Justification	Yes	No	Unclear	N/A
Bias related to selection and allocation						
1	Was true randomization used for assignment of participants to treatment groups?	Yes	X	☐	☐	☐
2	Was allocation to treatment groups concealed?	Yes double blind placebo controlled trial		X☐	X	☐
3	Were treatment groups similar at the baseline?	Some differences in clinical characteristics including tumour aggressiveness which could influence results.	X	☐	☐	☐
Bias related to administration of intervention/exposure						
4	Were participants blind to treatment assignment?	Yes double blind placebo controlled trial	☐	X	☐	☐
5	Were those delivering the treatment blind to treatment assignment?	Yes double blind	☐	X	☐	☐
6	Were treatment groups treated identically other than the intervention of interest?	Yes -no to 6 as tumour aggressiveness was stat -Treated identically yes as in outcomes etc.	X	☐	☐	☐
Bias related to assessment, detection and measurement of the outcome						
7	Were outcome assessors blind to treatment assignment?	Yes, double blind intervention study.	Yes	No	Unclear	N/A
	Outcome 1	Anxiety and Depression	☐	☐	☐	☐
	Outcome 2	Patient health questionnaire	☐	☐	☐	☐
	Outcome 3	Fear of recurrence	☐	☐	☐	☐
	Outcome 4	Insomnia Severity Index	☐	☐	☐	☐
	Outcome 5	Faitgue Symptom Inventory	☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
8	Were outcomes measured in the same way for treatment groups?	Yes - all measures were measured in a similar way per treatment group	Yes	No	Unclear	N/A
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐
9	Were outcomes measured in a reliable way	Yes, reliable scales were used for all outcome measures- same for all outcomes	Yes	No	Unclear	N/A
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐
	Outcome 3		☐	☐	☐	☐
Bias related to participant retention						
10	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?	Follow up was completed up to a 12 month assessment for all outcomes. At each stage, reasons for incomplete follow up were identified in a flow diagram. Made clear via diagram how many participants were included in analysis for all results n=65.				
	Outcome 1		Yes	No	Unclear	N/A

Statistical Conclusion Validity

11	**Were participants analysed in the groups to which they were randomized?**	Yes for all outcomes and results, results were analysed in reference to intervention group vs. placebo				
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Treatment effects	☐	☐	☐	☐
	Result 2	clinical levels of symptoms	☐	☐	☐	☐
	Result 3	Sensitivity analysis	☐	☐	☐	☐
	Outcome 2		**Yes**	**No**	**Unclear**	**N/A**
12	**Was appropriate statistical analysis used?**	Yes- group demographics were compared using cochran-mantel-haenszel and wilcoxon tests. effects of supplementation were explored using linear mixed models with repeated measures including random effects for patients on each outcome. Controlled for potential confounding effects outlined from the literature. All analysis conducted using an intent to treat approach. Generalised linear models used to assess severity of patient symptoms.	Yes and yes for all results			
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
13	**Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?**	Yes, this was a double blind supplementation trial which was appropriate for study design, patient outcomes and patient cohort.	X	☐	☐	☐

Overall appraisal: **Include: X** **Exclude:** ☐ **Seek Further Info:** ☐

Comments:

Table 3 – The JBI Critical Appraisal Tool for RCTs

Assessor: Aideen Scriney	Date of Appraisal: 17/4/25	Record Number:
Study Author: Hermelink 2007	Study Title:	Study Year: 2007

	Internal Validity	Choice - Comments/Justification	Yes	No	Unclear	N/A
Bias related to selection and allocation						
1	Was true randomization used for assignment of participants to treatment groups?	Yes- participants were randomised Lorna- just said randomly assigned -not overly described	X	☐	☐	☐
2	Was allocation to treatment groups concealed?	unclear -Lorna aswell		☐	X	☐
3	Were treatment groups similar at the baseline?	Yes	X	☐	☐	☐
Bias related to administration of intervention/exposure						
4	Were participants blind to treatment assignment?	no- open label	☐	X	☐	☐
5	Were those delivering the treatment blind to treatment assignment?	no- open label	☐	X	☐	☐
6	Were treatment groups treated identically other than the intervention of interest?	yes - assessment of similar outcomes at same time points regardless of clinical regime	X	☐	☐	☐
Bias related to assessment, detection and measurement of the outcome						
7	Were outcome assessors blind to treatment assignment?		Yes	No	Unclear	N/A
	Outcome 1	unclear -this is an open label trial, so researchers knew which group participants were assigned to - this is the case for all outcomes. It is not explicitly stated that they were or were not aware.	☐	☐	X☐	☐

8	Were outcomes measured in the same way for treatment groups?	Yes- Outcomes were assessed the same way in both groups - this applies to all outcomes	Yes	No	Unclear	N/A
	Outcome 1	Cognitive function- self report	☐	☐	☐	☐
	Outcome 2	Cognitive function- objective	☐	☐	☐	☐
	Outcome 3	Premorbid intelligence	☐	☐	☐	☐
	Outcome 4	Depression and Anxiety	☐	☐	☐	☐
	Outcome 5	Trait negative & positive affectivity	☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

9	Were outcomes measured in a reliable way	Yes, reliable and standard measures were used to measure all outcomes of interest.	Yes	No	Unclear	N/A
	Outcome 1	Cognitive function- self report	☐	☐	☐	☐
	Outcome 2	Cognitive function- objective	☐	☐	☐	☐
	Outcome 3	Premorbid intelligence	☐	☐	☐	☐
	Outcome 4	Depression and Anxiety	☐	☐	☐	☐
	Outcome 5	Trait negative & positive affectivity		☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

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Bias related to participant retention						
10	**Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?**	Yes- paper refers to prior research to outline retention. For all results, analysis was only conducted on n=101 who completed follow up. n=93 datasets complete for T1 & T2				
	Outcome 1	Self report cog function	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	increased problems at T2 .	☐	☐	☐	☐
	Result 2	small but non sig correlations with ob scores. changes in SR cog were not associated sig with no. of deteriorated test results	☐	☐	☐	☐
	Result 3	both measures showed increase sig between T1 & T2.	☐	☐	☐	☐
	Outcome 2	Objective cog function	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	comparison against test norms conducted for n=101	☐	☐	☐	☐
	Result 2	T1-T2 improvement sig, n=93 of completed data sets for T1 & T2	☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 3	Premorbid Intelligence	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	correlation between premorbid intelligence & T1 ob cog function (n=101)	☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 4	**Depression and Anxiety**	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	not correlated with objective cog t1 (n-101)	☐	☐	☐	☐
	Result 2	not correlated with the no of deteriorated or improved test results.	☐	☐	☐	☐
	Result 3	Anxiety and depression sig correlation with self report cog complaints measures.	☐	☐	☐	☐
	Outcome 5	Trait neg and pos affectivity	**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐

Statistical Conclusion Validity

11	**Were participants analysed in the groups to which they were randomized?**	No - this was a secondary analysis of an RCT. Participants were analysed per time point. This is the case for all outcomes. -No lorna but agreed yes.	

12	**Was appropriate statistical analysis used?**	Yes, comparison of T1 & T2 test results was by MANOVA. RCI was used to assess chance of individual error or true change in CF. Spearman rank correlations calculated for no. of deteriorated test results. MANOVAs used to assess effects of darbepoetin and of therapy induced menopause.	Yes and yes for all results			
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐

13	**Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?**	Yes , this was a secondary analysis of an open label RCT design. Given the nature of the RCT being a clinical trial with chemotherapy regimes, an open label approach was appropriate.	X	☐	☐	☐

Overall appraisal: **Include: X** **Exclude:** ☐ **Seek Further Info:** ☐

Comments:

Table 3 – The JBI Critical Appraisal Tool for RCTs

Post-Viva Copy 19/08/2026

Assessor: Aideen Scriney	Date of Appraisal: 22/4/25	Record Number:
Study Author: Hermelink 2010	Study Title:	Study Year: 2010

Internal Validity		Choice - Comments/Justification	Yes	No	Unclear	N/A
Bias related to selection and allocation						
1	Was true randomization used for assignment of participants to treatment groups?	Yes- participants were randomised	X	☐	☐	☐
2	Was allocation to treatment groups concealed?	unclear		☐	X	☐
3	Were treatment groups similar at the baseline?	Yes -Paper refers to previous reports for demographic information including Hermelink 2007 which has been assessed as part of this review	X	☐	☐	☐
Bias related to administration of intervention/exposure						
4	Were participants blind to treatment assignment?	no- open label -Same trial as Hermelink 2007	☐	X	☐	☐
5	Were those delivering the treatment blind to treatment assignment?	no- open label -Same trial as Hermelink 2007	☐	X	☐	☐
6	Were treatment groups treated identically other than the intervention of interest?	yes - assessment of similar outcomes at same time points regardless of clinical regime	X	☐	☐	☐
Bias related to assessment, detection and measurement of the outcome						
7	Were outcome assessors blind to treatment assignment?		Yes	No	Unclear	N/A
	Outcome 1	unclear -this is an open label trial, so researchers knew which group participants were assigned to - this is the case for all outcomes. it is not explicitly stated that they were or were not aware.	☐	☐	☐	☐
	Outcome 2	Subjective CF	☐	☐	☐	☐
	Outcome 3	Objective CF	☐	☐	☐	☐
	Outcome 4	Premorbid Intelligence	☐	☐	☐	☐
	Outcome 5	Anxiety and Depression	☐	☐	☐	☐
	Outcome 6	Trait negative and positive affectivity	☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐
8	Were outcomes measured in the same way for treatment groups?	Yes- Outcomes were assessed the same way in both groups - this applies to all outcomes -Same as Hermelink 2007	Yes	No	Unclear	N/A
	Outcome 1	Cognitive function- self report	☐	☐	☐	☐
	Outcome 2	Cognitive function- objective	☐	☐	☐	☐
	Outcome 3	Premorbid intelligence	☐	☐	☐	☐
	Outcome 4	Depression and Anxiety	☐	☐	☐	☐
	Outcome 5	Trait negative & positive affectivity -only measured at T1	☐	☐	☐	☐
	Outcome 6		☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐

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9	**Were outcomes measured in a reliable way**	Yes, reliable and standard measures were used to measure all outcomes of interest.	**Yes**	**No**	**Unclear**	**N/A**

Outcome 1	Cognitive function- self report	☐	☐	☐	☐
Outcome 2	Cognitive function- objective	☐	☐	☐	☐
Outcome 3	Premorbid intelligence	☐	☐	☐	☐
Outcome 4	Depression and Anxiety	☐	☐	☐	☐
Outcome 5	Trait negative & positive affectivity		☐	☐	☐
Outcome 6		☐	☐	☐	☐
Outcome 7		☐	☐	☐	☐

Bias related to participant retention

10	**Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?**	Yes- paper refers to prior research to outline retention. For all results, analysis was only conducted on n=101 who completed follow up. Paper does not make clear the final N used in this analysis				
Outcome 1		Self report cog function	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Yes patient retention explained why some patients dropped out out T3.	☐	☐	☐	☐
	Result 2	Both tests showed decrease at t2	☐	☐	☐	☐
	Result 3	eortc cf and FEDA sig correlation at all timepoints	☐	☐	☐	☐
Outcome 2		Objective cog function	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Study refers to prior work (Hermelink 2007 included in this review) for a breakdown of objective CF results	☐	☐	☐	☐
	Result 2	Therapy arm or medication did not impact OB test results	☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
Outcome 3		Premorbid Intelligence	**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
Outcome 4		**Depression and Anxiety**	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	no sig differences between groups at T1 or T2, T3 patients in arm B reported more anxiety.	☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
Outcome 5		Trait neg and pos affectivity	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	N/A only recorded at T1	☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐

11	**Were participants analysed in the groups to which they were randomized?**	Yes - although secondary analysis primary patient resutls were broken down both written and by use of graphs by intervention regime.				
	Outcome 1	Self Report CF -yes	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Both groups showed deterioration and T2 and particle recovery T3.	☐	☐	☐	☐
	Result 2	Subjective CF was predicted by: current depression, trait neg affectivity and therapy arm.	☐	☐	☐	☐
	Result 3	At T2 higher levels of training pos affectivity associated with deterioration of EORTC CFS	☐	☐	☐	☐
	Outcome 2	Objective CF	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	change in sub CF as predicted by change in ob test score showed a sig increased in performance of executive function test and FEDA score at T2.	☐	☐	☐	☐
	Result 2		☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 3	depression and anxiety	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	no sig differences in intervention groups on depression at any timepoint.	☐	☐	☐	☐
	Result 2	No sig differences in anxiety T1 & T2. T3- patients in arm b reported more anxiety than arm A.	☐	☐	☐	☐
	Result 3	Depression was a sig predictor of self reported CF	☐	☐	☐	☐
	Outcome 4	**Neg and Pos affectivity**	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Chemo groups did not differ on negative or positive affectivity.	☐	☐	☐	☐
	Result 2	Self report CF was predicted by trait negative affectivity	☐	☐	☐	☐
	Result 3	even though depression and trait neg affectivity were correlated, neg trait affectivity still had a sig effect both on EORTC CFS and FEDA scores after adjustment	☐	☐	☐	☐

12	**Was appropriate statistical analysis used?**	Yes- Linear mixed models were used to determine factor effects on cog self reports. The analyses were conducted for the dependent variables of sub cf. Researchers chose to retain negative trait affectivity and the interaction of time and therapy arm in the model as they may be confounding based on the literature, so these were not subject to factor selection. They also looked at change in cog self reports was related to change in cog performance using models. pearson correlations conducted for associations.	Yes and yes for all results			
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
	Result 2		☐	☐	☐	☐

			Yes	**No**	**Unclear**	**N/A**
13	**Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?**	Yes , this was a secondary analysis of an open label RCT design. Given the nature of the RCT being a clinical trial with chemotherapy regimes, an open label approach was appropriate.	X	☐	☐	☐

Overall appraisal: **Include: X** **Exclude:** ☐ **Seek Further Info:** ☐

Comments:

Table 3 – The JBI Critical Appraisal Tool for RCTs

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Assessor: Aideen Scriney	Date of Appraisal: 22/4/25	Record Number:
Study Author: Francois	Study Title:	Study Year: 2024

	Internal Validity	Choice - Comments/Justification	Yes	No	Unclear	N/A
Bias related to selection and allocation						
1	Was true randomization used for assignment of participants to treatment groups?	Yes- this is a secondary analysis of a randomized research study	X	☐	☐	☐
2	Was allocation to treatment groups concealed?	No- this was a non-blinded study		X☐	X	☐
3	Were treatment groups similar at the baseline?	Yes - clinical and demographic characteristics were all similar to baseline- taken from the main paper. However paper notes that groups were sig difference on social functions, fatigue and diarrhea could impact QoL outcome.	X	☐	☐	☐
Bias related to administration of intervention/exposure						
4	Were participants blind to treatment assignment?	No this was a non blinded study	☐	X	☐	☐
5	Were those delivering the treatment blind to treatment assignment?	no this was a non blinded study	☐	X	☐	☐
6	Were treatment groups treated identically other than the intervention of interest?	Yes other than intervention -Lorna said unclear- check	X	☐	☐	☐
Bias related to assessment, detection and measurement of the outcome						
7	Were outcome assessors blind to treatment assignment?	No-this was a non blinded study, assessors were not blind to treatment conditions. -Lorna said unclear	Yes	No	Unclear	N/A
	Outcome 1	Quality of life	☐	☐	☐	☐
	Outcome 2	QLQ Elderly -Geriatic Assessment	☐	☐	☐	☐
	Outcome 3	ADL score/ walking speed - GA	☐	☐	☐	☐
	Outcome 4	MMSE-GA	☐	☐	☐	☐
	Outcome 5	Depression-GA	☐	☐	☐	☐
	Outcome 6	Nutritional Status -GA	☐	☐	☐	☐
	Outcome 7		☐	☐	☐	☐
8	Were outcomes measured in the same way for treatment groups?	Yes - all outcome measures were measured in the same way for treatment groups across all outcomes.	Yes	No	Unclear	N/A
9	Were outcomes measured in a reliable way	Yes- reliable measures were used for all outcomes.	Yes	No	Unclear	N/A
	Outcome 1		☐	☐	☐	☐
	Outcome 2		☐	☐	☐	☐

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Bias related to participant retention						
10	**Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analysed?**	Study was closed after 3 years due to poor accrual and a detailed flow diagram of recruitment and retention included in the main study paper. Only included patients who did undergo treatment in the study- same for all outcomes and results. -Yes /Lorna Unclear				
	Outcome 1	Quality of life	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	T0 no difference between groups or at any further timepoints.	☐	☐	☐	☐
	Result 2	3 months post- sig better CF, fatigue and appetite group B. 6 months - sig better CF, Insomnia and constipation group B.	☐	☐	☐	☐
	Result 3		☐	☐	☐	☐
	Outcome 2	Geriatric Assessment	**Yes**	**No**	**Unclear**	**N/A**
	Result 1	Burden of disease perceived larger in Group A	☐	☐	☐	☐
	Result 2	3 months post op sig difference in ADL, group B	☐	☐	☐	☐
	Result 3	Depression greater deterioration at 3m post op in group A	☐	☐	☐	☐
		MMSE scores no differences throughout.				
	Outcome 3		**Yes**	**No**	**Unclear**	**N/A**

11	**Were participants analysed in the groups to which they were randomized?**	Yes participants were analysed for all outcomes By group A or B.				
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
	Result 1		☐	☐	☐	☐
			☐	☐	☐	☐

12	**Was appropriate statistical analysis used?**	Yes, as this is a secondary analysis,only frequencies and % are explored and standard deviations compared using students test or Mann Whitney U test.	Yes and yes for all results			
	Outcome 1		**Yes**	**No**	**Unclear**	**N/A**
			☐	☐	☐	☐

13	**Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?**	Yes, this is a non blinded study as patients are receiving cancer treatment prior to surgery. Non blinded is appropriate for cancer and treatment context.	X	☐	☐	☐

Overall appraisal: **Include: X** **Exclude:** ☐ **Seek Further Info:** ☐

Comments:

Table 3 – The JBI Critical Appraisal Tool for RCTs

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Appendix B: Quality Appraisal for Systematic Review Chapter 3

Quality Assessment (Dunne et al., 2017)

Criteria - quantitative studies	Ambler et al., 1999	Belleau et al., 2001	Brahmbhatt et al., 2020	Can et al., 2009	de Moor et al., 2008	de Paleville et al., 2007	Foley et al., 2010	Garssen et al., 2013	Li et al., 2017	Millstein et al., 2019	Singh et al., 2017	Zaman et al., 2021	Galantino et al., 2012
1. Clearly stated aims	2	2	2	2	2	2	1	1	1	2	2	2	2
2. Participant eligibility and recruitment strategy clearly documented	1	2	2	2	1	1	2	2	1	2	2	2	2
3. Main features of population/design described	2	2	2	2	2	2	2	2	2	2	2	2	2
4. Non-responders (and non-participants) described	2	0	2	2	2	0	2	2	2	1	1	2	1
5. Presence of a control group	0	1	0	2	1	0	2	2	2	0	0	2	0
6. Main limitations identified and acceptable	2	1	2	2	2	0	1	1	0	2	1	2	1
7. Sample size justified	0	0	1	2	2	0	2	2	0	2	0	2	1
8. No evidence of selective reporting of results	2	2	2	2	2	2	2	2	2	2	2	2	0
9. Statistical methods described	1	2	2	2	2	1	2	2	2	2	2	2	1
10. Statistical methods appropriate	0	2	2	2	2	2	2	2	1	2	2	2	2
11. Measures relevant, validated and described adequately	2	2	2	2	1	2	2	2	2	2	2	2	2
12. Results discussed adequately	2	2	2	2	2	2	2	2	2	2	2	2	1
Total score	16	18	21	24	21	14	22	22	17	21	18	24	15

Note. Score Key: Y (Yes) = Score of 2; P (Partial) = Score of 1; N (No) = Score of 0; DK (Don't know) = Score of 0, Scoring: 17-24 = good quality; 9-16 = acceptable quality; 0-8 = low quality

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Appendix C: Chapter 4 Study Materials

C.1 Plain Language Statement

Participant Information Leaflet

Name of Study: PANO: The PANO Trial: Perioperative Exercise and Nutrition Optimisation Prehabilitation in Cancer Patients with Peritoneal Malignancy

Site	**Mater Misericordiae University Hospital and ExWell Medical.**
Principal Investigator(s) and Co-Investigator(s) (insert names, titles and contact details)	**Mr. Jurgen Mulsow** **Consultant Surgeon with a specialist interest in advanced lower gastrointestinal cancer, tumours of the appendix and peritoneal malignancy.** **Address:** Mater Misericordiae University Hospital **Contact:** 01 854 5091 **E-mail:** jmulsow@mater.ie **Co-Principal Investigators:** **Dr. Lorraine Boran** **Assistant Professor, School of Psychology, DCU** **Contact: 01 700 7923 lorraine.boran@dcu.ie** **Dr.Lisa Loughney** **Clinical Exercise Physiologist, RCSI** **lisa.loughney@gmail.com** **Co-Investigators:** **Dr. Noel Mc Caffrey** **Medical Director ExWell Medical** **Contact: noel.mccaff@gmail.com** **Professor Pamela Gallagher** **Professor of Psychology** **Contact: 01-7008958 pamela.gallagher@dcu.ie** **Dr. Claire Timon** **Research Fellow** **Contact: claire.timon@dcu.ie** **Dr. Alexander Eustace** **Research Lead for Molecular Therapeutics for Cancer in Ireland** **Contact: 01 700 7497 alex.eustace@dcu.ie** **Dr. Denis Collins** **PI in Cancer Biotherapeutics with the Molecular therapeutics for Cancer group at the NICB** **Contact: 01 700 5647 denis.collins@dcu.ie**

Study Organiser/ Sponsor (if applicable)	
Data Controllers	**Mater Misericordiae University Hospital -** Mr. Jurgen Mulsow **Dublin City University-** Dr. Lorraine Boran, Dr.Lisa Loughney and Post-Doctoral Researcher : Shauna Malone
Data Protection Officer	**Data Protection Officer of MMUH:** Data Protection Office at the Mater: Phone: 01 803 4311 email: dataprotection@mater.ie **Data Protection Officer of Dublin City University:** Martin Ward, Phone: Officer and Deputy Chief Operations Officer Phone: 01 700 7476.

Introductory Statement:

You are being invited to take part in a research study to be carried out at the Mater Misericordiae University Hospital (MMUH) by Mr. Jurgen Mulsow, consultant general and colorectal surgeon. This research is also being carried out along with Dublin City University School of Psychology, School of Biotechnology, the Royal College of Surgeons Ireland and ExWell Medical Ltd.

Before you decide whether or not you wish to take part, you should read the information provided below carefully and, if you wish, discuss it with your family, friends or GP (doctor). Take time to ask questions – don't feel rushed and don't feel under pressure to make a quick decision. Two of our researchers on the team, Shauna Malone or Aideen Scriney can follow up with a brief phone call after 72 hours of receiving information about the study to answer any questions you may have and/or to confirm your participation in the study. Shauna and Aideen's details can be found at the end of this information sheet.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you. This process is known as 'Informed Consent'.

You don't have to take part in this study. If you decide not to take part, it won't affect your future medical care.

You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You don't have to give us a reason. If you do opt out, rest assured it won't affect the quality of treatment you get in the future.

This leaflet has five main parts:

Part 1 – The Study

Part 2 – Data Protection
Part 3 – Costs, Funding and Approval
Part 4 – Future Research
Part 5 – Further Information

Part 1 – The Study

Why is this study being done?

This study is taking place in order to explore if exercise and nutrition in the period before cancer surgery will improve fitness, and also if it may also improve other important health measures such as strength, well-being and overall quality of life. Studies have shown that people with improved fitness recover better after major operations.

Why have I been invited to take part?

You have been invited to take part as we are most interested in patients who have been diagnosed with cancer of the colon/rectum/appendix that spreads into the lining of the tummy and some cancers or people with pseudomyxoma peritonei where chemotherapy is given whilst the person is having surgery - also known by doctors as surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). We are intending to include 50 patients with this condition.

Do I have to take part? Can I withdraw?

You do not have to take part in this study and your participation is completely voluntary. If you decide not to take part, it will not affect your current or future medical care in any way. You can also choose to opt-out at any time even after the study has started and this also will not affect your current or future medical care in any way. Even after the study is complete, you can choose to withdraw your data at a later date before anonymisation has occurred. You do not have to give a reason for not taking part or for opting out during the study. If you wish to opt out, please contact the postdoctoral researcher Ms. Shauna Malone or PhD researcher Ms. Aideen Scriney who will be able to organise this for you.

What happens if I change my mind?

You are free to change your mind at any time by contacting postdoctoral researcher Ms. Shauna Malone or PhD researcher Ms. Aideen Scriney. If you choose not to continue to take part, this will not affect your medical care in any

way. If you wish you can also ask for your data and samples to be destroyed. If you request this, we will destroy all samples and data that are still in our possession. We will no longer use or share your samples or data for research from this point onwards.

How will the study be carried out?

Once you agree to participate in the study, we will organise your first visit where you will be asked to sign an informed consent document. Involvement in this study will require you to undergo some assessments at the beginning of the study, before surgery, after surgery when you are clinically fit to do so and 6 weeks later. At your first visit, you will be asked to perform the following exercise-related tests: 6 Minute Walk Test, Handgrip Test and the Sit to Stand Test. We aim to complete your first set of assessments at your hospital visit with the surgeon. After this, we will also aim to complete your assessments at times that you would usually visit the hospital but this may not always be possible. Outside of your usual appointments, you will not have to attend the hospital if it is not convenient. Depending on your geographical location, you may attend an ExWell centre in your local area or we can visit your home to complete these assessments.

You will also answer questionnaires about your psychological wellbeing, quality of life and dietary and nutrition information. These can be completed either on site or remotely.

The assessments will be completed at four different times and will measure fitness, strength, activity, quality of life, nutrition/diet and you will also be asked to get a blood sample taken. We will also ask you to take part in a short interview which will take place at two times: before your surgery, and asurgery the end of the study. For the interview, a member of our research team will ask you some questions about your experience before and after your surgery and how you feel physically and emotionally during these times. If you consent, there will also be the opportunity to take part in a follow-up interview after 6 months. All interviews will be completed remotely (e.g.: via phone call or Zoom)

What will happen to me if I decide to take part?

Your assessments will take place at the Mater Hospital or ExWell Medical (wherever is most convenient for you, based on where you live). Please note, if it is not possible for you to attend any of the ExWell locations for assessment, we can accommodate you with a home visit. The assessments will be completed by a trained member of our research team.

Recruited patients will be divided into a control and exercise and nutrition intervention group. You will have 1:1 chances of being placed in the exercise and nutrition intervention group. If you are assigned to the exercise and nutrition intervention group, we will provide you with an individualised exercise programme based on your ability that you can carry out at one of our exercise centres if they’re near your home or at home if that is most convenient for you and a dietary plan for both before and after your surgery. Every effort will be made to arrange your visits to fit in with other hospital appointments. If you are randomly assigned to the control group, you will receive standard advice.

As part of the research project we would also like you to complete a fitness and strength assessments, height and weight measures, and complete quality of life questionnaires when you enter the study, before surgery, after surgery and 6 weeks later. These questionnaires are easy to fill in. In addition, we would like you to complete a nutrition/diet assessment. During the study period, we would also like to invite you to have 2 quality of life interviews remotely before and after your surgery. You will also undergo your routine tumour examination by CT and MRI scans.

As part of this research project, all patients recruited will have a blood test taken at the beginning of the study, before and after surgery, and 6 weeks later. These will be taken as best we can as the same time as your usual blood samples. We will use a small needle to take blood samples from a site at your arm. You may feel discomfort due to the needle stick and you may have bruising, bleeding or swelling at the blood site sample. You may feel faint and dizzy while your blood is being drawn and there is a slight risk of infection. In addition to your hospital blood sample, another research sample of 20 ml (4 teaspoons) will be taken at each of 4 times (two times before and two times after surgery). All of the blood tests will be completed in the Mater Hospital.

We are also interested in how much physical activity you typically do, and whether this changes during the study period. Therefore on 4 occasions (at the beginning of the study, before surgery, at your clinic visit after surgery, and 6 weeks later) we will ask you to wear an "accelerometer", which is a small device worn on the upper leg (mid-thigh). This will be worn on each occasion for a 7-day period (day and night). This unit will measure your typical physical activity levels and is unobtrusive. This will be fitted at your first visit and will be shuttled back and forth to you on all 3 other occasions, to cause you the least amount of inconvenience.

Calculating your Body Mass Index (BMI) based on factors such as your height and weight. We will use a nutritional screening tool to look at the likelihood you may need nutritional support. As part of this assessment, a blood sample will be taken. We will use a nutritional screening tool to look at the likelihood you may need nutritional support. We will also look at measures taken as part of your routine care, such as your CT scans and blood samples to look at your levels of iron, vitamins, bone health and other markers of nutritional health to decide on how best to support your nutrition during the intervention.

We will also need to assess your quality of life. We do this using two questionnaires that have been designed and tested specifically to measure this that you will complete. We will also assess your self-efficacy using a questionnaire designed especially to assess this. We will also test your overall psychological wellbeing through four questionnaires that will assess areas such as stress and memory and attention (cognitive function) . All of these questionnaires will be taken at the beginning of the program , before surgery , after surgery and during a 6 week follow up.

These will all be assessed at 4 timepoints:
1) Firstly when you agree to the study initially
2) Days before your surgery

3) Clinic appointment after your surgery (approximately 6 weeks post-surgery but this depends on your length of hospital stay)
4) And finally, about six weeks after the previous appointment
After surgery, we will assess how the surgery affected you using research tools. They will assess things like if you had any complications after your surgery or if you had to stay in hospital longer than expected. (The information needed to fill out these tools will be taken from your medical records. This information will be collected by a surgical doctor who is also involved in the research. No other or extra people will have access to your medical records.) These will be assessed on days 3,7 and 15 after your surgery.

If you decide to take part in the interviews you will be called by a member of the research team at two points: before your surgery and at the final assessment timepoint. This will be a short phone interview where the researcher will ask you some questions about your experience of your treatment pathway, and how you felt physically and emotionally before and after your surgery. Topics will include your experience of your treatment pathway, how you felt physically and emotionally before and after your surgery and also your experiences with your attention and memory (cognitive function) since your diagnosis. If you consent there will also be a third interview 6 months later about your experiences.

All of this information will be stored on a protected encrypted server at Mater Hospital and Dublin City University. As soon as the data is collected it will be made so that you cannot be identified by the data. The only way to convert this information back into identifiable information will be held securely in a 'Key' by the head investigators Dr. Lorraine Boran and Dr. Lisa Loughney.

This information will be stored for 10 years after the completion of the study in a secure location but it will not have any identifiable features at that time.

If you have been randomly assigned to the exercise and nutrition support group, we will give you a structured exercise programme and ask that you do it three to five times per week. This can take place either at an ExWell Medical centre or at home. You can do some sessions in ExWell Medical and sessions at home. We will give you weekly phone calls to see how you are getting on and to see if you are doing the programme at home. ExWell Medical is a community-based exercise rehabilitation programme who cater for individuals with various medical conditions, including cancer (https://www.exwell.ie/). They have approximately 600 patients visits per week and have a variety of locations across Ireland.

The structured exercise programme will be tailored to your fitness and will include light aerobic exercise set at your own pace. Then there will be some strength exercises for your upper body and lower body.

You will also receive continued nutritional support from Dieticians at the Mater Hospital. This will involve continued support from senior dieticians at MMUH to help you to identify how best to improve your nutrition as you prepare for treatment and how best to treat any individual issues with your nutritional intake. This will be done using validated nutritional screening tool (e.g. Malnutrition Screening Tool (MST). In addition you will be asked to record your dietary intake using an interactive platform called Foodbook24.

If you are not assigned to the exercise and nutrition intervention condition, you will receive the standard care currently available to all patients who are preparing for CRS -HIPEC treatment and peritoneal malignancy.

What will happen to my Samples and Data?

All data collected as part of the study will be made pseudo-anonymous , stored securely and used solely for the purpose of this research project.

Data collected during the course of the study, including questionnaires and results of physical and nutritional assessments will be stored electronically on a secured drive. However, in some circumstances where this may not be possible due to hospital location or wifi drop; SPSS processor etc data may need to be temporarily 'stored' to support processing on a laptop and then uploaded to the secure cloud. Only those on the research team will have access to study data at all timepoints. Data will also be made pseudonymised once it is collected and each patient will be assigned an identification number for their data. The identification numbers and patient details will be kept separately so that your study data cannot be matched to your indefinable details. Only the co-principal investigators will have access to both your identification number and personal details. The anonymised stored data will be stored on a secure shared drive accessible only through password protected devices across the MMUH, DCU , RCSI and ExWell Medical. Your pseudonymised data will be analysed at DCU and the RCSI. Data will also be completely anonymised in all publications as a result of the research project. All anonymous data will be deleted on or before April 2032.

Audio recordings will be taken using a dictaphone from DCU's School of Psychology. Recordings will be downloaded and stored on a secure server for transcription. Transcription will be done by Aideen Scriney (PhD candidate) and any all identifying information will be removed so that the transcribed copies will be pseudo-anonymised with patient ID. The transcription will not contain any information that could identify the participants beyond that. Transcribed soft copy files will be stored on a secure DCU server. In all cases, access will only be available to members of the research team. Audio files will be deleted once transcription and fidelity checking has occurred.

As part of the study, a number of blood samples will also be taken. These will also be pseudonymised using the identification key. The material given to researchers will not have any information that identifies you. Anonymised blood samples will be transferred to DCU for analysis and stored securely with access only available to those on the research time. After analysis is complete, all anonymised samples will be destroyed. All consent documents will also be kept until such a time that all research data is anonymised, this will be after a period of 6 years (April 2028).

Are there any benefits to taking part in this research?

You will also be generating information that may be used in future cancer care programmes that may help people who are diagnosed with cancer in the future. You will be helping the researchers, some of whom are completing this research for academic qualifications.

Potential Benefits for those taking part in the intervention may be:
-An increase in physical fitness
-An improved balanced nutritional intake
-Improvements in your recovery after your surgery
-Less days spent in hospital after your surgery

Are there any risks to me or others if I take part?

There are few risks to partaking in this research study. Nutrition support and exercise during cancer care has been recommended as a key part of cancer care when preparing for cancer treatment or surgery.

Exercise carries a small risk of muscle injury, occurring approximately once in every 1,000 hours of walking and <4 times for every 1,000 hours of running.

Exercise carries a risk of delayed onset muscle soreness. Training at a lower level of intensity can decrease this soreness.

The assessment will take several hours three to four on the occasions that they will need to be carried out. The exercise intervention will require a considerable time commitment approximately 6 to 10 hours per week.

Blood sampling can cause a small degree of pain and may lead to bruising, or a slight chance of infection.

There is a risk that persons not involved in the study may see your personal information or that the device it is stored on becomes lost or stolen. A great deal of thought and effort has gone into trying to minimise these risks but there is a small chance that they may occur.

What happens if something goes wrong when I'm taking part in the study? *(May not apply)*

During the study, you will be able to access all of the usual support offered to patients who are undergoing cancer treatment at MMUH.

If any problem arises while taking part in the exercise program, ExWell medical has personnel who are trained to deal with any emergencies that may arise in a safe and professional manner. The home booklet also contains safety advice and tips, and participants taking part solely at home will receive support calls from the research team who will advise them on any queries about their exercise program or safety concerns.

If any problems arise during the study please contact post-doctoral researcher Ms. Shauna Malone or PhD researcher Ms. Aideen Scriney.
For questions about your rights or if you wish to make a complaint while taking part in this study, you can call the Clinical Trials Office on 01 809 2373.

If you decide to no longer participate in this study, you may withdraw at any time without giving a reason. This will not affect the standard of care you receive.

What other treatments are available to me? (May not apply)

This study is not looking into a treatment. The exercise and nutritional elements of the study will be as well as your usual treatment. If you do not wish to take part in this study it will not affect your treatment in any way.

Will I be told the outcome of the study? Will I be told the results of any tests or investigations performed as part of this study that relate to me?

The results of the study will be reported in medical/scientific journals and disclosed at medical/scientific conferences. No information which reveals your identity will be disclosed. All participants will receive a report outlining their results at each testing timepoint, highlighting changes over the pre-operative and post-operative pathways. This report can be accessed on the study website which is available here:

Part 2 – Data Protection

What information about me (personal data) will be used as part of this study? Will my medical records be accessed?

Throughout the study we will collect:

- Participant details -These include: Demographic information including age, medical history, gender, ethnicity, height, weight, clinical characteristics

- Physical Assessments – These will include measures of cardiorespiratory fitness , strength and activity levels
- Self-report/Questionnaire Assessments – These will include self-report measures to assess psychological well-being and stress, self-efficacy and nutritional information.
- Nutrition Assessments
- Treatment-related data- This can include surgical and post-operative data, clinical staging , tumour profile, blood profile, hospital stay, CT scans.
- Interview data – An audio recording of the interview will be taken and transcribed. Questions will relate to your experiences pre and post-surgery and your overall quality of life post-surgery.

Medical records will only be accessed after the point of surgery, in order to record some information like how many days you were in hospital for and if there were any complications from the surgery. Once this data is collected it will be completely Pseudonymised using an identification key. This data will remain completely Pseudonymised from this point.

What will happen to my personal data?

In order to ensure that your personal data is handled properly, we have arrangements in place so that personal data will be processed only as is necessary to achieve the objective of this health research. All personal data will be pseudonymised and any information that could identify you kept separate from the study data and not assessed in any way that could cause you distress or damage any of your personal data.

Personal data will be pseudonymised and kept for a period of 10 years It is necessary to keep it for this length of time to ensure that data is stored in line with the 2018 Health research regulations act.

After this time, all study data will be archived at Dublin City University. Data will then be destroyed. In cases of hard copy data this will involve the shredding and GDPR compliant disposal of all documentation. Any data stored electronically will be deleted and removed from all shared storage drives and laptops. At all timepoints, your data will not leave the State.

Who will access and use my personal data as part of this study?

The investigators who will have access to your anonymised personal data will be: Mr. Jurgen Mulsow, Dr. Lorraine Boran, Dr.Lisa Loughney, Professor Pamela Gallagher, Dr. Claire Timon, Dr. Alexander Eustace, Ms Aideen Scriney, Ms. Shauna Malone, Prof Jan Sorensen and Dr. Denis Collins.

The investigators who will have access to your medical records are:
Mr. Jurgen Mulsow

Anonymised data will be disclosed during the analysis stage to a statistician based in the RCSI.

The data at no point will leave Ireland. We will have to contact your GP to inform them of your involvement in the study.

Will my personal data be kept confidential? How will my data be kept safe?

Your privacy is important to us. We take many steps to make sure that we protect your confidentiality and keep your data safe. Here are some examples of how we do this:

-All information collected as part of this study will be stored anonymously; therefore researchers will be unable to identify you based on the data collected.

-For all data collected, a data protected risk assessment has been carried out by the research staff and found the level of risk associated with this data to be low.

-All research staff involved will ensure the highest standards of research integrity and all researchers will have completed research and academic integrity training , as well as GDPR training.

-Some samples collected will be analysed in Dublin City University. These anonymised samples will be destroyed when analysis has ended and will not be kept for any future research.

-The PI (Mr Muslow) who will have access to medical records will be bound by a professional code of secrecy.

-All data to be published in any journals or articles as a result of this study will be completely anonymous.

However, if something did go wrong the details of the data breach would be immediately reported to the relevant Data protection officers of either MMUH or DCU. Consultation will then occur with the DPO about the nature of the breach and next necessary action.

What is the lawful basis to use my personal data?

By law, we can use your personal information for scientific research (in the public interest). We will also ask for your explicit consent to use your data as a requirement of the Irish Health Research Regulations.

What are my rights?

Should you choose to take part in the research study you will have the following rights:

1. You have the right to withdraw consent to your personal data being used in this research project. You will be able to do this by contacting Ms. Aideen Scriney at aideen.scriney2@mail.dcu.ie

2. You have the right to lodge a complaint with the data protection commissioner

3.You have a right to request access to your data and a copy of it. You will be able to do this by contacting post-doctoral researcher Ms. Shauna Malone or PhD researcher Ms. Aideen Scriney. There is no charge to access this information.

4. You have a right to restrict or object to processing e.g. you don't want your personal data shared but don't mind having it collected and stored.

5. You have a right to have any inaccurate information about you corrected or deleted, unless your request would make it impossible or make it very difficult to conduct the research. You will be able to do this by contacting Ms Shauna Malone or Ms. Aideen Scriney.

6. You have a right to have your personal data deleted, unless your request would make it impossible or make it very difficult to conduct the research. E.g. you wanted to delete their data at the end of the research project just before it is due to be published.

7.You have a right to data portability, meaning you have a right to move their data from one controller to another readable format.

By law you can exercise the following rights in relation to your personal data, unless the request would make it impossible or very difficult to conduct the research. You can exercise these rights by contacting your study Doctor Mr.Jurgen Mulsow email: jmulsow@mater.ie or the MMUH Data Protection Ronan O'Halloran ronanohaloran@mater.ie or DCU Data Protection Officer Martin Ward Phone: 01 700 7476, Ireland. Website: https://www.mater.ie/data-protection/ , https://www.dcu.ie/ocoo/data-protection

Part 3 – Costs, Funding and Approval

Has this study been approved by a research ethics committee?

Yes, this study has been approved by Mater Misericordiae University Hospital (date of approval) and Dublin City University (date of approval) Research Ethics Committee. The Principal Investigator is linked to the MMUH and several of the co-investigators are associated with Dublin City University.

Who is organising and funding this study? Will the results be used for commercial purposes?

This research is being funded by the Irish Research Councils Collaborative Alliances for Societal Challenges (COALESCE) fund for research into policy and society. The research has been organised by a team of researchers based in MMHU, DCU, RSCI and ExWell Medical. Results of this research will not be used for commercial purposes. The PhD researcher Ms. Aideen Scriney is funded by the

Irish Research Council enterprise partnership scheme with Breakthrough Cancer Research.

Is there any payment for taking part? Will it cost me anything if I agree to take part?

No, we are not paying patients to take part in the study. However the costs of the exercise classes are funded as part of this study. (*you will be reimbursed for travel expenses if you need to make any visits that you would not normally have made as part of your routine clinical care).*

Part 4 – Future Research

Will my personal data and/or biological material be used in future studies? (May not apply)

No, none of your personal data or biological material will be used in any future studies as part of open or shared access with third parties. As part of a follow-up study to the PANO trial by PhD researcher Ms. Aideen Scriney, your pseudonymised personal data will be used for the purpose of understanding any long-term impacts of prehabilitation.

Will I be contacted about any future studies?

You will only be contacted by Ms. Aideen Scriney about an interview-based follow-up study, if you consent to us doing so (See Consent form).

Part 5 – Further Information

Who should I contact for information or complaints?

If you have any further questions about the study or if you want to opt out of the study, you can rest assured it won't affect the quality of treatment you get in the future. If you need any further information now or at any time please contact:

Primary Investigator MMUH: Mr. Jurgen Mulsow email: jmulsow@mater.ie

Co-Primary Investigator: Dr. Lorraine Boran email: lorraine.boran@dcu.ie

PhD Researcher: Ms. Aideen Scriney email: aideen.scriney@mail.dcu.ie Phone number: xxxxxx

Postdoctoral Researcher: Ms. Shauna Malone email: shauna.malone25@mail.dcu.ie Phone number: xxxxx

Data Protection Officers:

- Data Protection Officer of MMUH Ronan O'Halloran: email: ronanohalloran@mater.ie
- Data Protection Officer of Dublin City University: Martin Ward, Officer and Deputy Chief Operations Officer Phone: 01 700 7476.

Under GDPR, if you are not satisfied with how your data is being processed, you have the right to lodge a complaint with the Office of the Data Protection Commission, 21 Fitzwilliam Square South, Dublin 2, Ireland. Website: www.dataprotection.ie.If you have concerns about this study and wish to contact an independent person, please contact: The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000, e-mail rec@dcu.ie

Will I be contacted again?

If you would like to take part in this study, you will be asked to sign the Consent Form on the next page. Either Shauna or Aideen will contact you 72 hours after receiving this information leaflet to answer any questions and/or to confirm your participation in this study.

C.2 Informed Consent Document

STUDY NAME: PANO: Perioperative Exercise and Nutrition Optimization Prehabilitation in Cancer Patients with Peritoneal Malignancy **Centre ID:** xxx **Identification Number for study:** xxx
Consent Form
The below section should always be included in consent forms. The consents should be reviewed by the Principal Investigator and research team and amended as appropriate in line with the specific requirements and consents being sought from participants.
There are 17 sections in this form. Each section has a statement and asks you to initial if you agree. The end of this form is for the researchers to complete. **Please ask <u>any</u> questions you may have when reading each of the statements.** **Thank you for participating.** **Please <u>Initial</u> the box if you agree with the statement. Please feel free to ask questions if there is something you do not understand.**

General	**Tick box**
I confirm I have read and understood the **Information Leaflet** for the above study. The information has been fully explained to me and I have been able to ask questions, all of which have been answered to my satisfaction.	
I understand that this study **is entirely voluntary, and if I decide that I do not want to take part, I can stop taking part in this study at any time without giving a reason**. I understand that deciding not to take part will not affect my future medical care.	
I understand that my **medical notes and records** may be looked at by my surgeon Mr.Jurgen Mulsow and his team, Ms. Aideen Scriney, Ms. Shauna Malone and Mater Misercordiae University Hospital dietitians working on the PANO trial (Christina Molloy and Mary McKiernan at Mater Misercordiae University Hospital where it is relevant to the	

research. I agree that these individuals can access my records. I understand that all information will be kept private and confidential and that my name will not be disclosed.	
I understand that I **will not be paid for taking part in this study**.	
I know how to contact the research team if I need to.	
I agree to take part in this research study having been fully informed of the **risks, and benefits** which are set out in full in the information leaflet which I have been provided with.	
I agree to being contacted by researchers by email and phone as part of this research study.	
I agree to being contacted at before and after surgery by phone for the purposes of a short interview by PhD researcher Ms. Aideen Scriney.	
I agree to being contacted six months after completion of this study by PhD researcher Aideen Scriney for a follow-up interview about my experience of the trial.	
Data processing	**Tick box**
I understand that personal information about me will be protected in accordance with the General Data Protection Regulation.	
I understand that there are **no direct benefits to me** from participating in this study.	
I understand that **I can stop taking part in this study** at any time without giving a reason and this will not affect my future medical care.	

The following section of this consent form is relevant if <u>you are collecting biological samples</u> each element of the consent should be reviewed to determine if relevant to the particular research study.		
BIOLOGICAL SAMPLES	**Y**	**N**
I agree to provide up to and including four separate samples of 20mls of blood (4 teaspoons) for use in this study as described in the Information leaflet. The risk of taking samples has been explained to me.		

I agree for my blood samples to be shared with DCU and RCSI for the purpose of this study, as described in this information leaflet.		
I understand that my blood samples will be disposed of in a lawful and respectful way.		
I understand that I can **stop taking part in** this study and **request withdrawal of my blood samples** and request that my blood samples are destroyed at any time before my samples become anonymous, without any negative impact on my medical care.		
I understand that I will not be paid for the use of my blood samples.		

Patient Name (Block Capitals) Patient Signature Date

Witness Name (Block Capitals) Witness Signature Date

To be completed by the Principal Investigator or nominee.

I, the undersigned, have taken the time to fully explain to the above patient the nature and purpose of this study in a way that they could understand. I have explained the risks and possible benefits involved. I have invited them to ask questions on any aspect of the study that concerned them.
I have given a copy of the information leaflet and consent form to the participant with contacts of the study team

Researcher name

Title and qualifications

Signature

Date

C.3 Semi-Structured Interview Topic Guide for Preoperative Interviews

Interview to capture your journey so far since diagnoses
First time you might think about - may bring up emotions. we are here to listen and support and will call later/check is someone at home if needed
Quiet place - nobody in room
Anon (all identifying info erased)

1) Intervention Group Before Surgery Topic Guide:

Topic 1: Feelings about exercise
a. Can you tell me about your experience of the exercise programme overall?
b. Were there any aspects of the exercise programme you enjoyed?
c. Were there any aspects of the exercise that you did not like?
d. Is there anything else you would like to add about your experience or things we could improve on?

Topic 2: Feeling about diet
a. Can you tell a bit about your experience of dietary support?
b. Were there any aspects of the dietary support you enjoyed?
c. Were there any aspects of the dietary support that you did not like?
d. Do you have any observations about your experience with the programme
i: Prompt: Mental and Physical wellbeing, has this changed
e. Is there anything else you would like to add about your experience or things we could improve on?

Topic 3. Perception of Surgery
a. How are you feeling about your upcoming surgery?
i: Prompts if not explored – are you "confident, worried, just want it over" etc.
b. Can you describe any feelings or expectations you may have about your recovery?
i: Prompt- expectations about how they will experience recovery and return to "normal"

Topic 4: Cognitive health

Sometimes some people with cancer will report changes in their concentration, attention in memory in their day to day life, we want to explore this topic more.

a. Can you tell me a bit about your experience with things like your memory, attention and concentration since your diagnosis?

i. Prompt: If you did notice any changes, how are these making you feel? (worry, concern etc)

ii. Prompt: When did you first notice these issues?

b. How do you think your friends and family would describe things like your memory, attention and concentration?

c. How would you describe your overall thoughts / feelings at the moment?

Topic 5: Attitudes towards own health and behaviour change

a. How would you describe your overall health/energy etc at the moment?

b. How would you describe your quality of life?

c. What do you think is important for you to become healthy after surgery?

On starting: ID, Initials, Interviewer, Day and Time

2) Control Group Before Surgery Topic Guide:

Topic 1: Experience before surgery

a. Can you tell me about any ways that you may have prepared for your upcoming surgery?

i. Prompt: Physically and Mentally, Information seeking – Has this changed

Topic 2. Perception of Surgery

a. How are you feeling about your upcoming surgery?

i. Prompts if not explored – are you "confident, worried, just want it over" etc.

b. Can you describe any feelings or expectations you may have about your recovery?

i. Prompt- expectations about how they will experience recovery

Topic 3: Cognitive health

Sometimes some patients will report changes in their concentration, attention in memory, we want to explore this topic more. This can include even slight day to day changes.

a. Can you tell me a bit about your experience with things like your memory, attention and concentration since your diagnosis?

i. Prompt: If you did notice any changes, how are these making you feel? (worry, concern etc)

ii. Prompt: When did you first notice these issues?

iii. Prompt: How have you coped with these issues?

b. How do you think your friends and family would describe things like your memory, attention and concentration?

c. How would you describe your overall thoughts / feelings at the moment?

Topic 4: Attitudes towards own health and behaviour change

a. How would you describe your overall health/energy etc at the moment?

b. How would you describe your quality of life?

c. What do you think is important for you to become healthy after surgery?

Anything else you would like to add?

C.4 Sample Extract of Thematic Map for Preoperative Thematic Analysis



Appendix D: Chapter 5 Study Materials

D.1 Semi-structured Interview Topic Guide Postoperative Interview

1) Intervention Group After Surgery Topic Guide:

Theme 1: Feelings about Recovery

- Can you tell me about how the experience of recovery has been for you?
  - Prompt: How have you been feeling physically? Mobility? Energy? Lethargy?
  - Prompt: How have you been feeling emotionally? Prompt: How is your ability to take part in daily activities?
- Can you tell me about any new or unexpected experiences since your surgery?
  - Prompt: Prompt: Issues/ Post-op complications/Mental Health : Relief? Apprehension? Expectations?
- What do you consider important to aid in your recovery?

Theme 2: Impact on Health and quality of life

- How would you describe your day to day life since the operation?
  - Shopping, going for walks, going to work
- Have you returned to any daily or leisure activities you used to take part in before your surgery?
  - Prompt: Can you tell me a bit more about these?
- Has your cancer experience caused you to change your health behaviours in any way?

Theme 3: Reflection on the Intervention Experience

- How would you describe your experience overall with exercise intervention?
  - Prompt: Both physically and emotionally
- How was your experience of adapting your lifestyle to include the intervention?
  - How did you take part in the intervention? (if not stated)
- Did your friends or family notice a change in your physical activity?
  - Prompt: This can include daily activities not just physical structured exercise
- Can you describe your experience with dietary support intervention?
- How was your experience of adapting your lifestyle to include the intervention?
  - Did you face any challenges? Ie. cost, time for meal prep, family
- Did you notice any changes as a result of nutrition support? (Prompt for nausea, bowel issues, appetite etc)
- Have any comments on how we could have improved upon the interventions?

Theme 4: Reflection on experience of cognition from pre to post surgery

The next few questions I am going to ask you are about how you feel about your memory attention and focus, in research this is known as your cognitive function.

- When we first spoke, I asked you about your memory, attention and concentration. Can you tell me about your experience of this since your surgery
- Reflecting on your experiences from diagnosis to today, have you noticed any cognitive changes overall?
  - Prompts: Do you read books? Do you remember where you leave objects? Can you focus on a task for a long time? Can you remember appointments
  - Have any of the above deteriorated since surgery? (if not stated)

c. Can you tell me about any specific areas that may have been affected?
    - Prompt: How have you coped with these experiences?
    - Prompt: If you did notice any changes, how are these making you feel? (worry, concern etc)

d. Would you say that your friends or family have noticed any changes?

e. Do you think you would have/ could benefit from support in these areas?
    - Prompt: memory aids, professional support etc.

Theme 5: Support during the cancer experience

- Reflecting on your experience, do you think you were prepared for the experience of recovery?
- Did you engage in any information seeking about your surgery or recovery?
- Were you made aware of any supports available to you post-surgery?
- Do you think you people would benefit from an increased awareness about the experience of recovery?
    - Prompt: what could this look like

2) Intervention Group After Surgery Topic Guide:

Theme 1: Feelings about Recovery

- Can you tell me about how the experience of recovery has been for you?
    - Prompt: How have you been feeling physically? Mobility? Energy? Lethargy?
    - Prompt: How have you been feeling emotionally? Prompt: How is your ability to take part in daily activities?
- Can you tell me about any new or unexpected experiences since your surgery?
    - Prompt: Prompt: Issues/ Post-op complications/Mental Health: Relief? Apprehension? Expectations?
- What do you consider important to aid in your recovery?

Theme 2: Impact on Health and quality of life

- How would you describe your day-to-day life since the operation?
    - Shopping, going for walks, going to work
- Have you returned to any daily or leisure activities you used to take part in before your surgery?
    - Prompt: Can you tell me a bit more about these?
- Has your cancer experience caused you to change your health behaviours in any way?

Theme 3: Reflection on the Diet and Exercise Experience

a) Did you make any changes to your day-to-day diet or exercise during your recovery?

    i) Prompt: -if so, can you tell me a bit more about these?

b) Could you tell me about any changes in your physical function since surgery?

    i) Daily function, day to day physicality, eating habits

c) Do you think that patients would benefit from support in these areas generally?

Theme 4: Reflection on experience of cognition from pre to post surgery

The next few questions I am going to ask you are about how you feel about your memory attention and focus, in research this is known as your cognitive function.

- When we first spoke, I asked you about your memory, attention and concentration. Can you tell me about your experience of this since your surgery
- Reflecting on your experiences from diagnosis to today, have you noticed any cognitive changes overall?
    - Prompts: Do you read books? Do you remember where you leave objects? Can you focus on a task for a long time? Can you remember appointments
    - Have any of the above deteriorated since surgery? (if not stated)

c. Can you tell me about any specific areas that may have been affected?
    - Prompt: How have you coped with these experiences?
    - Prompt: If you did notice any changes, how are these making you feel? (worry, concern etc)

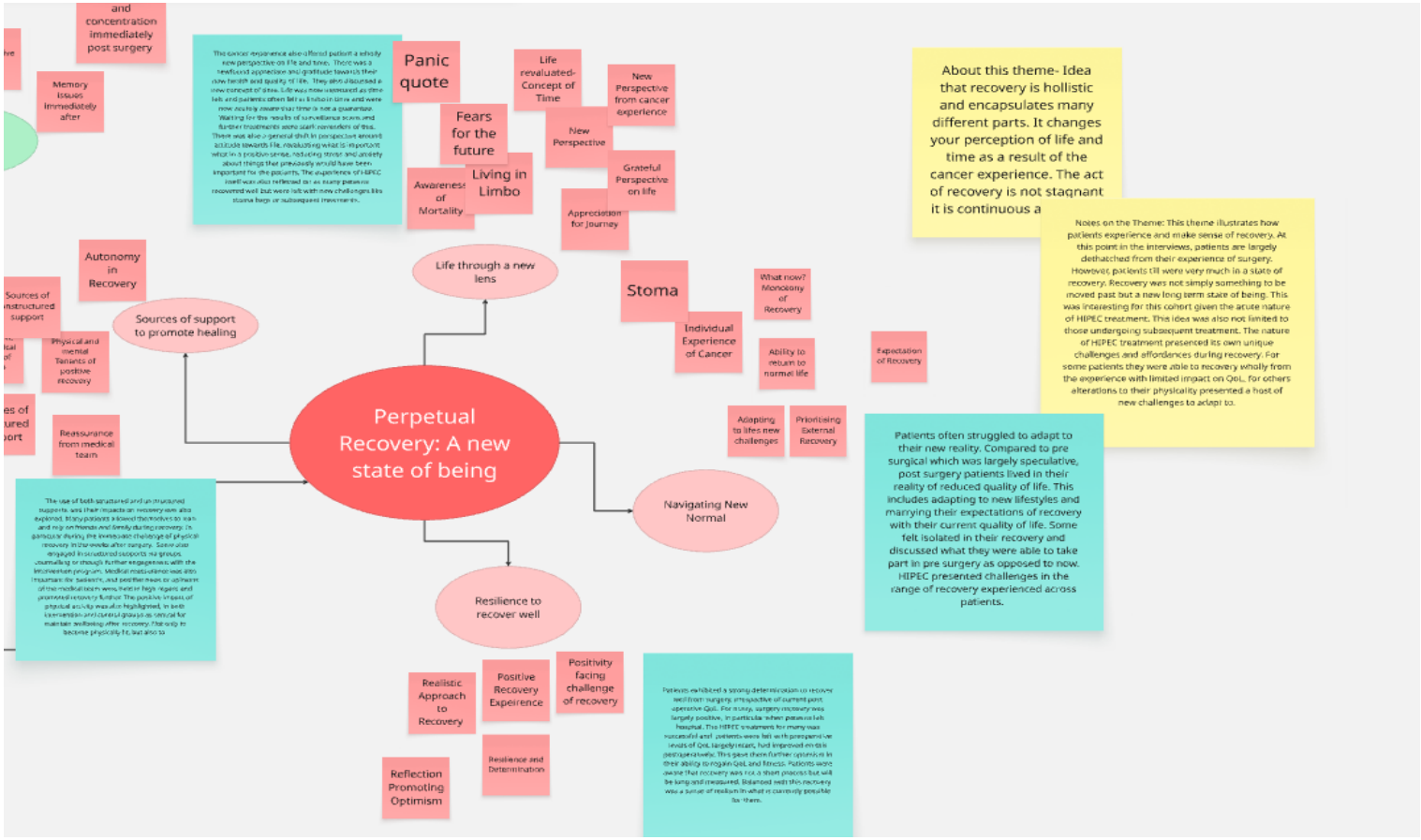
d. Would you say that your friends or family have noticed any changes?

e. Do you think you would have/ could benefit from support in these areas?
    - Prompt: memory aids, professional support etc.

Theme 5: Support during the cancer experience

- Reflecting on your experience, do you think you were prepared for the experience of recovery?
- Did you engage in any information seeking about your surgery or recovery?
- Were you made aware of any supports available to you post-surgery?
- Do you think you people would benefit from an increased awareness about the experience of recovery?
    - Prompt: what could this look like?

D.2 Sample Extract of Thematic Map for Postoperative Thematic Analysis



Appendix E: Chapter 6 Study Materials

E.1 Plain Language Statement Follow-up Study (Chapter 6)

Plain Language Statement For Participants

Introduction to the Research Study

This research titled " PreCog: Exploring the impact and expression of pre-treatment cancer related cognitive impairment in patients to improve postoperative cognitive function - Study 2" is being conducted as part of the PhD thesis of PhD candidate and principal investigator, Miss Aideen Scriney at Dublin City University (DCU) School of Psychology. This PhD research is under the supervision of Dr. Lorraine Boran (DCU), Dr. Lisa Loughney (RCSI) and Professor Pamela Gallagher (DCU). This work is a continuation of research that commenced during your time with the PANO trial. This work is being funded by the Irish Research Council in partnership with Breakthrough cancer research.

What is this research about?
You have been contacted about this research study as you previously took part in "The PANO trial:xxxxxx" and indicated that you consent to being contacted about follow-up research. As you may be aware, the PANO trial aimed to understand the effect of exercise and nutrition before and after surgery for patients who underwent CRS-HIPEC treatment. Within the PANO trial, we used questionnaires to look at things like your quality of life, self-efficacy and your cognitive function (your memory, attention and concentration). You also may have taken part in two interviews where you talked about your experiences before and after your treatment. This study wants to look at these questions again, to learn about your experiences with these things 6 months later. We also want to add to this research by also giving you a short cognitive assessment (this looks at things like your memory, concentration and attention). We advise that you read the contents of the plain language statement carefully and decide whether or not you would be interested in taking part in this research.

Why is this research being conducted?
This research is being conducted as currently we know very little about what changes people may experience to their cognitive function before, during and after treatment for cancer. We also know very little about the experiences of patients who undergo the CRS-HIPEC procedure. Learning more about these two aspects could potentially help the support patients undergoing CRS-HIPEC treatment in the future.

What will I be asked to do?
If you agree to participate, you will be asked to take part in a short audio recorded interview about your experience of recovery as well as some written questionnaires about your quality of life, self-efficacy and cognitive function. You will also be asked to take part in a short cognitive test to assess your cognitive function. The full assessment will take approximately one hour to complete. We will arrange for the assessment to take place at a time and location that is convenient for you. Ideally, assessments will take place in person. All information you provide during the assessment will be made pseudonymous meaning the information will not be able to be linked to you personally by anyone other than principal investigator Aideen Scriney. After analysis, all data will be then made completely anonymous.

How will my privacy be protected?

We are taking a number of measures to ensure your privacy during your participation in our study.

- All data collected during the study will be pseudo-anonymised, which means that only principal investigator Aideen Scriney will be able to trace any data back to you.
- Once data is analysed it will then be made completely anonymous.
- All data will be collected and stored in line with GDPR guidelines.
- All study data will be stored in a secure location at Dublin City University or on a secure encrypted drive.
- The key to re-identify data back to you will only be accessed by principal investigator, Aideen Scriney.

Privacy Notice

- The data controller for the present study is DCU, the data processor is Aideen Scriney.
- The DCU Data Protection Officer is Mr. Martin Ward (data.protection@dcu.ie Ph.: 7005118 / 7008257)
- For the purpose of this project, personal health data is being processed in the form of information you may provide us about your healthcare experiences and cognitive function. This data is being processed for the purpose of completion of the study.

- You have a right to access your own personal data, if you wish to do so you can do this before data analysis occurs and data is anonymised. If you wish to do so please contact aideen.scriney2@mail.dcu.ie
- Confidentiality of information can only be protected within the limitations of the law - i.e., it is possible for data to be subject to subpoena, freedom of information claim or mandated reporting by some professions.

How long will data be retained?

All study data is being retained for a period of 10 years in line with GDPR guidance on data for research purposes.

Are there any risks to taking part?

This risk to you should you agree to participate is minimal. There is a chance that you may decide to self-disclose emotional information with the researcher, if this is the case the researcher will offer to do a check up call with you to make sure you have not been negatively impacted. As part of the research, you will be also asked to take part in a short cognitive assessment by the PhD researcher, in some cases it may be necessary to discuss the results of this assessment with a medical professional within the research team and if deemed necessary your wider care team/GP.

Are there any benefits to taking part?

If you choose to take part in this study, you will be contributing to a much needed area of research that has the benefit to help patients who undergo CRS-HIPEC treatment in the future.

Do I have to take part?

You are in no way obligated to take part in this study and if you choose not to do so, it will not affect your care in any way. If you decide to take part, you are free to withdraw your data from the study at any point before data analysis has occurred.

If you have any other questions or concerns, please contact aideen.scriney2@mail.dcu.ie , for further information.

Principal Investigator: Aideen Scriney email: aideen.scriney2@mail.dcu.ie
Primary Supervisor: Dr. Lorraine Boran email: Lorraine.boran@dcu.ie

You have the right to lodge a complaint with the *Irish Data Protection Commission.* regarding the handling of your personal data, should you wish to do so.

If participants have concerns about this study and wish to contact an independent person, please contact:

The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000, e-mail rec@dcu.ie

E.2 Follow-Up Study (Chapter 6) Consent Form

Informed Consent Document

Research Study Title

Title: "PreCog: Exploring the impact and expression of pre-treatment cancer related cognitive impairment in patients to improve postoperative cognitive function - Study 2", Dublin City University, School of Psychology

Clarification of the purpose of the research
Personal data in the form of data concerning health will be collected and processed as part of this research project to ensure completion of the project. The named data controller is Dublin City University and the named data processor is Miss. Aideen Scriney.

Confirmation of particular requirements as highlighted in the Plain Language Statement
Requirements of my participation included: Involvement in an audio recorded interview, completion of questionnaires and completion of cognitive assessment.

Participant – please complete the following (Circle Yes or No for each question)

I have read the Plain Language Statement (or had it read to me)	*Yes/No*
I understand that my participation in this research is voluntary	*Yes/No*
I understand the information provided	*Yes/No*
I understand the information provided in relation to data protection	*Yes/No*
I understand the arrangements made to protect my confidentiality and the legal limitations of these	*Yes/No*
I understand that it may be necessary for the researcher to discuss the results of my assessment with a clinical professional	*Yes/No*
I have had an opportunity to ask questions and discuss this study	*Yes/No*
I have received satisfactory answers to all my questions	*Yes/No*
I am aware that my interview will be audiotaped	*Yes/No*

Signature:

I have read and understood the information in this form. My questions and concerns have been answered by the researchers, and I have a copy of this consent form. Therefore, I consent to take part in this research project

Participants Signature: _____

Name in Block Capitals: _____

Witness: _____

_____

Date: _____

_____

Debriefing Statement

Thank you for taking part in this research study. The purpose of this study was to explore the long term effects of CRS-HIPEC treatment, as well as exercise and nutrition on cognitive function and quality of life after 6 months. As part of the study you were asked to take part in an audio taped interview, answer written questionnaires and take part in a short assessment of your cognitive function (memory, attention and concentration). This data will be analysed as part of the PhD research thesis of the primary investigator, Aideen Scriney.

What will happen to my data?
Your data once collected will be analysed and interview data will be transcribed. At this time all identifiable data will be removed from interview transcripts. Once analysed all data will be made completely anonymous. The final data will be reported as part of a PhD thesis of primary investigator, Aideen Scriney. Data may also be used at academic conferences and at patient outreach events. Data may also be published as an journal article in a relevant academic article. All published data will be completely anonymous.

Can I withdraw my data?
If you wish to withdraw your data, please contact aideen.scriney2@mail.dcu.ie . Data can only be withdrawn up to the point that analysis occurs, at which point all data will be completely anonymous.

[illegible]his research we spoke with you about issues you may have with things like [illegible], concentration and attention. If you feel concerned by your experiences of

these, we suggest that you contact your multidisciplinary care team or general practitioner to discuss this with a medical professional.

Sometimes discussing aspects of past cancer treatments can be distressing, if you have experienced any distress as a result of this research. Below are a list of helplines that may be of benefit to you:

Irish Cancer Society Support Line: 1800 200 700

ARC Cancer Support Phone line: 01 215 0250

We would like to take this opportunity again to thank you for your valuable support to this area of research and wish you all the best on your survivorship journey.

If you would like to contact someone about this research, please contact aideen.scriney2@mail.dcu.ie

If participants have concerns about this study and wish to contact an independent person, please contact:

The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000, e-mail rec@dcu.ie

Mater Misericordiae University Hospital

E.4 Montreal Cognitive Assessment Training Certificates

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Eirinn



MoCA
COGNITIVE ASSESSMENT

CERTIFICATE OF COMPLETION

This certificate acknowledges that

Aideen Scriney

has successfully completed a one hour training and certification to administer and score the Montreal Cognitive Assessment, MoCA. Only health professionals with expertise in cognition can interpret test results.

Completion date: 2025/02/06

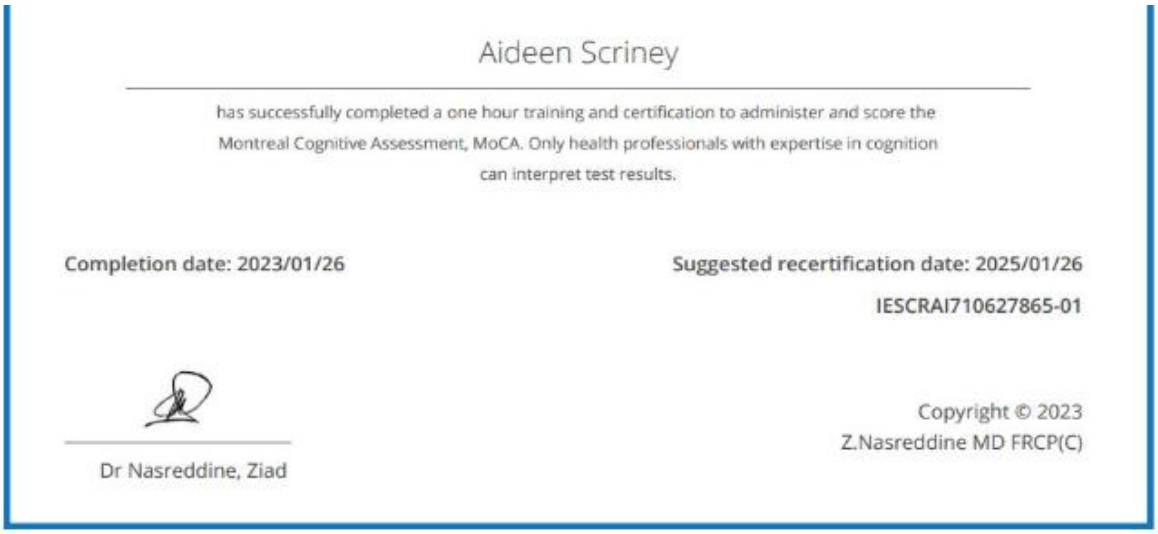
Suggested recertification date: 2027/02/06

16504026

IESCRAI710627865-02

Dr Nasreddine, Ziad

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Z.Nasreddine MD FRCP(C)



Aideen Scriney

has successfully completed a one hour training and certification to administer and score the Montreal Cognitive Assessment, MoCA. Only health professionals with expertise in cognition can interpret test results.

Completion date: 2023/01/26

Suggested recertification date: 2025/01/26

IESCRAI710627865-01

Dr Nasreddine, Ziad

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Appendix F: Ethical Approvals

F.1 DCU Research Ethics Committee (REC) DCUREC/2022/158 Ethical Approval Chapters 4 and 5

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

DCU

Aideen Scriney
DCU School of Psychology

11th October 2022

REC Reference: **DCUREC/2022/158**

Proposal Title: **PreCog: Exploring the impact and expression of pre-treatment cancer related cognitive impairment in patients to improve postoperative cognitive function**

Applicant(s): **Aideen Scriney, Dr Lorraine Boran, Dr Lisa Loughney, Prof. Pamela Gallagher**

Dear Colleagues,

Thank you for your application to DCU Research Ethics Committee (REC). Further to full committee review, DCU REC is pleased to issue approval for this research proposal.

DCU REC's consideration of all ethics applications is dependent upon the information supplied by the researcher. This information is expected to be truthful and accurate. Researchers are responsible for ensuring that their research is carried out in accordance with the information provided in their ethics application.

Materials used to recruit participants should note that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee. As part of DCU REC's ongoing monitoring process, during your research you may be asked to provide DCU REC with a progress report. Should substantial modifications to the research protocol be required at a later stage, a further amendment submission should be made to the REC.

Yours sincerely,

Dr. Melrona Kirrane
Chairperson
DCU Research Ethics Committee

DCU
Research & Innovation

Taighde & Nuálaíocht Tacaíocht
Ollscoil Chathair Bhaile Átha Cliath,
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Note: Please retain this approval letter for future publication purposes (for research students, this includes incorporating the letter within their thesis appendices).

F.2 DCU Research Ethics Committee (REC) DCUREC/2023/047 Ethical Approval Chapter 6

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

Dr Lorraine Boran
School of Psychology

17h May 2023

REC Reference: **DCUREC/2023/047**

Proposal Title: **PreCog: Exploring the impact and expression of pre-treatment cancer related cognitive impairment in patients to improve postoperative cognitive function - Study 2**

Applicant(s): **Dr Lorraine Boran, Ms Aideen Scriney, Dr Lisa Loughney, Prof Pamela Gallagher**

Dear Colleagues,

Thank you for your application to DCU Research Ethics Committee (REC). Further to full committee review, DCU REC is pleased to issue approval for this research proposal.

DCU REC's consideration of all ethics applications is dependent upon the information supplied by the researcher. This information is expected to be truthful and accurate. Researchers are responsible for ensuring that their research is carried out in accordance with the information provided in their ethics application.

Materials used to recruit participants should note that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee. As part of DCU REC's ongoing monitoring process, during your research you may be asked to provide DCU REC with a progress report. Should substantial modifications to the research protocol be required at a later stage, a further amendment submission should be made to the REC.

Yours sincerely,

Dr. Melrona Kirrane
Chairperson
DCU Research Ethics Committee

DCU Research & Innovation

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Note: Please retain this approval letter for future publication purposes (for research students, this includes incorporating the letter within their thesis appendices).

Appendix G: List of Publications and Conference Attendance Realted to the Thesis

Conferences Attendance & Presentations: Aideen Scriney

Title	Conference & Location	Date
Poster: The impact of prehabilitation interventions on affective and functional outcomes for young to midlife adult cancer patients: a systematic review.	International Society for Behavioural Nutrition and Physical Activity Annual Meeting (Online)	18/5/22
Preparing for Treatment Mind and Body: Applying Systematic Evidence to Explore Affective Outcomes During Cancer Prehabilitation: Oral Presentation	Psychological Society of Ireland Annual Conference: Midlands Park Hotel, Portlaoise	11/11/22
Posters X2 PreCog: Exploring the Impact and Expression of Pre-treatment Cancer Related Cognitive Impairment (CRCI) in patients to Support Postoperative Cognitive Function: Study Protocol Patient Experiences of Wellbeing and Cancer Related Cognitive Impairment during a bimodal Prehabilitation Programme: Preliminary Findings	EBPOM World Congress of Prehabilitation, University College London	July 2023
Poster: PreCog: Exploring the Impact and Expression of Pre-treatment Cancer Related Cognitive Impairment(CRCI) in Patients to Support Postoperative Cognitive Function: Study Protocol	Neuroscience Society of Ireland Annual Conference, RCSI	August 2023
Poster: The Impact of Public Patient Involvement in a Randomised Control Trial Exploring Bimodal Exercise and Nutrition Prehabilitation among Patients with Peritoneal Malignancy Scheduled for CRS-HIPEC and Associated Research.	Engaged Research Festival 2023, Dublin City University	December 2023

Poster: Exploring the Impact and Expression of Pre-treatment Cancer Related Cognitive Impairment (CRCI) in Patients to Support Postoperative Cognitive Function: Study Protocol & Preliminary Findings	Irish Association for Cancer Research Satellite Meeting 2024	February 2024
Poster Patient Experiences of Wellbeing and Cancer Related Cognitive Impairment during a bimodal Prehabilitation Programme: Preliminary Findings	38th Annual Conference of the European Health Psychology S Cognitive Neuroscience Society Annual Meeting	Portugal, September 2024
Poster: Psychological Risk Factors Associated with Pretreatment Cancer Related Cognitive Impairment: A Systematic Review	Cognitive Neuroscience Society Annual Meeting	Boston, April 2025

Publications:

Year	Reference
2022	The impact of prehabilitation interventions on affective and functional outcomes for young to midlife adult cancer patients: a systematic review. Scriney, A., Russell, A., Loughney, L., Gallagher, P., & Boran, L. (2022). Psycho-Oncology, 31(12), 2050-2062.
2025 (Accepted, pending final proof)	Scriney, A., Gurren, L., Gallagher, P., Loughney, L., & Boran, L. Psychological Factors Associated with Objective and Subjective Pretreatment Cancer-Related Cognitive Impairment: A Systematic Review. *Frontiers in Psychology*, *16*, 1682455.
2024 RTE Brainstorm	How Can We Prevent "Chemobrain" for Cancer Patients? RTE Brainstorm, Online Publication https://www.rte.ie/brainstorm/2024/0524/1450563-cancer-chemotherapy-chemobrain-treatment-prehabilitation/