THE EVALUATION OF A WEB-BASED COGNITIVE REHABILITATION THERAPY INTERVENTION IN ADULT CANCER SURVIVORS

By

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ABSTRACT

Cancer-related cognitive impairment (CRCI) associated with diagnosis and treatment is frequently reported by cancer survivors and has been well documented in the literature. A subset of cancer survivors reports problems with memory, attention, processing speed, executive functioning and other cognitive domains prior to, during, or after completion of primary curative treatments. These cognitive changes can reduce long-term daily functioning and quality of life (QoL). Cognitive rehabilitation therapy (CRT) has been demonstrated to be an effective method for mitigating symptoms of cognitive dysfunction through the re-attainment of cognitive skills lost or altered due to injury and can improve functioning on everyday tasks.

The purpose of this research was to adapt an existing CRT program for cancer survivors, ReCog, into a web-based version, eReCog, and evaluate its efficacy in two studies: a pilot study (Study One) and a randomised controlled trial (Study Two). The primary outcome variable in both studies was subjective cognitive functioning, with secondary outcomes being objective cognitive functioning, QoL, psychological distress, and illness perceptions. A secondary aim was to examine the degree to which participants engage in web-based interventions by investigating a new method for quantifying engagement that examines the number of activities completed in the program modules rather than utilising typical methods described in the literature. The final aim of this research project was to investigate potential mediating factors by assessing the psychological needs of competence, autonomy, and relatedness through a Self-Determination Theory (SDT) framework. SDT is a macro theory of human motivation, which purports that self-motivation stems from the extent to which an individual is able to meet innate psychological needs within their social network. As
such, human beings strive to maximise their potential through self-movement in order to increase their behavioura...al functioning over time. These psychological needs have previously been...d to mediate the relationships between intervention programs and improved physical activity, communication, and QoL in cancer survivors.

Firstly, it was hypothesised participants in the intervention program would demonstrate significant improvements in subjective cognitive functioning compared to waitlist groups in both studies. Secondly it was expected treatment participants would show improvements on objective cognitive functioning and perform better on outcome measures than waitlisted groups. Lastly it was hypothesised that the effects of treatment on subjective cognitive functioning would be mediated by the variables of competence, autonomy, and relatedness.

To test these hypotheses, Study One was conducted with a cohort of cancer survivors, community dwelling adults, and a waitlist non-cancer group, followed by Study Two with cancer survivors assigned to intervention and waitlist groups. A few statistically significant interaction effects on measures of subjective cognitive functioning were found, although many of the improvements were observed in the waitlisted groups as well albeit to a smaller degree. Both improvements and deteriorations were observed on some domains of objective cognitive functioning in both intervention and waitlist groups. Improved QoL was observed in both the intervention and waitlist group in the RCT. Significant changes in competence, autonomy and relatedness were not observed in either study indicating these constructs were not factors that mediated the relationship between treatment and outcome variables. Overall, these results suggest that brief 4-week online cognitive rehabilitation has the potential to improve self-reported cognitive functioning and QoL in cancer survivors.
STATEMENT OF ORIGINALITY

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

Mary E. Mihuta
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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>ii</td>
</tr>
<tr>
<td>STATEMENT OF ORIGINALITY</td>
<td>iv</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>v</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vii</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>viii</td>
</tr>
<tr>
<td>LIST OF APPENDICES</td>
<td>ix</td>
</tr>
<tr>
<td>LIST OF ABBREVIATIONS</td>
<td>x</td>
</tr>
<tr>
<td>STATEMENT ABOUT THIS THESIS</td>
<td>xiii</td>
</tr>
<tr>
<td>ACKNOWLEDGMENT OF PAPERS INCLUDED IN THIS THESIS</td>
<td>xiv</td>
</tr>
<tr>
<td>CHAPTER I: INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>CHAPTER II: REVIEW OF THE LITERATURE</td>
<td>5</td>
</tr>
<tr>
<td>Cancer Survivorship in Australia</td>
<td>5</td>
</tr>
<tr>
<td>Cancer-Related Cognitive Impairment</td>
<td>9</td>
</tr>
<tr>
<td>Objective and Subjective Cognitive Function</td>
<td>22</td>
</tr>
<tr>
<td>Cognitive Rehabilitation for Cancer Survivors</td>
<td>26</td>
</tr>
<tr>
<td>Web-Based Interventions in Cancer Survivorship</td>
<td>37</td>
</tr>
<tr>
<td>Psychological Mechanisms and Self-Determination Theory</td>
<td>47</td>
</tr>
<tr>
<td>Current Study</td>
<td>50</td>
</tr>
<tr>
<td>CHAPTER III: PROJECT METHODS</td>
<td>53</td>
</tr>
<tr>
<td>Development of eReCog</td>
<td>54</td>
</tr>
<tr>
<td>Study One Methods (Pilot)</td>
<td>63</td>
</tr>
<tr>
<td>Study Two Methods (RCT)</td>
<td>77</td>
</tr>
<tr>
<td>CHAPTER IV: EFFICACY OF A WEB-BASED COGNITIVE REHABILITATION INTERVENTION FOR ADULT CANCER SURVIVORS: A PILOT STUDY</td>
<td>81</td>
</tr>
<tr>
<td>STATEMENT OF CONTRIBUTION TO CO-AUTHORED PAPER</td>
<td>82</td>
</tr>
<tr>
<td>Abstract</td>
<td>83</td>
</tr>
<tr>
<td>Introduction</td>
<td>84</td>
</tr>
<tr>
<td>Methods</td>
<td>87</td>
</tr>
<tr>
<td>Results</td>
<td>94</td>
</tr>
<tr>
<td>Discussion</td>
<td>100</td>
</tr>
<tr>
<td>References</td>
<td>106</td>
</tr>
</tbody>
</table>
LIST OF TABLES

Table 2.1 Cognitive rehabilitation interventions for adult cancer survivors ............... 29
Table 3.1 WebNeuro tasks and outcome measurements .............................................. 70
Table 4.1 Demographic and medical characteristics .................................................... 95
Table 4.2 Effect sizes, means (and SD) for outcome variables ................................... 97
Table 5.1 Baseline demographic and medical characteristics ..................................... 124
Table 5.2 Effect sizes, means (and SD) for outcome variables ................................... 125
Table 6.1 Engagement points by module .................................................................. 143
Table 6.2 Participant demographic data and medical characteristics ......................... 146
Table 6.3 Module engagement for intervention participants ....................................... 148
Table 6.4 Email contact with facilitator during participation ..................................... 149
Table 7.1 Correlations between PCI and other outcome variables.............................. 168
Table 7.2 FACT-Cog 3 PCI means (and SD) for CRT and CT interventions ............. 170
Table 7.3 Clinical impairment by group at three time points ..................................... 172
LIST OF FIGURES

Figure 1.1 Schematic overview of the content and structure of the thesis ......................... 4
Figure 2.1 COSA model for wellness in cancer survivorship .............................................. 8
Figure 2.2 Conceptual model of chemotherapy-related changes in cognitive function 18
Figure 2.3 Proposed model of objective and subjective cognitive impairment ................. 25
Figure 3.1 Timeline and development process for adapting the FOCUS intervention to web-based format ........................................................................................................... 57
Figure 3.2 Webpage for creating a sequence of learning activities .................................. 58
Figure 3.3 Welcome page to Module One of eReCog ....................................................... 59
Figure 3.4 Example page where participants type in personalised responses .................. 60
Figure 3.5 Downloadable homework practice sheets ....................................................... 61
Figure 3.6 Relaxation audio file embedded in modules .................................................... 62
Figure 4.1 Participant flowchart ...................................................................................... 89
Figure 5.1 Participant CONSORT flowchart ................................................................. 123
Figure 7.1 Path diagram showing direct and indirect effects expected in a mediating relationship .............................................................................................................. 161
LIST OF APPENDICES

APPENDIX A ReCog Program Content ................................................................. 232
APPENDIX B Broadcast Email Study One ................................................................. 233
APPENDIX Recruitment Flyer .................................................................................. 234
APPENDIX D Initial Phone Screening Interview ......................................................... 235
APPENDIX E Information Sheet .............................................................................. 238
APPENDIX F Consent Form ...................................................................................... 241
APPENDIX G Broadcast Email Study Two ................................................................. 242
APPENDIX H Study One Questionnaire Results ......................................................... 243
APPENDIX I Study Two Questionnaire Results ......................................................... 244
APPENDIX J Study One WebNeuro Results ............................................................... 245
APPENDIX K Study Two WebNeuro Results ............................................................. 246
LIST OF ABBREVIATIONS

ADT = androgen deprivation therapy
ANOVA = analysis of variance
BADL = basic activities of daily living
BAPM = Brief Assessment of Prospective Memory
BCC = Behaviour Change Consortium
BCNA = Breast Cancer Network Australia
BIPQ = Brief Illness Perception Questionnaire
BRIEF = Behavioural Rating Inventory of Executive Function
BSC = breast cancer survivor
CBMEM = Cognitive Behavioural Model of Everyday Memory
CBT = cognitive behavioural therapy
CFQ = Cognitive Failures Questionnaire
CogFun = cognitive function scale of the EORTC QLQ-C30
COSA = Clinical Oncology Society of Australia
CRCI = cancer-related cognitive impairment
CRT = cognitive rehabilitation therapy
CT = cognitive training
DNA = deoxyribonucleic acid
EF = executive functioning
EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire
eReCog = Web-based Responding to Cognitive Concerns
FACT-Cog 3 = Functional Assessment of Cancer Therapy Cognitive Function
fMRI = function magnetic resonance imaging
IADL = instrumental activities of daily living
InfoProc = information processing efficiency
IQ = intelligence quotient
K10 = Kessler Psychological Distress Scale
LHRH = luteinizing hormone-releasing hormone
MAAT = Memory and Attention Adaptation Training
MASQ = Multiple Ability Self-Report Questionnaire
MSEQ = Memory Self-Efficacy Questionnaire
NIH = The National Institutes of Health
NPT = neuropsychological training
OCFI = Overall Cognitive Function Index
OCFI-I = Overall Cognitive Function Index – Impaired
OCFI-NI = Overall Cognitive Function Index – Not impaired
OTH = comments from others
PAOFI = Patient’s Assessment of Own Functioning
PASAT = Paced Auditory Serial Addition Test
PC = computer training
PCA = perceived cognitive abilities
PCI = perceived cognitive impairment
PM = prospective memory
PMP = pseudomyxoma peritonei
POMS = Profile of Mood Status
QoL = quality of life
RBANS = Repeatable Battery for Assessment of Neuropsychological Status
RCT = randomised controlled trial
ReCog = Responding to Cognitive Concerns
RS = response speed
SCC = squamous cell carcinoma
SD = standard deviation
SDT = Self-Determination Theory
ST = supportive therapy
VM = verbal memory
WCST = Wisconsin Card Sorting Test
WM = working memory
STATEMENT ABOUT THIS THESIS

The presentation of this thesis is in a format that contains a series of papers that have been submitted for publication. There are eight chapters in this thesis: an introduction, review of the literature, methods chapter that includes the development of the web-based intervention (Chapters I - III), unpublished results (Chapter VII), discussion (Chapter VIII), and three results chapters (Chapters IV - VI). The results chapters are in the form of manuscripts formatted to meet the requirements of the peer reviewed academic journals where they have been submitted for publication. Each of the results chapters begins with a detailed literature review in accordance with the requirements of the journals. As a result, there is some repetition among the results chapters, including the introductions, study methods, and reference lists. The results chapters have their own reference list at the end of each chapter, whilst the references for the remaining chapters are located at the end of the thesis. The tables and figures throughout are numbered by chapter to indicate placement within the thesis.
ACKNOWLEDGMENT OF PAPERS INCLUDED IN THIS THESIS

Included in this thesis are papers in Chapters IV, V and VI, which are co-authored with other researchers. My contribution to each co-authored paper is outlined at the front of the relevant chapter. The status for these papers including all authors, are:

- Chapter IV: Submitted to the *European Journal of Cancer Care* on 7 November 2016. Revisions to the manuscript were resubmitted 3 April 2017.
- Chapter V: Submitted to *Psycho-Oncology* on 30 January 2017. Revisions to the manuscript were resubmitted 3 April 2017, and 6 July 2017.
- Chapter VI: Submitted to *Supportive Care in Cancer* on 21 February 2017. Revisions to the manuscript were resubmitted 28 June 2017.

Appropriate acknowledgements of those who contributed to the research but did not qualify as authors are included in each paper.

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Principal Supervisor: Heather Green

Countersigned: ________________________________ Date: 27 July 2017
Secondary Supervisor: David Shum
CHAPTER I: INTRODUCTION

A subset of cancer survivors reports changes with their cognitive functioning following diagnosis and treatment (Asher, 2011; Correa & Ahles, 2008; Vardy, 2008). These changes are often referred to as cancer-related cognitive impairment (CRCI) in the literature and have been a popular area of investigation within the field of psycho-oncology during the last two decades. Cancer survivors have identified coping with changes in memory and attention as a primary “unmet need” in their survivorship journey (Campbell et al., 2010; Knobf et al., 2012). As a result, a number of cognitive training (CT) and cognitive rehabilitation therapy (CRT) interventions have emerged with the aim of alleviating symptoms of cognitive dysfunction experienced by this clinical group. Chapter II of this thesis provides a comprehensive literature review on cancer survivorship in Australia, the association between cancer and cognition, the theoretical models of CRCI, the relationship between subjective and objective cognitive functioning, and outlines the currently available cognitive rehabilitation interventions within the psychosocial contexts of cancer survivorship.

One of the challenges associated with most of the available interventions is that they are conducted in a face-to-face format in a clinical setting, which can limit their dissemination to a broader audience of cancer survivors, including individuals who are homebound or geographically isolated (Zulman et al., 2012). Web-based interventions have the potential to improve access to rehabilitative services for individuals with cognitive problems, yet there are limited interventions of this sort available. There are currently three published studies that have assessed the effectiveness of online CT for cancer survivors (Bray et al., 2017; Damholdt et al., 2016; Kesler et al., 2013), and the researchers reported positive results. However, there are no known published studies
that offer web-based CRT to cancer survivors. This research project aimed to examine the efficacy of a web-based CRT intervention called eReCog in cohorts of adult cancer survivors and community dwelling adults. The program was adapted from the face-to-face version called, “Responding to Cognitive Concerns” (ReCog; Schuurs & Green, 2009a, 2009b) and the adaptation and development process of the online version is detailed in Chapter III of this thesis.

To assess the efficacy of online CRT and investigate whether participation in the intervention led to improvements in subjective and objective cognitive functioning, and in psychosocial variables such as quality of life (QoL) and illness perceptions, two experimental studies were conducted. Study One was a pilot study that recruited cancer survivors and community dwelling adults without a history of cancer who were randomly allocated to intervention or waitlist groups. Chapter IV of this thesis contains a manuscript submitted for publication, which details the methodology, results and conclusions of the pilot study.

Study two was a larger scale randomised controlled trial (RCT) conducted subsequent to the pilot study. The RCT recruited cancer survivors who were randomly allocated to either an intervention or waitlist control group. The results and conclusions of Study Two are presented in manuscript format in Chapter V.

The second aim of this research was to examine the process of implementing online CRT in the two studies presented in this thesis. The software used to develop the web-based intervention did not include automated communications and therefore required monitoring and emails to be sent out to participants manually. However, the software allowed for the examination of participant engagement and level of activity completed within the training modules. Chapter VI presents a manuscript that quantified engagement and investigated the treatment fidelity of the eReCog program.
The final aim of this research was to investigate the underlying mechanisms contributing to the effectiveness of eReCog through a Self-Determination Theory (SDT) framework by evaluating whether the variables competence, autonomy, and relatedness mediated the relationship between treatment and outcome variables. The results and discussion about the mediation pathway are presented in Chapter VII of this thesis and were not included in the manuscripts submitted for publication. Chapter VII also includes additional results and discussion that were outside the scope of the submitted manuscripts. The final chapter of the thesis is the general discussion, Chapter VIII. To guide readers on the format of this thesis, a structural model providing a schematic overview of the document is presented in Figure 1.1 on the next page.
Figure 1.1 Schematic overview of the content and structure of the thesis.
CHAPTER II: REVIEW OF THE LITERATURE

Cancer Survivorship in Australia

A diagnosis of cancer may be one of the most terrifying and life-altering events that an individual will experience during their lifetime. Cancer is the leading cause of burden of disease in Australia, accounting for nearly one-fifth (19%) of the total burden of disease and injury in 2011 (Australian Institute of Health and Welfare, 2016). It was estimated in 2016 that around 130,000 new cases of cancer would be diagnosed in Australia excluding basal and squamous cell carcinomas of the skin (Australian Institute of Health and Welfare, 2016) and the incidence rate is expected to grow in the coming years, mainly due to an aging population (Jefford, 2009). Although the number of newly diagnosed cases continues to rise, the survival rates for many types of cancer are improving due to early detection and more effective targeted treatments (Deimling, Bowman, & Wagner, 2007; Jefford, 2009; Jefford et al., 2013).

The five-year survival rate for all types of cancers combined increased from 47% in the early 1980s to 67% by the end of 2010, which amounted to about 385,000 Australians living with a diagnosis during the past 5 years (Australian Institute of Health and Welfare, 2016). As a result, research has shifted to give more emphasis to survivorship care, or more specifically, the history and life of a person living with a cancer diagnosis beyond the acute care phase of diagnosis and treatment (Aziz, 2007).

Physician and cancer survivor Fitzhugh Mullan first introduced the term survivorship in 1985 and co-founded the National Coalition for Cancer Survivors the following year. In 1986, the National Coalition for Cancer Survivors was the first organisation to develop an operational definition of survivorship and defines an individual as a cancer survivor “from the moment of diagnosis and for the balance of life” (National Coalition for Cancer Survivors, 1995). This definition was later
expanded to include any family members, friends or voluntary caregivers who are affected by the cancer diagnosis. According to Mullan, survival is not a singular condition, but rather an agglomeration of many circumstances that disrupt normal life patterns, impact QoL, and affect the physical and mental health of everybody diagnosed with cancer regardless of course of illness (Mullan, 1985).

In reflections of his cancer experience, Mullan described three “seasons” of survival: acute survival, extended survival, and permanent survival (Mullan, 1985). The first season begins with the cancer diagnosis and is dominated by medical intervention, including diagnostic and therapeutic efforts to control or eradicate the disease. Fear and anxiety are dominant psychological factors in the first season, along with physical changes (e.g., cognitive impairment, fatigue, reduced strength, altered physical appearance, or pain). During the second season, patients transition from active treatment into post-treatment care and enter a phase of watchful waiting with periodic examinations by their physician. Psychologically, this period is dominated by fear of recurrence and adjustment to cope with the physical changes in the home, community and work place. The third season is permanent survival when the likelihood of the cancer’s return is sufficiently small that the patient is “cured” because the disease is considered permanently eradicated.

The extended survival phase where a patient transitions from active treatment to post-treatment is a crucial stage for promoting long-term health and survival (Institute of Medicine, 2005). With this stage of survivorship comes a whole new set of challenges. Although cancer survivors are contented to be completing their treatment, many survivors report that they feel unprepared to manage the lasting effects cancer and its treatment have on their physical and emotional wellbeing and worry about the late adverse effects that may arise in the months or years to come (Alfano & Rowland, 2006). In 2005 the Institute of Medicine formally assessed the
transition period from acute care to extended survival in its report, “From Cancer Patient to Cancer Survivor: Lost in Transition” (Institute of Medicine, 2005). The report focused on adult cancer survivors during the phase following primary treatment and (a) examined the medical and psychosocial consequences of cancer and its treatment, (b) provided a definition of quality care and strategies to achieve it, (c) examined social and economic hardships facing cancer survivors, and (d) described a process for improving quality of care and QoL for cancer survivors and their families.

Subsequently, a number of models of survivorship care began to emerge as researchers began to assess patients’ self-perceived supportive care needs during the period immediately following treatment (Armes et al., 2009). In 2016 the Clinical Oncology Society of Australia released a model for wellness in cancer survivorship (see Figure 2.1), which highlighted the key principles of care to promote long-term health and survival during the cancer journey from diagnosis to extended survivorship (Clinical Oncology Society of Australia Model of Survivorship Care Working Group, 2016). It is important to identify survivors’ needs and ensure referral to services able to deliver rehabilitative support for these needs. Providing cancer survivors with rehabilitative services during this phase of their cancer journey is essential for optimising individuals’ health, functioning, and QoL.
Figure 2.1 COSA model for wellness in cancer survivorship. From “Model of Survivorship Care: Critical Components of Cancer Survivorship Care in Australia Position Statement”, by Clinical Oncology Society of Australia Model of Survivorship Care Working Group. Copyright (2016) by Clinical Oncology Society of Australia. Reprinted with permission.
Conducting an appropriate needs assessment allows professionals to determine important needs that cancer survivors experience after finishing primary treatment. Survivors of cancer have identified a number of “unmet needs” in areas where rehabilitation and intervention support could benefit long-term outcomes, including: (a) managing treatment side-effects such as poor memory and concentration; (b) psychoeducation about what to expect post-treatment; (c) information about rehabilitation health services and counselling, or support groups; (d) and access to a social support network of individuals who have shared a similar cancer experience (Campbell et al., 2010; Jefford et al., 2008; Knobf et al., 2012).

Through this process, it has been identified that one frequent complaint amongst cancer survivors is changes in cognition and mental functioning (Baxter, Dulworth, & Smith, 2011), which is known to doctors and researchers as CRCI. According to the American Cancer Society, CRCI includes: memory difficulties such as forgetting things that are usually not difficult to recall and remembering details (e.g., names, dates, events) or common words; difficulties concentrating and multi-tasking; and slower thinking and processing (American Cancer Society, 2017). These sorts of impairments in cognitive functioning as a result of cancer diagnosis and treatment have been well documented in the literature (Ahles, Root, & Ryan, 2012; Correa & Ahles, 2008; Janselsins, Kesler, Ahles, & Morrow, 2014; Wefel, Kesler, Noll, & Schagen, 2015; Wefel & Schagen, 2012). The following section of this chapter discusses the theoretical foundations of CRCI and provides additional insight into how cancer diagnosis and treatment affect cognitive functioning.

**Cancer-Related Cognitive Impairment**

Cognitive impairment is the term used to describe cognitive changes that negatively impact on higher-order mental processes (Hess & Insel, 2007). Impaired cognitive functioning associated with cancer and treatments is a common complaint
amongst cancer survivors with non-central nervous system adult-onset malignancies following cancer treatment (Asher, 2011), and it can be one of the most distressing and difficult symptoms to treat (Von Ah, 2015). Similar or more pronounced neuropsychological deficits have been reported in the literature for paediatric cancers and cancers associated with the central nervous system (e.g., brain tumours), however these cancers are outside the scope of this thesis (for reviews see Gehrke, Baisley, Sonck, Wronski, & Feuerstein, 2013; Hutchinson, Pfieffer, & Wilson, 2017). There is evidence in the literature to suggest that up to 30% of adult cancer patients with no known central nervous system malignancy demonstrated evidence of CRCI on neuropsychological or self-report measures prior to beginning treatment; up to 75% show cognitive dysfunction during treatment; and as many as 35% demonstrate long-term changes in their cognitive functioning after treatment completion (Janelinsins et al., 2014; Janelinsins et al., 2011). The degree to which this subgroup of cancer survivors experiences CRCI varies from subtle to pronounced, interim to permanent, and stable to progressive (Ahles et al., 2012).

CRCI has been shown to impact on a variety of cognitive domains, although the findings on which domains are most impacted are not consistent in the literature (Von Ah, 2015). The majority of studies assess various cognitive domains, yet they only find impairment on some of the domains or on none at all. A recent meta-analysis conducted by Ono et al. (2015) evaluated the cognitive domains where impairment was reported on neuropsychological outcomes in 27 breast cancer studies involving 4361 participants. The analysis included 14 studies reporting cross-sectional data only, eight studies with both cross-sectional and longitudinal data, and five studies reporting only longitudinal data. The results demonstrated that in cross-sectional studies, breast cancer survivors (BCS) treated with chemotherapy performed significantly worse than (healthy or cancer) controls on measures of attention, executive function, motor
function, processing speed, and short-term memory, where the grand mean weighted effect size for fixed effects \( (d = -0.12) \) was significant. Their results were reasonably consistent with a previous meta-analysis conducted by Falleti et al. (2005) who reported significant impairment in domains of attention, executive functioning, motor function, verbal ability, visuospatial ability, and memory in the same population. On prospective longitudinal studies Ono et al. (2015) found no post-chemotherapy cognitive decline, and reported improvement on long-term memory over time. Other studies, however, have found clinically relevant long-term cognitive deficits in domains of verbal memory (Weis, Poppelreuter, & Bartsch, 2009) and psychomotor functioning (Ahles et al., 2002). The meta-analysis by Ono et al. (2015) was limited to BCS treated with chemotherapy and did not analyse other cancer or treatment types, which have also been associated with cognitive decline as will be discussed later in this chapter.

An area of cognition that has not been widely evaluated in cancer survivorship research is prospective memory (PM). This type of memory is described as the process of forming intentions to complete specific actions and then realising those intentions at an appropriate time in the future (McDaniel & Einstein, 2000). Essentially, PM is remembering to remember despite ongoing distractions occurring in the external or internal environment. Everyday life is filled with PM tasks such as remembering to ring a friend, or remembering to buy an item from the shops on the way home from work, or remembering to water the house plants, or remembering to lock the doors when leaving the house in the morning. It is believed that when people speak of “memory” problems, they are likely referring to examples of PM failures (Fish, Wilson, & Manly, 2010). Recent studies have demonstrated impaired PM functioning in BCS following treatment with chemotherapy compared to healthy controls (Bedard,
Verma, Collins, Song, & Paquet, 2016; Cheng et al., 2013; Paquet et al., 2013), but further research is needed regarding PM in other types of cancer and treatments.

Although there are some inconsistencies in the functional domains affected and long-term effects of cognitive dysfunction, the overall evidence suggests that cognitive impairment, although typically subtle, does occur in some cancer survivors and that it is sufficient to impact on occupational, educational and social functioning (Wefel, Witgert, & Meyers, 2008), QoL (Mehnert et al., 2007; Von Ah, Russell, Storniolo, & Carpenter, 2009), and functional ability on everyday activities (Munir, Burrows, Yarker, Kalawsky, & Bains, 2010; Player, Mackenzie, Willis, & Loh, 2014; Poppelreuter et al., 2004). A qualitative study on the impact of changes in cognition was conducted with nine breast cancer survivors treated with chemotherapy in Australia and found that six themes emerged: (a) uncertainty about the origin of the cognitive problems; (b) persistent but inconsistent impacts on functioning; (c) simple functions became complex; (d) a loss of functional independence in the family environment; (e) the need for adaptive strategies to maintain function; and (f) the need for recognition of the subjective experience of these individuals (Player et al., 2014). One area that did not emerge as a theme in their study was the impact of these changes of functioning in the work environment.

An estimated two-thirds of cancer survivors return to work 18 months after diagnosis (de Boer et al., 2008; Groeneveld, de Boer, & Frings-Dresen, 2013; Mehnert & Koch, 2013), however, the rate of unemployment in this clinical group is significantly higher than individuals without a history of cancer (Feuerstein et al., 2010). A qualitative study conducted by Boykoff, Moieni, and Subramanian (2009) on a group of 74 breast cancer survivors in the United States found that women reported unrealistic expectations from employers and co-workers, a diminished capacity to focus, work duties were more difficult and required more time to complete, they were
unable to function at the same level professionally or remain in the same role, and some women were forced to leave their jobs or reduce their working hours as a result of their cognitive changes. As a result, many women reported problems with financial stability and personal self-worth (Boykoff et al., 2009) due to these occupational challenges following breast cancer.

Historically, a large majority of the body of literature on CRCI has focused on breast cancer in women, which is likely to be due in part to its high prevalence rate as the most common cancer diagnosed in women worldwide (Jemal et al., 2011; Yu et al., 2014), increased rates of self-reported cognitive problems in breast cancer survivors compared to some other cancer groups (Janelinsins et al., 2014; Von Ah, Habermann, Carpenter, & Schneider, 2013), and the higher likelihood of females volunteering to participate in research compared to their male counterparts (Wymer, 2011). The cognitive complaints expressed by breast cancer survivors have been supported in the literature with multiple studies reporting evidence of CRCI during their cancer journey (Mihuta, Green, Man, & Shum, 2016; Ono et al., 2015; Paquet et al., 2013; Root, Andreotti, Tsu, Ellmore, & Ahles, 2016; Schagen, Muller, Boogerd, Mellenbergh, & van Dam, 2006; Von Ah & Tallman, 2015). In addition to breast cancer, cognitive dysfunction has been reported in patients with prostate cancer (Green et al., 2002; Green et al., 2004; Jenkins, Bloomfield, Shilling, & Edginton, 2005; Jim, Small, Patterson, Salup, & Jacobsen, 2010; Salminen et al., 2003), myelogenous leukaemia (Meyers, Albitar, & Estey, 2005), lung cancer (Simo et al., 2016), colorectal cancer (Vardy et al., 2006), ovarian cancer (Hess et al., 2010), gynaecologic cancer (Craig, Monk, Farley, & Chase, 2014), and testicular cancer (Amidi et al., 2015; Wefel, Vidrine, et al., 2011), among others.

The aetiology of cognitive impairment following cancer diagnosis and treatment is not well understood. Many cancer treatments are aggressive and often
include multimodal strategies for combating the disease including surgery, radiation, chemotherapy, immunotherapy, and hormone therapy (Asher, 2011). Because cancer diagnosis and treatment is a complex process, it is difficult for researchers to pinpoint the specific mechanisms responsible for the cognitive impairment demonstrated in this clinical group. Generally the aetiology of CRCI can be divided into four underlying mechanistic categories: direct effects of chemotherapy, indirect effects of chemotherapy, effects related to cancer biology alone, and other (Craig et al., 2014).

**Direct and Indirect Effects of Chemotherapy**

There is a large body of evidence to suggest that the effects of systemic chemotherapy treatment may be one of the contributing factors of cognitive decline in cancer patients (Janelinsins et al., 2011; Ono et al., 2015). The lay terms *chemobrain* or *chemofog* (Castellon et al., 2004; Shilling, Jenkins, & Trapala, 2006) emerged in the breast cancer community to first describe the mental “fogginess” associated with chemotherapy treatment and quickly became a catch phrase amongst survivors. Although the term emerged amongst patients with breast cancer, the description of associated symptoms of cognitive dysfunction applies to many patients with other types of cancer (Asher, 2011). The terms themselves are misleading since impairments in cognitive functioning do not result solely following chemotherapy treatment but may be caused by a number of other factors, which will be discussed in a later section of this chapter.

Chemotherapy and other oncological therapies used to treat cancer have the potential to cause neurotoxicity in the brain, which is well documented in the literature (Ahles & Saykin, 2002; Castellon et al., 2004; Cheng et al., 2013; Falleti et al., 2005; Meyers, 2008). The blood-brain barrier offers some protection from the penetration of chemotherapeutic agents into the brain, but evidence suggests that a degree of toxicity is still evident with some chemotherapy drugs (Evenden, 2013). Since chemotherapy is
not specific to targeted areas where tumours are located, other organs and tissues of the body are also exposed (Meyers, 2008). In fact, some chemotherapeutic agents have demonstrated a preference of targeting non-cancer cells over cancer cells (Craig et al., 2014; Dietrich, Han, Yang, Mayer-Proschel, & Noble, 2006). Some of the proposed direct effects on the body caused by chemotherapy include damage to myelin on nerve cells, histone acetylation in gene regulation, decreased cell proliferation, telomere shortening, and decreased levels of hippocampal catecholamine (Briones & Woods, 2011; Craig et al., 2014).

In addition to the direct effects on the body, chemotherapeutic agents can indirectly alter other processes and responses in the body, which are considered indirect effects of chemotherapy. One of the proposed indirect effects of certain cytotoxic agents is that they affect the inflammatory process in the body by causing prolonged activation of the cytokine pathways; and these proinflammatory agents subsequently cross the blood-brain barrier and cause impairments to cognition (Aluise et al., 2010; Lutgendorf et al., 2008). Another potential indirect effect of chemotherapeutic agents is that they can lead to oxidative stress through the production of reactive oxygen and nitrogen, which has been implicated in CRCI (Ahles et al., 2012; Joshi et al., 2005; Tangpong et al., 2008). Additional proposed indirect effects of chemotherapeutic treatment include the activation of microglia, potential obstructions in the cerebrovascular system, and hormonal changes in women (Craig et al., 2014). There is evidence to suggest that these direct and indirect effects of chemotherapy may lead to functional and structural changes to the brain, as described below.

A number of imaging studies have reported functional and structural changes in the brain following exposure to chemotherapeutic agents (de Ruiter et al., 2011; Deprez et al., 2011; Inagaki et al., 2007; Raffa, 2010; Silverman et al., 2007). For
example, one study assessed functional changes using functional magnetic resonance imaging (fMRI) in a cohort of BCS treated with high-dose chemotherapy 10 years earlier and compared the results to a group of BCS who had not received chemotherapy treatment (de Ruiter et al., 2011). The women in the chemotherapy group demonstrated task-specific hyporesponsiveness of the dorsolateral prefrontal cortex and parahippocampal gyrus, and generalised hyporesponsiveness of the lateral posterior parietal cortex compared to the control group. These three brain regions have been associated with executive functioning, episodic memory, and attentional processing, respectively. Moreover, the chemotherapy group demonstrated significantly impaired planning performance and marginally significant impaired recognition memory when compared to the control group.

In addition to functional changes, structural changes in the brain have also been observed following chemotherapy treatment. A study that used diffusion tensor imaging to examine the integrity of cerebral white matter found structural changes in the frontal and temporal axonal tracts of women treated with chemotherapy for breast cancer when compared to BCS not treated with chemotherapy and a group of healthy controls (Deprez et al., 2011). Similarly, structural MRI techniques have demonstrated reduced white and grey matter volumes in specific regions of the brain including the prefrontal cortex, parahippocampal gyrus, the cingulate gyrus, and the precuneus, one year post-chemotherapy in a group of BCS when compared to survivors treated without chemotherapy (Inagaki et al., 2007). Although changes in brain anatomy and function have been reported in association with chemotherapy exposure, there are additional hypotheses about the way in which chemotherapeutic agents may affect cognitive functioning.

Leading investigators in the field, Ahles and Saykin (2007), have proposed several candidate mechanisms that may be responsible for chemotherapy-induced
cognitive changes, including genetic susceptibility, blood-brain barrier integrity and associated neurotoxicity, damage to DNA at a cellular level, cytokine deregulation, and changes in hormonal balance. Many of these components are incorporated in Hess and Insel’s (2007) conceptual model of chemotherapy-related changes in cognitive function (Figure 2.2), which integrates other proposed mediating, moderating and psychosocial factors that may contribute to cognitive changes.

Hess and Insel’s model is based on Miller’s theory of human thought and cognition (Miller, 1909), a model which suggests that events (e.g., changes in cognitive function) result from identifiable inputs (e.g., antecedents) that lead to certain outcomes (e.g., consequences) whereby a series of processes (e.g., mediators and moderators) are involved. This occurs via Walker and Avant’s (2005) two identified distinct and interacting pathways: psychosocial and physiological (see Figure 2.2). As the model depicts, cancer treatment is associated with a variety of physiological factors that can affect human biology, and the cancer diagnosis impacts on psychosocial factors such as stress, depression, anxiety and distress. According to the model, both of these pathways can lead to associated toxicities, which are considered indirect effects of the treatment, and the toxicities can further exacerbate psychosocial symptoms. Each of these pathways, along with additional moderating variables (e.g., age, education, intelligence), influences subjective and objective cognitive functioning, which can lead to a reduction in health-related QoL and everyday functional abilities in individuals treated with chemotherapy.
Figure 2.2 Conceptual model of chemotherapy-related changes in cognitive function. From “Chemotherapy-Related Change in Cognitive Function: A Conceptual Model”, by L. M. Hess & K. C. Insel, 2007, Oncology Nursing Forum, 34, 981-991. Copyright (2007) by Oncology Nursing Society. All rights reserved. Reprinted with permission.

The conceptual model of chemotherapy-related changes in cognitive function proposed by Hess and Insel offers a complex conceptualisation of antecedents potentially leading to cognitive dysfunction following treatment with chemotherapy, however, the model has some limitations. Firstly, the model groups together self-report and formally assessed neuropsychological outcomes. Associations between the two are often weak and data suggest impairment can be found on one measure but not the other, which is discussed in greater detail in the section on objective and subjective cognitive function later in this chapter. Secondly, the model implies that only cancer treatments have physiologic impacts affecting cognition and that the impact of the diagnosis is psychological (e.g., distress, anxiety, depression, or stress), implying that without knowledge of the diagnosis, a cancer patient would not experience cognitive decline. Both of these implications exclude the possibility that biological effects of malignancy may contribute to CRCI, such as anaemia, fatigue, pain, altered immune
system functioning, or the impact of malignancy on other body systems (Craig et al., 2014). In other words, the model as presented appears to exclude the possibility that the presence of cancer itself may be a contributing factor to cognitive decline in some cancer patients (Vardy et al., 2014). The proposed aetiology of underlying mechanisms related to biological factors is supported by numerous studies that reported cognitive impairment prior to beginning cancer treatment, as discussed below.

**Biological Mechanisms**

The biological processes underlying cancer are potential mechanisms implicated in CRCI. Craig et al. (2014) suggested that this category arose after many studies reported cognitive dysfunction in cancer patients prior to beginning any treatment regimen, suggesting that the presence of cancer itself may have an effect on physiological processes. Pre-treatment cognitive dysfunction has been reported in a number of studies measuring baseline cognitive function prior to the start of treatment (Ahles et al., 2008; Meyers et al., 2005; Meyers, Byrne, & Komaki, 1995; Wefel et al., 2004). One study examining pre-treatment cognitive functioning in a cohort of 84 women with breast carcinoma reported 35% of the women demonstrated impaired cognitive functioning on a comprehensive neuropsychological evaluation prior to beginning systemic therapy (Wefel et al., 2004). Another study assessing cognitive impairment in 54 patients with acute myelogenous leukaemia or myelodysplastic syndrome found more than 40% of patients had impairments in learning new information, 33% had impaired fine motor coordination, and 25% had difficulties with executive functioning or visual motor scanning speed prior to starting treatment (Meyers et al., 2005). Furthermore, 65% of patients reported significant levels of fatigue at baseline assessment (Meyers et al., 2005).

The presence of cancer can affect individuals in different ways and genetic vulnerabilities (e.g., carrying the E4 variant of the apolipoprotein E gene) might also
play a role in the presence of cognitive impairment in this clinical population (Wefel et al., 2015). Some of the biological mechanisms that have been indicated as potential contributors to CRCI are fatigue, pain, and anaemia, which have been linked to self-reported cognitive impairment in previous research (Craig et al., 2014; Meyers, 2000). Treatment effects such as inflammatory mechanisms, surgery and its associated effects (e.g., those associated with anaesthesia), and hormone dysregulation are some additional proposed biological mechanisms that have been implicated in CRCI in psycho-oncology research (Amidi et al., 2015). Disruption to hormone status has received considerable attention in the literature, which is discussed in further detail in the next section of this chapter.

Hormonal Dysregulation

Changes to hormonal status are another proposed underlying mechanism involved in the aetiology of CRCI. As noted in the model on chemotherapy-related changes in cognitive changes, chemotherapy drugs can have an indirect effect on hormonal status in some cancer patients. One way that chemotherapy can alter a cancer patient’s hormone balance is through chemotherapy-induced menopause, which reportedly occurs in approximately 70% of pre-menopausal women treated with cytotoxic drugs for early stage breast cancer (Vearncombe et al., 2011). The cytotoxic drugs abruptly disrupt ovarian function and are associated with more favourable outcomes in younger women; however, they are also believed to potentially impact on cognitive functioning in these patients (Ahles & Saykin, 2007; Jenkins et al., 2006). Another method of cancer treatment that can alter hormone action is the use of adjuvant treatments in certain types of breast cancer. For example, women diagnosed with hormone receptor-positive breast cancer are often treated with oestrogen agonists (e.g., Tamoxifen) or aromatase inhibitors (e.g., anastrozole), both of which alter hormone action and have been associated with impaired cognitive functioning in
women with breast cancer (Baum et al., 2003; Bender et al., 2007; Jenkins, Shilling, Fallowfield, Howell, & Hutton, 2004).

Hormonal dysregulation associated with treatments, however, is not specific to breast cancer. For example, there is a body of evidence to show that treatment with luteinizing hormone-releasing hormone (LHRH) agonists and androgen deprivation therapy (ADT) for men with prostate cancer may be associated with reduced cognitive functioning (Cherrier, Aubin, & Higano, 2009; Green et al., 2002; Jenkins et al., 2005). Cherrier et al. (2009) compared 20 men treated with ADT consisting of nine months of complete androgen blockade to a cohort of 20 healthy controls without cancer. Significant group by time interaction effects were found on the total compilation of neuropsychological measures, and on individual tasks assessing visual working memory, spatial reasoning, and spatial ability three months after beginning treatment, demonstrating deterioration in the ADT group. Differences between groups were not significant at 9 months or 12 months, indicating the effects of ADT may be transient.

Similarly, Green et al. (2002) randomly allocated 82 men with prostate cancer to two LHRH analogue groups, a steroidal antiandrogen group, or clinical monitoring group. Significant group by time interactions were reported on verbal learning and a trend was found on a measure of visual scanning and motor performance. Both LHRH treatments were associated with decreased or slower performance compared to the other groups, indicating hormone treatments may have an impact on cognitive functioning. It is evident that understanding the aetiology of cognitive dysfunction in cancer survivors is a complex and intertwined process that likely involves a combination of treatment, biological, and psychological factors.

Thus far, this chapter has focused mainly on the chemical, biological, and hormonal factors associated with cancer treatment. It is also important to explore how
psychosocial variables related to cancer diagnosis impact on cognitive functioning. As conceptualised earlier in Hess and Insel’s (2007) model of chemotherapy-related cognitive changes, both physiologic and psychosocial factors are believed to influence cognitive functioning. The manner in which they do so, however, may be quite distinct. In the literature, cognitive impairment is generally assessed from a dual perspective by measuring both objective and subjective cognitive functioning. The difference is that objective cognitive functioning is assessed using a battery of neuropsychological measures whereas subjective cognitive functioning is evaluated with self-report measures pertaining to perceptions of everyday functioning. The relationship between these two areas of cognitive functioning, however, is complex. The aim of the next section of this chapter is to explore and evaluate this association.

**Objective and Subjective Cognitive Function**

The relationship between objective tests of cognitive functioning and subjective reports of impairment is convoluted and a topic that receives much attention in psycho-oncology research. Objective cognitive functioning is generally assessed using standardised neuropsychological measures designed to tap into specified cognitive domains of functioning, such as different types of memory, attention, processing speed or executive functions. These measures are designed to meet certain psychometric criteria (Green, Pakenham, & Gardiner, 2005), however, they often lack ecological validity and are distinct from tasks performed in everyday life (Munir et al., 2010). In contrast, subjective cognitive functioning is assessed with self-report questionnaires that reflect an individual’s perception of their cognitive functioning. The correlations between the two amongst cancer survivors are incongruous in the literature (Collins, Paquet, Dominelli, White, & MacKenzie, 2017; Cull et al., 1996; Green et al., 2005; Mihuta et al., 2016; Poppelreuter et al., 2004) and often demonstrate little association (Collins et al., 2017; Evenden, 2013). This lack of
correlation suggests that theoretically, objective and subjective measures of cognitive functioning may not be assessing the same construct.

The rates of subjective complaints about problems with memory and attention are often higher than rates of cognitive dysfunction observed on neuropsychological tests (Shilling et al., 2006). Subjective cognition is an important concept to understand because poorer self-reported cognitive functioning has been associated with behaviour changes such as delaying return to work (Schuurs & Green, 2013), or declining to participate in intervention programs (Cameron, Booth, Schlatter, Ziginskas, & Harman, 2007), and may affect an individual’s underlying motivation to engage in activities promoting health and wellbeing. For this reason, assessing both subjective cognitive complaints and objective performance on cognitive tasks is important for understanding an individual’s level of impairment.

Subjective cognitive functioning appears to be more closely related to negative affect (e.g., anxiety, depression, distress) and QoL than to performance on objective cognitive measures (Castellon et al., 2004; Collins et al., 2017; Green et al., 2005; Shilling & Jenkins, 2007; Vardy & Tannock, 2007). It has been suggested that reduced self-reported cognition may be a reflection of an individual’s inability to cope with a stressful event rather than objective cognitive dysfunction (Reid-Arndt & Cox, 2012). Cancer can be a highly distressing experience, therefore increased complaints about problems with poor memory and concentration would be expected in this clinical group (Mehlsen, Pedersen, Jensen, & Zachariae, 2009).

A study conducted by Cull et al. (1996) assessed 91 adult lymphoma patients who were at least six months post treatment to examine factors influencing patients’ complaints by comparing objective and subjective cognitive functioning. Participants were divided into groups of complainers or non-complainers on measures of concentration and memory. The researchers found that complaints of reduced
cognitive functioning on the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) were significantly correlated with anxiety and depression scores measured on the Hospital Anxiety and Depression Scale and self-reported fatigue measured on the Multi-Dimensional Fatigue Inventory. However, subjective complaints were not correlated with objective measures of cognitive functioning in their study.

In another study conducted by Collins, Paquet, Dominelli, White, and MacKenzie (2017), the researchers compared performance on objective and subjective measures of cognitive functioning in 54 women with early stage breast cancer and 54 healthy women matched on age and education. They also assessed mood using the Profile of Mood States (POMS), which measures mood dyads such as tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia, and confusion-bewilderment. The researchers found that Total Mood Disturbance on the POMS was significantly correlated with subjective cognitive functioning, in both the breast cancer group and the control group, but was not correlated with objective cognitive functioning measures. These results exemplify the discordance between self-report measures of cognition and objective cognitive testing, and highlight the importance of conducting a comprehensive neuropsychological assessment to fully understand an individual’s level of cognitive functioning both subjectively and objectively (Wefel et al., 2008).

To provide a better understanding of the relationship between objective and subjective cognitive functioning, Green, Pakenham, and Gardiner (2005) developed a conceptual model of the factors contributing to cognitive impairment in cancer survivors where they pinpointed a number of variables believed to affect subjective and objective cognitive impairment (Figure 2.3). Unlike Hess and Insel’s model, their model separates subjective and objective cognitive impairment whereby subjective
impairment is viewed as being influenced by both emotional health and objective cognitive impairment. Furthermore, the model indicates that physiologic changes can be affected by factors other than cancer treatment alone (e.g., physical health) and that emotional health is not exclusively related to the cancer diagnosis and physical changes, but is also impacted by a variety of other psychosocial variables.


Identifying variables that contribute to objective and subjective cognitive dysfunction and the theoretical relationship between them is an important step for researchers. More research is still needed, but research designs that investigate possible underlying mechanisms contributing to cognitive impairment have the potential to help provide a better understanding of the complex relationship between
these two constructs. Cognitive rehabilitation interventions that evaluate both subjective and objective functioning as outcomes can also assist researchers to better understand this association. The next section of this chapter examines the current body of literature on cognitive rehabilitation programs developed to address cognitive concerns in cancer survivors.

**Cognitive Rehabilitation for Cancer Survivors**

Many cancer survivors feel unprepared to manage long-term side effects associated with cancer and treatment including CRCI as they transition into the extended survivorship phase (Alfano & Rowland, 2006). Cognitive rehabilitation has the potential to mitigate the symptoms of cognitive dysfunction associated with cancer treatment. In the literature, the terms “cognitive training” and “cognitive rehabilitation” are employed somewhat interchangeably, which tends to blur the important distinctions between them conceptually and in their individual application (Clare & Woods, 2004).

Cognitive training (CT) is a behavioural method of treatment based on models of neuroplasticity, which suggest that cognitive abilities can be improved through progressive drills designed to exercise the brain (Kesler et al., 2013; G. E. Smith et al., 2009). As such, CT generally involves guided practice on a set of standardised tasks that target certain cognitive domains, such as memory, attention, processing speed, language, or executive functioning (Clare & Woods, 2004). These tasks typically have a range of difficulty levels, which allows individuals to select the level most appropriate for them. The first underlying assumption of CT methods is that regular practice has the potential to improve or at least maintain functioning in targeted cognitive domains; therefore, outcomes in research are generally assessed with standard neuropsychological tests with the expectation of improvement or maintenance in the intervention group (Clare & Woods, 2004). The second assumption is that these
practice effects will generalise to contexts beyond the training environment (Bahar-Fuchs, Clare, & Woods, 2013), an assumption that has not been consistently supported (Bahar-Fuchs et al., 2013; A. M. Owen et al., 2010; Papp, Walsh, & Snyder, 2009).

Owen et al. (2010) argue that the important question regarding CT is not whether performance on cognitive tests can be improved with training, but whether the observed benefits transfer into other untrained tasks or leads to overall improved cognitive functioning. These researchers recruited 11,430 participants aged 18 to 60 years old who were assigned to one of two experimental groups or a control group that was asked five obscure knowledge questions related to cognitive domains. Participants in experimental group 1 were assigned six training tasks focused on reasoning, planning, and problem solving, whereas experimental group 2 trained on a broader range of cognitive functions. Participants completed at least two training sessions during the six-week intervention period, and the average number of training sessions was 24.47 ($SD = 16.95$). The researchers found that improvements were observed post-intervention on every one of the cognitive domains trained, even in the control group, but found no evidence that the effects of training were transferred to untrained tasks, including those that were closely related to the trained cognitive domain. These findings call into question the generalisation of CT to everyday life.

Cognitive rehabilitation therapy (CRT), on the other hand, is based on biopsychosocial models and can be described as the process of reattaining cognitive skills lost or altered due to injury whereby the goal of treatment is to assist individuals achieve optimal levels of physical, psychological and social functioning (Clare & Woods, 2004; van Schouwen-van Kranen, 2014). Unlike CT, the emphasis of CRT is not on strengthening performance on cognitive tasks, but rather improving functioning in the context of everyday tasks (Wilson, 1997). CRT is an individualised approach to treatment for cognitive impairment where the individual collaborates with their family.
and health care professionals to identify personal goals and strategies for achieving them (Wilson, 2002). As such, typical CRT interventions often incorporate elements of cognitive behaviour therapy (CBT) such as psychoeducation, skills training, goal-setting, strategy training, and functional activity training that allows participants to implement these strategies in real-world settings. Outcomes are typically assessed with both neuropsychological tests and self-report measures.

There are no set guidelines for the application of CT or CRT interventions to different clinical populations, and selection of an intervention is mostly dependent on the main goal of treatment. The CRT approach was developed mainly through working with younger individuals following traumatic brain injury (Clare, Wilson, Carter, Hodges, & Adams, 2001); however, it has the potential to benefit a wide variety of clinical populations. A main advantage of CRT is that it focuses on learning new skills to adapt in everyday life where recovery from an injury is less predictable or unknown such as stroke, traumatic brain injury, schizophrenia, or cancer. On the other hand, CT which is theoretically designed to at least maintain functioning on certain cognitive skills, may have potential benefits in clinical populations where progressive deterioration is likely such as Parkinson’s disease (Walton, Naismith, Lampit, Mowszowski, & Lewis, 2016), Alzheimer’s Disease or other types of dementia (Bahar-Fuchs et al., 2013; Clare & Woods, 2004; Sitzer, Twamley, & Jeste, 2006) and multiple sclerosis (Brenk, Laun, & Haase, 2008).

In the last decade, researchers in psycho-oncology have published a number of studies investigating the efficacy of CRT and CT intervention programs in adult cancer survivors. Table 2.1 describes 15 studies that have been published on cognitive rehabilitation or training programs to treat cognitive dysfunction in cancer survivors and has been adapted from a publication by King and Green (2015) to include an additional five studies that have since been published.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Design</th>
<th>Participants</th>
<th>Intervention</th>
<th>Results</th>
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<tbody>
<tr>
<td>McDougall (2001)</td>
<td>Single arm, with 4 chronic health conditions</td>
<td>( n = 78 ), aged 65+ years with history of chronic disease ((n = 11 \text{ history of cancer}))</td>
<td>CRT: Cognitive Behavioral Model of Everyday Memory (CBMEM); self-efficacy theory, group treatment, 8 x 1.25 hour sessions over 4 weeks.</td>
<td>Cancer group showed improved short-term memory, memory self-efficacy, and metamemory post-intervention. (Note: study was not planned as a cancer substudy)</td>
</tr>
<tr>
<td>Ferguson et al. (2007)</td>
<td>Single arm</td>
<td>( n = 29 ), BCS, &gt; 3 years post-chemotherapy</td>
<td>CRT: Memory and Attention Adaptation Training (MAAT); individual, CBT-based, 4 x 30-50 min monthly sessions, plus 3 phone calls</td>
<td>Significant improvements on verbal and executive function, subjective cognitive function, and QoL</td>
</tr>
<tr>
<td>Poppelreuter, Weis, and Bartsch (2009)</td>
<td>Partial RCT (two interventions vs. care as usual)</td>
<td>( n = 96 ) female BCS post chemotherapy, undergoing inpatient rehab</td>
<td>CRT: Neuropsychological Training (NPT), group functional training for memory/attention; Computer training (PC) for memory/attention with individual support, 4 x 1 hour sessions per week for 3-5 weeks.</td>
<td>Significant improvements in performance on most neuropsychological tests and self-report measures in all three study groups.</td>
</tr>
<tr>
<td>McDougall, Becker, Acee, Vaughan, and Delville (2011)</td>
<td>RCT (intervention vs. attentional control)</td>
<td>( n = 267, 22 ) cancer survivors ((n = 8 \text{ intervention}; n = 14 \text{ comparison}))</td>
<td>CRT: CBMEM (see above)</td>
<td>Significant improvements on visual memory and self-reported memory CBMEM group compared to comparison. (Note: study not planned as cancer substudy)</td>
</tr>
<tr>
<td>Ferguson et al. (2012)</td>
<td>RCT (intervention vs. waitlist)</td>
<td>( n = 40 ), BCS &gt;18 months post-treatment</td>
<td>CRT: MAAT (see above)</td>
<td>Significant improvements on verbal memory and QoL in intervention group compared to control</td>
</tr>
<tr>
<td>Von Ah et al. (2012)</td>
<td>RCT (two interventions vs. waitlist)</td>
<td>( n = 88 ) BCS, &gt; 1 year post chemotherapy treatment</td>
<td>CT: Memory training: group memory exercises. Speed of processing: computerised training. Both groups had 10 x 1 hour training sessions in small groups over 6-8 weeks</td>
<td>Significant improvements in both intervention groups compared to waitlist, but processing speed group showed earlier benefits than memory group. Both showed improvements in subjective cognition, QoL, and distress.</td>
</tr>
<tr>
<td>Schuurs and Green (2013)</td>
<td>Non-randomised controlled trial (intervention vs. waitlist vs. community)</td>
<td>( n = 55, 32 ) cancer survivors &gt; 4 months post treatment; 23 community comparison</td>
<td>CRT: Responding to Cognitive Concerns (ReCog), CBT-based, group treatment, 4 x 2-hour weekly session, participant workbook/homework.</td>
<td>Significant improvements for overall cognitive function, immediate memory, visuospatial, and delayed memory in intervention compared to waitlist. Intervention group reported improved subjective cognitive function and reduced distress.</td>
</tr>
<tr>
<td>Study</td>
<td>Design Type</td>
<td>N &amp; Length</td>
<td>Intervention Description</td>
<td>Outcome Measures</td>
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<tr>
<td>Kesler et al. (2013)</td>
<td>RCT (I vs. W)</td>
<td>n = 41</td>
<td>CT: Online cognitive training program for executive function, 4 x 20-30 minute sessions weekly for 12 weeks (48 sessions total)</td>
<td>Significant improvements in intervention group in cognitive flexibility, verbal fluency, processing speed; self-rated executive function including planning, organising, and task monitoring compared to waitlist</td>
</tr>
<tr>
<td>Cherrier et al. (2013)</td>
<td>RCT (I vs. W)</td>
<td>n = 28</td>
<td>CRT: Group memory workshops consisting of 7 x 1 hour sessions for 7 weeks; homework</td>
<td>Significant improvements in intervention group compared to waitlist on subjective cognitive function and digit span</td>
</tr>
<tr>
<td>Ercoli et al. (2013)</td>
<td>Single-arm</td>
<td>n = 27</td>
<td>CRT: Cognitive rehabilitation targeting memory, attention and executive function. 5 x 2 hour group sessions over 5 weeks; homework</td>
<td>Significant improvements on processing speed, reaction time, visual attention, verbal learning, and self-reported cognitive functioning, memory and executive functions</td>
</tr>
<tr>
<td>Ercoli et al. (2015)</td>
<td>RCT (I vs. W)</td>
<td>n = 48</td>
<td>CRT: Cognitive rehabilitation (see above research by same author)</td>
<td>Significant improvements on self-reported cognitive functioning and memory, and verbal learning in intervention group compared to waitlist</td>
</tr>
<tr>
<td>King and Green (2015)</td>
<td>RCT (I vs. W)</td>
<td>n = 45</td>
<td>CRT: ReCog (see above)</td>
<td>Significant improvements on processing speed/visual scanning, perceived cognitive impairment, and cognitive self-efficacy showing effects in intervention group</td>
</tr>
<tr>
<td>Ferguson et al. (2016)</td>
<td>RCT (I vs. ST)</td>
<td>n = 47</td>
<td>CRT: MAAT (see above) delivered over videoconference device, 8 x 30-45 minutes sessions (weekly); ST for controls had same time demands</td>
<td>Significant improvements in subjective cognitive function and processing speed in intervention compared to ST group</td>
</tr>
<tr>
<td>Damholdt et al. (2016)</td>
<td>RCT (I vs. W)</td>
<td>n = 157</td>
<td>CT: Web-based cognitive training (eCogT): tasks on 6 cognitive domains; recommended 30min/day, 5days/week for 6 weeks</td>
<td>Significant improvements on verbal learning and digit span backwards in intervention group compared to waitlist. Interaction on primary outcome PASAT not significant</td>
</tr>
<tr>
<td>Bray et al. (2017)</td>
<td>RCT (I vs. W)</td>
<td>n = 242</td>
<td>CT: Web-based cognitive training: 5 cognitive domains; recommended 4 x 40 minute session per week for 15 weeks (40 hours total)</td>
<td>Significant improvements on subjective cognitive functioning in intervention group compared to control. Intervention group had better global QoL and reduced stress at follow-up</td>
</tr>
</tbody>
</table>

The studies published thus far have demonstrated beneficial effects of CRT and CT to address cognitive problems experienced by cancer survivors in both group and individual format (King & Green, 2015). Included in the summary are 11 CRT interventions and four CT programs. Whilst the majority of the studies presented in Table 2.1 were conducted with female BCS (Damholdt et al., 2016; Ercoli et al., 2013; Ercoli et al., 2015; Ferguson et al., 2007; Ferguson et al., 2012; Ferguson et al., 2016; Kesler et al., 2013; Poppelreuter et al., 2009; Von Ah et al., 2012), there have been a handful of studies published with cancer survivors of mixed tumour types (Bray et al., 2017; Cherrier et al., 2013; King & Green, 2015; McDougall, 2001; McDougall et al., 2011; Schuurs & Green, 2013).

Two of the studies described in Table 2.1 utilised a cognitive rehabilitation program designed to treat memory problems in older adults aged over 65 years and included participants with a variety of chronic illnesses (McDougall, 2001; McDougall et al., 2011), therefore were not specific to the cancer context and analyses with the cancer group were conducted post hoc by collapsing across groups. The second study by McDougall et al. (2011) included a matched attentional control condition where participants were assigned to a health promotion class, which was designed to keep participants engaged over the course of the study. The curriculum covered 18 different health-related topics about successful ageing, but did not include any specific health information related to CRCI. The study results found additional intervention effects compared to the health information arm. It is unclear whether an attentional control that specifically focuses on issues relevant to cancer and cognitive impairment might have provided additional benefits (King & Green, 2015; McDougall et al., 2011).

Popp and Schneider (2015) have claimed that attention placebo control arms should be included in the design methodology of psychosocial interventions in order to test the specific effect of psychosocial treatment. Such methodologies have the
potential to reduce dropouts by offering participants a more attractive treatment option than being added to a waitlist, and also address the ethical dilemma of withholding potentially beneficial treatment to participant who would benefit from being involved in the intervention. Despite the benefits of including attentional control arms, only two cognitive rehabilitation studies presented in Table 2.1 have used attentional control arms to date (Ferguson et al., 2016; McDougall et al., 2011).

There was one study that did not report additional benefits of participating in cognitive rehabilitation in the treatment group compared to the care-as-usual group, however, the intervention was conducted in conjunction with inpatient cancer rehabilitation received by all participants in the study (Poppelreuter et al., 2009). All three groups in that study demonstrated improvement, which may have occurred as an effect of the rehabilitation program despite it not specifically targeting cognition. It is also possible that some or all of the improvements could have been due to practice effects. Except for this study, each of the other studies that utilised a comparison arm demonstrated greater improvements in the intervention groups than the comparison groups.

The five additional studies added to the original table published by King and Green (2015) include three CRT studies (Ercoli et al., 2015; Ferguson et al., 2016; King & Green, 2015) and two web-based CT studies, which will be discussed in greater detail in the next section of this chapter on web-based cognitive rehabilitation interventions (Bray et al., 2017; Damholdt et al., 2016). In the study conducted by Ercoli et al. (2015), 48 breast cancer survivors were randomly assigned to participate in a 5-week cognitive rehabilitation intervention or to a waitlist control group. The primary outcome measure of the study was total score on a subjective measure of cognitive functioning called the Patient’s Assessment of Own Functioning (PAOFI); the secondary outcome was objective cognitive functioning assessed on six validated
neuropsychological measures, and a measure of premorbid intelligence. The results from the study found that the intervention group improved significantly more than the waitlist control group on the PAOFI total and the PAOFI memory scale, and on two scales of the Rey Auditory Verbal Learning Test (i.e., total verbal learning and delayed recall). Significant group differences were not observed on any of the other five neuropsychological measures, supporting the earlier claim that group differences on objective cognitive functioning measures are generally found on only few if any of the total measures administered.

Ferguson et al. (2016) conducted a randomised controlled trial of a videoconference-delivered Memory and Attention Adaptation Training (MAAT) intervention, which was previously delivered in face-to-face format in two published studies (Ferguson et al., 2007; Ferguson et al., 2012). Forty-seven breast cancer survivors with self-reported chemotherapy-related cognitive dysfunction were randomly allocated to the intervention group or an attentional control condition that received supportive therapy. This study was the first time that MAAT was tested against an active treatment control condition, which was designed to account for the effects of social support and attention. The primary outcome measures used were two self-report subscales of subjective cognitive functioning. Secondary outcomes included several validated neuropsychological tests and psychosocial variables. The results from the study demonstrated the intervention group made significantly greater gains in the self-report measure assessing perceived cognitive impairments at follow-up and on a measure of processing speed at post-treatment compared to the supportive therapy group. The reported effect sizes were moderate on both perceived cognitive impairments ($d = .52$) and processing speed ($d = .50$).

The study conducted by King and Green (2015) was a randomised controlled trial with a CRT intervention program entitled “Responding to Cognitive Concerns” or...
ReCog. The ReCog intervention serves as a cornerstone in the current research project because it was the intervention program that was adapted into web-based format and implemented in the two studies presented within this thesis. ReCog was developed as a manualised intervention to address cognitive dysfunction in cancer survivors (Schuurs & Green, 2013). Based on the principles of CBT, the program consists of four sessions containing elements of psychoeducation, relaxation training, mindfulness practices, strategy training, discussion questions, and homework. The intervention is offered in group format over the course of four weeks (i.e., one session per week), with each session lasting about two hours. The sessions of the program are divided into the following themes: (a) aging, health, cancer and cognitive function, (b) memory, (c) attention, and (d) fatigue, emotions and cognition. Participants involved in the program receive a workbook to keep, which may be used as a reference for the content of the program at a future time.

As described in Table 2.1, the ReCog intervention has been evaluated twice in cohorts of cancer survivors with complaints of cognitive dysfunction (King & Green, 2015; Schuurs & Green, 2013). The first published study to evaluate the feasibility of the intervention was conducted by Schuurs and Green (2013). In their study, the researchers recruited three groups of adults who were assigned to the cancer intervention group \( (n = 23) \), cancer comparison group \( (n = 9) \), or community sample group without a history of cancer \( (n = 23) \). The results from the study found a significant interaction effect on overall cognitive functioning as measured on the Repeatable Battery for Assessment of Neuropsychological Status (RBANS) whereby the intervention group improved to a significantly greater extent than the two comparison groups. Significant interactions were reported on subscales of immediate memory, visuospatial performance, and delayed memory. No significant interaction effects were reported on subjective measures of cognitive functioning, however the
researchers stated that the power to detect those interactions was low. They found that participants started and finished in the normal range on measures of subjective cognitive functioning, which is atypical for cancer survivors.

The second study conducted with ReCog was an RCT that included 29 cancer survivors assigned to either the intervention group (n = 16) or waitlist control group (n = 13) by random allocation (King & Green, 2015). Their study also contained a third group of 16 demographically matched community dwelling adults without a history of cancer. The results were analysed comparing the cancer groups only and comparing all three groups. When comparing the two cancer groups, the results demonstrated a significant interaction effect on an objective measure of cognitive functioning assessing processing speed/visual scanning whereby the intervention group improved significantly more than the control group at both post-intervention and follow-up. A trend was reported on the subjective measure subscale of perceived cognitive impairments, whereby the intervention group tended to report reduced cognitive impairments to a greater extent than the control group. When all three groups were included in the analyses at two time points, a significant interaction was reported on the total RBANS measure with both the intervention group and cancer control group demonstrating improvements to a greater extent than the community dwelling comparison group. There was a significant interaction effect on the visuospatial/constructional index of the RBANS with the cancer groups performing significantly worse than the community group at baseline, but there was no difference between groups at post-intervention. On the subscale measuring perceived cognitive impairments, a significant interaction effect was found where the intervention group improved significantly more than the other two groups at post-intervention. A trend was noted on the impact on QoL subscale with the intervention group reporting a
tendency towards improved QoL to a greater extent than the other two groups at post-intervention.

Thus far, the evidence for CRT and CT programs to treat cognitive dysfunction in cancer survivors has shown promise. However, there are some limitations associated with the research presented. First, despite showing promise for mitigating cognitive symptoms in cancer survivors, the application of these research findings into everyday clinical practice is challenging. Furthermore, many of the CRT interventions have been conducted with relatively small sample sizes, meaning the findings associated with intervention effects have varied greatly between studies on both objective and subjective measures of cognitive functioning. Additionally, the measures used to assess these outcomes have varied, making comparisons between studies a challenge. Lastly, there has been a larger focus on CRT compared to CT (i.e., only four studies) in this clinical population (refer to Table 2.1) and few comparisons evaluating which types of interventions are more beneficial for cancer survivors. Notably, all of the CRT studies were conducted using in-person format, including both ReCog studies, whereas three of the four CT interventions were delivered online and completed by participants in the home environment. To date, there are no known web-based CRT programs offering cognitive remediation to cancer survivors. The first aim of this research project was to develop a web-based CRT intervention by adapting the existing ReCog program into online format. To provide theoretical support for the development of an online CRT intervention, the next section of this chapter examines the scope and effectiveness of web-based interventions in cancer survivorship research. More specifically, it aims to discuss the effectiveness of the three existing published online CT interventions that have been assessed in cancer survivors to date and to compare the potential benefits offered by CRT and CT programs.
Web-Based Interventions in Cancer Survivorship

In recent years, web-based delivery designs have become a prominent methodology for administering psychosocial and therapeutic interventions within the healthcare field. Terms such as e-therapy, online therapy, Internet therapy, cybertherapy, web-based therapy, ehealth, or telehealth are used to describe these online therapeutic activities. There are several advantages to using web-based interventions over traditional in-person methodologies. First and foremost, interventions that are conducted online have the potential to reach a wider population and provide increased access to health care services to populations with difficulties accessing traditional treatment methods, such as those living in rural communities or individuals with mobility issues (Cuijpers, van Straten, & Andersson, 2008; Lintvedt et al., 2013; Ritterband et al., 2012). Additionally, web-based interventions provide flexibility to participants by allowing them to complete tasks on their own time (Barak, Klein, & Proudfoot, 2009), they are cost-effective (Blom, Bosmans, Cuijpers, Zarit, & Pot, 2013; Warmerdam, Smit, van Straten, Riper, & Cuijpers, 2010), and in some circumstances can provide anonymity when discussing sensitive health issues (White & Dorman, 2001).

Psycho-oncology has seen an increase in emerging web-based intervention programs in recent years targeting a variety of different health outcomes in adult cancer survivors, including cancer-related distress (Beatty, Koczvara, & Wade, 2016; Braamse et al., 2016; Gorlick, Bantum, & Owen, 2014; Lepore, Buzaglo, Lieberman, Golant, & Davey, 2011; J. E. Owen, Bantum, Gorlick, & Stanton, 2015; Ruland et al., 2013; Wootten et al., 2015), cancer-related fatigue and sleep problems (Bruggeman Everts, van der Lee, & de Jager Meezenbroek, 2015; Foster et al., 2016; Ritterband et al., 2012), depression and anxiety (Duffecy et al., 2013; Klemm, 2012; Willems et al., 2016), diet and exercise (Galiano-Castillo et al., 2016; Goode, Lawler, Brakenridge,
Reeves, & Eakin, 2015; Hatchett, Hallam, & Ford, 2013; Lee et al., 2014), sexual
dysfunction and distress (Classen et al., 2013; Schover et al., 2013), and cognitive
functioning (Bray et al., 2017; Damholdt et al., 2016; Kesler et al., 2013) amongst
other psychosocial variables.

Systematic reviews conducted to evaluate the effectiveness of online interventions in cancer survivors have found that some web-based interventions are as effective as in-person interventions (Bouma et al., 2015; Kim & Park, 2015). Bouma et al. (2015) conducted a review of the literature of web-based randomised and non-randomised controlled trials that aimed to rehabilitate or support cancer survivors with psychosocial and/or physical symptoms resulting from diagnosis and treatment. The studies selected were conducted with adult cancer survivors and included a comparison group. The results yielded 16 studies comprising 2620 cancer survivors. All but one of the studies provided education with the program, and the majority of the programs offered participants the opportunity to communicate with peers or professionals. Except for one support program, all other programs were facilitated by a moderator whose role varied from introducing discussion topics, providing expertise on question topics, or active involvement in the intervention (e.g., email support or participating in discussions). Positive effects of the web-based programs were observed in nine of the studies; two studies reported insufficient participants to detect significant results and two studies reported significant within group effects over time, but not between group effects. Three studies that used psychological distress as an outcome measure did not find significant results. One of the main limitations of the review was that the studies included used many different outcomes, therefore the review lacked homogeneity amongst samples. There were no web-based RCT or CT interventions included in Bouma et al.’s literature review, likely due to the scarcity of published web-based
cognitive rehabilitation programs. The existing published web-based cognitive rehabilitation studies are discussed in the next section of this chapter.

**Web-Based Cognitive Rehabilitation**

As mentioned in the previous section, to date there have been three published RCT studies evaluating the effectiveness of CT in cancer survivors. The first study was published by Kesler et al. (2013), and evaluated the effectiveness of an executive functioning (EF) training program in a group of BCS treated with chemotherapy. The EF Training Program was comprised of 13 exercises designed to improve core EFs and were selected by a clinical neuropsychologist from existing cognitive exercises created by Lumos Labs Inc. (San Francisco, CA). The study included a total of 41 BCS on average six years post-treatment that were assigned to the intervention group ($n = 21$) or waitlist group ($n = 20$). Assessments were completed at baseline and post-intervention. Participants assigned to the EF Training Program group were required to login to their account and complete five exercises four times per week over the course of 12 weeks for a total of 48 training sessions. Each training session lasted 20 to 30 minutes. The exercises were adapted to individual ability and progressively increased in difficulty over the course of the program. To increase adherence, the researchers contacted participants via telephone or email once per week to remind them to complete the required exercises. The primary outcome measure was performance on the Wisconsin Card Sorting Test (WCST), a measure of cognitive flexibility. Secondary outcomes included measures of verbal memory, verbal fluency, working memory, processing speed, and a self-report measure of EF measured by the Behavioural Rating Inventory of Executive Function (BRIEF). The researchers also evaluated psychiatric distress in order to control for any effects it might produce on cognitive outcome measures. Reported attrition rates were 5% in the active treatment group and 10% in the waitlist group. Results from the study found that the treatment
group demonstrated significant improvement to a greater extent than the control group post-intervention on objective cognitive measures including the WCST, verbal fluency, and processing speed. The groups did not differ significantly on subjective EF on the BRIEF, however, the intervention group improved significantly more than the control group on subscales of planning/organisation and task monitoring. Effect sizes were medium to large ranging from $d = .43$ to $d = .87$. Participants in the active treatment arm demonstrated 95% compliance as measured by program completion, and completed an average of 4 ($SD = 0.42$) sessions per week and required an average of 13.0 ($SD = 0.92$) weeks to complete the program and assessments.

The second study was conducted by Danish researchers Damholdt, Mehlsen, O’Toole, Andreasen, Pedersen, and Zachariae (2016) who recruited 157 BCS who were randomly allocated to receive web-based CT (eCogT) with email support ($n = 94$) or to a waitlist control condition ($n = 63$). They utilised a customised training program comprised of 12 tasks centred on six cognitive domains from the web-based program Happyneuron Pro© (Scientific Brain Training, Villeurbanne Cedex, France). Participants were randomised to groups after completing baseline assessments, and were reassessed post-intervention or waiting period at 7-8 weeks post-randomisation and again at follow-up at 27 weeks. Neuropsychological assessments were conducted over the telephone and self-report questionnaires were completed online. Participants began at the same level of difficulty, but advanced at an individual pace when two error-free trials were completed in a row. Participants were asked to complete a minimum of 30 minutes per day, five days per week over the course of six weeks for a total of 15 hours of training. The primary outcome measure was working memory assessed with the Paced Auditory Serial Addition Test. Secondary outcomes included self-reported cognitive function assessed with the Cognitive Failures Questionnaire, verbal memory and learning, working memory, and EF. Attrition was 23% in the
intervention group and 10% in the waitlist group; intent-to-treat analyses were performed. Significant group differences were not found on the primary outcome measure for working memory. There were significant interaction effects on verbal learning and working memory measured by Digit Span Backwards whereby the eCogT group improved to a greater extent than the control group. No significant differences were found between groups on subjective cognitive functioning. The average time spent engaging in cognitive training exercises was 16.78 ($SD = 7.97$, range 1 to 40 hours), which was slightly above the recommended 15 hours of participation. The researchers reported that 65% of participants used the program for 15 hours or more during the intervention period, which is indicative of relatively high adherence to the program instructions.

The third study to evaluate web-based CT in adult cancer survivors was conducted by Bray et al. (2017). Their study did not focus solely on BCS like the previous two CT studies and included 242 cancer survivors with mixed tumour types who had received three or more cycles of chemotherapy completed within the previous 6 to 60 months. Participants were recruited from 18 sites throughout Australia and were randomly allocated to the CT intervention group ($n = 122$) or waitlist control group ($n = 121$). Assessments occurred at baseline, post-intervention or wait period, and at 6-month follow-up. The intervention program used was Insight (Posit Science Corporation, San Francisco, CA), a program designed to target five cognitive domains frequently affected in cancer patients. Participants in the intervention group were recommended to train for four 40-minute sessions over the course of 15 weeks for a total of 40 hours of training. Unlike the previous two CT interventions discussed, the primary outcome in their study was subjective cognitive functioning rather than objective cognitive functioning. The outcome was assessed with the Functional Assessment of Cancer Therapy Cognitive Function (FACT-Cog version 3), with a
primary emphasis on the perceived cognitive impairment (PCI) and the perceived
cognitive abilities (PCA) subscales. Secondary outcomes included objective
neuropsychological functioning assessed by the CogState computerised battery
evaluating seven domains of cognition, anxiety/depression, QoL, fatigue, and stress.
Outcome data at 6-month follow-up were available for 184 participants with attrition
rates of 21% in the intervention group and 26% in the waitlist control group. Intent-to-
treat analysis was performed with missing data. The results found significant
interactions where the intervention group reported significantly less PCI than the
control group at T2, and this was sustained at T3. PCA were significantly better in the
intervention group at T2 and T3; the intervention group reported significantly less
impact on QoL at T2, but this was not sustained at T3; the intervention group reported
fewer comments from others about their cognitive impairment at T2, but there was no
difference between groups at T3. Reported effect sizes were small at T2 for PCI ($d = .28$) and for PCA ($d = .31$). No significant differences between groups were reported
on objective neuropsychological functioning. The average time spent training by the
intervention group was 25.08 hours (range 0.19 to 55.82 hours), which was less than
the recommended 40 hours. Only 27% of participants completed the program in the
recommended 15-week timeframe, and 14% of participants never began the program after being randomly assigned to the intervention group.

In summary, the three studies evaluating web-based CT in adult cancer
survivors have shown promise in providing remediation to address cognitive
dysfunction in BCS and survivors of various tumour types. Significant intervention
effects were observed on outcome measures of objective cognitive functioning
(Damholdt et al., 2016), subjective cognitive functioning (Bray et al., 2017), or both
(Kesler et al., 2013). The total time recommended engaging in training varied across
studies from 15 hours to 40 hours. In the study where 40 hours were recommended,
participants were found to engage less than recommended averaging around 25 hours over the course of the program. In the other two studies where approximately 15 hours was recommended, compliance was high. Attrition rates in the intervention group ranged from 5 to 23% and 10 to 26% in the waitlist group, with the highest overall attrition occurring in the intervention recommending 40 hours of training. This may have occurred as a result of the time demands required to complete the intervention, especially noting that only 27% of participants were able to complete the program in the recommended timeframe (Bray et al., 2017). The duration of the intervention (i.e., 15 weeks) was longer than the other two (i.e., 6 and 12 weeks). Another possible explanation for the higher drop-out rate was that participants had less interaction with the facilitator than the other two studies, which included weekly reminder emails or telephone calls (Kesler et al., 2013) and standard email support (Damholdt et al., 2016). Studies with online interventions have demonstrated that users are more likely to adhere to a program if they are held accountable to another person, a theory known as “Supportive Accountability” (Mohr, Cuijpers, & Lehman, 2011). As mentioned in the previous section, one of the underlying assumptions of CT is that improvements in certain cognitive domains will generalise to other contexts, an assumption that has not been universally supported (Bahar-Fuchs et al., 2013; A. M. Owen et al., 2010; Papp et al., 2009). In these studies it is not known how improvements on objective neuropsychological measures translate into functional improvement in everyday life, however the two studies demonstrating improvements in subjective cognitive functioning may be a reflection of improvement on everyday tasks.

As mentioned earlier in this chapter, no web-based CRT intervention studies designed to treat cognitive problems in cancer survivors have been published in the literature. A potential advantage of developing online CRT interventions is that CRT aims at improving functioning on tasks identified by the individual as problematic in
everyday life, which is unlike CT interventions that focus on improving a specific cognitive domain (Wilson, 1997). The focus of CRT is to teach participants strategies and skills for managing cognitive dysfunction, therefore successful implementation and rehearsal of these strategies from day to day may increase their likelihood of generalising to a broader context of tasks. These daily improvements are likely to be reflected in subjective measures of cognitive functioning and self-reported QoL. Another potential advantage is that many of the existing CRT interventions have lesser time demands than CT programs and generally occur over a shorter overall duration. For example the ReCog intervention requires eight hours of participation (i.e., two hours per week for four weeks); and the group memory workshops by Cherrier et al. (2013) require seven hours of participation (i.e., one hour per week for seven weeks). Less intensive time commitments may increase the likelihood that participants actually complete the program, thereby reducing dropout rates and increasing intervention effectiveness in terms of the proportion of participants who benefit (Mohr et al., 2011; Schubart, Stuckey, Ganeshamoorthy, & Sciamanna, 2011).

**Engagement in Web-Based Interventions**

Difficulties with participant engagement and attrition have been problematic in online interventions (J. E. Owen et al., 2015). Generally the reported overall engagement rates across studies implementing web-based interventions in cancer survivors are low (David, Schlenker, Prudlo, & Larbig, 2013). Engagement is defined as how individuals use an intervention program, which can be measured through a variety of different approaches (J. E. Owen et al., 2015). In web-based interventions, researchers will typically report participant engagement as the number of messages posted on a website or webpage (Classen et al., 2013; Han et al., 2012), the number of times a participant logged in to a program (Beatty et al., 2016; Duffecy et al., 2013), the number of modules completed (Beatty, Koczwara, & Wade, 2011), or the amount
of time spent visiting a particular website or program (Bray et al., 2017; Schover et al., 2013). Whilst these methods of measuring engagement are common in the literature, the question of whether they provide a sufficient gauge for assessing participant engagement is debatable (Morrison & Doherty, 2014).

One reason for low engagement levels is that many online interventions have higher dropout rates than typical face-to-face programs with reported attrition rates approaching nearly 40% in some studies (David et al., 2013; Foster et al., 2016). This phenomenon of participants discontinuing usage of the program and/or being lost to follow-up has been termed the law of attrition (Eysenbach, 2005) and is a methodological challenge in web-based research. Another reason that reported engagement rates are low may be that the current methodologies used in the literature are insufficient to meaningfully quantify engagement. The number of logins to a program does not provide information about whether the participant actually navigated through the program or received the intended intervention. The participant could have logged in and immediately logged back out. Similarly, calculating time spent in the program is not a valid indication of time engaged in the program as the participant may have left their computer for a lengthy time period during the recorded session. Given the challenges with the current methods of defining engagement, the second aim of the current research project is to develop a new strategy for quantifying engagement that is hopefully a more meaningful reflection of participants’ engagement in key learning activities of the online program.

Exploring the science of engagement in online interventions is an important factor to consider when developing web-based interventions. Understanding the ways in which participants engage in the intervention program has the potential to increase the likelihood of real-life behaviour change in an external environment (Danaher & Seeley, 2009). Furthermore, poor engagement can pose a significant threat to treatment
fidelity. The concept of treatment fidelity refers to the methodological strategies used by researchers to monitor and reinforce for reliability and validity of behavioural interventions (Bellg et al., 2004). The guidelines established by the National Institutes of Health Behaviour Change Consortium provide a framework that includes five essential elements related to treatment fidelity: (a) study design, (b) provider training, (c) treatment delivery, (d) receipt of treatment, and (e) enactment of skills (Bellg et al., 2004). Since web-based interventions are typically self-administered, researchers are challenged with the task of determining whether participants are receiving the proper dosage of the intervention and whether the program is being completed as intended by the clinician (Eaton, Doorenbos, Schmitz, Carpenter, & McGregor, 2011). Challenges of this sort make it difficult for researchers to replicate studies in future research or draw accurate conclusions about the outcomes of the study.

In addition to considering participant engagement during the process of developing web-based interventions, there are additional design elements that have been demonstrated to increase the validity and effectiveness of online programs. Barak and colleagues (Barak, Hen, Boniel-Nissim, & Shapira, 2008) conducted a meta-analysis of 92 web-based interventions for a variety of psychological problems and explored variables that contribute to the overall effectiveness of online intervention programs. They considered a variety of moderating variables in their analysis such as intervention method (e.g., CBT, psychoeducation, behavioural), types of outcome measures, type of problem being treated, Internet modalities, participant age, and other variables that may affect the effectiveness of the intervention. After a thorough investigation, the researchers concluded that: CBT was more effective than either psychoeducation or behaviour therapy alone (effect sizes 0.83, 0.46, 0.23, respectively); interactive websites were more effective than static websites (effect sizes 0.65 and 0.52, respectively); individual e-therapy was more effective than group e-
therapy (effect sizes 0.57 and 0.36, respectively); and in respect to modality, audio was more effective than chat, email, forum and webcam (effect sizes 0.91, 0.53, 0.51, 0.34 and 0.31, respectively). Considering these factors is a critical step during the development process of web-based intervention programs and should be carefully premeditated during the design process.

This section has examined the published studies on CT for cancer survivors, and discussed some of the limitations of CT as well as some of the potential advantages of CRT as an alternative intervention approach. It also explored the importance of designing web-based intervention programs that incorporate a valid measure of participant engagement and online elements that assist to maximise intervention effectiveness (e.g. interactive versus static, or individual therapy versus group therapy). Despite having some evidence of design methods that can improve the development of online interventions, there has been little research published exploring the underlying mechanisms by which an intervention achieves its positive effects (Stanton, Luecken, MacKinnon, & Thompson, 2013). The third aim of this research project is to examine whether underlying motivation is a factor that contributes to the effectiveness of CRT. The next section of this chapter presents a theoretical framework for understanding the potential underlying mechanisms that may contribute to the effectiveness of cognitive rehabilitation interventions in cancer survivors.

**Psychological Mechanisms and Self-Determination Theory**

One potential factor that may contribute to the overall effectiveness of cognitive rehabilitation interventions is how well the interventions target participants’ cognitive and psychosocial needs. As discussed at the beginning of this chapter (p. 9), there are a number of issues and unmet needs that cancer survivors have reported in association with extended survival, including addressing memory and attention, psychoeducation about what to expect after treatment, rehabilitation services available,
and access to social support groups with other cancer survivors (Campbell et al., 2010; Jefford et al., 2008; Knobf et al., 2012). Many of the existing CRT interventions, including ReCog, address and provide support for these unmet needs, which may, in part, account for participants’ improved cognitive performance and social functioning post-treatment (King & Green, 2015; Schuurs & Green, 2013). However, other factors may also contribute to intervention effectiveness.

Cognitive self-efficacy, which refers to a person’s confidence and/or perceptions related to the effectiveness of their cognitive functioning in particular situations (King & Green, 2015), was evaluated as a potential mechanism for change in a previous ReCog study. The researchers found that improved cognitive self-efficacy was significantly correlated with improved self-reported impact on QoL (King & Green, 2015). According to leading research in the field of social cognitive theory, Bandura (1990), self-efficacy provides the foundation for human motivation and largely influences human behaviour. Therefore, there is theoretical support to suggest that human motivation may be an underlying factor influencing participation in cognitive rehabilitation programs and could impact on outcomes in such research.

The third aim of this research project is to evaluate whether human motivation mediates the relationship between intervention effects and improved outcomes in web-based cognitive rehabilitation therapy, a topic that has not yet been widely examined in the literature on cognitive rehabilitation in this clinical population. From a holistic approach, it is believed that cognitive functions are associated with emotions, motivation and other noncognitive functions (Wilson, 1997). This may explain why CRT is potentially more beneficial than targeting specific cognitive domains in CT alone. The next paragraphs of this chapter present a theory of human motivation called Self-Determination Theory (SDT), which was evaluated in relation to potential mediators in the current research project.
SDT is a broad theory of human motivation that suggests self-motivation stems from the extent to which an individual’s innate psychological needs or growth tendencies are met within their social network (Ryan & Deci, 2000). The theory has its roots in organismic perspectives, which share a few basic assumptions with SDT: humans are active more than they are reactive, and they seek out problems and ways to solve them; human beings have an ongoing potential which guides them in seeking out different levels of expression and functioning in their lives; and from a dialectical perspective, life is viewed as an “ongoing struggle characterised by cyclical movement between impeding challenges, coping responses, creative resolutions, and new challenges” (Sheldon, Williams, & Joiner, 2003, p. 16). According to the organismic perspective, human beings try to maximise their potential through self-movement with the ultimate goal of increasing the complexity of their behavioural functioning over time. Within the SDT framework, this is referred to as intrinsic motivation whereby individuals strive to better themselves by meeting three inherent, psychological needs that foster well-being and health: competence, autonomy, and relatedness (Deci & Ryan, 1985).

According to Deci and Ryan (1985), intrinsic human motivation is influenced by fulfilling the psychological needs of competence, autonomy and relatedness. Perceived competence refers to one’s ability to interact effectively within their environment when confronted with challenging tasks; autonomy is defined as the perception that one’s actions and experiences are voluntary rather than controlled by external forces; and relatedness refers to the degree to which an individual feels connected to those in their immediate environment. When these three psychological needs are not being met, motivation levels for engaging in certain behaviours may become diminished. From a theoretical perspective, it could be argued that an innate drive to satisfy these needs underlies human motivation, which in turn influences the
extent to which an individual engages in and benefits from cognitive rehabilitation interventions.

Evaluating potential mediating processes in psycho-oncology interventions has the potential to assist researchers to better understand how interventions are effective in producing change and is considered an important step for integrating theory, research, and practice (Stanton et al., 2013). Human motivation from an SDT framework has been evaluated in interventions targeting exercise and physical activity behaviours in cancer survivorship research (Milne, Wallman, Guilfoyle, Gordon, & Corneya, 2008; Peddle, Plotnikoff, Wild, Au, & Courneya, 2008). One study found that BCS who met the recommended public health physical activity guidelines demonstrated higher intrinsic motivation, autonomy support, and competence than the BCS group not meeting physical activity guidelines (Milne et al., 2008). Furthermore, intrinsic motivation was significantly correlated with autonomy support and competence in their study. The second study reported that exercise behaviour and intrinsic motivation were both significantly correlated with autonomy support, competence, and relatedness in an exercise intervention for colorectal cancer survivors (Peddle et al., 2008). A third study examined the SDT constructs competence, autonomy, and relatedness as mediators in a communication intervention for BCS and found that all three constructs mediated the effect between intervention treatment and QoL (Hawkins et al., 2010). As such, the following section of this thesis reiterates the aims of the current research project and states the hypothesis for the project.

**Current Study**

This chapter has provided a literature review addressing the sequelae of cognitive and psychosocial issues associated with extended cancer survivorship. Many cancer survivors experience cognitive impairment following cancer treatment, and the effects can last many years after treatment completion and can affect daily functioning
and QoL. Some cancer survivors experience cognitive dysfunction prior to the start of treatment, which suggests that psychosocial and biological factors can also impact on cognition.

In addition to cognitive impairment, cancer survivors report that there is often a lack of additional support following treatment, such as psychoeducation about what to expect after treatment, strategies for managing cognitive impairment, rehabilitation services to assist in improving their daily functioning, and support network services for sharing their experiences with other cancer survivors. As noted earlier in this chapter, cognitive rehabilitation interventions for cancer survivors have the capacity to address each of these unmet needs by teaching compensatory strategies for managing cognitive difficulties, providing information about cancer and its impact on cognition, and introducing cancer survivors to others who have had similar experiences.

The first aim of this project was to develop a web-based CRT intervention through the adaptation of an in-person program and to evaluate whether it was an effective way to assist with the cognitive problems reported by cancer survivors. Currently there are no published web-based CRT interventions available for cancer survivors, and only three published online CT programs with a similar aim.

The second aim of this research was to investigate the way in which participants engage in the web-based CRT intervention programs. Participant engagement is an important mechanism that has the potential to explain intervention effects, yet is currently not well evaluated in the literature. Typical methods used to measure engagement do not capture the full picture of the way in which participants navigate through online interventions.

The final aim of this study was to explore the mechanisms of the intervention that contribute to its effectiveness, which will be considered from an SDT theoretical framework. As discussed earlier, fulfilment of the three basic psychological needs of
competence, autonomy and relatedness can provide motivation for individuals to engage in therapeutic and behaviour change. This project examined whether the effects treatment has on cognitive functioning are mediated by these three psychological needs.

**Hypotheses**

1. Intervention groups would improve to a significantly greater extent on measures of subjective cognitive functioning compared to waitlist control groups post-treatment.

2. Intervention groups would improve to a significantly greater extent on measures of objective cognitive functioning compared to waitlisted groups post-treatment.

3. By using an improved index for measuring engagement, significant correlations would be found between participant engagement and improved subjective cognitive functioning.

4. Motivation (e.g., competence, autonomy, and relatedness) would mediate the effects of treatment on subjective cognitive functioning.
CHAPTER III: PROJECT METHODS

The previous chapter provided a literature review of the effects that cancer and its treatment can have on cognitive functioning and discussed how cognitive rehabilitation interventions have the potential to mitigate the symptoms of cognitive dysfunction experienced by some cancer survivors. As discussed in Chapter II, the research presented in this thesis adapted the “Responding to Cognitive Concerns (ReCog)” intervention program into a web-based format (eReCog) based on the program content contained in the ReCog Clinician’s Manual (Schuurs & Green, 2009a). A description of the program content is presented in Appendix A.

Web-based eReCog is divided into four training modules that correspond with the four group sessions of ReCog. Module 1 focuses on cognition and ageing providing psychoeducation on ageing, cognition, and the impact of cancer treatments on cognitive functioning. There are group discussion pages where participants can discuss their own experiences of cancer-related changes in cognition and how they have coped with the changes. Additional activities in the module include relaxation training using an embedded video file, goal setting and problem solving activities, and assigned homework tasks. The second module relates primarily to memory and provides psychoeducation on understanding different types of memory and provides participants with various compensatory and enhancement strategies for improving memory functioning. There is a group discussion for participants to discuss changes in memory, coping strategies, and the effectiveness of these strategies. The assigned homework task is to elect a new memory strategy to practise over the following week along with continued relaxation practice. Module 3 pertains to attention and offers psychoeducation and compensatory and enhancement strategies for improving
attention. Participants are able to share their experiences of difficulties with attention in group discussions and select a new attention strategy to implement as homework during the next week. The final module focuses on the impact fatigue and emotional changes can have on cognition. Strategies for managing fatigue and self-care are presented along with a group discussion about personal experiences. Participants are instructed to continue applying strategies learnt from the program and implement self-care strategies for their final homework assignment. Feedback about participation in the program is also requested in the final module.

The eReCog intervention was implemented in two studies that comprised this research project: Study One (pilot study) and Study Two (RCT). The same measures and procedures were implemented for the two studies; however, the participants and recruitment were distinct. This chapter first describes the development process of creating eReCog, and then provides the study methods for Study One and Two of this research project.

**Development of eReCog**

A considerable amount of preparation is required in the development and evaluation of behavioural interventions. A Stage Model of Behavioural Therapies Research was developed to delineate the three progressive stages involved in the scientific process leading from initial efficacy research to effectiveness research (Onken, Blaine, & Battjes, 1997). The activities involved in Stage I include piloting and feasibility testing, developing a written manual, clinician training, and developing measures for assessing adherence/competence. Stage II research is focused on implementing RCT experimental designs to evaluate the efficacy of interventions that showed promise during Stage I research. The final Stage III of research focuses on translating efficacious interventions from the laboratory into a real-world setting focusing on generalisability, issues associated with implementation, cost-effectiveness,
and acceptability of the intervention program to consumers and policy makers. This model is also relevant to the development of web-based interventions in order to ensure that the process from inception to dissemination incorporates a rigorous design phase comparable to research conducted in more controlled research settings (Danaher & Seeley, 2009).

The in-person ReCog intervention was developed by doctoral candidate Dr Alana Schuurs and supervisor Dr Heather Green in 2009. Stage I of the research process involved writing a clinician’s manual (Schuurs & Green, 2009a) and participant’s manual (Schuurs & Green, 2009b), and conducting an initial feasibility study with a sample of cancer survivors, comparison group of waitlisted cancer survivors, and community dwelling adults who had never had cancer (Schuurs & Green, 2013). Stage II of the scientific process was carried out by another doctoral candidate Dr Summer King and supervisor Dr Heather Green through conducting a RCT with a cohort of cancer survivors randomly allocated to intervention or waitlist groups and demographically matched community volunteers (King & Green, 2015). Part of the final Stage III process of translating the intervention into real-world contexts by evaluating the implementation process, and improving availability and cost-effectiveness involved the adaptation of the intervention into web-based format. Creating a web-based version of the intervention, however, also meant returning to Stages I and II of the scientific process in order to validate the intervention in its new format and to complement existing research with the program. In this research project, Study One fulfilled the activities of Stage I (i.e., piloting and feasibility) whereas Study Two involved the activities typical of Stage II (i.e., RCT experimental design).

The design methodology used to develop web-based interventions is an important factor in creating effective online interventions. There is mounting evidence in the literature to demonstrate that participants engage in online interventions less
than envisioned by program developers (Eysenbach, 2005). As discussed in Chapter II of this thesis, researchers have identified elements of web-based interventions that may increase effectiveness and participant engagement, including the use of CBT, interactive websites, individual treatment rather than groups, and the inclusion of audio elements in the program (Barak et al., 2009). Ritterband, Thorndike, Cox, Kovatchev, and Gonder-Frederick (2009) noted in their model of Internet interventions that a website’s appearance, content, source and style of the content, delivery method, burdens of using the website, ability to engage users through interaction and reinforcement, prescriptions to instruct the user on how to address the targeted problem, and the ability to personalise the program can affect overall participant engagement in web-based interventions. Each of these elements was considered during the conceptualisation and development of the eReCog intervention.

The process of adapting an in-person intervention into web-based format has previously been described in a patient-caregiver communication intervention for improving communication, support, and emotional well being in cancer survivors. Zulman et al. (2012) created a model that outlined the timeline and development process for adapting the FOCUS intervention into a tailored, web-based delivery format (see Figure 3.1). There were two multidisciplinary teams involved in the development process, namely the Content Development Team and the Program Design and Development Team. The first phase consisted of ideation and prototyping, which involved the research team conducting focus groups with patients and their caregivers, and periodic review by the FOCUS intervention staff. The next phase was the iterative design and development phase, which included usability testing conducted by usability specialists and a nurse from the team. The final phase consisted of internal testing and final development of the program by the developers and behavioural scientists. The
total adaptation and development of the web-based program took about 12 months for the researchers to complete.

![Timeline and development process for adapting the FOCUS intervention to web-based format.](image)


The development of eReCog utilised aspects of the model detailed in Figure 3.1, however, limitations in the budget for PhD research precluded involvement of a multidisciplinary team of program developers, design specialists, and behavioural scientists. Rather than using completely customised software, web-based eReCog was created by translating the ReCog content and structure into LessonLAMS, which is open source Learning Activity Management System (LAMS) software developed by LAMS International (LAMS International Pty Ltd, 2002). This software is used for designing, managing and delivering online collaborative learning activities. The author is able to create a learning activity (e.g., module) comprised of a sequence of activity pages and give learners (e.g., participants) permission to access the content by registering their email address. The software is openly available for use at no charge with up to 30 learners and can be purchased on a monthly or yearly basis for use with
more than 30 learners. Creating an account to develop and deliver learning activities is accomplished by signing up for an account on the software website www.lessonlams.com with an active email address and password.

Once an account has been created, the author can begin creating a learning sequence either by building a lesson from scratch or utilising one of the ready-to-use templates available. Educators who choose to make their lessons available to others may also share lessons on the Internet. The author can select from a variety of different activities, which are located in a toolbar on the left side of the computer screen (see Figure 3.2). By double-clicking on the activity box, the author creates a new page whereupon desired learning material including text, videos, graphics, and audio files are inputted. Arrows are then used to connect the activity boxes to create the appropriate sequencing order.

![Figure 3.2 Webpage for creating a sequence of learning activities.](image)

There are some valuable features that add to the quality of the LessonLAMS software. One feature is the scrolling sequencing toolbar located on the left side of the
screen of the learning activity (see Figure 3.3). This allows participants to see the total number of pages included in the module and track their progress. Double-clicking on the page icons in the sequencing toolbar allows participants to return to view pages already completed. The “next activity” button located at the bottom right hand of the screen allows participants to complete the pages at their own desired pace.

**Figure 3.3 Welcome page to Module One of eReCog.**

**Key Elements of eReCog**

In the development of eReCog, there were a few critical elements to capture in the modules. Since interactive websites are more engaging for participants and have been demonstrated to be more effective than static websites (Barak et al., 2009), interactivity was a desirable element to include in the program. Each module contained several pages where participants could type in personalised responses to activity and discussion questions (see Figure 3.4). Anonymous responses from other participants were visible on some activities (e.g., discussion questions) after participants had submitted their own responses. This feature was also intended to capture a social
element of interacting with other participants in the program. In feedback provided from participants who completed the face-to-face ReCog intervention, interacting with other participants in the group was a valued aspect of the program (King & Green, 2015). Additionally, the feasibility study conducted with ReCog found that the intervention group improved significantly on a subscale of social function from baseline to post-intervention (Schuurs & Green, 2013), and the RCT study found a significant interaction effect on the same subscale where the cancer group reported significantly improved social functioning post-intervention compared to the waitlist group and the community group (King & Green, 2015). Since social functioning is an area that demonstrated improvements in the face-to-face intervention studies, it was important to attempt to incorporate this component in the eReCog program.

Figure 3.4 Example page where participants type in personalised responses.

Another key element included in the modules was downloadable practice recording sheets, tip sheets, and other relevant printable content from the module. At
the end of each module, the homework tasks to be completed during the next week were listed for participants along with access to the downloadable PDF or Microsoft Word files (see Figure 3.5). By clicking on the homework sheet, the file would automatically download to the participants’ computer, laptop, or personal device and could be saved for future reference.

Figure 3.5 Downloadable homework practice sheets.

The inclusion of audio elements is another feature that has been demonstrated to increase intervention effectiveness (Barak et al., 2009). Since each module contained relaxation training practice, an audio mp3 file was recorded by Dr Heather Green and embedded in the modules (see Figure 3.6). The settings were chosen so that the audio file began when the activity page opened, however, participants had the option to pause, stop, rewind, and adjust the volume on the tool bar located below the photo. The relaxation script was available in the homework section of the modules so
that participants could retain a copy of the text. The audio file could be emailed to participants upon request in mp3 or wma formats.

![Relaxation audio file](image)

*Figure 3.6 Relaxation audio file embedded in modules.*

**Pre-Piloting of eReCog**

After creating the four modules comprising the eReCog program (see p. 33-34), a full review of the content and design of the modules was conducted by the current PhD candidate and primary supervisor. The next step was to conduct usability testing as recommended by Zulman et al. (2012). To facilitate this next step, two personal acquaintances and three post-graduate candidates from Griffith University were recruited to individually assess the usability, user-friendliness, content, and aesthetics of the modules. Feedback from the reviewers was assessed and recommended changes were implemented. One of the primary recommendations was to allow participants the option to leave activity fields blank if they desired. The
settings on individual activities were therefore changed so that participants were not required to type in a response. When an activity field was left blank, participants would receive the following message after clicking on the “submit” button, “One or more question(s) are not answered. Do you want to continue anyway?” Participants then had the option to continue without responding or return to the previous page and submit a response. Additional amendments to the modules included minor wording changes, corrections to spelling and punctuation, photo changes, and the restructuring of some content. Once the recommended changes were made, the final development stage was achieved and the PhD candidate and primary supervisor conducted a final review. No further recommendations were made and the online modules were ready for trialling with Study One; the methods are described in the next section.

**Study One Methods (Pilot)**

Study One was a partially randomised trial that included both participants with a history of cancer and community dwelling adults without a history of cancer. Two non-cancer groups were included based on the recommendations outlined by The International Cognition and Cancer Task Force on the types of control groups to include in this research area. The task force recommends that disease specific and healthy controls who complete cognitive assessments at the same time intervals as the group of interest be included in research designs (Wefel, Vardy, Ahles, & Schagen, 2011). The first aim of Study One was to assess the usability and functionality of the intervention program by eliciting feedback from participants on any technical, operational, functional, or aesthetic changes that could be adjusted prior to beginning data collection for the main study. The second aim of the study was to assess primary and secondary outcome measures in order to determine the preliminary feasibility and efficacy of the web-based intervention.
Participants

For Study One, participants were recruited through a university email network (see Appendix B), the intervention website www.recogintervention.org, and the volunteer section of the career website www.indeed.com.au (see Appendix C) between November 2015 and March 2016. Volunteers were eligible for the cancer group if they reported a history of adult-onset cancer without central nervous system tumours, were at least 18 years of age, had self-reported problems with memory or concentration as a result of their cancer as demonstrated in a semi-structured interview (see Appendix D) and the EORTC QLQ-C30 cognitive functioning subscale (Aaronson et al., 1993), completed primary treatment at least six months prior to enrolment, and reported no known cancer recurrence at the time of participation. Volunteers were eligible for the non-cancer groups if they were over the age of 35 years, which was selected in order to obtain an age-matched sample to the cancer group. Volunteers were required to have no reported neurological or medical problems that could affect their participation. All participants were required to speak and read English fluently, have access to a desktop or laptop computer with a mouse, and have Internet access with an active email account. Volunteers were excluded if their English skills were not sufficient, reported any neurological problems or severe head trauma, did not have access to the required technology, or were currently undergoing cancer treatment or had incurable disease.

Measures

The assessment measures used in both Study One and Study Two comprised a series of tests and questionnaires. The primary outcome measure in both studies was subjective cognitive functioning. Secondary outcomes were objective cognitive functioning, QoL, psychological distress, illness perceptions, and satisfaction with eReCog. The basic psychological needs of competence, autonomy and relatedness were assessed to examine whether participating in the intervention mediated
participants’ performance on primary outcome measures. Participant engagement was examined for intervention groups from both studies.

**Subjective Cognitive Functioning**

Three different measures were used to assess self-reported cognitive functioning. The Functional Assessment of Cancer Therapy – Cognitive scale (FACT-Cog 3) was selected because the measure was created specifically to assess cognitive functioning in individuals with a history of cancer and can easily be administered online (Wagner, Sweet, Butt, Lai, & Cella, 2009). The second questionnaire selected was the Brief Assessment of Prospective Memory (BAPM) to assess prospective remembering. This type of memory is involved in many everyday tasks and may provide insight into a person’s everyday memory that may not be evident in formal laboratory assessments (Man, Fleming, Hohaus, & Shum, 2011). The third measure selected was the European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire (EORTC QLQ-C30), which was also developed for use with cancer survivors. The questionnaire assesses QoL in several dimensions of a person’s life, including a cognitive functioning subscale (Aaronson et al., 1993).

**FACT-Cog 3.** This measure is a 37-item self-report questionnaire designed to assess memory, attention, concentration, language and thinking abilities in cancer patients (Wagner et al., 2009). It contains four different subscales: Perceived Cognitive Impairments (PCI), Perceived Cognitive Abilities (PCA), deficits perceived by others on Comments from Others (OTH), and cognitive problems’ Impact on Quality of Life (QoL). Participants’ responses range on a scale from 0 (*never or not at all*) to 4 (*several times a day or very much*) and are rated based on participants’ experiences over the past seven days. A sample item from the PCI subscale is, “I have trouble forming thoughts”; from the PCA subscale, “I have been able to concentrate”; from the OTH subscale, “Other people have told me I seem confused”; and the QoL subscale, “I
have been upset about these problems”. Each subscale is scored by summing the individual item scores, multiplying the summed score by the total number of items on the subscale, and then dividing by the number of items answered. Three of the subscales are reverse scored (i.e., PCI, PCA and QoL). The PCI and PCA subscales each contain two optional items that are excluded from standard scoring of the scales, but these items can be included in the total score if a measure of internal consistency and individual item-total score correlation coefficients indicate that the items are a good fit with the scale (FACIT Measurement System, 2010). In this research project, the optional items were not scored. Psychometric properties for the English version of the FACT-Cog 3 have not been published, but many of the items are the same as the FACT-Cog 2, which demonstrated high internal consistency on subscales with Cronbach’s alpha levels ranging from $\alpha = .90$ to $\alpha = .92$ (Lai et al., 2009). Version 3 demonstrated sensitivity to the ReCog intervention when delivered in in-person format (Schuurs & Green, 2013).

**BAPM.** This is a 16-item self-report questionnaire designed to evaluate the frequency of prospective memory (PM) failures in individuals with acquired brain injury (Man et al., 2011) and is the shortened form of the Comprehensive Assessment of Prospective Memory measure (Chau, Lee, Fleming, Roche, & Shum, 2007; Roche, Fleming, & Shum, 2002). Responses are indicated with the frequency that each item is experienced over the last month where 1 = *never*, 2 = *rarely*, 3 = *occasionally*, 4 = *often*, 5 = *very often*, and 6 = *not applicable*. There are eight items that comprise the instrumental activities of daily life (IADL) subscale and eight items that form the basic activities of daily life (BADL) subscale. The IADL assesses common memory lapses such as household and financial management tasks. An example item from this subscale is, “Forgetting to take tablets at the prescribed time”. The BADL subscale assesses uncommon forgetting such as, “Forgetting to eat a meal”. To score the
measure, items from each subscale are summed and divided by the total number of items answered excluding items responded to as not applicable. The range for each subscale is from 0 to 5. Evaluation of the measure’s psychometric properties indicated that the BAPM total score had acceptable internal consistencies in three different samples with Cronbach’s alpha ranging from \( \alpha = .83 \) to \( \alpha = .90 \), good content and criterion validity, and sound test-retest reliability (Man et al., 2011).

**EORTC QLQ-C30.** This is a 30-item questionnaire developed to assess QoL in cancer patients (Aaronson et al., 1993). The measure has 28 questions that incorporate five functional scales (i.e., physical, role, cognitive, emotional, and social) and nine symptom scales (i.e., fatigue, insomnia, pain, financial difficulties, nausea and vomiting, dyspnoea, appetite loss, constipation, and diarrhoea). For this research project, only the fatigue, insomnia, pain, and financial difficulties subscales were evaluated because they are more likely to be associated with extended survivorship. The cognitive functioning scale contains two questions that related to the individual’s cognitive functioning over the last seven days. The type of item included on this measure is, “Have you had difficulty remembering things?” Individuals’ responses are scored on a Likert-type scale from one to four where 1 = not at all, 2 = a little, 3 = quite a bit, and 4 = very much. There are two additional items to assess global health and overall QoL. These two items are reported on a scale from one to seven, with the lowest score indicating very poor and the highest score indicating excellent. The developers reported that the measure is a reliable and valid instrument for assessing QoL in cancer patients with Cronbach’s alpha ranging from \( \alpha = .52 \) to \( \alpha = .89 \) for multiple-item scales (Aaronson et al., 1993).

**Objective Cognitive Functioning**

The WebNeuro online cognitive test battery was used to assess objective cognitive functioning (Brain Resource Ltd, 2010a) in both studies. The program
consists of 11 computerised tasks that assess seven thinking domains and two emotion domains: verbal memory, working memory capacity, attention and concentration, response speed, information processing efficiency, executive functioning, impulsivity, emotion identification, and emotion bias. In this research project, the emotion domains were not evaluated. The complete assessment battery takes approximately 40 minutes and requires the use of a desktop or laptop computer with a mouse.

To determine the variables that comprised each thinking domain, the developers used principal components analysis whereby factor loadings >.30 were used to identify variables comprising each domain. For example, the verbal memory domain consisted of two variables from a Memory Recognition Task: (a) total immediate recognition for trials 1-3, and (b) delayed recognition for trials 1-3. A complete list of the tasks with their associated cognitive domains and outcome measurements is presented in Table 3.1. The working memory domain was calculated by two variables from a Digit Span test: (a) recall span of visually presented digits, and (b) total number of correct trials in forward digit span. Attention was evaluated with a Continuous Performance Test and included two variables: (a) reaction time via space-bar presses averaged across all correctly identified target stimuli, and (b) omission errors where the space-bar was not pressed following a target stimulus. Information processing efficiency was measured with four variables on three different tasks: (a) total time taken to complete the whole sequence of digits and letters on Switching of Attention, (b) reaction time on a Choice Reaction Time test, (c) speed with visual interference on a Verbal Interference (Word) test, and (d) speed with verbal interference on a Verbal Interference (Colour) test. A Motor Tapping test was used to measure response speed on two variables: (a) tapping speed (mouse clicks) with the dominant hand, and (b) tapping variability measured by the standard deviation of the time between taps with the dominant hand. Executive functioning was assessed with a
Maze Task on two variables: (a) time taken to complete the maze without errors twice consecutively, and (b) number of overrun errors made across all trials until completing task twice consecutively. A Go/No-Go task was used to assess impulsivity on two variables: (a) reaction time via space-bar press averaged across all correctly performed green ‘press’ stimuli, and (b) number of times space-bar was pressed in response to a red ‘don’t press’ stimulus.

The online WebNeuro neurocognitive battery was validated against the computerised IntegNeuro (Silverstein et al., 2007), a program that demonstrates convergent and divergent validity with standardised paper-and-pencil tests such as Digit Span (Wechsler Adult Intelligence Scale III), Spatial Span (Wechsler Memory Scale III), California Verbal Learning Test, Trail Making Test, Stroop Test, Finger Tapping Test, and other neuropsychological measures (Paul et al., 2005). Data from the participants in the research reported in this thesis were compared to norms published by the developers, which were drawn from a naturalistic population sample of 1,317 individuals (Brain Resource Ltd, 2010a). The normative sample was 51% female and had an age range from 6 to 92 ($M = 38, SD =20.6$). When a participant completed WebNeuro, the raw score and standardised Z-score for each variable were provided by the developers in an Excel spreadsheet based on the normative sample using relevant age, sex, and education. Domain Z-scores were then calculated by averaging the relevant variables for that domain. An Overall Cognitive Function Index (OCFI) was calculated by averaging Z-scores from all seven thinking domains. Verbal memory and response speed domains were positively skewed and log transformations were conducted, however the results were not affected so the untransformed data were used in the analyses.
### Table 3.1

*WebNeuro tasks and outcome measurements*

<table>
<thead>
<tr>
<th>Task Name</th>
<th>Cognitive Domain</th>
<th>Outcome Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor Tapping</td>
<td>Response speed/ sensory motor processing</td>
<td>Number of taps in 30 seconds</td>
</tr>
<tr>
<td>Go/No-Go</td>
<td>Impulsivity (executive function)</td>
<td>Reaction time speed, errors of commission and omission</td>
</tr>
<tr>
<td>Continuous Performance Test</td>
<td>Attention and concentration</td>
<td>Speed and accuracy for detecting repetitions</td>
</tr>
<tr>
<td>Choice Reaction Time</td>
<td>Information processing efficiency</td>
<td>Mean reaction time to click on correct circle</td>
</tr>
<tr>
<td>Verbal Interference</td>
<td>Information processing efficiency</td>
<td>Words correctly identified with visual and verbal interference</td>
</tr>
<tr>
<td>Switching of Attention</td>
<td>Information processing efficiency</td>
<td>Completion time and errors</td>
</tr>
<tr>
<td>Memory Recognition</td>
<td>Memory</td>
<td>Total scores for immediate and delayed recognition</td>
</tr>
<tr>
<td>Digit Span</td>
<td>Working memory capacity</td>
<td>Maximum length of sequence and total correct trials</td>
</tr>
<tr>
<td>Maze</td>
<td>Executive function</td>
<td>Completion time and number of errors</td>
</tr>
<tr>
<td>Emotion Recognition</td>
<td>Emotion identification</td>
<td>Number of correct responses, accuracy, and response time</td>
</tr>
<tr>
<td>Delayed Emotion Recognition</td>
<td>Emotion bias</td>
<td>Number of correct responses, accuracy, and response time</td>
</tr>
</tbody>
</table>

*aNot analysed in the present research*

The program has demonstrated high test-retest reliability on all domains, with Chronbach’s alpha ranging from 0.62 on the memory recognition task to 0.89 on the motor tapping task (Brain Resource Ltd, 2010a; Silverstein et al., 2007). Dozens of studies demonstrating the usefulness of WebNeuro in a variety of clinical populations...
have been published in the past decade, including research on patients with brain
tumours (Burger, Vernimmen, Dugmore, Parkes, & Balchin, 2014), mild cognitive
impairment and dementia (Snyder et al., 2011), adult obesity (Gunstad et al., 2007;
Spitznagel, Galioto, Limbach, Gunstad, & Heinberg, 2013), and alcohol use disorder
(Lookatch et al., 2017).

This test battery was selected because it can be completed online without
requiring an administrator, and this research project aimed to have the assessments and
intervention modules to be completed online. However, the use of online cognitive
testing programs is controversial. On one side of the spectrum, there are several
advantages to online testing including that it is efficient and can administered remotely
at any time; it is cost efficient by reducing expenses related to administration,
equipment, and travel; and some organisations believe it is viewed positively by
participants (Lievens & Burke, 2011). Online cognitive testing can be particularly
useful when testing large numbers of individuals or when repeated assessments are
required (Darby et al., 2014). On the other end of the spectrum, a less controlled
testing environment can lead to reduced reliability and validity since it is difficult to
control cheating or participants receiving assistance from others during testing
(Lievens & Burke, 2011). In addition, it is argued that fixed scheduling introduces
more testing variability in relation to optimal testing circumstances for some
participants (Darby et al., 2014). However, there is no reason to suspect that potential
problems associated with online testing would differentially affect different arms of
the study in research of the type presented in this thesis.

Another disadvantage to online testing, which also affects self-report measures,
is the bias that is potentially introduced by the social desirability phenomenon. Social
desirability is the tendency for respondents to distort their self reports or performance
in a favourable direction so that their responses are consistent with their beliefs about
social norms and expectation (Crutzen & Goritz, 2010), which also affects the reliability and validity of the obtained results. Typically, social desirability bias is present in self-reports of public health risky behaviours (e.g., smoking, alcohol consumption) but less prevalent in non-risky behaviours in non-adolescents (Jago, Baranowski, Baranowski, Cullen, & Thompson, 2007); therefore, there is little reason to suspect a substantial degree of bias in the current study.

**Quality of Life**

This construct was assessed using two measures described earlier in this section: the EORTC QLQ-C30 and the QoL subscale of the FACT-Cog questionnaire.

**Psychological Distress**

The Kessler Psychological Distress Scale (K10) was used to assess reported distress (Kessler et al., 2002). The measure is a 10-item self-report questionnaire that obtains a global measure of psychological distress based on responses to questions about levels of depression and anxiety over the most recent 4-week period. A sample item from this measure is, “In the last four weeks, about how often did you feel nervous?” Normative data gathered from Australia and New Zealand found the measure to be valid for assessing and screening affective disorders in clinical populations (Andrews & Slade, 2001). The measure has demonstrated high internal consistency and concurrent validity (Hides et al., 2007). Cronbach’s alpha has been reported as $\alpha = .93$ and there is good criterion validity with respect to one-month DSM-IV diagnoses of depression and anxiety disorders (Fassaert et al., 2009).

**Illness Perceptions**

This construct was assessed using the Brief Illness Perception Questionnaire (BIPQ), which is a 9-item questionnaire that assesses cognitive and emotional symptoms of illness (Broadbent, Petrie, Main, & Weinman, 2006). The measure contains five items on the cognitive representation of illness perception: consequences,
timeline, personal control, treatment control, and identity. There are two items on emotional representation: concern and emotions. There is one item on illness comprehensibility and an additional item on perceived cause of illness. The general word “illness” can be replaced with a specific term relative to the phenomenon (Broadbent et al., 2006). For this research project, the word illness was substituted with the term “cognitive difficulties” as previously examined with cancer survivors (King & Green, 2015). A sample item from this questionnaire is, “How much do your cognitive difficulties affect your life?”

This measure was selected because the illness perceptions construct provides a broader perspective on how individuals perceive a health problem that goes beyond perceived severity. In contrast to a measure of perceived severity of cognitive problems such as the FACT-Cog 3, this measure evaluates multiple aspects of cognitive difficulties including whether the problems are perceived as manageable and how long they are likely to persist. Cognitive and emotional threats of illness are processed through three stages including: (a) representation of the health threat, (b) behaviours for coping with the threat, and (c) appraised efficacy of the behaviours for coping. Emotional representations of illness are often associated with negative emotions such as fear, anger, and distress, which impact on a patient’s behaviour and are worthwhile assessing in this clinical population (Broadbent et al., 2006). The Brief IPQ has good test-retest reliability, moderate to good correlations in tested concurrent validity with the 80-item full version of the Illness Perception Questionnaire – Revised (IPQ-R), and acceptable discriminant validity (Broadbent et al., 2006).

Competence, Autonomy and Relatedness

These constructs were assessed with the Basic Psychological Needs Satisfaction Scale – General version (BPNS), which is a 21-item measure assessing satisfaction on three psychological needs: competence, autonomy, and relatedness
(Gagne, 2003). Each item is rated on how true the statement is to the respondent and is scored on a 7-point Likert scale ranging from 1 = not at all true to 7 = very true. There are 7 items on the autonomy scale, 6 items on the competence scale, and 8 items on the relatedness scale. Each of these scales contains 3 items that are reverse scored. An example question from the autonomy subscale is, “I feel like I am free to decide for myself how to live my life”; an example from the competence subscale is, “Often, I do not feel very competent”; and a sample item from the relatedness subscale is, “I get along with people I come into contact with.” Higher scores on the measure indicate greater satisfaction. Coefficient alphas for the scales were reported at .71, .69, and .90 for competence, autonomy, and relatedness, respectively (Gagne, 2003).

**Participant Satisfaction**

Participants in the intervention groups rated their satisfaction with the program using the same 5-point Likert scale used in the two previous ReCog studies (King & Green, 2015; Schuurs & Green, 2013). They rated their: (a) satisfaction with the online treatment program where 1 = strongly dissatisfied and 5 = strongly satisfied; (b) level of change in cognitive functioning where 1 = got a lot worse and 5 = improved a lot; and (c) likelihood of recommending the program to a friend with similar problems where 1 = very unlikely and 5 = very likely. Participants also rated the overall program on a 1 to 10 scale where 1 = very poor and 10 = excellent, and were provided with the opportunity to comment on aspects of the program they found the most enjoyable or helpful, the aspects they found least enjoyable or helpful, and any additional comments about their participation experience.

**Participant Engagement**

The method used for evaluating participant engagement was developed for this research project because the program used (i.e., LessonLAMS) did not allow for measurement of some of the typical engagement parameters in web-based research that
were outlined in Chapter II (p. 44). In addition, the standard methods for assessing engagement are not meaningful for evaluating a participant’s activity level in the program. Each of the four modules comprising the eReCog intervention contained activity and discussion pages where participants could freely type in a response to the questions posed. For each valid response that a participant typed into the text box they received one point. A total engagement score was calculating by summing the points from all four modules, allowing for a maximum total score of 76 points. The number of emails received from the program facilitator was also calculated to provide a measure of facilitator engagement required. These engagement measures are described further in Chapter VI.

Procedure

The same procedure was implemented for Study One and Two in this research project. The project was approved by the university ethics committee and was preregistered at www.anzctr.org.au (ACTRN12615000878572). Volunteers who were interested in participating in the project contacted the research team via email. There were no incentives or monetary awards offered for participation in this project, only free access to the cognitive rehabilitation intervention. To determine eligibility, the PhD candidate conducted an initial standardised telephone interview with potential participants (see Appendix D). If participants were deemed eligible to participate they were informed of their group allocation over the telephone, which was predetermined by a computerised random number generator when receiving their initial expression of interest. They were emailed an information sheet (Appendix E) and consent form (Appendix F) and instructed to provide written consent via return email.

Upon providing written consent, participants were emailed links to complete the baseline (T1) assessment. Each assessment was comprised of the WebNeuro online test battery (Brain Resource Ltd, 2010b) and online questionnaires created using
Qualtrics software (2013; Qualtrics, Provo, UT, USA). The total time required to complete the assessment was approximately 60 minutes. Once both portions of the assessment were completed, participants in the waitlist groups were sent a follow-up email thanking them for completing the assessment and advising them they would receive an email with links to the next assessment (T2) in approximately four weeks. Participants in the intervention groups were immediately emailed a link with their username and password to access Module 1 of the program. The program modules were emailed sequentially on a weekly basis from the day they completed the first module, allowing approximately seven days to implement the homework strategies from the previous module. Participants were not emailed the next module until the previous module was completed, therefore if the modules were not completed on time then the sequencing “reset” to seven days from when the module was completed. The recommended completion time of the program was 21 days from finishing the first module.

Reminder emails were sent to participants on average five days after receiving either the assessment or module links if they had not yet been completed. On some occasions, participants completed only one of the two assessment components and were sent a follow-up email informing them that their assessment was not yet completed. After three reminders or follow-up emails were sent to participants without further activity, they were contacted via email or telephone to discuss their continued participation in the research project. Most participants received completion emails from the facilitator after finishing the post-intervention assessments (T2), which advised them they would receive links to the follow-up assessment (T3) in approximately three months. The long-term follow-up of 3 months was selected to allow for comparison to previous ReCog intervention research that also used a 3-month follow-up period. After completing the final assessment, participants were sent
a concluding email informing them that their participation in the study was finished and thanking them for volunteering to be involved in the research project. Participants in the waitlist groups were offered the opportunity to complete the intervention program if they desired.

**Data Analyses**

An intent-to-treat analysis was applied to manage missing data for participants who completed at least two time point assessments, where the last data point was carried forward. Outcome variables were examined for outliers, skewness, and kurtosis. No outliers were excluded for any of the outcome variables. Executive functioning demonstrated excess kurtosis and the BADL subscale was largely positively skewed. Transformations to the data did not produce a significant difference in the results; therefore untransformed data were reported in the final analyses. Main analyses were 3x3 mixed ANOVAs to examine the effects of group, time, and Group x Time interactions. Where there were violations of Mauchley’s test of sphericity, the Huynh-Feldt correction for degrees of freedom were reported. A significance level of $p \leq .05$ was set for all analyses. Effect sizes for interactions were calculated using $\eta^2$ and Cohen’s $d$ was calculated to evaluate between groups effect sizes for change scores from baseline to T2 and T3.

**Study Two Methods (RCT)**

After Study One closed, the quantitative and qualitative feedback from the participant satisfaction ratings was evaluated. Overall, participants in the intervention groups were relatively satisfied with the program; these results are presented in the next chapter. The open-ended comments regarding the most enjoyable or beneficial and least enjoyable aspects of the program were evaluated. The positive feedback received from participants indicated that no additional changes to the intervention modules were required. However, an additional modification was implemented for
Study Two in order to evaluate whether facilitator feedback would increase participant engagement. In Study Two, participants received individualised feedback from the facilitator on the goal-setting activity from Module 1, the implementation of a new memory strategy from Module 2, or in most cases, both. Study Two was an RCT that recruited a sample of cancer survivors from throughout Australia. The recruitment process and participant sample are described in the next section.

Participants

Volunteers for Study Two were recruited through emails sent to Breast Cancer Network Australia (see Appendix G) and Griffith University staff and students (Appendix B) from March to June 2016. A sample of 54 participants was sought based on a priori power analysis demonstrating 80% power for detecting an interaction effect on the primary outcome measure with $\alpha = .05$. An additional 20% (11 participants) was added to the desired sample size to allow for attrition, which meant recruiting a total of 65 participants for the study. Volunteers were eligible to enrol in the study if they had a history of adult-onset cancer excluding central nervous system tumours, were at least 18 years of age, reported cognitive complaints with memory or concentration as assessed with two questions from the cognitive functioning scale of the EORTC QLQ-C30 and attributed these complaints to cancer and/or treatment, completed primary treatment at least six months prior to enrolment (ongoing hormone treatment was acceptable), were currently cancer-free, were able to speak and read English, and had access to a desktop or laptop computer with a mouse, Internet and an active email account. Volunteers were excluded if they were currently undergoing primary treatment for cancer, had a history of traumatic brain injury or a neurological disorder, had poorly managed anxiety or depression, or had inadequate English language skills.
Measures and Procedure

As mentioned earlier in this section, the measures and procedure for Study Two were mostly equivalent to those presented in Study One except for the addition of module feedback to participants in Study Two.

Data Analyses

A sample size of 54 participants was sought based on a priori power analysis demonstrating 95% power for detecting an interaction effect of $d = 0.5$ (estimated from previous ReCog studies) on the primary outcome measure with $\alpha = 0.05$. An additional 20% (11 participants) was added to the desired sample size to allow for attrition, which meant recruiting a total of 65 participants for Study Two. Intent-to-treat analysis was applied to missing T3 data whereby scores from T2 were carried forward. The outcome variables were examined for outliers, skewness, and kurtosis. The variables response speed and FACT-Cog 3 OTH subscale showed negative skew and excess kurtosis. Log transformations were performed, however the results did not differ significantly therefore the untransformed data were used in the reported analyses.

Violations to Mauchly’s test of sphericity were adjusted with the Huynh-Felt correction. The main analyses were 2x3 ANOVAs to examine main effects for group and time, and interaction effects. Within-group planned comparisons were computed across time and Cohen’s $d$ was calculated to determine between-group effect sizes from baseline to T2 and T3.

The results from Study One are described in a manuscript presented in Chapter IV of this thesis, which at the time of the submission of this thesis, is under review with the European Journal of Cancer Care. Study Two’s results are described in the manuscript in Chapter V, which at the time of the submission of this thesis, is under review with the journal Psycho-Oncology. A manuscript that examines participant engagement in the eReCog intervention groups from both Study One and Two is
presented as Chapter VI, and at the time of the submission of this thesis, is under review with the journal *Supportive Care in Cancer*. 
CHAPTER IV: EFFICACY OF A WEB-BASED COGNITIVE REHABILITATION INTERVENTION FOR ADULT CANCER SURVIVORS:
A PILOT STUDY

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Running Head: WEB-BASED COGNITIVE REHABILITATION CANCER

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Ethical Standards:
The authors confirm that this research complies with the ethical standards of the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC) and was performed in accordance with the Helsinki Declaration.
STATEMENT OF CONTRIBUTION TO CO-AUTHORED PAPER

This chapter includes a paper that was co-authored by my thesis supervisors, Dr Heather Green and Professor David Shum. The manuscript is currently under review by the *European Journal of Cancer Care* and has been formatted to that journal style. As such, there is some repetition in sections of this chapter with other sections of this thesis. Tables and Figures are numbered to correspond with Chapter numbers. The citation is as follows: Mihuta, M. E., Green, H. J., & Shum, D. H. K. (Manuscript in submission). *Efficacy of a web-based cognitive rehabilitation intervention for adult cancer survivors: a pilot study.*

- My contribution to the manuscript involved: review of the literature, initial concept and experimental design, data collection and analysis, and preparation of the manuscript.
- The contributions of Heather Green and David Shum involved: supervision of the project design, data collection and analysis; and revisions to the manuscript.

Signed: ________________________________ Date: 4 April 2017
Mary E. Mihuta

Countersigned: __________________________ Date: 4 April 2017
Co-author of paper: Heather Green

Countersigned: __________________________ Date: 4 April 2017
Co-author of paper: David Shum
Abstract

The purpose of this study was to evaluate the efficacy of a web-based cognitive rehabilitation intervention in survivors of adult-onset cancer and a sample of non-cancer community dwelling adults. Fifty-one participants were recruited and allocated to a cancer intervention group, a non-cancer intervention group, or a non-cancer waitlist group. Intervention groups completed a 4-week online program and all participants were assessed at baseline, post-intervention and 3-month follow-up. The primary outcome measure was subjective cognitive functioning. Secondary outcome measures included objective cognitive functioning, distress, quality of life (QoL), illness perception and program satisfaction. Results from the study found significant improvements on self-report measures of cognitive functioning in both treatment groups, as well as improvements on objective measures assessing attention and executive functioning. No intervention effects were observed for distress, QoL or illness perception. High participant satisfaction was observed with 75% of participants in the cancer group reporting being either “satisfied” or “very satisfied” with the program compared to 87% in the non-cancer treatment group. Initial evaluation of the program suggests the web-based cognitive rehabilitation intervention shows potential for improving subjective and objective cognitive functioning in cancer survivors and community dwelling adults.

Keywords: adult cancer survivors, chemotherapy, cognitive rehabilitation, supportive care, web-based.
Introduction

According to the National Cancer Institute, an individual with cancer is considered a survivor from the time of diagnosis until the end of life regardless of treatment status or prognosis (National Cancer Institute, 2016). Survivors of cancer can face a number of physical and psychological challenges as they transition into the survivorship phase as a result of their diagnosis and treatment. Some of these challenges include cognitive impairment, peripheral neuropathy, lymphedema, sexual dysfunction, pain, fatigue, sleep problems, anxiety, and depression (Lavoie Smith et al., 2012).

Cognitive dysfunction associated with cancer diagnosis and treatment has been well-documented in the literature for a variety of different types of cancer including breast (Ahles & Saykin, 2007; Brezden, Phillips, Abdolell, Bunston, & Tannock, 2000; Castellon et al., 2004; Myers, Wick, & Klemp, 2015; Schagen, Muller, Boogerd, Mellenbergh, & van Dam, 2006; Vardy et al., 2014), colorectal cancer (Vardy et al., 2014), prostate cancer (Green et al., 2002; Jenkins, Bloomfield, Shilling, & Edginton, 2005; Jim, Small, Patterson, Salup, & Jacobsen, 2010), lung cancer (Meyers, Byrne, & Komaki, 1995), and myelogenous leukaemia (Meyers, Albitar, & Estey, 2005). Although reports in the literature vary, a substantial subgroup of cancer survivors (17-34%) is estimated to experience long-term post-treatment cognitive changes (Ahles & Saykin, 2007). Given this, providing these cancer survivors with access to services that address their cognitive changes is an important part of survivorship care. Cancer survivors themselves have identified a number of unmet needs associated with survivorship, including managing treatment side-effects such as poor memory and attention, receiving psychoeducation about expectations post-treatment, and information about rehabilitation services, counselling and support groups (Jefford et al., 2008).
The aetiology of cognitive impairment associated with cancer is not well understood, however four underlying mechanistic categories often proposed in the literature are direct effects of chemotherapy, indirect effects of chemotherapy, effects related to cancer biology alone, and other (e.g., stress, hormone dysregulation; Craig, Monk, Farley, & Chase, 2014). Cognitive rehabilitation intervention and training programs have the potential to mitigate the symptoms of cognitive impairment through strategy and skills training and have demonstrated positive outcomes for managing cognitive dysfunction in this clinical group (Cherrier et al., 2013; Ercoli et al., 2013; Ercoli et al., 2015; R. J. Ferguson et al., 2007; R. J. Ferguson & Martinson, 2011; Kesler et al., 2013; King & Green, 2015; Schuurs & Green, 2013; Von Ah et al., 2012). However these interventions have most often been implemented in face-to-face format, which may reduce their dissemination and accessibility. Alternatively, web-based programs are increasingly being used as a delivery method to increase access to healthcare services, in particular to individuals in rural communities or people limited by mobility problems (Cuijpers, van Straten, & Andersson, 2008; Ritterband et al., 2012).

Web-based intervention programs offer several advantages over face-to-face methodologies. Apart from reaching a wider population and increased access to certain demographic groups, interventions administered over the Internet are cost-effective (Blom, Bosmans, Cuijpers, Zarit, & Pot, 2013), they provide participants with flexibility to complete tasks on their own time (Barak, Klein, & Proudfoot, 2009), and they allow for greater anonymity particularly when discussing sensitive information (White & Dorman, 2001).

We have limited knowledge about the effectiveness of utilising web-based interventions to provide cognitive remediation to cancer survivors in the community. Only three randomised controlled trials (RCTs) evaluating the efficacy of online
cognitive training programs in cancer survivors have been published (Bray et al., 2017; Damholdt et al., 2016; Kesler et al., 2013). Results from these studies found improved cognitive flexibility, verbal fluency, processing speed, and self-reported executive function skills in the treatment group compared to the waitlist group (Kesler et al., 2013); improved verbal learning and working memory at follow-up in the intervention group compared to the waitlist group (Damholdt et al., 2016); and significantly improved perceived cognitive impairment, perceived cognitive abilities, and impact on QoL in the treatment group at post-intervention compared to the waitlist group (Bray et al., 2017).

The aim of this pilot study was to examine the efficacy of a web-based cognitive rehabilitation program adapted from its original face-to-face format into online modules. Based on principles of cognitive behavioural therapy, the intervention program provides other components in addition to skills practice. These components include psychoeducation, goal setting, relaxation training, and weekly homework tasks. The primary outcome measure was perceived cognitive impairment (PCI), with secondary outcome measures of additional self-report measures of cognitive functioning, objective cognitive functioning, and psychosocial variables of distress and perception of threat of illness. It was hypothesised that the intervention groups would demonstrate significant improvements on measures of subjective cognitive functioning and domains of objective cognitive functioning compared to the control group, and the cancer group would show greater benefits than the non-cancer treatment group.

This study is unique in that the intervention program was administered to a non-cancer control group, which has not previously been done to the authors’ knowledge. The International Cognition and Cancer Task Force recommends including several control groups including healthy controls, which can help establish whether cognitive impairment is present in the target group (Wefel, Vardy, Ahles, &
Schagen, 2011). The reasons for including a healthy non-cancer intervention group in the pilot study were threefold. First, an additional non-cancer group allowed for further comparison to assess for baseline impairment in the cancer group. Second, an additional intervention group created a larger sample to determine whether a larger scale RCT trial was warranted. Third, mild cognitive impairment (MCI) is found among some members of the general population during middle age. For example, the estimated prevalence of MCI in late middle-age (i.e., late 40s and early 50s) in individuals with a parental history of Alzheimer’s disease ranges from 3% to 49% depending on classification scheme (Clark et al., 2016), and some middle-aged patients with a history of type 2 diabetes are also at risk for MCI (Chen et al., 2012). Two published studies showed that cognitive behavioural memory training designed for older adults in the community with concerns about cognitive functioning was also helpful for cancer survivors (McDougall, 2001; McDougall, Becker, Acee, Vaughan, & Delville, 2011), therefore it was speculated that the online program in the present study might also be helpful for individuals who have not had cancer, but to a lesser extent.

**Methods**

**Participants**

Initially, 86 potential participants were screened for eligibility via telephone interview. After exclusions and withdrawals (see Figure 4.1), 59 participants were enrolled and allocated into three groups, and 51 of these completed the initial assessment. The participant flowchart is presented in Figure 1. Those with a history of cancer were allocated to the cancer group \( (n = 13) \), and participants without a history of cancer were randomly allocated to the intervention \( (n = 21) \) or waitlist \( (n = 17) \) groups. Participants in the cancer group were eligible if they had a history of adult onset cancer (age 18+) with non central nervous system (CNS) tumours, reported
cognitive complaints associated with their cancer or treatment, completed primary
treatment at least 6 months prior to enrolling in the study, and were disease-free at the
time of participation. Current hormonal treatment was not an exclusion criterion.
Participants in the non-cancer groups were eligible if they were aged 35+ years, which
was selected based on the typical age profile of cancer survivors recruited using
similar methods in previous cognitive rehabilitation studies (King & Green, 2015;
Schuurs & Green, 2013). A lower age cut-off might have created an imbalance as a
result of a younger age profile than the cancer survivors. Non-cancer volunteers were
excluded if they reported neurological problems or medical issues that could hinder
their participation in the program. All participants had to speak and read English
fluently, have access to a desktop or laptop computer with a mouse, and have Internet
access.
Figure 4.1 Participant flowchart.
Measures

**Subjective Cognitive Functioning** was assessed with the Functional Assessment of Cancer Therapy – Cognitive Function (FACT-Cog) version 3 (Wagner, Sweet, Butt, Lai, & Cella, 2009). The Fact-Cog 3 is a 37-item self-report questionnaire on cognitive complaints in cancer patients. The measure has subscale scores in four domains: Perceived Cognitive Impairment (PCI), Comments from Others (OTH), Perceived Cognitive Abilities (PCA), and Impact on Quality of Life (QoL). The FACT-Cog-3 was supplemented with the Brief Assessment of Prospective Memory (BAPM), a 16-item self-report questionnaire that evaluates the frequency of prospective memory (PM) failures (Man, Fleming, Hohaus, & Shum, 2011). The measure has two subscales each with eight items: basic activities of daily living (BADL) and instrumental activities of daily living (IADL). In addition, the cognitive functioning scale from the European Organisation for Research and Treatment of Cancer – Quality of Life Questionnaire (EORTC QLQ-C30) was administered (Aaronson et al., 1993), which contains two questions pertaining to memory functioning and concentration over the previous week.

**Objective Cognitive Functioning** was assessed with the WebNeuro online cognitive test battery (Brain Resource Ltd, 2010b). The program consists of 11 computerised tasks assessing seven thinking domains: verbal memory (VM), working memory capacity (WM), attention/concentration, response speed (RS), information processing efficiency (InfoProc), executive functioning (EF), and impulsivity. The program has demonstrated high test-retest reliability on all domains, and acceptable internal consistency and validity (Brain Resource Ltd, 2010b; Silverstein et al., 2007). Participants’ individualised Z-scores, adjusted for age and sex from the large sample in the WebNeuro database, were used as outcome variables. Each of the tasks has
between 33 and 60 parallel versions available to reduce practice effects, and participants completed different parallel versions for each assessment.

*Illness Perceptions* was assessed with the Brief Illness Perception Questionnaire (BIPQ), a 9-item questionnaire assessing cognitive and emotional symptoms of illness (Broadbent, Petrie, Main, & Weinman, 2006). The term “illness” was substituted with the term “cognitive difficulties” for this study as done in a previous study with cancer survivors (King & Green, 2015).

*Psychological Distress* was assessed using the Kessler Psychological Distress Scale (K10), a 10-item self-report questionnaire measuring global distress based on responses to questions related to levels of anxiety and depression over the past 4-week period (Kessler et al., 2002).

*Participant Satisfaction* was measured with the intervention groups using a 5-point Likert scale to rate: (a) satisfaction with the online treatment program (1= *strongly dissatisfied* to 5= *strongly satisfied*); (b) level of change in cognitive functioning (1= *got a lot worse* to 5= *improved a lot*); and (c) likelihood of recommending the program to a friend with similar problems (1= *very unlikely* to 5= *very likely*). Participants rated the overall program on a 1 to 10 scale (1= *very poor*, 10= *excellent*), and were asked to report which aspects of the program they found most enjoyable or helpful, state which aspects they least enjoyed or found least helpful, and provide any additional comments (King & Green, 2015).

**Procedure**

This study was conducted in accordance with the Helsinki Declaration and preregistered at www.ANZCTR.org.au (ACTRN12615000878572). Approval was obtained from a university ethics committee. Participants were recruited through a university email network, the intervention website www.recogintervention.org, and the career website Indeed.com.au between November 2015 and March 2016. To volunteer,
potential participants emailed the research team and completed telephone eligibility screening. Participants emailed to provide consent along with medical, demographic and psychosocial variables. The online baseline assessment consisted of the 40-minute WebNeuro battery and questionnaires, which took about 20 to 30 minutes. Those allocated to the intervention groups then completed the online intervention program. Each week they were emailed a link and their password to access the modules. Reminder emails were sent to keep participants on track for completing the program in 4 weeks. Participants were reassessed post-intervention, or 4 weeks after the baseline assessment for the waitlist group. A follow-up assessment was completed 3 months after the second assessment.

**Intervention.** Responding to Cognitive Concerns (ReCog) is a manualised, 4-session cognitive rehabilitation program based on principles from cognitive-behavioural therapy that offers adult cancer survivors psychoeducation on cognitive dysfunction associated with cancer treatment, skills training for improving memory and attention, relaxation training, tips for improving sleep hygiene, and weekly homework tasks to reinforce new learning (Appendix A). The face-to-face program consists of four weekly sessions lasting about two hours each. The intervention program has been evaluated twice in cohorts of adult cancer survivors with complaints of cognitive impairment (King & Green, 2015; Schuurs & Green, 2013) and demonstrated improvements in self-report and objective cognitive functioning.

**Development of eReCog.** The development of eReCog involved adapting the 4-week face-to-face ReCog intervention into four online training modules using existing guidelines for adapting an in-person communication intervention into a web-based program for cancer patients (Zulman et al., 2012). The process consisted of three phases: module development, usability testing, and pre-piloting and feedback.
During the module development phase, four training modules were created using LessonLAMS software (LAMS International Pty Ltd, 2002). The content and key components of the in-person intervention were added to web-based modules, along with written instructions that are delivered orally during the face-to-face program. Imagery in the form of graphs, pictures, and comics was added to make the pages more aesthetically pleasing. Relaxation training audio files were recorded by the second author and embedded into the modules. Group discussion pages were created so participants could share their experiences with other members of the group. To make the modules interactive, participants were asked questions where they could type in their responses (e.g., goal-setting task) and, in some cases, view anonymous responses of previous participants (e.g., personal experiences of memory problems). Participants were instructed to download homework practice sheets to record their practice over the next week.

The next phase consisted of testing the usability of the modules to ensure links, audio files and downloading pages worked correctly, which was completed by the first two authors. During the pre-piloting stage, three Masters degree candidates completed the online modules and provided feedback on the user friendliness and overall usability of the training modules.

Statistical analyses. An intent-to-treat analysis was applied to manage missing data, where the last data point was carried forward for participants who completed at least two time point assessments. This occurred for three participants, all of whom were in the non-cancer treatment group. Main analyses were conducted with 3x3 mixed ANOVAs to examine the effects of group (cancer, non-cancer treatment and non-cancer waitlist), time (T1, T2 and T3), and Group x Time interaction. Huynh-Feldt corrections for degrees of freedom were used where there were violations of Mauchley’s test of sphericity. Planned comparisons with Bonferroni corrections were
conducted to further examine effects of time within each group. Significance level of all analyses was set at $p \leq .05$. Effect sizes for 3x3 interactions are reported using $\eta^2$ to correct for sampling error due to a smaller sample size (C. J. Ferguson, 2009). Cohen’s $d$ was calculated to evaluate differences in effect sizes for changes from baseline between the cancer group and non-cancer groups at T2 and T3.

**Results**

Demographic and medical data are presented in Table 1. The three groups were comparable in age, years of education, distress level, marital status, language and country of birth. The cancer group was entirely female, whereas males participated in the non-cancer groups. Overall attrition rates in the study were 8% in the cancer group, 24% in the non-cancer treatment group, and 12% in the non-cancer waitlist group.

At baseline the cancer group reported more PCI than the non-cancer groups; worse PCA than the non-cancer groups; and an increased impact on QoL than the non-cancer waitlist group only (see Table 2 for means and standard deviations). Their reported cognitive functioning on the cognitive scale of the EORTC QLQ-C30 was worse than the non-cancer groups; they reported more PM failures on the IADL and BADL than the non-cancer groups; and they reported increased perception of illness threat than the non-cancer groups. None of the groups differed at baseline on any of the objective domains.
Table 4.1

Demographic and medical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cancer Group (n = 12)</th>
<th>Non-Cancer Treatment (n = 16)</th>
<th>Non-Cancer Waitlist (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (SD)</td>
<td>45.4 (10.3)</td>
<td>47.6 (10.0)</td>
<td>45.9 (7.4)</td>
</tr>
<tr>
<td>Mean Education (SD)</td>
<td>16.1 (3.4)</td>
<td>16.1 (3.9)</td>
<td>17.2 (2.4)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>100.0</td>
<td>75.0</td>
<td>73.3</td>
</tr>
<tr>
<td>Male (%)</td>
<td>0.0</td>
<td>25.0</td>
<td>26.7</td>
</tr>
<tr>
<td>Born in Australia (%)</td>
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<td>68.8</td>
<td>53.3</td>
</tr>
<tr>
<td>Other (%)</td>
<td>41.7</td>
<td>31.2</td>
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<tr>
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<td>73.3</td>
</tr>
<tr>
<td>Other (%)</td>
<td>8.3</td>
<td>12.5</td>
<td>26.7</td>
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<tr>
<td>Marital Status (%)</td>
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<tr>
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<td>16.7</td>
<td>25.0</td>
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<td>De facto</td>
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<td>6.3</td>
<td>6.7</td>
</tr>
<tr>
<td>Partnered</td>
<td>16.7</td>
<td>6.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Married</td>
<td>33.3</td>
<td>50.0</td>
<td>46.7</td>
</tr>
<tr>
<td>Separated</td>
<td>0.0</td>
<td>6.3</td>
<td>6.7</td>
</tr>
<tr>
<td>Divorced</td>
<td>25.0</td>
<td>6.3</td>
<td>20.0</td>
</tr>
<tr>
<td>Cancer Type (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>50.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bowel</td>
<td>8.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Endometrial</td>
<td>8.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>16.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PMP Appendix</td>
<td>8.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>SCC Vulva</td>
<td>8.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Treatment (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>83.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>100.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>58.3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Months since treatment Range (6 – 125)</td>
<td>52.3 (46.8)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Subjective Cognitive Function

Descriptive statistics are shown in Table 4.2. There was a significant Group x Time interaction for BADL, $F(4, 75) = 3.2, p = .019, \eta^2 = 0.13$. The BADL also showed main effects for time, $F(2, 75) = 4.3, p = .018, \eta^2 = 0.09$, and group, $F(2, 40) = 4.9, p = .012, \eta^2 = 0.20$. The time effect occurred because participants reported more PM failures at T1 than T2 and T3 and the group effect because the cancer group reported significantly more PM failures on this subscale than the both the other groups. The interaction occurred because the cancer group showed a trend towards reporting reduced PM failures at both T2, $F(1, 11) = 4.1, p = .067, \eta^2 = .27$, and T3, $F(1, 11) = 4.7, p = .053, \eta^2 = .30$; the non-cancer treatment group reported reduced PM failures at T2 only, $F(1, 15) = 4.6, p = .049, \eta^2 = 0.24$; and no changes over time were reported by the non-cancer waitlist group.

Similarly, there was a trend towards a Group x Time interaction for IADL, $F(4, 80) = 2.0, p = .096, \eta^2 = 0.08$. There was a main effect for time on IADL, $F(2, 80) = 7.2, p = .001, \eta^2 = 0.14$, with participants reporting significantly fewer PM failures from T1 to T3. The main effect for group was also significant, $F(2, 40) = 5.9, p = .006, \eta^2 = 0.23$, with the cancer group reporting significantly more PM failures than the waitlist group. The interaction approached significance because the cancer group reported a trend towards reduced PM failures at T2, $F(1, 11) = 4.2, p = .066, \eta^2 = .27$, and significantly reduced PM failures at T3, $F(1, 11) = 7.7, p = .018, \eta^2 = .41$, whereas the non-cancer groups reported no changes in IADL over time.
### Table 4.2

**Effect sizes, means (and SD) for outcome variables**

<table>
<thead>
<tr>
<th></th>
<th>Cancer Group ($n = 12$)</th>
<th>Non-Cancer Treatment Group ($n = 16$)</th>
<th>Non-Cancer Waitlist Group ($n = 15$)</th>
<th>$d_{Ca-Treat}$</th>
<th>$d_{Ca-WL}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2/3</td>
<td>T2/3</td>
<td>T2/T3</td>
<td>T2/T3</td>
</tr>
<tr>
<td><strong>Subjective</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI</td>
<td>33.8 (18.7)</td>
<td>42.3 (18.3)**</td>
<td>42.8 (18.2)**</td>
<td>0.35 / 0.38</td>
<td>0.35 / 0.39</td>
</tr>
<tr>
<td></td>
<td>50.6 (10.8)</td>
<td>53.8 (11.6)**</td>
<td>53.8 (10.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCA</td>
<td>13.3 (5.2)</td>
<td>15.8 (7.1)</td>
<td>15.7 (6.6)</td>
<td>0.52 / 0.50</td>
<td>0.19 / 0.07</td>
</tr>
<tr>
<td>OTH</td>
<td>13.8 (2.1)</td>
<td>14.7 (1.4)</td>
<td>13.8 (3.0)</td>
<td>0.44 / -0.27</td>
<td>0.26 / -0.26</td>
</tr>
<tr>
<td>QoL</td>
<td>9.3 (5.5)</td>
<td>11.8 (4.7)</td>
<td>11.3 (5.2)</td>
<td>0.31 / 0.17</td>
<td>0.68 / 0.32</td>
</tr>
<tr>
<td>CogFun</td>
<td>54.2 (21.5)</td>
<td>69.4 (23.4)**</td>
<td>61.1 (29.6)</td>
<td>0.61 / 0.19</td>
<td>0.72 / 0.06</td>
</tr>
<tr>
<td>IADL</td>
<td>2.50 (0.78)</td>
<td>2.28 (0.59)</td>
<td>1.95 (0.46)**</td>
<td>0.15 / 0.62</td>
<td>0.25 / 0.59</td>
</tr>
<tr>
<td>BADL</td>
<td>1.67 (0.73)</td>
<td>1.46 (0.48)</td>
<td>1.35 (0.36)**</td>
<td>0.19 / 0.51</td>
<td>0.48 / 0.61</td>
</tr>
<tr>
<td><strong>Psychosocial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distress</td>
<td>19.9 (7.3)</td>
<td>18.3 (5.5)</td>
<td>18.6 (6.7)</td>
<td>0.51 / 0.63</td>
<td>0.36 / 0.26</td>
</tr>
<tr>
<td></td>
<td>16.6 (4.9)</td>
<td>18.2 (6.3)</td>
<td>19.2 (6.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15.1 (4.5)</td>
<td>15.7 (4.9)</td>
<td>15.4 (6.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIPQ</td>
<td>44.2 (12.5)</td>
<td>41.8 (8.6)</td>
<td>41.2 (12.9)</td>
<td>0.14 / 0.18</td>
<td>0.37 / -0.13</td>
</tr>
<tr>
<td></td>
<td>31.3 (13.7)</td>
<td>30.8 (10.5)</td>
<td>30.8 (10.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.6 (12.8)</td>
<td>31.0 (12.5)</td>
<td>23.9 (9.9)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VM</td>
<td>0.07 (0.66)</td>
<td>0.04 (0.55)</td>
<td>-0.50 (1.12)</td>
<td>0.64 / -0.08</td>
<td>0.68 / -0.20</td>
</tr>
<tr>
<td></td>
<td>0.04 (0.50)</td>
<td>-0.37 (1.03)</td>
<td>-0.48 (0.85)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WM</td>
<td>-0.12 (0.79)</td>
<td>-0.06 (1.05)</td>
<td>-0.08 (0.95)</td>
<td>0.29 / 0.21</td>
<td>0.21 / 0.39</td>
</tr>
<tr>
<td></td>
<td>0.00 (1.09)</td>
<td>-0.23 (1.14)</td>
<td>-0.17 (0.91)</td>
<td>0.29 / 0.21</td>
<td>0.21 / 0.39</td>
</tr>
<tr>
<td>Attention</td>
<td>-0.71 (0.91)</td>
<td>-0.37 (0.62)</td>
<td>-0.30 (0.58)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.22 (0.91)</td>
<td>-0.35 (0.90)</td>
<td>-0.56 (1.00)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF</td>
<td>0.46 (0.63)</td>
<td>0.77 (0.72)</td>
<td>0.77 (0.70)</td>
<td>0.22 / 0.02</td>
<td>0.15 / -0.03</td>
</tr>
<tr>
<td></td>
<td>-0.16 (0.97)</td>
<td>0.46 (1.19)**</td>
<td>0.36 (1.12)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.14 (1.05)</td>
<td>0.35 (0.67)</td>
<td>0.45 (0.78)</td>
<td>-2.13 / -0.24</td>
<td>0.11 / 0.00</td>
</tr>
<tr>
<td>InfoProc</td>
<td>-0.11 (0.62)</td>
<td>-0.16 (0.56)</td>
<td>-0.21 (0.67)</td>
<td>-0.42 / 0.06</td>
<td>0.15 / -0.03</td>
</tr>
<tr>
<td></td>
<td>-0.25 (0.60)</td>
<td>-0.16 (0.62)</td>
<td>-0.36 (0.67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.32 (0.70)</td>
<td>-0.47 (0.67)</td>
<td>-0.40 (0.56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>0.27 (0.85)</td>
<td>0.36 (0.81)</td>
<td>0.42 (0.75)</td>
<td>0.41 / 0.77</td>
<td>0.37 / 0.54</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>-0.36 (0.30)</td>
<td>-0.32 (0.26)</td>
<td>-0.30 (0.42)</td>
<td>0.07 / 0.00</td>
<td>-0.19 / 0.25</td>
</tr>
<tr>
<td></td>
<td>-0.35 (0.29)</td>
<td>-0.33 (0.41)</td>
<td>-0.29 (0.32)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lower scores on the IADL, BADL, Distress, and BIPQ indicate better functioning. *** $p < .001$, ** $p < .01$, * $p < .05$ for planned comparison to T1 score within the allocated group, $d_{Ca-Treat} = $ Cohen’s effect sizes for change in Cancer Group corrected for change in Non-Cancer Treatment Group; $d_{Ca-WL} = $ Cohen’s effect sizes for change in Cancer Group compared to change in Waitlist Group whereby positive values indicate greater improvement in the cancer group than the comparison group.
Other subjective cognitive measures showed some statistically significant main effects and planned comparisons but no other interaction effects for subjective cognition approached statistical significance. On the PCI subscale a main effect was found for time, $F(2, 72) = 11.0, p < .001, \eta^2 = 0.20$, and for group $F(2, 40) = 8.5, p = .001, \eta^2 = 0.30$. The time effect occurred because participants reported significantly more PCI at T1 compared to T2 and T3. Planned comparisons within the cancer group demonstrated a significant improvement in PCI from T1 to T2 on the PCI subscale, $F(1, 11) = 9.6, p = .010, \eta^2 = .47$. This effect remained significant at T3, $F(1, 11) = 5.9, p = .033, \eta^2 = .35$. The non-cancer treatment group also reported a significant reduction in PCI from T1 to T2, $F(1, 15) = 4.6, p = .048, \eta^2 = .24$, however this effect was not maintained at T3.

There was a main effect for group on the PCA subscale, $F(2, 40) = 6.9, p = .003, \eta^2 = 0.26$, whereby the cancer group reported significantly worse PCA than the waitlist group. Similarly, a main effect for group was found on the EORTC QLQ-C30 cognitive scale, $F(2, 40) = 9.9, p < .001, \eta^2 = .33$, where the cancer group reported significantly poorer cognitive functioning than the other two groups. Also on the EORTC QLQ-C30 cognitive scale, planned comparisons in the cancer group showed significantly fewer reported cognitive impairments from T1 to T2, $F(1, 11) = 5.9, p = .043, \eta^2 = .35$, however these effects were not maintained at T3. Neither the non-cancer treatment group nor the non-cancer waitlist group reported significant changes in their cognitive functioning at different time points.

On the Impact on QoL subscale, there was a main effect of group, $F(2, 40) = 3.8, p = .031, \eta^2 = .16$. The cancer group reported significantly lower QoL than the non-cancer waitlist group. There were no significant effects of time on QoL reports for any of the groups.
Objective Cognitive Function

Table 4.2 shows descriptive statistics for objective cognitive measures. There was one significant Group x Time interaction found, in the Attention domain, $F(4, 80) = 3.1, p = .020, \eta^2 = .13$. The interaction occurred because there was a significant improvement from T1 to T3 for both the cancer group, $F(1, 11) = 5.5, p = .039, \eta^2 = .33$, and the non-cancer waitlist group, $F(1, 14) = 5.2, p = .038, \eta^2 = .27$, but a significant decline for the non-cancer treatment group, $F(1, 15) = 7.0, p = .018, \eta^2 = .32$.

There was a main effect for time on the VM domain, $F(2, 80) = 5.7, p = .005, \eta^2 = .12$, with participants performing significantly worse at T3 compared to T1. A main effect for time was also found on the EF domain, $F(2, 80) = 8.1, p = .001, \eta^2 = .16$. Participants significantly improved their performance from T1 to T2 and from T1 to T3. Planned comparisons showed that participants in the non-cancer treatment group demonstrated a significant improvement in performance on the EF domain from T1 to T2, $F(1, 15) = 27.0, p < .001, \eta^2 = .64$, and these effects were maintained at T3, $F(1, 15) = 12.8, p = .003, \eta^2 = .46$. The other two groups did not demonstrate significant effects of time on this global domain.

On the RS domain there were no omnibus effects but there were some effects within specific groups. The non-cancer treatment group performed significantly slower on this domain overall at T3 compared to T1, $F(1, 15) = 4.5, p = .051, \eta^2 = .23$. There were no significant main effects on InfoProc, WM or Impulsivity domains.

Psychosocial Variables

Descriptive statistics are presented in Table 2. There were no significant Group x Time interaction effects on any of the psychosocial variables. The main effects of time and group were not significant for the measure of distress and there were no significant effects of time at the individual group level.
There was a significant main effect of group on the perception of illness threat measure, $F(2, 40) = 6.7, p = .003, \eta^2 = .25$. The cancer group reported a significantly higher perception of threat associated with illness than both the non-cancer treatment group and the waitlist group. There were no significant effects of time for the cancer group or the non-cancer treatment group. Interestingly, the non-cancer waitlist group reported significantly lower perceived threat of illness at T3 compared to T1, $F(1, 14) = 6.5, p = .023, \eta^2 = .32$.

**Participant Satisfaction**

The data from this pilot study showed that participants in the intervention groups were satisfied overall with the newly developed intervention program. In the cancer group, 75% of participants were either satisfied or very satisfied with the online program whereas 25% were neither satisfied nor dissatisfied. Ninety-two per cent reported their cognitive problems improved a little or improved a lot, 83% were likely or very likely to recommend the program to a friend with similar problems, and the mean overall program rating was 7.8 out of 10.

The non-cancer treatment group reported similar levels of satisfaction with the program, and the two groups did not differ significantly in their reported satisfaction levels, $\chi^2 (2, N = 27) = .95, p = .62$. Eighty-seven per cent of these participants were either satisfied or very satisfied with the program whereas 13% reported they were neither satisfied nor dissatisfied; 87% reported their cognitive problems improved a little or improved a lot; 80% were likely or very likely to recommend the program to a friend; and the mean overall rating score was 7.7.

**Discussion**

This pilot study sought to evaluate the efficacy of a newly developed web-based cognitive rehabilitation program for cancer survivors with subjective complaints of cognitive impairment. A cancer group and two additional non-cancer groups were
recruited for comparison, including a second intervention group. This design allowed investigation of the degree to which benefits of the intervention, if any, were specific to cancer survivors. Attrition was low and satisfaction was high. Group x Time interactions indicating larger and/or more sustained improvements over time for cancer participants than non-cancer participants were found in a measure of prospective memory, the BAPM. One objective domain, Attention, showed a significant interaction whereby the cancer group and the non-cancer waitlist group improved over time but the non-cancer treatment group declined. Planned comparisons within groups also showed a number of changes over time in all groups.

Attrition rates for the online program were acceptable with 8% of participants withdrawing from the cancer group, 24% from the non-cancer treatment group, and 12% from the waitlist group. The attrition rate of the cancer group is comparable to the aforementioned studies assessing web-based cognitive training in cancer survivors. In the randomised controlled trial examining whether web-based cognitive training can alleviate cognitive complaints in breast cancer survivors the attrition rate was 5% (Damholdt et al., 2016), and the online cognitive training for improving executive function in cancer survivor study reported an attrition rate of 7% (Kesler et al., 2013). Since the current intervention was designed to address cognitive concerns associated with cancer and treatment, it is possible that the rate of attrition was higher in the non-cancer group because some of the content may not be related to their personal experience. Additionally, these participants may not have the same motivation to complete the program if their symptoms of cognitive impairment were milder compared to the cancer group.

Satisfaction ratings for the program were also acceptable. Participants in the intervention groups reported high satisfaction with the online program, and of surprising note is that the non-cancer treatment group had a slightly higher percentage
of “very satisfied” or “satisfied” responses (81%) than the cancer group (75%). Since
the program is designed for cancer survivors and the text in the modules makes direct
reference to issues associated with cancer and cancer treatment, this was an
unexpected finding. It may be that non-cancer participants found the cognitive and
other program components relevant and helpful despite some content being most
pertinent to cancer survivors. It is also possible that contact with significant others
with cancer during their lifetime may have made some aspects of psychoeducation in
the modules useful for understanding the cancer experience. Participants were likely to
recommend the program to friends with similar cognitive problems in both the cancer
group (83%) and in the non-cancer control group (75%), which suggests that the
majority of participants were satisfied with the treatment they received with the
program.

The reported cognitive improvements on the satisfaction survey are promising
for examining the efficacy of the web-based cognitive rehabilitation program. In the
cancer group, 92% of participants reported their cognitive function had improved “a
lot” or “a little”, and 81% of the non-cancer treatment group reported similar changes.

A significant interaction was not found on the primary outcome measure PCI,
however within group improvements were observed on this and other subscales
assessing subjective cognitive functioning. The cancer group reported significant
improvements post-intervention on four subscales, the non-cancer treatment group on
two subscales, whereas no significant changes were reported with the waitlist control
group. On the PCI subscale, improvements from baseline to follow-up were 9.0 in the
intervention group, 3.2 in the non-cancer intervention group, and 2.8 in the non-cancer
waitlist group where an estimated minimally important difference on this measure is
6.5 (Bray et al., 2017). In previous ReCog studies the cancer intervention groups
improved at follow-up by 8.9 (Schuurs & Green, 2013) and 16.5 (King & Green,
Despite significant improvements in the cancer group, the mean PCI scores at follow-up ($M = 42.8$, $SD = 18.2$) remained lower than baseline scores in the non-cancer treatment group, ($M = 50.6$, $SD = 10.8$) and the non-cancer waitlist group, ($M = 57.3$, $SD = 11.9$), indicating lower perceived functioning than a healthy population even after treatment.

Differential benefit of the program for cancer survivors was further supported by a significant interaction for the BADL scale and a trend towards an interaction for the IADL scale (both measures of PM). Moderate effect sizes were found for change scores on the BADL and IADL when comparing the cancer group to the other two non-cancer groups ($d = 0.51$ to $d = 0.62$). A reduction in PM failures on the BADL was noted at follow-up in both intervention groups, and in the cancer group only on the IADL subscale at follow-up. These results indicate that participants’ perception of their cognitive functioning improved over time as a result of participating in the online program. Since subjective cognitive impairment generally correlates more to psychosocial factors such as QoL, fatigue, anxiety, and depression than to objective measures (Hutchinson, Hosking, Kichenadasse, Mattiske, & Wilson, 2012), it would not be uncommon to find reports of cognitive dysfunction amongst community dwelling adults. The results of this study provide preliminary support for improved subjective cognitive functioning following participation in a web-based cognitive rehabilitation program.

Objective outcome measures showed some improvements over time, but also worsening performance in some instances. There was one significant Group x Time interaction, for Attention. In this domain, both the cancer and waitlist groups showed significant improvement on their performance from T1 to T3, whereas the non-cancer treatment group showed the opposite effect, performing significantly more poorly at T3 than T1. The attention domain is comprised of two tasks including measures of
reaction time and omission errors on a continuous performance test. Inspection of means suggested that the non-cancer treatment group performed at the same accuracy at T3 as T1, but at a slower speed.

On the VM domain, both the non-cancer groups performed significantly more poorly at follow-up compared to their baseline assessment. The VM domain is comprised of two tasks, a total verbal memory recognition score and a delayed recognition score. Both tasks have a minimum of 33 parallel versions available to reduce practice effects, therefore the word lists presented would not have had any overlapping words between assessments (Brain Resource Ltd, 2010a). It is unclear why two of the groups performed more poorly over time and why a similar pattern was not observed in the cancer group.

The non-cancer intervention group demonstrated improved performance on the global EF domain at T2, which was maintained at T3. The EF domain was comprised of two variables: maze completion time and number of overrun errors. Both the cancer group and non-cancer treatment group significantly improved completion time of the maze from T1 to T3, and the non-cancer treatment group significantly reduced their overrun errors from T1 to T2. These improvements on either of these tasks were not observed in the non-cancer waitlist group. Significant improvements on standardised objective measures of executive function have been demonstrated as a result of cognitive training interventions in cancer survivors (Kesler et al., 2013), and the results of this study seem to support those researchers’ findings that improvements are possible. However, it is possible that these results may have been an effect of participants becoming more familiar with the task at each assessment time point, rather than a benefit specific to the intervention.

There are some limitations of this study. Firstly there was a relatively small sample size, which is typical of pilot studies. The study used multiple comparisons;
therefore the results presented should be interpreted with caution. Secondly, participants in the cancer group were not randomly assigned like the non-cancer participants in the study, which may have biased the results when comparing cancer survivor and non-cancer participants. Furthermore this study was lacking a cancer waitlist comparison group for comparisons with the cancer group. Practice effects would be expected on the neuropsychological tests and were not formally assessed or controlled for apart from the use of parallel versions of tasks at retest. However, there is no reason to expect that the size of any practice effects would differ between the groups. Despite these limitations, the initial results suggest the eReCog online program may be an effective method for improving cognitive functioning in individuals treated for cancer and the normal adult population. A larger randomised controlled trial is currently underway to further investigate the efficacy of this cognitive rehabilitation program.
References


CHAPTER V: WEB-BASED COGNITIVE REHABILITATION FOR SURVIVORS OF ADULT CANCER: A RANDOMISED CONTROLLED TRIAL

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Running Head: WEB-BASED COGNITIVE REHABILITATION FOR CANCER

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Ethical Standards:
This research project complies with the ethical standards of the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC) and was conducted in accordance with the Helsinki Declaration

Keywords: Cancer, oncology, adult, survivors, cognitive rehabilitation, web-based, online
STATEMENT OF CONTRIBUTION TO CO-AUTHORED PAPER

This chapter includes a paper that was co-authored by my thesis supervisors, Dr Heather Green and Professor David Shum. The manuscript is currently under review by the journal *Psycho-Oncology* and has been formatted to that journal style. As such, there is some repetition in sections of this chapter with other sections of this thesis. Tables and Figures are numbered to correspond with Chapter numbers. The citation is as follows: Mihuta, M. E., Green, H. J., & Shum, D. H. K. (Manuscript in submission). *Web-based cognitive rehabilitation for survivors of adult cancer: a randomised controlled trial.*

- My contribution to the manuscript involved: review of the literature, initial concept and experimental design, data collection and analysis, and preparation of the manuscript.

- The contributions of Heather Green and David Shum involved: supervision of the project design, data collection and analysis; and revisions to the manuscript.

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Abstract

**Objective:** Cognitive dysfunction associated with cancer is frequently reported and can reduce quality of life. This study evaluated a web-based cognitive rehabilitation therapy program (eReCog) in cancer survivors compared to a waitlist control group.

**Methods:** Adult cancer survivors with self-reported cognitive symptoms who had completed primary treatment at least 6 months prior were recruited. Participants completed telephone screening and were randomly allocated to the 4-week online intervention or waitlist. Primary outcome was perceived cognitive impairment assessed with the Functional Assessment of Cancer Therapy – Cognitive Function version 3. Secondary outcomes were additional measures of subjective cognitive functioning, objective cognitive functioning and psychosocial variables.

**Results:** 76 women were allocated to the intervention (n=40) or waitlist (n=36). A significant interaction was found on the instrumental activities of daily living measure of self-reported prospective memory (PM) whereby the intervention group reported a greater reduction in PM failures than the waitlist group. Interaction trends were noted on Perceived Cognitive Impairments (p=.089) and Executive Functioning (p=.074). No significant interactions were observed on other measures of objective cognitive functioning or psychosocial variables.

**Conclusions:** The web-based intervention shows promise for improving self-reported cognitive functioning in adult cancer survivors. Further research is warranted to better understand the mechanisms by which the intervention might contribute to improved self-reported cognition.
Background

Advances in cancer treatments have led to improved survival rates, but adverse effects of diagnosis and treatment can impact quality of life. Cancer-related cognitive impairment (CRCI) is frequently reported by patients and has been well documented.\textsuperscript{1,2} Up to 30% of cancer patients experience CRCI before beginning treatment; as many as 75% experience cognitive dysfunction during treatment; and up to 35% experience long-term CRCI after treatment completion.\textsuperscript{1,3} CRCI impacts vary from subtle to pronounced, interim to permanent, and stable to progressive\textsuperscript{4} and can involve cognitive domains including memory, attention, processing speed, motor function, and executive functioning.\textsuperscript{3,5}

Many cancer survivors are unprepared for CRCI and coping with poor memory and attention has been identified as a primary “unmet need” in survivorship care.\textsuperscript{6} Research has demonstrated that self-reported cognitive impairment is often associated with increased psychological distress, fatigue, and poorer quality of life (QoL),\textsuperscript{7,8} and this impairment generally correlates poorly with performance on standardised neuropsychological measures.\textsuperscript{9} Therefore, assessing both subjective and objective CRCI is advisable.

Cognitive rehabilitation has the potential to mitigate symptoms of objective and self-reported CRCI. Several randomised controlled trials have been published with reported benefits of such intervention programs for cancer survivors.\textsuperscript{10-13} The terms “cognitive rehabilitation” and “cognitive training” are often used interchangeably, which masks important conceptual differences between them. Cognitive training (CT) is a behavioural method of treatment based on models of neuroplasticity, which suggest that cognitive abilities can be improved by progressive drills that exercise the brain.\textsuperscript{14,15} In contrast, cognitive rehabilitation therapy (CRT) is the process of re-attaining cognitive skills that have been lost or altered due to injury whereby the goal
of treatment is to improve functioning on everyday tasks. CRT incorporates psychoeducation, skills training, strategy training, and functional activity training to apply the strategies in everyday life.

Web-based interventions in this area have been scarce. There are no published studies evaluating online CRT in cancer survivors and only three online CT interventions. Kesler and colleagues conducted an RCT with 41 breast cancer survivors, 21 of whom received web-based CT four times per week for 12 weeks. Improved objective executive functioning (EF), processing speed, verbal fluency, and improved subjective EF skills were reported in the treatment group post intervention. In another study Damholdt and colleagues recruited 157 breast cancer survivors and randomly allocated 94 to web-based CT with email support (eCogT) compared to waitlist. They reported no significant group differences on primary or secondary outcome measures of working memory and perceived cognitive functioning, but found significant improvements for verbal learning and another working memory test in the eCogT group at follow-up. Most recently Bray and colleagues conducted an RCT with 242 adult cancer survivors, 121 of whom were assigned to CT with a recommended four 40-minute sessions per week for 15 weeks. They reported significantly less perceived cognitive impairment (PCI), and reduced psychological distress and fatigue at post-intervention and follow-up in the intervention group.

The objective of our study was to evaluate the efficacy of a web-based CRT program called eReCog. The program was adapted from the face-to-face Responding to Cognitive Concerns (ReCog) intervention and piloted with small samples of cancer survivors and community dwelling adults with beneficial results. The main hypothesis was that participants in eReCog would improve more on self-reported cognition compared to a waitlist control group at post-intervention and follow-up. Objective cognition; psychosocial variables of distress, quality of life, illness
perception and fatigue; and program satisfaction were assessed as secondary outcomes relevant to this population\textsuperscript{12,20,21}.

**Methods**

**Intervention**

Responding to Cognitive Concerns (ReCog) was developed as a manualised face-to-face, 4-session, group intervention to address cognitive dysfunction in cancer survivors\textsuperscript{12,21,22}. This intervention was adapted into a web-based version (eReCog). Its development process and piloting trial are described elsewhere\textsuperscript{19}. Based on the principles of cognitive behavioural therapy (CBT), the program contains four modules, each including psychoeducation, relaxation, strategy training, discussion questions that allow viewing of others’ anonymised responses, and homework\textsuperscript{23}. Modules take approximately 30 to 60 minutes and participants are expected to complete one module per week over four weeks. Module topics are (1) Aging, health, cancer and cognitive function, (2) Memory, (3) Attention, and (4) Fatigue, emotions, and cognition.

**Participants**

A sample size of 65 participants was sought based on a priori power analysis demonstrating 95\% power for detecting an interaction effect of $d=0.5$ with $\alpha=0.05$. An additional 20\% (11 participants) were added to allow for attrition. A total of 76 participants were eligible and randomly allocated to intervention ($n=40$) or waitlist ($n=36$) groups. Eligibility criteria were: diagnosed with adult-onset cancer excluding central nervous system tumours, aged 18+ years, reported cognitive complaints with memory or concentration, completed primary treatment at least 6 months prior (excluding hormonal treatment, which could be ongoing), were disease-free at the time of enrolment, and able to read and write English fluently. Exclusion criteria were: currently undergoing primary treatment, history of traumatic brain injury or
neurological disorder, poorly managed anxiety or depression, or insufficient English skills.

**Procedure**

The study was approved by Griffith University’s ethics committee and preregistered at www.ANZCTR.org.au (ACTRN12615000878572). Individuals were recruited through emails sent to Breast Cancer Network Australia (BCNA) and Griffith University staff and students from March to June 2016. Group allocation was determined via computerised random number generation. Volunteers were allocated to a group upon receiving their initial email expressing interest. During subsequent eligibility screening conducted via telephone by the first author, sociodemographic and medical data were collected. Cognitive complaints were evaluated using the two-item cognitive functioning scale of the European Organisation for Research and Treatment of Cancer – Core Quality of Life Questionnaire (EORTC QLQ-C30). Volunteers answered item #20, “have you had difficulty in concentrating on things, like reading a newspaper or watching television?” and item #25, “have you had difficulty remembering things?” Possible responses were 1=not at all, 2=a little, 3=quite a bit, and 4=very much. Eligible volunteers scored 2 or more on either item and believed these impairments were associated with their cancer experience. Volunteers on medication for anxiety or depression were asked whether they believed their symptoms were adequately managed with current treatment.

Eligible participants were informed of group allocation and were requested to confirm consent via email. Upon receiving written consent, participants were emailed links to complete the first assessment (T1). Intervention participants then completed the 4-week online program and control participants underwent a 4-week waiting period. Participants were reassessed after the intervention or wait period (T2) and
completed a follow-up assessment after a further 3 months (T3). After T3 assessment, participants in the waitlist group could choose to complete the intervention.

**Email Delivery and Support**

Links to WebNeuro assessment\(^{25}\), questionnaires via Qualtrics Software (2013; Qualtrics, Provo, UT, USA), and program modules via LessonLAMS (2002; LAMS International) were emailed to participants for online completion. Reminder emails were sent approximately 5 days later if the task was uncompleted. After 3 reminder emails with no response, participants were contacted via telephone or assumed to withdraw. Encouragement emails were sent to participants after completing Module 1 with individualised feedback on the goal-setting activity. Additional email support was available for questions regarding content or technical problems.

**Measures**

*Subjective cognitive functioning*

*Functional Assessment of Cancer Therapy – Cognitive Scale (FACT-Cog 3).*

This 37-item measure assesses memory, concentration, language, and thinking abilities in cancer patients.\(^{26}\) It contains four subscales: PCI, Perceived Cognitive Abilities (PCA), Comments from Others (OTH), and Impact on Quality of Life (QOL). As recommended, PCI was used as the primary measure of subjective cognitive functioning.\(^{26}\)

*Brief Assessment of Prospective Memory (BAPM).* This 16-item self-report measure was designed to evaluate frequency of prospective memory (PM) failures in individuals with brain injury.\(^{27}\) Eight items comprise the instrumental activities of daily living (IADL) subscale, which assesses common memory lapses such as household and financial management tasks, and 8 items comprise the basic activities of daily living (BADL) subscale assessing uncommon forgetting such as dressing and
eating. The mean score for answered items (1 to 5 response scale) is calculated for each subscale. The measure has demonstrated sensitivity in breast cancer survivors.\textsuperscript{28}

**Objective cognitive functioning**

The online test battery WebNeuro comprises 11 computerised tasks assessing seven cognitive domains: verbal memory (VM), working memory (WM), attention, response speed (RS), information processing efficiency (InfoProc), executive functioning (EF), and impulsivity.\textsuperscript{25} Online WebNeuro was validated against the computerised IntegNeuro battery,\textsuperscript{29} which demonstrated convergent and divergent validity with standardised paper-and-pencil neuropsychological tests including Digit Span (Wechsler Adult Intelligence Scale III), Spatial Span (Wechsler Memory Scale III), California Verbal Learning Test, Trail Making Test, Stroop Test, Finger Tapping Test, Rey Complex Figure Test and others.\textsuperscript{30} For each cognitive domain, individualised Z-scores adjusted for age, sex and education based on the developers’ normative sample were calculated. Between 33 and 60 parallel forms are used for each task to reduce practice effects.\textsuperscript{31} Participants were instructed to complete the WebNeuro assessment in a single sitting of approximately 40 minutes, when unlikely to be interrupted.

**Psychosocial variables**

*Kessler Psychological Distress Scale (K10).* This 10-item self-report measure assesses levels of anxiety and depressive symptoms in the past 4 weeks.\textsuperscript{32}

*Brief Illness Perception Questionnaire (BIPQ).* Perceived threat of illness was assessed with an 8-item questionnaire. The term “illness” can be substituted with other terms relevant to the phenomenon.\textsuperscript{33} In this study, “illness” was substituted with “cognitive difficulties”, as previously examined with cancer survivors.\textsuperscript{12}

*Fatigue.* Symptoms of fatigue were assessed with the 3-item EORTC QLQ-C30 fatigue symptom scale.\textsuperscript{24}
Program satisfaction

Satisfaction was measured by intervention participants’ ratings of: (1) satisfaction with the program, (2) change in cognitive functioning, and (3) likelihood of recommending the program to others on a 5-point Likert scale.\textsuperscript{12,21} They provided an overall program rating from 1 (very poor) to 10 (excellent) and were asked to comment on aspects of the program found most enjoyable, least enjoyable, or otherwise noteworthy.

Statistical Analyses

The main analyses used 2(Group) x 3(Time) analyses of variance. Imputation of missing T3 scores was performed for 3 participants (2 waitlist; 1 intervention) by carrying forward their T2 scores. Since results did not differ with and without imputation, results included this imputed data. Where Mauchly’s Test indicated violations to the sphericity assumption, the Huynh-Feldt correction was used. Within-group planned comparisons across time were computed. Cohen’s $d$ was calculated to determine differences between intervention and waitlist effect sizes at T2 and T3, computed such that positive values of $d$ represented improvement and positive values of differences in $d$ represented greater improvement in intervention than waitlist participants.\textsuperscript{34}

Results

Five women did not complete baseline assessments (Figure 5.1), therefore 37 women commenced the intervention and 34 the waitlist. T3 assessments were completed by 31 women in each group indicating 16.2% and 8.8% attrition in intervention and waitlist groups, respectively. Participants who withdrew were less likely to have had hormonal treatment, more likely to be unpartnered, and completed primary treatment longer ago on average ($M=97.78$, $SD=44.14$) than completers.
$M=42.97, SD=37.79)$. Intervention and waitlist group demographic and medical characteristics did not differ at baseline (see Table 5.1).

*Figure 5.1 Participant CONSORT flowchart.*
Table 5.1

Baseline demographic and medical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 32)</th>
<th>Waitlist (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Age (SD)</td>
<td>55.1 (9.2)</td>
<td>56.9 (9.2)</td>
</tr>
<tr>
<td>Mean Education (SD)</td>
<td>15.3 (2.6)</td>
<td>15.1 (2.9)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Born in Australia (%)</td>
<td>81.3</td>
<td>81.8</td>
</tr>
<tr>
<td>First Language English (%)</td>
<td>93.8</td>
<td>97.0</td>
</tr>
<tr>
<td>Living with partner (%)</td>
<td>65.6</td>
<td>81.8</td>
</tr>
<tr>
<td>State or Territory (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New South Wales</td>
<td>43.8</td>
<td>42.4</td>
</tr>
<tr>
<td>Other</td>
<td>56.2</td>
<td>57.6</td>
</tr>
<tr>
<td><strong>Medical characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Type (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>96.9</td>
<td>100</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>3.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Treatment (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>87.5</td>
<td>81.8</td>
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<tr>
<td>Radiotherapy</td>
<td>68.8</td>
<td>66.7</td>
</tr>
<tr>
<td>Hormone Therapy</td>
<td>84.4</td>
<td>93.9</td>
</tr>
<tr>
<td>Current Hormone</td>
<td>68.8</td>
<td>63.6</td>
</tr>
<tr>
<td>Mean years since primary treatment (SD)</td>
<td>3.4 (2.7)</td>
<td>4.1 (3.7)</td>
</tr>
</tbody>
</table>

**Subjective Cognitive Functioning**

Descriptive statistics for outcome measures are presented in Table 5.2. Main effects for time were observed on all 6 subscales of subjective cognitive functioning, representing improvements over time; there were no main effects of group. A significant interaction was observed on the IADL, $F(2,126) = 3.80, p = .025$, $\eta^2 = 0.045$, which occurred because the intervention group reported a reduction in PM failures at T2, $F(1,31) = 9.11, p = .005$, and T3, $F(1,31) = 33.00, p < .001$, and the waitlist group a reduction at T3 only, $F(1,32) = 5.99, p = .020$. An interaction trend was noted on the PCI ($p = .089$), whereby intervention participants tended to report greater improvement in PCI over time than waitlist participants.
<table>
<thead>
<tr>
<th>Measures (Ranges)</th>
<th>Intervention (n=32)</th>
<th>Waitlist (n=33)</th>
<th>Interaction (p)</th>
<th>d_{Int-Wait}</th>
<th>d_{Int-Wait}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>FACT-Cog-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI (0-72)</td>
<td>41.6(15.4)</td>
<td>44.1(14.8)</td>
<td>50.5(12.7)***</td>
<td>42.5(16.0)</td>
<td>46.2(14.1)**</td>
</tr>
<tr>
<td>PCA (0-28)</td>
<td>15.6(5.4)</td>
<td>17.2(4.9)**</td>
<td>18.2(5.7)**</td>
<td>17.3(5.9)</td>
<td>17.8(6.4)</td>
</tr>
<tr>
<td>OTH (0-16)</td>
<td>14.9(1.9)</td>
<td>14.6(2.4)</td>
<td>15.6(1.7)</td>
<td>14.1(3.0)</td>
<td>14.2(2.9)</td>
</tr>
<tr>
<td>QOL (0-16)</td>
<td>11.9(4.4)</td>
<td>13.1(3.0)**</td>
<td>14.1(2.6)**</td>
<td>11.5(3.6)</td>
<td>12.1(3.4)</td>
</tr>
<tr>
<td>BAPM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IADL (0-5)</td>
<td>2.05(0.58)</td>
<td>1.78(0.46)**</td>
<td>1.67(0.52)***</td>
<td>1.83(0.52)</td>
<td>1.79(0.53)</td>
</tr>
<tr>
<td>BADL (0-5)</td>
<td>1.28(0.26)</td>
<td>1.19(0.34)*</td>
<td>1.18(0.29)</td>
<td>1.33(0.34)</td>
<td>1.31(0.39)</td>
</tr>
<tr>
<td>EORTC-QLQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cog Scale (0-100)</td>
<td>64.1(23.6)</td>
<td>70.8(18.0)</td>
<td>71.9(20.9)</td>
<td>65.7(23.9)</td>
<td>73.2(21.1)**</td>
</tr>
<tr>
<td>WebNeuro</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VM</td>
<td>0.07(0.71)</td>
<td>0.02(0.66)</td>
<td>-0.38(1.17)*</td>
<td>-0.07(0.73)</td>
<td>-0.51(1.48)</td>
</tr>
<tr>
<td>WM</td>
<td>-0.34(1.04)</td>
<td>-0.35(1.08)</td>
<td>-0.37(1.15)</td>
<td>-0.60(1.10)</td>
<td>-0.51(0.70)</td>
</tr>
<tr>
<td>Attention</td>
<td>-0.24(0.80)</td>
<td>-0.15(0.85)</td>
<td>-0.19(0.73)</td>
<td>-0.15(0.80)</td>
<td>-0.19(0.63)</td>
</tr>
<tr>
<td>InfoProc</td>
<td>0.09(0.55)</td>
<td>-0.09(0.66)*</td>
<td>0.02(0.58)</td>
<td>0.01(0.62)</td>
<td>-0.11(0.81)</td>
</tr>
<tr>
<td>EF</td>
<td>-0.20(0.66)</td>
<td>0.54(0.69)**</td>
<td>0.43(0.73)**</td>
<td>0.04(0.63)</td>
<td>0.36(0.68)**</td>
</tr>
<tr>
<td>RS</td>
<td>-0.03(1.12)</td>
<td>-0.19(1.20)</td>
<td>-0.12(0.85)</td>
<td>-0.37(1.46)</td>
<td>-0.05(1.12)</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>-0.46(0.41)</td>
<td>-0.23(0.41)*</td>
<td>-0.24(0.29)*</td>
<td>-0.29(0.42)</td>
<td>-0.23(0.49)</td>
</tr>
<tr>
<td>Psychosocial</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Fatigue (0-100)</td>
<td>31.9(19.5)</td>
<td>27.1(15.7)*</td>
<td>30.6(17.4)</td>
<td>39.4(20.0)</td>
<td>35.7(18.0)</td>
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<tr>
<td>Distress (10-50)</td>
<td>16.3(6.1)</td>
<td>16.3(6.5)</td>
<td>16.4(6.6)</td>
<td>18.0(6.4)</td>
<td>18.1(6.1)</td>
</tr>
<tr>
<td>BIPQ (0-80)</td>
<td>39.0(11.9)</td>
<td>39.7(11.4)</td>
<td>36.8(10.7)</td>
<td>39.8(12.2)</td>
<td>41.7(12.1)</td>
</tr>
</tbody>
</table>

Note: *p<.05, **p<.01, ***p<.001 for within group comparisons to Time 1. Raw scores and possible ranges are shown for self-report measures and Z-scores for objective cognitive domains. Lower scores indicate better functioning on IADL, BADL, fatigue, distress, and BIPQ. $d_{Int-Wait}$=effect size for intervention improvement corrected for waitlist improvement.
Objective Cognitive Functioning

No significant Group x Time interactions were found but main effects for time were noted on four of seven domains. A significant main effect for time indicating worsening performance was found on InfoProc, \( F(2,126)=3.42, p=.036, \eta^2=0.050 \), and VM, \( F(2,120)=10.21, p=.001, \eta^2=0.139 \); see means and within group comparisons in Table 5.2. EF produced a main effect in a positive direction, \( F(2,112)=19.11, p<.001, \eta^2=.256 \), with both groups improving performance over time. On Impulsivity there was a significant main effect for time, \( F(2,124)=3.78, p=.025, \eta^2=.056 \); within group comparisons showed improvements for the intervention group at T2 (\( p=.023, d=.56 \)) and T3 (\( p=.017, d=.61 \)). No significant changes over time were observed on the WM, Attention, or RS domains.

Psychosocial Variables

No interactions were found on psychosocial variables. The intervention group reported reduced symptoms of fatigue at T2, \( F(1,31)=4.32, p=.046, d=.27 \), but this effect was not maintained at follow-up, \( F(1,31)=0.19, p=.670, d=-.08 \). No significant effects were found on measures of distress or illness perceptions.

Participant Satisfaction

Among intervention participants, 94% were “satisfied” or “very satisfied” and 6% were “neither satisfied nor dissatisfied”; 84% were “likely” or “very likely” to recommend the program; 68% reported their cognitive functioning had improved “a little” or “a lot”, whereas 32% reported “no change”. The mean rating of the program was 7.7/10 ranging from 5 (average) to 10 (excellent).

Discussion

This RCT aimed to evaluate the efficacy of web-based CRT in adult cancer survivors and is the first published study to do so. We hypothesised that intervention participants would report improved subjective cognition compared to waitlist
participants, a hypothesis that was partially supported. A significant Group x Time interaction and two trends towards interactions were found, all representing greater improvements in the intervention than the waitlist group.

The primary outcome measure PCI demonstrated a trend towards an interaction ($p=0.089$). Mean improvements from baseline to follow-up were 8.9 for intervention and 5.6 for waitlist participants, compared to an estimated minimally important difference of 6.5 for this measure. Participants reported higher PCI at baseline than previous cancer cognitive rehabilitation studies. Having more stringent inclusion criteria (e.g., reporting “quite a bit” of difficulty with memory or concentration) might have resulted in a more impaired sample allowing for greater improvement. Notwithstanding, baseline PCI scores in this study were still lower than non-cancer comparison groups indicating some degree of impairment, and their follow-up scores, although improved, remained below baseline scores for healthy individuals.

Improved PCI on the FACT-Cog-3 was observed in both groups, similar to previous research with cancer survivors. King and Green’s RCT utilising the ReCog intervention showed 73% of intervention and 50% of waitlist participants demonstrated clinically significant improvement on PCI at follow-up. The authors suggested the improvements in the waitlist group might have resulted from increased awareness and improved perceptions of their cognitive functioning due to assessment sessions. These researchers also reported similar improvements on other FACT-Cog subscales for both intervention and waitlist groups, which was seen in the current study on both PCA and QOL subscales.

The interaction on the IADL subscale assessing PM was significant. PM is the ability to remember to complete intended actions in the future despite everyday distractions and it is believed that when people refer to “poor memory” they are
referring to PM failures\textsuperscript{38}. Only one other published cognitive rehabilitation study with cancer survivors has assessed PM\textsuperscript{12}, although PM failures have been reported in chemotherapy-treated breast cancer survivors compared to healthy participants.\textsuperscript{28} This type of impairment is likely to be noticed on everyday activities and potentially provides an acceptable measure of memory functioning on daily tasks. Despite both groups reporting reduced PM failures, the effect size was larger for intervention than waitlist participants at T3 (difference in \(d=.38\)). This effect may be due to the successful implementation of memory compensatory strategies learnt during the intervention.

Improved subjective cognition in this study may also be explained by the similarity of the computerised WebNeuro assessment to typical CT programs. Participants reported to investigators that WebNeuro was comparable to previously trialled “brain training” programs. Evidence suggests placebo effects can occur in cognitive interventions when participants know the intended outcome.\textsuperscript{39} For example, Foroughi and colleagues\textsuperscript{39} intentionally created a placebo effect by using suggestive flyers advertising “Brain Training and Cognitive Enhancement” versus a control flyer “Email Today and Participate in a Study”. The placebo condition showed improvements after a single 1-hour cognitive training session whereas the nonsuggestive flyer group showed no improvements. Recruitment materials for the current study advised prospective participants they would have the opportunity to participate in “a 4-week online interactive program, which aims to improve cancer-related cognitive issues such as memory and concentration”. Participant expectations to receive an intervention coupled with the similarity of WebNeuro assessments to CT training may have influenced self-report measures of cognition.

On objective cognitive functioning domains a trend towards an interaction occurred on EF, which was not observed in the pilot study.\textsuperscript{19} These results may have
occurred because participants became more familiar with the maze task and completed the task more quickly with fewer overrun errors, although improved EF performance has been demonstrated following cognitive training in cancer survivors.\textsuperscript{14} Clinical implications of improved EF are an improved ability to plan, initiate, and execute daily tasks, which has the potential to enhance QOL if improvements transfer into everyday life.

Within group comparisons for Impulsivity showed significant improvements for intervention participants at T2 and T3, which did not occur with waitlist participants. Theoretically it has been postulated that impulsivity is the “antipode” to EF.\textsuperscript{40} That is to say executive \textit{dysfunction} is the equivalent of certain types of impulsivity. As a result, improvements in EF could result in improvements on measures of impulsivity, which was demonstrated in the intervention group only. It could be argued the reduced impulsivity resulted from an increased level of attention to the task, which was fostered by learning from Module 2 of the intervention.

A pattern of poorer performance across time on VM was observed in the pilot study\textsuperscript{19} and current study, which is not believed to be associated with interference from previous word lists since parallel versions of the tasks were used. Practice effects were not formally assessed, but by design, any practice effects would have been expected to affect both groups equally.

\textit{Strengths and limitations}

A notable strength is that this is the first known RCT to assess online CRT in cancer survivors. We utilised an intervention previously implemented successfully in face-to-face and web-based format (i.e., pilot study). This provides preliminary evidence that online cognitive rehabilitation interventions translated from face-to-face format can be effective. Secondly, the online intervention was created with a software program (LessonLAMS) that is readily available to researchers at no cost for small
samples (<30) and a low cost ($199AUD/year) for larger samples (up to 90 participants). Furthermore, our study conducted a comprehensive assessment of subjective and objective cognitive function, as well as psychosocial variables typically reported as problematic in this clinical group.

There are some limitations to note. No published studies have used WebNeuro to measure cognitive functioning in adult cancer survivors and further investigation into its appropriateness for this purpose seems warranted. Participants completed the WebNeuro assessments in an uncontrolled environment (e.g., home), therefore performance on tasks is susceptible to unknown influences (e.g., telephone interruptions). In addition, recruitment predominantly occurring through BCNA resulted in a sample that was 100% female and 98.5% survivors of breast cancer limiting the generalisation of findings to males and survivors of other types of cancer. Statistical significance and trends should be interpreted with caution as multiple comparisons were conducted in this study; descriptive statistics and effect sizes provide further interpretative information.

Clinical implications

The web-based cognitive rehabilitation program eReCog shows some promise for improving subjective cognitive functioning and possibly objective cognitive functioning in female adult cancer survivors. Many improvements were found in the waitlist group also, but effect sizes tended to be larger for intervention than waitlist. Development of online cognitive remediation interventions has the potential to provide accessible supportive care to alleviate cognitive symptoms in cancer survivors, particularly those living in smaller communities or with limited mobility.
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CHAPTER VI: THE IMPLEMENTATION OF WEB-BASED COGNITIVE REHABILITATION IN ADULT CANCER SURVIVORS: EXAMINING PARTICIPANT ENGAGEMENT, ATTRITION, AND TREATMENT FIDELITY

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Running Head: IMPLEMENTATION OF WEB-BASED COGNITIVE REHABILITATION

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Ethical Standards: This research complies with the ethical standards of the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC) and was performed in accordance with the Helsinki Declaration.
STATEMENT OF CONTRIBUTION TO CO-AUTHORED PAPER

This chapter includes a paper that was co-authored by my principal thesis supervisor, Dr Heather Green. The manuscript is currently under review by the journal *Supportive Care in Cancer* and has been formatted to that journal style. As such, there are some repetitions in sections of the paper and other sections of this thesis. Tables and Figures are numbered to correspond with Chapter numbers. The citation is as follows: Mihuta, M. E. & Green, H. J. (Manuscript in submission). *Implementation of web-based cognitive rehabilitation in adult cancer survivors: examining participant engagement, attrition, and treatment fidelity.*

- My contribution to the manuscript involved: review of the literature, initial concept and experimental design, data collection and analysis, and preparation of the manuscript.
- The contributions of Heather Green involved: supervision of the project design, data collection and analysis, and revisions to the manuscript.
- Acknowledgement is given to David Shum for his involvement in research projects associated with the results presented in this paper.

Signed: ____________________________  Date: 4 April 2017
Mary E. Mihuta

Countersigned: ________________________  Date: 4 April 2017
Co-author of paper: Heather Green
Abstract

Purpose: Low engagement and high attrition are common challenges in web-based interventions. Typical measures of engagement reported in the literature are not meaningful for describing participant activity within the intervention and can be misleading. This research aimed to develop a more meaningful method of measuring engagement in an online cognitive rehabilitation program whilst monitoring treatment fidelity.

Methods: A pilot study and randomised controlled trial (RCT) were conducted. Data from 60 participants were analysed from three intervention groups: pilot cancer group, pilot non-cancer group, and RCT cancer group. Groups completed the 4-week eReCog program comprised of four online modules. Engagement scores were calculated based on activities completed in each module. Attrition, interaction with the program facilitator, and correlations with outcome measures were analysed.

Results: Overall engagement in the intervention was high. The non-cancer group participated significantly less than the cancer groups ($p = < .001$), whereby the percentage of activity items completed was 92%, 87%, and 78% in the pilot cancer, RCT cancer, and pilot non-cancer groups, respectively. Attrition was higher in the pilot non-cancer group (24%) compared to the pilot cancer group (8%) and the RCT cancer group (16%). Total engagement was correlated with fewer prospective memory problems on Instrumental Activities of Daily Living ($p = .018$).

Conclusions: Measuring completed activities in online interventions appears a more meaningful measure of engagement than other conventional methods described in the literature and has the potential to increase treatment fidelity in web-based research.

Keywords: Cancer, cognitive rehabilitation, web-based, online, engagement, treatment fidelity
Background

There has been an increase in the number of web-based interventions aimed at improving psychosocial and physical outcomes in cancer survivors, but low levels of engagement and high attrition rates have been problematic in this area of research [1]. Some researchers have suggested that using methodological approaches that analyse the science of engagement, or the way in which individuals engage in web-based interventions, has the potential to increase the efficacy and cost-effectiveness of these interventions [2, 3] improve treatment outcomes, and increase the possibility of their adoption into real-life behaviour change [4, 5].

Engagement is the process of how individuals utilise an intervention program, which can be defined in a variety of ways [1]. Some of the most common measures of engagement include number of messages posted [6-9], number of logins [10-13], number of modules completed [14], and time spent on the program or website [15, 16]. Whilst each of these measures of engagement provides some level of understanding about how individuals participate in an intervention program, their validity in some cases can be troublesome. For example, the number of messages posted may be insufficient to adequately describe participant engagement since individuals do not uniformly post responses in web-based forums. A study on breast cancer support groups reported that 54% of participants did not post any messages and did not meet their criteria for active participation [17]. Similarly, a simple count of participant logins may be misrepresentative of their participation for a range of reasons including logging in without engaging with the content or multiple logins due to Internet connectivity problems. These sorts of methodological issues may be one factor contributing to the low levels of engagement often reported in the literature.

It is recognised that participant engagement often declines over time [18], which has been described by Eysenbach as “the law of attrition” [5]. Eysenbach’s
“law” is referring to the phenomenon of participants’ discontinued usage of the program and/or loss to follow-up, which is a methodological challenge posed by many web-based intervention programs. Attrition rates as high as nearly 40% have been reported in some web-based interventions for cancer survivors. Foster and colleagues conducted a multi-centre randomised controlled trial (RCT) to assess the effectiveness of a web-based intervention for managing cancer-related fatigue after finishing primary cancer treatment and reported an attrition rate of 36% by the 12-week follow-up assessment [19]. Similarly, David and colleagues performed an RCT to assess a 4-week internet-based program for coping with cancer in a cohort of hematologic cancer patients and reported a dropout rate of 36% at post-intervention [20].

Low levels of engagement and high levels of attrition pose a threat to the treatment fidelity of web-based interventions. The concept of treatment fidelity refers to the methodological strategies that are used to monitor and enhance both the reliability and validity of behavioural intervention programs, which is often underreported in the literature [21]. The National Institutes of Health (NIH) Behaviour Change Consortium (BCC) created guidelines to provide a framework for the discussion of treatment strategies [21]. These guidelines include five key elements associated with treatment fidelity: (a) study design, (b) provider training, (c) treatment delivery, (d) receipt of treatment, and (e) enactment of treatment skills. Since Web-based interventions are generally self-administered, it can be difficult to ensure participants are receiving the proper dose of the intervention and that the intervention is being completed as intended [22]. This makes it difficult for researchers to replicate studies and draw accurate conclusions about outcomes.

The aim of the current research was to develop and evaluate an alternative and potentially more meaningful measure of participant engagement, using the example of a web-based cognitive rehabilitation therapy (CRT) program called eReCog. This
interactive online intervention comprises four online training modules that were adapted from the manualised in-person intervention “Responding to Cognitive Concerns (ReCog)” [23, 24]. The program is based on models of cognitive-behavioural therapy (CBT) and contains elements of psychoeducation, strategy training, and enactment of skills on topics such as cancer, cognition, normal ageing, memory, attention, fatigue, and emotional changes associated with cancer and treatment. Rather than using the conventional methods described earlier for measuring engagement (e.g., number of logins, number of modules completed) we incorporated a more rigorous approach to monitoring the intervention and were able to calculate the number and percentage of activities completed within each of the four program modules. Engagement data were analysed from a pilot study with adult cancer survivors and community dwelling adults conducted between November 2015 and March 2016 [25] and an RCT of adult cancer survivors completed from March to October 2016 [26]. The primary outcome for these studies was subjective cognitive functioning assessed on seven subscales from validated measures. We also measured facilitator interaction in order to enhance our understanding of the implementation process required in web-based intervention research.

**Method**

**Participants**

In total, 71 participants were assigned to complete the web-based eReCog intervention in one of three groups. Eleven participants withdrew prior to completing the post-intervention assessment and were therefore excluded from analysis. The results are based on data from 60 participants: pilot cancer group (n=12), pilot non-cancer group (n=16), and RCT cancer group (n=32).
Inclusion criteria for the cancer groups included: diagnosed with adult onset cancer excluding central nervous system tumours, aged 18+ years, had self-reported cognitive complaints related to memory or concentration, had completed primary treatment at least 6 months prior to enrolment (excluding ongoing hormone therapy, which was permissible), and were currently disease free. Participants in the non-cancer group were eligible if they were aged 35+ and had no neurological, medical or psychological problems affecting their participation in the study. All participants were required to speak and read English fluently, and have access to a laptop or desktop computer with Internet and an active email account.

**Quantifying Module Engagement**

Online eReCog was created using LessonLams [27], an open source Learning Activity Management system. Each module has a fixed number of pages, which participants progress through consecutively until reaching the end of the module. There is a tracking bar located on the left of the screen indicating the total number of pages in the module that allows participants to monitor their progress.

Each module contains interactive pages where reflective and discussion questions relating to the module are presented. Participants are not required to type in a response, but the module instructions encourage them to respond. Since not all participants in the pilot study had a history of cancer, the following instructions were included: “If you have not had cancer and are participating in the second group, then some of these questions may not be relevant to you. If you can relate in another way to the experience (e.g., you have been really tired before and noticed you could not concentrate), then feel free to share your experiences. Or if you prefer, you can leave those fields blank”. After participants type in their personalised response, they are able to view anonymised responses from other participants in the program. Module engagement was calculated for each module based on the number of responses typed.
in by each participant. Participant responses were analysed by the researchers to ensure
the quality of their responses whereby arbitrary text responses such as non-words or
blank responses received zero points for that activity. A total engagement score was
calculated by combining the four modules for a maximum score of 76 points. The
allocation of points by module is presented in Table 6.1.

Table 6.1

*Engagement points by module*

<table>
<thead>
<tr>
<th>Module Tasks</th>
<th>Allocated Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Module 1 (40 pages)</strong></td>
<td></td>
</tr>
<tr>
<td>Defining cognition</td>
<td>1 point</td>
</tr>
<tr>
<td>Group discussion (3 questions)</td>
<td>3 points</td>
</tr>
<tr>
<td>Goal-setting (7 steps)</td>
<td>7 points</td>
</tr>
<tr>
<td>Problem-solving (8 steps)</td>
<td>8 points</td>
</tr>
<tr>
<td>Relaxation training exercise</td>
<td>1 point</td>
</tr>
<tr>
<td><strong>Total Engagement Module 1</strong></td>
<td>20 points</td>
</tr>
<tr>
<td><strong>Module 2 (30 pages)</strong></td>
<td></td>
</tr>
<tr>
<td>Homework (3 questions)</td>
<td>3 points</td>
</tr>
<tr>
<td>Defining memory and impact (2 questions)</td>
<td>2 points</td>
</tr>
<tr>
<td>Group discussion (4 questions)</td>
<td>4 points</td>
</tr>
<tr>
<td>Strategies and application (11 questions)</td>
<td>11 points</td>
</tr>
<tr>
<td><strong>Total Engagement Module 2</strong></td>
<td>20 points</td>
</tr>
<tr>
<td><strong>Module 3 (24 pages)</strong></td>
<td></td>
</tr>
<tr>
<td>Homework (2 questions)</td>
<td>2 points</td>
</tr>
<tr>
<td>Attention exercise and feedback (4 questions)</td>
<td>4 points</td>
</tr>
<tr>
<td>Group Discussion (6 questions)</td>
<td>6 points</td>
</tr>
<tr>
<td>Applying strategies (7 questions)</td>
<td>7 points</td>
</tr>
<tr>
<td><strong>Total Engagement Module 3</strong></td>
<td>19 points</td>
</tr>
<tr>
<td><strong>Module 4 (27 pages)</strong></td>
<td></td>
</tr>
<tr>
<td>Homework (3 questions)</td>
<td>3 points</td>
</tr>
<tr>
<td>Emotions and fatigue (6 questions)</td>
<td>6 points</td>
</tr>
<tr>
<td>Group discussion (2 questions)</td>
<td>2 points</td>
</tr>
<tr>
<td>Self-care activity (6 questions)</td>
<td>6 points</td>
</tr>
<tr>
<td><strong>Total Engagement Module 4</strong></td>
<td>17 points</td>
</tr>
<tr>
<td><strong>Total number of possible engagement points</strong></td>
<td>76 points</td>
</tr>
</tbody>
</table>
Interaction with Facilitator

The number of emails received from the program facilitator (postgraduate provisionally registered psychologist) after consenting to participate was summed as an additional measure of engagement during the intervention and assessment phases. A minimum of seven emails was required to send links for pre- and post-assessments and each of the four individual modules. Emails were grouped into reminder, follow-up, CBT feedback, completion, technical, and other emails.

Procedure

Participants were recruited from around Australia through a university broadcast email, Breast Cancer Network Australia (BCNA), and the volunteer section of the employment website Indeed.com.au. Cancer participants in the pilot study were all assigned to the intervention group and non-cancer community adults were randomly allocated using a random number generator to either the intervention or waitlist control group. Participants with a cancer history in the main RCT were randomly allocated to intervention or waitlist. After providing written consent via email, participants were emailed links to complete the baseline (T1) assessment. Online assessments were completed using WebNeuro online test battery [28] and Qualtrics software (2013; Qualtrics, Provo, UT, USA). When both components of the T1 assessment were complete, participants were emailed a link with a username and password to access the first module of the program. They received sequential modules weekly on the day they completed the first module, allowing seven days to implement homework strategies. Participants were not sent the next module until the previous module was complete, therefore the sequencing “reset” to seven days from when the previous module was completed if participants did not complete the modules on time. The recommended completion time of the intervention was 21 days after the completion of module 1.
Reminder emails were sent on average five days after the modules or assessment materials were sent if they had not been completed. Follow-up emails were sent if participants completed only one of the assessment components or discontinued during the module. Up to three reminder emails or follow-up emails were sent before the participant was contacted via telephone to discuss their continued participation. During the main RCT, participants in the intervention group received individualised feedback on the goal-setting activity from module 1, the implementation of a new memory strategy from module 2, or in most cases, both. Most participants received completion emails after finishing the post-intervention assessment (T2), which advised the participant they would receive another email in 3 months for the final (T3) assessment, and after finishing the T3 assessment notifying them their participation in the study was finished.

**Statistical Analyses**

Analyses of variance (ANOVAs) and post hoc comparisons were conducted to compare group statistics on engagement variables, module activities, and facilitator interaction. ANOVA and $\chi^2$ tests were used for completer analyses to compare groups on baseline characteristics. Independent groups $t$-tests were used to compare the two cancer groups on baseline medical characteristics related to their cancer treatment. Statistical significance was determined by $\alpha \leq .05$ for all analyses.

**Results**

At baseline the RCT cancer group was significantly older than the pilot cancer group ($p=.014$) and the pilot non-cancer group ($p=.041$), which is presented in Table 6.2. Both cancer groups had significantly more females than the pilot non-cancer group ($p=.003$). Amongst the cancer groups, the RCT cancer group had a significantly higher percentage of breast cancer participants ($p<.001$), a higher rate of participants who received surgery as part of their treatment ($p=.018$), received hormone therapy
and had finished their primary treatment significantly \((p=.011)\) fewer months ago on average \((M=40.4, SD=31.9)\) than the pilot cancer group \((M=52.3, SD=46.8)\).

### Table 6.2

**Participant demographic data and medical characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Pilot Cancer ((n=12))</th>
<th>Pilot Non-Cancer ((n=16))</th>
<th>RCT Cancer ((n=32))</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>45.4 (10.3)(^a)</td>
<td>47.6 (10.0)(^a)</td>
<td>55.1 (9.2)(^b)</td>
<td>.005</td>
</tr>
<tr>
<td>Mean years of education (SD)</td>
<td>15.7 (2.6)</td>
<td>14.9 (3.0)</td>
<td>15.3 (2.6)</td>
<td>.731</td>
</tr>
<tr>
<td>Female (%)</td>
<td>100.0(^a)</td>
<td>75.0(^b)</td>
<td>100.0(^a)</td>
<td>.003</td>
</tr>
<tr>
<td>Born in Australia (%)</td>
<td>58.3</td>
<td>68.8</td>
<td>81.2</td>
<td>.276</td>
</tr>
<tr>
<td>First language English (%)</td>
<td>91.7</td>
<td>87.5</td>
<td>93.8</td>
<td>.761</td>
</tr>
<tr>
<td>Living with partner (%)</td>
<td>58.3</td>
<td>62.5</td>
<td>65.6</td>
<td>.902</td>
</tr>
<tr>
<td><strong>Medical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer (%)</td>
<td>50.0</td>
<td>-</td>
<td>96.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Surgery (%)</td>
<td>83.3</td>
<td>-</td>
<td>100.0</td>
<td>.018</td>
</tr>
<tr>
<td>Chemotherapy (%)</td>
<td>100</td>
<td>-</td>
<td>87.5</td>
<td>.199</td>
</tr>
<tr>
<td>Radiotherapy (%)</td>
<td>58.3</td>
<td>-</td>
<td>68.6</td>
<td>.516</td>
</tr>
<tr>
<td>Hormone therapy (%)</td>
<td>33.3</td>
<td>-</td>
<td>84.4</td>
<td>.001</td>
</tr>
<tr>
<td>Time since treatment (months)</td>
<td>52.3 (46.8)</td>
<td>-</td>
<td>40.4 (31.9)</td>
<td>.011</td>
</tr>
</tbody>
</table>

*Note. Superscript indicates statistical difference from post hoc comparisons whereby groups with the same superscript are not significantly different from each other.*

### Intervention Completion

The pilot non-cancer group had a higher attrition rate (24%) compared to the pilot cancer group (8%) and the RCT cancer group (16%). Non-completers who withdrew from the study had a longer average time since completion of primary treatment \((M=85.7, SD=57.3)\) than intervention completers \((M=43.6, SD=36.4)\), a difference that was significant \(F(1, 49)=6.11, p=.017\). The mean time from completion of module 1 to the completion of module 4 was 29.5 \((SD=10.6)\) days \((median=25.5; range=16-57)\) and was not significant between groups, \(F(2, 59)=0.54, p=.587\).
Module Engagement

There was a significant group difference on total engagement scores, $F(2, 59) = 11.41, p=<.001$ where the pilot non-cancer group participated in the modules significantly less than the cancer groups (Table 6.3). A significant group difference on participation in overall discussion activities was found, $F(2, 59)=11.41, p<.001$, where the pilot non-cancer group participated significantly less in discussion activities than both cancer groups. The three groups did not differ significantly on their reported weekly homework practice, $F(2, 59)=0.99, p=.378$. Significant group differences were found on the problem-solving activity, $F(2, 59)=3.69, p=.031$, the memory strategies activity, $F(2, 59)=4.41, p=.017$, and on the emotions/fatigue activity, $F(2, 59)=16.58, p<.001$.

Interaction with Facilitator

The groups did not differ significantly on the total number of emails received from the program facilitator during participation in the study ($M=20.7, SD=4.4$). These results are presented in Table 6.4. Significant group differences were found on the number of reminder emails, $F(2, 59)=3.47, p=.038$, follow-up emails, $F(2, 59)=5.30, p=.008$, and CBT feedback emails sent to participants, $F(2, 59)=111.9, p<.001$. 

147
Table 6.3

Module engagement for intervention participants

<table>
<thead>
<tr>
<th></th>
<th>Pilot Cancer (n = 12)</th>
<th>Pilot Non-Cancer (n = 16)</th>
<th>RCT Cancer (n = 32)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) Intervention Completion (days)</td>
<td>30.1 (13.2)</td>
<td>31.6 (10.5)</td>
<td>28.3 (9.8)</td>
<td>0.54</td>
<td>.587</td>
</tr>
<tr>
<td>Module 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Define cognition</td>
<td>1.00 (0.00)</td>
<td>1.00 (0.00)</td>
<td>1.00 (0.00)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Discussion</td>
<td>1.75 (1.42)</td>
<td>0.69 (1.08)</td>
<td>1.28 (1.37)</td>
<td>2.33</td>
</tr>
<tr>
<td></td>
<td>Goal-setting</td>
<td>7.00 (0.00)</td>
<td>6.75 (0.45)</td>
<td>6.94 (0.25)</td>
<td>3.07</td>
</tr>
<tr>
<td></td>
<td>Problem-solving</td>
<td>7.75 (0.45)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.94 (2.84)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.25 (1.65)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>3.69</td>
</tr>
<tr>
<td></td>
<td>Relaxation</td>
<td>1.00 (0.00)</td>
<td>0.94 (0.25)</td>
<td>1.00 (0.00)</td>
<td>1.39</td>
</tr>
<tr>
<td></td>
<td>Engagement</td>
<td>18.5 (1.7)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.3 (3.6)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.5 (2.4)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.49</td>
</tr>
<tr>
<td>Module 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Homework</td>
<td>2.58 (0.69)</td>
<td>2.69 (0.60)</td>
<td>2.56 (0.76)</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>Define memory</td>
<td>2.00 (0.00)</td>
<td>1.94 (0.25)</td>
<td>2.00 (0.00)</td>
<td>1.39</td>
</tr>
<tr>
<td></td>
<td>Discussion</td>
<td>2.42 (1.56)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.44 (1.09)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.03 (1.69)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.49</td>
</tr>
<tr>
<td></td>
<td>Strategies</td>
<td>11.0 (0.0)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.8 (0.5)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>10.5 (0.6)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.41</td>
</tr>
<tr>
<td></td>
<td>Engagement</td>
<td>18.0 (1.7)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.9 (1.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>17.1 (2.3)&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>4.43</td>
</tr>
<tr>
<td>Module 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Homework</td>
<td>1.92 (0.29)</td>
<td>1.88 (0.50)</td>
<td>1.78 (0.42)</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>Attention exercise</td>
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<td>4.00 (0.00)</td>
<td>3.94 (0.25)</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>Discussion</td>
<td>5.00 (0.74)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.50 (1.55)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.38 (1.04)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19.82</td>
</tr>
<tr>
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<td>Strategies</td>
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<td>6.72 (0.52)</td>
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</tr>
<tr>
<td></td>
<td>Engagement</td>
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<td>14.9 (1.8)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>16.8 (1.3)&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Module 4</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Homework</td>
<td>2.75 (0.45)</td>
<td>2.31 (0.95)</td>
<td>2.25 (0.84)</td>
<td>1.70</td>
</tr>
<tr>
<td></td>
<td>Emotions/fatigue</td>
<td>6.00 (0.00)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.81 (1.38)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.00 (0.00)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16.58</td>
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<tr>
<td></td>
<td>Discussion</td>
<td>0.75 (0.97)</td>
<td>0.25 (0.58)</td>
<td>0.84 (0.95)</td>
<td>2.53</td>
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<td>Self-care</td>
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<td>5.88 (0.34)</td>
<td>5.91 (0.30)</td>
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</tr>
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<td>Engagement</td>
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<td>13.3 (2.1)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>15.0 (1.5)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8.04</td>
</tr>
<tr>
<td></td>
<td>Total engagement</td>
<td>69.8 (3.8)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>59.4 (6.4)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>66.4 (6.2)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.40</td>
</tr>
<tr>
<td></td>
<td>(maximum of 76 points)</td>
<td>92%</td>
<td>78%</td>
<td>87%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total discussion</td>
<td>9.92 (3.26)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.88 (3.01)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8.53 (4.14)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>(maximum of 15 points)</td>
<td>66%</td>
<td>26%</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total homework</td>
<td>7.25 (1.06)</td>
<td>6.88 (1.50)</td>
<td>6.59 (1.46)</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>(maximum of 8 points)</td>
<td>91%</td>
<td>86%</td>
<td>82%</td>
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</table>

Note. Superscript indicates statistical difference from post hoc comparisons whereby groups with the same superscript are not significantly different from each other.
Table 6.4

*Email contact with facilitator during participation*

<table>
<thead>
<tr>
<th></th>
<th>Pilot Cancer (n = 12)</th>
<th>Pilot Non-Cancer (n = 16)</th>
<th>RCT Cancer (n = 32)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reminder emails</td>
<td>2.92 (2.64)</td>
<td>5.31 (3.14)</td>
<td>3.06 (3.02)</td>
<td>3.47</td>
<td>.038</td>
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<td>Follow-up emails</td>
<td>1.33 (1.15)</td>
<td>2.06 (1.24)</td>
<td>0.88 (1.18)</td>
<td>5.30</td>
<td>.008</td>
</tr>
<tr>
<td>CBT feedback emails</td>
<td>0.08 (0.29)</td>
<td>0.06 (0.25)</td>
<td>1.72 (0.52)</td>
<td>111.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Completion emails</td>
<td>1.75 (0.45)</td>
<td>1.63 (0.72)</td>
<td>2.06 (0.62)</td>
<td>3.01</td>
<td>.057</td>
</tr>
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<td>Technical emails</td>
<td>0.25 (0.45)</td>
<td>0.56 (0.73)</td>
<td>0.84 (1.37)</td>
<td>1.35</td>
<td>.267</td>
</tr>
<tr>
<td>Total emails</td>
<td>18.5 (4.08)</td>
<td>22.4 (3.12)</td>
<td>20.5 (4.69)</td>
<td>3.02</td>
<td>.056</td>
</tr>
</tbody>
</table>

*Note.* Superscript indicates statistical difference from post hoc comparisons whereby groups with the same superscript are not significantly different from each other. All participants received 7 routine emails (3 assessments and 4 modules).

**Correlates of Engagement**

Three outcome variables in the main RCT differentiated between intervention and waitlist groups: a self-reported measure of prospective memory called instrumental activities of daily living (IADL), perceived cognitive impairment (PCI), and executive functioning (EF). Pearson correlations between total engagement scores and change scores on these measures showed that higher levels of engagement were associated with reduced prospective memory problems on IADL, \( r(60) = -.31, p=.018 \), indicating a moderate association [29]. Engagement did not correlate with change scores on PCI or EF.

**Discussion**

The purpose of this study was to address methodological concerns associated with current measures of assessing participant engagement in web-based interventions.
Researchers have highlighted the need to implement more rigorous approaches to designing online interventions in order to increase the quality and quantity of engagement [3]. Current methods typically reported in the literature provide some measurement of participant engagement, but do not adequately ensure treatment fidelity through measurement of treatment delivery, receipt of treatment, and enactment of treatment skills. Low levels of engagement and high rates of attrition at follow-up are common in online interventions, which is a problem for evaluating intervention effectiveness [30]. We compared three intervention groups from our pilot study and main RCT, and quantified the level of participant engagement by measuring individual participation in each of the activities from four training modules.

Each module of the program contained several pages where participants could voluntarily type in responses to questions in the modules. Across all four modules, there were a total of 76 fields allowing for participants to type in their personal responses to activity and discussion questions. Overall participant engagement in the program was high with the pilot cancer group responding to 92% of the activity questions, the cancer RCT group responding to 87% of questions, and the pilot non-cancer group responding to 78% of activity questions. As mentioned previously, engagement data may be an important mechanism to explain treatment effects in web-based interventions and improve outcomes [4]. Total engagement scores demonstrated consistency in the differences observed between groups where higher attrition was associated with lower engagement and lower attrition rates with higher engagement levels. Engagement was also associated with reduced self-reported prospective memory failures on the IADL. These results provide preliminary evidence to support the validity of this method for measuring engagement.

The non-cancer group's overall engagement in the program was significantly lower than that of the two cancer groups. This was partially explained by Modules 2, 3...
and 4 containing discussion questions pertaining directly to their cancer experience (e.g., “Since going through the experience of cancer and cancer treatment, have you noticed any changes in your memory?”). Expectedly, the non-cancer group responded to significantly fewer discussion questions in Module 2 ($p=.001$) and Module 3 ($p<.001$) than the cancer groups. Similarly, the emotions activity in Module 4 contained questions associated with the cancer experience, which likely resulted in a significantly lower response rate from non-cancer participants on this activity ($p<.001$). When discussion questions associated with cancer and treatment were excluded from analysis, the non-cancer group did not differ significantly on total engagement scores from the RCT cancer group ($p=.131$), and groups did not differ on remaining items in Modules 2 through 4. However, with cancer-specific items excluded, the non-cancer group's overall engagement remained significantly lower than that of the pilot cancer group ($p=.009$) and Module 1 group participation differences remained.

Several implementation elements have been associated with higher participant engagement in web-based interventions. Researchers have reported that scribing personal messages and feedback to participants [31, 32] and providing professional support [32, 33] are associated with increased engagement. A theoretical model called “Supportive Accountability” suggests that users of individual Internet interventions are more likely to adhere to a program if they are accountable to another person [13, 34]. Participants in the eReCog intervention groups received on average between 18.5 and 22.4 email correspondences from the facilitator of the program, including feedback and professional support on module activities, reminder emails to complete necessary tasks, and follow-up emails if tasks were not completed in full. These email exchanges between the facilitator and participant likely contributed to their high level of engagement in the program and made them feel like a valued participant in the
Another element associated with higher engagement is the facilitation of social networking opportunities for participants to share their experiences with one another [33, 35]. Participants in eReCog were able to read and respond to other participants’ responses in the discussion sections of the modules, which may have also been a feature of the program design that contributed to the high participant engagement.

The eReCog program was developed to ensure that the modules were delivered in a standardised way to all participants. After logging into the modules, participants were required to navigate continuously through each page of the module until reaching the end page. Facilitators could monitor their progress each week and participants were not emailed the next module until the previous module was completed. The average completion time for the three intervention groups was 29.5 ($SD=10.6$) days, which meant that participants on average completed one module every 9.83 days. The face-to-face ReCog program was delivered every 7 days [23, 24], meaning the web-based version took slightly longer for participants to complete. Nonetheless, the delivery process ensured that all modules were completed over the course of the program, which provides evidence that treatment fidelity was upheld in the delivery and receipt of the intervention program [21].

Another notable feature to the design of the eReCog intervention is the follow-up questions pertaining to homework tasks at the beginning of Modules 2, 3 and 4. As noted previously, the enactment of learnt skills is an important concept to measure as part of assessing treatment fidelity [21]. Participants in this research self-reported their skills practise each week at the start of the next module. Across the entire program the pilot cancer group reported practising newly learnt skills at a rate of 91%, the pilot non-cancer group 86%, and the RCT cancer group 82%. The most common reasons for not completing homework tasks were being too busy or forgetting to practise.
Implementing a design method that measures the enactment of skills is critical in psychosocial interventions because skills practise reinforces knowledge or behaviours related to the outcome of interest [4], thereby enhancing the potential efficacy of the intervention program.

As previously mentioned, high attrition is a common challenge encountered in web-based interventions. Rates approaching nearly 40% have been reported in some online studies with cancer survivors [19, 20]. The attrition rates for the research conducted with the eReCog program were found to be acceptable, with the highest drop-out occurring in the non-cancer group (24%), and lower rates were observed in the RCT cancer group (16%) and pilot cancer group (8%). The higher attrition in the non-cancer group was expected since the intervention was designed for cancer survivors and has elements specifically relating to cancer and its treatment. Attrition in web-based eReCog was slightly higher than the in-person ReCog randomised controlled trial, which had an attrition rate of 7% [23]. However, these results are not uncommon as attrition is often higher in online interventions compared to in-person programs.

This research is not without limitations. The LessonLAMS software used to develop the program modules did not allow researchers to track some of the typical methods for measuring engagement such as number of logins, time spent on individual pages, or time taken to complete each module. In addition, the researchers had to manually extract the data of participants’ posts from each page of the modules in order for the data to be analysed qualitatively. Another limitation to the study was that occasional telephone contact occurred between facilitator and participants, however these were not recorded or included in the analysis. Participants’ motivation was not assessed directly, which would have been a helpful component in interpreting engagement and attrition data.
Conclusions

The science of participant engagement in web-based interventions is an area of research in its infancy. Researchers have identified a number of methods of reporting engagement, but the quality of these methods and the quantity of engagement remain relatively low. Future research ought to focus on the design process of developing online interventions that incorporate the fundamental objectives of psychological and behavioural interventions: ensure delivery and receipt of the intervention, and skills practise. Low engagement levels are a potential indication that participants are not receiving the intended dose of the intervention, which can reduce overall effectiveness. By designing web-based programs that maximise engagement and measure it in meaningful ways, researchers can augment treatment fidelity and likely increase the effectiveness of online intervention program.
References


155


CHAPTER VII: MEDIATION AND SUPPLEMENTARY ANALYSES

The previous three results chapters IV, V, and VI detailed results from Study One (pilot study) and Study Two (RCT) on the evaluation of the primary outcome measure PCI, and secondary outcomes of other subjective cognitive measures, objective cognitive functioning and psychosocial variables. The results also examined participant engagement in the eReCog intervention. At the time of submission of this thesis, these three sets of results are under consideration for publication. This chapter presents results from this research project that were not included in the manuscripts submitted for publication.

As discussed in the literature review Chapter II of this thesis, another aim of this research was to evaluate the mediating effect of the variables of autonomy, competence, and relatedness within the Self-Determination Theory (SDT) framework. SDT is a broad theory of human motivation, which purports that motivation is influenced by the fulfilment of the psychological needs of autonomy, competence, and relatedness within an individual’s social network and that people engage in behaviours that will lead to desired outcomes and goals (Deci & Ryan, 2000). The next section discusses the results from the mediation analyses conducted for Study One and Two.

Additional analyses included in this chapter are the results of between-group comparisons on functional and symptom scales of the EORTC QLQ-C30; Pearson’s correlations calculated to evaluate the association between the primary outcome PCI and other outcome variables; a comparison of PCI scores from this research project to other cognitive rehabilitation interventions for cancer survivors; and Overall Cognitive Function Index (OCFI) scores derived from the WebNeuro assessment. Results are presented first followed by a discussion section at the end of the chapter.
Mediation Analyses

To test for mediation, Baron and Kenny (1986) recommended that a series of regression models should be estimated rather than ANOVA because it provides a better test of a mediational hypothesis. If there are not more than two levels of a variable, however, the results from ANOVA and linear regression are the same. It is recommended to calculate the following three regression equations: (a) regressing the mediating variable on the independent variable, (b) regressing the dependent variable on the independent variable, and (c) regressing the dependent variable on the mediating variable whilst holding the independent variable constant. Figure 7.1 presents a pictorial representation of the target variables from this study and the outlined pathways such that regression equation 1 is represented as Path a’, equation 2 is represented as Path c’, and equation 3 is represented as Path b’.

Figure 7.1 Path diagram showing direct and indirect effects expected in a mediating relationship. Based on Baron and Kenny (1986).
To test for mediation, the first step was to evaluate the association between the independent variable (i.e., group membership) and the mediating variables (i.e., path a’). Both ANOVAs and linear regression were conducted for Study One and only linear regression equations for Study Two since there were only two levels of the independent variable.

**Study One**

As reported in Chapter IV of this thesis, Study One involved three participant groups: cancer intervention group, non-cancer intervention group, and non-cancer control group. Using data from Study One, mediation analyses were conducted for the potential mediating effect of the variables of autonomy, competence, and relatedness. Means and standard deviations for the potential mediators are shown in Appendix H.

**Autonomy.** For the variable autonomy, an ANOVA was first performed to analyse the effect of group membership on change scores in autonomy from baseline (T1) to post-intervention (T2) because this entire pathway must be significant in order for mediation to occur. These results were not significant, $F(2, 42) = 0.63, p = .540$. To examine whether participation in the intervention program increased autonomy from T1 to T2, linear regression was performed using a dummy coding combining intervention groups, which was compared to change scores in the waitlist group. The results were not significant, $F(1, 42) = 0.53, p = .473$. Comparing the cancer group to the non-cancer groups on autonomy change scores was also not significant, $F(1, 42) = 1.22, p = .277$. Analysis of within-group effects demonstrated no significant changes from T1 to T2 on autonomy in the cancer treatment group, $F(1, 11) = 0.79, p = .394$; the non-cancer treatment group, $F(1, 15) = 0.37, p = .551$; or the non-cancer waitlist group, $F(1, 14) = 0.77, p = .394$. This lack of association between the independent variable and mediation variable did not provide evidence of a mediating effect.
**Competence.** The second variable analysed was competence. An ANOVA assessing the relationship between group and change scores from T1 to T2 on the measure of competence was conducted. The results were not significant, $F(2, 42) = 0.40, p = .676$. A linear regression model was conducted using dummy coding to combine intervention groups and compare change scores on competence to the waitlist group; the results were not significant, $F(1, 42) = 0.27, p = .607$. The association between the cancer group and non-cancer groups on changes in feelings of competence was also not significant, $F(1, 42) = 0.79, p = .378$. Within group analyses found no significant differences in competence scores from T1 to T2 in the cancer group, $F(1, 11) = 0.56, p = .470$; the non-cancer treatment group, $F(1, 15) = 0.02, p = .879$; or the waitlist control group, $F(1, 14) = 0.15, p = .700$.

**Relatedness.** An ANOVA was performed to evaluate the relationship between group and change scores on the relatedness variable from T1 to T2. This association was not found to be significant, $F(2, 42) = 0.50, p = .611$. Linear regression was performed with dummy coding to compare the intervention groups to the waitlist group on changes in feelings of relatedness; the results of the model were not significant, $F(1, 42) = 0.61, p = .437$. Comparison of the cancer group to the non-cancer groups was also not significant, $F(1, 42) = 0.85, p = .363$. Significant improvements on changes in feelings of relatedness were not observed from T1 to T2 in the cancer group, $F(1, 11) = 1.06, p = .325$; the non-cancer treatment group, $F(1, 15) = 0.04, p = .854$; or the non-cancer waitlist group, $F(1, 14) = 0.13, p = .726$.

**Study Two**

As described in Chapter V of this thesis, Study Two was an RCT that involved a cancer treatment group and a cancer waitlist control group. The data from this study were analysed to evaluate for mediation effects. Only linear regression data are presented since the results from ANOVA are the same. The first step in the process
was similar to Study One and involved investigating the association between group membership and each of the proposed mediating variables as described below. Means and standard deviations for mediating variables are presented in Appendix I.

**Autonomy.** Linear regression was performed to evaluate the relationship between treatment group and change scores on the autonomy measure from T1 to T2. No significant association between group and autonomy change scores was found, $F(1, 64) = 2.11, p = .151$, indicating that a mediation effect did not occur. Within-group analyses found the intervention group reported increased autonomy at T2, $F(1, 31) = 6.00, p = .020$, whereas the waitlist control group did not.

**Competence.** The results of the linear regression model found no significant association between group membership and change scores on the competence measure, $F(1, 64) = 1.34, p = .252$. Within group analyses demonstrated no significant changes in either group from T1 to T2.

**Relatedness.** Linear regression was conducted to examine the association between group and change scores on relatedness and found no significant association between these variables, $F(1, 64) = 1.40, p = .240$. The waitlist group reported significantly reduced feelings of relatedness from T1 to T2, $F(1,32) = 4.31, p = .046$, whereas the treatment group demonstrated no significant change.

**Quality of Life**

The EORTC QLQ-C30 was used to evaluate QoL on several functional and symptom domains in both studies of this research project as outlined in Chapter II (p. 66). The cognitive function scale was reported in results Chapters IV and V for both studies, however, most other subscales were not included in the manuscripts due to word limitations for journal articles. Results from four other functional scales, four symptom scales, and a measure of global health status are presented in this chapter.
Mixed ANOVAs were conducted to examine interaction and main effects. Baseline differences were calculated with one-way ANOVAs.

**Study One**

Group means and standard deviations for the three assessment points are presented in a table in Appendix H. At baseline, the cancer group reported significantly poorer social functioning than the non-cancer intervention group, $F(1, 26) = 4.95, p = .035$. Compared to the non-cancer waitlist group, the cancer group reported significantly poorer social functioning, $F(1, 25) = 11.53, p = .002$; poorer role functioning, $F(1, 25) = 4.41, p = .012$; worse physical functioning, $F(1, 25) = 6.30, p = .019$; more symptoms of pain, $F(1, 25) = 4.44, p = .045$; more symptoms of fatigue, $F(1, 25) = 5.40, p = .029$; and more financial difficulties, $F(1, 25) = 15.30, p = .001$.

Interaction effects on the subscales were analysed with Group (3) x Time (3) ANOVAs. No significant interaction effects were found on the following subscales: global health status, $F(4, 80) = 0.55, p = .702$; physical functioning, $F(3, 70) = 0.37, p = .832$; role functioning, $F(4, 74) = 1.49, p = .214$; emotional functioning, $F(4, 80) = 0.33, p = .856$; social functioning, $F(4, 80) = 0.98, p = .423$; symptoms of fatigue, $F(4, 75) = 0.79, p = .531$; symptoms of pain, $F(4, 80) = 0.30, p = .875$; and symptoms of insomnia, $F(4, 80) = 0.53, p = .717$. A significant interaction effect was found on the symptoms of financial difficulties subscale, $F(4, 80) = 4.95, p = .001$. The interaction resulted from the cancer group reporting a significant reduction in financial difficulties from T1 to T2, $F(1, 11), 6.06, p = .032$, whereas the other groups did not report any significant changes on this subscale.

A main effect for group was found on the social functioning scale, $F(2, 40) = 5.06, p = .011$. The cancer group reported poorer social functioning than the non-cancer waitlist group ($p = .009$), but not the non-cancer treatment group ($p = .182$). A significant main effect for group was also noted on symptoms of fatigue, $F(2, 40) =$
5.78, \( p = .006 \). This main effect occurred because the cancer group reported significantly more symptoms of fatigue than the non-cancer waitlist group (\( p = .005 \)), but not the non-cancer treatment group (\( p = .276 \)). There was a main effect for group on the symptoms of financial difficulties scale, \( F(2, 40) = 6.18, p = .005 \), which occurred because the cancer group reported more financial difficulties than the non-cancer waitlist group (\( p = .003 \)), but not the non-cancer treatment group (\( p = .256 \)). A significant main effect for time was observed on the symptoms of pain scale, \( F(2, 80) = 3.54, p = .034 \) because participants reported fewer symptoms of pain at T3 compared to T1.

**Study Two**

In the RCT study, the intervention group did not differ from the waitlist control group on any of the functional or symptom scales of the EORTC QLQ-C30 at baseline assessment. Means and standard deviations for the three assessments are presented in Appendix I. There were no significant interaction effects on global health status, \( F(2, 126) = 2.11, p = .125 \); physical functioning, \( F(2, 126) = 0.13, p = .875 \); role functioning, \( F(2, 126) = 0.17, p = .842 \); emotional functioning, \( F(2, 126) = 0.04, p = .963 \); social functioning, \( F(1, 126) = 0.26, p = .770 \); symptoms of fatigue, \( F(2, 113) = 0.41, p = .639 \); symptoms of pain, \( F(2, 126) = 0.66, p = .518 \); symptoms of insomnia, \( F(2, 126) = 1.21, p = .301 \); or symptoms of financial difficulties, \( F(2, 126) = 0.60, p = .550 \).

There was a significant main effect for group on the symptoms of pain scale, \( F(1, 63) = 4.52, p = .037 \), which occurred because the intervention group reported fewer symptoms of pain than the waitlist group. A significant main effect for time was reported on the financial difficulties scale, \( F(2, 126) = 4.68, p = .011 \), with participants reporting fewer financial difficulties over time.
Within group comparisons found a significant reduction in fatigue symptoms in the intervention group from T1 to T2, \( F(1, 31) = 4.33, p = .046 \), and significantly poorer global health status in the waitlist group from T1 to T3, \( F(1, 32) = 4.27, p = .047 \). There were no other significant within group effects on any of the other EORTC-QLQ-C30 scales.

**Perceived Cognitive Impairment Correlations**

As described in Chapter II of this thesis (p. 23), subjective cognitive functioning typically demonstrates stronger correlations with negative affect and QoL than with performance on standardised neuropsychological measures. To evaluate this relationship, Pearson’s correlations were computed to examine whether change scores on PCI from T1 to T2 were associated with change scores on other measures of subjective cognitive functioning (i.e., IADL, BADL, and impact on QoL); on psychosocial variables (i.e., psychological distress and perceptions of illness related to cognitive difficulties); and on objective measures of cognitive functioning (i.e., total WebNeuro Z-score and EF domain Z-score). The variables selected were those that demonstrated significant changes or trends in Study One and/or Two. The Pearson’s correlation coefficients are presented in Table 7.1.

**Study One**

In Study One, correlation analyses found that improved PCI was associated with improved impact on QoL; a reduction in PM failures on the IADL; reduced psychological distress; and improved EF. PCI was not correlated with a reduction in the threat of illness associated with cognitive problems; a reduction in PM failures on the BADL; or total WebNeuro scores (see Table 7.1).
Table 7.1

Correlations between PCI and other outcome variables

<table>
<thead>
<tr>
<th></th>
<th>Study One</th>
<th>Study Two</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>p</td>
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<tr>
<td>Impact on QoL</td>
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<td>IADL</td>
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<td>.016</td>
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<td>.037</td>
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<tr>
<td>Illness Perceptions</td>
<td>-.22</td>
<td>.166</td>
</tr>
<tr>
<td>WebNeuro Total</td>
<td>.13</td>
<td>.424</td>
</tr>
<tr>
<td>Executive Functioning</td>
<td>.34</td>
<td>.026</td>
</tr>
</tbody>
</table>

Study Two

A slightly different pattern of correlations was observed in Study Two. Improved PCI from T1 to T2 was correlated with improved impact on QoL, and a reduction in PM failures on the IADL. The PCI was not correlated with reduced PM failures on the BADL; reduced psychological distress; a reduced threat of illness related to cognitive difficulties; improved EF; or total WebNeuro scores (see Table 7.1).

Perceived Cognitive Impairment Subscale Comparisons

PCI was the primary outcome variable in this research project and is also a frequently used subscale measure in other studies of cognitive remediation for cancer survivors. It is therefore possible to compare PCI and other characteristics (e.g., age and years of education) between studies to examine similarities and differences among study participant characteristics and outcome measures. As discussed in Chapter III (p. 64), alternate scoring options are available for two subscales of the FACT-Cog-3 (i.e., PCI and PCA). The developers of the measure (i.e., FACIT) recommend in the scoring
guidelines that the PCI be used as the primary subscale measure, and suggest the use of the PCA as well. These two subscales, however, have two different scoring options available. The standard scoring method includes 18 items on the PCI scale, which produces a range from 0 to 72 on the scale. There are two additional items (i.e., CogMT1 and CogMT2) that can be included in the scoring if a measure of internal consistency and individual item-total score correlation coefficients indicate that these items fit with the scale, which is a recommended step since these items were added after the initial validation process. If researchers opt to include the two additional items, the range for the scale becomes 0 to 80. Similarly the PCA scale includes seven standard items with a scoring range from 0 to 28, but provides the option of including two additional items (i.e., PMT1 and PMT2) to create a scoring range from 0 to 36.

Given the two scoring options available for the PCI and PCA subscales, it is not always clear in published research which option was employed. Table 7.2 presents PCI scores from seven different CRT and CT studies that utilised the FACT-Cog-3 measure to assess subjective cognitive functioning, including the two studies from this research project. The standard scoring method was implemented in both Study One and Study Two, which meant the optional items were not included in the analyses. King et al. (2015) and Schuurs et al. (2013) used the extended scoring method and included the optional items in their analyses. Data from the researchers for these two studies were available to recalculate the results excluding the optional items, which are the data presented in Table 8.1. Personal communication from the authors of the study published by Bray et al. (2017) confirmed use of the standard scoring method, however, it is not clear whether the other studies presented in Table 7.2 used the standard scoring or extended scoring option and the data for the other studies are from publication materials (Cherrier et al., 2013; Ferguson et al., 2016).
The mean scores recorded at the bottom of Table 7.2 are weighted by sample size and include pooled standard deviations. Age and education variables for the study by Bray et al. (2017) were excluded from the mean scores because standard deviations were not reported to be included in the analysis. The grand mean scores should be interpreted with caution since there are two studies that potentially may have used the extended scoring version rather than the assumed standard scoring.

Table 7.2

FACT-Cog-3 PCI means (and SD) for CRT and CT interventions

<table>
<thead>
<tr>
<th>Authors</th>
<th>PCI Time 1</th>
<th>PCI Time 2</th>
<th>PCI Time 3</th>
<th>Age</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cherrier et al. (2013)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 12)</td>
<td>35.7 (6.3)</td>
<td>51.0 (5.7)</td>
<td>-</td>
<td>60.5 (2.3)</td>
<td>17.8 (0.5)</td>
</tr>
<tr>
<td>Waitlist control (n = 16)</td>
<td>37.7 (5.1)</td>
<td>42.9 (4.7)</td>
<td>-</td>
<td>57.3 (3.8)</td>
<td>16.5 (0.5)</td>
</tr>
<tr>
<td>Schuurs et al. (2013)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 10)</td>
<td>35.2 (15.3)</td>
<td>42.5 (14.6)</td>
<td>43.5 (14.4)</td>
<td>58.2 (11.8)</td>
<td>15.4 (3.2)</td>
</tr>
<tr>
<td>Cancer comparison (n = 8)</td>
<td>56.4 (14.2)</td>
<td>61.0 (10.4)</td>
<td>-</td>
<td>58.3 (8.6)</td>
<td>13.6 (3.4)</td>
</tr>
<tr>
<td>King et al. (2015)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 15)</td>
<td>30.8 (13.8)</td>
<td>42.1 (13.4)</td>
<td>45.4 (13.4)</td>
<td>50.4 (8.8)</td>
<td>15.8 (4.0)</td>
</tr>
<tr>
<td>Waitlist control (n = 12)</td>
<td>31.1 (14.1)</td>
<td>31.4 (15.3)</td>
<td>41.4 (15.2)</td>
<td>51.8 (9.4)</td>
<td>13.8 (3.5)</td>
</tr>
<tr>
<td>Non-cancer control (n = 16)</td>
<td>67.5 (5.2)</td>
<td>65.9 (7.6)</td>
<td>52.9 (17.0)</td>
<td>13.9 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Ferguson et al. (2016)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 22)</td>
<td>29.3 (12.8)</td>
<td>41.2 (14.5)</td>
<td>44.8 (14.2)</td>
<td>54.0 (12.8)</td>
<td>15.6 (2.9)</td>
</tr>
<tr>
<td>Supportive therapy (n = 13)</td>
<td>31.6 (11.1)</td>
<td>37.3 (15.6)</td>
<td>37.1 (15.3)</td>
<td>55.6 (11.4)</td>
<td>15.6 (2.7)</td>
</tr>
<tr>
<td>Bray et al. (2017)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 121)</td>
<td>38.6 (14.3)</td>
<td>-</td>
<td>-</td>
<td>52.0</td>
<td>14.0</td>
</tr>
<tr>
<td>Waitlist control (n = 121)</td>
<td>41.9 (15.1)</td>
<td>-</td>
<td>-</td>
<td>54.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Study One</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer intervention (n = 12)</td>
<td>33.8 (18.7)</td>
<td>42.3 (18.3)</td>
<td>42.8 (18.2)</td>
<td>45.4 (10.3)</td>
<td>16.1 (3.4)</td>
</tr>
<tr>
<td>Non-cancer intervention (n = 16)</td>
<td>50.6 (10.8)</td>
<td>53.8 (11.6)</td>
<td>53.8 (10.0)</td>
<td>47.6 (10.0)</td>
<td>16.1 (3.9)</td>
</tr>
<tr>
<td>Non-cancer control (n = 15)</td>
<td>57.3 (11.9)</td>
<td>60.3 (10.0)</td>
<td>60.1 (9.1)</td>
<td>45.9 (7.4)</td>
<td>17.2 (2.4)</td>
</tr>
<tr>
<td>Study Two</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention (n = 32)</td>
<td>41.6 (15.4)</td>
<td>44.1 (14.8)</td>
<td>50.5 (12.7)</td>
<td>55.1 (9.2)</td>
<td>15.3 (2.6)</td>
</tr>
<tr>
<td>Waitlist Control (n = 33)</td>
<td>42.5 (16.0)</td>
<td>46.2 (14.1)</td>
<td>48.2 (15.0)</td>
<td>56.9 (9.2)</td>
<td>15.1 (2.9)</td>
</tr>
</tbody>
</table>

Groups: Mean PCI | Mean PCI | Mean PCI | Mean Age | Mean Edu
Cancer intervention (k = 7) | 37.0 (14.3)| 43.6 (14.2)| 46.5 (14.2)| 54.0 (10.0)| 15.8 (2.9)
Cancer comparison (k = 6)  | 40.9 (14.4)| 43.4 (13.0)| 44.3 (15.1)| 56.2 (8.8)| 15.1 (2.7)
Non-cancer comparison (k = 2) | 62.6 (9.0)| 63.2 (8.8)| 60.1 (9.1)| 49.5 (13.3)| 15.5 (3.2)
Non-cancer intervention (k = 1) | 50.6 (10.8)| 53.8 (11.6)| 53.8 (10.0)| 47.6 (10.0)| 16.1 (3.9)

Note. Study by Von Ah et al. (2012) utilised the FACT-Cog-3, but reported a total score on the measure combining four subscales, therefore performance across time was not available for the PCI subscale. k = number of studies contributing to the pooled mean and standard deviation.
Overall Cognitive Function Index

In Chapter II it was noted that performance on objective neuropsychological measures varies amongst cancer survivors with some studies finding improvements on some cognitive domains following rehabilitation whilst others found no improvements. Based on the Z-scores obtained from participants’ WebNeuro performance, it was possible to calculate an OCFI for each participant, which was previously conducted with other neuropsychological measures (Wefel et al., 2004). The Z-scores for individual variables and cognitive domains for Study One are presented in Appendix J and for Study Two in Appendix K. Participants were considered to have impaired functioning (OCFI-I) if: (a) the participant had two or more Z-scores ≤ -1.5 SD on any of the seven cognitive domains, or (b) if the participant had only one cognitive domain meeting the first criterion, then that single domain Z-score had to be ≤ -2.0 SD. Participants who did not meet the aforementioned criteria were classified as not impaired (OCFI-NI). Rates of OCFI-I and descriptive statistics by group are presented in Table 7.3.
Table 7.3

Clinical impairment by group at three time points

<table>
<thead>
<tr>
<th>Groups at T1</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>Min to Max</th>
<th>OCFI-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot intervention cancer (n = 12)</td>
<td>-0.07 (0.44)</td>
<td>-0.35 to 0.21</td>
<td>-0.92 to 0.54</td>
<td>17%</td>
</tr>
<tr>
<td>Pilot intervention non-cancer (n = 16)</td>
<td>-0.11 (0.40)</td>
<td>-0.33 to 0.10</td>
<td>-1.23 to 0.24</td>
<td>13%</td>
</tr>
<tr>
<td>Pilot waitlist non-cancer (n = 15)</td>
<td>-0.17 (0.46)</td>
<td>-0.43 to 0.08</td>
<td>-1.07 to 0.49</td>
<td>27%</td>
</tr>
<tr>
<td>RCT intervention cancer (n = 32)</td>
<td>-0.16 (0.35)</td>
<td>-0.28 to -0.03</td>
<td>-0.99 to 0.45</td>
<td>16%</td>
</tr>
<tr>
<td>RCT waitlist cancer (n = 33)</td>
<td>-0.20 (0.52)</td>
<td>-0.38 to -0.02</td>
<td>-2.11 to 0.51</td>
<td>15%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Groups at T2</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>Min to Max</th>
<th>OCFI-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot intervention cancer (n = 12)</td>
<td>0.04 (0.43)</td>
<td>-0.24 to 0.31</td>
<td>-0.55 to 0.63</td>
<td>0%</td>
</tr>
<tr>
<td>Pilot intervention non-cancer (n = 16)</td>
<td>-0.16 (0.57)</td>
<td>-0.47 to 0.15</td>
<td>-1.84 to 0.47</td>
<td>19%</td>
</tr>
<tr>
<td>Pilot waitlist non-cancer (n = 15)</td>
<td>-0.24 (0.50)</td>
<td>-0.52 to 0.04</td>
<td>-1.25 to 0.55</td>
<td>27%</td>
</tr>
<tr>
<td>RCT intervention cancer (n = 32)</td>
<td>-0.06 (0.42)</td>
<td>-0.22 to 0.09</td>
<td>-1.15 to 0.61</td>
<td>13%</td>
</tr>
<tr>
<td>RCT waitlist cancer (n = 33)</td>
<td>-0.18 (0.53)</td>
<td>-0.37 to 0.01</td>
<td>-1.54 to 0.82</td>
<td>18%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Groups at T3</th>
<th>Mean (SD)</th>
<th>95% CI</th>
<th>Min to Max</th>
<th>OCFI-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot intervention cancer (n = 12)</td>
<td>-0.03 (0.50)</td>
<td>-0.35 to 0.29</td>
<td>-0.92 to 0.61</td>
<td>17%</td>
</tr>
<tr>
<td>Pilot intervention non-cancer (n = 16)</td>
<td>-0.26 (0.58)</td>
<td>-0.57 to 0.05</td>
<td>-1.69 to 0.58</td>
<td>25%</td>
</tr>
<tr>
<td>Pilot waitlist non-cancer (n = 15)</td>
<td>-0.26 (0.46)</td>
<td>-0.52 to -0.01</td>
<td>-1.33 to 0.56</td>
<td>13%</td>
</tr>
<tr>
<td>RCT intervention cancer (n = 32)</td>
<td>-0.13 (0.40)</td>
<td>-0.27 to 0.02</td>
<td>-0.95 to 0.53</td>
<td>16%</td>
</tr>
<tr>
<td>RCT waitlist cancer (n = 33)</td>
<td>-0.21 (0.54)</td>
<td>-0.41 to -0.02</td>
<td>-1.39 to 0.53</td>
<td>12%</td>
</tr>
</tbody>
</table>

**Discussion**

The results contained in this chapter describe analyses conducted to evaluate mediation with SDT variables, outcomes on the QoL measure, correlations between PCI and other outcome variables, comparisons between PCI scores in this study and other cognitive rehabilitation interventions, and OCFI scores obtained on the neuropsychological assessment measure.

Mediation analysis in this research project demonstrated that the variables autonomy, competence, and relatedness did not mediate the relationship between intervention effects and outcome measures. In Study One it was found that group membership was not correlated with any of the hypothesised mediating variables of...
autonomy, competence, or relatedness. It was expected that participants in the intervention groups would show increased feelings of autonomy, competence and relatedness post-intervention compared to the waitlist group; however, none of the three groups from the study demonstrated any significant changes in these variables from T1 to T2. A similar relationship between the mediation variables and group membership was observed in Study Two whereby group membership was not correlated with change scores on the variables autonomy, competence, or relatedness. The intervention group demonstrated an increase in feelings of autonomy at T2 and the waitlist group had worse feelings of relatedness at T2 compared to T1, however these changes were not related to a mediation effect. Further discussion regarding the implications of this study hypothesis is included in the Chapter VIII in the General Discussion.

The QoL measure did not produce any significant interaction effects in either study apart from financial difficulties in Study One, which resulted from the cancer group having more financial trouble than the non-cancer groups. This is likely due to medical costs and reduced capacity to work. Baseline differences between the cancer group and non-cancer waitlist group were significant on the majority of the functional and symptoms scales in Study One, which would be expected since the waitlist group did not have a history of cancer. Similar baseline performance would be expected in the non-cancer intervention group, however, a significant difference was found on only the social functioning scale. These results suggest that the non-cancer treatment group reported lower functioning and higher symptomatology than the other non-cancer group. Self-reported functioning can be influenced by a number of factors, such as current mood, attitudes, anxieties, expectations, memory, reporting biases, and situational demands (Simmonds, 2002). Participants’ awareness of their allocation to the cognitive rehabilitation intervention group may have influenced their perception of
their functional abilities in this situation, causing them to report more functional problems and symptoms at the time of assessment than they might otherwise report. Main effects for group on social functioning, symptoms of fatigue and financial difficulties were not surprising as they were indicative of the cancer group reporting more problems than the non-cancer groups. Interestingly, a main effect for time was observed on the pain subscale with participants reporting fewer symptoms of pain over time, although the intervention did not discuss pain associated with cancer.

In Study Two, no significant interaction effects occurred on the subscales of the QoL measure. A main effect for group was found on the pain subscale as a result of the intervention group reporting fewer symptoms of pain than the waitlist group. This difference was seen at baseline so is unlikely to be related to the intervention. A main effect for time was found on the financial difficulties subscale with participants reporting fewer financial troubles over time. These reductions may be associated with the obtainment of new employment or other psychological factors. The intervention group did report fewer symptoms of fatigue post-intervention, which may have resulted from learning about good sleep hygiene in the eReCog program, however this effect was not statistically significant at follow-up.

Chapter II discussed the relationship between subjective cognitive functioning and objective cognitive functioning. Researchers typically find that subjective cognitive functioning correlates more strongly with negative affect and QoL than with performance on neuropsychological measures (Collins et al., 2017; Green et al., 2005; Reid-Arndt & Cox, 2012). To address this issue in the current research project, correlations were computed between pre- and post- scores on PCI and change scores on PM, psychological distress, illness perceptions related to cognitive difficulties, impact on QoL, EF, and total WebNeuro Z-scores of objective cognitive functioning. The findings support the notion that self-reported cognitive function shows stronger...
correlations with affect and QoL than neuropsychological performance. Associations were found between PCI and impact on QoL, and PM failures in both studies, as well as psychological distress in Study One only. An association between PCI and the EF domain was found in Study One, but this was not replicated in Study Two. Neither study found significant correlations between PCI and total scores on WebNeuro. These results suggest that self-reported cognitive functioning may be partly influenced by psychological factors (i.e., distress), but that it could also be related to changes in functional ability on everyday tasks. Since PM is more closely related to everyday cognitive problems than many neuropsychological tasks, measures of PM have the potential to demonstrate more correlations with self-report measures than typical objective cognitive functioning measures (Mihuta et al., 2016).

An evaluation of PCI scores across cognitive rehabilitation interventions for cancer survivors that utilised the FACT-Cog 3 allowed for comparison of the results from this research project with other studies. Of the seven published studies there were seven cancer intervention groups, six cancer comparison groups, two non-cancer comparison groups, and one non-cancer intervention group. Comparison of the cancer group in Study One to the weighted mean across studies demonstrated that the cancer intervention group’s baseline PCI score ($M = 33.8, SD = 18.7$) was slightly lower than the overall mean for cancer intervention groups ($M = 37.0, SD = 14.3$). In Study Two however, the cancer intervention group had a slightly higher baseline score ($M = 41.6, SD = 15.4$) than the overall mean for cancer intervention groups. Higher baseline scores can have an impact on finding significant group differences, a topic that is discussed in greater detail in the General Discussion chapter of this thesis. Similarly, the cancer comparison group in Study Two had a slightly higher baseline score ($M = 42.5, SD = 16.0$) than the overall means for cancer comparison groups ($M = 40.9, SD = 14.4$). It is noteworthy to mention that the non-cancer group’s PCI scores were higher
at baseline than the cancer groups (see Table 7.2). Even at post-intervention and follow-up, the cancer group’s PCI scores did not obtain the same level as reported by the non-cancer groups at baseline, which is addressed in more detail in the General Discussion.

The final analysis conducted in this chapter was comparing total WebNeuro performance across groups from both studies in this research project. As previously mentioned in this thesis, comparing cancer groups to healthy control groups allows for researchers to determine the level of impairment present (Wefel, Vardy, et al., 2011). When comparing mean Z-scores across the five groups, there were not many discernible differences (refer to Table 7.3). Unexpectedly, the pilot cancer group demonstrated the best overall performance across the seven cognitive domains when comparing mean Z-scores ($M = -0.07, SD = 0.44$), whereas the RCT waitlist cancer group demonstrated the worst performance ($M = -0.20, SD = 0.52$). Even the group with the worst performance did not extend beyond 0.2 standard deviations from the mean of a normative sample matched on age and education levels. There were no notable differences between the cancer groups and the non-cancer groups. In fact, the pilot waitlist non-cancer group had the highest rate of baseline clinical cognitive impairment (27%) of all the five groups.

Apart from the pilot cancer group, the rates of OCFI-I did not produce large changes at T2 or T3. The pilot cancer group reduced from 17% OCFI-I to 0% at T2, but this resulted from a small sample size where two participants demonstrated improved performance on at least one of the cognitive domains. These effects, however, were not maintained at T3. The WebNeuro results provide further evidence to support the claim that cognitive deficits in cancer survivors are typically subtle, and may not be apparent on standardised neuropsychological test measures (Wefel et al., 2008), however are sufficient to impact on everyday functioning as evidenced by
significant findings on self-reported subjective cognition. The final chapter of this thesis provides a general discussion of the findings presented in results Chapters IV - VII and discusses their implications along with directions for future research.
CHAPTER VIII: GENERAL DISCUSSION

Summary of Results

The primary aim of the current project was to develop a web-based CRT program and investigate its effectiveness for adult cancer survivors. The project was comprised of two studies, namely Study One (pilot study) and Study Two (RCT) that evaluated participant outcomes on measures of subjective cognitive functioning, objective cognitive functioning, and psychosocial variables of distress, fatigue, QoL, and illness perceptions. The second aim of the project was to examine the patterns of participant engagement in the newly developed online CRT program by creating a more meaningful method of measuring engagement than what is typically described in the literature on web-based interventions. Participant engagement was evaluated using data from intervention groups in both studies. The final aim of this research project was to examine potential psychological mechanisms that contribute to the effectiveness of cognitive rehabilitation therapy interventions by evaluating key Self Determination Theory variables of autonomy, competence, and relatedness as potential mediators of intervention effects.

The results from Study One indicated that the intervention groups improved to a significantly greater extent on reported PM failures on the BADL than the waitlist group, and a trend towards an interaction was noted on the IADL subscale where the cancer group reported a reduction in PM failures whereas the non-cancer groups did not. PCI showed significant main effects for time and group, with the cancer group reporting more impairment at baseline than the non-cancer groups and participants reporting more problems with cognitive impairments at baseline compared to post-intervention and follow-up. Trends towards time effects were observed on PCA and cognitive QoL subscales, and both variables demonstrated significant group effects.
with the cancer group reporting worse PCA and cognitive QoL than the waitlist group only. On objective cognitive functioning, a significant interaction was found on the Attention domain with the cancer intervention group and waitlist group improving over time, whereas the non-cancer treatment group performed more poorly on the domain over time. Main effects for time were observed on the Verbal Memory domain indicating worse performance over time whereas there was significantly improved performance on the Executive Function domain. There were no significant interaction or main effects on the functional or symptom subscales of the EORTC QLQ, psychological distress, or illness perceptions. Participants in the cancer group were satisfied with the program with 75% reporting being either “satisfied” or “very satisfied”, and their overall rating of the program was 7.8/10. In the non-cancer group, 87% of participants were either “satisfied” or “very satisfied”, and they provided an overall rating of 7.7/10. Total participant engagement was lower in the non-cancer intervention group (78%) compared to the cancer intervention group (92%), which was an expected outcome in this study.

In Study Two the intervention group reported a reduction in PM failures on the IADL to a significantly greater extent than the waitlist group. A similar trend was noted on PCI. Main effects for time were observed on all seven measures of subjective cognitive functioning representing improvements over time. There were no significant interactions on domains of objective cognitive functioning, but a trend was noted on Executive Functioning towards greater improvement in the intervention group compared to the waitlist group. Main effects of time were observed on four of the seven objective cognitive domains with improvements observed on Executive Functioning and Impulsivity domains, and worsening performance on Information Processing Efficiency and Verbal Memory domains. Similar to Study One, there were no significant interactions to report on functional or symptom subscales of the QoL.
measure, psychological distress, or illness perceptions. Satisfaction with the intervention program was high amongst those assigned to the treatment group with 94% of participants reporting they were either “satisfied” or “very satisfied”, and the overall rating of the program was 7.7/10. Total engagement in the intervention program was acceptable with participants completing 87% of activities within the four program modules.

**Hypothesis 1**

The results from these two studies provided partial support of Hypothesis 1, which predicted that the intervention groups would demonstrate improvement to a significantly greater extent than the waitlist control groups. In both studies, significant improvements in the intervention groups were observed on subscales assessing PM functioning to a greater extent than in comparison groups.

PM is a type of memory that has been widely assessed in individuals with traumatic brain injury (Fleming et al., 2008; Kinsella, 2010), schizophrenia (Raskin et al., 2014; Xiang, Shum, Chiu, Tang, & Ungvari, 2010), Parkinson’s disease (Raskin et al., 2011; S. J. Smith, Souchay, & Moulin, 2011), stroke (Kant et al., 2014), Alzheimer’s disease (Shelton et al., 2016), mild cognitive impairment (Costa et al., 2010), and more recently in breast cancer survivors (Mihuta et al., 2016; Paquet et al., 2013). However, this type of memory functioning has not been widely assessed in cancer survivors within the context of CRT interventions.

One of the main aims of CRT interventions, as described in Chapter II, is to improve everyday functioning. PM may provide a better indication of memory functioning on everyday tasks than neuropsychological measures that generally lack ecological validity (Mihuta et al., 2016) or self-report measures, which can be susceptible to over-reporting due to negative affect. The first study to evaluate PM was a previous ReCog study, which unlike the current research project found no significant
intervention effects on the self-report BAPM measure (King & Green, 2015). Since PM has not been evaluated in cognitive rehabilitation more broadly, it is difficult to compare the results from the two studies in this project to other published studies on cognitive rehabilitation. Notwithstanding, incorporating subjective or objective measures that assess PM functioning in CRT interventions may assist researchers to evaluate memory functioning post-intervention and help to improve the effectiveness of these programs on outcomes that are relevant to everyday living.

The primary advantage to having a standardised recommended measure for assessing subjective cognitive functioning in psycho-oncology research is that it allows researchers to compare results across studies. The International Cognition and Cancer Task Force made recommendations for researchers on which neuropsychological measures to use in order to assess objective cognitive functioning (Wefel, Vardy, et al., 2011), however their recommendations did not specify which self-report measures were most appropriate. The majority of recently published cognitive rehabilitation studies for cancer survivors has used the FACT-Cog-3 as a primary measure for assessing self-reported cognitive functioning (Bray et al., 2017; Cherrier et al., 2013; Ferguson et al., 2016; King & Green, 2015; Schuurs & Green, 2013; Von Ah et al., 2012), although others have used the Multiple Ability Self-Report Questionnaire (MASQ; Ferguson et al., 2007; Ferguson et al., 2012; Schuurs & Green, 2013), the Cognitive Failures Questionnaire (CFQ; Damholdt et al., 2016), the Memory Self-Efficacy Questionnaire (MSEQ; McDougall et al., 2011), or the Patient’s Assessment of Own Functioning Inventory (PAOFI; Ercoli et al., 2013; Ercoli et al., 2015).

The widespread use of the FACT-Cog-3 for assessing subjective cognitive functioning led to its selection in this research project in order to compare across studies. Recommendations from the International Cognition and Cancer Task Force
suggest including multiple control groups in psycho-oncology research on cognitive functions after cancer including healthy controls and disease specific controls, which will allow researchers to determine whether cognitive impairment is present and to discern whether changes in cognitive functioning are a result of practice effects or true improvement (Wefel, Vardy, et al., 2011), which was implemented in Study One.

The compilation of scores on the PCI measure presented in Chapter VII demonstrates a clear discrepancy in reported impairment between healthy individuals from the community and cancer survivors, a difference that was still present after completing the intervention. In Study Two, the cancer group’s baseline scores were somewhat higher than the mean baseline scores across studies. These higher baseline scores in both groups may in part explain why the interaction effect on PCI did not achieve significance, since higher baseline functioning provides less room for improvement. However these scores would not be considered a ceiling effect since the comparison groups without cancer had higher baseline scores than the cancer groups post intervention. This suggests that despite improvements over time, cognitive problems are still present to a degree amongst the cancer survivors.

Improvements in the control groups on the PCI measure may also have reduced the probability of a significant interaction effect. As noted in the Results section of Chapter V, a significant main effect for time was observed in Study Two with the intervention group improving 8.9 points compared to 5.7 points for the waitlist group. The latter change was slightly below the estimated minimally important difference of 6.5 points (Bray et al., 2017). Improvements on the PCI in waitlist groups have occurred in other studies also (Cherrier et al., 2013; Ferguson et al., 2016; Schuurs & Green, 2013), as presented in Table 7.2 (p. 166). These improvements may have resulted from participants acquiring an increased awareness into their own cognitive functioning as a result of the assessment sessions, despite receiving no feedback on
performance until after participation in the research project was complete. The act of being involved in a study itself may have fostered an improvement in psychological well-being (e.g., anxiety or depressive symptoms), which has been associated with improved self-reported cognitive functioning (Collins et al., 2017). The results presented in Chapter VII demonstrated that improved PCI was associated with an improvement on the impact of cognitive problems on QoL in both studies, and with improved psychological distress in Study One.

In summary, the findings from this research project suggest that web-based CRT has the potential to assuage some symptoms associated with self-reported memory problems and cognitive functioning for cancer survivors, and may even be associated with slight benefits for individuals participating in waitlist groups.

**Hypothesis 2**

Results from this research project provided little support for Hypothesis 2, that intervention groups would improve to a greater extent on objective cognitive function domains than the waitlist groups. There was a significant interaction on the Attention domain, but this occurred because the cancer group and waitlist group improved, whereas the non-cancer treatment group performed worse over time. This inconsistent pattern of performance is not likely a reflection of a true intervention effect. An interaction trend was noted on the EF domain in the expected direction of greater improvement in the intervention group in Study Two. Some improvements were observed on Impulsivity, whilst worsening performance occurred on InfoProc and VM.

The pattern of worsening performance on the VM domain occurred in both studies in this research project, which was not likely due to direct interference from previous trials since parallel versions of the tasks were used for each assessment without repetitions of stimuli. This pattern of deterioration is unexplained on the VM
domain in this research project. Deterioration was also observed on the InfoProc domain, particularly for the Verbal Interference task, which required participants to select the correct word while ignoring the colour of the word. In both studies participants’ baseline scores were better than the T2 and T3 assessments. This deterioration in performance may be associated with general task difficulty or the order in which the tasks were presented. Fatigue, testing anxiety, or lack of motivation are other factors that might explain this pattern or performance.

Improved EF was found across all groups in both studies. The domain consists of a maze task where completion time and number of overrun errors are scored. Global improvements for the domain suggest that participants in each of the groups completed the task more quickly with fewer errors as they became familiar with the task. However, the improvements in the intervention group in Study Two were larger than those in the waitlist group, which may indicate intervention effects. As discussed in Chapter V, one published study found improved EF on subjective and objective measures of cognitive functioning following participation in a CT intervention (Kesler et al., 2013). Improvements on this cognitive domain have the potential to translate into improved functioning on everyday tasks that involve planning, problem-solving and working memory capacity.

According to the International Cognition and Cancer Task Force’s recommendations, validated objective neuropsychological test measures are the gold standard for measuring cognitive function as opposed to self-report measures (Wefel, Vardy, et al., 2011). Based on the cortical profile of the cognitive effects generally associated with chemotherapy treatment, the Task Force recommends three validated tests that measure learning and memory, processing speed, and executive functioning. These three tests are: the Hopkins Verbal Learning Test – Revised, Trail Making Test, and the Controlled Oral Word Association. Due to the desire to conduct this research
project in a completely web-based modality, it was not possible to use the tests recommended by the Task Force. The WebNeuro battery contains testing tasks that measure similar cognitive domains, however, neither the Task Force’s recommended tests nor the WebNeuro tests provide pure measures of domains and the online WebNeuro assessment does not provide direct equivalents to the recommended pencil-and-paper tests.

In the literature, there are no other cognitive rehabilitation studies that have utilised the WebNeuro online assessment tool; therefore the results presented here cannot be compared to other similar studies. The assessment battery has been used to measure changes in cognitive functioning in cancer patients receiving intracranial stereotactic irradiation for benign cranial and base of skull lesions (Burger et al., 2014). The WebNeuro assessment tool appeared to be a reliable program for assessing cognitive functioning in these patients, however, further investigation into the reliability and validity of the WebNeuro assessment battery with cancer survivors is a warranted research avenue.

**Hypothesis 3**

The third hypothesis of this research project purported that participant engagement would correlate with outcomes on subjective cognitive functioning measures, which was partially supported in this research project. Data evaluated from the intervention groups from both studies demonstrated that higher engagement was associated with greater reductions in PM failures and a trend was observed towards less PCI. Reported engagement levels in web-based research with cancer survivors are generally low (David et al., 2013), which may reduce the effectiveness of the intervention. One of the reasons for this is that the typical methods used to measure engagement may be lacking insight into users’ behaviours whilst participating in the intervention (Morrison & Doherty, 2014). As described in Chapter VI of this thesis,
this research project developed a distinct method for quantifying participant engagement and the results from the studies in this project found higher levels of engagement than those typically reported with web-based interventions. In the future, researchers should consider alternative methods for measuring engagement during the development process of the interventions and incorporate these methods into the intervention design. This has the potential to improve future reported rates of engagement in web-based interventions.

It has been suggested that higher level of participant engagement has the potential to improve outcomes in web-based research (Danaher & Seeley, 2009), however, the associations between engagement levels and outcome measures are not often reported. Of the three published web-based CT interventions (Bray et al., 2017; Damholdt et al., 2016; Kesler et al., 2013), only one of them reported correlations between measures of engagement and outcome variables. Bray et al. (2017) measured engagement as the number of training hours during the course of the intervention and reported a mean of 25.08 hours. The researchers conducted dose-response analyses using regression models to determine if training time was associated with change scores on the PCI or on the neuropsychological measure CogState total and found no strong evidence of a significant dose-response relationship for either outcome. Participants who trained more than the mean training time demonstrated a change of 16.3 points on the PCI compared to a 12.6 point change for those who trained less than the mean.

The researchers did not report correlations between training time and improved PCI, however the change scores, which exceeded the minimally important difference (Bray et al., 2017) likely showed significant correlations with number of training hours. Essentially what the authors are emphasising in their study is that training more than the mean 25.08 hours or less than the mean hours does not significantly affect
change scores on PCI. If this is the case, than the number of hours spent training does not provide a meaningful measure of engagement since training for 10 hours could be as effective as training for 30 hours. One of the aims of psychological interventions is to maximise treatment fidelity, as discussed in Chapter II of this thesis, in order to ensure that participants receive the proper dosage of an intervention program as intended. Evaluating treatment fidelity of an intervention program is difficult if the number of training hours required to improve self-reported cognitive functioning is not known.

In conclusion, the association between increased engagement and improved functioning on outcome measures in this research project provides some evidence that participant engagement may be an underlying mechanism for explaining intervention effectiveness, but this has yet to be fully investigated. Incorporating valid methods for measuring participant engagement is an important step that should be considered during the development phase of web-based intervention programs in future research.

**Hypothesis 4**

The fourth hypothesis, that the variables competence, autonomy, and relatedness would mediate the intervention effects on outcome measures of subjective cognitive functioning, was not supported based on the results from the two studies presented in this thesis. One of the conditions for mediation is that the independent variable demonstrates a significant correlation with the mediating variables. In both studies, change scores on each of these variables were not associated with group membership (e.g., whether participants were in the intervention or control groups). In Study One, no significant changes on any of these variables were observed from T1 to T2 for any of the three groups. In Study Two, the intervention group reported increased feelings of autonomy from T1 to T2, whereas the waitlist group reported
decreased feelings of relatedness. These changes, however, were not associated with a mediation effect.

Autonomy, competence and relatedness have not been investigated as mediators in any published cognitive rehabilitation interventions thus far, however, they have been evaluated in a computer-mediated support intervention with breast cancer survivors (Hull et al., 2016). The researchers used path analysis to examine whether engagement in an interactive health system affected autonomy, competence, and relatedness, and whether this relationship was in turn associated with QoL and wellbeing. The results reported in the correlated parallel model suggested that the effects of engaging in the intervention and outcome on functional wellbeing were mediated by perceptions of relatedness, but not autonomy or competence.

One reason that Hull et al. (2016) may have found significant associations is because they selected different measures that were related to autonomy, competence and relatedness within a health context. For example, the autonomy scale they selected used four items from the Health Care Climate Questionnaire, which contained questions assessing participants’ comfort and confidence in discussing treatment options and being assertive with their healthcare. The competence scale contained questions about how capable and knowledgeable participants felt with respect to their health. The current project used the Basic Psychological Needs Satisfaction Scale – General form, which contained more general items not specifically related to cognitive functioning or health associated with cancer. The use of a different measure may have produced significant results; therefore, there remains an open question about the potential for a SDT approach to help explain psychological mechanisms of treatment effects in future cognitive rehabilitation research.

Potential psychosocial mechanisms have been investigated in cognitive rehabilitation with cancer survivors, however none of the studies described in Chapter
II reported mediation analyses of this type. For example, King and Green (2015) evaluated whether change scores on measures of cognitive self-efficacy and illness perceptions were correlated with group and change scores for objective and subjective measures of cognitive functioning in the previous ReCog study. They found that improved cognitive self-efficacy was correlated with improved impact on QoL. In addition, trends toward improved PCA and illness perceptions associated with cognitive self-efficacy were reported. In psycho-oncology research, few cognitive rehabilitation studies have investigated the underlying mechanisms or psychosocial factors associated with intervention effects. Further investigation into potential mechanism of change is discussed at the end of this chapter in possibilities for future research.

**Strengths and Limitations**

The design of the research project was a notable strength. Conducting two individual studies allowed for an extensive evaluation of novel a online CRT intervention in samples of cancer survivors and community dwelling adults. The inclusion of two healthy control groups assisted with the comparison of the clinical sample to a normal population, which provided a better understanding of the level of impairment present at baseline on subjective and objective measures of cognitive functioning. Furthermore a comprehensive assessment battery was incorporated to assess self-reported functioning, psychosocial functioning, and neuropsychological task performance in the targeted clinical group.

The sample size recruited for this research project was adequate and within the desired limits for this type of intervention program. The selected recruitment strategies were effective and provided a cohort of participants from various states, territories, and regions throughout Australia.
There are noteworthy benefits of the online intervention program developed for this research project. First, the program required minimal involvement from a facilitator in comparison to the time requirements typically needed for the facilitation of face-to-face interventions, indicating that the program could be implemented with minimal additional resources required in the community, although cost-effectiveness was not directly evaluated in this project. The online delivery modality of the intervention program makes it easily accessible and readily available for potential wider dissemination. Participants in this research project found the program engaging as evidenced by their involvement in multiple aspects of the modules and adherence to weekly homework tasks presented in results Chapter VI. Low attrition rates (i.e., 8%, 16% for cancer intervention groups and 9% for the cancer waitlist group) in this research project provide a good indication that the program was administered and received as intended. In addition, low attrition supports the internal validity of the results.

The current research project is not without limitations. One potential disadvantage to online CRT is that the process does not typically involve a network of supporting individuals. According to Wilson (2002), a leading proponent for cognitive rehabilitation, the process of cognitive rehabilitation is meant to be interactive between the impaired individual and a variety of persons surrounding them (e.g., healthcare professionals, family members, and the wider community). The impaired individual works together with those in their environment to attempt to remediate or mitigate the cognitive deficits resulting from the injury or damage. The process of online CRT can be very individually based and might include only minimal support and interaction from a trained professional or facilitator, or even from other participants in the group. Nevertheless, it is argued that the experience of an individual in a program such as eReCog fits more closely with a cognitive rehabilitation paradigm than with a
cognitive training paradigm, which is why the intervention used in the current project has been described as online cognitive rehabilitation.

The difficulty associated with incorporating the social element of sharing cancer experiences with other participants in the program is another potential disadvantage of online CRT. As mentioned in the project methods section in Chapter III of this thesis, participant feedback from the in-person ReCog interventions indicated that sharing personal experiences from the cancer journey was a valuable part of their involvement in the program. In the initial feasibility study of ReCog, non-parametric tests were used for data analysis so interaction effects were not investigated on the social functioning scale, however within group effects demonstrated the intervention group demonstrated significant improvements in reported social functioning after the intervention, which was not observed in the comparison group (Schuurs & Green, 2013). In the ReCog RCT study a trend towards a significant interaction was noted, and within group analysis demonstrated improvements in social functioning in the intervention group post treatment (King & Green, 2015). Similar feedback regarding the sharing of cancer experiences was obtained from the online version of the program; participants commented to the facilitator that reading responses from other participants was an enjoyable aspect of the intervention. For feasibility purposes, it was decided in this research project to allow participants to commence the program on their own time schedule. Moreover, the software used did not allow for online chatting or simultaneous engagement with other participants. Incorporating a platform that allows participants to interact with one another whilst completing the intervention simultaneously might create a stronger social component in future research.

Another potential challenge with online CRT is the difficulty associated with assessing and treating multiple problems at once. Individuals who participate in
cognitive rehabilitation generally present with multiple cognitive problems rather than a single isolated deficit, and may have a number of emotional, social and behaviour problems associated with their injury (Wilson, 2002). Given the complex presentation of problems, CRT interventions should address a variety of symptoms that have real-life consequences for these individuals, which is difficult to execute in an online platform.

The design of this project may have limited the investigation of underlying mechanisms attributing to the effectiveness of the intervention. The principal aim of this research was to develop and evaluate the effectiveness of a CRT intervention, whereas the investigation of mediating factors was a secondary aim. Examining potential mediating relationships might require a design that focuses on evaluation of the mediating relationship between target variables as the main purpose.

Restrictions on the capabilities of the software tools used in this research project provided some limitations. The WebNeuro neuropsychological assessment battery was convenient for the current project because it could be administered online so that participants were able to complete the assessments at home. This, however, meant completing assessments in a less controlled environment compared to administration in a laboratory setting. WebNeuro has not been utilised in published research with cancer survivors causing speculation for whether the measure was appropriate for assessing cognitive dysfunction in this clinical group. The LessonLAMS software also had some drawbacks. The software is open access and can be used by other researchers, which makes for easy replication and dissemination of the program, however, the simplicity of the software meant that some more engaging elements could not be incorporated into the modules (e.g., chat features or external videos). In addition, important quantitative data (e.g., time spent on pages, time to complete modules, number of homework downloads) were not available.
In regards to participant demographic characteristics, the cancer groups in both studies were entirely female and predominantly survivors of breast cancer. Whether or not the current findings can be replicated in other samples of mixed tumour types and men could be addressed in future research. To enrol in the studies participants had to report at least “a little” trouble with either memory or concentration as assessed by the two items comprising the EORCT QLQ cognitive subscale. Given the cancer group’s comparable performance to the non-cancer groups on objective cognitive functioning domains, it might be beneficial to screen for eligibility using neuropsychological measures rather than self-report measures. A sample of cancer survivors with demonstrated impairment on objective measures may potentially show greater intervention effects than the current studies demonstrated.

**Future Research**

The current research project has generated a number of ideas for future research directions with web-based CRT. One area for further investigation is the inclusion of an attentional control condition, which has been recommended for psychosocial research to test for the specific effects of the treatment whilst keeping participants engaged during the wait period (Papp et al., 2009). Due to the time constraints for a PhD project, recruiting sufficient participants for three groups was a challenge. In the context of online cognitive rehabilitation, attentional control conditions might include online education modules with information about other physical aspects associated with cancer survivorship (e.g., fatigue, pain, lymphedema, body image) or healthy lifestyle changes (e.g., exercise, diet). Including an attentional control condition has the benefit of reducing attrition by keeping participants engaged during the typical waiting period, which should be considered for web-based interventions where high attrition rates are problematic.
An alternative protocol or comparison condition could be a group that receives immediate feedback after completing the assessment checkpoints, rather than feedback at the end of the study. The number of participants in the waitlist groups who engage in the intervention after completing the waitlist period is often low, suggesting that the experience of participating in assessments may sufficiently address concerns about cognition for some waitlist participants such that they no longer wish to participate in an intervention. In Study Two of the current project only 24% of participants from the waitlist group completed the intervention program after the final assessment. An additional 15% of participants began the intervention, but discontinued halfway through the program or prior and demonstrated a lack of interest in participating after finishing the assessment checkpoints. A number of studies have indicated that neuropsychological assessment with feedback may have indirect benefits on general health and wellbeing in an array of patient groups demonstrating cognitive dysfunction and potential direct psychological benefits as well (Braun et al., 2011; Longley, Tate, & Brown, 2012), yet it is an area that has not been investigated in cognitive rehabilitation interventions targeting cognitive dysfunction. Participants in this research project received feedback on the general findings from the study; individualised feedback was offered to participants who enquired about their personal performance, however all feedback was only available to them after they completed the final assessment and their participation in the project had ended. Providing immediate feedback on their cognitive performance during their involvement may provide additional psychological and wellbeing benefits.

Investigating psychosocial and underlying mechanisms potentially contributing to the effectiveness of online cognitive rehabilitation is another area for further exploration. The current research project examined mechanisms of motivation (SDT theory) as mediators of intervention effects, and found little association. Nevertheless,
alternative SDT measures more specific to the context of the behaviour (i.e., cognitive dysfunction) may produce varying results. Other variables of motivation from alternative theoretical frameworks should also be assessed. As mentioned earlier in this chapter, investigating participant engagement and alternative measures of engagement may also be useful mechanisms for describing intervention effects, which was not fully analysed in this research project.

The process of emotion management is another potential underlying mechanism that could assist researchers to better understand intervention effects in cognitive rehabilitation research. A longitudinal study in a group of individuals with early schizophrenia investigated the effects of cognitive enhancement therapy (CET) and found that emotion management mediated the effects of CET on functioning (Eack, Pogue-Geile, Greenwald, Hogarty, & Keshavan, 2011). Since increased self-reported cognitive dysfunction has been associated with negative affect and psychological distress, improved emotion management may be a mechanism associated with improved outcomes. Researchers often evaluate the emotion itself (e.g., distress, anxiety, depression) but do not investigate emotion regulation skills per se. To conclude that a reduction in distress is due to better stress management is deceiving because changes in psychological variables are not always maintained at long-term follow-up. Since some CRT interventions include components designed to manage emotional distress, such as relaxation training or meditation, assessing the management of emotions may be worthwhile.

Web-based CRT programs might be beneficial for other clinical populations, including those who were excluded from the current research project. Volunteers that experienced paediatric cancers or had a history of tumours of the central nervous system were not eligible to participate, but additional research with these cancer survivors might find that the program is beneficial for them as well. The participants
involved in the research, particularly in Study Two, had a relatively high level of baseline functioning therefore it is not known whether a group of more severely impaired individuals, such as cancer patients currently undergoing treatment or patients with impairment from tumours in the brain, would find similar benefits.

The extent to which the CRT intervention program might benefit individuals closely involved in the cancer experience is another possible area for future research. As described in Chapter II of this thesis, the National Coalition for Cancer Survivorship’s definition of a cancer survivor was extended to include not just the individual diagnosed with the disease, but also relatives, caregivers and anyone else involved in the cancer experience. Since cognitive rehabilitation is meant to be an interactive process between the individual cancer and persons in their immediate environment, it might be useful for caregivers or close family members to participate in the intervention in order to better understand the cancer journey and become an active participant in the cognitive rehabilitation process. In fact, there were a few volunteers for Study One from the community group who reported that they volunteered because they had a close family member or friend who had experienced cognitive problems and they wanted to better understand the experience of their loved one. Encouraging family or friends to participate along with a cancer survivor could make the experience more enjoyable for both parties completing the program.

Conclusions

In conclusion, this research project makes four valuable contributions to the existing literature on cognitive rehabilitation interventions for cancer survivors. First, the findings from these studies indicated that the development and implementation of web-based CRT interventions has the potential to alleviate some of the symptoms of cognitive dysfunction reported by cancer survivors. Online CRT appears to be a feasible method for delivering facilitator-enhanced cognitive rehabilitation to cancer
survivors in the community. Second, the studies from this project demonstrated that subjective cognitive functioning is not only associated with negative affect and QoL, but also with memory difficulties on everyday tasks. PM failures are correlated with self-reported cognitive functioning, yet apart from one other study these types of memory failures have not been assessed in cognitive rehabilitation interventions in this clinical group. Third, this project showed the importance of analysing participant engagement in online interventions and considering different approaches to measuring engagement during the process of developing interventions. Higher level of engagement is associated with improved outcomes, thus interventions designed to maximise engagement can lead to more effective treatments. Finally, results from this project did not support the proposition that motivation to meet basic psychological needs from an SDT framework would mediate intervention effects on subjective cognitive functioning. Investigating other potential mechanisms of change is an important avenue for future research in order to assist researchers to better understand the positive effects of cognitive rehabilitation interventions.
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**APPENDICES**

**APPENDIX A**

ReCog Program Content

Table A.1

*Group Cognitive Intervention Program Summary*

<table>
<thead>
<tr>
<th>Session</th>
<th>Topic</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cognition and Normal Aging</td>
<td>• Introduction to program, housekeeping, icebreaker&lt;br&gt;• Psychoeducation: Aging and cognitive function, cancer and cognitive function&lt;br&gt;• Group Discussion: Experiences of impact of cancer, cognitive changes, coping strategies&lt;br&gt;• Relaxation training, problem solving, goal setting&lt;br&gt;• Homework: Finalise goal setting, relaxation practice</td>
</tr>
<tr>
<td>2</td>
<td>Memory</td>
<td>• Psychoeducation: Understanding memory&lt;br&gt;• Compensatory strategies, enhancement strategies: List and discuss, advantages/ disadvantages&lt;br&gt;• Group Discussion: Experiences of changes in memory, coping strategies, effectiveness of strategies&lt;br&gt;• Homework: Practise a memory strategy and record information, relaxation practice</td>
</tr>
<tr>
<td>3</td>
<td>Attention</td>
<td>• Psychoeducation: Understanding attention&lt;br&gt;• Group discussion: Personal experiences of difficulties with attention&lt;br&gt;• Improving attention: Enhancement strategies, applying strategies, meta-cognition approach&lt;br&gt;• Homework: Practise one attention strategy and record information, continue practising previous memory strategy or pick new strategy, relaxation practice</td>
</tr>
<tr>
<td>4</td>
<td>Fatigue, Emotions and Cognition</td>
<td>• Psychoeducation: Understanding emotions and fatigue&lt;br&gt;• Group discussion: Personal experiences of fatigue&lt;br&gt;• Managing fatigue, self-care, summary/feedback, relaxation practice&lt;br&gt;• Homework: Continue to apply strategies learnt in program, implement self-care strategies, relaxation practice</td>
</tr>
</tbody>
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APPENDIX B

Broadcast Email Study One

Cognition in cancer survivors: The aim is to provide cancer survivors with a free assessment of their current cognitive abilities, and the opportunity to participate in an online rehabilitation program to address cognitive difficulties.

Type of volunteers needed: Cancer survivors who experience cognitive problems, such as difficulties with memory and concentration, following cancer and cancer treatment, AND adults with no history of cancer or cancer treatment.

Volunteers: need to be over 18, have been diagnosed with cancer previously, and have finished major treatments at least 6 months previously, OR be over age 35 and have never been diagnosed with cancer. Access to a computer, active email account, and Internet connection are required.

What would I be asked to do? How much time would it take?: Complete an online rehabilitation program once a week over 4 weeks (1 hour/week), and complete 3 online assessment sessions (approximately 1 hour each). You will have the flexibility to complete the online modules at your convenience and in the comfort of your own home or office.

What’s in it for me?: As part of helping with this research, you would receive free assessment and treatment. Do you know someone who is the cancer survivor with cognitive difficulties? Please forward this information to them.

How can I volunteer or find out more? Please contact Dr Heather Green at h.green@griffith.edu.au or phone 5678 9086.

Research element School of Applied Psychology. This project has gained ethical approval from the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC).
RESEARCH VOLUNTEERS NEEDED

We are researching problems in memory, attention, and concentration in people who have been treated for cancer

Want to get involved?
• Must be aged 18 or above
• Have been diagnosed with cancer during adulthood (excluding brain tumour)
• Completed treatments for cancer at least 6 months ago
• Not be awaiting further treatment (current hormone treatments are okay)
• Have access to a computer, an active email account, and Internet services

OR
• Must be aged 35 or above
• Have no history of cancer
• Have access to a computer, an active email account, and Internet services

What’s involved?
• Participation in a free online treatment program targeting problems with memory, attention and concentration
• Learning about cognitive functions
• Working on skills and practical exercises to help cognitive functioning
• Completing 4 online modules (1 hour each) and 3 online assessment

This research project has gained ethical approval from the Human Research Ethics Committee at Griffith University (PSY/F4/14/HREC)

If you are interested in participating or wish to know more information, please contact the researcher, Dr Heather Green, by email h.green@griffith.edu.au or phone (07) 5678 9086. All queries and questions are welcome.
APPENDIX D

Initial Phone Screening Interview

Hi ___,

I’m [name] from [organisation]. You contacted my team about a research project for cancer survivors. I’d like to ask you a few questions for the study. Do you have a few minutes to do this now or would another time be better?

[Wait for response]

First, can you tell me if you received and read the Participant Information and Consent Form? Is there anything you would like to ask me before we go further?

[Wait for responses between each question]

Next, I would like to ask a couple of questions that relate to your cognitive functioning over the past week. Would this be OK with you?

[Wait for response]

In response, could you please answer either: Not at all, A little, Quite a bit, or Very much.

<table>
<thead>
<tr>
<th>During the past week:</th>
<th>Not at All</th>
<th>A Little</th>
<th>Quite a Bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Have you had difficulty remembering things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

*If answer “Not at all” to both questions, say:*

Unfortunately for this study we need people who are currently experiencing some level of difficulty in areas like memory or attention. Thank you very much for your time. Would you like to stay on our contact list in case there are other studies in future that might interest you?

*If cumulative score of 3 or more on questions, say:*

Thank you. Can I check some more information for the study? This would take about 10 minutes. We can do this now or make another time, if you prefer.
Telephone Interview

Date of Interview: .................. Participant Code: .....................


4. Highest level of education completed: .................. 5. Years of Education:...........

6. Marital status: ..................................................

7. What was your first language? English / Other (specify) ....................

8. What country were you born in? Australia / Other (specify) ..................

9. Type of cancer:............................

10. Past cancer treatment:..........................................................

11. How long is it since you were first diagnosed with cancer (approximately how many months)?:..................................................

12. How long is it since you finished your main treatments for cancer, such as surgery, chemotherapy or radiotherapy (approximately how many months)?:.............

13. Do you have any medical problems at the moment? If yes, could you tell me what they are?:
..............................................................................................
..............................................................................................
..............................................................................................

14. Current medications/treatments:
..............................................................................................
..............................................................................................
..............................................................................................

15. Have you ever experienced a neurological problem? E.g. Epilepsy, Parkinson’s disease etc.:
..............................................................................................
..............................................................................................
..............................................................................................
16. Do you think that you have experienced any cognitive difficulties that were directly related to your cancer or your cancer treatment? If so, what would you say was the most severe example?

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…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
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…………………………………………………………………………………………

17. If you experienced changes, are they still current?
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………

18. If you experienced changes, what adaptations did you have to make in areas of your life?
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………

19. Is there anything in particular you think we should be aware of that might affect your performance on the tests?
…………………………………………………………………………………………
…………………………………………………………………………………………

Do you have any questions for me regarding the research? Thank you so much for your kind offer to help with this research.

INTERVIEWER: Space is provided here for any other relevant information/observations
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………
…………………………………………………………………………………………

237
APPENDIX E

Information Sheet

An Online Intervention to Target Cognitive Impairments Associated with Cancer and Cancer Treatments

Who is conducting the research

Name: Dr Heather Green & Ms Mary Mihuta
School / Centre: School of Applied Psychology & Behavioural Basis of Health Program
Contact Phone: (07) 5678 9086
Contact Email: h.green@griffith.edu.au or mary.mihuta@griffithuni.edu.au

Why is the research being conducted?
This research is being conducted as part of the requirements for a Doctor of Philosophy in Clinical Psychology for Mary Mihuta. The research will help to find out whether an online intervention can help cancer survivors improve cognitive functions, such as memory and concentration. The study builds on previous research that has shown cognitive rehabilitation interventions can help to improve areas of cognition, including problems with memory and concentration. All information collected for this study is confidential.

What you will be asked to do
If you agree to participate in the research, you will be participating in study 1 (pilot study) or study 2 (main study). If you are participating in the pilot study, you will be allocated to either the cancer survivor group (A), non-cancer group (B), or non-cancer waitlist group (C). You will be participating in an online intervention, which consists of 4 modules that you will complete over the course of 4 weeks. Each module will take you about 60 minutes to complete, and they will teach you about cognitive functions and provide you with some skills and practical exercises to practice at home. You will be emailed a link with a username and password and instructions on how to access the intervention website. In addition, you will complete 3 online assessments consisting of questionnaires and standard computerised tasks which will take you about 60 minutes to do. These will be completed prior to beginning the intervention, upon completion of the intervention, and again at a 3-month follow-up interval. If you are participating in the main study, you will be assigned at random to one of two groups: the treatment group (D) or the waitlist group (E). If you are assigned to Group D, you will be completing the same online rehabilitation interventions as Groups A and B outlined above. If you are assigned to Group E you will complete the online questionnaires and standard computerised tasks at the same time intervals as Group D, and you will be provided with access to the online intervention after you have finished all assessments.

The basis by which participants will be selected or screened
The pilot study is for adults aged 18 years or over who have previously been diagnosed with cancer in adulthood (excluding primary and secondary brain tumours) and for
healthy adults without a history of cancer. If you have a history of cancer, you can take part in this study if you have completed all treatments and are not waiting for any further treatment (such as chemotherapy, surgery or radiotherapy) and if your only current treatment is a hormone therapy such as Tamoxifen or Zoladex. If you are over age 18 and never been diagnosed with cancer before, then you are also eligible to participate. The main study is for adults with a history of cancer in adulthood (excluding primary and secondary brain tumours) who have completed all treatments (current hormone therapy is acceptable). If you are not sure about whether you can take part, please discuss it with the researcher.

The expected benefits of the research
This research will help the researchers to assess whether an online cognitive rehabilitation program helps individuals who have been treated for cancer to improve their cognitive functioning. As the study is being conducted to see if the treatment is helpful, it may or may not have these benefits for you. Once you have completed the whole study, you will be able to receive feedback on your individual results from the research team if desired.

Risks to you
Some people may find it mildly challenging or stressful to do some of the tests or treatment tasks. You may take breaks when needed or stop at any time if you no longer wish to continue. If you continue to feel distressed afterwards you may contact Dr Green or telephone the free Cancer Helpline on 13 11 20 (available 8 am to 8 pm, Monday to Friday) for support.

Your confidentiality
All information collected for this study is confidential. The computerised results from your tests will be stored in a database that does not contain any identifying information. Your name will be recorded only for the purposes of matching up the data and so that you can receive individual feedback if you request this. Computerised data from this study, including the code for matching names with results, will be stored securely for 5 years past the end of the year of the final publication from this study and will then be destroyed. Your individual information will not be able to be identified in any reports resulting from this research.

Your participation is voluntary
Your participation is voluntary. You are free to withdraw from the study at any time.

Questions / further information
If you need any additional information, you may contact Dr Green (contact details on page 1).

The ethical conduct of this research
Griffith University conducts research in accordance with the National Statement on the Ethical Conduct of Human Research (2007). If potential participants have any concerns or complaints about the ethical conduct of the research project they should contact the Manager, Research Ethics on 3735 5585 or research-ethics@griffith.edu.au

Feedback to you
If you would like individual feedback on your test scores after you have finished the study, please contact Dr Heather Green via email h.green@griffith.edu.au or (07) 5678 9086.
Privacy Statement
Please note that the Commonwealth Privacy Commissioner has classified opinions as personal information. The conduct of this research involves the collection, access and/or use of your identified personal information. As outlined elsewhere in this information sheet, your identified personal information may appear in the publications/reports arising from this research. This is occurring with your consent. Any additional personal information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal or other regulatory authority requirements. A de-identified copy of this data may be used for other research purposes. However, your anonymity will at all times be safeguarded, except where you have consented otherwise. For further information consult the University’s Privacy Plan at http://www.griffith.edu.au/about-griffith/plans-publications/griffith-university-privacy-plan or telephone (07) 3735 4375.
APPENDIX F

Consent Form

An Online Intervention to Target Cognitive Impairments Associated with Cancer and Cancer Treatments

Research Team
Name: Dr Heather Green & Ms Mary Mihuta
School / Centre: School of Applied Psychology & Behavioural Basis of Health Program
Contact Phone: (07) 5678 9086
Contact Email: h.green@griffith.edu.au or mary.mihuta@griffithuni.edu.au

I have read and understood the information package and in particular have noted that:

- I understand that my involvement in this research will include participating in 3 online assessment sessions, and completing 4 online treatment modules lasting 1 hour each if I am chosen for Group A, B, or D. If I am chosen for Group C or E, I will complete the 3 online assessment sessions and will be able to complete the 4 treatment modules when I have finished the assessment sessions, and;
- I have had any questions answered to my satisfaction;
- I understand the risks involved;
- I understand that there will be no direct benefit to me from my participation in this research;
- I understand that my participation in this research is voluntary;
- I understand that if I have any additional questions I can contact the research team;
- I understand that I am free to withdraw at any time, without comment or penalty;
- I understand that I can contact the Manager, Research Ethics, at Griffith University Human Research Ethics Committee on 3735 4375 (or research-ethics@griffith.edu.au) if I have any concerns about the ethical conduct of the project; and
- I agree to participate in the project.

Participation in this research project requires your **verbal** or **written** consent, which will be obtained by the research team prior to the commencement of your participation. The details of your consent will be recorded by the research team [see below].

On [date] _____________________, at [time] ____________________, participant [name] __________________________ read or had read to him/her the participant information/verbal consent script, confirmed they understood the nature of the research and their participation, and agreed to proceed with the interview.
APPENDIX G

Broadcast Email Study Two

Dear (Name)

Women affected by breast cancer may experience a number of cancer-related side effects, including trouble with concentration, multi-tasking and memory.

Researchers at Griffith University have developed a four-week online, interactive program, which aims to improve cancer-related cognitive issues such as memory and concentration.

**Who can participate?** You are eligible to participate if you:
- Are over 18 years
- Have been diagnosed with cancer during adulthood
- Have completed active treatment (surgery and/or chemotherapy and/or radiotherapy)
- You are eligible to participate if you are currently receiving hormone therapy (e.g. tamoxifen, Arimidex, Femara, Aromasin)
- Have access to a computer with the Internet
- Have an active email account.

**What's involved in the study?** If you participate in the study, you will be 'randomly assigned' to one of two groups. Being “randomly assigned” means that you have an equal chance of being selected for each group.

Group 1: If you are allocated to the first group, you will begin participating in the online program immediately. The program has four modules, each of which will take about 60 minutes to complete.

You will also be asked to complete three assessments, which involve answering an online survey and completing some computerised tasks. You will be asked to take the first assessment before starting the program, the second assessment at the end of the four week program, and the third assessment three months after you finish the program.

Group 2: If you are allocated to the second group, you will be asked to complete the three assessments, which involve answering an online survey and completing some computerised tasks. After you complete the three assessments, you will be able to participate in the 4-week program.

**How to participate?** If you are interested in being involved, please contact Dr Heather Green on h.green@griffith.edu.au or Ms Mary Mihuta on mary.mihuta@griffithuni.edu.au to indicate you would like to participate in the project. For more information, please see the Participant Information Statement.
### APPENDIX H

**Study One Questionnaire Results**

**Table H.1**

*Study One outcomes on self-report questionnaires*

<table>
<thead>
<tr>
<th></th>
<th>Cancer Group (n = 12)</th>
<th>Non-Cancer Treatment Group (n = 16)</th>
<th>Non-Cancer Waitlist Group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
</tr>
<tr>
<td>FACT-Cog 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived cognitive impairments</td>
<td>33.8 (18.7)</td>
<td>42.3 (18.3)**</td>
<td>42.8 (18.2)*</td>
</tr>
<tr>
<td>Perceived cognitive abilities</td>
<td>13.3 (5.2)</td>
<td>15.8 (7.1)</td>
<td>15.7 (6.6)</td>
</tr>
<tr>
<td>Comments from others</td>
<td>13.8 (2.1)</td>
<td>14.7 (1.4)</td>
<td>13.8 (3.0)</td>
</tr>
<tr>
<td>Impact on quality of life</td>
<td>9.3 (5.5)</td>
<td>11.8 (4.7)</td>
<td>11.3 (5.2)</td>
</tr>
<tr>
<td>BAPM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instrumental activities daily life</td>
<td>2.50 (0.78)</td>
<td>2.28 (0.59)</td>
<td>1.95 (0.46)*</td>
</tr>
<tr>
<td>Basic activities of daily life</td>
<td>1.67 (0.73)</td>
<td>1.46 (0.48)</td>
<td>1.35 (0.36)*</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global health quality of life</td>
<td>63.9 (21.7)</td>
<td>70.8 (23.7)</td>
<td>62.5 (26.0)</td>
</tr>
<tr>
<td>Physical function</td>
<td>79.4 (17.9)</td>
<td>83.9 (12.5)</td>
<td>80.0 (16.1)</td>
</tr>
<tr>
<td>Role function</td>
<td>76.4 (27.9)</td>
<td>80.6 (30.8)</td>
<td>69.4 (30.0)</td>
</tr>
<tr>
<td>Emotion function</td>
<td>66.0 (21.5)</td>
<td>68.8 (16.7)</td>
<td>69.4 (25.0)</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>54.2 (21.5)</td>
<td>69.4 (23.4)*</td>
<td>61.1 (29.6)</td>
</tr>
<tr>
<td>Social function</td>
<td>62.5 (28.5)</td>
<td>77.8 (29.6)</td>
<td>70.8 (22.6)</td>
</tr>
<tr>
<td>Symptoms of fatigue</td>
<td>45.4 (28.2)</td>
<td>44.4 (25.9)</td>
<td>43.5 (23.4)</td>
</tr>
<tr>
<td>Symptoms of pain</td>
<td>41.7 (28.0)</td>
<td>43.1 (33.7)</td>
<td>31.9 (32.9)</td>
</tr>
<tr>
<td>Symptoms of insomnia</td>
<td>44.4 (29.6)</td>
<td>44.4 (32.8)</td>
<td>36.1 (33.2)</td>
</tr>
<tr>
<td>Symptoms of finance difficulties</td>
<td>47.2 (43.7)</td>
<td>22.2 (25.9)*</td>
<td>41.7 (37.9)</td>
</tr>
<tr>
<td>K10 Psychological distress</td>
<td>19.9 (7.3)</td>
<td>18.3 (5.5)</td>
<td>18.6 (6.7)</td>
</tr>
<tr>
<td>Brief illness perception questionnaire</td>
<td>44.2 (12.5)</td>
<td>41.8 (8.6)</td>
<td>41.2 (12.9)</td>
</tr>
<tr>
<td>Autonomy</td>
<td>34.6 (6.7)</td>
<td>33.9 (5.9)</td>
<td>35.8 (6.1)</td>
</tr>
<tr>
<td>Competence</td>
<td>28.0 (6.4)</td>
<td>29.1 (5.7)</td>
<td>28.7 (5.6)</td>
</tr>
<tr>
<td>Relatedness</td>
<td>40.5 (8.6)</td>
<td>41.8 (7.6)</td>
<td>43.3 (6.7)</td>
</tr>
</tbody>
</table>

*Note.*** p < .001, ** p < .01, * p < .05*
### APPENDIX I

#### Study Two Questionnaire Results

**Table I.1: Study Two outcomes on self-report questionnaires**

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group ($n = 32$)</th>
<th>Waitlist Control Group ($n = 33$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td>FACT-Cog 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perceived cognitive impairments</td>
<td>41.6 (15.4)</td>
<td>44.1 (14.8)</td>
</tr>
<tr>
<td>Perceived cognitive abilities</td>
<td>15.6 (5.4)</td>
<td>17.2 (4.9)**</td>
</tr>
<tr>
<td>Comments from others</td>
<td>14.9 (1.9)</td>
<td>14.6 (2.4)</td>
</tr>
<tr>
<td>Impact on quality of life</td>
<td>11.9 (4.4)</td>
<td>13.1 (3.0)**</td>
</tr>
<tr>
<td>BAPM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instrumental activities daily life</td>
<td>2.05 (0.58)</td>
<td>1.78 (0.46)**</td>
</tr>
<tr>
<td>Basic activities of daily life</td>
<td>1.28 (0.26)</td>
<td>1.19 (0.34)*</td>
</tr>
<tr>
<td>EORTC QLQ-C30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global health quality of life</td>
<td>74.2 (19.7)</td>
<td>77.3 (15.3)</td>
</tr>
<tr>
<td>Physical function</td>
<td>86.5 (12.4)</td>
<td>87.1 (12.3)</td>
</tr>
<tr>
<td>Role function</td>
<td>91.1 (18.9)</td>
<td>90.1 (17.4)</td>
</tr>
<tr>
<td>Emotion function</td>
<td>68.8 (22.0)</td>
<td>71.6 (22.8)</td>
</tr>
<tr>
<td>Cognitive function</td>
<td>64.1 (23.6)</td>
<td>70.8 (18.0)*</td>
</tr>
<tr>
<td>Social function</td>
<td>77.6 (28.9)</td>
<td>79.2 (28.1)</td>
</tr>
<tr>
<td>Symptoms of fatigue</td>
<td>31.9 (19.5)</td>
<td>27.1 (15.7)*</td>
</tr>
<tr>
<td>Symptoms of pain</td>
<td>22.4 (23.0)</td>
<td>20.8 (24.7)</td>
</tr>
<tr>
<td>Symptoms of insomnia</td>
<td>43.8 (32.2)</td>
<td>42.7 (37.1)</td>
</tr>
<tr>
<td>Symptoms of financial difficulties</td>
<td>30.2 (37.3)</td>
<td>21.9 (34.5)**</td>
</tr>
<tr>
<td>K10 Psychological distress</td>
<td>16.3 (6.1)</td>
<td>16.3 (6.5)</td>
</tr>
<tr>
<td>Brief illness perception questionnaire</td>
<td>39.0 (11.9)</td>
<td>39.7 (11.4)</td>
</tr>
<tr>
<td>Autonomy</td>
<td>36.9 (5.7)</td>
<td>38.4 (6.5)*</td>
</tr>
<tr>
<td>Competence</td>
<td>28.2 (4.8)</td>
<td>29.6 (5.1)</td>
</tr>
<tr>
<td>Relatedness</td>
<td>45.5 (7.4)</td>
<td>45.2 (7.5)</td>
</tr>
</tbody>
</table>

*Note.*** $p < .001$, ** $p < .01$, * $p < .05$*
## APPENDIX J

**Study One WebNeuro Results**

### Study One outcomes on WebNeuro online test battery of objective cognitive functioning

<table>
<thead>
<tr>
<th></th>
<th>Cancer Group (n = 12)</th>
<th>Non-Cancer Treatment Group (n = 16)</th>
<th>Non-Cancer Waitlist Group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
</tr>
<tr>
<td><strong>Verbal Memory</strong></td>
<td>0.07 (0.66)</td>
<td>0.04 (0.55)</td>
<td>-0.50 (1.12)</td>
</tr>
<tr>
<td>Immediate recognition</td>
<td>57.2 (3.2)</td>
<td>57.3 (2.1)</td>
<td>54.4 (5.4)</td>
</tr>
<tr>
<td>Delayed recognition</td>
<td>19.1 (1.1)</td>
<td>19.0 (1.2)</td>
<td>18.1 (2.4)</td>
</tr>
<tr>
<td><strong>Working Memory</strong></td>
<td>-0.12 (0.79)</td>
<td>-0.06 (1.05)</td>
<td>-0.08 (0.95)</td>
</tr>
<tr>
<td>Recall span (digits)</td>
<td>6.83 (1.12)</td>
<td>6.92 (1.44)</td>
<td>6.75 (1.29)</td>
</tr>
<tr>
<td>Recall total</td>
<td>8.17 (2.13)</td>
<td>8.25 (2.60)</td>
<td>8.50 (2.43)</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>-0.71 (0.91)</td>
<td>-0.37 (0.62)</td>
<td>-0.30 (0.58)*</td>
</tr>
<tr>
<td>Reaction time (CPT)</td>
<td>593 (124)</td>
<td>556 (81)</td>
<td>558 (77)</td>
</tr>
<tr>
<td>Omission errors (CPT)</td>
<td>1.00 (1.60)</td>
<td>0.50 (0.90)</td>
<td>0.33 (0.65)</td>
</tr>
<tr>
<td><strong>Executive Function</strong></td>
<td>0.46 (0.63)</td>
<td>0.77 (0.72)</td>
<td>0.77 (0.70)</td>
</tr>
<tr>
<td>Maze completion time</td>
<td>261 (109)</td>
<td>205 (76)**</td>
<td>204 (89)**</td>
</tr>
<tr>
<td>Maze overrun errors</td>
<td>11.3 (5.4)</td>
<td>12.0 (9.3)</td>
<td>12.1 (6.7)</td>
</tr>
<tr>
<td><strong>Info Processing</strong></td>
<td>-0.11 (0.62)</td>
<td>-0.16 (0.56)</td>
<td>-0.21 (0.67)</td>
</tr>
<tr>
<td>Completion time</td>
<td>57.3 (15.2)</td>
<td>51.3 (14.2)**</td>
<td>50.9 (17.5)*</td>
</tr>
<tr>
<td>Reaction time (CRT)</td>
<td>431 (89)</td>
<td>414 (68)</td>
<td>425 (73)</td>
</tr>
<tr>
<td>Correct word (VIT)</td>
<td>16.2 (5.3)</td>
<td>10.9 (6.8)**</td>
<td>11.0 (5.3)**</td>
</tr>
<tr>
<td>Correct colour (VIT)</td>
<td>10.6 (2.9)</td>
<td>11.8 (3.7)</td>
<td>11.5 (5.1)</td>
</tr>
<tr>
<td><strong>Response Speed</strong></td>
<td>0.27 (0.85)</td>
<td>0.36 (0.81)</td>
<td>0.42 (0.75)</td>
</tr>
<tr>
<td>Number of taps</td>
<td>188 (25)</td>
<td>189 (25)</td>
<td>190 (25)</td>
</tr>
<tr>
<td>SD time between taps</td>
<td>18.7 (8.1)</td>
<td>18.0 (9.5)</td>
<td>17.5 (9.7)</td>
</tr>
<tr>
<td><strong>Impulsivity</strong></td>
<td>-0.36 (0.30)</td>
<td>-0.32 (0.26)</td>
<td>-0.30 (0.42)</td>
</tr>
<tr>
<td>Go/No-Go speed</td>
<td>341 (48)</td>
<td>322 (56)</td>
<td>328 (57)</td>
</tr>
<tr>
<td>Commission errors</td>
<td>4.08 (3.00)</td>
<td>4.58 (2.87)</td>
<td>4.50 (3.40)</td>
</tr>
</tbody>
</table>

*Note.*** p < .001, ** p < .01, * p < .05; CPT = continuous performance test, CRT = choice reaction time, VIT = verbal interference task, SD = standard deviation.*
## APPENDIX K

### Study Two WebNeuro Results

**Table K.1**  
*Study Two outcomes on WebNeuro online test battery of objective cognitive functioning*

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group (n = 32)</th>
<th>Waitlist Control Group (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
</tr>
<tr>
<td><strong>Verbal Memory</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate recognition</td>
<td>0.07 (0.71)</td>
<td>0.02 (0.66)</td>
</tr>
<tr>
<td>Delayed recognition</td>
<td>56.4 (4.0)</td>
<td>56.5 (3.2)</td>
</tr>
<tr>
<td><strong>Working Memory</strong></td>
<td>-0.34 (1.04)</td>
<td>-0.35 (1.08)</td>
</tr>
<tr>
<td>Recall span (digits)</td>
<td>6.34 (1.64)</td>
<td>6.34 (1.41)</td>
</tr>
<tr>
<td>Recall total</td>
<td>7.69 (2.46)</td>
<td>7.66 (2.73)</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction time (CPT)</td>
<td>-0.24 (0.80)</td>
<td>-0.15 (0.85)</td>
</tr>
<tr>
<td>Omission errors (CPT)</td>
<td>543 (104)</td>
<td>547 (112)</td>
</tr>
<tr>
<td><strong>Executive Function</strong></td>
<td>0.56 (0.95)</td>
<td>0.34 (0.70)</td>
</tr>
<tr>
<td>Maze completion time</td>
<td>-0.20 (0.66)</td>
<td>0.54 (0.69)**</td>
</tr>
<tr>
<td>Maze overrun errors</td>
<td>331 (87)</td>
<td>269 (81)**</td>
</tr>
<tr>
<td><strong>Info Processing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion time</td>
<td>58.7 (14.1)</td>
<td>57.4 (14.0)</td>
</tr>
<tr>
<td>Reaction time (CRT)</td>
<td>451 (77)</td>
<td>423 (70)</td>
</tr>
<tr>
<td>Correct words (VIT)</td>
<td>15.4 (3.7)</td>
<td>10.9 (5.4)**</td>
</tr>
<tr>
<td>Correct colour (VIT)</td>
<td>10.0 (3.8)</td>
<td>9.7 (4.0)</td>
</tr>
<tr>
<td><strong>Response Speed</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of taps</td>
<td>-0.03 (1.12)</td>
<td>-0.19 (1.20)</td>
</tr>
<tr>
<td>SD time between taps</td>
<td>174 (24)</td>
<td>171 (28)</td>
</tr>
<tr>
<td><strong>Impulsivity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go/No-Go speed</td>
<td>26.9 (40.2)</td>
<td>28.4 (45.3)</td>
</tr>
<tr>
<td>Commission errors</td>
<td>6.46 (0.41)</td>
<td>-0.23 (0.41)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note.* ***p < .001, **p < .01, *p < .05; CPT = continuous performance test, CRT = choice reaction time, VIT = verbal interference task, SD = standard deviation.*