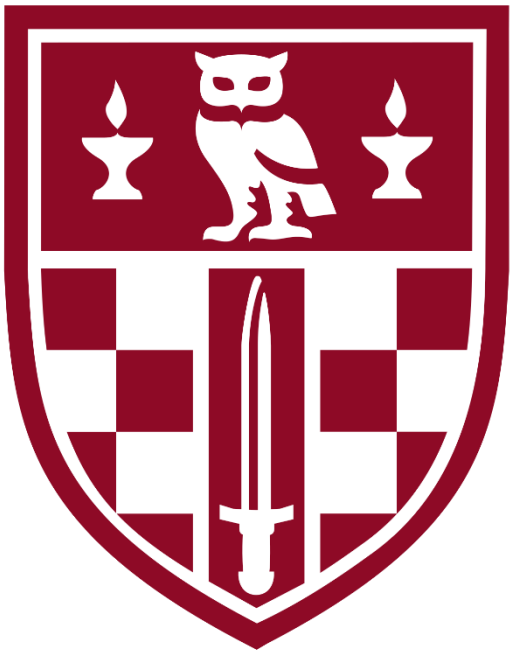
# Investigating the efficacy of adaptive cognitive training and understanding the role of work-related factors on the cognitive and emotional health of women with a history of breast cancer

# Investigating the efficacy of adaptive cognitive training and understanding the role of work-related factors on the cognitive and emotional health of women with a history of breast cancer

**Bethany Louise Chapman**

A thesis submitted for the degree of Doctor of Philosophy (PhD) in the Department of Psychological Sciences

Birkbeck, University of London



# Declaration.

‘I, Bethany Louise Chapman, confirm the work presented in this thesis is my own’.

Date: 22nd of August 2022

# Acknowledgements

I would first like to thank my primary supervisor Professor Nazanin Derakshan who encouraged me from the start and gave me the amazing opportunity to write and apply for an ESRC grant to fund my PhD research. I would also like to thank you for your invaluable support, inspiration, and guidance, as well as the generosity of your knowledge and time throughout my PhD. Naz, you truly are an inspiration! I would also like to thank my second supervisor Professor Beth Grunfeld who has provided me with incredible guidance and support throughout my PhD, particularly when it came to conducting my first piece of qualitative research. Further, I am immensely grateful to Jason Moser and Courtney Louis for sharing their expertise in analysing ERP data. I also owe a special thanks to Jessica Swainston and Trish Beloe for supporting my early EEG training and to Alex, Ryan, Delia and Lou for helping with my EEG testing sessions.

My thesis would not have been possible without the women who kindly gave up their time to participate in my studies, to these women I would like to say a massive thank you! I am also incredibly grateful to the many online breast cancer support groups who generously advertised my research studies and encouraged their members to take part. I would also like to say thank you to the amazing team at the Birkbeck Centre for Building Resilience in Breast Cancer (BRiC) who voluntarily offer their time to help support women living with a diagnosis of primary or secondary breast cancer in the UK.

Finally, thank you to my amazing family and friends who have unreservedly supported and encouraged me throughout this four-year journey. I would especially like to thank my wonderful parents Andrew and Deryn, sister Amber and brothers Jake and Liam, who have always believed in me and always told me to never give up! I could not have achieved this without you!

The work presented in this thesis was funded by an Economic and Social Research Council grant (Grant reference: ES/P000592/1) (https://esrc.ukri.org/).

The thesis includes work that appears in the following papers:

## Chapter 3:

Chapman, B., Derakshan, N., & Grunfeld, E. A. (2021). Exploring primary breast cancer survivor's self-management of sustained cancer-related cognitive impairment in the workplace. *Psycho-Oncology*. https://doi.org/10.1002/pon.5844

## Chapter 4:

Chapman, B., Derakshan, N., & Grunfeld, E. A. (accepted in BJHP). Experiences of cognitive training on primary breast cancer survivor's cognitive impairments at work: A longitudinal qualitative study. *British Journal of Health Psychology*.

## Chapter 5:

Chapman, B., Louis, C. C., Moser, J., Grunfeld, E. A., & Derakshan, N. (In preparation). A randomised control trial on the efficacy of adaptive cognitive training as an intervention to help breast cancer survivors improve and sustain their workability.

## Chapter 6:

Chapman, B., Grunfeld, E. A., Derakshan, N. (2022). Quality of working life can protect against cognitive and emotional vulnerability in women living with metastatic breast cancer: A cross-sectional study. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-022-01169-0

**Chapter 7**: (Chapman & Swainston share the first authorship)

Swainston, J., Chapman, B., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 Lockdown and its adverse impact on psychological health in breast cancer. *Frontiers in Psychol.* 11:2033. http://doi:10.3389/fpsyg.2020.02033.

## Chapter 7:

Chapman, B., Swainston, J., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 outbreak effects on job security and emotional functioning amongst women living with breast cancer. *Frontiers in Psychol.* 11:582014. doi: 10.3389/fpsyg.2020.582014.

During my PhD, I also contributed to the following work:

Choobim, M. H., Mirabolfathi, V., Chapman, B., Moradi, A. R., Grunfeld, E. A., & Derakshan, N. (2021). The impact of COVID-19 outbreak on emotional and cognitive vulnerability in Iranian women with breast cancer. *Frontiers in Psychol.* 12: 663310. doi: 10.3389/fpsyg.2021.663310.

# Abstract

Worldwide breast cancer is the most common form of cancer diagnosed in women, with more than 150 new cases each day in the UK alone. The overall aim of this PhD thesis was to provide a more comprehensive understanding of how cognitive function and emotional vulnerability (anxiety and depression) relate to workability and work-related factors in women diagnosed with breast cancer, as well as ascertain the longer-term efficacy of adaptive cognitive training (see box 1) to empower women's workability which is known to be crucial in promoting better cognitive and emotional health. This PhD thesis was two-fold. A mixed-methods approach was utilised. First, this thesis will present and discuss the 'BRiCatWork' study which aimed to examine the efficacy of adaptive dual *n*-back training as an intervention for helping women affected by primary breast cancer sustain workability over time by targeting impaired cognitive function. To this end, the study also investigated women's experiences with sustained cancer-related cognitive impairment (CRCI) and its impact at work before receiving the intervention. This thesis will then go on to present a study that aimed to investigate the role of quality of working life in predicting perceived cognitive impairment and anxiety and depression in women with metastatic breast cancer (MBC), a population who are understudied and minimised in society. As a result of the Coronavirus disease (COVID-19) outbreak during this PhD, the final study focused on exploring the impact of COVID-19 on cognitive and emotional health.

Findings from the 'BRiCatWork' study are outlined in **Chapters 3**, **4**, and **5**. **Chapter 3** found women can experience CRCI up to five years after active treatment, adversely affecting their workability. Women had mixed experiences and feelings with self-management coping strategies. **Chapter 4** found women who received dual *n*-back training perceived experiencing sustained improvements in their cognitive functioning. These perceived improvements were associated with self-confidence and emotional wellbeing, as well as dependency on work-related self-management methods for cognitive impairment and career progression or development, increasing workability. In addition, findings revealed that women found dual *n*-back training to be highly engaging, with experiences indicating that dual *n*-back training can be flexibly offered six- to 12 months after active treatment. **Chapter 5** evidenced that dual *n*-back training elicited improvements in perceived cognitive ability and

workability, as well as in transfer-related gains in depression, with effects sustained up to one year. Significant increases in working memory capacity and P3 amplitude, as well as a reduction in post-error slowing, were also found. The 'BRiCatWork' study corroborates that dual *n*-back training can be offered to women treated for primary breast cancer to promote cognitive functioning and workability, as well as reduce vulnerability to depression, a known risk factor for recurrence and premature mortality.

**Chapter 6** found women's experiences with their employers following their MBC diagnosis was associated with their perceived quality of working life, such that a better experience met with a greater quality of working life. Importantly, a greater self-reported quality of working life predicted a better perceived cognitive function and quality of life, as well as reduced vulnerability to depression. **Chapter 7** found women affected by primary breast cancer may be at an increased risk for developing more severe emotional distress and poorer perceived cognitive functioning as a result of the COVID-19 outbreak. Taken together, the studies presented in **Chapters 6** and **7** indicate that work-related factors including job security and quality of working life play an important role in protecting against escalating cognitive and emotional vulnerability in women diagnosed with breast cancer.

Overall, this thesis has made important contributions to theory as well as method while providing strong implications for informing oncologists and oncology services including occupational health, as well as employers, on supporting women diagnosed with breast cancer in sustaining their workability over time.

# Table of Contents

# Abbreviations

| | |
|---|---|
| **ACC** | Anterior cingulate cortex |
| **AD** | Alzheimer's disease |
| **AIs** | Aromatase inhibitors |
| **ANOVA** | Analysis of variance |
| **CBT** | Cognitive behavioural therapy |
| **CCI** | Charlson Comorbidity Index |
| **CDT** | Change Detection Task |
| **CES-D** | Center for Epidemiologic Studies Depression Scale |
| **CFO** | Comments from others |
| **COVID-19** | Coronavirus disease 2019 |
| **CRCI** | Cancer-related cognitive impairment |
| **CRF** | Cancer-related fatigue |
| **CRN** | Correct-response negativity |
| **DCIS** | Ductal carcinoma in situ |
| **DLPFC** | Dorsolateral prefrontal cortex |
| **DMN** | Default mode network |
| **EEG** | Electroencephalogram |
| **EOG** | Electrooculogram |
| **EORTC-QLQ-C30** | European Organization for Research and Treatment of Cancer Quality of Life |
| **ERN** | Error-related negativity |
| **ER+** | Oestrogen receptor-positive |
| **FACT-Cog** | Functional Assessment of Cancer Therapy-Cognitive Scale |
| **GM** | Gray matter |
| **IDC** | Invasive ductal carcinoma |
| **HADS** | Hospital Anxiety and Depression Scale |

| | |
|---|---|
| **HER2+** | Human epidermal growth factor receptor 2 |
| **HPA** | Hypothalamus-pituitary-adrenal |
| **HRT** | Hormone replacement therapy |
| **ILC** | Invasive lobular carcinoma |
| **ITT** | Intention-to-treat |
| **MBC** | Metastatic breast cancer |
| **MLM** | Multilevel modelling |
| **MRI** | Magnetic resonance imaging |
| **NST** | No special type |
| **NOS** | Not otherwise specified |
| **OPSAN** | Operation Span Task |
| **PCC** | Posterior cingulate cortex |
| **Pe** | Error Positivity |
| **PPC** | Posterior parietal cortex |
| **PCA** | Perceived cognitive ability |
| **PCI** | Perceived cognitive impairment |
| **PROM** | Patient report outcome measure |
| **PP** | Per-protocell |
| **PSWQ** | Penn State Worry Questionnaire |
| **PTSD** | Post-traumatic stress disorder |
| **QoL** | Quality of life |
| **QWLQ-CS** | Quality of Working Life for Cancer Survivors |
| **RCT** | Randomised control trial |
| **rIFG** | Right inferior frontal gyrus |
| **RRS** | Rumination Response Scale |
| **RT** | Reaction time |
| **RTW** | Return-to-work |

| | |
|---|---|
| **SBC** | Secondary breast cancer |
| **SERMs** | Selective oestrogen receptor modulators |
| **SD** | Standard deviation |
| **TBV** | Total brain volume |
| **TNM** | Tumour, Node, Metastasis |
| **UK** | United Kingdom |
| **WMC** | Working memory capacity |
| **WM** | Working memory |
| **WLQ** | Work Limitations Questionnaire |
| **WPAI: SHP** | Work Productivity and Activity Impairment Questionnaire: Specific Health Problem |
| **WPEQ** | Workplace Experience Questions |
| **5-HT** | Five hydroxyl tryptophan |

# List of Figures

## Chapter 2:



## Chapter 3:



## Chapter 4:



## Chapter 5:

## Chapter 6:

### Chapter 7:



# List of Tables

### Chapter 3:



### Chapter 5:



### Chapter 6:

## Chapter 7:

# **Chapter 1:** General Introduction

## 1.1. **Chapter Overview**

The current chapter will start by providing an overview of breast cancer including epidemiology, diagnosis and treatment to give context and facilitate the comprehension of the terminology used in the studies presented throughout this thesis. The chapter will then proceed to describe the impact of breast cancer diagnosis and treatment, presenting literature on the prominent cancer-related sequelae including fatigue, emotional distress and cancer-related cognitive impairment (CRCI) impacting the everyday quality of life and work-related outcomes such as workability and work productivity. Following this, the chapter will introduce literature focusing on coping methods and cognitive training interventions implemented in the breast cancer population to target cognitive impairment and cancer-related sequelae including the adaptive dual *n*-back training task a central method implemented in the 'BRiCatWork' study presented in **Chapters 3, 4** and **5** (see **box 1** below for a description of dual *n*-back training**)**. Finally, an overview of the existing interventions and work-based adaptions utilised to support work-related outcomes in women living with a history of breast cancer will be presented. This chapter will conclude with a thesis outline and summaries for the remaining chapters.

**Box 1**: Dual *n*-back training and dual 1-back training

Standard versions of the dual *n*-back training and dual 1-back training were utilised in the study presented in this thesis. During each trial, a single green square appeared in one of eight positions on a 3x3 grid accompanied by a single spoken letter consonant. Participants were asked to remember both the location of the green square and its paired spoken consonant and respond using the keyboard.

Task difficulty for dual *n*-back training adapted depending on average accuracy for both stimuli on the previous block of trials (1-back, 2-back, 3-back, 4-back). In contrast, the task difficulty for dual 1-back training (active control) remained unchanged regardless of performance accuracy (see **Chapter 1 section 1.6.3** and **Chapter 2 section 2.9** for a more comprehensive description of training).

## 1.2. **Breast Cancer: Epidemiology, Type and Risk Factors**

As it stands, breast cancer is the most prevalent malignancy diagnosed worldwide, accounting for 11.7% of all new cancer cases (World Health Organization, 2020). In the United Kingdom (UK), a breast cancer diagnosis is received every 10 minutes (Breast Cancer Now, 2021), a figure that is expected to continuously increase due to advances in screening and a longer lifespan. Breast cancer is also the leading cause of death in women under the age of 50 in the UK (Breast Cancer Now, 2021). Over the last four decades, the number of women surviving primary breast cancer has doubled, with recent figures showing that 85% will survive at least five years after diagnosis. It is predicted that approximately 1.2 million women in the UK will be living with a diagnosis of breast cancer by 2030 (Breast Cancer Now, n.d.). Improvements in the rate of long-term survivorship have been attributed to a range of factors including advances in screening technology, earlier detection, as well as more efficient diagnosis and treatment (e.g., multimodality treatment programs).

Breast cancer is defined by the formation of abnormal cells that grow uncontrollably and divide beyond their usual boundaries to form a (benign or cancerous) tumour. Most forms of breast cancers start in the cells lining the ducts or lobes of the breast before spreading into the neighbouring breast tissue. Ductal carcinoma in situ (DCIS) is a pre-invasive or non-invasive form of cancer diagnosed when the cancer cells are contained within the ducts or lobules of the breast. DCIS is the earliest form of diagnoseable breast cancer and is most commonly detected during routine screening (i.e., a mammogram), as most women show no visible symptoms (Macmillan, 2018a). If it is left untreated DCIS can, however, become invasive. Invasive breast cancer is diagnosed when the cancer cells have spread beyond the ducts or lobules into the surrounding breast tissue and/or lymph nodes, this requires prompt treatment to prevent spreading (metastasising) to distant regions of the body.

Approximately 70% of invasive tumours diagnosed in women are invasive ductal carcinoma (IDC) also known as invasive carcinoma of no special type (NST) or breast cancer not otherwise specified (NOS), this is because when examined the cancer cells show no special (differentiating) features. Much like DCIS many cases of NST (or IDC) are detected through routine screening, however,

it is more common to notice visible symptoms such as changes or differences on or around the breasts, for example, a lump, change in size or shape or change in skin texture (i.e., dimpling). There are also many special types or rarer forms of breast cancer that can be diagnosed. The most prevalent is invasive lobular carcinoma (ILC), accounting for approximately 15%. Younger women between the ages of 45 and 55 are most likely to receive a diagnosis of ILC (Cancer Research UK, 2020a).

Both non-invasive and invasive breast cancer is defined by the stage (i.e., size of cancer and spreading) and grade (i.e., the severity of difference in abnormal cells compared to healthy cells) of the cancer cells. In the UK there are many staging systems used, however, the most common is the TNM (Tumour, Node, Metastasis) and number staging where stage 0 refers to DCIS and invasive cancer ranges from stage 1 to 4. Stage 4 denotes that the cancer cells have metastasised (spread) beyond the sentinel nodes of the breast to other distant regions of the body including, the visceral organs such as the brain, lungs, liver or bones (Macmillan, 2018b). Stage 4 breast cancer is interchangeably referred to as secondary breast cancer (SBC), advanced cancer, and metastatic breast cancer (MBC) which is incurable. One in three women with a diagnosis of primary breast cancer will go on to develop MBC despite the advances in treatment and early screening (Breast cancer org, 2022). A diagnosis of "*de novo"* MBC is given to approximately 5% of women when the cancer cells have spread beyond the breast before detection (i.e., there is no primary diagnosis) (Breast Cancer Now, 2021). Primary breast cancer can be graded as low (grade 1), intermediate (grade 2) or high (grade 3) depending on the ability to differentiate between cancer cells and healthy cells. High grade represents cancer cells that are significantly different and have much faster growth and spreading rate. In clinical practice, both stage and grade are used to guide the program of treatment administered and provide statistics for prognosis.

Multiple biological, genetic and lifestyle factors have been associated with an increased risk of developing breast cancer. The greatest risk factor for women is their age followed by inheriting either the BRCA1 or BRCA2 (BReast CAncer) gene, for example, 55% to 72% of women carrying the mutated BRCA1 gene will develop breast cancer by the age of 80 (National Cancer Institute, 2020).

## 1.3. **Treatment**

Most commonly women diagnosed with breast cancer receive multimodality treatment which may include, surgical procedure(s), chemotherapy and radiation, as well as more long-term daily anti-oestrogen (i.e., hormone or endocrine therapy) medications such as Tamoxifen, biological (targeted) therapy medications (i.e., Herceptin) or six-monthly bisphosphonate infusions. The specific combination of treatment given depends on multiple factors including, the stage and grade of breast cancer cells, location, menopause status and type of breast cancer diagnosed. For most, treatment begins with a surgical procedure such as a lumpectomy (also known as breast-conserving surgery) or a mastectomy to remove the cancer cells. There are many different forms of mastectomy performed by breast surgeons including, skin-sparing mastectomy, nipple-sparing mastectomy, radical mastectomy or most commonly a standard (simple or total) mastectomy involving the complete removal of the breast tissue including the skin and nipple (NHS, 2021). A mastectomy can be unilateral (one breast) or bilateral (both breasts). Breast reconstruction surgery is often also offered to women receiving a mastectomy as part of their treatment. In some instances, neo-adjuvant chemotherapy or hormone therapy will be administered before surgical treatment to shrink the size of the tumour and reduce the risk of cancer recurrence (Masood., 2016). Adjuvant chemotherapy is given after a surgical procedure to target any remaining cancer cells that have spread into neighbouring tissue or lymph nodes (Ahles & Root, 2018). Radiotherapy sessions are given for the same reason and are often the final form of active treatment received by women with primary breast cancer. In cases of MBC, chemotherapy and radiotherapy are used continuously (e.g., once a week or once every three weeks) until they are no longer effectively controlling the adverse symptoms or slowing down the rate of MBC tumour growth.

Hormone (or endocrine) therapy is selectively given to women diagnosed with oestrogen receptor-positive (ER+) or progesterone receptor-positive (PR+) breast cancer for up to 10 years to reduce the risk of cancer recurrence. In ER+ and PR+ breast cancer, the circulating oestrogen and/or progesterone stimulates the growth of cancer by binding to receptors on the tumour. Hormone therapy medications, therefore, function by preventing oestrogen and progesterone binding or by suppressing the natural production of oestrogen throughout the body (Cancer Research UK, 2020c). The type of

hormone therapy prescribed depends on menopause status at the time of diagnosis and treatment, risk of recurrence and side effects experienced (e.g., vasomotor, gynaecological, cognitive complaints). Pre/perimenopausal women with ER+ breast cancer, for example, are usually given selective oestrogen receptor modulators (SERMs) such as Tamoxifen (i.e., a receptor blocker) and postmenopausal women are more often given Aromatase inhibitors (AIs) such as anastrozole or exemestane (i.e., a production suppressor). Biological (targeted) therapy such as Herceptin (Trastuzumab) is administered every three weeks for the first year after the completion of active treatment if the cancer cells have human epidermal growth factor receptor 2 (HER2+) (NICE, 2018). Similar, to Tamoxifen, Herceptin binds to the HER2 receptors on the cell's surface to prevent growth and possible breast cancer recurrence (Cancer Research UK, 2020e). Breast cancer is defined as being triple-positive when the tumour is HER2+, ER+ and PR+. Both target therapy and hormone therapy are routinely offered alongside treatment (i.e., chemotherapy or radiotherapy) to women living with a diagnosis of ER+ and/or HER2+ MBC (Tarantino et al., 2020). In one in five cases breast cancer is triple-negative, meaning that hormone therapy and biological (targeted) therapy will not work (Macmillan, 2018).

## 1.4. **Impact of Diagnosis and Treatment**

Whilst the combination of early detection and implementation of multimodality treatment has significantly improved survival rates, with approximately 76% (i.e., 3 out of 4) of women now surviving at least 10 years (Cancer Research UK, 2020a). Both diagnosis and treatment have been associated with a cluster of ongoing physical, psychological, emotional and cognitive sequelae that can persist for many years (Burgess et al., 2005; de Ruiter et al., 2011; Koppelmans et al., 2012; van der Willik et al., 2018; Maass et al., 2021). Such sequelae have been shown to profoundly influence women's quality of life, relationships, everyday functioning (i.e., ability to carry out household duties), self-esteem and confidence, as well as impede their workability and performance. In a study by Dieluweit et al., (2011), it was shown that individuals affected by various forms of cancer who experienced cognitive impairment had half the odds of being employed more than five years after diagnosis. Workability is

defined as an individual's perception of their ability to do their work with respect to the work demands, as well as their health and mental resources (Ilmarinen et al., 2005). Substantiating evidence has shown that women diagnosed with breast cancer are more likely to experience a reduced (or poorer) workability compared to other forms of cancer such as melanoma and non-cancer reference groups (Hansen et al., 2008; Dahl et al., 2019), with studies showing that nearly 50% of women diagnosed with breast cancer report reduced workability upon returning to work (Musti et al., 2018). The standard set of value-based patient-centred outcomes for breast cancer developed by the international consortium for health outcomes measures (ICHOM) initiative has identified the ability to work as a key outcome impact breast cancer patients' longer-term quality of life (Ong et al., 2017).

### 1.4.1. **Physical Sequelae**

For many women changes in their physical function and wellbeing are triggered by the start of cancer treatment and persist throughout the treatment period before slowly recovering. Some physical sequelae such as pain and fatigue, however, can last for many months or even years after active treatment (i.e., chemotherapy) has finished (Biering et al., 2020; Voute et al., 2020; Maass et al., 2021), significantly impacting quality of life and ability to engage in work, as well as personal activities (Schmidt et al., 2012; Costa et al., 2017; Ho et al., 2018). Studies have shown a high level of interindividual variability associated with the severity and trajectory of fatigue and other physical sequelae (i.e., pain) amongst women treated for breast cancer (Dhruva et al., 2010; Schmidt et al., 2012; Voute et al., 2020). Such variability is said to be related to a range of factors including, the histology and physiology of cancer, comorbidities, type of treatment, age, education, psychological (emotional) distress or response to diagnosis (i.e., anxiety and depression), pain as well as inflammatory markers and regulation patterns (e.g., cortisol) (Bower et al., 2006; Von Ah et al., 2008; Knobf & Sun, 2005). In a study by Menning et al., (2016), for example, it was shown that women who had received systemic treatment (e.g., chemotherapy) reported worse physical function and fatigue compared to women

treated without chemotherapy and healthy controls; although it should be noted that women receiving alternative (i.e., non-systemic treatment) also had greater fatigue compared with the control group.

#### 1.4.1.1. *Fatigue*

Fatigue is one of the most common sequelae experienced by women diagnosed with breast cancer (see Joly et al., 2019, for a review), with approximately one in three (30%) reporting moderate to severe levels of fatigue after completion of active treatment (see Ganz & Bower, 2007, for a review). Compared to healthy controls, women living with a diagnosis of breast cancer are at a greater risk of experiencing fatigue (Carreira et al., 2020, 2021). It is well-documented that cancer-related fatigue (CRF) is far more debilitating than the general fatigue caused by poor sleep quality or over-exhaustion (Poulson, 2001). Many mechanisms have been suggested to explain CRF including, dysregulation of the hypothalamus-pituitary-adrenal (HPA) axis, dysregulation of five hydroxyl tryptophan (5-HT), as well as inflammation (Bower et al., 2002; Bower, 2007; Orre et al., 2011). In cancer patients, fatigue is not eased by good quality sleep and episodes of relaxation (Poulson, 2001) and frequently co-occurs with pain, insomnia, weight gain, hot flushes and emotional distress (anxiety and depression) (Bjerkeset et al., 2020). High levels of fatigue escalate feelings of tearfulness and vulnerability in everyday life, as well as induce a generally low mood amongst women affected by breast cancer (Mackereth et al., 2015). When assessing long-term fatigue, Maass et al., (2021) found that 81.1% of women with symptoms of depression and 60.0% with symptoms of anxiety were experiencing (multidimensional) fatigue. Fatigue is also associated with both subjective and objective cognitive performance (Von Ah & Tallman, 2015; Gullett et al., 2019), with elevated levels of fatigue predicting a poorer cognitive function. Whilst, studies have shown that both radiotherapy (Irvine et al., 1998) and chemotherapy (Gullett et al., 2019) independently exacerbate levels of fatigue across the treatment period which improve significantly within the first year of survivorship, recent research conducted by Maass et al., (2021) revealed 26.6% of women experience heightened fatigue symptoms up to 10 years after diagnosis. Recovery has been shown to be more complex for individuals who receive a combination of

treatments compared to those receiving chemotherapy and/or radiotherapy only (see Ruiz-Casado et al., 2021, for a review).

#### 1.4.1.2. *Other common physical sequalae*

A plethora of studies have also shown that elevated levels of sleep disturbance (or poor sleep quality), sleep disorders such as insomnia, pain, aching muscles and joints, as well as amenorrhea, sudden menopause and hot flashes are common amongst women who receive cancer treatment including, chemotherapy, radiotherapy or hormone therapy (Liou et al., 2019; Carreira et al., 2021). Koopman et al., (2002), for example, found that 63% of women with MBC reported experiencing one or more sleep disturbance(s). In a recent meta-analysis by Drijver et al., (2022), it was found that sleep quality was associated with self-reported cognitive impairment, such that poorer sleep quality met with greater perceived cognitive impairment. Studies have also shown that between 65-78% of women living with a diagnosis of breast cancer experience menopause symptoms such as vasomotor symptoms (e.g., hot flashes) and sexual dysfunction following diagnosis and treatment (Gupta et al., 2006). In a recent study by Vega et al., (2018), it was found that women treated with chemotherapy experience more menopausal symptoms (as measured by the menopause symptom checklist) compared to women without a cancer diagnosis. Premature menopause induced by chemotherapy has been found to occur in approximately 40% of women at age 40 and nearly all women over the age of 50 (Goodwin et al., 1999). For many younger (working-aged) women, the loss of their menstrual functioning and fertility results in significant emotional distress (anxiety and depression) and poorer quality of life outcomes (see Rosenberg & Partridge, 2013, for a review). Furthermore, studies have shown that many women diagnosed and treated for breast cancer experience persistent and chronic joint pain (or aching) which limits their ability to function in everyday life. When compared to a non-cancer control group, findings have revealed that the severity of joint pain experienced by women with breast cancer is significantly greater (Fenlon et al., 2013), with many studies linking this severe pain to the use of AI and Tamoxifen

hormone therapies which limit the production of oestrogen and inhibit the absorption of oestrogen (Sherwin et al., 1996).

#### 1.4.1.3. *Relationship between physical sequelae and work-related outcomes*

The relationships between physical fatigue and work-related outcomes such as workability in women affected by breast cancer have been well explored, with many studies corroborating that fatigue adversely influences work function and workability (Hansen et al., 2008; Carlsen et al., 2013; Ho et al., 2018; Dorland et al., 2018; Wolvers et al., 2019), as well as reduces the likelihood of returning to work following the completion of treatment (Pryce et al., 2007; Lee et al., 2017). In an early study by Hansen et al., (2008), it was found that women who were approximately four years post-treatment for breast cancer had significantly greater work limitations compared to a non-cancer control (5.5 vs. 2.8). Further, their findings showed that physical fatigue accounted for the majority of variance in work limitations in women with breast cancer, with greater fatigue predicting higher work limitations scores. Similarly, Carlsen et al., (2013) reported that fatigue was more strongly associated with reduced workability in women affected by breast cancer. Extending this, Dahl and colleagues (2019) showed that poorer workability was significantly related to increased levels of fatigue and depression up to 16 years after diagnosis, evidencing that cancer-related sequelae can affect workability long into survivorship and perhaps beyond the initial return-to-work (RTW) period. Physical fatigue has been found to cause high levels of frustration amongst workers affected by cancer, as well as result in them prioritising and reserving their energy levels for work duties over activities outside of work (i.e., socialising) according to managers and professionals active in the field of guidance and support of the working population (Boelhouwer et al., 2021). When describing their experiences with fatigue, many women reported encountering a lack of understanding and even hostility from colleagues (Machereth et al., 2015), causing them to take early retirement or reduce their working hours. Numerous studies have shown that physical sequelae such as hot flashes, nausea, lymphedema, pain and aching joints are also significantly associated with workability and sustainment of work across time (Fenlon & Rogers, 2007; Lavigne et

al., 2008; Quinlan et al., 2011; Ho et al., 2018), with findings corroborating that greater symptom severity met with worse work-related outcomes.

### 1.4.2. **Emotional Distress**

#### 1.4.2.1. ***Prevalence and trajectory of emotional distress***

Substantiating evidence from meta-analyses conducted by Carreira and colleagues (2018, 2021), has shown that women living with a diagnosis of breast cancer are at a greater risk for developing anxiety and depression compared to the wider population (or non-cancer reference control). Indeed, Burgess et al., (2005) found that the prevalence of depression and/or anxiety amongst women diagnosed with early-stage breast cancer was double that of the general population in the first year after diagnosis, with a high prevalence sustained long into survivorship. Claus et al., (2006), for example, found significantly higher depression scores (as measured by the CES-D) in women living with a history of breast cancer compared to a reference control group approximately 6 years after diagnosis. Similar findings have been identified when assessing the long-term trajectory of anxiety (see Carreira et al., 2018, for a review). Anxiety and depression are even more prevalent after breast cancer recurrence, with 45% expressing symptoms (Burgess et al., 2005). In recent meta-analyses, it was shown that the global prevalence of anxiety and depression in women affected by breast cancer was 41.9% and 32.2%, respectively (Hashemi et al., 2020; Pilevarzadeh et al., 2019). Importantly the standard set of value-based patient-centered outcomes for breast cancer developed by the International Consortium for Health Outcomes Measures (ICHOM) includes both anxiety and depression (Ong et al., 2017). In recent years studies have shown that women affected by breast cancer are also susceptible to developing anxiety-related disorders including Post-Traumatic Stress Disorder (PTSD), with studies showing that approximately 10% of women diagnosed with breast cancer will develop PTSD after diagnosis (see L. C. Brown et al., 2020, for a review).

### 1.4.2.2. *Determinants of emotional distress*

In individuals living with a diagnosis of cancer, escalating levels of anxiety and depression have been associated with fear of cancer recurrence (or cancer metastasis) and possible premature mortality, as well as the post-treatment sequelae (i.e., pain, fatigue, cancer-related cognitive impairment) commonly experienced (Vahdaninia et al., 2010; Baqutayan., 2012). Studies have shown a high level of interindividual variability associated with the development risk, severity and trajectory of anxiety and depression amongst women living with a diagnosis of breast cancer, with factors such as sociodemographic (i.e., age, education, marital status), lifestyle (i.e., exercise), workability, pre-existing comorbidity (i.e., heart disease, rheumatoid arthritis), past psychopathology, genetic predisposition such as Catechol-O-Methyltransferase Met (*COMT Met/Met*) (Hajj et al., 2021; See Bayer et al., 2022, for a review), cancer and treatment characteristics (i.e. chemotherapy) attributed (Bidstrup et al., 2015; Ho et al., 2018; Tsaras et al., 2018; see Carreira et al., 2018, 2020, 2021, for reviews). It is well-documented, for example, that younger women (≤ 60 years) are at a higher risk for developing both anxiety and depression compared to older women given the same diagnosis and treatment (Hashemi et al., 2020; Pilevarzadeh et al., 2019). Chemotherapy has also been shown to increase the risk of emotional distress compared to alternative treatments such as radiotherapy. It has been suggested that chemotherapy agents increase anxiety and depression by promoting inflammatory markers and reducing dopaminergic transmission, as well as by reducing physical and cognitive function in everyday life (Smith, 2015). A study by Restevska-Dimitrovska et al., (2016), found lower resilience to predict greater depression amongst women living with breast cancer, showing the importance of promoting cognitive, psychological and emotional resilience to protect against escalating levels of depression. Much like emotional distress (anxiety and depression), PTSD has been linked to multiple factors including women's fear of cancer recurrence (see L. C. Brown et al., 2020, for a review).

### 1.4.2.3. *Impact of emotional distress on survivorship*

In the most recent meta-analysis conducted by Wang et al., (2020), it was revealed that depression increased the risk of cancer recurrence, all-cause mortality and breast cancer-specific mortality by 24%, 30% and 29%, respectively. Extending this, Wang et al., evidenced that younger women affected by breast cancer (< 60 years) are at a higher risk of mortality compared to older women (≥ 60 years) living with the same diagnosis. Such a finding substantiates the importance of providing accessible support to younger women diagnosed with breast cancer to promote longer-term survival. Importantly, they also found that length of follow-up after diagnosis was associated with the risk of recurrence and mortality, such that women are most vulnerable in the first five years after diagnosis. Corroborating Wang et al., (2020), Shim et al., (2020) also found anxiety, depression and comorbid anxiety and depression to be predictive of all-cause mortality. In an early study by Groenvold and colleagues (2007), it was shown that anxiety was associated with the duration of recurrence-free survival, such that worse anxiety predicted a shorter recurrence-free survival. One possible explanation is greater levels of anxiety and depression have been associated with poorer adherence to treatment (DiMatteo & Haskard, 2011), with findings showing that depressed cancer patients are three times more likely to not adhere to planned treatment which could lead to poorer prognosis (DiMatteo et al., 2000). Further, they have also been linked to an increased risk of suicide among breast cancer patients (Akechi et al., 2000; Kim et al., 2013). Carreira and colleagues (2018) reported that women had a 37% to 60% higher risk of suicide compared to non-cancer reference control groups. It is important to mention that depression and anxiety are associated with biological mechanisms such as abnormal activation of the hypothalamic-pituitary-adrenal axis (HPA axis) and higher levels of norepinephrine and cortisol (Pruessner et al., 2003; Sephton et al., 2000) which may play a key role in underpinning the relationship between emotional vulnerability and escalating risk of recurrence and mortality in women with a history of breast cancer. In a study by Thaker and colleagues (2006), for example, it was validated that chronic levels of stress can lead to escalating levels of tissue catecholamines, greater tumour burden and more invasive growth of ovarian carcinoma. Similarly, Cui et al., (2019) found that stress-induced epinephrine increases lactate dehydrogenase A and promotes breast cancer stem-like cells.

Substantiating evidence has shown that chronic stress accelerates cancer growth and progression by stimulating the sympathetic neural nerves in cancer tumours (Kamiya et al., 2019). Given Wang et al., (2020) robust meta-analysis future research should work towards developing a greater understanding of biological mechanisms underpinning the relationships between depression and cancer recurrence as well as cancer-specific mortality. Despite these findings, anxiety and depression are frequently overlooked and under-treated in women with breast cancer. It has been suggested that this is due to the commonality between the symptoms of cancer and anti-cancer treatment and the symptoms of anxiety and depression including fatigue, appetite loss and sleep disturbance (Newport & Nemeroff, 1998), making it difficult to reliably diagnose. A study by Fallowfield et al., (2001) found that approximately 35% of cancer patients' level of psychiatric morbidity was misclassified by health care professionals, resulting in a reduced likelihood of patients being adequately assessed and treated for anxiety and/or depression.

#### 1.4.2.4. *Relationship between emotional distress and work-related outcomes*

Of focal importance, a plethora of studies have shown a significant (bidirectional) relationship between emotional distress (anxiety and depression) and work-related outcomes such as workability and work productivity (see Tan et al., 2021, for a review). In a study by Zeng et al., (2016), for example, it was shown that escalating levels of depression predicted greater work productivity loss (as measured by the WLQ) amongst women living with a diagnosis of primary breast cancer. Most recently, Kim et al., (2022) revealed that work productivity loss was approximately four-fold higher (2.73 vs. 10.3) in depressed women with breast cancer. In addition, they also evinced that depression was associated with all four of the WLQ subscales (time management demands, physical demands, mental/interpersonal demands, work output demands), with greater depression meeting greater workplace difficulty. History of anxiety was associated with worse mental/interpersonal demands and work output demands. Liu et al., (2021) found that work productivity loss predicted quality of life. Another study by Carlsen et al., (2013) similarly found that higher levels of anxiety were associated with poorer workability in women

up to five years after a breast cancer diagnosis, indicating that emotional distress has a long-term impact on the working life of women living with breast cancer. Correspondingly, Ho et al., (2018) found that depression was also associated with self-reported workability, with findings showing that greater depression predicted poorer workability (as measured by the workability index) in women with breast cancer. Further, they found that more women with suboptimal workability had borderline abnormal anxiety and depression scores, as well as poorer emotional functioning, quality of life (global health status) and a poorer future perspective. Such findings indicate that escalating levels of emotional vulnerability to anxiety and depression may significantly contribute to reducing workability and work productivity in women living with a history of breast cancer, potentially risking longer-term sustainment of work.

It is well documented that RTW after a cancer diagnosis and treatment is highly beneficial for emotional wellbeing, providing women with a sense of normality and contentment in everyday life, as well as familiarity following a greatly distressing and uncertain period of time in their life (Rasmussen & Elverdam, 2008). For many women, work functions as part of a coping mechanism distracting them from their cancer experience, providing purpose and reaffirming their identity outside of the cancer patient label (Amir et al., 2008; Kennedy et al., 2007; Raque-Bogdan et al., 2015; MacLennan et al., 2021). In a recent study by Inhestern and colleagues (2017), it was shown that unemployment was predictive of greater depression in working-age individuals living with a diagnosis of cancer. Extending this, Maruthappu et al., (2015) found that unemployment was significantly associated with an increased risk of breast cancer mortality, postulating that this is due to increasing levels of emotional distress and harmful behaviours associated with employment loss. Studies have shown that sustaining long-term work beyond the initial RTW is crucial for many women living with a diagnosis of breast cancer as it provides a source of socialisation and support, as well as financial stability (Amir et al., 2008; van Maarschalkerweerd et al., 2020). When exploring the relationship between financial instability and emotional wellbeing in women with breast cancer, Perry et al (2020) found that worse financial instability was predictive of greater anxiety and depression. Financial instability has also been identified as a key factor contributing to poorer quality of life in breast cancer (Meneses et al., 2012; Keim-

Malpass et al., 2017), showing the importance of supporting women with breast cancer to maintain long-term work. Greater social support in the workplace after diagnosis and treatment reduces the likelihood of leaving work (Mehnert, 2011) and enhances the quality of working life in primary breast cancer (Jin., 2021). Inhestern et al., (2017) found that lower general social support predicted greater anxiety and depression in working-age cancer survivors, suggesting that better social support (or employer support) in the workplace may play an important role in protecting against escalating levels of anxiety and depression. Taken together, the existing literature highlights the importance of researching the role of work-related factors such as employer support and job insecurity in predicting anxiety and depression in women living with breast cancer.

### 1.4.3. **Cancer-Related Cognitive Impairment (CRCI)**

#### 1.4.3.1. ***What is cancer-related cognitive impairment (CRCI)***

Over the last two decades, it has become increasingly acknowledged that women diagnosed and treated for breast cancer are more susceptible to experiencing cognitive impairment or complaints compared to the wider population (see Joly et al., 2019, for a review). In the early years, such cognitive complaints were referred to by researchers as ‘chemo-brain’ or ‘chemo-fog’ due to their high association with the neurotoxic effects of chemotherapy (Kesler et al., 2011), however, over time as prospective and longitudinal research has continued to advance the assumptions of ‘chemo-brain’ have been challenged (Ahles, 2012; see Ahles and Hurria, 2018, for a review). Indeed, the concept ‘chemo-brain’ assumes that women diagnosed with breast cancer have a typical (or normal) cognitive functioning before the onset of treatment challenging this, studies by Wefel et al., (2004, 2010) have found that approximately 21% of women diagnosed with breast cancer experience cognitive difficulty before starting chemotherapy treatment, with pronounced difficulties in psychomotor processing speed and executive function recorded. In a similar study by Janelsins et al., (2018), it was shown that prior to treatment women had worse scores on objective measures of memory, attention and executive function compared to a matched non-cancer control. As it stands, there is no single explanation or

mechanism attributed as the cause of pre-treatment cognitive difficulties, however, two main hypotheses have been suggested, this includes the biology/physiology of cancer (e.g., Patel et al., (2015) found evidence that elevated levels of the pro-inflammatory cytokine sTNF-RII were associated with poorer memory performance in women diagnosed with breast cancer before treatment) and DNA damage hypothesis (also known as common risk factors hypothesis). The DNA damage hypothesis proposes that factors such as oxidative stress, damaged DNA and the inability to repair damaged DNA are associated with both the development of neurodegenerative disorders (i.e., Alzheimer's' disease) and breast cancer exist (Ahles & Saykin, 2007). Elevated levels of emotional distress (anxiety and depression) and PTSD have also been associated with a decline in self-reported cognitive function before the start of treatment (Janelsins et al., 2017; Hermlink et al., 2015), indicating that emotional (or psychological) distress in reaction to a breast cancer diagnosis may play a role in inducing early cognitive difficulties. Neuroimaging has provided evidence of structural and functional brain changes in regions associated with cognitive function in individuals with PTSD (Villarreal et al., 2002).

The second assumption widely challenged is that cognitive difficulties result from receiving chemotherapy treatment only as substantiating evidence has shown that women treated with alternative or complementary therapies with and without chemotherapy also experience sustained cognitive difficulties, suggesting that multiple cancer treatments contribute to the difficulties encountered. In a study by Van Dyk et al., (2018), for example, it was shown that women who received a surgical procedure (i.e., mastectomy) only as their treatment had comparable levels of cognitive impairment to women who received radiotherapy, chemotherapy or chemotherapy plus radiotherapy. Another study by Phillips et al., (2012) similarly found no significant difference in executive function performance in women treated with chemotherapy plus radiotherapy or radiotherapy only at both six- and 36 months post-active treatment. Corroborating this notion, neuroimaging research by McDonald et al., (2012) found evidence of hyperactivation in the left frontal lobe during a verbal *n*-back task (working memory (WM) task) for women treated with and without chemotherapy at one-year post-treatment. Further, they found increased left parietal activation for those treated without chemotherapy, suggesting that regardless of treatment type women diagnosed with breast cancer recruit from neighbouring brain

regions to compensate for the deficit in the WM circulatory. It is important to note, that although both treatment groups showed frontal hyperactivation at one-year this activity was greater in women treated with chemotherapy, indicating that chemotherapy causes more excessive functional brain changes. In line with this de Ruiter et al., (2011) compared women treated with chemotherapy at least 10 years earlier to the non-chemotherapy breast cancer group and found sustained hypoactivation in the dorsolateral prefrontal cortex (DLPFC) and bilateral posterior parietal cortex (PPC), with these reductions in activity accompanied by significantly worse performance on the Tower of London Task, Paired Associates task for the chemotherapy group.

In recent years, studies have also provided extensive evidence showing that taking hormone (or endocrine) therapies such as Tamoxifen and AIs to reduce the risk of breast cancer recurrence or metastasising also results in adverse cognitive changes, for example, in an early study by Jenkins and colleagues (2004), it was shown that women actively taking Tamoxifen, Anastrozole (a form of AI) or combined therapy who had not previously received chemotherapy had poorer verbal memory and processing speed compared to a healthy reference control group. Extending on this, Castellon et al., (2004) found that women treated with chemotherapy and Tamoxifen performed worse on a global neurocognitive performance measure compared to women treated only with chemotherapy two to five years after diagnosis. More recently, Wagner and colleagues (2020) revealed that women treated with chemotherapy plus hormone (endocrine) therapy reported greater perceived cognitive impairment (as measured by the FACT-Cog) compared to women receiving hormone therapy only at both a three- and six-month follow-up. Interestingly, however, their findings showed that at 12-, 24- and 36- months perceived cognitive impairment was comparable between the two treatment groups, with women in the hormone therapy group reporting a worse perceived cognitive impairment over time. Taken together, these findings indicate that taking hormone therapy alone or in combination with other treatments leads to excessive cognitive impairment in women diagnosed with breast cancer. Studies suggest that AI medications reduce the conversion of androgens to oestradiol (the main form of oestrogen in women) limiting the binding of oestradiol to receptors in major memory and executive function brain regions including the hypothalamus, amygdala, hippocampus and DLPFC. It is well documented that oestradiol

also plays a significant role in modulating neurotransmitters (i.e., noradrenaline, and dopamine) associated with cognitive function (see Haggstrom et al., 2022, for a review).

Finally, the concept 'chemo-brain' assumes that chemotherapy is the only risk factor for cognitive impairment, however, multiple contributing risk factors have now been identified (see **section 1.4.3.3.** for more detail). As a result of these challenges, Hurria and colleagues (2007) coined the more inclusive (or multi-factorial) term 'cancer- and cancer treatment-associated cognitive change', however, over time this has become more commonly referred to in the literature as 'cancer-related cognitive impairment' (CRCI) (Padgett et al., 2020; accc-cancer.org). CRCI is a singular term describing the cluster of cognitive complaints reported by women diagnosed and treated for breast cancer (see Padgett et al., 2020; Ahles & Root, 2018 for a review). A plethora of studies have shown that women affected by breast cancer experience pronounced difficulties in memory (verbal and visual), concentration/attention, language, verbal fluency, processing speed and executive functions including, WM, cognitive flexibility, multitasking, decision making and planning (Jenkins et al., 2004; Von Ah et al., 2013; Janelsins et al., 2018; Bolton et al., 2018). Impaired memory and attention are, however, most frequently reported and considered by many women to be the most impacting on their ability to function in everyday life (Von Ah et al., 2013; Bolton et al., 2018; Von Ah & Crouch, 2021). The severity of cognitive impairment experienced can be subtle or dramatic (Ahles & Root, 2018).

At present, multiple biological mechanisms have been proposed to try and explain the underlying cause of longer-term CRCI in women affected by breast cancer, however, these mechanisms are not well understood (Joly et al., 2015). Neuroimaging using structural and functional magnetic resonance imaging (MRI) has shown significant alterations in multiple brain regions including the prefrontal and frontal cortex and hippocampus (McDonald & Saykin, 2013; Kelser et al, 2013) in women diagnosed and treated for breast cancer. Recent imaging has identified structural changes such as brain gray volume loss, white matter, microstructural disruption, reduced gray matter (GM) density and impaired cerebral blood flow (see Simó et al., 2013; Andryszak et al.,2017; for reviews). When exploring the long-term effect of chemotherapy in women approximately 21 years post-active treatment, Koppelmans et al., (2012a) found that compared to a non-cancer reference control group

women exposed to chemotherapy had a significantly smaller GM volume and total brain volume (TBV), with the effects observed comparable to that of 4 years of natural ageing effects on GM volume. In a study by Conroy et al., (2013), it was also shown that greater oxidative damage was associated with lower GM density. Evidence suggests that dysregulation of the HPA axis and dysregulation of the immune system (i.e., resulting in elevated inflammatory markers), as well as decreased telomere activity, may also play a key role in sustaining cognitive impairment over time. Indeed, van der Willik et al., (2018), found higher levels of inflammatory markers including GRL, PLR, and SII in women up to 20 years after the completion of active treatment. Further, their findings showed that the level of inflammatory markers was significantly associated with cognitive performance, such that greater (higher elevation) inflammation met with poorer cognitive performance. High levels of CRP and cytokines (e.g., interleukin (IL)) have been identified in women experiencing cognitive difficulties (Vardy et al., 2007; Patel et al., 2015; Toh et al.,2020). Using neuroimaging techniques, Kesler et al., (2013) confirmed that reduced hippocampal volume was associated with higher levels of IL-6 and TNF-α in women affected by breast cancer. Taken together, the body of literature suggests that the long-term cognitive impairment experienced by women diagnosed with breast cancer is likely underpinned by an interplay between these proposed mechanisms, as opposed to a singular cause.

#### 1.4.3.2. ***Prevalence and trajectory of CRCI***

Cognitive complaints (or difficulties) are one of the most common and debilitating changes reported by women following diagnosis and treatment (Boykoff et al., 2009; Schmidt et al., 2016; Joly et al., 2019), with approximately one in three women experiencing clinically significant cognitive impairment (see Whittaker et al., 2022, for a review). Substantiating evidence from across the body of existing literature has revealed that the exact prevalence of cognitive impairment amongst women affected by breast cancer is highly variable (15-90%), with factors such as the assessment method (i.e., self-report vs. objective neuropsychological test), sociodemographic (i.e., age), time since diagnosis and treatment and treatment (i.e., chemotherapy) characteristics thought to be responsible (Whittaker et al., 2022). Indeed, Lange et al., (2019a) disclosed that although over 50% of women report experiencing

cognitive complaints on self-report questionnaires following chemotherapy, only 15-25% show objective cognitive impairment. Such a difference in findings has been attributed to a range of potential causes including the use of traditional neuropsychological tests, compensatory activation (i.e., recruiting from neighbouring brain regions to maintain performance effectiveness) on objective tasks, inflation in self-reporting, as well as the use of traditional statistical methods to analyse data (See Ahles & Hurria, 2018, for a review). In a recent neural study by Swainston et al., (2021), it was shown that in the absence of performance differences on a modified flanker task (see **Chapter 2 section 2.5.1.3** for a description of this task) women with a history of primary breast cancer expressed a greater ΔERN and Pe, well-known neural indices of error processing and monitoring compared to a non-cancer reference control. Such findings suggest that women with breast cancer use greater neural compensatory activation to maintain high-performance effectiveness on objective laboratory-based tasks. In further support of this notion, Swainston and colleagues found a significant difference in perceived cognitive function (as measured by the FACT-Cog), with women diagnosed with breast cancer perceiving poorer cognitive function in everyday life.

In individuals diagnosed with cancer the cognitive impairment experienced can be temporary or permanent, and stable or progressive (Ahles et al., 2012). In a longitudinal study conducted by Janelsins et al., (2018), it was revealed that cognitive deficits found before treatment in memory, attention and executive function were most pronounced six months after the completion of active chemotherapy compared to immediately post-treatment, indicating a persistent and continuous decline likely associated with the accumulative effects of chemotherapy toxins. The study also provided evidence for a delay in the onset of decline in a subset of cognitive domains including, visual memory. Similarly, Wefel et al., (2010) identified that approximately seven months after treatment 29% of women showed a new onset of cognitive impairment that was not present immediately after treatment. Whilst, the other 71% showed a continuous decline across both follow-up assessment sessions. Such findings suggest that the rate of cognitive impairment may vary across different cognitive domains and individuals. Furthermore, studies have confirmed that complaints in some cognitive domains (i.e., memory) can be ongoing for many years, for example, Koppelmans et al., (2012b) showed memory

difficulties including word-finding and regularly forgetting tasks or pursuits were experienced by women up to 20 years after the completion of active treatment.

### 1.4.3.3. *Determinants of CRCI*

A series of fixed and modifiable risk (or predictive) factors have been associated with the cognitive impairment experienced by women living with a diagnosis of breast cancer this includes sociodemographic and lifestyle factors such as age, race, weight (or BMI), menopausal status, social support and education, as well as physiological (i.e., neuropathy, fatigue, insomnia, quality of sleep, comorbidity), psychological (i.e., anxiety and depression, cognitive reserve) and allostatic load (i.e., cardiovascular). In recent years, studies have focused on exploring the impact of age, with the findings showing that younger (working-aged) women report experiencing worse cognitive impairment compared to older women given the same treatment (Janelsins et al., 2017; Gregorowitsch et al., 2019). This difference may be attributed to the fact that younger women are often diagnosed with high-stage breast cancer and thus have more aggressive chemotherapy treatment resulting in greater neurotoxic effects (i.e., worse oxidative DNA damage or pro-inflammatory markers). Equally, younger women are more likely to have returned to work after the completion of treatment and therefore may report noticing cognitive changes more routinely in everyday life compared to women no longer working.

Studies have also identified multiple genetic risk factors that increase women's susceptibility to cognitive impairment, for instance, Catechol-O-Methyltransferase valine (*COMT-Val*) was linked to worse attention, motor speed and verbal fluency in women given chemotherapy (Small et al., 2011). Likewise, women who expressed the *APOE e*4 allele were shown to have worse visual memory and spatial ability deficits (Ahles et al., 2003; Ahles et al., 2014). The *APOE e*4 allele has been linked to the development of Alzheimer's disease (AD) (Lloret et al., 2015), development of breast cancer (Cibeira et al., 2014) and higher stage of breast cancer (Kesler et al., 2017), as well as cognitive impairment, indicating that it is a shared risk factor. Recent research conducted by Kelser et al., (2017) showed that women diagnosed with breast cancer regardless of treatment type had a higher probability

of developing AD compared to healthy controls. Moreover, they also showed that the *APOE e*4 allele and education were significantly associated with the probability of AD in women treated with chemotherapy.

### 1.4.3.4. *Impact of CRCI on quality of life and survivorship*

Many studies have investigated the effects of cognitive impairment on everyday life and quality of life, for instance, Chapman et al., (2019) showed worse perceived cognitive function predicted poorer quality of life amongst women diagnosed with primary or metastatic breast cancer. The working group developing the minimal standard set of value-based patient outcome measures for breast cancer identified cognitive functioning as an outcome impacting patients' long-term quality of life (Ong et al., 2017). Interviewing 23 women, Von Ah and colleagues (2013) found evidence that CRCI adversely impacts women's relationships with family and friends, as well as reduces their self-confidence and self-esteem in everyday life. Further, many of their women reported that their impairment had significantly "changed" them and left them with a sense that they were no longer the same person. Extending this, Bolton et al., (2018) found cognitive impairment was associated with a loss of confidence to try out new things and socialise, resulting in higher levels of social isolation and withdrawal. Much like emotional distress (anxiety and depression; see **section 1.4.2.3**), worse cognitive impairment has been linked to reduced adherence to medication and treatment (Stilley et al., 2010), potentially increasing the risk of premature mortality and recurrence. Alatawi and colleagues (2020) reported that women diagnosed with breast cancer who were experiencing cognitive impairment prior to diagnosis had a higher risk of cancer-specific mortality, all-cause mortality and non-cancer cause mortality compared to those women without cognitive impairment. Such a finding suggests that sustained CRCI long into survivorship may also play a role in escalating women's risk of recurrence and premature mortality. Despite these findings, CRCI is still poorly addressed and managed by oncology services, with findings showing that approximately only one-third of women experiencing cognitive difficulties discuss these issues with health care professionals (Buchanan et al., 2015). It has been suggested that this is partly due to health care professionals' uncertainty of how to best manage (or 'fix') the cognitive difficulties experienced (Smidt et al., 2016). Similar reports have been made

about the workplace, with many stating that occupational health services lacked knowledge regarding supportive care options for managing CRCI at work (Klaver et al., 2020).

#### 1.4.3.5. ***Relationship between CRCI and work-related outcomes***

Importantly, CRCI has been shown to adversely affect work-related outcomes such as workability, work productivity and long-term sustainment of work in women living with a diagnosis of breast cancer (see Von Ah et al., 2016, for a review). In an early study conducted by Bradley et al., (2007), it was found that up to 39% of women report experiencing cognitive limitations in the workplace including difficulties with concentration, analysis and learning new things, as well as struggling to keep up with their co-workers. Extending this, Munir et al., (2011) found approximately 71% (12 of 17) of women in their study also reported problems remembering tasks at work, limiting their work performance. An integrative review by Von Ah et al., (2016) confirmed that tasks involving memory, concentration/attention and executive function were the most problematic in the workplace. Supporting this, Calvio et al., (2010) showed that self-reported memory and executive function predicted work output difficulty (as measured by the WLQ), such that worse perceived impairment met with greater work output difficulty amongst women affected by breast cancer. Von Ah and colleagues (2018) revealed that greater perceived cognitive impairment was also significantly associated with greater time management difficulties, physical difficulties and mental/interpersonal difficulties in the workplace, as well as higher work productivity loss. Greater impaired cognitive function has been linked to loss of self-confidence in workability, feelings of being overwhelmed and frustrated in the workplace, as well as feelings of letting down employers and co-workers (Kennedy et al., 2007; Munir et al., 2010) as a result of decreased work productivity and efficiency.

Substantiating evidence has revealed that women affected by CRCI have a higher likelihood of being unable to sustain long-term employment (Obserst et al., 2010; Peipins et al., 2021). Recent research by Peipins et al., (2021), for example, reported that a higher percentage of women with breast cancer who lost employment experienced memory complaints associated with reduced workability

compared to those without (17.4% vs. 5.9%). It is speculated that women experiencing reductions or changes to their employment (i.e., working fewer hours or unemployment) may be adversely affected by the reduced amounts of positive cognitive stimulation (i.e., learning new information, socialising with colleagues) and physiological support to the brain (i.e., having a schedule) (Vance et al., 2016), risking a further escalation of CRCI and development of neurogenerative diseases such as AD. Previous studies have confirmed that women diagnosed with breast cancer are at a greater risk of developing AD regardless of treatment type (Kesler et al., 2017), highlighting the importance of targeting CRCI to support long-term employment and workability for women living with a history of breast cancer.

## 1.5. **Metastatic Breast Cancer in the literature**

It is important to highlight that much of the research described in the sections above has focused on investigating the impact of diagnosis and treatment on the cognitive and emotional health of women with primary breast cancer, with most studies excluding women with MBC. Mayer and colleagues (2010) reported that when directly asked most women with MBC (52%) felt that there was not enough attention and societal awareness given to MBC compared with primary breast cancer, an issue that appears to still exist. This is surprising as figures estimate that in the UK alone there are around 35,000 women with this diagnosis (Breast Cancer Now, 2021). The experience of receiving a diagnosis of MBC is distinctively different from primary breast cancer, with survival in MBC dependent on the availability of effective anti-cancer treatments. As a result of these ongoing treatments, many women experience cumulative and highly debilitating side effects such as chronic pain, fatigue and nausea that adversely impact and potentially limit their everyday life. Typically, as MBC progresses, new treatments administered work for shorter and shorter amounts of time, and with lower effectiveness. Considering this it is not surprising that women with MBC reported experiencing a high level of uncertainty about their future, escalating vulnerability to anxiety and depression, as well as cognitive impairment. In a meta-analysis by Willis et al., (2015), it was found that women with MBC are significantly more likely to experience poorer emotional functioning, as well as higher levels of clinical

levels of anxiety and depression compared to women with a history of primary breast cancer only. In a study by Giese-Davis et al., (2011), it was shown that depression can significantly influence the duration of survival of women with MBC, with findings showing that reducing levels of depression increased survival by approximately 29 months. Such evidence affirms the importance of investigating the risk factors including work-related factors that have the potential to escalate vulnerability to anxiety and depression. Most recently, Dobretsova and Derakshan (2021) conducted an online study focusing on the cognitive and emotional well-being of women with MBC in the UK. The findings firstly confirmed that much like in primary breast cancer there is a significant association between perceived cognitive function and anxiety and depression, as well as with PTSD, with worse perceived cognitive function meeting with worse levels of emotional distress and PTSD. Importantly, the study also evidenced that social support significantly moderates the relationship between perceived cognitive function and depression, with the findings indicating that women with low levels of social support and poorer cognitive functioning are at a greater risk of experiencing depression. Such findings highlight the importance of good social support and cognitive health for protecting against vulnerability to depression in women with MBC. As many women with MBC decide to continue working following their diagnosis it is important to extend this research into the workplace. To date, there are very few studies exploring workability and work in women with MBC.

## 1.6. **Coping Methods and Cognitive Training Interventions**

### 1.6.1. ***Self-management coping methods and adaptations applied by women diagnosed with breast cancer***

As it stands, there is no method of prevention or cure available for women experiencing CRCI, however, numerous interventions and coping methods including pharmacological such as erythropoietin, psychostimulants and cholinesterase inhibitor, exercise, cognitive behavioural therapy (CBT) and cognitive training have been studied to assess their efficacy in reducing and/or managing CRCI in everyday life (see Von Ah et al., 2013b, Bai &Yu, 2021, for reviews). Interviewing 18 women

with a diagnosis of primary or secondary breast cancer who were experiencing CRCI, Myers et al., (2012) found that notetaking ("*writing things down*") was the most common coping strategy employed by women to manage their CRCI, with 88% reporting the need to create notes soon after receiving information to avoid forgetting. Women also described using coping methods like addressing one task at a time, giving themselves more time, permitting themselves to make mistakes, receiving support and validation, helping others and depending on others to help with their CRCI. Implementing such coping methods reflects the consequences of CRCI on women's health-related quality of life and alternations in their ability to function in everyday life. Myers et al., (2012) proposed the life with chemobrain thematic framework which can be applied to help guide content to include information about experiences of CRCI, common coping strategies (or methods) and information important for inclusion in the development educational programmes for healthcare providers. Expanding on this research, Henderson and colleagues (2019) found that the use of planning, preparation and notetaking to compensate for CRCI was highly valued by all women, however, those who perceived their CRCI to be part of a transitory phase or curable placed more emphasis on '*being mindful*' and '*trying their best*'. Whereas, women who considered their CRCI to be a long-term or permanent sequelae described greater reliance on external coping strategies (e.g., reminder cues) to function in everyday life. In a qualitative study by Von Ah et al., (2013), working women disclosed that developing and implementing coping strategies such as notetaking was essential to supporting their workability and enabling them to overcome the cognitive difficulties experienced in the workplace. Strategies such as working in quiet environments, using feedback from others to monitor work accuracy and recording conversation or meetings, pre-empting work, as well as putting in extra effort to meet others' expectations (i.e., colleagues) are commonly reported by individuals living with a diagnosis of cancer (Sandberg et al., 2014; Klaver et al., 2020). Whilst it is well-acknowledged that women affected by breast cancer implement a series of self-management coping strategies to support their everyday functioning and reduce the impact of their cognitive impairment, women's experiences with such self-management coping strategies, particularly in the workplace are understudied.

Numerous studies have explored the work-based adaptations made by women diagnosed with breast cancer to manage their cancer-related sequelae (i.e., cognitive impairment, fatigue) and enable greater work functioning. Evidence suggests that changes to the number of working hours followed by changes to the workload are the most common work-based adaptions applied (Torp et al., 2012; Sandberg et al., 2014; see de Boer et al., 2020, for a review). Hamood et al., (2019) found that approximately 48% of women in their study had changed from working full-time hours to part-time hours following their RTW, with this change having adverse effects on quality of life. Other common adaptions include working from home more frequently to reserve energy levels and minimise the impact of distraction on work productivity, as well as limiting work-related activities outside of the typical working hours (i.e., networking or socialising).

### 1.6.2. *Cognitive training interventions in breast cancer*

A recent qualitative study by Crouch & Von Ah (2017) outlined that women with a history of breast cancer have a preference to engage in interventions to target their CRCI that do not include the use of (pharmacological) medication, for example, Modafinil (Kohli et al., 2009), expressing that the use of medication generated apprehension. Convenience including flexibility and accessibility (e.g., online computerised training) was also described as essential to facilitating the completion of the intervention whilst allowing the continuation of existing schedules and commitments (i.e., work). Using a web-based survey, Lange and colleagues (2019b) found that 75% of cancer survivors wanted support for their CRCI, with cognitive training (72%) most requested in comparison to psychological support (48%) and physical activity (32%). Cognitive training is defined as a behavioural method based on models of neuroplasticity that aims to improve or restore cognitive function via adaptive tasks that exercise the brain and strengthen neuroplasticity (Kesler et al., 2013b).

Several cognitive training studies have been performed with women living with a history of breast cancer, for example, Von Ah et al., (2012) conducted a randomised control trial (RCT) to compare women who received 10 one-hour sessions of memory training or speed of processing training

to a waiting-list control. Results showed sustained near (i.e., an improvement on trained cognitive domains) and far (i.e., improvement on untrained cognitive domains or a distinctively different process) transfer effects for both groups up to two months, with improvements in memory, processing speed, self-reported cognitive function (as measured by FACT-Cog and SSMQ), symptom distress, fatigue and depression noted. Similarly, Kesler et al., (2013b) explored the effects of receiving 48 sessions of visual executive function training in women at least 18 months post-chemotherapy and found significant improvements in the Wisconsin card sorting test (WSCST), letter fluency and symbol search. They concluded that their training successfully improved cognitive flexibility, processing speed and verbal fluency, however, found no improvement in WM despite including several WM training tasks. Kesler and colleagues suggest this finding could be due to many factors such as the outcome measure utilised or the training exclusively employing visual-based tasks, arguing that training that encompasses both visual and auditory stimuli may have yielded greater improvements in domains of WM. Damholdt et al., (2016) used the web-based cognitive training app known as Happyneuron Pro (Scientific Brain Training, Villeurbanne, Cedex, France) and observed sustained improvements in verbal learning and WM (as measured on digit span backwards). Bray et al., (2017) also showed improvements in self-reported cancer-related sequelae after 40 hours (15 weeks) of the Insight app-based intervention, with sustained effects up to six months found for self-reported cognitive function. Notably, all of these cognitive training studies were conducted in the absence of an active control group, provoking questions about the training's true effectiveness in women with breast cancer. It is widely acknowledged by researchers that an active control group which controls for participants' training expectancy and ensures both training groups have an equal interaction with the researchers is required to draw any reliable conclusions (See Simons et al., 2016, for a review).

In a recent breakthrough, Swainston and Derakshan (2018) compared the effects of receiving 12 sessions of adaptive dual *n*-back training with dual 1-back training (active control group) in women living with a history of breast cancer. A significant improvement in the level of '*n*' from day 1 to day 12 was observed, indicating an increase in WM functioning. Further, improvements in self-reported rumination and anxiety symptomatology were also found, with these effects sustained up to

approximately 15 months after the completion of training. It is important to note, that no measure of cognitive transfer was assessed in this study. Such findings provide support for a direct relationship between WMC and attentional control and vulnerability to emotional distress (anxiety and depression) (see Derakshan, 2020; Koster et al., 2017, for reviews). Indeed, a recent meta-analysis by Moran (2016) demonstrated that self-reported anxiety was significantly associated with WM, with greater anxiety symptomology meeting worse performance on WM tasks including the *n*-back task. The attentional control theory (ACT; Eysenck et al., 2007) proposes attentional control plays a central role as a determinant of emotional vulnerability to anxiety and depression (DeRaedt & Koster, 2010). Evidence suggests that poor attentional control can result in greater attendance and maintenance of worrisome and ruminative thoughts, thereby reducing the WM resource available for task-relevant information. By training WMC via tasks such as dual *n*-back the efficacy of attentional control is likely to improve, which should, in turn, reduce vulnerability to anxiety and depression, as there will be more resources to exert control over negative (more salient) emotional thoughts. The findings from Swainston and Derakshan (2018, 2021), therefore, indicate that dual *n*-back training may play an important role in protecting against escalating levels of anxiety in women with breast cancer by enhancing the WMC (as measured by the level of '*n*' achieved) subsequently improving attentional control over attending to anxiety-inducing information.

### 1.6.3. ***Dual n-back training (Adaptive cognitive training)***

Cognitive neuroscience research has shown that the brain is plastic, meaning it can reorganise its structure, function and connections as a result of cognitive training. Adaptive dual *n*-back training was pioneered by Jaeggi and colleagues in 2003 as a dual task intervention for targeting WMC. Substantiating evidence from Jaeggi et al., (2008, 2012) has affirmed that dual *n*-back has the potential to elicit both near and far transfer effects, increasing its popularity amongst researchers. Adaptive dual *n*-back training is a common form of computerised WM training often referred to as a WM updating measure (Szmalec et al., 2011) that also reflects the active maintenance or working memory capacity

(WMC) of an individual (see Soveri et al., 2017, for a review). This online computerised training is known for its challenging exercise of prefrontal functions, in a systematic and adaptive manner. Indeed, the successful performance on the *n*-back training task involves the engagement and exercising of multiple cognitive processes including WM updating (i.e., encoding of current stimuli, monitoring, maintenance, and updating of information, as well as stimulus matching), inhibition, switching and cognitive flexibility, as well as other higher-order executive function such as problem-solving, decision making and selective attention (Kane & Engle, 2002; Pergher et al., 2018; Derakshan 2020). Interference control processes are also needed when lures appear in the task, for example, when participants are presented with a 2-back match but are performing at a 3-back level (Pergher et al., 2018).

Adaptive dual *n*-back training involves presenting participants with continuous pairs of auditory (i.e., letters such as 'A') and visuospatial stimuli (see **Chapter 2 section 2.9** for an example). This task requires participants to decide whether the current pair of stimuli or one of the stimuli in that pair (i.e., the spoken letter or visuospatial stimuli) matches the stimuli presented '*n*' number of trials earlier, for example, if *n* was two participants would be expected to match the current stimuli with the stimuli presented two trials before. The value of '*n*' adapts across the blocks of trials depending on performance, increasing by one level (i.e., from 1-back to 2-back) when performance is higher than the designated threshold and decreasing by one level when performance is lower than the accuracy threshold. The adaptive element of *n*-back training is fundamental to ensure that the task remains demanding and engaging for the participant (Jaeggi et al., 2014), preventing the development of task-specific strategies and automatic processing and stimulating increases in WM function and thus attentional control. Substantiating evidence suggests that cognitive training will only cause neural plasticity changes if cognitive processes are challenged by new demands exceeding routine functioning (Diamond & Ling, 2019). In a study by Holmes and colleagues (2009), it was shown that gains from WM training were significantly greater in participants who received adaptive training compared to those with non-adaptive training. Evidence suggests that training using an adaptive threshold of 90% accuracy is more likely to result in far transfer effects compared with using a threshold of below 90% (8.3% vs.

29.4%). Transfer occurs if cognitive processes depend on shared neural networks. In line with these findings, dual *n*-back training provided as part of the 'BRiCatWork' study presented in this thesis applied a threshold value of 95%, an accuracy threshold also used by Swainston and Derakshan (2018, 2021).

A plethora of studies performed with both clinical and non-clinical populations has provided substantiating evidence that receiving *n*-back training can result in improvements (or gains) in a series of executive processes including WM, cognitive control, general fluid intelligence and inhibition (Au et al., 2015; Jaeggi et al., 2008; Jaeggi et al., 2014; Owens et al., 2013; Sari et al., 2016; Hotton et al., 2018). Owens et al., (2013), for instance, found that eight sessions of adaptive dual *n*-back training in a sub-clinical depressed group resulted in transfer effects in both behavioural and neural measures of WMC, as well as filtering efficiency of irrelevant information. Similarly, Sari et al., (2016) revealed that 15 sessions of dual *n*-back training improved attentional control on a modified flanker task, suggesting that WM training enhances the effectiveness of the regulatory processes in top-down attention reducing the bias for the bottoms-up system (parietal system). Further, they found higher engagement with dual *n*-back training met with a greater improvement in trait anxiety scores. Correspondingly, Hotton et al., (2018) showed improvement on *n*-back training was associated with improvement in self-reported worry and perfectionism as well as WMC in high worries and Course-Choi et al., (2017) found higher (or greater) engagement with *n*-back training met with greater improvements in antisaccade latencies, worry symptomology as well as resilience scores. In the most recent study conducted by Beloe and Derakshan (2020), it was shown that 20 sessions of dual *n*-back training resulted in sustained improvements in depression up to one-month post-training in secondary school-aged adolescents. Notably, this is the first study to find reductions in depression following sessions of dual *n*-back training. When assessing the effects of a modified version of the emotional dual *n*-back training task in high anxious adults, Lotfi et al., (2020) found nine sessions of training to elicit greater reductions in self-reported trait anxiety, in addition to meaningful transfer gains on the spatial span task relative to the control group. The findings also revealed larger increases in the magnitude of the error-related negativity (ERN; a known neural marker of error processing and cognitive functioning;

see **Chapter 5** for a more comprehensive description) following the completion of training for the *n*-back group. Such findings suggest that *n*-back training was more impacting on underlying cognitive processes supporting higher-order monitoring and updating systems of WM compared to active control training.

Of focal importance evidence from neuroimaging studies has shown that dual *n*-back training also results in significant functional and structural brain changes, with improvements detected for both gray and white matter (Colom et al., 2016; Salminen et al., 2016; Salminen et al., 2020). In a study by Salminen and colleagues (2016), it was shown that participating in 16 sessions of dual *n*-back training induced significantly greater increases in white matter integrity in multiple white matter pathways connecting the brain regions underpinning WM performance compared to single *n*-back training (active control training) and a no training passive control group. In a second study, Salminen et al (2020) found that dual *n*-back training also resulted in far transfer effects as evidenced by improvements on an untrained dual WM task and increased functional connectivity of the ventral default mode network (DMN) in right inferior frontal gyrus (rIFG). Further, they found that change in functional connectivity (pre- to post-training) significantly correlated with performance gains on the dual WM task for dual *n*-back training but not the single *n*-back or passive control group. Miró et al., (2020) found *n*-back training to result in a decrease in activation in the anterior dorsolateral prefrontal cortex indicative of improved neural efficiency, with findings sustained at a later follow-up. When comparing dual *n*-back training to complex span WM training and permuted rule operations, Blacker et al (2017), revealed that *n*-back training elicited robust near transfer effects and significant neural grains, indicating that *n*-back training was a much more reliable and effective training intervention compared to complex span training.

In the most recent study conducted by Swainston and Derakshan (2021), it was found that dual *n*-back training resulted in the greatest reduction in trait anxiety in women living with primary breast cancer compared with an active control group who completed dual 1-back training and mindfulness training groups, with these effects sustained at the longer six-month follow-up. Such a finding replicates the findings from their earlier cognitive training study (Swainston &Derakshan, 2018). Specifically,

Swainston and Derakshan (2018) found a sustained reduction in levels of trait anxiety and rumination up to approximately 15 months after the completion of 12 sessions of dual *n*-back training. Of focal importance, Swainston and Derakshan's (2018, 2021) work is the first to provide evidence that receiving a program of 12 sessions of online adaptive dual *n*-back training which targets impaired cognitive function promotes cognitive and emotional resilience in women diagnosed with breast cancer longer term.

### 1.6.4. ***Interventions supporting work-related outcomes in breast cancer***

Despite the promising effects of adaptive cognitive training (i.e., dual *n*-back training) in both health and clinical populations, as well as the results from cognitive training studies conducted in the breast cancer population no research to date has explored the impact of targeting impaired cognitive function using dual *n*-back training on workability and work-related outcomes. In fact, at present, there are little-to-no interventions specifically targeting the CRCI experienced at work (Duijts et al., 2017a), even though figures have shown that nearly 45% of women attribute reductions or discontinuation of work after breast cancer diagnosis and treatment to memory and attention problems (Schmidt et al., 2019). As it stands, research exploring work-related interventions has largely focused on supporting the process of RTW during or after the completion of cancer treatment (see de Boer et al., 2015; Lamore et al., 2019, for reviews), as well as addressing cancer-related sequelae such as fatigue (Purcell et al., 2011; Dolgoy et al., 2020). It is well-documented that RTW after a diagnosis of breast cancer is highly complex, with many individuals facing a series of work-based (e.g., discrimination, lack of social support) and cancer-related (e.g., cognitive impairment) challenges. Figures show that individuals diagnosed with cancer are 1.4 times more likely to become unemployed compared with healthy individuals (Verdechhia et al., 2009). To date, many different forms of work-related interventions have been trialled including psycho-educational (e.g., counselling, training in self-management or coping, problem-solving therapy), psychological (e.g. CBT), vocational (e.g., person-directed or work-directed interventions focusing on employment), physical (e.g., exercise, vocal training), medical or

pharmacological (e.g., surgical procedure or medication), as well as multidisciplinary (i.e., a combination of psycho-educational and physical exercise), with mixed findings reported about their successfulness in supporting RTW (see de Boer et al., 2015, for a review). In addition, work-directed and person-directed informational tools such as RTW discussion guides, work accommodation requests and preparatory plans for encouraging RTW have also been explored (Cimprich et al., 2005; Munir et al., 2013; Tamminga et al., 2013; Hoffmann et al., 2014). A recent meta-analysis conducted by Bilodeau et al., (2017) revealed that the majority (81%) of RTW interventions offered to women affected by breast cancer are provided by multiple health care professionals such as occupational health therapists or nurses, with most offered during the survivorship period, in hospital or external rehabilitation centres as opposed to in the workplace.

In one of the few studies assessing workability in addition to RTW outcomes amongst cancer survivors (83.9% were breast cancer), it was found that receiving a multidisciplinary rehabilitation programme combining personal counselling on work-related issues and supervised physical exercise resulted in significant reductions in fatigue, as well as improved the rate of RTW, perceived workability (as measured by the workability index) and views of the importance of work. The study, however, found no significant improvements in self-reported measures of work limitations (as measured by the work limitations questionnaire) which were only completed by working participants (Leensen et al., 2017). Previous research by Von Ah et al., (2018) has shown that perceived cognitive function significantly predicted work limitations, such that a poorer perceived cognitive function met with greater work limitations in women affected by breast cancer indicating, that interventions targeting cognitive impairment may play an important role in diminishing limitations experienced in the workplace.

## 1.7. **Thesis Overview**

To address gaps in the current literature and to find ways to empower workability, the present PhD thesis used a mixed-methods approach to better understand how cognitive function and emotional distress (anxiety and depression) relate to workability and work-related factors such as quality of

working life in women affected by breast cancer, as well as to understand the effectiveness and usability of adaptive cognitive training in targeting impaired cognitive function and improving workability. Up to now, women's experiences in the workplace and with their employers beyond the initial RTW period are not well studied. The aim of the current PhD thesis was two-fold. First, the thesis will present findings from the 'BRiCatWork' study which aimed to investigate the longer-term efficacy of adaptive dual *n*-back training as a possible intervention for helping women living with a diagnosis of primary breast cancer sustain their workability and work over time by targeting impaired cognitive function (See **Chapters 4**, **5**). To this end, the study also explored women's experience with sustained cancer-related cognitive impairment and its impact on workability prior to receiving the adaptive cognitive training (See **Chapter 3**).

In order to build on existing literature focusing on breast cancer and work, the thesis will then go on to address its second aim by presenting findings from two cross-sectional studies that aimed to investigate the role of work-related factors such as experience with employers, quality of working life and job security in predicting cognitive impairment and vulnerability to anxiety and depression, known risk factors for reducing workability and quality of life, as well as increasing recurrence and premature mortality risk. It is crucial to gain a greater understanding of the impact of work-related factors on the perceived cognitive function and emotional health of women affected by breast cancer, as this will enable supporting services such as occupational health and breast cancer nurses to provide more informed guidance to women and their employers beyond the initial RTW period, reducing the risk of adverse work-related outcomes such as suboptimal workability and unemployment. The study presented in **Chapter 6** aimed to explore the relationship between self-reported quality of working life with perceived cognitive function, anxiety, depression and global health status, in addition to exploring experience with employers amongst women living with MBC. As it stands, there is little-to-no research focusing on women with MBC in the workplace despite figures showing that approximately 35,000 women are living with this diagnosis in the UK. As a result of the unexpected Coronavirus disease (COVID-19) outbreak during this PhD, the study presented in **Chapter 7** focused on exploring the impact of COVID-19 and its associative restrictive measures on the general cognitive and emotional

health of women with primary breast cancer, as no previous studies had been conducted in this research area.

## 1.8 **Chapter Summaries**

**Chapter 2:** In **Chapter 2** the methods and materials implemented in the BRiCatWork study **(Chapter 3, 4, and 5)** and the two cross-sectional studies **(Chapter 6** and **7**) presented throughout this thesis are described.

**Chapter 3:** The findings from the baseline interviews conducted as part of the larger 'BRiCatWork' study are presented in **Chapter 3**. Firstly, this chapter aimed to understand women's experiences of sustained post-treatment CRCI and its impact on workability in long-term survivorship beyond the initial RTW. The chapter then aimed to explore women's experiences of self-management coping strategies including cognitive support methods and work-based adaptations applied to manage CRCI and known cancer-related sequelae at work.

**Chapter 4:** The findings from the semi-structured telephone interviews conducted as part of the 'BRiCatWork' study at one-month, six-months and one-year post-training are then presented in **Chapter 4**. The main aim of **Chapter 4** was to investigate the perceived impact of receiving 12 sessions of adaptive cognitive training (dual *n*-back training) or active control training (dual 1-back training) on self-reported CRCI impacting workability. The chapter also aimed to examine the perceived transfer effects of training on women's work-related self-management methods for cognitive impairment and on career development or progression. In addition, women's experiences of participating in the 12 sessions of online training including, their engagement with the training and challenges or difficulties experienced, as well as their views on the timing of the training were explored.

**Chapter 5:** The findings from the self-report questionnaires, objective assessments of WM and neural indices collected as part of the 'BRiCatWork' study are presented in **Chapter 5**. The main aim of this chapter was to investigate the efficacy of dual *n*-back training on improving impaired cognitive functioning and its transfer effect on workability anxiety, depression and quality of life.

**Chapter 6:** The main aim of the cross-sectional study presented in **Chapter 6** was to examine how the self-reported quality of working life of women living with MBC related to their global health, perceived cognitive function, anxiety and depression. To this end, the study also aimed to investigate women's experience with their employers after MBC diagnosis and its relationships with self-reported quality of life.

**Chapter 7:** The overarching aim of the study presented in **Chapter 7** was to investigate the impact of the COVID-19 outbreak and its associated restrictive measures on the cognitive and emotional health of women living with a diagnosis of primary breast cancer. The study first aimed to investigate the impact of the UK Government shielding letter and disruption to scheduled oncology appointments on self-reported cognitive function, anxiety and depression, in addition to exploring the relationship between COVID-19-related emotional vulnerability (COVID-EMV) and perceived cognitive function, anxiety and depression after allowing for the effects of rumination, pathological worry and key sociodemographic and clinical factors. The study then aimed to explore the relationship between job insecurity created by the COVID-19 outbreak and perceived cognitive and emotional vulnerability. To this end, the impact of changes in employment status (i.e., furloughed) on perceived cognitive and emotional health as well as on women's perceptions of work was also explored.

**Chapter 8:** In **Chapter 8** the main findings from the three studies presented throughout this thesis (see **Chapters 3**,**4**, **5**, **6**, and **7**) will be summarised and discussed. This is followed by general implications of the findings and suggestions for future direction, as well as the limitations.

# **Chapter 2:** Methods

## 2.1. **Chapter Overview**

In **Chapter 2** the methods and materials applied in the two cross-sectional studies (**Chapters 6** and **7**) and the longitudinal randomised control trial (BRiCatWork study) (**Chapters 3**, **4**, and **5**) presented in this thesis will be outlined. First, the ethical approval (see **section 2.2**) and participant recruitment procedure (see **section 2.3**) for each of the studies will be described. This is followed by an overview of the quantitative methods and materials used, including the self-report questionnaires (see **section 2.4**; **Chapters 5**, **6** and **7**), objective neuropsychological tests (see **section 2.5**; **Chapter 5**) and electroencephalogram (EEG, see **section 2.6**.; **Chapter 5**). An overview of the qualitative methods and materials covering the interview schedules (see **section 2.7**; **appendix 4**; **Chapters 3**, and **4**) and qualitative analysis approach (see **section 2.8**; **Chapters 3**, and **4**) will then follow. Lastly, the cognitive training tasks (see **section 2.9**; dual *n*-back training see **section 2.9.1** and dual 1-back training see **section 2.9.2**) implemented in the BRiCatWork study will be introduced (**Chapters 4**, and **5**).

## 2.2. **Ethics**

The studies presented in this thesis received ethical approval from the Research Ethics Committee of the Department of Psychological Sciences, the College Research Ethics Committee at Birkbeck College, University of London, and the Economic and Social Research Council (Reference: 181935, 192078). The BRiCatwork study presented in **Chapters 3, 4, and 5** was also prospectively registered with the International Standard Registered Clinical/soCial sTudy Number (ISRCTN) on 14th January 2019 (study number: ISRCTN11333136).

Participants were asked to provide written consent before any data was collected (see **appendix 1** for information sheets and consent forms). Per ethical guidelines and the British Psychological Society's code of ethics and conduct (BPS, 2018), participants were provided with a study ID number (i.e., A123) to ensure their information remained anonymous. In the instance that identifiable

information was unintentionally disclosed, for example, during an interview, the information was discarded during transcription and replaced with a generic label representing the form of information removed (i.e., partner's name, location, name of employer). In line with the General Data Protection Regulation law (GDPR, 2018) all data were stored in encrypted files on either a password-protected computer or on an encrypted external hard drive.

## 2.3. **Participant Recruitment**

All participants were recruited using volunteer response sampling, a form of purposive sampling via advertisements placed on online social media platforms including Facebook, Twitter and Instagram. Recruitment posters were displayed on both public and private breast cancer support group's media pages including the Birkbeck Centre for Building Resilience in Breast Cancer (BRiC; http://briccentre.bbk.ac.uk/), Breast Friends, Inflammatory Breast Cancer Network, Mastectomy Network, Macmillan, Breast Cancer Now, True Cancer Bodies (TCB) and Breast Cancer Now, as well as MET UP UK, and Stage4needsmore.

Participants who responded to one of the online advertisements were sent an email containing the study information sheet and participant inclusion criteria (see individual chapters for a more comprehensive description of each study's inclusion criteria) to assess their eligibility before they agreed to participate. Upon confirmation of eligibility, further instructions and study materials (i.e., URL links to access the online questionnaires) were emailed.

## 2.4. Self-Report Questionnaire Measures

### 2.4.1. Demographic Information:

Demographics questionnaires were employed in each of the studies presented in this thesis to collect information relating to sociodemographic and lifestyle factors including, age, civil status, education and ethnic origin, as well as alcohol consumption, smoking (e.g., do you smoke) and substance abuse (e.g., tobacco). Information regarding breast cancer and treatment characteristics (i.e., grade, type of breast diagnosed, size of tumour(s), lymph node involvement, hormone receptor status, treatments received), psychiatric history (i.e., current medication, previously suffered from any psychiatric condition), neurological conditions (i.e., previously suffered from a neurological condition) and current employment (i.e., work sector, working hours, size of the company) was also collected. All information was self-reported by participants

### 2.4.2. Perceived Cognitive Function:

In the 'BRiCatWork' study (**Chapters 5)**, impact of quality of working life in metastatic breast cancer study (**Chapter 6)** and impact of COVID-19 in primary breast cancer study (**Chapter 7**), perceived cognitive function was measured by the ***Functional Assessment of Cancer Therapy-Cognitive Scale (FACT-Cog, version 3)*** (Wagner et al., 2004; Wagner et al., 2009), a 37-item self-report questionnaire composed of four subscales including perceived cognitive impairment (PCI; 20 items, score range = 0-80), perceived cognitive ability (PCA; 9 items; score range =0-36), comments from others (CFO; 4 items; score range = 0-16) and impact on quality of life (QoL; 4 items, score range = 0-16). Items are measured on a five-point Likert scale from 0 ('*never*' or '*not at all*') to 4 ('*several*

*times a day*' or '*very much*'), with a total score ranging from 0 to 148[1]. Higher scores (for each subscale and total) indicate a better perceived cognitive function or quality of life. The Fact-cog (version 3) has been widely used in both primary breast cancer (Von Ah & Tallman, 2015; Janelsins et al., 2017; Von Ah et al., 2018) and metastatic breast cancer (MBC) (Dobretsova & Derakshan, 2021) research. Excellent Cronbach's α scores were found for each of the studies reported in this thesis (α ≥.95).

### 2.4.3. **Rumination:**

In the 'BRiCatWork study (**Chapters 5)** and impact of COVID-19 in primary breast cancer study (**Chapter 7)**, rumination was assessed using the ***Rumination Response Scale (RRS)*** (Treynor et al., 2003), a 22-item self-report questionnaire composed of three factors including brooding (5 items, score range = 5-20), reflection (5 items, score range = 5-20) and depression (12 items; score range = 12-48). Items are rated on a four-point Likert scale ranging from 1 ('*never*') to 4 ('*almost always*'), with the total score ranging from 22 to 88. A higher total score reflects a greater level of rumination. The RRS is a highly reliable and valid questionnaire that has been implemented in breast cancer research (Swainston & Derakshan, 2018). Excellent Cronbach's α scores were found for each of the studies presented in this thesis (both α = .94). In line with research conducted by Swainston and Derakshan (2018, 2021; Swainston et al., 2021), the total score was selected as the variable of interest.

### 2.4.4. **Anxiety:**

In all three studies presented in this thesis (see **Chapters 5**, **6** and **7)**, anxiety was assessed using the anxiety subscale of the highly reliable and valid ***Hospital Anxiety and Depression- Anxiety Scale (HADS-A)*** (Zigmond & Snaith, 1983), a seven-item self-report questionnaire with a four-point Likert

[1] In line with the recommendation from FACIT.org individual item-total score correlation coefficients were explored for PCI, PCA and FACT-Cog total. Results showed that all 37-items should be included in the total score and analysis.

scale ranging from 0 to 3. The total score ranges from 0 to 21, with a higher score reflecting worse (trait) anxiety in the last seven days. The HADS-A has been implemented in both primary breast cancer (Osborne et al., 2004; Ho et al., 2018; Swainston et al., 2021) and metastatic breast cancer (Park et al., 2018) studies. Good Cronbach's scores were found for each of the studies ($\alpha \geq .84$).

### 2.4.5. **Depression:**

In the impact of quality of working life in metastatic breast cancer study (**Chapter 6**) and impact of COVID-19 in primary breast cancer study (**Chapters 7)**, depression was measured with the ***Hospital Anxiety and Depression- Depression Scale (HADS-D)*** (Zigmond & Snaith, 1983), a seven-item subscale. Items are rated on a four-point Likert scale, with scores ranging from 0 to 3. The total score is calculated from the summation of scores, with the possible total ranging from 0 to 21. A higher score indicates a greater level of depression. The HADS-D is a highly reliable and valid self-report questionnaire that has been implemented in previous breast cancer research (Ho et al., 2018; Park et al., 2018; Gregorowitsch et al., 2019). Good Cronbach's scores were found for each of the studies ($\alpha \geq .78$).

Depression was measured by the ***Center for Epidemiologic Studies Depression Scale (CES-D)*** (Radloff, 1977) in the 'BRiCatWork' study presented in **Chapter 5**. CES-D is a highly reliable and valid 20-item self-report inventory with a four-point Likert scale ranging from 0 ('*Rarely or not of the time (less than 1 day)*') to 3 ('*Most or all of the time (5-7 days*)'). The overall score ranges from 0 to 60, with a higher score indicating greater depression in the last seven days. The CES-D has been widely used in RCTs conducted with the breast cancer population (Stagl et al., 2015; Bower et al., 2021). An excellent Cronbach's α score was found in the RCT reported in **Chapter 5** ($\alpha = .92$).

### 2.4.6. **Quality of life:**

In the 'BRiCatWork study **(Chapter 5)** and impact of quality of working in metastatic breast cancer study (**Chapter 6)**, quality of life was assessed by the ***European Organization for Research***

***and Treatment of Cancer Quality of Life (EORTC-QLQ-C30)*** (Aaronson et al., 1993), a reliable and valid self-report questionnaire composed of five functional scales (physical, 5 items; role, 2 items; social, 2 items; emotional, 4 items and cognitive, 2 items), three symptom scales (fatigue, 3 items; nausea and vomiting, 2 items and pain, 2 items) and six individual symptom item statements (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties), as well as a global health status scale (2 items). Items in the functional scales, symptom scales and individual symptom statements are measured on a four-point Likert scale ranging from 1 ('*not at all*') to 4 ('*very much*'). Global health status items are rated on a seven-point scale from 1 ('*very poor*') to 7 ('*excellen*t'). Scores are calculated by adding the responses and then dividing by the number of answered items. The raw score for each subscale and individual symptom item is then converted using transformation to create a score ranging from 0 to 100. Higher scores for the five functional scales and global health status demonstrate a greater quality of life and functioning. Whilst, higher scores for the symptoms (subscale and individual items) indicate more severe symptomology in everyday life. The EORTC-QLQ-C30 has been widely used in primary breast cancer and MBC research (McLachlan et al., 1999; Menning et al., 2016; Ho et al., 2018; Mierzynska et al., 2020). Excellent Cronbach's α scores were found for each of the studies (Global health $\alpha \geq .85$).

### 2.4.7. **Pathological Worry:**

In the impact of COVID-19 in primary breast cancer study presented in **Chapter 7**, worry was measured by the ***Penn State Worry Questionnaire*** (***PSWQ***) (Meyer et al., 1990), a 16-item self-report questionnaire with a five-point Likert scale ranging from 1 ('*not typical of me*') to 5 ('*very typical of me*'). The total score ranges from 16 to 80, with a higher score showing a greater level of pathological worry. The PSWQ is a highly reliable and valid questionnaire that has been widely applied in breast cancer research (Swainston & Derakshan, 2018; Renna et al., 2020). An excellent Cronbach's score was found for the study presented in this thesis ($\alpha = .94$).

### 2.4.8. **Comorbidity:**

In the impact of COVID-19 in primary breast cancer study (**Chapter 7)**, current health comorbidity was assessed using the ***modified Charlson Comorbidity Index*** (***CCI***) (Charlson et al., 1987), a nine-item (comorbidities: (1) asthma, emphysema or chronic bronchitis, (2) arthritis or rheumatism, (3) diabetes, (4) digestive problems, (5) heart trouble, (6) HIV illness or AIDS, (7) kidney disease, (8) liver problems, (9) stroke) self-report questionnaire with 'yes' or 'no' responses. Each comorbidity item has a weighted value of 1, 2, 3 or 6 (determined by the relative risk of mortality within 1 year), with more severe health comorbidities assigned higher values (i.e., 'HIV illness or AIDS' has a value of 6). The nine items included are the most common comorbidities associated with the risk of mortality. An overall score is formed by summing the nine responses ('yes' responses are given the weighted value and 'no' responses are given a value of 0). A higher overall score reflects a worse level of current health comorbidity. The CCI has previously been used in breast cancer research to record comorbidity (Fu et al., 2015).

### 2.4.9. **Work Limitations:**

In the 'BRiCatWork' study (**Chapter 5)** and impact of COVID-19 in primary breast cancer study (**Chapter 6)**, workplace performance and productivity loss were measured using the 25-item ***Work Limitations Questionnaire*** (***WLQ***) (Lerner et al., 2001; 2003), a highly reliable and valid self-report inventory (Lerner et al. 2002). Items compose four subscales including time management demands scale (TMD-S; 5 items), physical demands scale (PD-S; 6 items), mental/interpersonal demands scale (MID-S; 9 items) and work output demands scale (WOD-S; 5 items). All items are rated on a five-point Likert scale ranging from 1 ('*difficult all of the time (100%)* or *able all of the time (100%)*') to 5 ('*difficult none of the time (0%)* or *able none of the time (0%)*'), with reverse scoring for negatively phrased TMD-S, MID-S, and WOD-S items. Work productivity loss (%) over the last 14 days is calculated using the four subscales. Scores are calculated by adding the scores from the answered items and dividing by the number of answers provided. The WLQ formula is then applied to form a

total score ranging from 0 to 100, with higher subscale scores reflecting a greater level of difficulty in the workplace. Applying the exponential formula, a percentage score for work productivity loss is created (the maximum attainable score for work productivity loss is 24.9%). The WLQ has been widely applied in previous breast cancer studies (Hansen et al., 2008; Calvio et al., 2010; Zeng et al., 2016; Von Ah et al., 2018). High Cronbach's α scores were found for the studies included in this thesis (all α's ≥.83).

### 2.4.10. **Work and Activity Impairment:**

In the quality of working life in metastatic breast cancer study (**Chapter 6**), work and activity impairment due to MBC was measured using the ***Work Productivity and Activity Impairment Questionnaire: Specific Health Problem*** (***WPAI: SHP***, ***version, 2***) (Reilly et al., 1993), a highly reliable and valid self-report questionnaire made up of six individual items assessing (1) current employment status, (2) work hours missed because of MBC in the last seven days, (3) work hours missed for other reasons in the last seven days, (4) hours worked in the last seven days, (5) MBC effect on productivity at work and (6) MBC effect on the ability to engage in regular daily activities outside of work. Items five and six are measured on a Likert scale ranging from 0 to 10, with higher scores showing a greater level of impairment as a result of MBC. Four subscale scores expressed as a percentage are formed: work time missed due to MBC, impairment at work due to MBC, overall work impairment due to MBC and activity impairment due to MBC. Higher scores demonstrate worse impairment and productivity loss due to MBC. The WPAI: SHP has been widely applied in MBC research (Cleeland et al., 2014; Bajaj et al., 2017; Verrill et al., 2020).

### 2.4.11. **Quality of Working Life:**

In the quality of working life in metastatic breast cancer study (**Chapter 6**), quality of working life was assessed with ***Quality of Working Life for Cancer Survivors*** (***QWLQ-CS***) (de Jong et al., 2018), a 23-item self-report questionnaire composed of five subscales including meaning of work (4

items), perception of the work situation (5 items), atmosphere in the work environment (5 items), understanding and recognition (5 items) and problems due to health (4 items). Items are rated on a six-point Likert scale from "Totally disagree" to "Totally agree", with reverse scoring for negatively phrased items. Scores for the five subscales and the QWLQ-CS total are converted to a standardised score ranging from 0 to 100 with the formula: ((sum of items – lowest possible sum score) / range between lowest and highest score) x 100). Higher scores reflect better quality of working life in cancer survivors. Excellent Cronbach's α scores were found for the study presented in **Chapter 6** (Meaning of work: Cronbach's α = .96, Perception of the work situation: Cronbach's α = .86, Atmosphere in work environment: Cronbach's α = .85, Understanding and recognition: Cronbach's α = .81, Problems due to health: Cronbach's α = .82, Overall QWLQ-CS score: Cronbach's α = .91).

### 2.4.12. **Women's experience with employers after MBC diagnosis:**

In the quality of working life in metastatic breast cancer study (**Chapter 6**), experience with employers following MBC diagnosis was assessed using the ***Workplace Experience Questions*** (***WPEQ***) (developed by BC) composed of 22 individual items. Multiple-choice items were used to record the influence of employers on current employment status, factor(s) that prompted the decision to leave the workforce and financial burden, as well as the required work-based adjustments. Ten Likert scale items assessed women's experiences with employer support, understanding, awareness and the impact on confidence at work, with scores ranging from 0 ('*not at all*' or '*much less*') to 5 ('*extremely*' or '*much more*'). Higher scores reflect a more positive experience with employers and better views of work. Two composite mean scores were formed and referred to as experience of employers score (MBC-EE score; Cronbach's α = .88) and personal views of work score (MBC-PVW score; Cronbach's α = .85) (see **appendix 2** for questions and **appendix 3** for item reliability and factor analysis).

### 2.4.13. **Coronavirus Disease 2019 (COVID-19) Impact:**

In the impact of COVID-19 in primary breast cancer study (**Chapter 7)**, the effect of COVID-19 and its restrictive measures on women living with a diagnosis of breast cancer was examined during the peak of the pandemic in the UK using the self-report ***COVID-19 Impact Questions*** (developed by BC) composed of 24 individual items. At this time the UK government introduced three restrictive measures including (1) requiring people to stay at home including working from home, except for very limited purposes, (2) closing certain businesses and venues not providing essential services and (3) stopping all gatherings of more than two people in a public space (UK Government, 2020). Items composed two subsections referred to as COVID-19 impact items (section A, 16 items) and COVID-19 work items (section B, 8 items). In section A, multiple-choice questions were used to record women's isolation status, the UK Government shielding letter and disruption(s) to scheduled appointments, as well as personal experience with COVID-19 including the symptoms experienced[2]. Five Likert scale items assessed the effect of the COVID-19 outbreak on women's emotional wellbeing ('*Has the COVID-19 outbreak made you feel more*: (1) anxious, (2) upset, (3) fearful than usual' or '*Has the COVID-19 outbreak made you feel less*: (4) in control or (5) less confident than usual'), with scores ranging from 0 ('*not at all*') to 5 ('*extremely*'). Higher scores indicate a greater COVID-19-related emotional vulnerability. A composite score was derived from the five emotional vulnerability items and referred to as COVID-EMV (Cronbach's $\alpha = .89$) (see **appendix 2** for questions and **appendix 3** for item reliability, factor analysis and COVID-EMV correlations).

In section B, multiple-choice items were used to record current employment status and employers' support with the required work-based adaptations. A single open item assessed the impact of COVID-19 on women's typical working day and work duties (e.g., working as normal or not working due to COVID-19) and five items rated on a 0 ('*not at all*' or '*much less*') to 5 ('*extremely*' or '*much more*') scale measured employers support, work importance, job satisfaction, confidence and job security. Higher scores reflect more positive views of work and better employer support in response to the COVID-19 outbreak at work. A good Cronbach's $\alpha$ score was found for subsection B ($\alpha = .74$).

[2] COVID-19 symptoms were taken from the NHS and Government public support page/advise page.

## 2.5. **Objective Measures of Cognitive Function**

### Computerised Working Memory Tasks:

The three computerised working memory tasks (described below) presented in **Chapter 5** ('BRiCatWork' study) were carried out in a soundproof experimental booth in the MERLiN laboratory (Birkbeck, University of London) using E-Prime 2.0 Professional Software (Schneider et al. 2012). All tasks were presented at a distance of 70 cm on a 24-inch LED Asus VG248QE LCD computer screen with a resolution of 1920 x1080, a refresh speed of 60Hz and a response time of one millisecond.

### 2.5.1. **Working Memory Capacity:**

Working memory capacity (WMC) was measured using the ***automated Operation Span Task*** (***OSpan task***) (Unsworth et al., 2005; Foster et al., 2015; Turner & Engle, 1989) and the ***shortened version of the Change Detection Task*** (***CDT***) (Vogel et al, 2005; Owens et al., 2012, 2013) replicated from earlier research conducted by Swainston & Derakshan (2021) with women from the breast cancer population.

#### 2.5.1.1. **Operation Span Task:**

The ***automated OSPAN task*** is a reliable and valid complex maths-letter span task composed of three practice sessions ((1) letters only (4 trials), (2) maths equations only (15 trials) and (3) a combination of letter and maths equations (3 trials)) and three experimental blocks of 15 trials (75 letters and 75 maths equations) completed independently by the participant using the computer mouse.

During the first practice session, participants were asked to remember and recall a sequence of two to three unrelated letters each shown on the computer screen for 800ms. Participants were first presented with the letters (successively) before a 4 x 3 matrix of 12 possible letters ('F, H, J, K, L, N,

P, Q, R, S, T and Y') was displayed, using the computer mouse participants had to select the box next to the letters shown in the correct serial order. The practice session was untimed and feedback regarding the number of letters correctly recalled was provided. Participants then practised answering the maths equations. Participants were shown a simple maths equation (e.g., 2 + 4 =?) and told to solve the equation as quickly as possible before clicking on the mouse button to advance to the next computer screen. On the following screen, a single numerical answer (e.g., 6) was presented alongside 'true' and 'false' boxes, using the answer participants had to select the appropriate response box. Feedback was provided after each equation. The practice session was used to determine the participants' average response time. In the final practice session, participants were instructed to remember a sequence of unrelated letters ('F, H, J, K, L, N, P, Q, R, S, T and Y'; *memory task component*) presented between simple maths equations (i.e., 2 + 2 =?; *distractor task component*), duplicating the experimental trials.

Throughout the last practice session and experimental trials, participants were first shown a simple maths equation, after clicking on the mouse 'true' and 'false' boxes appeared with a numerical answer. This was followed by the presentation of a single letter. Whilst there was no overall time limit for the task, participants were only given 2.5 standard deviations of their average response time (as determined by the math equation practice session) to select a 'true' or 'false' response. This aimed to stop the rehearsal of any letters shown earlier in the sequence. If no response was made within that time limit an error response was counted and the program automatically moved on to the next letter. The number of letters presented in each experimental trial varied randomly from three to seven. At the end of each trial, the same 12 letters were displayed. Feedback regarding the number of correct letters, number of errors made on the maths equations and percentage accuracy on the maths equation for the entire experiment was provided at the end of each trial.

Participants were informed at the start of the experimental trials that it was important to maintain a performance accuracy of at least 85% on the maths equations, as only data equal to or above this percentage could be used. They were also told that to attend future experiments they must score at least 85% on the maths equations whilst maintaining good performance on the letter recall. The number

of correct letters recalled from the three blocks of trials was added together to provide an OSpan score (also known as the partial score).

### 2.5.1.2. **Change Detection Task:**

The shortened version of the CDT (Vogel et al.,2005; Owens et al., 2012, 2013) is a highly reliable and valid visual working memory task composed of a short practice session (12 trials, 4 per condition) and 192 experimental trials split into four blocks of 48 trials. Participants started on the practice session before moving on to the experimental trials once they had reached ≥ 50% accuracy on the practise session.

During both the practice session and experimental trials, participants were asked to remember and then compare the orientation of red rectangles (*target items*) shown in two sets of stimulus array, referred to as the (1) memory array and (2) accuracy-test array. Participants were first shown a white fixation cross positioned in the centre of the screen closely followed by the appearance of a white arrow (acting as a cue) directly above, pointing either to the left or right side of the screen for 700ms. Participants were told to maintain their focus on the fixation cross and only attend to the set of rectangles displayed on the side indicated by the white arrow. The memory array of two or four rectangles was then shown for 100ms, this was followed by a 900ms retention array and finally the accuracy-test array in which the rectangles reappeared for 2,000ms (see **figure 2.1** for an example of the CDT). Participants were asked to respond as accurately as possible by pressing the '1' key on the computer keyboard if there was a change in orientation of one of the red rectangles and the '0' key if there was no change in the orientation between the (1) memory array and (2) accuracy-test array.

For each trial, participants were shown one of three different possible rectangle (0.64º x 1.21º) conditions including two red rectangles (2), four red rectangles (4) or two red rectangles and two blue rectangles (4D; *distractor items*). The red (*target items*) and blue (*distracter items*) rectangles were randomly oriented in one of four positions (vertical, horizontal, left 45º, right 45º) and spaced

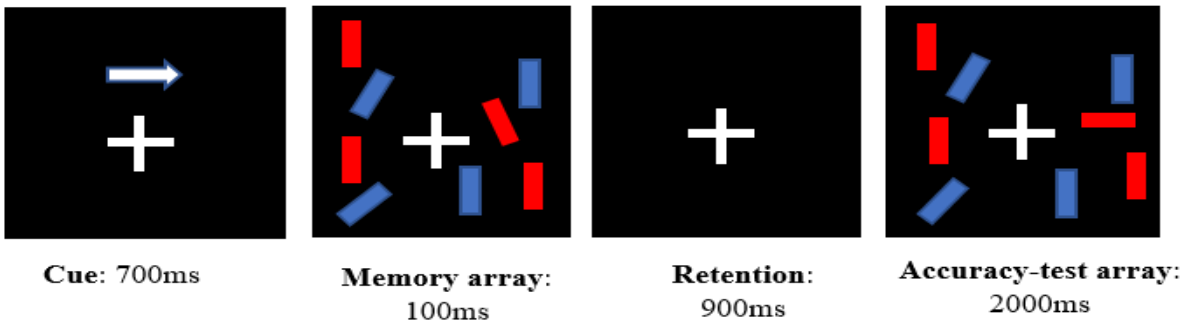
approximately 2º apart within a 4º x 7.2º rectangular region. The two regions were centred 3º from a white central fixation cross presented on a black background.

In half of the trials, the orientation of the red rectangles presented in the (1) memory array matched the (2) accuracy-test array (i.e., there was no change in orientation) and in the other half, the orientation of one red rectangle changed from the (1) memory array to (2) accuracy-test array. Throughout the trials, the rectangle condition (two red rectangles, four rectangles or two red rectangles and two blue rectangles), orientation change (i.e., change or no change) and direction of the arrow (right or left) were randomised and presented equally. The same set of stimuli was not shown more than once during the experimental trials.

WMC was calculated using the formula K = S x (H – F) / (1 -F) (Pashler, 1988), where S was the size of the array, H was the proportion of correct responses when the orientation of one of the red rectangles had changed (also known as the hit rate) and F was the proportion of incorrect response when the orientation of the red rectangles had not changed (also referred to as the false alarm rate). In the BRiCatWork study presented in **Chapter 5**, S was equal to the four red rectangle condition to avoid the ceiling or floor effects that can occur in the two-item condition and the four-item distracter condition (Owens et al., 2013).

**Figure 2.1**

*An example of the CDT*




*Note.* Participants were instructed to remember the orientation of the red rectangles shown in the memory array and then compare them to the orientation of the red rectangles in the accuracy-test array.

Using the keyboard participants responded by pressing '1' if there was a change and '0' if there was no change. In the example presented in **figure 2.1**, participants would need to press '1' as the orientation of one of the red rectangles presented on the right side has changed.

### 2.5.1.3. **Distractor Interference:**

Distractor interference was assessed using the ***modified standard letter flanker*** (Eriksen & Eriksen, 1974, replicated from Moser et al., 2011), a highly reliable and valid conflict paradigm that has been used in previous breast cancer research to assess neural markers of error monitoring (Swainston & Derakshan, 2021). Participants were asked to respond rapidly and accurately using the left and right computer mouse buttons to identify the central letter (*target letter*) shown within a string of five letters (i.e., MM**N**MM), for example, participants were told to press the left button if the central letter was **M** or press the right button if the central letter was **N**. For each trial, the central letter was either congruent (i.e., VV**V**VV) or incongruent (i.e., VV**U**VV) to the four distractor (*flanking*) letters. Participants completed a short practise session of 24 trials before moving on to 480 experimental trials divided into 12 blocks of 40 trials.

In half of the trials, the target letter was congruent and in the other half, the target letter was incongruent to the four distractor letters. To increase the number of error responses produced and ensure reliable ERN analysis (Olvet & Hajcak 2009a; see **section 2.6**), the letters differed across the 12 blocks of trials (block 1 and 2: M + N, block 3 and 4: E + F, block 5 and 6: O + Q, block 7 and 8: T + I, block 9 and 10: V + U, and block 11 and 12: P + R) and response requirements were reversed between the blocks (i.e., in block 1 the target letter M corresponded to a left mouse response and in block 2 the letter M corresponded to a right mouse response). No feedback was provided during the task.

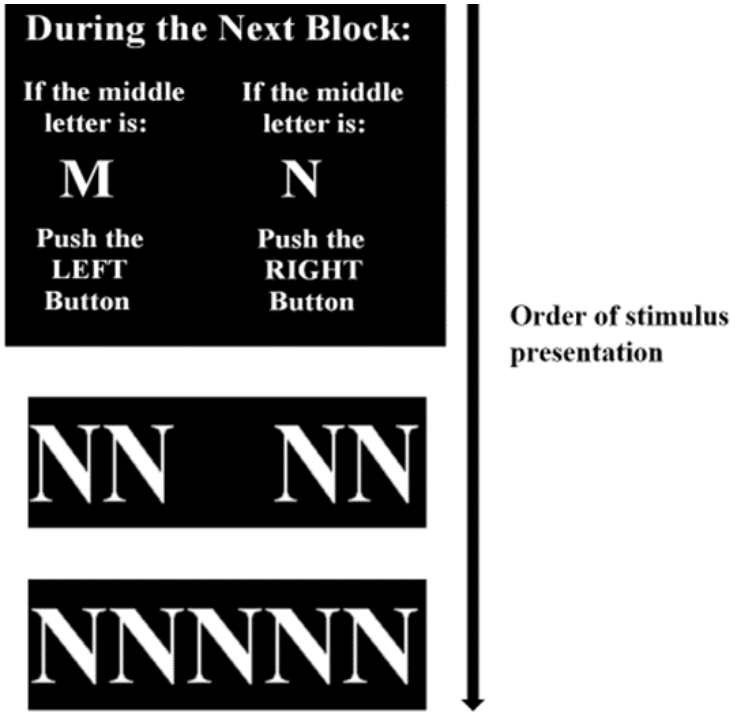
Across all of the trials, the white letter stimuli appeared subtended 1.38º of the visual angle vertically and 9.28º horizontally on a black background. Participants were shown the four distractor letters for 35ms before the central target letter was displayed. The string of five letters then remained

visible on the screen for 100ms (a total trial time of 135ms). A variable intertrial interval with a white fixation cross was presented for between 1,200ms to 1,700ms after each letter trial.

Participants' reaction times and response accuracies were calculated for both congruent and incongruent trials, as well as the total number of error responses produced. Corrections were applied for switching block failure (> = 60% errors).

**Figure 2.2**

*An example of a congruent trial included in the Modified Standard Letter Flanker*




*Note.* Participants were instructed to use the computer mouse buttons to respond to the central letter shown between four flanking letters (distractors). In the example presented in **figure 2.2**, participants would need to press the right mouse button to signal that the central letter was N. Please note this image is not to scale.

## 2.6. **Electroencephalogram (EEG)**

In the 'BRiCatWork' study (**Chapter 5)**, neural markers of error processing and attentional control were assessed noninvasively using EEG. Neural activity was recorded continuously using BrainVision Recorder (Brain Products, Gilching, Germany) from 32 6 mm central opening Ag-AgCl passive electrodes embedded in a standard BrainVision BrainCap (EasyCap) in accordance with the international standard 10/20 system (Jasper, 1958) including, both left and right mastoids (TP9 and TP10) during the modified flanker task (see **section 2.5.1.3** for a comprehensive description of the task). The online reference electrode was located at FCz and the ground electrode was at AFz. Electrooculogram (EOG) activity created by vertical eye movements and blinks was recorded at FP2 and via an electrode placed approximately 1 cm below the right pupil (EOGV). Horizontal eye movement was recorded by electrodes placed on the left and right outer canthi (EOGH). Throughout data acquisition, BrainVision recorder software digitized all electrical signals at 1024 Hz and impedances were kept between 0-10kΩ. The signal was amplified with a BrainVision BrainAmp standard amplifier with a sampling rate of 1000 Hz, resolution of 0.1μV and a low cutoff of 10s (0.016 Hz) and a high cutoff of 1000 Hz. Online filters included a low cutoff filter of 0.531 Hz and a high cutoff of 70 Hz (slope for the low and high cutoff is 12 dB/octave).

Offline analyses were conducted using BrainVision Analyzer 2.2 (Brain Products, Gilching, Germany). Failed switch blocks (or failed switched mappings) (> = 60% errors) were accounted for and removed to be consistent with behavioural analyses. Spherical splines method (Perrin et al., 1989) was used for interpolation. Scalp electrode recordings were re-referenced to the mean of the mastoids and band-pass filtered using Butterworth zero-phase filters with a low cut-off of 0.1Hz and a high cut-off of 30 Hz (12 Db/octave roll-off). Gratton, Coles and Donchin's (1983) method was applied to correct ocular artefacts. Response-locked data were segmented into individual epochs beginning 200ms before the response discharge and continuing for 800ms after the response production. Stimulus-locked data were also segmented into individual epochs beginning 200ms before the stimulus onset and continuing for 800ms. A computer-based algorithm within BrainVision software was employed to detect

physiological artefacts (i.e., muscle movement) and trials were rejected if the following criteria were met: (1) a voltage step exceeding 50 μV between contiguous sampling points, (2) a voltage difference of more than 200μV within a trial, or (3) a maximum voltage difference less than 0.5μV within a trial. The remaining response-locked and stimulus-locked data were segmented, averaged and then baseline corrected (beginning at -199.22ms and ending at 0.00ms) separately.

## Overview of Qualitative Materials and Methods

### 2.7. **Interview Schedule**

Baseline and post-training interviews were conducted as part of the 'BRiCatWork' RCT study (see **Chapters 3**, and **4**). Interview schedules were developed by reviewing qualitative research studies (i.e., Maunsell et al., 1999; Kennedy et al., 2007; Von Ah et al., 2013; Bolton et al., 2018; Klaver et al., 2020) to identify key issues experienced by working cancer survivors. After the initial interview schedules were devised by the principal researcher (BC) they were reviewed and refined by a second researcher (EAG), with a few changes made to the wording and phrasing of questions. The baseline interview schedule was then piloted with two women before the study[3] to assess the appropriateness and feasibility of the interview questions. The women were approached by the researcher to participate after expressing an interest in the study. After the interviews, verbatim transcripts were reviewed to check that the wording of the questions elicited detailed and in-depth responses. No changes were made to the wording of the questions; however, further probing questions (such as 'can you tell me something about how experiencing these changes in cognitive (thinking) skills make you feel?') were included and agreed by consensus. No changes were made to the interview schedules during data collection.

[3] Pilot participant one was unable to participate in the study as she was over 60 months post active treatment but matched all of the other criteria and participant two was mainly working voluntarily at the time of the interview.

Baseline interview schedules started by asking participants a series of questions relating to their breast cancer history, as well as the physical, social, psychological and emotional sequelae they had experienced throughout the treatment period. Participants were also asked to talk about their work experiences and work status during and after their active treatment. The interview schedule then focussed on investigating the perceived cancer-related cognitive sequelae, the impact of these sequelae on workability and work performance, as well as the self-management coping strategies and work-based adaptions implemented including changes to work commitments (i.e., decreased hours). Women's contentment at work was also discussed (see **appendix 4** for the baseline interview schedule).

Post-training interviews were conducted at one-month, six-months and one-year using the same interview schedule. The interview first focused on exploring the perceived effects of cognitive training (dual *n*-back training or dual 1-back training) on the cancer-related cognitive sequelae affecting workability and performance, work commitments, self-management coping methods and adaptions applied and level of contentment at work. Participants were then asked a series of questions relating to their training experience, earlier expectations and perceived benefits from training (e.g., on workability, confidence, and emotional wellbeing). Preference regarding the timing of the training was also explored (see **appendix 4** for the post-training interview schedule). Interview questions followed the flow of the discussion. Open discussions were encouraged alongside the planned questions to allow participants to comprehensively outline their experiences without restriction.

## 2.8. **Qualitative Analysis**

Participant interviews were recorded using an encrypted audio recorder digital App and were transcribed verbatim by the principal researcher using Express Scribe Transcription Software. Transcripts were then accuracy checked against the original recording. Grammatical errors made during the interviews were retained to reflect the voice of the participants. A "framework" analysis approach introduced by Ritchie and Spencer, (1994; Ritchie et al., 2003) was selected to analyse the interviews collected for the BRiCatWork study (see **Chapters 3**, and **4**) because of its systematic approach to

managing large data sets ($N$ = 126) and flexible nature allowing the complete collection of data before starting the analysis, which was key in enabling the interviews to be conducted at the required time points. Besides, it was also selected due to its compatible nature with participants with more heterogeneous (or varied) sample characteristics, for example, women in the BRiCatWork study ranged from six- to 60-months post-active treatment.

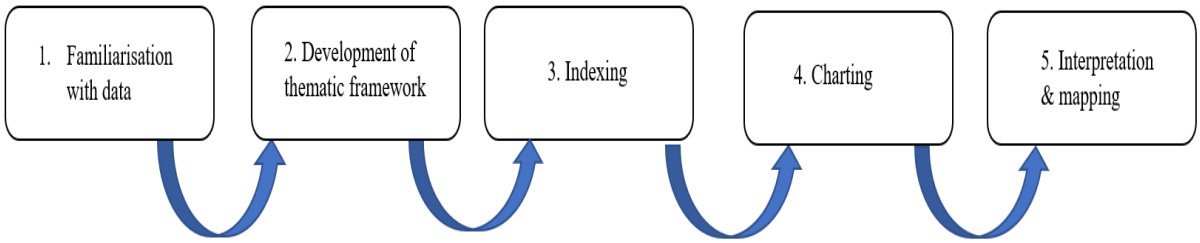
Framework analysis is defined as a highly systematic and pragmatic qualitative approach that utilises a thematic framework to manage, analyse and identify themes in large sets of data (Gale et al., 2013). Framework which was originally developed for the development of social research policy (Ritchie and Spencer, 1994), is a continuous, flexible, reflective and iterative approach that is not aligned to any epistemology, philosophical or theoretical approach (Gale et al., 2013). The framework approach primarily follows a constant comparison method (Glaser, 1965) to refine themes grounded within the data, this involves systematically comparing interviews to detect similarities and differences within and between participants' experiences. One main advantage of using the framework approach is it allows for comparisons across both the themes (thematic analysis) and individual cases (case analysis). It is also a highly transparent approach due to its systematic nature and compatibility with software such as NVivo (NVivo, 2018), enabling the production of an audit trail from the original data.

Transcripts were analysed via a series of five systematic interconnecting steps including (1) familiarisation, (2) formation of the thematic framework, (3) indexing, (4) charting and (5) interpretation and mapping using NVivo Pro 12 software (NVivo, 2018). Initially, the researcher became immersed in the data (familiarisation) through reading and re-reading the transcripts and taking note of relevant units of meaning and creating free codes (open coding). These free codes were then grouped into a series of coherent themes to produce a list of superordinate and subordinate themes that reflected women's shared experiences, forming the thematic framework (also known as the coding index). The thematic framework was then applied to all of the interview transcripts (indexing) before thematic charts were constructed to summarise the indexed data for each of the themes (charting). In the final interpretative step, the relationships and interactions between the themes and subthemes were explored and established to draw 'bottom-up' conclusions.

Interviews were conducted, coded and analysed by the principal researcher (BC, MSc) under the supervision of EAG, an expert in qualitative analysis. Throughout the process, BC considered her own position in relation to the research topic as a female researcher with no personal experience of breast cancer, as well as what her knowledge, views and beliefs on the effects of adaptive cognitive training and of impaired cognitive function at work in women with breast cancer brought to the interviews to avoid obvious, conscious or systematic bias and achieve an 'empathic neutrality' (Ritchie & Spencer, 1994; Ritchie et al., 2003). The first ten interviews were selected at each time point before analysis and independently coded and analysed by BC and EAG to assess constancy in data interpretation. Only minor differences emerged in the identified themes and these were resolved by mutual agreement. Emerging themes in the remaining interviews were discussed as part of an ongoing process to increase rigor and trustworthiness. Interview transcripts were not returned to participants for review or correction due to the sensitive nature of the research and to also ensure that they remained blind to their training group allocation until after the completion of the BRiCatWork study.

**Figure 2.3**

*The five interconnecting stages forming the 'framework' analysis approach*




*Note.* The framework analysis approach is highly flexible, allowing the researcher to move back and forth between these five interconnecting stages

## 2.9. **Cognitive Training**

Standard versions of dual *n*-back training and dual 1-back training (replicated from Jaeggi et al., 2008; Owens et al., 2013) were utilised in the 'BRiCatWork' study (see **Chapters 4**, and **5**). Participants were shown a 3 x 3 grid with a green fixation cross located in the central square (see **figure 2.4** for an example of dual *n*-back training). During each trial, a single green square flashed up in one of eight possible positions on the grid at a presentation rate of 500ms. At the same time, a single letter consonant (h, l, c, q, s, r, k and t) was spoken by an automated female voice. The position of the green square (visuospatial stimuli) and letter consonant (auditory stimuli) was randomly distributed across each of the trial blocks. Participants were instructed to simultaneously remember the location of the green square shown and its paired spoken consonant. Responses were made using the computer keypad when either a single stimulus (press 'A' for a visual match ***or*** press 'L' for an auditory match) or the pair of stimuli (press 'A' ***and*** 'L' at the same time) matched what was presented '*n*' number of trials beforehand. For example, if $n = 2$, participants respond when the location of the green square and/or the spoken letter matched the stimuli presented two trials earlier. No response was required for a non-match. Participants were asked to respond to each trial as rapidly and accurately as possible. Each trial was separated by a 2,500ms interval. Blocks of trials were designed to contain an equal number of visuospatial and auditory matches (i.e., four visuospatial ***or*** four auditory and two visuospatial ***and*** auditory).

Participants were asked to complete 12 sessions of training at home as consecutively as possible over a period of two weeks. Sessions lasted approximately 30 minutes each regardless of training condition (i.e., dual *n*-back or dual 1-back). Participants were given a unique ID number which they entered at the start of each session, allowing the researcher to track their progress. The rationale for selecting 12 sessions was driven by findings from earlier research conducted by Swainston & Derakshan (2018, 2021), showing that women with a history of breast cancer experienced sustained improvements in emotional resilience as evidenced by reductions in (trait) anxiety and rumination after participating in 12 sessions of training. A recent meta-analysis by Pergher et al., (2019) revealed that approximately 61% of studies providing 10 sessions or more of *n*-back training found robust near transfer effects and

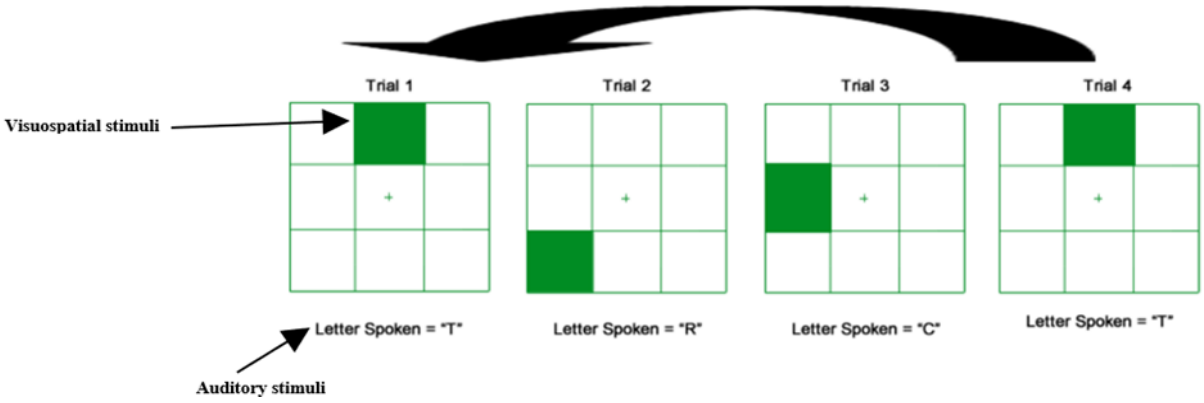
approximately 26% found far transfer effects, this compares to studies implementing less than 10 sessions where near and far transfer effects were reported less frequently (50% and 20%, respectively).

### 2.9.1. **Dual *n*-Back Training (Adaptive cognitive training; Intervention group)**

The level of task difficulty for dual *n*-back training (intervention; 1-back, 2-back, 3-back and 4-back) was determined by the average performance accuracy for both (visuospatial and auditory) stimuli on the previous block of trials. Participants were required to complete 20 blocks of 20 + *n* trials, for instance, a block of dual 2-back included 22 trials. Each training session started on 1-back and then adapted across the remaining trials according to the level of match accuracy. A score of 95% or higher for both stimuli resulted in the difficulty level of '*n*' increasing by one, a performance of below 75% caused '*n*' to decrease by one and when the performance was maintained between 75-95% the difficulty on the next block remained at the same level. Dual 4-back was the highest achievable level of '*n*' (replicated from Swainston & Derakshan, 2018, 2021).

**Figure 2.4**

*An example of a dual 3-back training trial with a visual and auditory stimuli match*



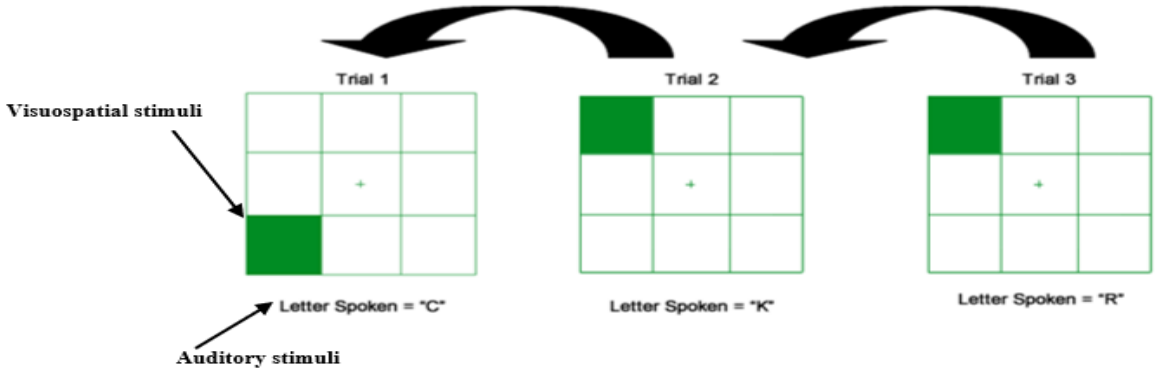

*Note.* Participants in the intervention group were instructed to remember the position of the green box and its paired spoken consonant and respond using the keypad (press 'A' for a visuospatial match, 'L' for an auditory match and both 'A' and 'L' at the same time for a dual match) when the stimulus or stimuli matched what was shown 3 trials earlier.

## 2.9.2. **Dual 1-Back Training (Non-adaptive cognitive training; Active Control group)**

Dual 1-back training (active control) task difficulty remained unchanged at the 1-back level for all 20 blocks of trials regardless of performance accuracy, making the training far less taxing on working memory.

**Figure 2.5**

*An example of dual 1-back training completed by participants in the active control group*




*Note.* Participants in the active control group were told to remember the position of the green box and its paired spoken consonant presented in the previous trial and respond using the keypad (‘A’ for a visuospatial match, ‘L’ for auditory match and ‘A’ and ‘L’ at the same time for a dual match).

# **Chapter 3:** Understanding the experience of cancer-related cognitive impairment and self-management coping strategies implemented by breast cancer survivors in the workplace beyond the initial return-to-work period

## 3.1. **Chapter Overview**

It is well acknowledged that work plays a crucial role in the return to a more 'normal' life for women affected by breast cancer. Although, developments in multimodality-based treatments have significantly improved the long-term survival rate (76% of women will survive 10 or more years) it is also associated with a series of ongoing cancer-related issues such as fatigue and cancer-related cognitive impairment (CRCI) that adversely impact everyday life including workability. The aim of **Chapter 3** was two-fold. Firstly, the chapter aimed to understand women's experiences of sustained post-treatment CRCI and its impact on workability beyond the initial return-to-work period. The chapter then aimed to explore women's experiences of self-management coping strategies applied to manage CRCI and cancer-related sequelae (i.e., fatigue) at work.

## 3.2. **Introduction**

Work plays a fundamental role in the recovery process following a breast cancer diagnosis and active treatment and significantly contributes to re-establishing a sense of normality and daily routine as well as often providing women with a purpose, value and meaning in life (Kennedy et al., 2007; Duijts et al., 2017b). Returning to work (RTW) following diagnosis or active treatment for breast cancer has been shown to improve quality of life, wellbeing and reduce financial difficulties (Ferrell et al., 1997; Waddell & Burton, 2006; van Maarschalkerweerd et al., 2020). Over half of all breast cancers

diagnosed are to women in their working years (< 65 years). Studies have shown that whilst the majority of women are working before their diagnosis and treatment they are at an increased risk of unemployment (or job loss) (de Boer et al., 2009; Paalman et al., 2016) or experiencing unwanted work adjustments and changes including, reduced responsibility, independence and demotion following their RTW (Maunsell et al., 1999).

In the UK, the age of retirement has continuously increased with more women deciding to retire in their late 60s. One key reason for this increase is thought to be the limited availability of early retirement pension programmes (Cribb et al., 2013; Cribb & Emmerson, 2018). Greater financial difficulty (or burden) is associated with worse quality of life (Gupta et al., 2007), emotional distress (Perry et al., 2020) and workability (Ho et al., 2018) in women affected by breast cancer. As it stands, women diagnosed with breast cancer are entitled to statutory sick pay (£99.35 per week) for up to 28 weeks, as well as universal credit or disability benefit (Breast Cancer Now, 2021), however, this is often considerably lower than their salary. Despite the wide range of benefits of work, for example, greater financial stability, socialisation and better overall quality of life, many women report a plethora of work- and cancer-related issues that impact both the initial RTW and long-term sustainability (Mehnert et al., 2013; Calvio et al., 2010; Islam et al., 2014; Musti et al., 2018).

One of the most common and ongoing complaints described by women with breast cancer is CRCI (Hurria et al., 2007; Padgett et al., 2020). Indeed, CRCI has been shown to affect women up to 20 years after the completion of their active treatment (Koppelmans et al., 2012). More recently the cause of CRCI has been defined as multimodality (see Lange et al., 2019a; Ahles & Root, 2018, Joly et al., 2019, for recent reviews) as strong linkages between alternative treatments such as radiotherapy (Phillips et al., 2012) and Tamoxifen (Jenkins et al., 2004; Schilder et al., 2010; Breckenridge et al., 2010) have also been found. Studies have found evidence of cancer-related impairment in multiple cognitive domains such as memory (visual and verbal), attention/concentration, processing speed and executive functions including, WM, cognitive flexibility, decision making, multitasking and planning (Von Ah et al., 2013). Previous qualitative research studies indicate that memory and attention are the most affected (Von Ah et al., 2013; Bolton et al., 2018). In recent years, greater (or worse) cognitive

impairment has been linked to several modifiable factors including fatigue (Todd et al., 2011; Von Ah & Tallman 2015), sleep quality (Henneghan et al., 2018), PTSD (Boscher et al., 2020), anxiety and depression (Von Ah & Tallman, 2015; Janelsins et al., 2017). CRCI has also been identified as a key predictor of quality of life (Chapman et al., 2019).

Importantly, it has been shown that CRCI is strongly related to reduced workability and work productivity in cancer survivors (Calvio et al., 2010; Zeng et al., 2016; Von Ah et al., 2018; Ho et al., 2018). Workability is defined as the individuals' perception of how able they are to do their work with respect to the work demands, health and mental resources, either presently or in the future (Ilmarinen et al., 2005). In a study by Von Ah et al., (2017), it was shown that self-reported attentional fatigue was related to lower workability in breast cancer survivors 4.97 years after active treatment. Similarly, Calvio et al., (2010) found that self-reported memory and executive function were significant predictors of work output (as measured by the WLQ), such that greater cognitive impairments meet a poorer work output. Studies have shown that women reporting cognitive impairment such as memory problems that affect their ability to work are at much greater risk of unemployment (Obserst et al., 2010; Peipins et al., 2021).

Emotional distress including anxiety (Carlsen et al., 2013) and depression (Zeng et al., 2016; Ho et al., 2018) have also been linked to workability in women affected by breast cancer. Ho et al., (2018), found that over one-third (37%) of women in their sample had suboptimal workability and those women were at a greater risk of developing worse levels of anxiety and depression. Women with reduced workability experience worse levels of fatigue (Hansen et al., 2008; Carlsen et al., 2013; Ho et al., 2018; Dahl et al., 2019), poorer overall quality of life (Keim-Malpass et al., 2016), greater financial concerns and have a poor future perspective of their health (Ho et al., 2018).

Although workability and absenteeism can slowly improve over time after RTW (de Boer et al., 2008; Gregorowitsch et al., 2019b) and many women can sustain long-term employment (Bradley & Bedneck, 2002), women often report experiencing ongoing suboptimal workability and require continuous work-based adaptions including, reduced hours or workload (Torp et al., 2012; Sandberg et

al., 2014; Gregorowitsch et al., 2019b; Klaver et al., 2020). According to Von Ah et al., (2013), additional self-management coping methods are required by most women to compensate at work.

Despite the growing body of evidence demonstrating that sustained CRCI affects emotional distress, fatigue and workability in women with a history of breast cancer, few studies have explored working women's experiences of post-treatment sequelae (i.e., CRCI) and their consequences at work in survivorship beyond the initial RTW period. Given, that women affected by breast cancer can experience CRCI for up to 20 years (Koppelmans et al., 2012b) and evidence has shown CRCI significantly increases the risk of unemployment (Peipins et al., 2021), there is an urgent need to investigate the longer-term impact of CRCI on workability. In spite of studies substantiating that cancer survivors commonly need to implement self-management coping strategies at work, no study to date has examined women's experiences of self-management coping strategies. Self-management coping strategies refer to cognitive support methods such as notetaking and work-based adaptions to changes in working hours or workload to help manage CRCI and cancer-related sequelae in the workplace.

### 3.2.1. **Aims**

The aim of **Chapter 3** was two-fold. The chapter first aimed to understand women's experiences of the post-active treatment CRCI and its impact on work and workability in long-term survivorship beyond the initial RTW period. The chapter then explored women's experiences of self-management coping strategies such as cognitive support methods and work-based adaptations applied to manage CRCI and known cancer-related sequelae at work. In **Chapter 3**, work was defined as paid employment or self-employment. Developing a greater understanding of the consequences of sustained CRCI and self-management coping strategies applied by women can help inform employers and healthcare professionals managing work-based survivorship care.

## 3.3. **Method**

### 3.3.1. **Participants**

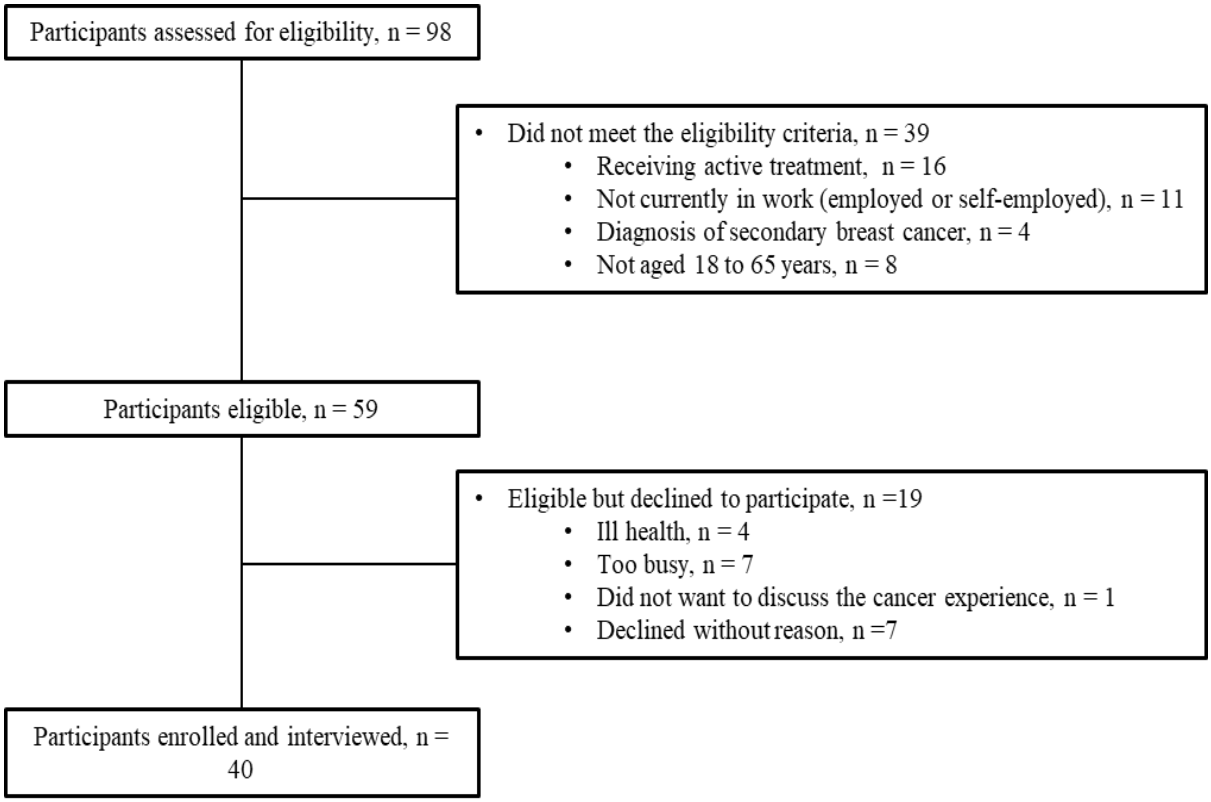
Primary breast cancer survivors were voluntarily recruited from advertisements placed on social media platforms including, Facebook and Twitter between the 1st of February 2019 and the 29th of February 2020 using purposeful sampling. Reasons for not participating when eligible included ill-health (n = 4), being too busy (n = 7) and not wanting to reflect on their cancer experience (n =1) (see **figure 3.1** for the flowchart of participants). The first 40 women enrolled on the 'BRiCatWork' study were selected to participate in the interview.

Inclusion criteria included: (1) a history of primary breast cancer, (2) aged 18 to 65 at the time of enrolment, (3) six to 60 post-active active treatment for chemotherapy and/or radiotherapy (whichever came last), (4) receiving hormone replacement therapy, hormone blocker therapies or target therapies, (5) attending paid work (employed or self-employed) at the time of recruitment and (6) experiencing a decline in workability because of cognitive difficulties (see **table 3.1** for more detailed clinical and demographic figures).

Exclusion criteria included (1) receiving active treatment(s) such as chemotherapy and/or radiotherapy, (2) under six months or over 65 months post-active treatment, (3) under 18 years old or over 65 years old, (4) not attending paid work (i.e., volunteering), (5) not experiencing any difficulties with workability associated with cognitive impairments and (7) unable to read or understand English.

**Figure 3.1**

*Flowchart of participants*




## 3.3.2. **Procedure**

Participants who confirmed their eligibility via the emailed checklist were enrolled on the 'BRiCatWork' study and were then allocated to either the adaptive cognitive training (dual *n*-back training) or active control training (dual 1 back-training) group using randomisation software (Sealed Envelope Ltd., 2017). Participants were asked to give online consent to take part in the 'BRiCatWork' study, as well as verbal consent at the start of the semi-structured telephone interview to confirm that the principal researcher (BC) could audio-record their discussion. Participants were informed that the information provided during the interview would be used for research purposes only. In addition, participants were also informed that any identifiable information given during the interview such as the name of their employer would be removed from the final transcript to ensure their confidentiality. Participants were contacted via email to arrange a suitable time for their baseline interview. Only the

principal researcher (BC) and participant were present during the telephone interview. Interviews lasted on average 57.72 minutes (range 39.10 to 97.27 minutes)[4]. Fieldnotes were made throughout to help guide the conversation. All clinical information relating to the breast cancer diagnosis was self-reported by the participant. Three repeat interviews were conducted as part of the larger 'BRiCatWork' randomised control trial (see **Chapter 5** for longitudinal study findings). Findings from the baseline interviews are reported in the current chapter.

### 3.3.3. **Interview Schedules**

Baseline interviews asked participants a series of questions relating to their breast cancer history and experience during the treatment period, as well as post-active treatment CRCI, impact of these sequelae on workability, current work contentment and self-management coping strategies applied (see **Chapter 2 section 2.7** for a more comprehensive description of the baseline interview schedule and **appendix 4** for the interview schedule). Questions followed the flow of the discussion.

## 3.4. **Qualitative Analysis**

As outlined in **Chapter 2**, "framework" analysis (Ritchie & Spencer, 1994; Ritchie et al., 2003) was used to analyse the baseline interviews due to its systematic approach to managing and analysing large data sets ($N = 40$) (See **Chapter 2 section 2.8** for a more comprehensive description of the analysis approach). Data saturation was reached after analysing 28 interviews; however, the remaining 12 interviews were analysed.

As Tamoxifen can cause more excessive cognitive impairment (Castellon et al., 2004), preliminary analysis was conducted to compare the differences between the CRCI experienced by women who were receiving ongoing hormone therapy such as Tamoxifen and those not taking hormone

[4] All interviews were conducted prior to the COVID-19 outbreak in the UK.

therapy at the time of the interview. No significant differences were found. Furthermore, preliminary analysis was also performed to examine the sustainability of CRCI over time by comparing women who had finished their active treatment above and below the mean (*M* = 23 months). Although some women felt that there had been a natural improvement when they compared their active treatment period to their post-treatment period, the CRCI and its consequences on workability remained relatively stable and persistent across time (six to 60-months). Only one participant was still receiving an extended phased return at the time of her baseline interview. This interview was compared to all other interviews and no significant differences were identified, as a result, all 40 interviews were included in the final analysis reported in this chapter.

## 3.5. **Results**

### 3.5.1. **Sample characteristics**

A total of 40 women living with a history of primary breast cancer completed the baseline telephone interview. Mean time since the completion of active treatment was approximately 23 months (*SD* =13.03) and mean age at diagnosis was approximately 46 years (*SD* = 6.24, ranging from 33 to 58 years, see demographics and clinical demographics in **table 3.1**). Most women reported working full-time (65%) at the time of the interview. Six (15%) women had changed their job role and/or employer since receiving their cancer diagnosis and treatment.

**Table 3.1**

*Participant sociodemographic, clinical characteristics and work information*

| | ***N = 40*** | ***%*** |
|---|---|---|
| ***Sociodemographic*** | | |
| Age | Mean = 48.8 (Min = 34, Max = 60) | |
| Education | | |
| Secondary education | 2 | 5.0 |

| | | |
|---|---|---|
| Further education | 8 | 20.0 |
| Higher education | 24 | 60.0 |
| ***Work*** | | |
| Full-time | 26 | 65.0 |
| Worked through treatment | 19 | 47.5 |
| ***Clinical*** | | |
| Age at diagnosis | Mean = 46.2 (Min = 33, Max = 58) | |
| Type of breast cancer | | |
| Ductal Carcinoma in Situ (DCIS) | 3 | 7.5 |
| Invasive Ductal Carcinoma (IDC) | 23 | 57.5 |
| Invasive Lobular Breast Cancer | 3 | 7.5 |
| Mixed IDC and DCIS | 10 | 25.0 |
| Ductal Carcinoma and Invasive Lobular | 1 | 2.5 |
| Grade of breast cancer | | |
| Grade 1 | 5 | 12.5 |
| Grade 2 | 10 | 25.0 |
| Grade 3 | 24 | 60.0 |
| Type of treatment received | | |
| Chemotherapy | 30 | 75.0 |
| Radiotherapy | 38 | 95.0 |
| Surgical Procedure | 40 | 100.0 |
| Time since active treatment (months) | Mean = 23.10 (Min = 6, Max = 59) | |
| Endocrine Therapy | | |
| Yes | 29 | 72.5 |
| No | 7 | 17.5 |
| Prescribed but stopped | 4 | 10.0 |
| Herceptin | 9 | 22.5 |
| History of a psychiatric condition | 8 | 20.0 |

*Note.* [a] Six participants did not disclose their highest level of education, [b] Nine participants did not disclose whether they received a phrased return, [c] One participant did not state the grade of their breast cancer, [e] Three participants did not specify if they received Herceptin

### 3.5.2. **Themes and subthemes**

Two main themes and six subthemes were found across the baseline interviews. The main themes were categorised as (1) “Sustained consequences of cancer-related cognitive impairment” and

(2) “Self-management coping strategies to support work-related performance” (see **table 3.2** for a list of subordinate themes).

**Table 3.2**

*Main themes and subthemes from qualitative analysis*

| Main Themes | Subthemes |
|---|---|
| ***(1) Sustained consequences of cancer-related cognitive impairment*** | *Impact of changes in cognitive function*<br>*Emotional impact of cognitive changes*<br>*Impact of fatigue on work-related performance*<br>*Reduced confidence resulting from cognitive changes* |
| ***(2) Self-management coping strategies to support work-related performance*** | *Cognitive support methods used to aid work-related performance*<br>*Work-based adaptions applied to manage work-related challenges* |

## Theme 1: Sustained consequences of cancer-related cognitive impairment

### *Impact of changes in cognitive function*

In line with previous studies, women reported experiencing a series of noticeable cognitive impairments in memory (short-term and long-term), attention/concentration, word-finding/recall, decision making, planning and processing of complex information, significantly impacting their ability to engage in routine tasks or duties at work. Short-term memory deficits and inability to maintain attention/concentration, however, were reported most frequently as being disruptive to everyday

workability and performance. Women mentioned experiencing a reduced work output (or lower turnover of work) and longer completion times because of time lost to forgetting key information and inability to block out distractors:

> "*Hard, really hard. I can't concentrate, I get easily distracted, things take me hours and hours and hours and hours whereas it wouldn't have before something that I might have taken an hour on before it can now take me all day and a lot of that is because I can't concentrate but also, I don't know my brain doesn't work the same anymore*." [Participant 38]

> "*The majority of my work, as I say, is kind of sat at a computer drafting things so if I can't concentrate then I can't get much done*". [Participant 38]

> "*I just feel very scatty. I feel that I can start one job and then I am…my brain has gone to something else and I can't concentrate on something for too long*". [Participant 13]

Two women spoke of how their memory had become increasingly fragmented and key parts of their (long-term) work information was missing since RTW:

> "*I describe my brain as swiss cheese*". [Participant 10]

For many, cognitive impairment resulted in "mistakes" or "errors" being made often without any awareness until brought to light by a co-worker or an issue arose (i.e., missed meetings). Such errors were contributing to a loss of confidence and questioning about sustainability of work:

> "*What I found was that my manager just had this expectation I think that well…she actually said to me a couple of months ago you're well enough to work…but I was basically forgetting a few things…but she was basically saying you're well enough to work and I think she was thinking I just wasn't performing as I should be*". [Participant 7]

Besides, a few women spoke of how their career progression had been completely stalled since their RTW because of their decision to not take on mandatory work development courses or training that were required to progress. These decisions were linked to concerns and worries about the post-treatment CRCI and its impact on the ability to learn and retain new information. One woman discussed

how this had reduced her contentment at work as she knew her future career development depended on her completing work-specific training:

> "*So, now my…my career is at a standstill because you can't really get on without that qualification and now people are throwing the idea at me to start studying again but [I] really don't…and I want to because I… you know I want to push myself, etc but I just don't know whether I am capable of retaining the information and things to* study*".* [Participant 15]

> *"I suppose that is what caused the issues the fact that my memory isn't as good and my concentration isn't as good means that I can't retain information so I don't feel that I can study*". [Participant 15]

## *Emotional impact of cognitive changes*

Initial coding of the interviews showed that there were strong linkages between CRCI and emotional distress. Women consistently spoke of how their cognitive impairment made them feel "sad", "embarrassed", "frustrated", "stupid", "rubbish", "vulnerable" and sometimes "panicked" in the workplace. Many women implied these emotional distresses were due to the fear of judgement and others' perception of them and their ability to work efficiently:

> "*I just feel that people that meet me for the first time just think o god this woman is a complete ditz*". [Participant 36]

> "*I suppose I worry I am going to get the reputation o my god [name of participant] has forgotten that again but then doesn't she always sort of thing*". [Participant 35]

> "*I just feel stupid sometimes you know and I know I am not but I feel stupid and I think what must people think of me, do people think I am stupid… you know…. do people think why can't she speak properly and they probably don't you know…. but I worry that people think differently about me now because I do*". [Participant 20]

One participant spoke of how changes in her forgetfulness and inability to understand more complex technical (or job-specific) information led to her withdrawing at work particularly when her co-workers around her seemed to find the work simple. Her withdrawal was associated with feelings of embarrassment and fear of the judgement she might face from her co-workers:

> *"That is really frustrating because I don't like that…I mean I wouldn't…the thing with that is I would just be quiet then and think well I don't want to look stupid so I just don't say anything".* [Participant 31]

Other women spoke of their emotional distress triggered by their awareness and insecurities (or self-doubts) concerning their inabilities to function in the workplace. In particular, they were concerned about their capability to engage and contribute to work effectively and felt guilty and annoyed that additional work was created by mistakes or errors, leading to self-doubt. Some women discussed how their self-doubts led to worry and apprehension about attending work and caused concerns about long-term work sustainment:

> "*I was worried going to work… about my brain working because I was really aware that you know I wasn't…my brain wasn't functioning that well*". [Participant 13]

> *"It is frustrating because you know things don't get done then you know I am going to have to re-go and do them or somethings got missed or I've made some mistakes then it's going to cause a problem in the immediate future so you know problems will pile up rather than be attended too. So, yeah it makes you feel down and anxious and a bit depressed about it, yeah and a bit worried and concerned really*". [Participant 35]

The relationship between CRCI and emotional distress seemed to be strongly bi-directional, with greater emotional distress further escalating the severity of the cognitive impairment, resulting in higher levels of stress.

### *Impact of fatigue on work-related performance*

Bidirectional linkages were found between post-active treatment fatigue and CRCI in the workplace. A large proportion of women reported noticing a worsening of fatigue as the working day and week progressed, intensifying cognitive challenges and limiting their ability to carry out work-related tasks. A few women spoke of how their employers had a lack of understanding of the impact of fatigue:

> "*It has been incredibly difficult; I am not going to lie it's still I get to about Wednesday and you can…I can really feel the fatigue kicking in Thursday. For sure by Friday afternoon my brain is just not capable of doing anything really complex*". [Participant 10]

Some women felt that additional energy and effort was required to deal with their cognitive difficulties at work to ensure that they were performing at an adequate level:

> "*It's quite exhausting trying to focus for the 4 days and Monday I can go in and I will be alright but yeah, I feel myself dip as the week goes on*". [Participant 3]

> "*If I have had an intense meeting with somebody then afterwards, I can feel completely shattered by the intensity of trying to remember what it was or… what [we were] was talking about or concentrating on the conversation*". [Participant 2]

Importantly, fatigue affected career development, playing a central role in limiting the types of work and number of hours they were able to accept from their employer, profoundly restricting their future career prospects and progression. One woman spoke of her frustration at not committing to new projects or contributing her ideas in team meetings often out of worry that she was unable to manage the extra work if she put herself forward. Another mentioned her anxiety about overdoing things because of the impact of her fatigue, for example, on her emotional wellbeing. She also spoke of how her fatigue reduced her resilience and induced a negative mood:

> "*I am tired and still suffering with fatigue and that really restricts how many hours I can take on and what sort of job I can do*". [Participant 30]

"*I think it's not too bad but if I overdo things, I know I can get significantly overwhelmed and I can get quite teary when I am exhausted so… and I can get low moods when I am tired where you know everything seems negative*". [Participant 11]

### *Reduced confidence resulting from cognitive changes*

Finally, the interviews revealed that a lack of confidence was affecting most women. The majority of women spoke of how their CRCI significantly knocked their confidence and often induced a sense of self-doubt about their ability to perform tasks. This was evident when women compared their current ability to pre-diagnosis ability. This lack of confidence frequently resulted in over-compensating to ensure no errors and mistakes had been made, creating delays in work production or completion. Some suggested that their cognitive impairments made them feel insufficient compared to others in the workplace, undermining their confidence and self-esteem:

"*I would say over the last two years I have found that my memory and concentration are not as good and I am really having to really concentrate hard on what I am doing and double-checking myself more which I was…I was very confident that I was dosing patients fine which I was but now I do double-check and a lot of it is to do with a loss of confidence I suppose in my memory*". [Participant 37]

"*I have to double, double-check everything…check, check, check*". [Participant 30]

Some women also spoke about how their lack of confidence in abilities underpinned their decisions to avoid applying for new job roles or turndown career opportunities such as managing a larger client base:

"*I just think they [employers] want more from me, they want me to progress which for anyone else would probably be great you are supposed to want to be promoted and things but that would just be more kind of client-facing and I haven't got the confidence to speak to clients anymore*". [Participant 38]

One woman spoke about her concerns taking on new projects or roles would make her feel "exposed" and "vulnerable" in the workplace. This seemed to be associated with confidence and the fear of judgement she may face if she is unable to perform. It may also be linked to fear that her employer will reconsider her employment on the grounds of her work performance. This could imply that avoiding career development or progression (i.e., taking on novel projects) is a masking (or safeguarding) technique driven by reduced confidence:

> "*So, its…works importance in my life overall has gone down as well and then my approach at work is whereas I would have hungrily taken on anything now I am much more measured in my approach about what I agree to do because I know am limited both in my capacity because my energy but also in my competence because of the cognitive impairment*". [Participant 8]

> "*I think it's probably curtailed a bit of my ambition in terms of not even a promotion actually even a sideways move because I feel I have lost a lot of…. I am very confident in what I do and what I know but stepping out of that into a new role, I would feel very exposed and vulnerable actually*". [Participant 8]

Further, a few women questioned whether they could sustain their employment in the long-term or whether the employer would begin to reconsider their employment on the grounds of their suboptimal workability and performance:

> "*They've [cognitive impairments] made my confidence drop really badly. I feel worried about my job, worried if I can keep my job and etc*". [Participant 15]

## Theme 2: Self-management coping strategies to support work-related performance

As a consequence of the CRCI, all women reported implementing at least one self-management coping strategy to help minimise the detrimental effect on their workability. Strategies included cognitive support methods such as notetaking and work-based adaptions including, a reduced workload,

number of hours per week and organising the workday more meticulously to account for the functional changes.

### *Cognitive support methods used to aid work-related performance*

A range of self-management cognitive support methods were employed by women in an attempt to manage CRCI, including memory aids, notetaking, as well as setting digital reminders in an attempt to avoid forgetting to attend work events or a deadline. Overwhelmingly there was a dependency on these cognitive support methods as "safety nets" or "parachutes". Some women discussed how a lack of "trust" and "confidence" in their cognition was underpinning that dependency:

> "*The way I get through my days is I have a book and I write everything down that has to be done every day".* [Participant 32]

> "*Yeah, I do it's become my way of working almost so I guess it's gone from being something that was unusual for me to do for it now to become the norm*". [Participant 28]

Although, cognitive support methods are regularly encouraged and supported women demonstrated evidence of mixed feelings (incorporating both positive and negative) towards using such methods in the workplace. Some women described that they made them feel more "efficient", "empowered", "in-control", "proactive" and "organised":

> "*I think it actually makes me feel in control and if this is what I have to do to allow me to do my work and to do it without getting you know pressure from my boss then it is actually good*". [Participant 7]

Others felt that cognitive support methods further highlighted their CRCI and made them feel "weak", "stupid", "exasperated", "embarrassed" and "frustrated". Some of these negative feelings towards the methods seemed to be due to concerns and fear of the judgement they may receive. Besides, some spoke of how relying on these methods added to their stress and anxiety as opposed to relieving it. This was partly because the methods exposed the true extent of the impairment and changes in their

workability and distractibility:

> "*I feel embarrassed that I have to go round with this bit of paper and nobody has ever said anything they probably don't even notice but it worries me that I do have to do that*". [Participant 37]

> "*I think it can be a bit irritating that I have to rely on these kinds of external mechanisms to help me function*". [Participant 35]

> "*Yeah, I do write lists but lists don't always help me because they just get bigger and bigger and I never seem to be able to tick anything off so that causes me more stress*". [Participant 38]

Interestingly, some women also raised the issue of requiring an adequate level of memory and concentration to compose the cognitive aids, suggesting that CRCI acts as a barrier to the self-management cognitive support methods:

> *"I try and write everything down but sometimes it's…, it's hard to remember to write stuff down*". [Participant 9]

> "*I am always writing myself a note, I am always putting a reminder on my phone to remind me to do things and as long as I remember to look at my phone, I am okay"*. [Participant 40]

### *Work-based adaptions applied to manage work-related challenges*

Women spoke about the work-based adaptions they made at work in an attempt to manage both their CRCI and factors that influence this impairment (i.e., fatigue). Many women spoke of reducing the number of hours or limiting their work to prevent excessive levels of fatigue and stress which can cause more errors and mistakes. For some, this decision induced greater financial concerns, worries about career development and emotional distress, with many stating their eagerness to work more hours, knowing they could not with their current physical function and CRCI:

"*Yeah, I mean in my head and in my dreams and my aspirations for myself I would love to have a full-time job you know I would absolutely love to. I would love to have a full-time job; I would love to be earning decent money you know I would love to be able to do that but I feel limited and that is the truth*". [Participant 18]

One woman spoke of actively decided to adjust her hours since her RTW as part of a safeguarding approach to avoid her employers and co-workers becoming aware of her sequelae and its impact on her workability, reflecting her loss of confidence as well as her fear of judgement from others:

"*Yeah, through my fear. I just want to work as little as possible so that no one finds me out [laugh]…that I am useless these days no one puts pressure on me or relies on me for anything*" [Participant 38]

In addition, some women outlined the need to structure their workday rigorously including, starting work earlier to ensure that they could take more frequent "rest" or "refresh" breaks and still allow enough time to meet deadlines. Women also spoke of structuring their day, chunking the type of work or addressing one task at a time to avoid switching or juggling to reduce the risk of errors and minimise fatigue and stress. Such adjustments, however, created challenges when unexpected work came up or rapid turnaround was required:

"*I try and start earlier because I know I am going to take more breaks while I am working, I know I am going to get distracted and I know it is going to take me longer*". [Participant 5]

"*It's like that thing of you don't know that you've made a mistake necessarily or that you've been inaccurate and the way to avoid that for me is to not juggle things it's to be a bit more one-tracked because I am less likely to make mistakes so it is a concern*". [Participant 33]

## 3.6. **Discussion**

The main aim of **Chapter 3** was to understand the effects of long-term post-active treatment CRCI affecting women's workability and self-management coping strategies, including cognitive

support methods and work-based adaptions applied by women in an attempt to manage these sequelae at work. The current findings revealed that ongoing CRCI (Calvio et al., 2010; Zeng et al., 2016; Von Ah et al., 2018) provoke emotional distress (Carlsen et al., 2013; Zeng et al., 2016; Ho et al., 2018), fatigue (Carlsen et al., 2013; Ho et al., 2018), and reduce confidence (Munir et al., 2010) adversely impacting work and workability beyond the initial RTW period. Given, that the 'BRiCatWork' study recruited women up to five years post-active treatment, it is evident that these sequelae can impact work long into survivorship. In contrast, to previous studies which have shown that workability, work-based adaptions and absenteeism improve gradually over time (de Boer et al., 2008; Gregorowitsch et al., 2019) the current findings provide in-depth support for the presence of a more ongoing and sustained suboptimal workability and implementation of self-management coping strategies. In a study by de Boer et al., (2008), it was found that the workability of women affected by breast cancer significantly improved by 18 months. It is plausible that the difference in findings is partly driven by the research inclusion criteria which stated that to be eligible for the current study women must have noticed some form of cognitive difficulty or challenge in the work environment.

Whilst there may be employer support and flexibility during the reintegration period (or initial phased return period) this often rapidly decreases (usually within the first six months) causing many to face a series of unrealistic expectations and work demands (Kennedy et al., 2007; Dorland et al., 2018). In line with this, the current findings showed that some women had experienced issues with their employers or co-workers when it came to their cognitive challenges (i.e., memory), confidence (i.e., to take on new responsibilities) and post-treatment fatigue. It is plausible that employers' possible lack of awareness or understanding of the sustainability of post-treatment sequelae is driving their unhelpful responses. These findings indicate that a higher level of awareness of the possible long-term impacts at work beyond the initial RTW is required. This is particularly important as previous research has shown that better employer support concerning cancer-related issues is significantly associated with greater workability and performance (Taskila et al., 2007; Torp et al., 2012; Musti et al., 2018) in women affected by breast cancer.

Further, findings from the baseline interviews revealed that women in the current study often feared how they would be viewed by their employers or co-workers when it came to their cognitive challenges. Women stated that their cognitive impairments made them feel "embarrassed", "frustrated", "vulnerable" and "panicked". Whilst it is well documented that emotional distress (anxiety and depression) reduces workability (Carlsen et al., 2013; Zeng et al., 2016; Ho et al., 2018) the underlying cause(s) has not been well explored. The present findings suggest that fear of judgement and concerns about others' views of them and their "new" workability are responsible for provoking these negative emotions. For some women, the embarrassment associated with their CRCI was causing withdrawal. It is plausible that this withdrawal is part of a masking (or safeguarding) technique being (un)consciously implemented to reduce the likelihood of others becoming aware of these difficulties and creating adverse judgements that may threaten employment. Although in the long-term such behaviour may end up contributing to job loss. Supporting this notion, recent figures reported by Peipins and colleagues (2021) revealed that loss of employment was almost three times higher in women experiencing memory problems that affected their ability to work (17.4% vs. 5.9%), validating the concerns of women in the current study.

In the current study, women spoke of how their CRCI detrimentally reduced their quality of work causing "mistakes" and "errors" to be made often without any awareness that they had happened until a problem or issue arose. A few women reported that the compensatory effort required to minimise the impact of these cognitive impairments on quality of work was compounded by fatigue, adversely affecting work quality. Further, cognitive impairments and their detrimental effects on work were significantly exacerbated by fatigue. Fatigue is defined as one of the most common complaints reported by breast cancer survivors (Joly et al., 2019). The findings indicate a strong bidirectional relationship between fatigue and cognitive impairment, such that the high effort and energy required to reduce the impact of cognitive impairments increases fatigue. This elevated fatigue in turn then further promotes cognitive impairment (i.e., inability to block out distractions), reducing workability. Trying to balance these two post-treatment sequelae to prevent them from becoming highly debilitating whilst also managing expectations to avoid underperforming is likely to be exceptionally challenging, exhausting

and highly stressful. Klaver et al., (2020) found that additional effort at work to manage CRCI and to meet the expectations from employers often resulted in over-exhaustion and deficits in processing efficiency in cancer survivors.

Extending on Raque-Bogdan et al., (2015), the current findings showed that CRCI, fatigue and loss of confidence induced by CRCI are key factors shaping women's views and decisions about their career development and progression beyond the RTW period. In particular, women reported turndown career opportunities such as training courses out of concern that they would not be able to learn and retain the information required to pass assessments with their current cognitive ability. Women also highlighted that they are often unable to take on more hours at work, projects or network with clients because of the undesirable impact this would have on their fatigue, increasing their self-doubts about their adequacy at work. Studies have shown that self-confidence is significantly associated with perceived workability and performance, as well as the rate of RTW (Amir et al., 2008; Wolvers et al., 2018).

**Chapter 3** is the first to provide an in-depth examination of women's experiences using self-management coping strategies, including cognitive support methods and work-based adaptions to support their workability. In line with previous research (Torp et al., 2012; Sandberg et al., 2014), women outlined using a series of common work-based adaptions and cognitive support methods such as notetaking to enhance workability and work function. Women, however, reported mixed experiences, with some stating that the cognitive support methods were ineffective and further heighten their emotional distress. These negative views of cognitive support methods seemed to be partly driven by fear of judgement or discrimination within the workplace, supporting earlier accounts suggesting that women affected by breast cancer often decide not to disclose their CRCI or "brain-fog" to their supervisors or co-workers (Sandberg et al., 2014). These negative experiences with the common cognitive support methods may further compound loss of confidence and add to their apprehensions, reducing some women's long-term work sustainability, as opposed to improving it.

Taken together the findings presented in **Chapter 3** have important clinical implications, as they can be used to help inform employers and healthcare professionals to better understand and manage

CRCI and self-management coping strategies in the workplace beyond the initial RTW period. Given the adverse effects of CRCI on fatigue, confidence and self-esteem the findings indicate that working women may significantly benefit from receiving adaptive cognitive training which is beneficial in promoting cognitive efficiency and protecting against emotional distress (See Derakshan, 2020, for a review).

### 3.6.1. **Limitations**

**Chapter 3** presents a few limitations that should be considered when interpreting the findings. Firstly, the semi-structured interview focused on CRCI and its consequences on work, as a result, other key cancer-related sequelae such as the physical effects (i.e., pain) which may also significantly impact work were not discussed. Studies have shown that women who experience limitations in their range of motion and arm pain after surgery have a high level of work productivity loss (Quinlan et al., 2009, 2011). Future qualitative research should therefore consider the physical sequelae experienced by women at work beyond the initial RTW period. Research should also aim to explore these post-treatment sequelae in an unpaid or invisible work capacity as this study restricted recruitment to women in paid (employed or self-employed) work. The sample was over-represented by participants who were well-educated (80%) and working full-time hours (65%). Although the aim of qualitative research is not to generalise findings, the results of this study should be considered in relation to the sample.

### 3.6.2. **Conclusion**

To conclude, the findings presented in **Chapter 3** show that CRCI was sustained up to five years after the completion of active treatment for primary breast cancer. It was evident that CRCI can elevate a series of negative emotions, reduce self-confidence and promote fatigue in the workplace, adversely affecting workability and work performance in women beyond the initial RTW period. Whilst women commonly use self-management coping strategies, such as cognitive support methods and

work-based adaptions to reduce the impact of cancer-related sequelae at work, mixed experiences were reported, with some women outlining that self-management coping strategies could be problematic (or ineffective) escalating adverse emotions and feelings of distress.

## Published paper associated with this chapter:

Chapman, B., Derakshan, N., & Grunfeld, E. A. (2021). Exploring primary breast cancer survivor's self-management of sustained cancer-related cognitive impairment in the workplace. *Psycho-Oncology*. https://doi.org/10.1002/pon.5844

# **Chapter 4:** Investigating the efficacy of adaptive cognitive training on primary breast cancer survivor's perceived cognitive impairment in the workplace: findings from the longitudinal post-training follow-up interviews

## 4.1. **Chapter Overview**

The findings from the baseline interviews reported in **Chapter 3** showed that working women living with a history of primary breast cancer can experience ongoing cancer-related cognitive impairment (CRCI) in the workplace which adversely affects their workability and work productivity up to five years after the completion of active treatment and beyond their initial return-to-work (RTW) period. As expected, strong linkages were found between changes in perceived cognitive function and emotional distress, fatigue and confidence. Whilst all women reported using at least one self-management coping strategy in the workplace to help manage their post-treatment sequelae and to function more effectively at work, mixed feelings (incorporating both positive and negative) towards the methods were found. Taken together, the findings presented in **Chapter 3** indicate that working women affected by primary breast cancer may benefit from interventions that promote cognitive efficiency and emotional resilience.

Previous research conducted by Swainston and Derakshan (2018) found sustained improvements in anxiety-related vulnerability up to 15 months after breast cancer survivors received 12 sessions of working memory training (dual *n*-back training). Similar studies exploring the efficacy of dual *n*-back training in clinical, sub-clinical and non-clinical populations have revealed a series of near and far transfer effects in working memory capacity (WMC), filtering efficiency, attentional control and general fluid intelligence (see Derakshan, 2020, for a review). Working memory is inherent to higher-order cognitive processes including, executive functions and attentional control. It is acknowledged that cognitive impairments (i.e., memory and attention deficits) associated with cancer

and anti-cancer treatments adversely impact performance and development in the workplace, however, no study has explored the efficacy of working memory training (dual *n*-back training) on perceived cognitive impairment experienced in the workplace and its impact on work-related outcomes in women with a history of primary breast cancer.

The primary aim of **Chapter 4** was to investigate the perceived impact of receiving 12 sessions of adaptive cognitive training (dual *n*-back training) or active control training (dual 1-back training) on the CRCI impacting women's workability over the period of one year. Further, the chapter also aimed to examine the perceived transfer effects of training on work-related self-management methods for cognitive impairment and on career development or progression. In addition, women's experiences of participating in the 12 sessions of online training including, their engagement with the training and challenges or difficulties experienced, as well as their views on the timing of the training were explored.

## 4.2. **Introduction**

Breast cancer is the most prevalent malignancy diagnosed worldwide, making up 11.7% of all new cancer cases (World Health Organization, 2020). Improvements in diagnostic techniques and treatment programs available have led to increased survival rates, with recent figures showing that 76% will survive for at least 10 years (Office for National Statistic, 2019). Despite this positive advance in survivorship many women diagnosed and treated for breast cancer endure a series of adverse short- and long-term sequelae including, CRCI, fatigue and emotional distress (anxiety and depression) (Joly et al., 2020; Carreira et al., 2021; Maass et al., 2021). Indeed, Kopplemans et al., (2012b) showed that women treated with chemotherapy experience cognitive complaints such as word finding and memory difficulties for up to 20 years. CRCI has been shown to act as a barrier in the RTW process (Mehnert et al., 2013; Nilsson et al., 2013; Sun et al., 2017) and adversely impacts work-related outcomes including workability and work productivity (Calvio et al., 2010; Von Ah et al., 2018; Von Ah et al., 2021). In a study by Buchanan et al., (2015), it was found that only 37% of women experiencing cognitive complaints report having discussions with their health care provider about these issues. Oncologists

attribute this lack of communication with survivors to uncertainty about how to best manage (or "fix") their CRCI given the limited number of pharmacological and behavioural interventions available (Smidt et al., 2016).

Work is considered central to the recovery process after a breast cancer diagnosis and treatment as it often signals the endpoint of the patient period and re-entry into a more 'normal' everyday life (Kennedy et al., 2007), in addition to promoting a greater quality of life (de Boer, 2014). Recent figures have shown that the number of women diagnosed with breast cancer out of work is more than double that of healthy control populations (35.6% vs. 15.2%) (The Economist Intelligence Unit, 2017). The economic burden created by the inability to work reduces quality of life (Meneses et al., 2012) in women living with breast cancer. Although absenteeism improves over time (Drolet et al., 2005; Gregorowitsch et al., 2019b) women are at a greater risk of becoming unemployed during the first five years of survivorship (Paalman et al, 2016; Grinshpun & Rottenberg, 2019) compared to the wider population. Higher risk of unemployment, sickness leave or not returning to previous work activities has been linked to multiple factors including mental disorders (Plym et al., 2019), post-cancer depression (Landeiro et al., 2018), cognitive impairment (Oberst et al., 2010), fatigue, pain-related conditions (Plym et al., 2019), high psychological job demands, employment support and suboptimal workability (Wang et al., 2018). Unemployment has also been associated with an increased risk of breast cancer mortality (Maruthappu et al., 2015), showing the importance of sustained workability for women affected by primary breast cancer.

Studies have shown that greater financial difficulty (or hardship), physical fatigue, cognitive impairment, emotional distress, and loss of confidence are significant predictors of suboptimal workability and work productivity loss in women living with a diagnosis of breast cancer (Calvio et al., 2010; Carlsen et al., 2013; Zeng et al., 2016). Suboptimal workability, in turn, has been shown to increase women's risk of anxiety and depression as well as limit their future perspective (Ho et al., 2018). In a study by Raque-Bogdan et al., (2015), it was found that breast cancer diagnosis and treatment slow down, block or re-direct the long-term career path for many women. Such effects were linked to the inability to attend learning opportunities in the workplace and the decision to reserve energy for

other aspects of life outside of work. Extending on this, the findings in **Chapter 3** from the baseline interviews revealed that CRCI triggered a loss of confidence and self-doubt in workability that significantly contributed to diminished career development and progression (Chapman et al., 2021). Norredam and colleagues (2009) found that women who were affected by cancer had a much lower level of confidence in their ability to secure a new job at the same level as their current position if they were to become unemployed.

In a study by Sandberg et al., (2014), it was revealed that women affected by breast cancer implement a series of coping strategies including changing the number of work hours, reducing the workload and using memory prompts to manage their work tasks following their diagnosis and treatment. The novel findings presented in **Chapter 3** identified, however, that women have mixed feelings towards the self-management coping strategies (i.e., cognitive support methods and work-based adaptions) implemented, with some reporting that strategies prompt a series of adverse emotions and feelings (i.e., frustration) and added to their distractibility. The findings also revealed that experiencing CRCI reduced the effectiveness of the cognitive support methods (Chapman et al., 2021).

Cognitive training programs such as memory training, processing speed training and executive function training have been shown to successfully improve both self-reported cognitive function and objective cognitive performance (Von Ah et al., 2012; Kesler et al., 2013b). Reductions in emotional vulnerability including anxiety and depressive-related symptoms were reported by Swainston and Derakshan (2018; 2021) when assessing the efficacy of 12 sessions of working memory training (dual *n*-back training) in reducing emotional vulnerability by enhancing processing efficiency, with effects sustained up to approximately 15 months post-training in women diagnosed with primary breast cancer. As it stands, there is no gold standard intervention for managing CRCI. When asked about their intervention preferences women with a history of breast cancer reported a desire to participate in interventions that did not involve pharmacological medications such as Modafinil (Kohli et al., 2009) and emphasised the importance of convenience (i.e., flexible and readily available online computer programs). Women also highlighted that endorsement and positive experience from others was key in facilitating their participation (Crouch & Von Ah, 2017). It is acknowledged by oncologists and

oncology services that to improve communication and management of CRCI research needs to be conducted to investigate the effectiveness and usability of (viable) interventions that target CRCI as this will promote the development of standard practice post-active treatment protocols.

### 4.2.1. **Aims**

In spite of the growing body of research demonstrating that breast cancer and its consequential cognitive impairment detrimentally impact work- and work-related outcomes, no study to date has explored the impact of adaptive cognitive training on CRCI affecting workability in women affected by primary breast cancer in early survivorship (≤ 5 years). Earlier research by Calvio et al., (2010) found that self-reported memory and executive function were associated with work output in women affected by breast cancer, such that greater perceived cognitive impairment met with greater work output difficulty. Studies have demonstrated that participating in adaptive cognitive training improves executive functions including working memory (See Derakshan, 2020, for a review). In a recent study by Blacker et al., (2017), it was found that dual *n*-back training was the most effective and reliable training intervention, with *n*-back eliciting both robust near transfer effects and significantly greater neural gains compared to other training groups. Substantiating evidence has also shown that receiving sessions of dual *n*-back training results in greater behavioural and neural training gains compared to the active control training (dual 1-back training) in emotionally vulnerable populations (Owens et al., 2013; Sari et al., 2016; Ciobotaru et al., 2021).

The main aim of **Chapter 4** was to investigate the perceived impact of receiving 12 sessions of adaptive cognitive training (dual *n*-back training) or active control training (dual 1-back training) on the self-reported cognitive impairment impacting women's workability for one year. Further, the chapter also aimed to examine the perceived transfer effects of training on work-related self-management methods for cognitive impairment and career development or progression. Work-related self-management methods for cognitive impairment refer to methods such as notetaking and calendar alerts implemented by women in the workplace to help manage their CRCI and support work. In addition,

**Chapter 4** examined women in the 'BRiCatWork' study's experiences with participating in adaptive cognitive training (dual *n*-back training) or an active control training (dual 1-back training) at one-month post-training. This included their engagement with the training sessions and challenges or difficulties experienced. To help guide the development and implementation of standard practice post-active treatment support protocols women's views of the timing of the training were also examined.

The rationale for providing participants in the 'BRiCatWork' study with 12 sessions of training to complete over a period of two-weeks was motivated by the earlier findings from Swainston & Derakshan (2018, 2021), in addition to the findings from the meta-analysis conducted by Pergher et al., (2019). Developing a greater understanding of the effectiveness of adaptive cognitive training on work-related outcomes will help promote the implementation of dual *n*-back training in the workplace, supporting women affected by primary breast cancer to sustain work and workability over time.

## 4.3. **Method**

Interviews were conducted as part of the 'BRiC at Work' study (see **Chapters 3 section 3.3.1** for a comprehensive description of participant recruitment, inclusion and exclusion criteria)**.**

### 4.3.1. **Procedure**

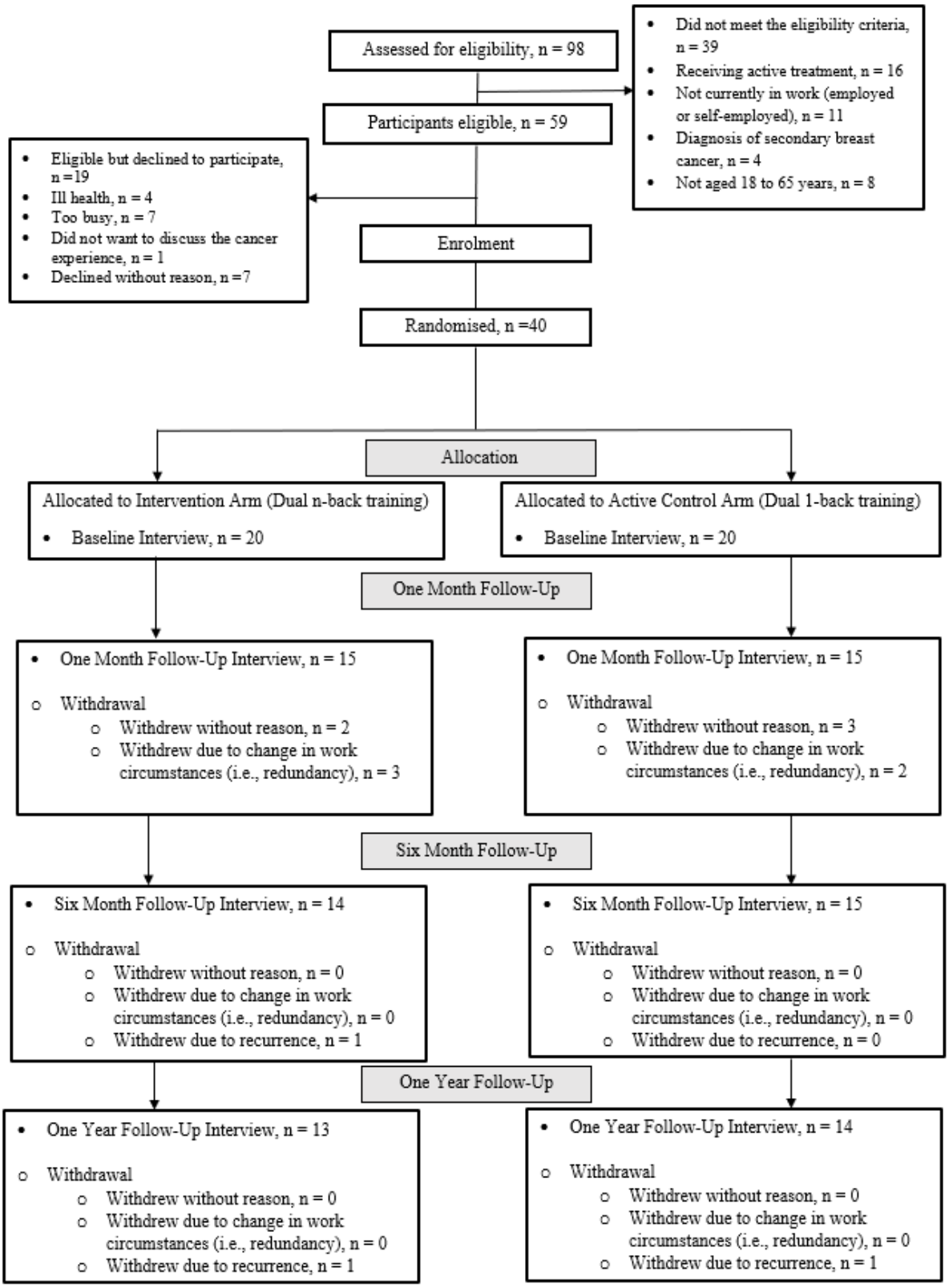
Using randomisation software (Sealed Envelope Ltd., 2017) eligible participants were assigned on a 1:1 ratio to either the adaptive cognitive training (dual *n*-back training) or the active control training (dual 1-back training) group. Participants were blind to their assigned training group and were given the same general information about the study to ensure their expectations of the training were matched. All participants were informed that they were participating in 12 sessions of online cognitive training that aimed to improve their cognitive function and workability. As studies have shown that expectations can influence cognitive outcomes (Boot et al., 2013; Foroughi et al., 2016), it was important to match

participants' training expectations to reduce the likelihood that findings from the dual *n*-back group were due to placebo effects or positive training expectancy.

Participants gave online consent to take part in the 'BRiCatWork' study and verbal consent at the start of the telephone interviews to affirm that the interview could be audio-recorded. Participants were told that the interviews were being conducted for research purposes only. Following enrolment, participants were approached via email to schedule a time to complete their baseline interview. Baseline interviews lasted on average 57.72 minutes (range 39.10 to 97.27 minutes; findings are presented in **Chapter 3**). After the interview, participants were instructed to complete 12 online sessions of adaptive cognitive training (dual *n*-back training) or active control training (dual 1-back training) at home as consecutively as possible over two weeks. Sessions lasted approximately 30 minutes each day (see **Chapter 2 section 2.9** for a more comprehensive description of the training). Upon completing the training sessions, participants were then emailed or asked during their face-to-face lab sessions to schedule their repeat follow-up interviews at one-month post-training, (interviews lasted on average 45.94 minutes; range 27.41 to 76.15 minutes), six months post-training (interviews lasted on average 55.47 minutes; range 39.10 to 84.21 minutes) and one-year post-training (interviews lased on average 55.33 minutes; range 34.02 to 84.33). Only the principal researcher (BC) and participant were present during the telephone interviews. Field notes were taken throughout to help guide the discussion. Participants remained blind to their training group until after the completion of the 'BRiCatWork' study.

**Figure 4.1**

*Flowchart of participants*



### 4.3.2. **Interview Schedules**

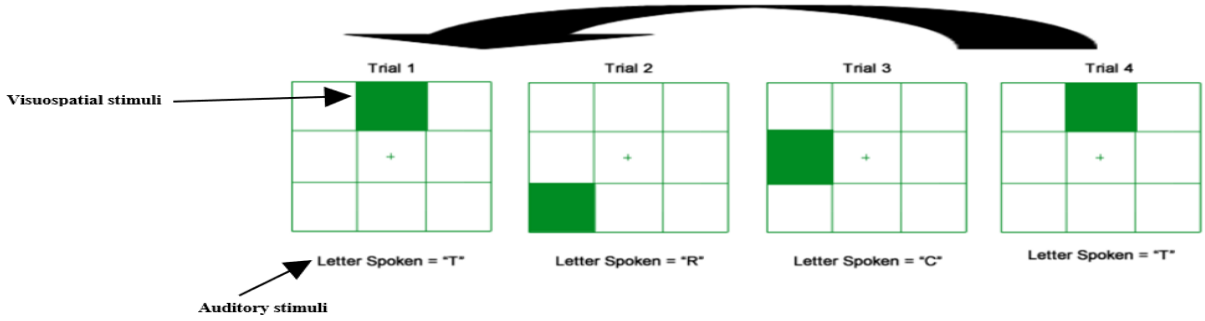
The same repeated post-training interview was conducted at one-month, six-months and one-year to enable comparisons between each of the time points. Participants were asked a series of questions relating to the perceived effects of the cognitive training on their cognitive impairment(s) affecting workability, self-management coping methods and work-based adaptations, as well as their contentment at work. Participants were also asked about their training experience, expectations, perceived benefits and preference regarding the timing of the training (see **Chapter 2 section 2.7** for a more comprehensive description of the interview).

## 4. 3.3. **Dual *n*-Back Training (Intervention) or Dual 1-Back Training (Active Control)**

As described in **Chapter 2**, standard versions of the dual *n*-back training and dual 1-back training task (replicated from Swainston & Derakshan, 2018, 2021) were used in the 'BRiCatWork' study (See **Chapter 2 section 2.9** for a comprehensive description of training; **figure 5.2** shows an example of dual 3-back training with a dual match).

**Figure 4.2**

*Dual 3-back training with a visuospatial and audio stimuli match*




*Note.* Participants were instructed to remember the position of the green box and its partnered spoken consonant and respond using the keypad when the stimulus (green box ***or*** spoken consonant) or stimuli

(green box ***and*** spoken consonant) matched what was presented 3 trials earlier. Task difficulty was determined by performance accuracy on the previous block of trials.

## 4.4. **Qualitative Analysis**

As outlined in **Chapter 2** (see **section 2.8**) a "framework" approach (Ritchie and Spencer, 1994; Ritchie et al., 2003) was utilised to analyse the interviews due to its systematic nature and compatibility with large volumes of interview data (Gale et al., 2013). Eight-five post-training interviews[5] were included in the final sample and analysed. To manage the data, all of the interviews collected at one time point were analysed before moving on to the next time point (i.e., one-month post-training interviews were analysed before six-months). One set of themes was produced for post-training interviews.

## 4.5. **Results**

### 4.5.1. **Sample Characteristics**

The sample consists of the same women presented in **Chapter 3** (see **section 3.5.1** and **table 3.1** for sample characteristics). The dropout rate was approximately 33% from baseline to one-year post-training (see **figure 4.1.** for the flowchart of participants).

[5] One of the one-year follow up interviews was excluded from the final analysis due to the participant being made redundant and unable to discuss the impact on work.

### 4.5.2. **Themes: Impact of adaptive cognitive training**

Three main themes were observed across the post-training interviews collected at one-month six-months and one-year post-training including (1) perceived impact of cognitive training on impaired cognitive function, (2) perceived effects of training on work-related self-management methods for cognitive impairment and (3) perceived impact on women's career development and progression. Clear relationships were found between the themes and subthemes reported by women in the work environment. See **Chapter 3** for the findings from the baseline interviews.

#### *One-month post-training*

#### **Dual *n*-back training:**

#### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Most women spoke of noticing small to moderate improvements in cognitive domains including decision making, concentration/attention, problem-solving, word-finding, and short-term memory, positively impacting their workability and work performance. As expected, short-term memory and concentration/attention were perceived to be the most impacted by the training. Many described that training had not completely eradicated their cognitive issues but reduced their severity and frequency. Linkages were found between perceived cognitive function, confidence and general emotions (i.e., frustration), with improvements in CRCI elevating confidence, optimism and contentment, as well as reducing feelings of frustration at work:

> "*I don't know where I've got this figure from but for some reason, I seem to think that I can concentrate for between 10 and 20 minutes longer than I did previously. I don't know why I think it is specifically 10 to 20 minutes longer, but… I don't know I've got this idea from somewhere maybe I have loosely timed*". [Participant 10]

"*I definitely feel better about myself and I do feel a bit more confident and much less tearful, much less victim like*". [Participant 30]

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

This boost in perceived cognitive ability reduced dependency and reliance on self-management methods (i.e., notetaking or double-checking) which, in turn, was promoting confidence in the workplace. One woman, for example, described feeling more professional and on par with her colleagues now that she was not as reliant on these methods. Women also described feeling more "normal" and "capable". Majority of women spoke of how their self-management cognitive support methods had become less detailed (i.e., single trigger word), more organised and more efficient since completing the 12 sessions of training:

"*Well, it feels…you feel more…I feel more confident because I feel like my brain is…is taking more of the strain as it were so I don't need those props quite so much*". [Participant 14]

A high acceptance of using the self-management methods in the workplace was reported by women experiencing little-to-no change in dependency.

### *Theme 3: Perceived impact on women's career development and progression*

Some women in the study were considering or had already started to increase their number of working hours (either in a paid or voluntary capacity) and workload. This seemed to reflect the improvements in perceived CRCI enhancing workability and confidence. A few women spoke of voluntarily putting themselves forward or applying for new work opportunities, something they would not necessarily have done before receiving the training. Such a change in behaviour suggests that dual *n*-back training provokes greater self-confidence in workability. One woman mentioned she would have taken on additional work before the training but would not have felt as certain in her ability. A couple

of women who stated that they were not content with their work situation before the training outlined feeling more motivated to make a change:

> "*Just had more… actually no I volunteered to let someone shadow me which I probably wouldn't have done before and that was a confidence thing, I think. So, I've done that and like I said I've got more cases as well and more complex cases*". [Participant 31]

> "*Before the training, I was considering quitting…I didn't want to do it anymore I just thought I can't do it…I feel like a fraud but now I am thinking of going a few hours on a Thursday as well so going from 21 hours to 25 hours*". [Participant 38]

## Dual 1-back training:

### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Many women in this group spoke of feeling marginally 'sharper' and less 'foggy' compared to before the training. 'Little' or 'slight' improvements in short-term memory and attention/concentration, were most commonly reported. As expected, perceived cognitive improvements had a positive effect on workability, emotional wellbeing and confidence. Interestingly, a few mentioned, however, that it was challenging to attribute these changes solely to the training, with one woman explaining she felt the improvements could be linked to a combination of factors including the training sessions, better awareness and natural recovery over time. This response could be underpinned by doubts or uncertainty around how a 'simple' or non-cognitively demanding task could be responsible for these improvements. Many women clearly stated that cognitive impairment could still be noticeably problematic. It seemed that these perceived cognitive issues were linked to worse periods of fatigue and stress:

> "*Even a little bit of memory coming back, and you feel more confident you don't feel like you are losing the plot".* [Participant 20]

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

Mixed views of dependency and reliance (incorporating both positive and negative) on the self-management methods were found, with a moderate proportion describing that although they still routinely applied the methods at work their reliance had lessened. A few women attributed this change to improvements in cognitive functioning and its impact on confidence. In contrast, others described no noticeable change in dependency since receiving the training, with many describing that self-management methods were crucial at work. A couple of women did, however, express that the methods had become more efficient and effective, reflecting a better perceived cognitive function, acceptance and more conscious awareness of the importance of using such methods to function:

> "*At work, I wouldn't say I have changed anything, but I am always… I am always trying to jot things down because I might be doing something at work and I think of something I need to do…actually, this is when I make mistakes a lot of the time when something comes into my mind that I need to do and I don't make a note of it and then just forget it and then I don't do it because I have forgotten it*". [Participant 15]

### *Theme 3: Perceived impact on women's career development and progression*

Most women outlined that there had been no change to their number of working hours or workload. Only a few in the active control group implied considering or were already starting to participate in new training courses or work opportunities. Women taking on new work opportunities or duties spoke about how growth in confidence associated with their perceived cognitive ability was one of the factors influencing their decision.

## *Six months post-training*

### Dual *n*-back training:

### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Most women experienced sustained improvements in their perceived cognitive abilities including memory and attention when compared to pre-training. Some, however, outlined starting to notice a decline. In particular, these women described experiencing issues with memory and word-finding again, adversely affecting mood (i.e., creating frustrations) and beginning to impact work-related outcomes. This decline seemed to be related to increased pressure, stress and fatigue, as well as the outbreak of COVID-19 and its consequence[6]. Despite these evident declines most described a sustained improvement in their overall confidence. Many spoke of still feeling more "worthy", "recovered", "proud" and "in control". For some, confidence had continued to grow, and this was contributing to a greater acceptance and less concern when cognitive issues arose:

> "*Well, there was an improvement in that, but I do know for a fact the last couple of weeks, in particular, that's kind of been a bit of a problem as well at work and home but mostly at work…I just couldn't find the word that I need and then it made me panic*". [participant 31, social care]

> "*I think it is more the feeling being confident you know thinking I can handle things…I am not completely….my brain is not completely disabled I can handle things and if I don't remember something, I can come back…it is the mindset that has changed for me*". [Participant 24]

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

In line with the one-month interviews, most women expressed that their self-management

[6] Many of the post-training interviews were conducted during the COVID-19 national lockdown in the UK.

methods (i.e., notetaking**)** were far less detailed and more efficient. Many also reported a sustained reduction in dependency and reliance which made them feel more "spontaneous", "better", "less tearful" and less "burdened" in the workplace. A few reported being highly dependent on self-management methods**,** however, delineated that use had become more of a habit, suggesting that for some using methods may not directly reflect their perceived cognitive function. Further, two women spoke of reverting back to using more methods, stating this was not linked to their perceived cognition or dependence but rather changes induced by the COVID-19 outbreak and its impact on work conditions (i.e., working from home). One woman mentioned that working from home because of COVID-19 had further lessened her need to use self-management methods as there were far fewer distractions than in the office environment:

> "*No, not at all and I mean I still write lists for things and I still do lists but not to the same extent as my work list used to be. I mean I have always used lists so that is never going to change but yeah…. Yeah, they are just not so…it is not such an integral part of work now".* [Participant 40]

## *Theme 3: Perceived impact on women's career development and progression*

Many women spoke of how improvements in perceived cognitive function and confidence impacted their desire to increase the number of working hours, workload, or types of work they were taking on, however, because of COVID-19 and circumstances outside of their control these developments had been curtailed for some. Women were taking on additional duties including, new projects or roles because of the growth in confidence associated with their perceived cognitive ability. One woman, for example, spoke of feeling more confident that she could take on additional work without making mistakes because her thought processing was much clearer:

> "*I seem to remember last time we spoke I had loads of improvement like I was thinking of increasing my working hours but that didn't happen because of COVID and everything anyway*". [Participant 38]

"*Prior to the training and prior to kind of…there was a big difference I noticed. I don't think I would have felt confident doing as much as I am doing now if I hadn't had the training*". [Participant 40]

## Dual 1-back training:

### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Some women reported a slight sustained improvement in their focus/concentration, positively affecting their capacity to engage in tasks and duties, however, most noticed a continuous decline. This seemed to be primarily linked to fatigue and work pressure (i.e., high workload), as well as the indirect effects of COVID-19. There were mixed experiences (incorporating both positive and negative) with memory, decision-making and word-finding, with most noticing a decline at work. Others felt they had remained stable over time albeit often attributing this to self-management coping methods or external changes within the company.

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

A moderate proportion of women outlined some noticeable improvements in the effectiveness and efficiency of their self-management methods despite there being no overall change in dependency, with many denoting a heavy reliance at work. Some described implementing more self-management methods at work, linking this to improvements in efficiency and general acceptance. Being able to effectively use the methods seemed to be contributing to workplace confidence for many women. Only a few in the group spoke of having a lower dependency which was still promoting their confidence:

"*I think so I mean I certainly feel that I am not forgetting as many things as I was you know maybe a year ago let's say. So, I am remembering to write things down. It is all very well saying*

*write things down to remind you, but you've got to remember to write them down, so I think I am actually better at writing things down and almost I think that is helping with my organisation as well*". [Participant 7]

"*I think it is less detailed now, so I plan my day and I plan marketing and who I want to phone up or just what is coming up and what I need to create for that, but I don't write down every last order and detail in it…no*". [Participant 32]

### *Theme 3: Perceived impact on women's career development and progression*

A moderate proportion spoke about how their workload or number of working hours had noticeably increased in recent months, however, for most this was due to external circumstances outside of their control (i.e., time of year, COVID-19 adaptions) as opposed to personal desire. One woman described how COVID-19 had completely limited the work opportunities available. Only a couple of women mentioned starting to put themselves forward for new projects or tasks, which could reflect an improvement in self-confidence at work:

"*I mean there has been a need in terms of some of the changes around me and I have been able to put my hand up for stuff and say yeah, I can take that on, so it has been obvious… my increased ability and confidence has enabled me to…to take things on*". [Participant 8]

"*Yeah, I mean I think there is always several factors to things so I had an opportunity to do this new thing I may well have done it before I don't know but I think that I felt more confident in being able to take it on*". [Participant 2]

## *One-year post-training*

### Dual *n*-back training:

### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Mixed views were found with perceived cognitive function (incorporating both positive and negative). Whilst many experienced a degree of sustained improvement in their concentration/attention and word-finding when compared to baseline, others felt there had been a clear and evident decline. Noticeable declines in memory (and recall), were most prevalently reported. Word-finding issues were also frequently discussed, although some felt they were still far less frequent and more 'normal' (e.g., a tip of the tongue experience). For a moderate proportion of women, this decline seemed to be associated with the unprecedented outbreak of COVID-19 and its adverse effects, as well as increasing levels of fatigue and stress. Women describing sustained improvements reported feeling more 'confident', 'happier', 'content' and less 'disadvantage' and 'stressed'. Some also described that the improvement(s) had a positive effect on work turnover and work productivity:

> *"Definitely because I am not…like I was making the same silly mistakes, again and again, say on…say if we had a similar claim something that I had already dealt with I still won't be able to get my head around it because I couldn't concentrate. Whereas now…yeah, the concentration… I can actually do it and focus on it"*. [Participant 38]

> "*Yeah, just I suppose it is easier to say it used to make me feel inadequate because I just felt like I can't do this job, I am useless and now I know I can again…I am doing it…successfully touchwood at the moment. So, yeah, I feel like my confidence has come back a lot".* [Participant 38]

> "*I did notice I had that slight improvement after I did the training but gradually that has sort of faded over and I do find myself now unless I am working without distractions and just left to do something then I do find that I lose concentration easily*". [participant 28]

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

In line with one-month and six-month interviews, most women reported a sustained reduction in their dependency on self-management methods, positively boosting their emotional wellbeing, workability and work productivity. Many also stated the methods such as notetaking were less detailed and more effective. Some discussed how these improvements were further contributing to increased confidence and better emotional wellbeing. Much like the six-month interviews, a few women highlighted that their use of self-management methods had changed since the COVID-19 outbreak and working remotely from home:

> "*Yeah, that lower level of dependency makes me feel…I can't even think of the word…it makes me feel good about myself. It makes me feel useful…I just felt like a fraud before like there must be so many people out there who would love to be doing this job and I've got it and I don't deserve it and I can't do it so yeah, now I feel deserving…I feel like I am a strong part of the team*". [Participant 38]

> "*I still like to use them but I suppose I use them as a function rather than an aid these days I think is what I am talking about…I don't use notes sort of to help me cognitively it is a function of what I am doing*" [participant 23]

### *Theme 3: Perceived impact on women's career development and progression*

Many women described continuing to increase their workload, work hours and taking on new (and more ambitious) duties or tasks, attributing this to improvements in perceived cognitive function and growing confidence over the year. One woman outlined how her gain in confidence and acceptance of her memory since the training contributed to her taking on two educational courses that would help progress her career:

*I have started taking on the odd extra shift which I definitely was not doing six months ago and actually I think I might apply for another job which I certainly wouldn't have done. I haven't actually done the application form but I am thinking I could probably do that whereas I wasn't feeling like I could do anything of any responsibility before*. [Participant 30]

## Dual 1-back training:

### *Theme 1: Perceived impact of cognitive training on impaired cognitive function*

Many described experiencing some level of sustained improvement in their memory and attention/concentration when compared to baseline, although most outlined noticing evident problems with their perceived cognitive function in the workplace. Women reported fluctuations day-to-day depending on fatigue and stress. Improvements were associated with workability, as well as general emotional wellbeing. Only a few women mentioned feeling more confident. A couple of women linked their sustained improvements to changes induced by COVID-19, for example, working from home.

### *Theme 2: Perceived effects of training on work-related self-management methods for cognitive impairment*

Many women spoke of how their self-management methods were still more effective and efficient, reflecting a sustained improvement over the year. A few delineated implementing more self-management methods such as calendar alert apps to support their workability and prevent mistakes, associated with the effects of COVID-19 (i.e., working remotely) and increasing workloads:

"*Well, it is like a little safety net so I know I have got it there… so I know it is there if I need to use it. So, it is just a backup really but it was crucial that I had it before… I think I would get a little bit nervous if I hadn't made notes knowing how bad my memory was at that point in time."* [Participant 22]

Most women experiencing a reduction in dependency at six months post-training stated that there had been no significant change.

### *Theme 3: Perceived impact on women's career development and progression*

Many outlined that they were starting to take on new projects, work duties or were diversifying their type of work. This seemed to be linked to growing confidence associated with perceived cognitive function and the self-management coping methods, as well as the consequences of the COVID-19 outbreak and its impact on work:

> "*I did have a project given to me recently which I don't usually do project work but we are writing a new project… but it was given to me and I had to stop and think about what I was doing and I was able to… and I think if it had been in the office, I probably wouldn't have been able to so much. It is easier at home to do it.*" [Participant 20]

> "*Yeah, I mean because there is often new innovates to work and focus on and certainly managing through the pandemic, we have had to completely change our way of working so that has been a huge piece of work to lead the team through so yeah, I'd say actually there has been quite a lot of change in terms of what I have been working on*". [Participant 8]

## 4.5.3. **Themes: Experience and engagement with adaptive cognitive training**

One-month post-training interviews revealed detailed descriptions of women's experiences and engagement with the 12 sessions of dual *n*-back training or dual 1-back training (active control). Two main themes were identified across the interview transcripts: (1) women's experiences with- and endorsement of the cognitive training sessions and (2) views on the timing of the cognitive training as part of post-active treatment recovery.

### *Theme 1: Women's experiences with- and endorsement of the cognitive training sessions*

Most women in the dual *n*-back group spoke of how they were able to highly engage with the 12 training sessions and found them to be "challenging", "enjoyable" and "fun". One woman described feeling inspired by the training as a result of the measurable improvement observed during each session. Women stated that they would recommend the training to others living with the effects of breast cancer and its treatment. Reasons primarily included the enjoyment of the training, as well as the improvements in confidence and perceived cognitive function. Some described how the training had exercised (or unlocked) their brain and demonstrated to them that the detrimental effects did not have to be permanent. Many outlined they would like to continue with the training (although less frequently) because of the positive and evident effects experienced:

> *"Well, going back to what I said now it's been a really positive experience, it's made me see myself as a proper human being again because before I was, I just felt like a shell of my…that sounds quite dramatic but that's you know I can't think of any way else to say it"*. [Participant 9, dual *n*-back training]

> *"I would really recommend it because it made me feel good about myself again and think that is a really common thing with people who have been through chemo this bubble your kind of… your brain being asleep in away…so that is the main thing it has woken my brain up and I don't know if anything else would have done that. So yeah, I am definitely glad I did it and I would recommend it".* "*I could have done more I was quite sad when it ended…not sad but I wanted to carry on*". [Participant 38, dual *n*-back training]

Most women (in both training groups) stated that completing 12 sessions over two weeks was manageable, however, a few women spoke of the logistical and time management issues they faced when trying to complete the sessions as consecutively as possible (e.g., at the same time each day) whilst also managing their work and family commitments:

"*Yes, I did. I made sure I put aside that…I think it was half an hour each day. I made sure I did that and I got on with it…yes and that. The only thing I did find…I remember at the start you said and I think in the notes it said to try and do it at the same time every day and I didn't find that possible at all*". [participant 18, dual *n*-back training]

"*Probably the only challenge was making sure that you allotted a time and actually, in my case making sure that other people were out of the way so that I could do the training*". [Participant 27, dual 1-back training]

"*The tests themselves I found quite easy to do…they worked quite well I tried them on a couple of computers and I had no problem doing them either on Mac or a PC it was fine so it was very accessible*". [Participant 36, dual *n*-back training]

In comparison to dual *n*-back training, one challenge experienced more commonly by women allocated to the active control (dual 1-back training) was sustaining a high level of engagement throughout the training sessions. Women described how they found the training to be "repetitive", "boring", "tedious" or a "chore":

"*The number of them is fine, it is quite a lot time at a time that you sit down and do it and I did find doing it a bit tedious*". [participant 32, dual 1-back training]

"*I guess the main thing was the more I did it…I did actually get bored [laugh] if I am honest because it is quite a boring task*". [Participant 8, dual 1-back training]

### *Theme 2: Views on the timing of cognitive training as part of post-active treatment recovery*

Majority of women in the early stages of survivorship spoke of how the dual *n*-back timing of the training felt right and they were able to see some improvements, for example, in perceived cognitive function or workability shortly after completing the sessions. As the survivorship period (or time since completion of active treatment) progressed, women more frequently described feeling that they would

have potentially benefited more from receiving the training closer to the end of the active treatment period. As this was the time when they were struggling most to come to terms with the post-treatment effects or had more available time to complete the training before they returned to work. Many women stated that they felt six- to 12- months after treatment would be an optimal time. One woman spoke of how she felt the training would have been instrumental in her recovery process. She also stated that she felt the training should be integrated into support programs that are offered to all women recovering from cancer treatment:

> "*I think actually afterwards but you know a few months after so when the dust settles because I think that is when you start realising o my goodness what has just happened to me. So, I think if it was a part of follow up treatment when you finish your active treatment, I think that would be brilliant you know if it could be part of…. almost like a recovery post active treatment sort of thing*". [Participant 24, dual *n*-back training]

Importantly, some women speculated that receiving dual *n*-back training during active treatment (i.e., during chemotherapy or radiotherapy) as opposed to waiting until the end of the treatment period could also have some potentially beneficial effects, for instance, lessening the severity of CRCI. Although, some indicated that the training would need modifying to make it manageable:

> "*I don't know maybe not so intense so maybe shorter sessions and not kind of every day might have been useful during chemo or during treatment but I think I would have struggled with it during chemo for so long so maybe sort of shorter periods of time might have been useful*". [Participant 40, dual *n*-back training]

Similarly, to dual *n*-back training, many women in the early survivorship stage stated that the timing of dual 1-back training felt right. Some, however, reported feeling they could have received their training slightly earlier than six months post-active treatment (as specified by the research inclusion criteria) and that this may have prevented the development (or build-up) of some of the debilitating post-treatment effects. This response may be driven by the non-adaptive nature of the task which makes it less cognitively demanding on working memory compared with the dual *n*-back training. Women

longer into survivorship demonstrated mixed feelings, with some stating that they could not have received the training any earlier. This seemed to be linked to receiving more aggressive treatment(s) or ongoing treatment and/or experiencing greater complications. Most women stated that they would have found it too challenging to complete during their active treatment:

> "*I would have said sooner after treatment actually would have been…I would have preferred…yeah, I think particularly because I went back to work a couple of months after I finished treatment. If it had then helped with cognitive function at work that would have again… I would have then been in a much more…much sort of better cycle of cognitive improvements so, therefore, confidence would have improved*". [Participant 8, dual 1-back training]

## 4.6. **Discussion**

**Chapter 4** aimed to investigate the perceived effects of adaptive cognitive training (i.e., dual *n*-back training) and active control training (i.e., dual 1-back training) on the self-reported experiences of cognitive impairment impacting the workability of women affected by primary breast cancer. The chapter also aimed to explore the perceived transfer effects of this cognitive training on work-related self-management methods implemented by women to manage their cognitive impairment and on career progression or development. In addition, the chapter also examined primary breast cancer survivors' experiences with dual *n*-back training (adaptive cognitive training group) or dual 1-back training (active control group) including, their views of the timing of the training. The findings revealed that women in the current study experienced improvements in perceived CRCI following 12 sessions of dual *n*-back training, enhancing confidence and general emotional wellbeing. Furthermore, these perceived improvements contributed to a reduced dependency on self-management methods at work and promoted career development and progression (i.e., increased workload or working hours). Whilst there were

sustained effects on perceived cognitive function for up to six months and one year, the outbreak of COVID-19 and its consequences in the UK had curtailed and changed work for many women.

In recent years, WM training such as dual *n*-back training has grown in popularity due to its potential to generate both near and far transfer effects (see Soveri et al., 2017, for a review). Substantiating studies have shown positive transfer effects in cognitive domains including attentional control, WMC, filtering efficiency and general fluid intelligence (See Derakshan, 2020, for a review). Swainston and Derakshan (2018) also showed sustained far transfer effects in self-reported rumination and (trait) anxiety in women affected by breast cancer following the completion of 12 sessions of online *n*-back training.

Comparisons between the baseline (see **Chapter 3** for the baseline interview findings) and the post-training interviews revealed that although dual *n*-back training had not completely eradicated CRCI, the majority of women had experienced some positive changes in their perceived cognitive function, compared to the active control group (dual 1-back training). Most commonly women in the adaptive dual *n*-back training group described noticing evident improvements (or perceived training gains) in their (short-term) memory and attention/concentration which was, in turn, positively boosting confidence and reducing emotional vulnerability. The possible similarities in improvements reported by women in the adaptive dual *n*-back training and active control training group can be explained by both groups' positive expectancy of the training effects (i.e., an individual's belief in the training effectiveness) or more general placebo effects, as participants were blind to their training group allocation and all believed that they were participating in a cognitive training study to improve their cognitive function and workability. In a study by Foroughi et al., (2016), it was found that placebo effects from recruitment posters significantly influenced cognitive training outcomes. Notably, however, more women in the active control group described attributing their positive changes to a combination of factors including natural recovery over time since completing treatment, suggesting a level of uncertainty about the plausibility of dual 1-back training as a cognitive intervention.

When comparing adaptive dual *n*-back training to active control dual 1-back training, Sari et al., (2016) found a greater improvement in attentional control as assessed by performance on a modified

flanker task under stress in high trait anxious participants. Equally, they also found significant training-related gains on neural measures of attentional control as assessed by a reduction in the SW/FW ratio (Sari et al., 2016), a known marker of trait attentional control (Putman et al., 2014). Similarly, dual *n*-back training compared with active control training has been shown to result in greater improvement in behavioural and neural measures of WMC in sub-clinically depressed participants (Owens et al., 2013). In a recent neuroimaging study by Colom et al., (2016), it was shown that *n*-back training also led to a greater grey matter volume in brain regions implicated in working memory and cognitive control. The findings of perceived cognitive function improvements between the adaptive dual *n*-back training and active control training (dual 1-back training) group presented in **Chapter 4** are in line with these objective markers.

In line with studies showing that greater self-efficacy and confidence are associated with better workplace wellbeing (Singh et al., 2019) and work performance (Stajkovic & Luthans, 1998), many women in the dual *n*-back group described experiencing improvements in confidence associated with their post-training cognitive ability, positively enhanced workability and work performance. In a study by Munir et al., (2010), it was shown that cognitive impairment adversely affects breast cancer survivors' confidence in their workability. Furthermore, another study by Amir et al., (2008), reported that loss of confidence was one of the key challenges experienced by cancer survivors after returning to work. Unexpectedly, from one-month post-training, some women in the dual *n*-back group reported that they were thinking of or had begun the process of increasing their working hours and workload (either in a paid or voluntary capacity). In comparison, far fewer women who received dual 1-back training spoke of career developments or progression. Studies have shown that reducing work hours and changing work duties are two of the most common adaptions made by cancer survivors (Torp et al., 2012; Sandberg et al., 2014). Of focal importance, Hamood et al., (2019) found that work transitions such as being downgraded (or demoted) adversely impact the quality of life of women affected by breast cancer. The findings presented in **Chapter 4**, therefore, suggest that perceived transfer effects of dual *n*-back training on cognitive function and the translation of this on career development or progression may have crucial implications for women's overall quality of life. One possible explanation for this

difference between the two groups which should, however, be considered is the availability of career opportunities. It is probable that for some women career opportunities or developments may not be obtainable regardless of their workability. Alternatively, it is also viable that women in the dual *n*-back group were experiencing greater and more long-term objective cognitive training gains (i.e., genuine effects from the training) compared to the active control group as evidenced by greater career progression, despite the similarities in the subjective reports.

In further support of this notion, women in the dual *n*-back group also spoke more frequently about noticing a change in dependence on work-related self-management methods such as notetaking, suggestive of greater cognitive effects. Interestingly, women in both training groups reported noticeable changes in the effectiveness and efficiency of their self-management methods at work regardless of dependency, for example, women outlined more concise or structured notes and a better ability to remember to use notetaking. It is possible that some of the changes experienced with the self-management methods may have been driven by women's reflections after the baseline interviews and their (un)conscious decision to make improvements to better support their workability. Given that the findings from the baseline interviews presented in **Chapter 3** revealed that some women find self-management coping strategies including cognitive support methods applied in the workplace to be problematic and to contribute to greater emotional distress (Chapman et al., 2021), these findings also have important implications.

Whilst women outlined experiencing some sustained effects following dual *n*-back training when compared to baseline, a proportion described noticing evident declines in their perceived cognitive function in the months before their six months follow-up and in the time between the six months and one-year follow-up, coinciding with the outbreak of COVID-19 in the UK. Despite this perceived decline many women in the dual *n*-back group described feeling more "worthy", "recovered" and "in-control" at six months post-training, as well as more "confident", "content" and less "disadvantage" at one-year, reflecting a sustained improvement in emotional wellbeing, confidence and self-esteem in the workplace. Comparisons between the groups show that improvements in self-confidence were greater at one year in the dual *n*-back training group compared to the active control

group. Whilst some women reported taking on new duties because of growing confidence and many others wanted to increase their work (i.e., number of hours), the outbreak of COVID-19 had curtailed opportunities and adjusted the work experience for many. Women across both training groups described a series of changes influenced by COVID-19 independent of the training effects including working from home and changes in work duties.

When asked about their experience women in the dual *n*-back group described their training as "challenging" and "enjoyable", with many reporting they would like to continue with the training although less intensely (e.g., training three times a week). Women in the active control (dual 1-back group), however, found it challenging to maintain engagement, with some describing the training as "tedious" and "boring" and stated that it became a "chore" to complete, despite showing a high-performance accuracy throughout, indicating that these views were not driven by performance. Such differing accounts of the training experience in terms of engagement and enjoyability suggest that long-term compliance would likely be higher in dual *n*-back training. Women's feedback (from both groups) about the challenges (i.e., logistical and time management issues) with the intensity of the training also suggests that longer-term training or follow-up ('top-up') training sessions after the initial 12 training sessions would need to be more flexible to ensure it is suitable for women regardless of their existing schedules and commitments (e.g.., work).

Most women who received dual *n*-back training in the early stages of survivorship described how the time of the training was right for them and they could see evident gains. Although women longer into survivorship outlined experiencing improvements, many felt the training would have been more effective closer to the end of their treatment or even immediately after treatment, as this was the period when the effects were most troublesome and difficult to come to terms with both at work and in their personal life. The findings suggest that dual *n*-back training could be offered flexibly to women six- to 12 months after the completion of active treatment. Further objective research should be conducted to compare and contrast the effectiveness of receiving dual *n*-back training at various stages (or time points) to identify if there is an optimal time.

Furthermore, some women who received dual *n*-back training stated that they felt it could also be beneficial to be offered the training during treatment (i.e., chemotherapy and/or radiotherapy) before the issues arose. Currently, there is no preventive (behavioural) intervention available to protect against CRCI (see Joly et al., 2019, for a review). Further longitudinal research should be conducted to investigate the viability of implementing this cognitive intervention during the treatment period, as plasticity-induced changes require a high level of rigour (i.e., 12 sessions of dual *n*-back training to be completed consecutively over two weeks) which may not be manageable. It is well documented that women can experience a series of debilitating physical and psychological effects during active treatment including pain, fatigue, insomnia, headaches, nausea and vomiting as well as depression and anxiety (Bower, 2008; Whisenant et al., 2020) that may hinder participation during this time, escalating existing levels of distress.

Taken together, the findings presented in **Chapter 4** have important implications for occupational health services as they suggest that women who receive dual *n*-back training perceive experiencing improvement in CRCI, which in turn, boosts emotional wellbeing and confidence. Further, they indicate that these perceived improvements may have a beneficial effect on career development and the self-management cognitive support methods implemented by women in the workplace. This research should be interpreted with caution, however, because of the COVID-19 outbreak and should be replicated after work (and the economy) starts to 'normalise' to determine the true efficacy of the training at six months and one year. Interestingly, the experiences reported by women imply that dual *n*-back training should be offered through oncology services six-to 12 months after the completion of treatment to target post-active treatment issues.

### 4.6.1. **Limitations**

**Chapter 4** bestows a few limitations that need to be taken into consideration. Given, that the study was longitudinal, and women with known CRCI (i.e., impaired short-term memory) were asked to recall their experiences over one year the impact of memory (or recall) bias should be considered

when interpreting the findings. Future research could ask women to keep a record of events or experiences to increase the reliability of their accounts. In addition, although women were encouraged to talk openly about their experiences with the training they may have focused on the positive outcomes and benefits as opposed to giving a more objective review of the training. This study was conducted during the COVID-19 outbreak in the UK which may confound the findings reported.

### 4.6.2. **Conclusion**

To conclude, the findings presented in **Chapter 4** show that working women who received 12 sessions of dual *n*-back training described experiencing positive improvements in their perceived cognitive function which significantly boosted their emotional wellbeing and confidence in the workplace. Although similar findings were reported by the active control group who received dual 1-back training, the perceived effects were much greater in the dual *n*-back group. Women also reported positive effects on dependency and effectiveness of the self-management cognitive support methods applied to support work, as well as on their career developments after the training, indicating that dual *n*-back training can be implemented as part of a standard protocol to help women affected by breast cancer sustain their work and workability over time. Importantly, the findings in this chapter revealed that women found dual *n*-back training to be "challenging" and "enjoyable", with many stating they would like to continue to receive the training. Further research should be conducted to examine the experiences of dual *n*-back training in women living with a diagnosis of metastatic breast cancer.

## Published paper associated with this chapter:

Chapman, B., Derakshan, N., & Grunfeld, E. A. (accepted in BJHP). Experiences of cognitive training on primary breast cancer survivor's cognitive impairments at work: A longitudinal qualitative study. *British Journal of Health Psychology*.

# **Chapter 5:** Exploring the efficacy of adaptive cognitive training on improving impaired cognitive function and workability: A multimodal assessment using self-report questionnaires, objective measures of cognitive function and electrophysiological measures

## 5.1. **Chapter Overview**

The findings presented in **Chapter 4** showed that working women who received 12 sessions of dual *n*-back training experienced sustained improvements in their perceived cognitive functioning up to one-year after the completion of training. These perceived improvements in cognitive function were associated with greater self-confidence and a better general emotional wellbeing in the workplace. A lower dependency on work-related self-management methods such as notetaking and greater career progression or development, previously shown to be stalled as a result of cancer-related cognitive impairment (CRCI) and cancer-related sequelae (see **Chapter 3** for baseline interviews) were also found.

Extending these findings, the primary aim of **Chapter 5** was to investigate the longer-term efficacy of dual *n*-back training on improving cognitive function (assessed using objective and subjective measures), as well as to examine the transfer effects of training on workability and quality of life, as well as on anxiety and depression, well-known predictors of reduced workability in women living with a diagnosis of breast cancer (see **Chapter** 1 **section 1.4.2.4.** for existing literature).

## 5.2. **Introduction**

Breast cancer is the most prevalent malignancy diagnosed in women worldwide, with more than 2.2 million cases recorded in 2020 alone (World Health Organisation, 2020). Developments in the

efficiency of early diagnostic techniques and greater awareness of the signs and symptoms of breast cancer alongside the advances in multimodality treatment have significantly improved long-term survival rates, with approximately 85% of women surviving at least five years in England (Cancer Research UK, n.d.). Notwithstanding the advances in survivorship, many women affected by breast cancer experience a series of short- and long-term cancer-related sequelae including, cancer-related cognitive impairment (CRCI; Joly et al., 2019), anxiety, depression (Carreira et al., 2018, 2021) and fatigue (Maass et al., 2021) which adversely impact everyday quality of life (Zeng et al., 2016; Chapman et al., 2019) and work-related outcomes such as work productivity (Calvio et al., 2010; Kim et al., 2022), in addition to reducing sustainment of work (Peipins et al., 2021).

Women affected by breast cancer are at a greater risk for developing anxiety and depression compared to the wider population (see Carreira et al., 2018, 2021, for reviews). In a study by Shim et al., (2020), it was shown that anxiety, depression and comorbid anxiety and depression predicted all-cause mortality amongst women living with a diagnosis of breast cancer. Extending this, Wang et al., (2020) found that depression increased the risk of recurrence, all-cause mortality and breast cancer-specific mortality by 24%, 30% and 29%, respectively (see **Chapter 1 section 1.4.2.3** for more comprehensive description). When assessing the role of depression and anxiety on workability, Kim et al., (2022) found that depression significantly impacted work productivity loss (as measured by the WLQ), such that depressed women with a history of breast cancer had approximately four-fold higher work productivity loss compared to those without depression (2.7 vs. 10.3). Further, findings showed that depression was adversely associated with the four WLQ subscales (time management demands, physical demands, mental/interpersonal demands, work output demands), with greater depression meeting worse reported workability. Greater work productivity loss has been shown to be predictive of poorer quality of life in women affected by breast cancer (Liu et al., 2021).

CRCI describes the symptom cluster of cognitive complaints (i.e., memory deficits, attentional lapse) experienced by individuals diagnosed and treated for cancer (Padgett et al., 2020; accc-cancer.org). Studies have shown that CRCI is one of the most common complaints reported by women living with a history of breast cancer (See Joly et al., 2019, for a review). Indeed, Lange et al., (2019b)

found that more than 50% of women in their study had self-reported cognitive complaints (e.g., attentional deficits) following the completion of chemotherapy; although only 15-25% showed objective cognitive impairment. The discrepancy between objective and subjective measures in this population has been attributed to a range of factors including compensatory effort and the use of traditional neuropsychological tests (See Ahles & Root, 2018; Ahles & Hurria, 2018, for reviews), indicating that subjective reports are an important indicator of women's cognitive vulnerability. In a study by Calvio et al., (2010), it was shown that self-reported memory and executive function significantly predicted breast cancer survivors' work output, however, no associations were found with performance-based tests assessing the same cognitive domains, suggesting that women affected by breast cancer may use compensatory effort to maintain their performance effectiveness on objective tests, for which there has been increasing evidence for (Menning et al., 2016; Swainston et al., 2021). A plethora of studies conducted by Von Ah and colleagues have provided substantiating evidence that self-reported cognitive function is significantly associated with work-related outcomes in women with a history of breast cancer, with findings showing that poorer perceived cognitive function predicts worse work-related outcomes including greater work productivity loss (Von Ah et al., 2013, 2017, 2018, 2021).

Memory and attention deficits are the most impacting on everyday life and workability in women affected by breast cancer (Bolton et al., 2018; Von Ah et al., 2013). In a series of electroencephalogram (EEG) studies conducted by Kreukels et al (2005, 2006, 2008), it was shown that women treated for breast cancer express a blunted P3 (or P300) amplitude and longer P3 latencies. The P3 is a well-established neural marker occurring approximately 350 to 550 ms after the stimulus onset over the centroparietal regions (i.e, Cz, Pz) (Polich, 2007). Functionally, the P3 has been associated with the allocation of cognitive to task-relevant information and allocation of attention resources for updating working memory (Polich, 2012), with a larger P3 amplitude reflecting a greater allocation of cognitive (or attention) resources to task-relevant information and more efficient allocation of attentional resources for updating working memory. Kam and colleagues (2016) found that greater reported cognitive deficits met with a smaller P3 amplitude compared to controls on a sustained-

attention-to-response task (SART). Further, they found higher alpha power at rest met with slower reaction times, suggestive of abnormal patterns of sustained attention and poorer allocation of attention to task-relevant information.

The error-related negativity (ERN) and error positivity (Pe) have also been utilised to investigate the impact of clinical affective disorders (i.e., anxiety) and neurotoxins such as chemotherapy on cognitive functioning. The ERN is a negative potential that peaks within 100ms of an erroneous response on reaction-time tasks (i.e., flanker task) (Gehring et al., 1993; Moser et al., 2013) and is detected in the frontocentral scalp regions (i.e., Cz). Neuroimaging indicates that the ERN is generated by the dorsal portion of the anterior cingulate cortex (ACC) and posterior cingulate cortex (PCC) (Debener et al., 2005; Grutzmann et al., 2016; Gilbertson et al., 2021) reflecting the conflict between error and correct responses (Yeung and Cohen, 2006; Hughes and Yeung, 2011). Dissociable from the ERN, the Pe is a positive potential found to be maximal in the centroparietal regions between 200 to 400ms after an erroneous response and is generated by the rostral portion of the ACC (Overbeek et al., 2005). It depicts the error awareness, allocation of attention to an error and the adjustment of response strategies (i.e., slowing down after an erroneous response) to optimise accuracy and performance (Falkenstein et al., 2000; Overbeek et al., 2005). A study by Simó et al., (2018) revealed smaller ERN amplitudes on a modified flanker task in individuals affected by lung cancer compared to healthy controls which they attributed to inefficient performance monitoring. Performance monitoring is defined as a regulation behaviour that involves the signalling and detection of an error, as well as the correction of the error response in a flexible manner to optimise performance usually measured by the ERN and its correct response counterpart, the CRN (correct-related negativity). Most recently, Swainston and Derakshan (2021) found women with a breast cancer diagnosis who had undergone chemotherapy compared to 'no cancer' controls showed different patterns of ERN/CRN responses and a larger Pe on a standard letter flanker in the absence of behavioural effects between groups, suggesting greater neural compensatory mechanisms and greater affective reactivity to errors.

The efficacy of adaptive cognitive training interventions such as the adaptive dual *n*-back training task on improving cognitive efficiency has been explored in both non-clinical (Jaeggi et al.,

2008, see Derakhshan, 2020, for a review) and clinical (or sub-clinical) populations including anxious (Sari et al., 2016), depressed (Owens et al., 2013), high worriers (Hotton et al., 2018), as well as with women affected by breast cancer (Swainston & Derakshan, 2018, 2021). In a study by Owens et al., (2013), it was found that eight sessions of adaptive dual *n*-back training significantly improved WMC and filtering efficiency of irrelevant information. Sari et al., (2016) also revealed improvements in attentional control on a modified flanker task in high anxious individuals as a result of dual *n*-back training. Besides, they found reductions in trait anxiety, with greater reductions in trait anxiety associated with higher dual *n*-back engagement. Using a modified version of the emotional dual *n*-back training task, Lotfi and colleagues (2021) found that nine sessions of training increased the amplitude of the ERN, a finding not replicated by the active control group. Similar increases have been reported for the P3 amplitude following cognitive training (Tusch et al., 2016; Gajewski & Falkenstien, 2012, 2018; Lotfi et al., 2020) in healthy older adults and children with dyslexia. Recently, Beloe and Derakshan (2020) evidenced that dual *n*-back training significantly reduced depression and anxiety in adolescents, with effects sustained up to one-month post-training. Of focal importance, Swainston and Derakshan (2018) substantiated that receiving 12 sessions of dual *n*-back training resulted in sustained reductions in rumination and anxiety in women living with a history of breast cancer up to 15 months after the completion of training, however, no measure of cognitive transfer was assessed.

In a recent study conducted by Lange et al., (2019b), it was shown that the majority of cancer survivors want support for their CRCI, with cognitive training (72%) most requested compared to psychological support (48%) and physical activity (32%). Importantly, Crouch and Von Ah (2017) found that women affected by breast cancer and CRCI preferentially wanted to participate in online computer-based cognitive training programs that were readily accessible, not too time-consuming and could be completed from anywhere (i.e., at home or work).

### 5.2.1. **Aims**

Given the promising findings from existing adaptive cognitive training (dual *n*-back training) research and the body of research showing that impairment of cognitive function significantly predicts worse work-related outcomes in women affected by breast cancer, it was crucial to investigate the efficacy of dual *n*-back training in working women living with a history of primary breast cancer. To this end, the overall aim of the current study (known as the 'BRiCatWork' study) was to examine the longer-term effects of online adaptive cognitive training (dual *n*-back training) on workability and sustaining work across time through targeting cognitive functioning. In doing so, **Chapter 5** first aimed to investigate the efficacy of dual *n*-back training on improving impaired cognitive function. The chapter then aimed to investigate the transfer effect on workability, anxiety and depression and quality of life. Studies have shown a significant association between perceived cognitive impairment and emotional distress amongst women affected by breast cancer (anxiety and depression) (Von Ah & Tallman, 2015; Janelsins et al., 2017). Of importance, greater anxiety and depression have also been linked to poorer work-related outcomes (Carlsen et al., 2013; Ho et al., 2018; Kim et al., 2022). In line with Swainston & Derakshan (2018; 2021), women were provided with 12 sessions of training to complete as consecutively as possible over two weeks (see **Chapter 2 section 2.9** for a more comprehensive description).

It was predicted that women who received dual *n*-back training would experience a greater level of improvement in their perceived cognitive function, self-reported emotional wellbeing (anxiety and depression) and quality of life compared with the active control group (dual 1-back training) post-training and at longer follow-up of one-year. It was also predicted that women who received dual *n*-back training would report a greater improvement in their workability (as measured by the WLQ -Work Output score and Work Productivity Loss) at six-months and one-year. The current study is the first to explore the impact of dual *n*-back training and dual 1-back training on neural indices of error processing, cognitive function and working memory (WM) assessed during a modified flanker task in women affected by primary breast cancer. Based on previous research we elected to examine three key neural markers including the P3 (P300), ERN and Pe. It was predicted that the dual *n*-back training group

would show better cognitive functioning on objective measures of WMC and neural indices of error processing (ERN, Pe), cognitive functioning and WM (P3) which may be implicated in workability compared to the dual 1-back training group at post-training.

## 5.3. **Method**

### 5.3.1. **Design**

A two-group single-blind, RCT comparing adaptive cognitive training (dual *n*-back training) to an active control group (dual 1-back training) was utilised. Self-report outcomes were measured at baseline, post-training, six-months and one year. Objective assessments of working memory, as well as neural indices of working memory and cognitive function, were measured at baseline and post-training[7].

### 5.3.2. **Participants**

Women living with a history of primary breast cancer ($N$ = 80) were recruited via advertisements displayed on the Birkbeck Centre for Building Resilience in Breast Cancer (BRiC) Facebook public page and other breast cancer support group webpages including Macmillan, Breast Cancer Network, Mastectomy Network, Breast Friends and True Cancer Bodies (TCB). Women were recruited between the 1st of February 2019 and the 29th of February 2020 using self-selected (voluntary) sampling. The first 40 women enrolled on the 'BRiCatWork' study were asked to additionally participate in the telephone interviews conducted at baseline, one-month post-training, six-months and one year (see **Chapter 3** for baseline findings and **Chapter 4** for post-training follow up interviews).

Inclusion criteria included: (1) aged 18 to 65 at the time of enrolment, (2) diagnosis of primary breast cancer, (3) six to 60 months post-active treatment for chemotherapy and/or radiotherapy at the

[7] Due to the Coronavirus disease outbreak and national lockdown in the UK the six-month and one-year follow up sessions were cancelled for the safety of the participants.

time of recruitment (whichever came last), (4) receiving hormone blocker therapies, hormone replacement therapies (HRT) or target therapies like Herceptin, (5) attending regular employed or self-employed paid work and (6) experiencing a decline in workability or performance as a result of cognitive difficulties.

Exclusion criteria included (1) receiving active treatment(s) such as chemotherapy and/or radiotherapy, (2) under six months or over 65 months post-active treatment, (3) under 18 years old or over 65 years old, (4) not attending paid work (i.e., volunteering), (5) not experiencing any difficulties with workability associated with cognitive impairments and (7) unable to read or understand English.

### 5.3.3. **Materials and Stimuli**

Participants' sociodemographic and clinical information was self-reported using the ***General Demographics Questionnaire (GDQ***; replicated from Swainston & Derakshan, 2018; see **Chapter 2 section 2.4.1** for a more comprehensive description).

#### 5.3.3.1. **Primary Outcomes and Measures**

#### *Objective Measures of Cognitive Function*

WMC was assessed by the ***automated operation task*** (***OSpan task***; Unsworth et al., 2005; Foster et al., 2015; Turner & Engle, 1989) presented on an Asus computer at Birkbeck University. Participants were asked to remember three to seven unrelated letters ('F, H, J, K, L, N, P, Q, R, S, T and Y'; *memory task component*) presented in between simple maths equations (e.g., 2 + 4 =?; *distractor task component*). At the end of each trial, participants were asked to recall the correct sequence of letters from a possible 12 letters. A higher OSpan score (also referred to as the partial score) reflects a greater WMC (see **Chapter 2 sections 2.5. and 2.5.1.1** for a more comprehensive description of OSpan task).

WMC was also measured using the shortened version of the ***Change Detection Task*** (***CDT,*** Vogel et al., 2005; Owens et al., 2012, 2013) presented on an Asus computer at Birkbeck University. Participants were asked to remember and then compare the orientation of red rectangles (target items) shown in two sets of stimulus arrays: (1) a memory array and (2) an accuracy-test array and respond by pressing the '1' key if the orientation of one of the red rectangles had changed between the two arrays and '0' if the two arrays matched. A higher score (K score) demonstrates a greater WMC (see **Chapter 2 sections 2.5. and 2.5.1.2** for a comprehensive description of CDT and Pashler's formula for the K score).

Distractor interference and information processing was measured with the ***modified standard letter flanker*** (Eriksen & Eriksen, 1974; replicated from Moser et al., 2011) shown on an Asus computer at Birkbeck University. Participants were asked to respond rapidly and accurately using the computer mouse to the central letter (*target letter*) shown within a string of five letters (i.e., MM**N**MM). For each trial, the central letter was either congruent (i.e., VV**V**VV) or incongruent (i.e., VV**U**VV) to the four distractor (flanking) letters. Participants' reaction times and response accuracy were calculated for both congruent and incongruent trials, as well as the total number of error responses produced and post-error slowing. Post-error slowing was calculated using the difference between response reaction times on correct trials following an error or correct response (EC – CC). Corrections were applied for switching block failure (> = 60% errors) (see **Chapter 2 section 2.5** and **2.5.1.3** for a more comprehensive description of the flanker task).

## *Questionnaires*

Perceived cognitive function was assessed by the ***Functional Assessment of Cancer Therapy-Cognitive Scale*** (***FACT-Cog, Version 3***; Wagner et al., 2004; Wagner et al., 2009). Higher scores (for each subscale and total score) reflect a greater perceived cognitive function. Cronbach's α scores were high in the current study: FACT-Cog total (α = .95), PCI (α = .95), PCA (α = .85), CFO (α = .82) and

QoL (α = .88). The FACT-Cog-perceived cognitive ability subscale (PCA) was selected as the variable of interest (see **Chapter 2 section 2.4.2** for a more comprehensive description).

Rumination was assessed using the 22-item ***Rumination Response Scale (RRS***; Treynor et al., 2003). A higher score demonstrates more severe rumination. Cronbach's α was excellent in the current study (α = .94) (see **Chapter 2 section 2.4.3** for a more comprehensive description).

Workability was measured with the 25-item ***Work Limitations Questionnaire*** (***WLQ***; Lerner et al., 2001; 2003). Higher scores for the subscale and work productivity loss indicate a greater level of difficulty in the workplace and more productivity loss. High Cronbach's α scores were found for productivity loss (= .95), time management (α = .83), physical (α = .86), mental/interpersonal (α = .88) and work output (α = .86), reflecting high reliability. The work output demands score and productivity loss score were used as the variables of interest (see **Chapter 2 section 2.4.9** for more detail).

### 5.3.3.2. **Secondary Outcomes** and **Measures**

#### *Electroencephalography (EEG)*

EEG activity was recorded using BrainVision Recorder software (Brain Products, Gilching, Germany) during the flanker task (see **Chapter 2 section 2.5.1.3** for a more comprehensive description of the task). Recordings were taken from 32 Ag-AgCl passive electrodes embedded in a standard mesh EEG cap (BrainVision, EasyCap) placed per the 10/20 system (Jasper, 1958) including, both left and right mastoids (TP9 and TP10) (see **Chapter 2 section 2.6** for a description of electroencephalogram setup).

Offline analyses were performed using BrainVision Analyzer 2.2 (Brain Products, Gilching, Germany). Failed switch blocks (or failed switched mappings) (> = 60% errors) on the flanker task were first removed to be in line with behavioural analyses. Interpolation was then conducted using Spherical splines method (Perrin et al., 1989). Twenty-seven participants needed interpolation at baseline and 15 participants needed interpolation at post-training, however, none of these participants

required interpolation exceeding four electrodes. Only one participant at post-training had central electrodes interpolated (Cz) that were included in the average for the ERN and CRN. Scalp electrode recordings were re-referenced to the mean of the mastoids and band-pass filtered with cut-offs of 0.1Hz and 30 Hz (12 Db/octave roll-off). Gratton, Coles and Donchin's (1983) method was applied to correct ocular artefacts. Event-related potentials (ERP) data (response-locked: ERN, CRN, Pe, stimulus-locked: P3) were segmented into individual epochs beginning 200ms before the stimulus onset or response discharge and continuing for 800ms after the stimulus onset or response production. A computer-based algorithm built in BrainVision was used to identify physiological artefacts. Trials that met the following three criteria were rejected: (1) a voltage step exceeding 50 μV between contiguous sampling points, (2) a voltage difference of more than 200μV within a trial, or (3) a maximum voltage difference less than 0.5μV within a trial. This resulted in a loss of an average of 2.28% and 2.43% trials at baseline and 1.19% and 0.92% at post-training for response-locked data and stimulus-locked data, respectively. The remaining response-locked data were segmented into erroneous and correct responses, averaged and then baseline correction (beginning at -199.22ms and ending at 0.00ms) was applied. Separately, the stimulus-locked data were segmented into incongruent and congruent stimuli on correct trials, averaged and then bassline corrected (beginning at -199.22ms and ending at 0.00ms).

Split-half reliability was assessed using Spearman-Brown-corrected Pearson correlation coefficients between odd and even trials ($SB = 2r_{xy}/ (1+r_{xy})$), **Baseline**: ERN: $r_{sb} = 0.89$, $p < .001$, CRN: $r_{sb} = 0.99$, $p < .001$, early pe (errors): $r_{sb} = 0.79$, $p < .001$, early pe (corrects): $r_{sb} = 0.96$, $p < .001$, late pe (errors): $r_{sb} = 0.70$, $p < .001$, late pe (correct): $r_{sb} = 0.96$, $p < .001$, P3 (incongruent trials): $r_{sb} = 0.96$, $p < .001$, P3(congruent trials): $r_{sb} = 0.96$, $p < .001$; **Post-training**: ERN: $r_{sb} = 0.82$, $p < .001$,CRN: $r_{sb} = 0.97$, $p < .001$, early pe (error): $r_{sb} = 0.72$, $p<.001$, early pe (correct): $r_{sb} = 0.98$, $p<.001$, late pe (error): $r_{sb} = 0.70$, $p <.001$, late pe (correct): $r_{sb} = 0.96$ $p <.001$,P3 (incongruent trials): $r_{sb} = 0.95$, $p <.001$, P3 (congruent trials): $r_{sb} = 0.98$, $p <.001$. The respective time windows for the ERN, early and late Pe, as well as early and late P3, were determined by visual inspection of the grand average waveforms (see ERP sections below for each of the respective time windows).

### *Error-related negativity (ERN)*

The ERN and the corresponding ERP amplitude on the correct (correct-response negativity; CRN) response trials were defined as the mean activity (i.e., mean amplitude) occurring in the post response time window from 0 to 100ms, at the Cz electrode, where the ERN and CRN were maximal. A larger negative ERN (or CRN) amplitude on the erroneous trials and correct trials reflects a greater level of early error processing. The number of trials included in the final analysis after artefact rejection (based on **PP.** sample) at baseline ranged from 6 to 72 for error trials ($M$ = 25.13, $SD$ = 16.67), and ranged from 29 to 468 for correct trials ($M$ = 420.90, $SD$ = 76.80). At post-training the number of trials included ranged from 6 to 40 for error trials ($M$ = 17.00, $SD$ = 8.72), and ranged from 394 to 470 for correct trials ($M$ = 452.81, $SD$ = 16.01)[8].

### *Error Positivity (Pe)*

The Pe was defined as the mean activity occurring in two sequential post response time windows from 150 to 350ms known as the early Pe and 350 to 550ms known as the late Pe at the Pz electrode, where the early and late Pe were maximal. A more positive Pe amplitude after erroneous trials represents a higher level of awareness and attention to errors produced (Hughes & Yeung, 2011). The number of trials included in the final analysis of the Pe was the same as the ERN.

### *Posterior P3b*

The P3b was defined as the mean activity occurring in two sequential time windows from 250 to 450ms known as the early P3 and 450 to 600ms known as the late P3 after incongruent and congruent stimulus onset on correct trials, at the Pz electrode, where the P3 was maximal. A more positive P3

[8] Seven participants were eliminated from the **PP.** ERN and Pe analysis as they did not produce enough errors trials (≤5) on the Flanker task

amplitude reflects a greater allocation of cognitive resources to task-relevant information and allocation of attentional control for updating working memory. The number of trials included in the final analysis after artefact rejection at baseline ranged from 10 to 238 for congruent trials ($M$ = 214, $SD$ = 34.43), and ranged from 16 to 235 for incongruent trials ($M$ = 205, $SD$ = 32.90). Number of trials included in post-training analysis ranged from 175 to 239 for congruent trials ($M$ = 229, $SD$ = 11.78), and ranged from 166 to 238 for incongruent trials ($M$ = 222, $SD$ = 12.47).

### *Questionnaires*

Anxiety was measured by the 7-item ***Hospital Anxiety and Depression - anxiety subscale (HADS-A***; Zigmond & Snaith, 1983). A higher score indicates a worse level of (trait) anxiety. Current study's Cronbach's α = .84, reflecting a good reliability (see **Chapter 2 section 2.4.4** for more detail).

Depression was measured by the ***Center for Epidemiologic Studies Depression Scale*** (***CES-D***; Radloff, 1977). A higher score represents a greater level of depression. Current study's Cronbach's α = .92, showing an excellent reliability (see **Chapter 2 section 2.4.5** for more detail).

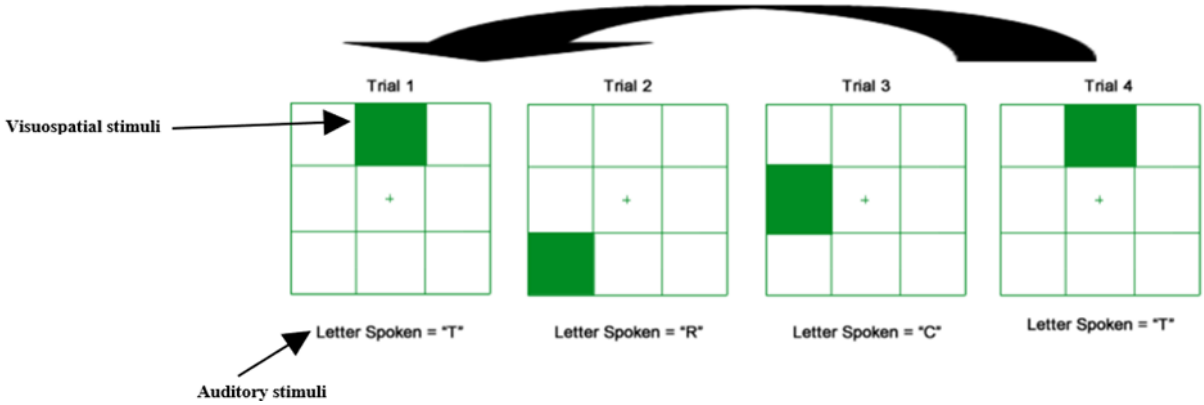
Quality of life (QoL) was assessed using the global health subscale from the ***European Organization for Research and Treatment of Cancer Quality of Life*** (***EORTC-QLQ-C30***; Aaronson et al., 1993). A higher score for global health status reflects a better global quality of life. Current study's study's Cronbach's α = .85, representing a good reliability (see **Chapter 2 section 2.4.6** for more detail).

## 5.3.4. **Dual *n*-Back Training (Intervention; Adaptive Cognitive Training) or Dual 1-Back Training (Active Control Training)**

Standard versions of the dual *n*-back training and dual 1-back training (replicated from Swainston & Derakshan, 2018) were used in the current study (see **Chapter 2 section 2.9** for a comprehensive description of training; **figure 5.1** shows an example of dual 3-back training with a dual match).

**Figure 5.1**

*An example of a dual 3-back training trial with a visuospatial and auditory stimuli match*




*Note.* Participants in the intervention arm were instructed to remember the position of the green box and its paired spoken consonant and respond using the keypad ('A' for a visuospatial match, 'L' for an auditory match and 'A' and 'L' at the same time for a dual match) when the stimulus or stimuli matched what was shown 3 trials earlier.

## 5.3.5. **Procedure**

Women were initially screened using an inclusion criteria checklist sent via email to assess their eligibility (see **section 5.3.2** for the participant criteria). Those who met the criteria and expressed an interest in participating were provided with a study identification number (i.e., A200) and were allocated on a 1:1 ratio to either the adaptive cognitive training group (dual *n*-back training) or active control group (dual 1-back training) using sealed envelope software (Sealed Envelope Ltd., 2017). Reasons for not completing baseline assessments after enrolment included the Coronavirus disease 2019 outbreak ($n$ = 9), ill-health ($n$ = 2) and cancer recurrence ($n$ = 2). Five participants did not give a reason for their decision to withdraw before baseline (see **figure 5.2** for CONSORT diagram).

Women were asked to provide informed consent at the start of each session. Women were first asked to complete a battery of online questionnaires measuring perceived cognitive function, rumination, emotional distress (anxiety and depression), global health status (quality of life), as well as workability. Following the completion of these questionnaires, women then completed the lab session

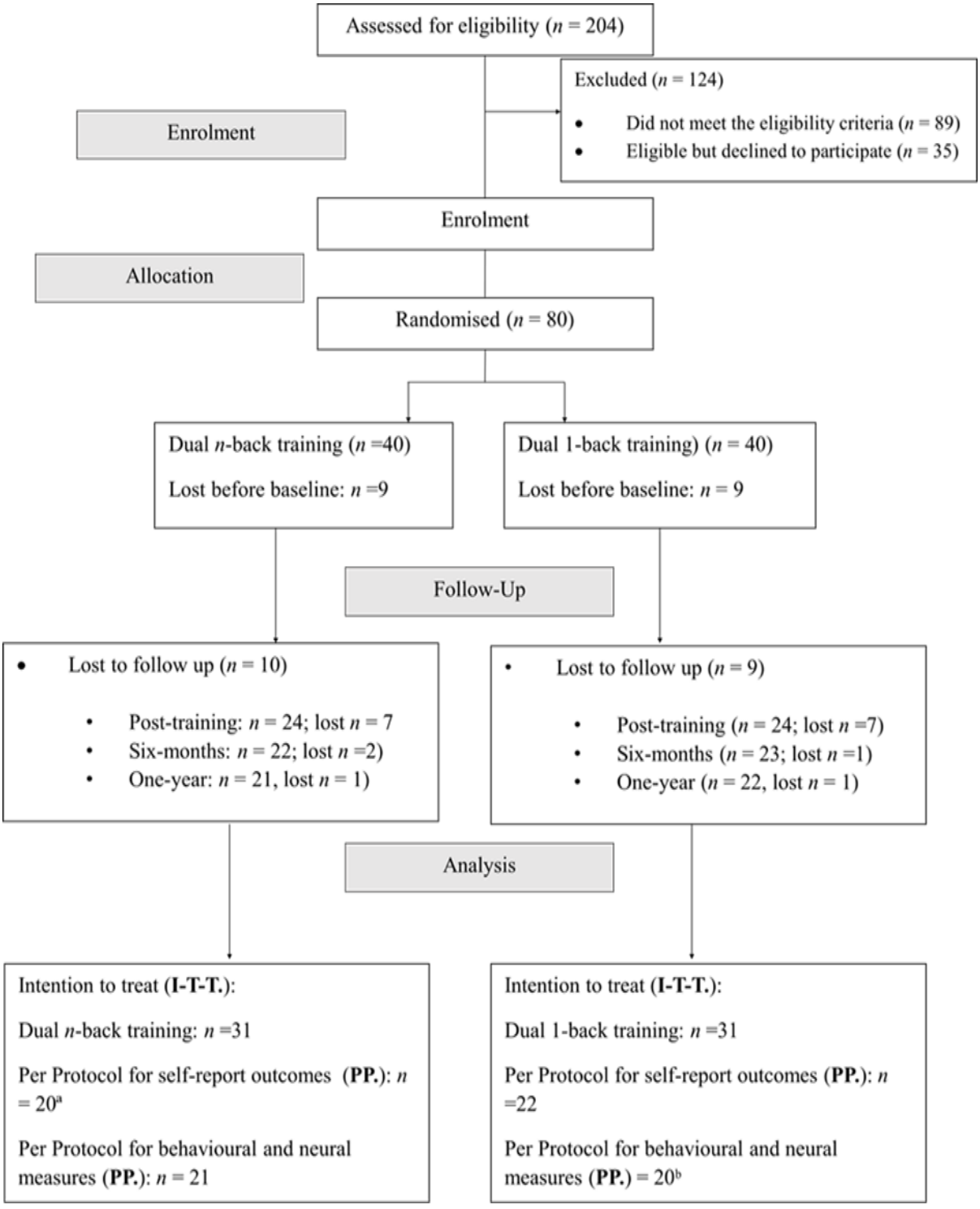
including the objective measures of WM (CDT and OSPAN) and an EEG to assess neural indices of cognitive function and WM implicated in workability whilst completing a modified Flanker task (replicated from Moser et al., 2011). The lab session lasted approximately two and a half hours. Upon completion of the lab session, women were then instructed to complete 12 sessions of online cognitive training (dual *n*-back training or dual 1-back training) lasting approximately 30 minutes as consecutively (i.e., approximately the same time each day) as possible over a period of two weeks. Post-training follow-ups[9] were completed within two weeks of the final training session.

An email was sent to inform women when they were due to complete their six months and one-year follow-up online questionnaires. Women remained blind to their training group until after all of the study data was collected. On completion of the study, women received a single payment of £120 and were given access to both of the training programs.

[9] Due to the COVID-19 outbreak four of the participants could only complete questionnaires at baseline and seven (including the four at baseline) were only able to complete questionnaires at post-training follow-up.

**Figure 5.2**

*Consolidation standards of reporting trials (CONSORT) diagram of the current study*




*Note.* [a] One participant was unable to complete the six-month post-training questionnaires due to ill health, however, did not withdraw from the study and completed the questionnaires at one-year. [b] Two participants were unable to complete behavioural and neural measures as a result of the outbreak of COVID-19 and subsequent closure of the MERLiN lab.

## 5.4. **Statistical Analysis**

Statistical analyses were conducted with the Statistical Package for the Social Sciences (IBM SPSS, version 28). Descriptive statistics were calculated for the sociodemographic, breast cancer history and work characteristics (see **table 5.1** for participant demographics). Chi-square tests and independent samples (bootstrapped) *t*-tests were conducted to examine the group differences between the dual *n*-back training (intervention) and active control group (dual 1-back training) at baseline. Paired *t*-tests (bootstrapped) were also performed to explore the improvement in working memory function (as measured by the level of '*n'*) in the dual *n*-back group from training day 1 to day 12. Performance accuracy was assessed in the active control group from day 1 to day 12.

A series of 2 (group: dual *n*-back training, active control) x 2 (time: baseline, post-training) mixed analysis of variance (ANOVA) were conducted to compare the dual *n*-back training group and the active control group's performance on objective measures of WM including the CDT and Ospan task, as well as on flanker task performance and ERP markers of cognitive function, WM (P3) and error processing (ERN, Pe) from pre- to post-training[10] (see footnote 10). Checks for violation of the assumption of normality and outliers were performed before the analysis. Outliers were examined using histograms and box plots and Winsorization which is recommended for small samples was applied to deal with individual outliers greater than 1$^{st}$ quartile – (1.5 x interquartile range (IQR) or 3$^{rd}$ quartile + (1.5 x IQR) by replacing the outlier with the nearest "non-outlier" value (Reifman & Keyton, 2010). Non-normally distributed data were transformed using square root transformation. Finally, checks for the assumptions of homogeneity of variance were performed using Levene's test. Partial eta squared effect sizes were calculated.

Multilevel modelling (Linear Mixed Effect Models; MLMs) with autoregressive 1 (AR1) was conducted to compare the dual *n*-back training and the active control group (dual 1-back training) on a battery of self-reported questionnaires over time. Two sets of independent analyses were conducted, the

[10] Due to the COVID-19 outbreak in the UK objective measures of WM and ERP markers were unable to be collected at six months and one year.

first utilised all participants who completed the baseline measures (intention-to-treat analysis; **I-T-T.**) regardless of whether they completed all of the intended follow-ups. The second set included participants who completed all of the follow-up sessions (per-protocol sample; **PP.**). Fixed effects in the MLM models were defined as the group (dual *n*-back training, active control), time (baseline, post-training, six months follow-up and one-year follow-up) and group x time interaction. Random effects were specified as participants. A maximum likelihood method was selected for model (parameter) estimation. In line with Swainston and Derakshan (2018) Cohen's *d* method was used to calculate the effect sizes for MLM [$d = 2*\sqrt{(F/df)}$]. Simple effects with Bonferroni-corrected pairwise comparisons were then performed to follow up on significant MLM. Cohen's *d* was calculated.

Additional bootstrapped Pearson's correlation analysis was performed between change (post – pre) in early and late P3 and self-reported outcome measures to explore whether change in P3 following dual *n*-back training or dual 1-back training related to changes in psychopathology, perceived cognitive function, quality of life and work-related outcomes.

## 5.5. **Results**

### 5.5.1. **Sample Characteristics**

**Table 5.1**. shows the demographic, clinical and work-related characteristics of the 62 women who completed baseline questionnaires. The dropout rate for the current study was 30.67 %.[11]

[11] A high dropout rate of 22.5% was found from enrolment to baseline questionnaire completion in this study because of the COVID-19 outbreak increasing job uncertainty and reducing the accessibility of computers. The figure under the sample characteristics section is the dropout rate from baseline to one-year follow-up excluding those enrolled who never started the study. This figure was also influenced by the outbreak of COVID-19.

No group differences were found for education, substance misuse, work hours, age at diagnosis, current age, time since active treatment, history of psychiatric disorder, hormone therapy status, grade, surgery, chemotherapy and radiotherapy (*p's* > .05).

### 5.5.2. **Baseline Characteristics**

**Table 5.2** displays the means and standard deviations (SD) for the self-reported questionnaires for each training group. Independent (bootstrapped) *t*-tests show significant group differences for perceived cognitive ability (as measured by the FACT-Cog) (BCa 95% CI [0.91, 5.48]. *t* (60) = 2.50, *p* = .02, *d* = .64), work output demands (BCa 95% CI [-23.24, -4.11], *t* (60) = -2.50, *p* = .02, *d* = .63) and work productivity loss (%) (BCa 95% CI [-4.76, -1.00], *t* (60) = 2.67, *p* = .01, *d* = .68), such that women in the dual *n*-back (intervention) group had worse perceived cognitive ability and work demands compared to the active control group at baseline. Women were randomly assigned on a 1:1 ratio to their training group using sealed envelope software (Sealed Envelope Ltd., 2017). No significant differences were found for global health status (quality of life), rumination, anxiety and depression (*p's* >.05).

No significant differences were found between training groups for WMC (as measured by the CDT and OSPAN), commission of flanker errors, error reaction time (RT), correct RT, error-correct trials (EC) RT, correct-correct trials (CC) RT, RT on congruent and incongruent correct flanker trials, RT on congruent and incongruent error flanker trials, early and late P3 amplitude on congruent and incongruent trials, ERN, CRN, early Pe and late Pe at baseline (see **table 5.3** for means and SDs for objective measures of working memory and ERPs).

**Table 5.1**

*Women's demographics, clinical and psychiatric history and work characteristics at baseline*

| | Intention-to-treat | | | | Per-Protocol | | | |
|---|---|---|---|---|---|---|---|---|
| | **Adaptive cognitive training** | | **Active control training** | | **Adaptive cognitive training** | | **Active control training** | |
| | ***n = 31*** | ***(%)*** | ***n = 31*** | ***(%)*** | ***n = 20*** | ***(%)*** | ***n = 22*** | ***(%)*** |
| ***Demographic*** | | | | | | | | |
| Current age (years) | 49.2 (Range 34-60) | | 47.5 (Range 36-61) | | 48.6 (Range 34-60) | | 48.2 (Range 36-61) | |
| *Education*[a] | | | | | | | | |
| Secondary/further education | 9 | 29.0 | 8 | 25.8 | 7 | 35.0 | 7 | 31.8 |
| Higher education | 18 | 58.1 | 20 | 64.5 | 13 | 65.0 | 15 | 68.2 |
| History of substance misuse | 1 | 3.2 | 1 | 3.2 | 1 | 5.0 | 1 | 5.0 |
| *Alcohol intake* | | | | | | | | |
| None | 8 | 25.8 | 7 | 22.6 | 6 | 30.0 | 6 | 27.3 |
| 1-6 units | 18 | 58.1 | 15 | 48.3 | 12 | 60.0 | 9 | 40.9 |
| 7-13 units | 3 | 9.7 | 6 | 19.3 | 1 | 5.0 | 4 | 18.2 |
| 14-20 units | 2 | 6.5 | 2 | 6.5 | 1 | 5.0 | 2 | 9.1 |
| >20 units | 0 | 0.0 | 1 | 3.2 | 0 | 0.0 | 1 | 4.5 |
| ***Clinical - Breast cancer history*** | | | | | | | | |
| Age at diagnosis (years) | 46.9 (Range 31-58) | | 45.0 (Range 35-59) | | 46.3 (Range 31-58) | | 45.6 (Range 35-59) | |
| *Grade*[b] | | | | | | | | |
| Grade 1 | 4 | 12.9 | 1 | 3.2 | 2 | 10.0 | 1 | 4.5 |
| Grade 2 | 9 | 29.0 | 7 | 22.6 | 5 | 25.0 | 5 | 22.7 |
| Grade 3 | 17 | 54.8 | 22 | 71.0 | 13 | 65.0 | 15 | 68.2 |
| *Type of treatment* | | | | | | | | |
| Chemotherapy | 23 | 74.2 | 25 | 80.6 | 16 | 80.0 | 18 | 81.8 |
| Radiotherapy | 27 | 87.1 | 26 | 83.9 | 17 | 85.0 | 19 | 86.4 |
| Surgical procedure | 31 | 100.0 | 31 | 100.0 | 20 | 100.0 | 22 | 100.0 |
| Time since active treatment finished [c] (months) | 20.9 (Range 6-37) | | 21.4 (Range 6-59) | | 19.6 (Range 6-37) | | 21.7 (Range 6-59) | |
| Endocrine therapy | 24 | 77.4 | 21 | 67.7 | 15 | 75.0 | 14 | 63.6 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *History of a psychiatric condition* | 9 | 29.0 | 6 | 19.4 | 6 | 30.0 | 4 | 18.2 |
| Anxiety | 1 | 3.2 | 0 | 0.0 | 1 | 5.0 | 0 | 0.0 |
| Depression | 1 | 3.2 | 4 | 12.9 | 1 | 5.0 | 3 | 13.6 |
| Anxiety and depression | 2 | 6.5 | 2 | 6.5 | 2 | 10.0 | 1 | 4.5 |
| **Work** | | | | | | | | |
| *Number of hours*[d] | | | | | | | | |
| Full-time | 20 | 64.5 | 17 | 54.8 | 11 | 55.0 | 14 | 63.6 |

*Note.* **Intention-to-treat**: [a] Seven women did not disclose their highest level of education, [b] Two women did not state the grade of their primary breast cancer diagnosis, [c] One woman did not state her specific time since diagnosis although did confirm she was between six to 60 months post-active treatment, [d]One woman did not state the number of hours they are employed to work; **Per-protocol**: [b] One participant did not state the grade of their primary breast cancer

**Table 5.2**

*Means and standard deviations for perceived cognitive ability, emotional symptomology, quality of life and work limitations*

| | **Baseline** | | **Post-training** | | **Six-Months** | | **One-Year** | |
|---|---|---|---|---|---|---|---|---|
| | **Training (*n* =31)** | **Control (*n* =31)** | **Training (*n* =24)** | **Control (*n* =24)** | **Training (*n* =21)** | **Control (*n* =23)** | **Training (*n* =21)** | **Control (*n* =22)** |
| **Perceived cognitive ability (FACT-Cog)** [a] | 11.94 (5.10) | 15.16 (5.06) | 13.46 (4.90) | 20.96 (6.52) | 18.10 (8.40) | 19.52 (6.43) | 19.24 (7.73) | 21.14 (7.31) |
| **Perceived cognitive impairment (FACT-Cog)** | 27.26 (15.10) | 36.32 (12.94) | 39.38 (14.32) | 51.08 (11.83) | 46.67 (16.05) | 54.43 (12.46) | 49.67 (14.02) | 59.18 (12.63) |
| **Comments from others (FACT-Cog)** | 12.55 (3.48) | 14.19 (2.12) | 12.63 (2.99) | 15.25 (1.15) | 14.29 (2.33) | 15.22 (1.83) | 14.29 (2.29) | 15.41 (1.33) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Impact on quality of life (FACT-Cog)** | 6.67 (3.70) | 8.00 (3.76) | 9.79 (3.96) | 12.63 (2.95) | 9.90 (4.69) | 11.17 (4.26) | 10.90 (4.72) | 12.77 (3.19) |
| **Perceived cognitive function (FACT-Cog total score)** | 59.06 (23.66) | 73.68 (17.99) | 75.25 (22.24) | 100.54 (17.91) | 88.95 (27.14) | 104.57 (12.59) | 94.10 (24.88) | 108.50 (22.68) |
| **Rumination (RRS)** | 53.39 (14.32) | 49.26 (12.58) | 48.33 (12.20) | 41.67 (8.75) | 45.57 (11.32) | 39.30 (6.46) | 43.19 (11.15) | 41.23 (12.86) |
| **Anxiety (HADS)** | 10.29 (5.00) | 9.23 (4.65) | 9.92 (3.80) | 7.79 (5.26) | 9.29 (4.78) | 6.22 (3.50) | 8.76 (5.11) | 6.41 (3.78) |
| **Depression (CES-D)** | 26.48 (11.41) | 21.42 (11.37) | 23.38 (10.75) | 13.08 (7.62) | 21.43 (12.03) | 11.83 (6.67) | 18.14 (11.85) | 15.95 (12.05) |
| **Global health status (QoL)** | 57.53 (23.80) | 66.93 (19.54) | 64.24 (21.06) | 74.65 (17.11) | 66.67 (17.87) | 75.72 (13.97) | 69.44 (16.53) | 75.76 (16.04) |
| **Work productivity loss (%) (WLQ)** | 12.07 (4.18) | 9.25 (4.12) | 10.01 (4.97) | 7.43 (4.45) | 8.19 (4.13) | 5.34 (3.43) | 6.58 (3.51) | 4.99 (2.50) |
| **Work output demands (WLQ)** | 51.25 (22.32) | 37.66 (20.45) | 39.35 (22.97) | 33.13 (24.90) | 33.43 (17.90) | 19.24 (12.87) | 26.25 (11.48) | 19.83 (13.94) |

*Note*. SD are in parentheses. Values are based on the total number of participants that completed the questionnaires at each phase of the study. [a] Perceived cognitive ability: higher score = greater perceived cognitive ability; Rumination: higher score = greater rumination; Anxiety: higher score = greater anxiety; Depression: higher score = greater depression; Global health status: higher scorer = better

global health; Work productivity loss: greater score = greater productivity loss; Work output demands: greater score = greater work output difficulty

**Table 5.3**

*Means and standard deviations for objective measures of working memory, flanker task performance and neural indices implicated in workability for Per-Protocol (PP.) sample*

| | **Baseline** | | **Post-Training** | |
|---|---|---|---|---|
| | **Training** | **Control** | **Training** | **Control** |
| **Working memory capacity (CDT)** | 0.69 (0.96) | 1.33 (1.01) | 1.68 (0.70) | 1.53 (0.90) |
| **Ospan partial score** | 51.05 (18.67) | 52.10 (12.51) | 55.24 (12.36) | 58.90 (11.00) |
| **Flanker task:** | | | | |
| **Number of errors** | 18.90 (17.60) | 24.70 (14.41) | 14.85 (10.64) | 15.00 (6.95) |
| **Accuracy (%)** | 96.00 (0.04) | 95.00 (0.03) | 97.00 (0.02) | 97.00 (0.02) |
| **Error RT (ms)** | 470.59 (61.65) | 420.31 (85.46) | 479.85 (102.21) | 446.13 (84.22) |
| **Correct RT (ms)** | 557.71 (44.59) | 525.95 (58.19) | 533.80 (54.61) | 511.74 (52.84) |
| **Post-error slowing (ms) (EC - CC)** | 50.75 (62.62) | 43.75 (55.29) | -12.10 (40.03) | 26.68 (45.44) |
| **Congruent errors RT (ms)** | 497.18 (101.48) | 428.40 (112.24) | 471.58 (108.50) | 494.13 (155.54) |
| **Incongruent errors RT (ms)** | 461.63 (80.79) | 409.92 (82.49) | 483.25 (103.19) | 423.70 (66.62) |
| **Congruent correct RT (ms)** | 535.37 (49.33) | 499.90 (56.42) | 503.43 (42.61) | 486.50 (51.98) |
| **Incongruent correct RT (ms)** | 580.57 (40.59) | 553.49 (61.67) | 554.18 (45.10) | 537.75 (55.58) |
| **Error correct response RT (ms)** | 606.19 (56.53) | 564.90 (93.53) | 518.24 (46.85) | 536.22 (78.50) |

| | | | | |
|---|---|---|---|---|
| **Correct-correct response RT (ms)** | 555.44 (46.85) | 522.30 (58.02) | 530.33 (50.52) | 509.54 (52.39) |
| **ERPs:** | | | | |
| **Error-related negativity (ERN) at Cz (μV)** | -0.20 (2.16) | -1.25 (1.42) | -0.53 (1.32) | -2.08 (2.55) |
| **Correct-response negativity (CRN) at Cz (μV)** | 0.60 (1.51) | -0.06 (1.39) | 0.30 (1.71) | 0.09 (1.18) |
| **ΔERN (μV)** | -0.77 (2.31) | -2.14 (3.91) | -0.99 (2.41) | -2.99 (3.74) |
| **Early Pe on error trials at Pz (μV)** | 1.02 (2.40) | 1.64 (4.07) | 0.49 (2.55) | 1.64 (5.01) |
| **Late Pe on error trials at Pz (μV)** | -0.09 (3.55) | 1.47 (3.59) | 0.19 (3.49) | 1.11 (3.20) |
| **Early P3 on congruent correct trials at Pz (μV)** | 4.52 (2.17) | 5.34 (1.79) | 5.52 (2.74) | 5.58 (1.90) |
| **Early P3 on incongruent correct trials at Pz (μV)** | 4.51 (2.14) | 4.80 (1.64) | 5.20 (2.72) | 5.72 (2.08) |
| **Late P3 on congruent correct trials at Pz (μV)** | 4.96 (3.21) | 4.11 (2.16) | 5.27 (3.05) | 3.61 (2.12) |
| **Late P3 on incongruent correct trials at Pz (μV)** | 5.26 (2.99) | 4.31 (2.02) | 5.49 (3.06) | 4.88 (2.28) |

*Note.* SD are in parentheses. [a]Seven participants were eliminated from the analysis as they did not produce enough errors (≤5) on the Flanker task; [b] Three participants had no error data following corrections; (ERN and Pe: Dual *n*-back training *n* =14; dual 1-back training *n* = 17)

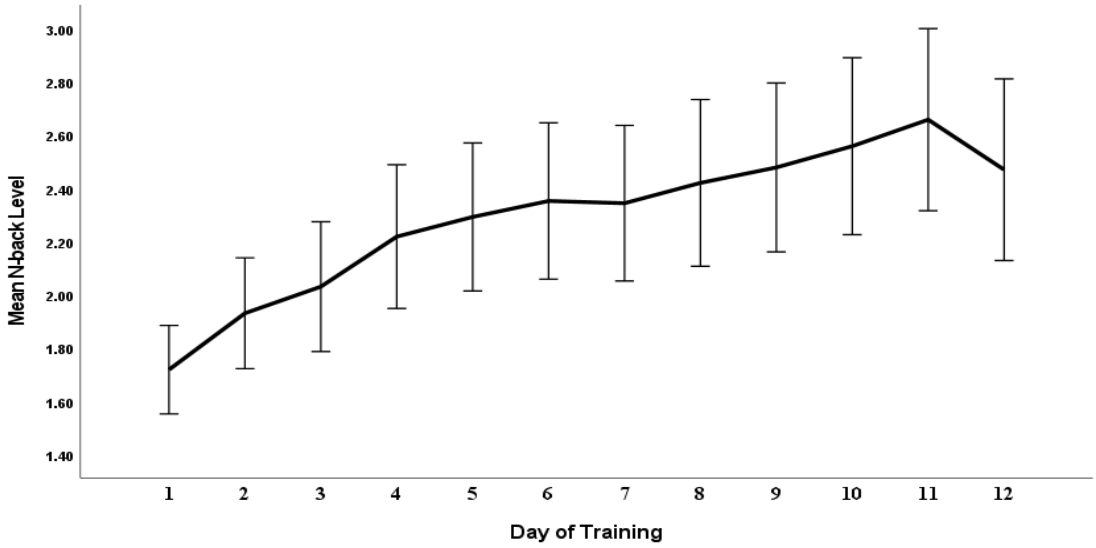
### 5.5.3. **Dual N-back Training Performance**

As **figure 5.3** shows, women in the dual *n*-back training (intervention) group experienced a significant improvement in their working memory (as measured by the level of '*n*') from day 1 (*M* = 1.72, *SD* = .40, BCa 95% CI [1.55, 1.89]) to the final session on day 12 (*M* = 2.47, *SD* = .83, BCa 95% CI [2.12, 2.84]), *M* difference = -.75, BCa 95% CI [-1.00, -.47], *t* (24) = 5.16, *p* < .001, *d* = 1.03. The

slope of improvement for dual *n*-back training was significantly different from zero, *M* difference = .07, BCa 95% CI [.05, .09], *t* (24) = 7.42, *p* <.001, *d* = 1.48.

**Figure 5.3**

*The average level of dual n-back achieved across the 12 days of training*




*Note***.** Error bars = CI 95%

## 5.5.4. **Dual 1-back Training Performance**

Women allocated to the active control group demonstrated a persistently high level of accuracy from day 1 (*M* = 93.78%, *SD* = 10.56, BCa 95% CI [89.03, 97.41]) to day 12 (*M* = 96.44%, *SD* = 11.40, BCa 95% CI [91.56, 99.21]).

## 5.5.5. **Primary Outcomes**

### *Change Detection Task (CDT)*

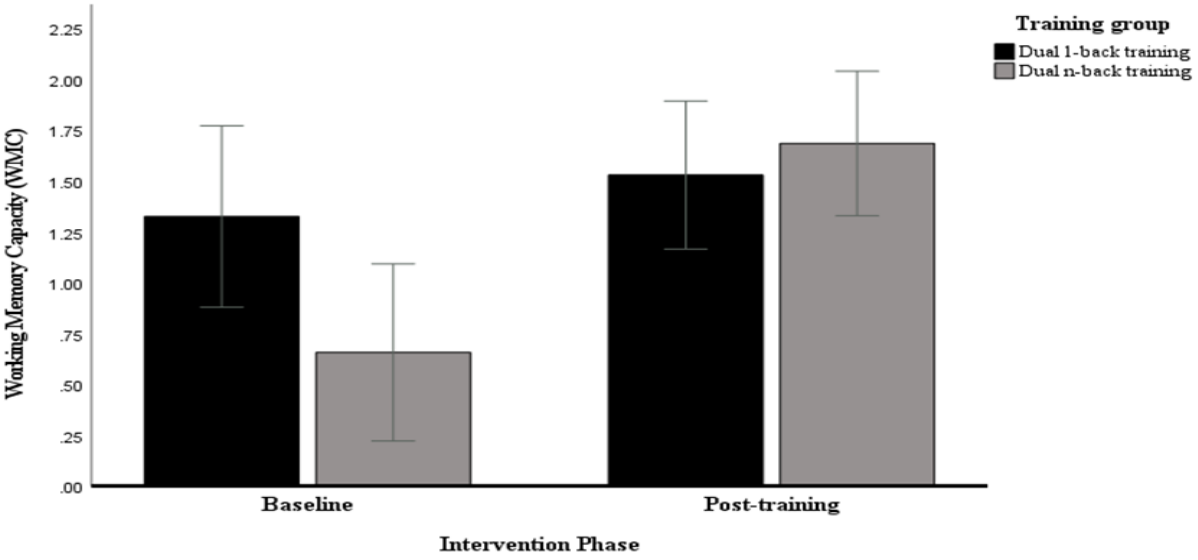
**Figure 5.4** indicates that women in the dual *n*-back training group experienced a greater increase in their WMC (as measured by the K score) following the completion of training compared to

women in the dual 1-back group. When WMC was entered, the mixed ANOVA revealed that there was a significant main effect of time, $F$ (1, 39) = 23.90, $p$ < .001, $\eta_p^2$ = .38 and a significant group x time interaction, $F$ (1, 39) = 10.69, $p$ <.01, $\eta_p^2$ = .22.

Simple effects with Bonferroni corrected pairwise comparisons confirmed that this interaction was driven by a significant increase in WMC for the dual *n*-back group, *M* difference = 1.03, $p$ < .001, $d$ = 1.14 which was not present in the dual 1-back group, *M* difference =.20, $p$ = .27, $d$ = 0.30 (see **table 5.3** for means and SDs at baseline and post-training for each group). No significant difference was found between the two groups at baseline ($p$ > 05).

**Figure 5.4**

*Mean working memory capacity scores on the change detection task for both training groups*




*Note***.** Error bars = 95% CI

## *Post-error slowing*

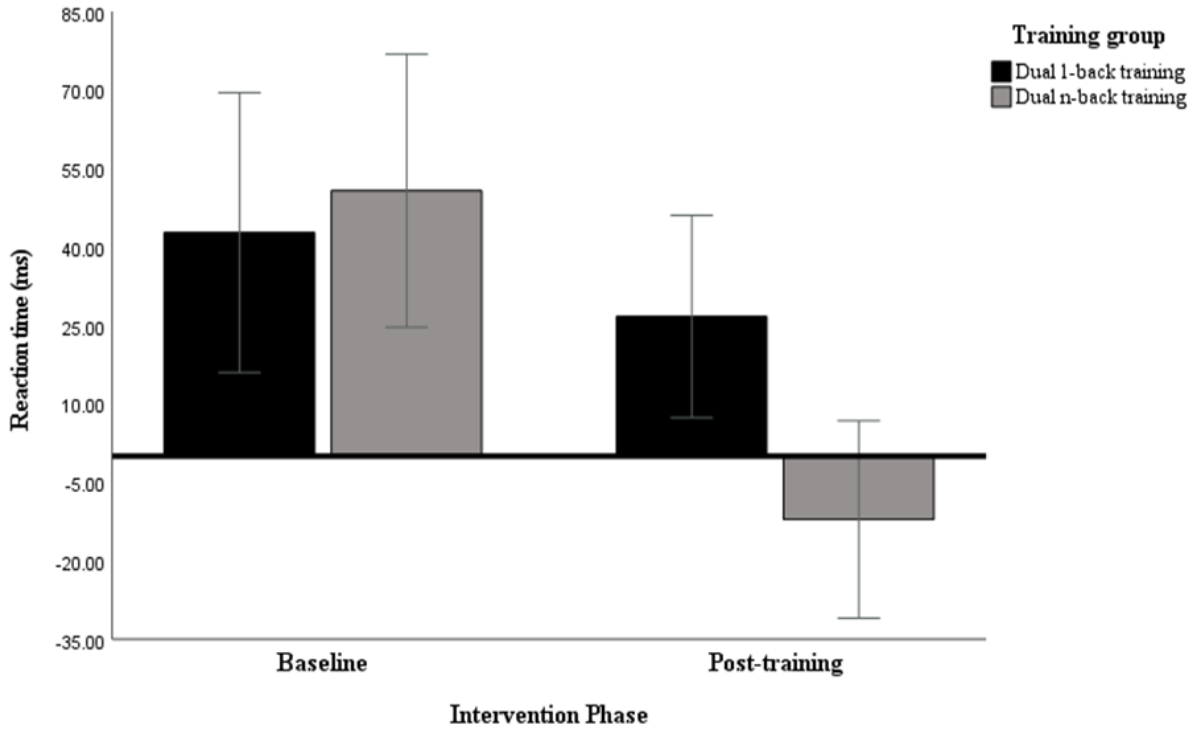
When the difference between response RT on correct trials following an error (EC) and correct response (CC; EC- CC) was entered as the dependent variable, the mixed ANOVA showed a main

effect of time ($F$ (1, 39) = 17.48, $p$ <.001, $\eta_p^2$ = .31) and significant group x time interaction ($F$ (1, 39) = 6.14, $p$ =.02, $\eta_p^2$ = .14).

Post hoc simple effects with Bonferroni corrected comparison with the **PP.** sample showed that post-error slowing RT did not significantly differ between the dual *n*-back training and dual 1-back training group at baseline ($p$ =.67), however, differed significantly following the completion of training ($p$ = .01). Further, the analysis revealed that dual *n*-back training experienced a significant reduction in post-error slowing RT ($M$ difference = 62.85ms, $p$ <.001, $d$ = 1.00) unlike the dual 1-back group ($M$ difference = 16.06ms, $p$ = .24, $d$ = 0.28), suggesting that post-error slowing diminishes after dual *n*-back training (see **figure 5.5** for mean RT (ms) for EC and CC trials and **table 5.3** for means and SDs for each group).

**Figure 5.5**

*Mean post-error slowing RT (ms) for both training groups*




*Note.* Error bars = 95% CI

### *Flanker reaction time (performance)*

When response type (correct, error) RT was entered as the dependent variable, the mixed ANOVA revealed no significant main effect of time ($F$ <1, *ns*) but a marginal main effect of group ($F$ (1,39) = 3.95, $p$ =.05, $\eta_p^2$ = .09). There was no significant group x time x response type ($F$ <1, *ns*), however, the was a significant time x response interaction ($F$ (1, 39) = 7.81, $p$ = .008, $\eta_p^2$ = .17 (see **table 5.3** for means and SDs for each group).

### *Commission of error responses*

When number of errors was entered as the dependent variable, the mixed ANOVA revealed a significant main effect of time ($F$ (1, 39) = 13.14, $p$ <.001, $\eta_p^2$ = .25), however, no significant main effect of group ($F$<1, *ns*) or group x time interaction was found ($F$ (1, 39) = 1.88, $p$ = .18, $\eta_p^2$ = .05) (see **table 5.3** for means and SDs for each group).

### *Total accuracy*

When total accuracy was entered as the dependent variable, the mixed ANOVA revealed a significant main effect of time ($F$ (1, 39) = 16.09, $p$ <.001, $\eta_p^2$ = .29) and a trend towards significance for the group x time interaction ($F$ (1, 39) = 3.61, $p$ =.07, $\eta_p^2$ = .09) (see **table 5.3** for means and SDs).

### *Perceived cognitive ability*

MLM revealed a main effect of time (**I-T-T.** $F$ (3,139.36) = 12.31, $p$ <.001, $d$ = 0.59; **PP**. $F$ (3, 118.54) =11.99, $p$ <.001, $d$ = 0.64) and a significant training group x time interaction (**I-T-T.** $F$ (3, 139.36) = 4.01, $p$ <.01, $d$ = 0.34*;* **PP.** $F$ (3, 118.54) = 3.23, $p$ =.02, $d$ = 0.33).

Simple effects with Bonferroni corrected pairwise comparisons showed a significant improvement from baseline to one-year post-training for both groups, however, this increase was greater for the dual *n*-back group (Dual *n*-back: **PP.** Baseline: $M$ = 11.05, $SD$ = 4.66, One-year: $M$ =

19.35, *SD* = 7.92, *M* difference = 8.30, *p* <.001, *d* = 0.98; Dual 1-back: **PP.** Baseline: *M* =15.23, *SD* = 4.66, One-year: *M* = 21.14, *SD* = 7.31, *M* difference = 5.91, *p* =.002, *d* = 1.02).

### *Automated Operation Span Task (Ospan)*

Using the OSpan partial score as the dependent variable, the mixed ANOVA showed a significant main effect of time, $F$ (1, 39) = 4.49, $p$ = .04, $\eta_p^2$ = .10 but no significant main effect of group ($F$ <1, *ns*) or group x time interaction, $F$ (1, 39) = 1.77, $p$ = .19, $\eta_p^2$ = .04, indicating that both training groups experienced an improvement in their WMC from baseline to post-training (see **table 5.3** for means and SDs at baseline and post-training for each group).

### *Rumination*

MLM analysis revealed that there was a significant main effect of time (**I-T-T.** $F$ (3, 130.04) = 12.62, $p$ <.001, $d$ = 0.62; **PP.** $F$ (3, 117.85) = 13.69, $p$ <.001, $d$ = 0.68) but no significant group x time interaction (**I-T-T.** $F$<1, *ns*; **PP.** $F$<.1, *ns*), indicating that both training groups experienced a reduction in rumination across time.

### *Work output demands*

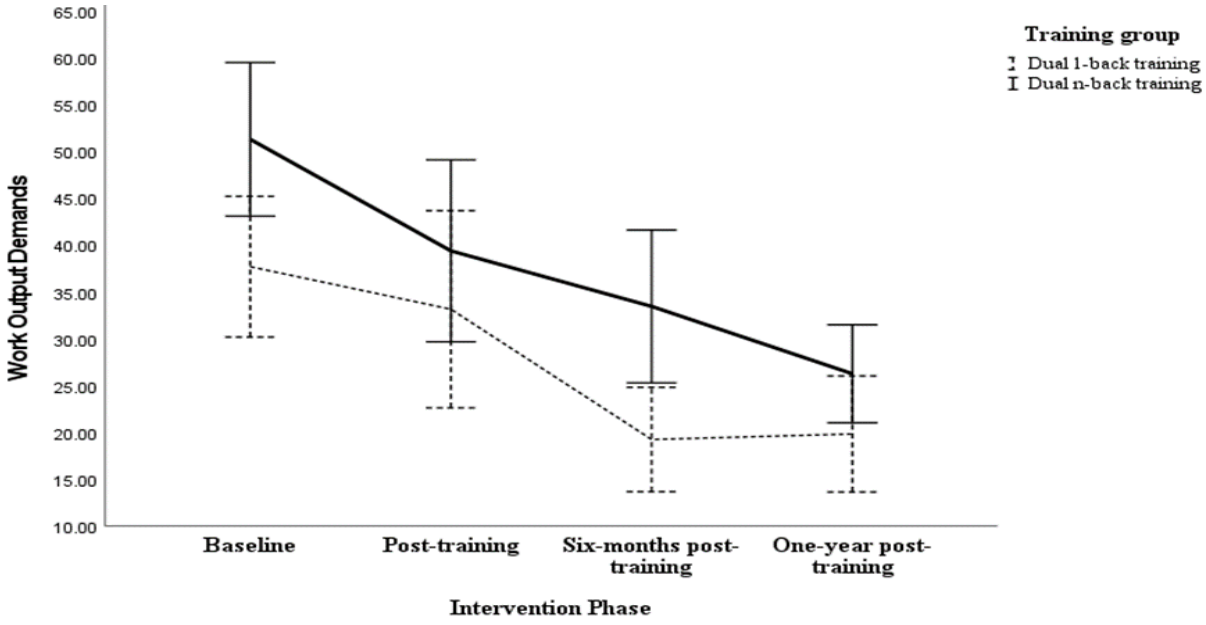
**Figure 5.6** shows that women in the dual *n*-back training group experienced a greater reduction in their work output difficulty compared to the dual 1-back group from baseline to one-year. MLM revealed a significant main effect of time (**I-T-T**. $F$ (3, 138.84) = 13.24, $p$ <.001, $d$ = 0.62; **PP.** $F$ (3, 121.71) = 15.43, $p$ <.001, $d$ = 0.71), indicating that both training groups experienced an improvement following training. No significant group x time interaction was found for the **I-T-T** analysis ($F$ (3, 138.84) = 2.02, $p$ = .11, $d$ = 0.24), however, there was a significant interaction was found for the **PP.** analysis ($F$ (3, 121.71) = 3.79, $p$ =.01, $d$ = 0.35) which indicated that the dual *n*-back group's

improvement in work output difficulty (*M* difference = 28.32, $p < .001$, $d = 1.37$) was greater than that of the active control group (*M* difference = 17.56, $p = .002$, $d = 0.80$).

As a matter of interest given the trend shown in **figure 5.6**, simple effect with Bonferroni corrected pairwise comparisons were also performed between baseline and post-training, with the findings substantiating that the dual *n*-back group experienced a significant improvement from baseline to post-training (*M* difference = 17.41, $p < .001$, $d = 0.96$) compared to the dual 1-back group (*M* difference = 3.13, $p = 1.00$, $d = 0.18$) (see **table 5.2** for means and SDs for each group).

**Figure 5.6**

*Mean work output demands score for both training groups over time*




*Note***.** Error bars = 95% CI

## *Work productivity loss*

MLM analysis revealed a significant main effect of time (**I-T-T**. $F$ (3, 137.44) = 18.22, $p < .001$, $d = 0.73$; **PP**. $F$ (3, 123.74) = 19.89, $p < .001$, $d = 0.80$ but no training group x time interaction (**I-T-T**. $F < 1$, *ns*; **PP.** $F$ (3, 123.74) = 1.83, $p = .14$, $d = 0.23$), indicating that both training groups improved

over time (Dual *n*-back: **PP.** Baseline: *M* = 12.54, *SD* = 4.23, One-year: *M* = 6.52, *SD* = 3.60; Dual 1-back: **PP.** Baseline: *M* = 8.96, *SD* = 3.95, One-year: *M* = 4.99 , *SD* = 2.50).

### 5.5.6. **Secondary Outcomes**

#### *Anxiety*

MLM analysis showed a main effect of time, **I-T-T.** *F* (3, 136.351) = 4.87, *p* < .01, *d* = 0.38; **PP.** *F* (3, 120.02) = 4.84, *p* <.01, *d* = 0.38) but no significant group x time interaction (**I-T-T.** *F*<1, *ns*; **PP.** *F* <1, *ns*), indicating that both training groups experienced a reduction in their level of anxiety over time) (see **table 5.2** for means and SDs for each group).

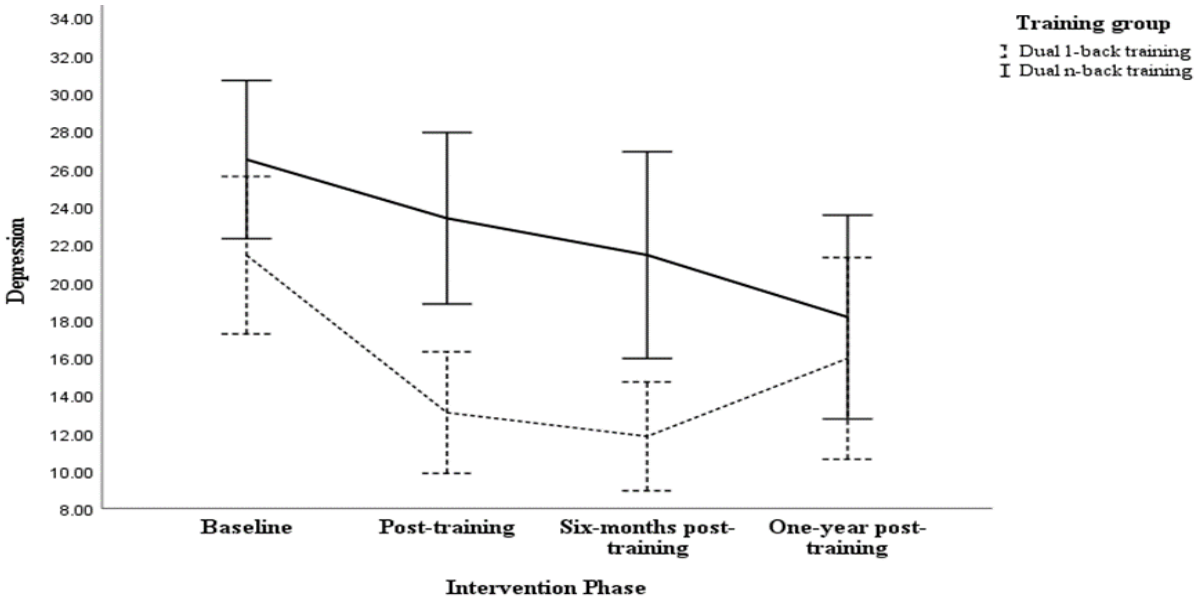
#### *Depression*

**Figure 5.7** shows that women in the dual *n*-back training group experienced a greater reduction in depression relative to the dual 1-back training group from baseline to one-year. MLM revealed a main effect of time (**I-T-T.** *F* (3, 130.39) = 10.39, *p* <.001, *d* = 0.56; **PP.** *F* (3, 118.04) = 10.54, p <.001, *d* = 0.60) and a training group x time interaction (**I-T-T.** *F* (3, 130.39) = 2.93, *p* =.04, *d* = 0.30; **PP**. *F* (3, 118.04) = 3.02, *p* = .03, *d* = 0.32).

Post hoc simple effects with Bonferroni corrected pairwise comparisons showed a significant reduction in the dual *n*-back group (*M* difference = 10.30, *p* <.001, *d* = 0.84) compared to the dual 1-back group (*M* difference = 4.18, *p* = .44, *d* = 0.47) from baseline to one-year post-training (see **table 5.2** for means and SDs for each group).

**Figure 5.7**

*Mean depression scores for both training groups across time*




*Note***.** Error bars = 95% CI

## *Quality of life*

MLM revealed that there was a main effect of time (**I-T-T.** *F* (3, 130.99) = 5.59, *p* <.001, *d* =; 0.41; **PP.** *F* (3, 119.39) = 7.98, *p* <.001, *d* = 0.52) but no group x time interaction (**I-T-T.** *F* <1, ns; **PP.** *F* <1, *ns*), indicating that both training groups improved over time (see **table 5.2** for means and SDs for each group).

## *P3 on correct trials in the Flanker task*

## *Flanker reaction time (performance) on correct trials*

When congruency (congruent, incongruent) RT on correct trials was entered as the dependent variable, the mixed ANOVA demonstrated a significant main effect of time, *F* (1.39) = 18.94, p <.001, $\eta_p^2$ = .33, however, no significant main effect of group (*F* (1,39) = 2.65, *p* = .11, $\eta_p^2$ = .06) or group x congruency x time interaction was found, *F* (1, 39) = 1.31, *p* = .26, $\eta_p^2$ = .03 (see **table 5.3** for means and SDs for each training group).

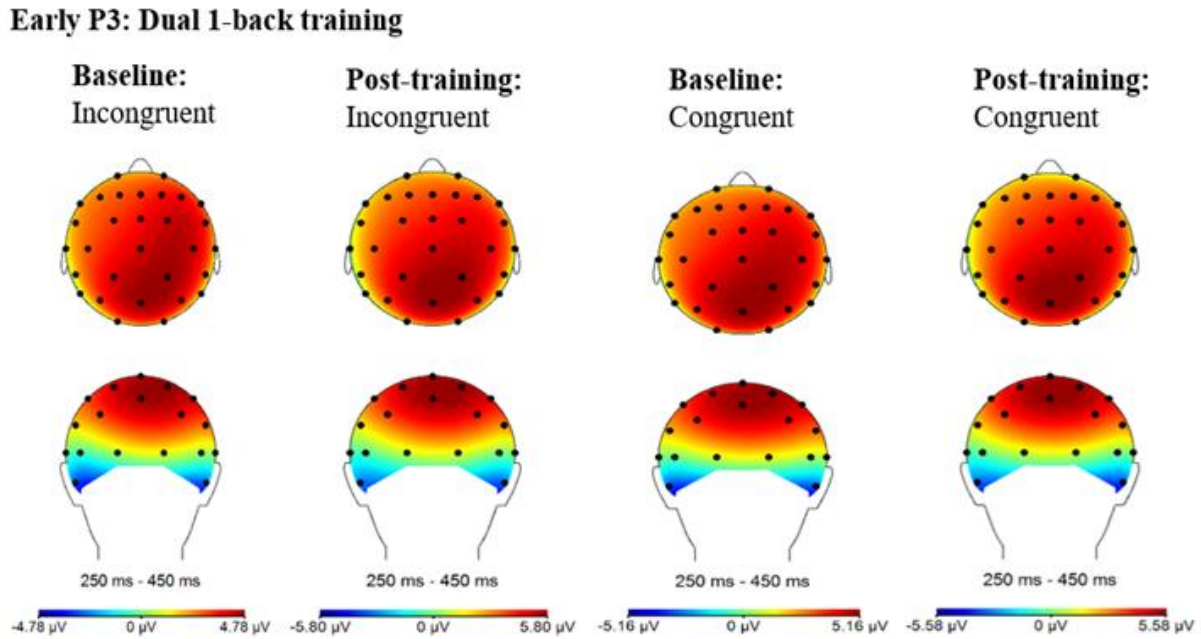
### *Early P3*

Using the early P3 (250-450ms) as the dependent variable, the mixed ANOVA showed a significant main effect of time, $F$ (1, 39) = 9.477, $p$ <.005, $\eta_p^2$ = .20 and a significant group x time x congruency interaction, $F$ (1, 39) = 8.70, $p$ = .005, $\eta_p^2$ = .18.

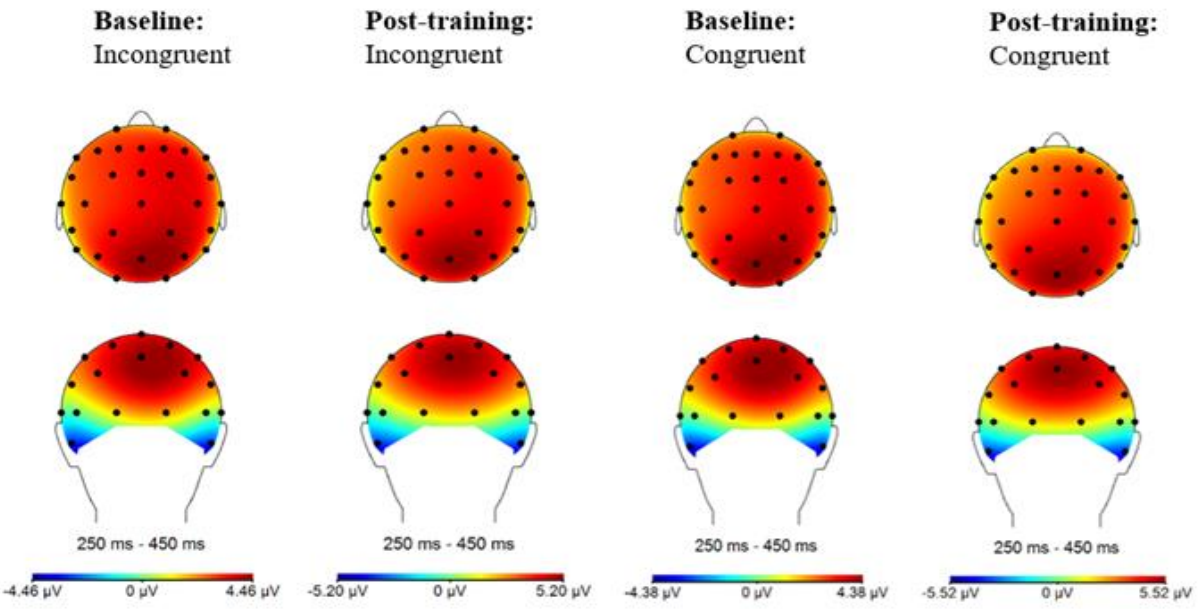
Post hoc simple effects with Bonferroni corrected pairwise comparisons revealed that women in the dual *n*-back training group showed a significant increase in early P3 amplitude on congruent correct trials (*M* difference = 1.00 μV, $p$ =.004, $d$ = 0.73) and trend towards significance on incongruent correct trials (*M* difference = 0.69 μV, $p$ = .06, $d$ = 0.56) trials following the completion of training compared to dual 1-back group who only showed a significant increase on incongruent trials (*M* difference = 0.92 μV, $p$ = .02, $d$ = 0.46; **Congruent trials**: *M* difference = 0.24 μV, $p$ = .48, $d$ = 0.15) (see **table 5.3** for means and SDs for each group, **figure 5.8** for scalp topography and **figure 5.10** for stimulus-locked data waveforms).

**Figure 5.8**

*Scalp topography representing the early P3 derived from the average waveform for incongruent and congruent correct trials*



**Early P3: Dual *n*-back training**




### *Late P3*

When the late P3 (450-600ms) was entered as dependent variable, the mixed ANOVA showed no significant main effect of time, $F<1$, *ns* or group ($F$ (1,39) = 1.81, $p$ =.19), however, a significant group x time x congruency interaction was found, $F$ (1, 39) = 5.28, $p$ = .03, $\eta_p^2$ = .12.

Post hoc simple effects with Bonferroni corrected pairwise comparisons revealed that women in the dual *n*-back training group experienced a non-significant increase in late P3 amplitude on both congruent (*M* difference = 0.31 µV, $p$ =.44, $d$ = 0.20) and incongruent (*M* difference = 0.24 µV, $p$ = .41, $d$ = 0.16) trials following the completion of training compared to dual 1-back group who showed a non-significant increase on incongruent trials (**Incongruent trials**: *M* difference = 0.57 µV, $p$ = .18, $d$ = 0.26) but a decrease on congruent trials (**Congruent trials**: *M* difference = -0.50 µV, $p$ = .22, $d$ = 0.25) (see **table 4.3** for means and SDs for each group, **figure 5.9** for scalp topography and **figure 5.10** for stimulus-locked data waveforms).

**Figure 5.9**

*Scalp topography representing the late P3 derived from the average waveform for incongruent and congruent correct trials*

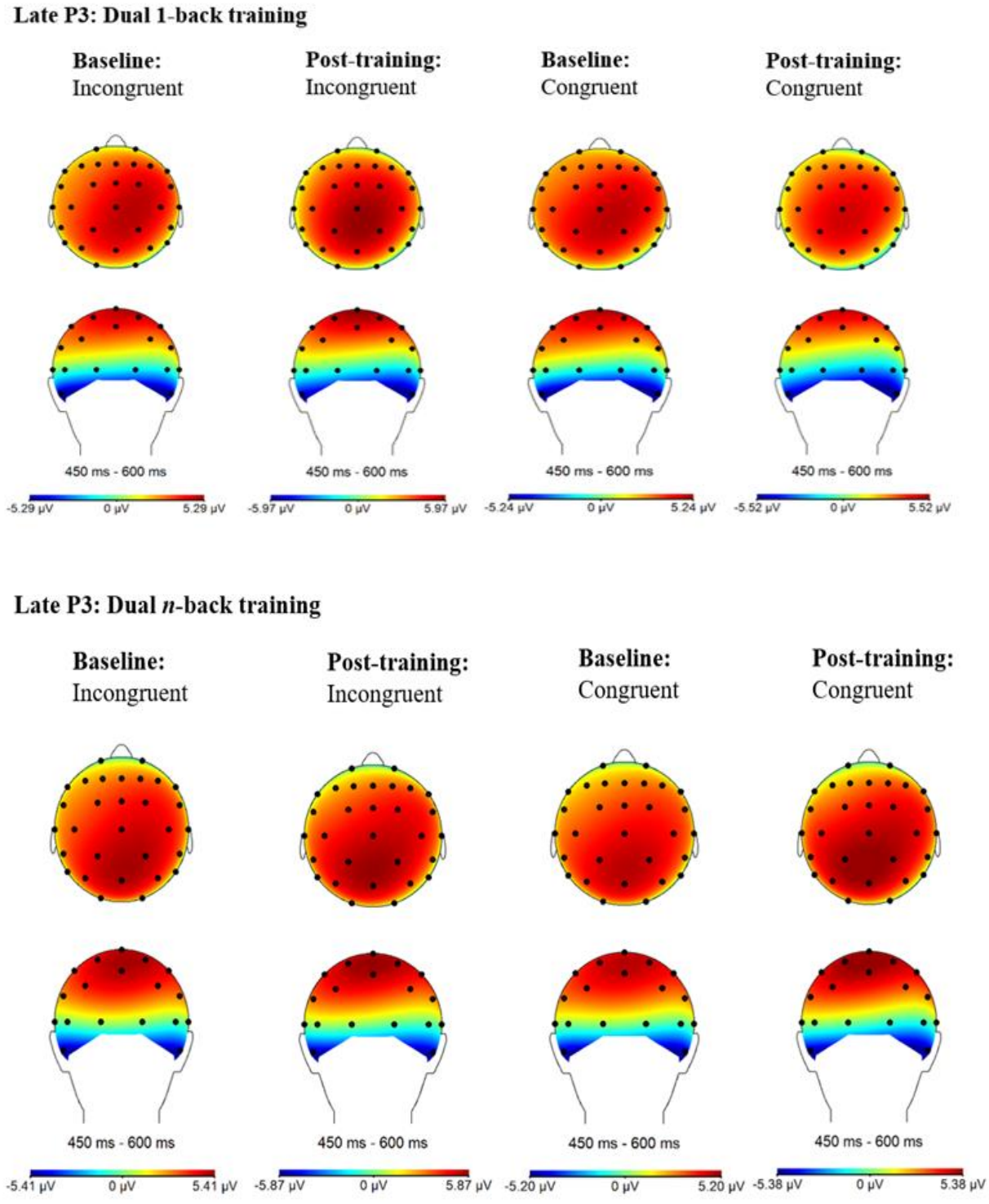
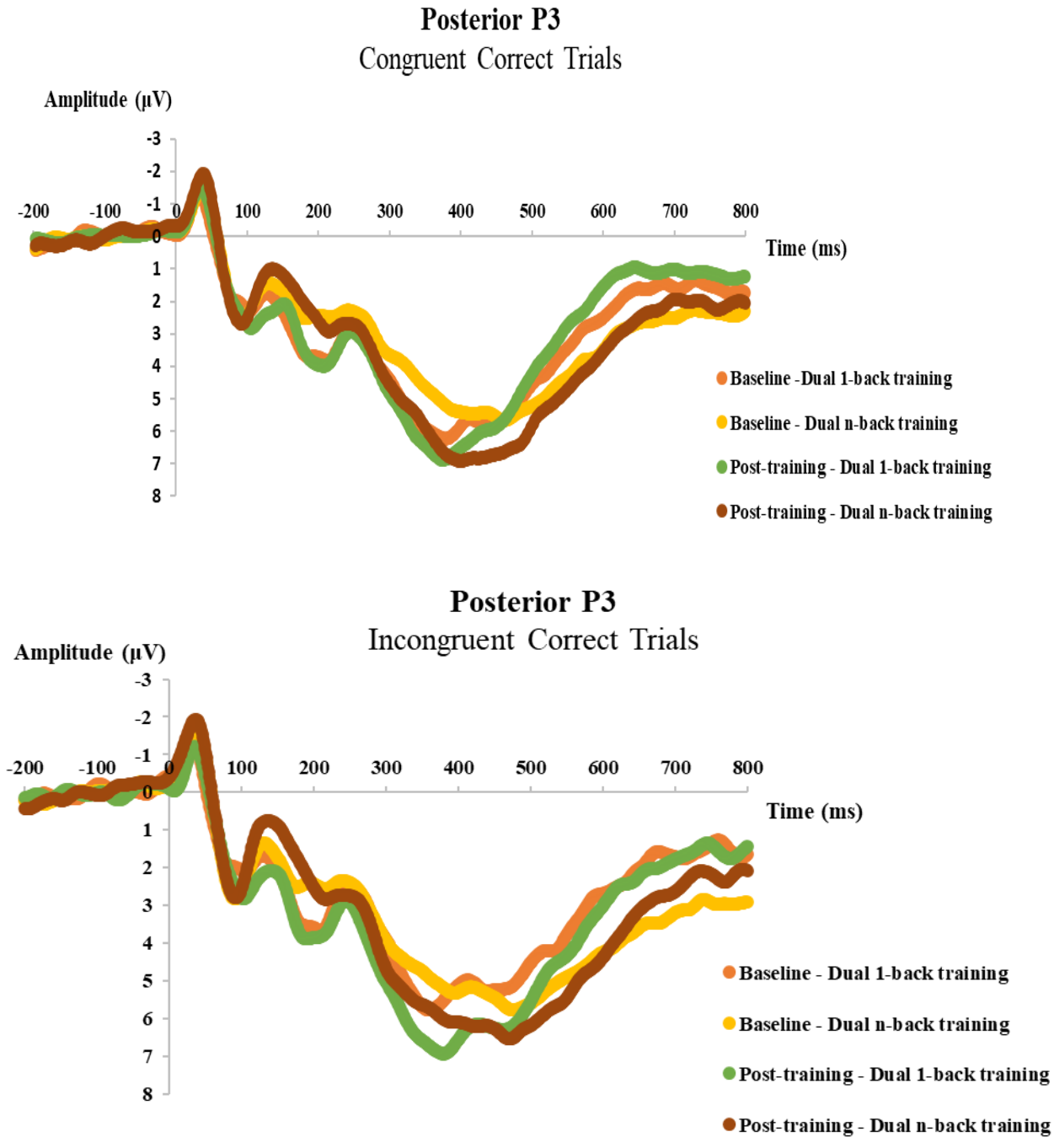


**Figure 5.10**

*Stimulus-locked ERP waveforms recorded from the flanker task at Pz for dual n-back and dual 1-back training*




*Note.* In the analysis conducted above the P3 was defined as the mean activity (i.e., mean amplitude) occurring in two sequential time windows after stimulus onset known as early P3 (250-450ms) and late P3 (450-600ms)

## Additional analyses

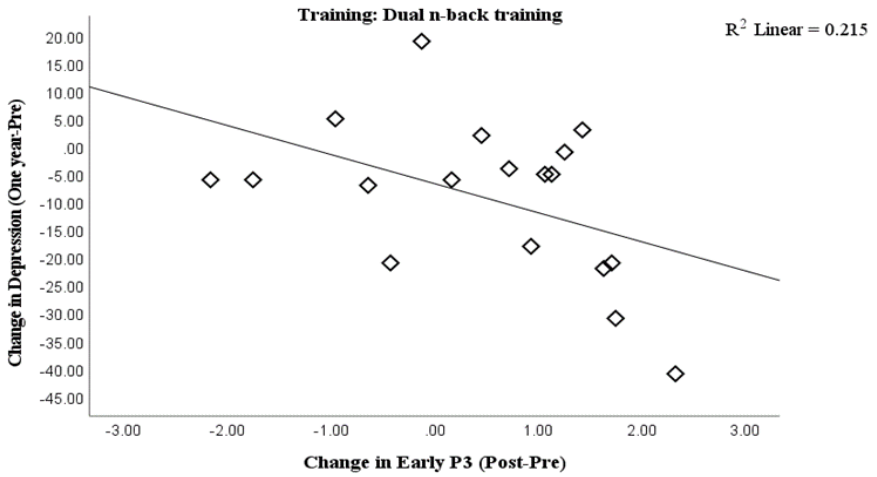
### *Relationship between P3 and self-reported outcomes*

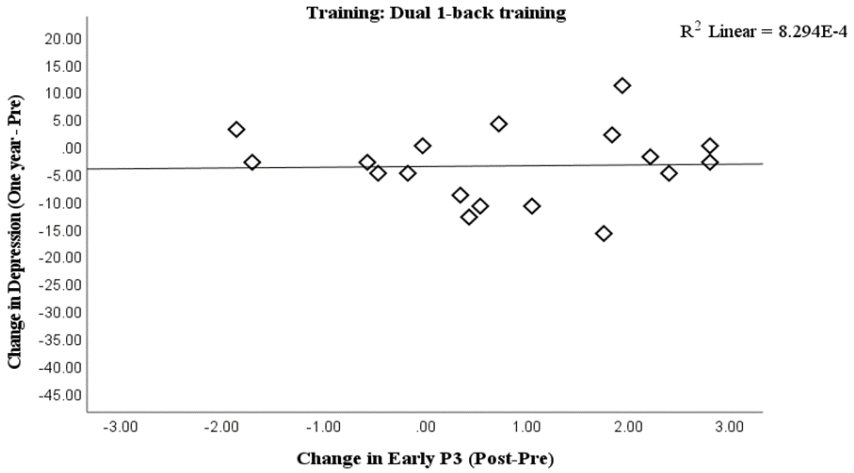
In the dual *n*-back training group, change (post – pre) in early P3 measured on RT (performance) on correct trials on the flanker task significantly correlated with change (one-year – pre) in rumination ($r$ (16) = -.52, BCa 95% CI [-.81, -.17], $p$ =.03), change in depression ($r$ (16) = -.46, BCa 95% CI [-.74, -.06], $p$ =.05) and change in work output difficulty ($r$ (16) = -.46, 95% CI [-.71, -.12], $p$ =.05), with findings suggesting a greater increase in P3 met with a greater reduction in rumination and depression, as well as a greater improvement in work output difficulty from baseline to one-year (see **figure 5.11** for correlations). In contrast, no significant correlations were found for the dual 1-back training group (all $p$'s ≥.10). Taken together, these findings suggest that a greater increase in early P3 amplitude on correct trials following 12 sessions of dual *n*-back training is met with positive changes in women's emotional vulnerability to depression, rumination and work output difficulty.

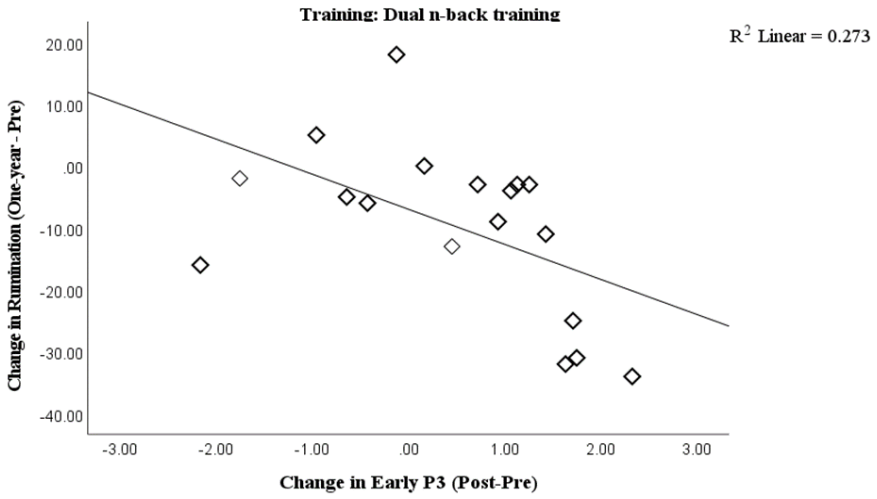
No significant correlations were found between change in late P3 measured on RT (performance) on correct trials and the self-reported outcomes for either of the training groups.

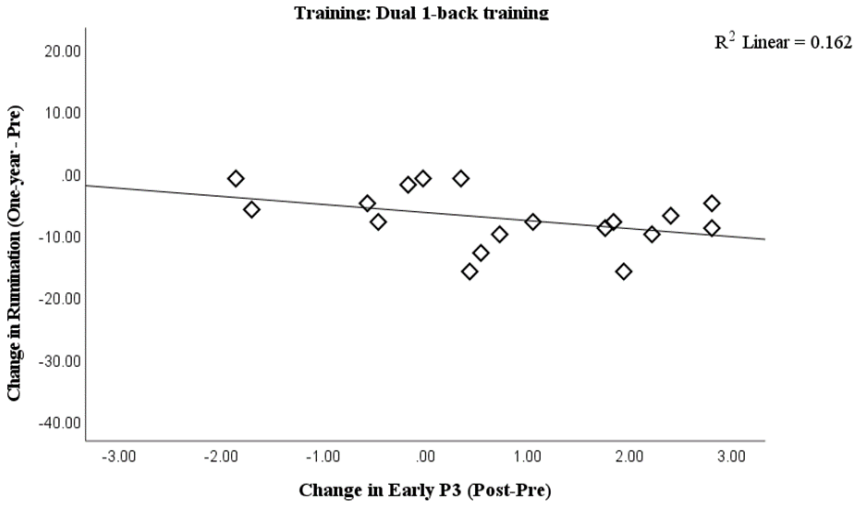
**Figure 5.11**

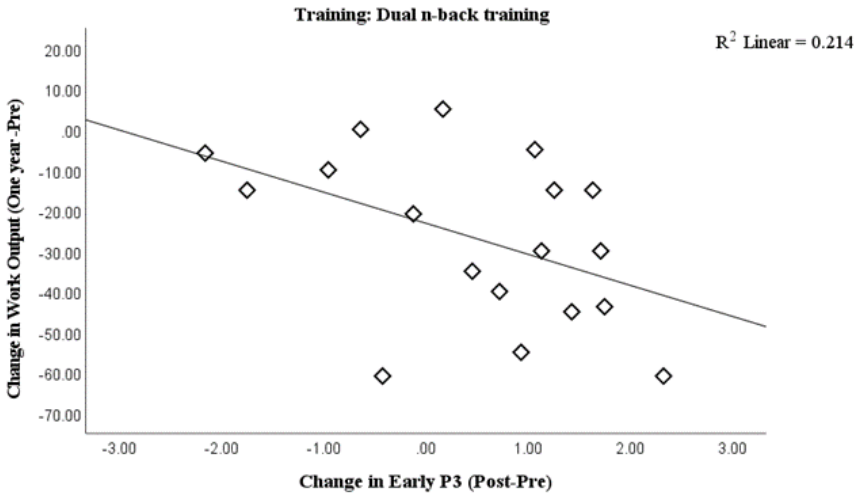
*Correlations between the change in early P3 (Post-training – Pre-training) and change in self-report outcomes (One-year – Pre-training)*

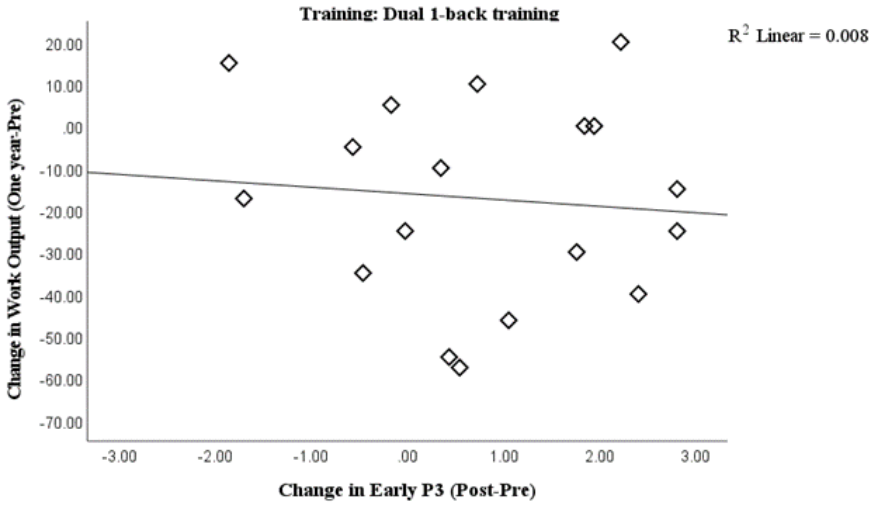



Training: Dual n-back training
R² Linear = 0.214
Change in Work Output (One year-Pre)
20.00
10.00
.00
-10.00
-20.00
-30.00
-40.00
-50.00
-60.00
-70.00
-3.00
-2.00
-1.00
.00
1.00
2.00
3.00
Change in Early P3 (Post-Pre)


Training: Dual 1-back training
R² Linear = 0.008
Change in Work Output (One year-Pre)
20.00
10.00
.00
-10.00
-20.00
-30.00
-40.00
-50.00
-60.00
-70.00
-3.00
-2.00
-1.00
.00
1.00
2.00
3.00
Change in Early P3 (Post-Pre)

## *Neural markers of error monitoring*

### *ERN*

Using ERN as dependent variable, the mixed ANOVA revealed a non-significant main effect of time ($F$ (1, 29) = 2.14, $p$ =.15, $\eta_p^2$ =. 07) and group x time interaction ($F$ <1, *ns*), however, a significant main effect of group was found ($F$ (1, 29) = 5.02, $p$ =.03, $\eta_p^2$ = .15) which indicate that dual 1-back group had a larger ERN (**PP.** $M$ = -1.58 , $SD$ = 1.55) compared to the dual *n*-back group (**PP.** $M$ = -.45, $SD$ = 1.55; $M$ difference = -1.14, $p$ =.03) (see **table 5.3** for means and SDs, **figure 5.12** for scalp topography and **figure 5.13** for stimulus-locked data waveforms).

**Figure 5.12**

*Scalp topography representing the ERN derived from the average waveform for error trials*

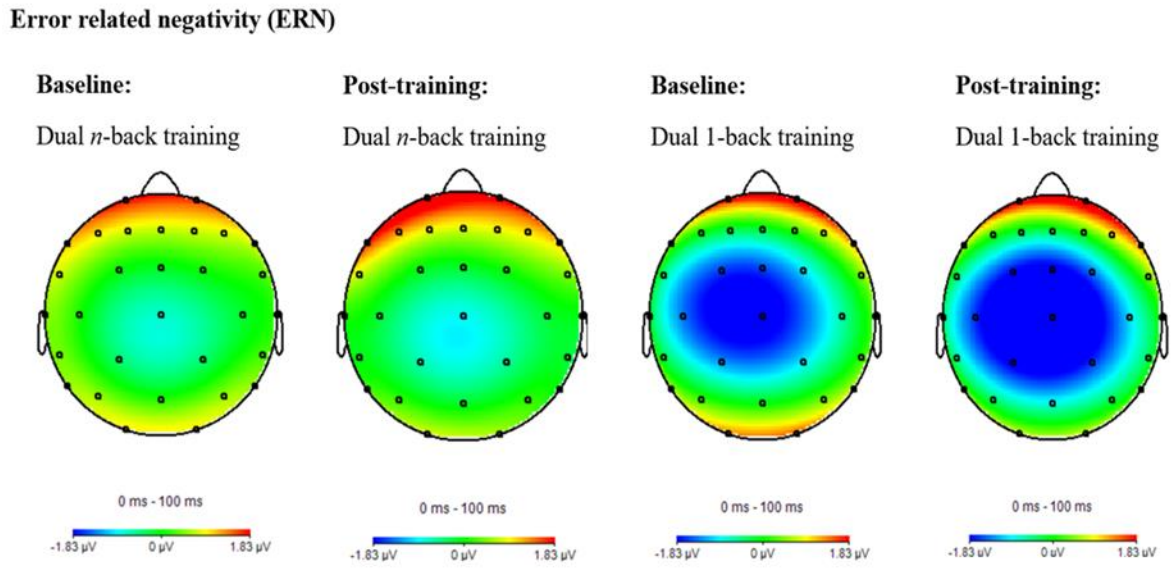
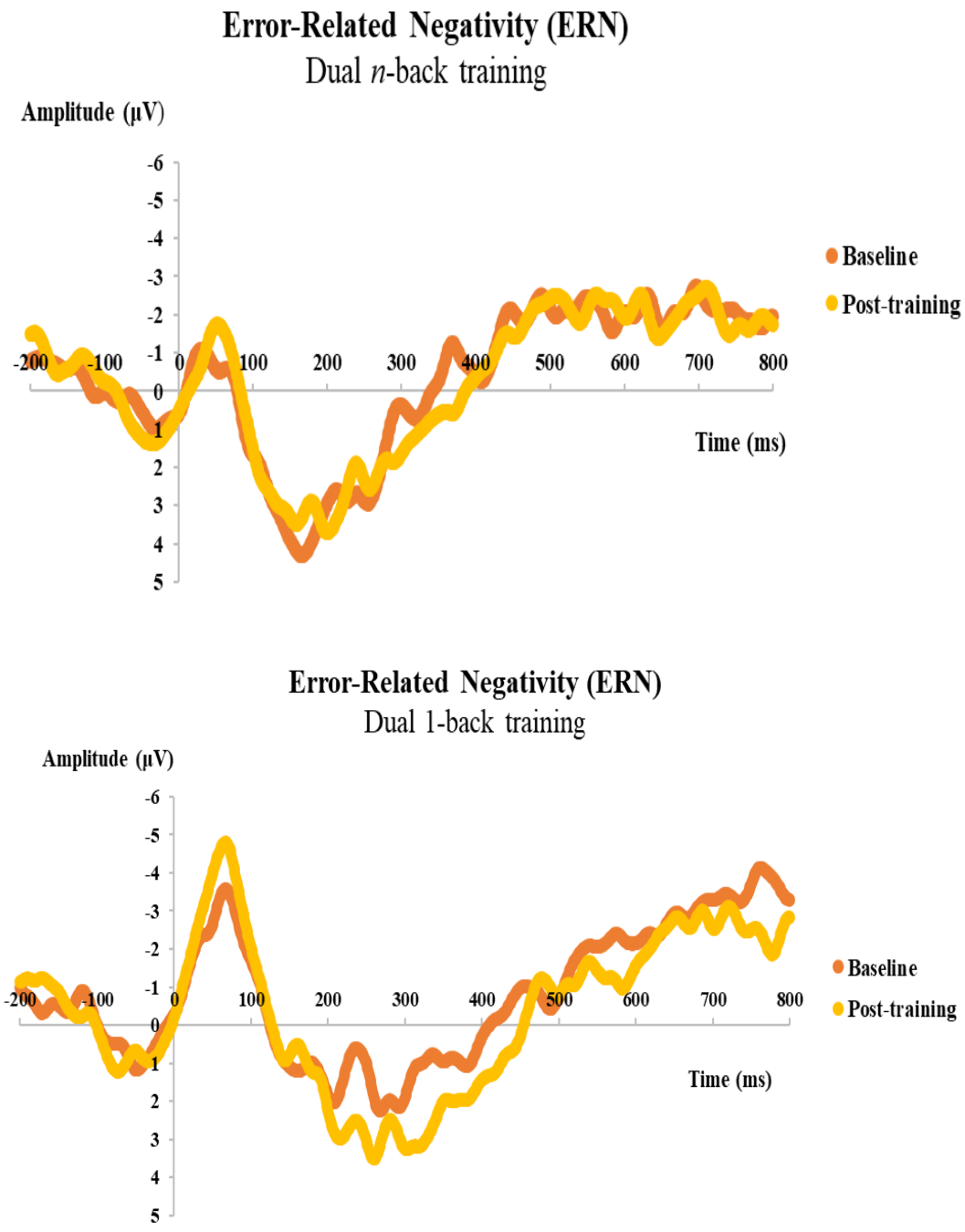


**Figure 5.13**

*Responses-locked ERP waveforms recorded from the flanker task on error trials at Cz for dual n-back and dual 1-back training*




*Note.* In the analysis conducted above the ERN was defined as the mean activity (i.e., mean amplitude) occurring in the post response window 0-100ms

### *Early and late Pe*

No significant effects were found for either early or late Pe (all *Fs* < 1) (see **figure 5.14** for scalp topography and **figure 5.15** for stimulus-locked waveforms).

**Figure 5.14**

*Scalp topography representing the early and late Pe derived from the average waveform for error trials*

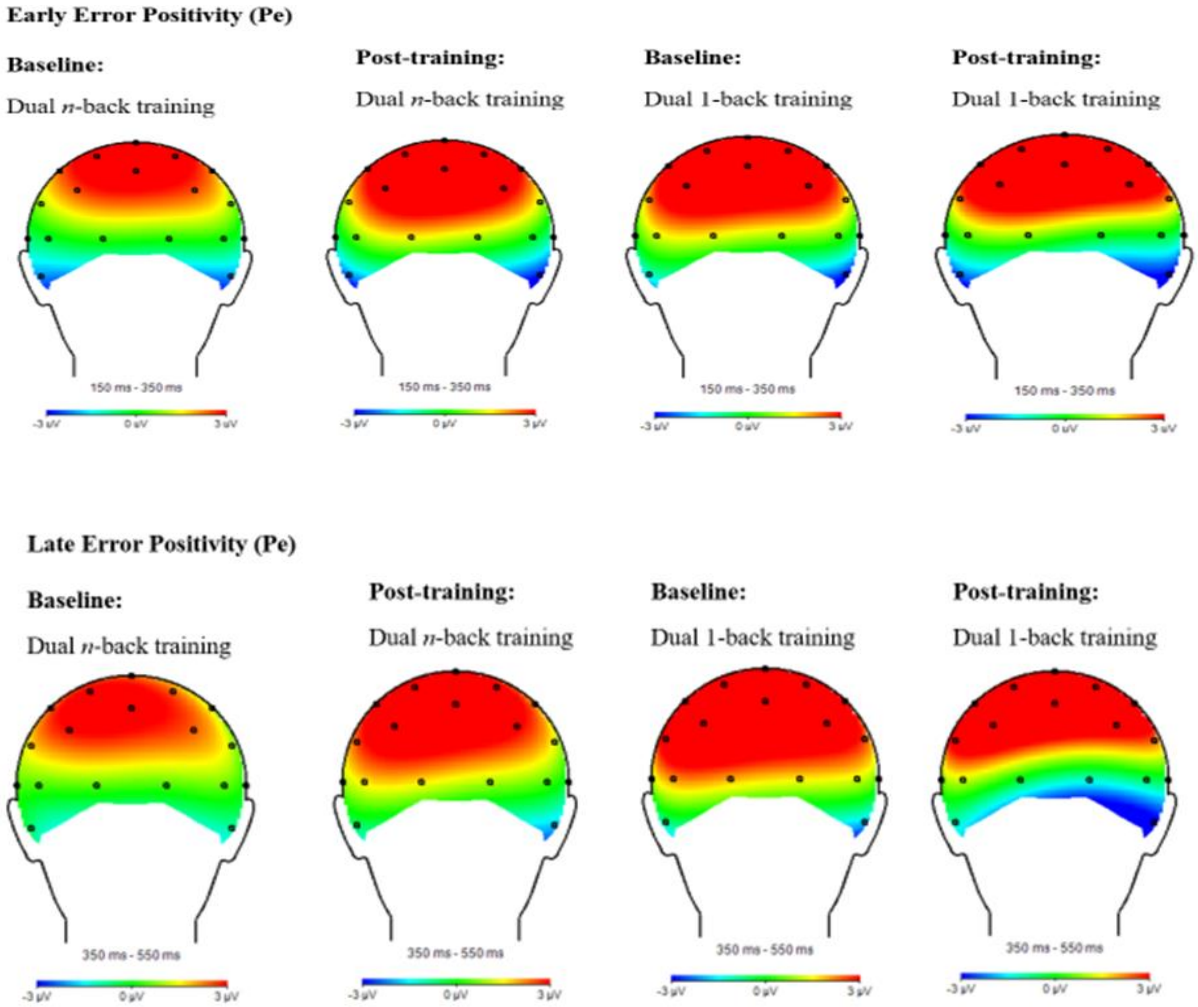
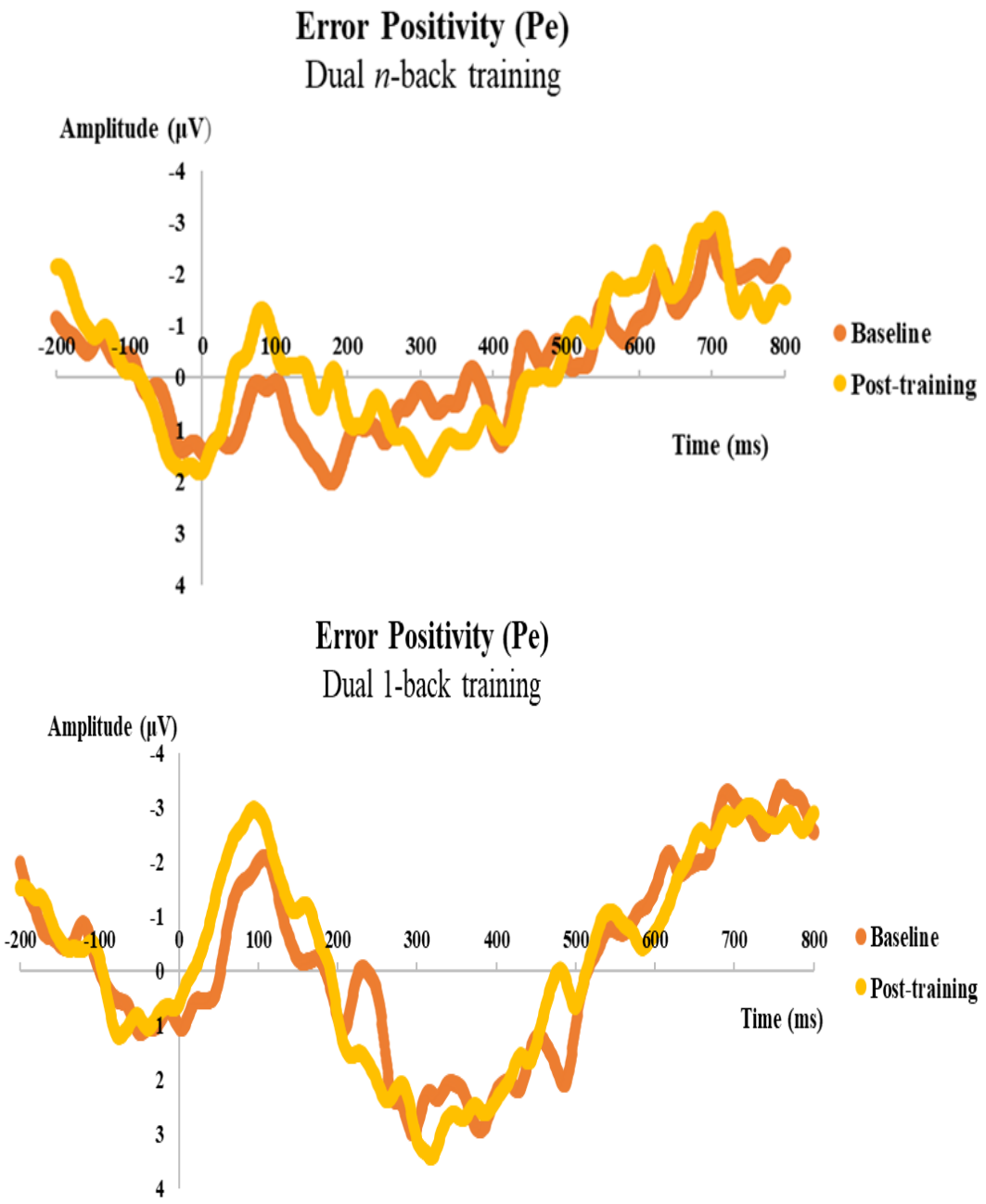


**Figure 5.15**

*Stimulus-locked ERP waveforms recorded from the flanker task on error trials at Pz for dual n-back and dual 1-back training*




*Note.* In the analysis conducted above the Pe was defined as the mean activity (i.e., mean amplitude) occurring in two sequential post response windows from 150-350ms (early Pe) and 350-550ms (late Pe)

## 5.6. **Discussion**

**Chapter 5** aimed to investigate the effects of adaptive cognitive training (dual *n*-back training) on improving impaired cognitive function and its transfer effect on workability, anxiety, depression and quality of life. As predicted, women who received dual *n*-back training experienced a greater improvement in their perceived cognitive ability and workability (as indexed by work output and work productivity loss), as well as transfer-related gains in depression, with improvements sustained at the longer follow-up of one-year post-training. Previous research conducted by Von Ah and colleagues (2013, 2016, 2018, 2021) has shown that poorer perceived cognitive function significantly predicts worse work-related outcomes in women affected by breast cancer. Von Ah et al., (2018), for example, found poorer perceived cognitive ability met with greater work productivity loss. Similarly, Calvio et al., (2010) found that self-reported cognitive limitations related to work output, with greater cognitive limitations predicting poorer work output. Extending this, studies have also shown that greater perceived cognitive impairment diminishes women's confidence in their workability (Munir et al., 2009; Chapman et al., 2021) and increases their likelihood of unemployment (Oberst et al., 2010). In a recent study by Peipins et al., (2021), it was shown that loss of employment was much greater in women with memory complaints (17.4% vs. 5.9%). Notably, the findings presented in **Chapter 3** revealed that perceived cancer-related cognitive impairment also adversely impacted career progression and development in women affected by primary breast cancer (Chapman et al., 2021). It is reasonable to argue that the significant improvement in perceived cognitive ability following dual *n*-back training has played an important role in boosting women's confidence and encouraging participation in work-specific training, resulting in a greater likelihood of sustainment of work across time. As unemployment has been associated with an escalating risk of developing depression and mortality in individuals affected by cancer (Maruthappu et al., 2015; Inhestern et al., 2017), this finding has important implications for working women affected by cognitive impairment.

Coupled with the improvement in perceived cognitive ability, **Chapter 5** found evidence of a significant increase in working memory capacity (WMC) on the Change Detection Task (CDT) but not the Ospan task for women in the dual *n*-back group, with both training groups showing an improvement

on the latter. The significant finding with the CDT is of focal importance as working memory is inherent to supporting higher-order cognitive processes such as reasoning and problem solving which are required in everyday life, particularly at work. Validating this finding, Owens et al., (2013) also found that eight sessions of dual *n*-back training elicited significantly greater increases in working memory capacity on the CDT compared to dual 1-back training in dysphoric individuals. It is important to note, that women in our dual *n*-back training group had a non-significantly lower WMC at baseline compared with the active control. The 'BRiCatWork' study is the first to use an unrelated measure of working memory to corroborate that in women affected by primary breast cancer working memory can be improved by dual *n*-back training, with the findings evidencing that adaptive training leads to generalisation or cognitive transfer effects.

In line with these findings, Blacker et al., (2017) also reported no significant transfer effect from dual *n*-back training or symmetry span training to the Ospan task, with both their training groups and active control improving over time. Similarly, Jaeggi et al., (2010) found no significant time by group (dual *n*-back training, single *n*-back training, a no-contact control) interaction for Ospan score, concluding that the Ospan task depends on active recall processes rather than recognition abilities which are recruited by *n*-back tasks. Further, Jaeggi et al postulated that *n*-back training may adversely interfere with Ospan performance post-training as participants depend more on recognition rather than recall, preventing significant performance gains. It is viable that the improvement on the Ospan task from baseline to post-training for both groups was due to test-retest effects or participants' familiarity with the task.

In terms of self-reported workability, the findings in this chapter confirm that the dual *n*-back group experienced greater improvements in both their work output difficulty and work productivity loss, with continuous reductions recorded at one-year. Interestingly, findings show a significant improvement from baseline to post-training for work output difficulty, a finding that was not a-prior predicted as it was anticipated that it would take time for the effects of training on cognitive impairment to consolidate before translating into evident changes in workability. This novel finding, however, does not match this expectation showing that the beneficial impact of dual *n*-back training on workability

was immediate, with improvements then continuing over time. It is plausible that the significant increase in working memory capacity (as detected by CDT) and perceived cognitive ability coupled with the reductions in depression and anxiety were underpinning this immediate improvement. This is a highly promising finding as it suggests that dual *n*-back training can be offered routinely by health care professionals or occupational health services to women struggling with their workability as a result of cancer-related cognitive difficulties, enabling them to enhance their work performance and potentially sustain work across time.

Importantly, when considering clinical psychological outcomes, the current findings show that women who received dual *n*-back training experienced a greater improvement in depression compared to women in the active control group (dual 1-back training), with continuous reductions shown at one-year post-training. Such a finding suggests that dual *n*-back training may play a sustained role in protecting against escalating levels of emotional vulnerability to depression in working women affected by primary breast cancer. This finding resembles the effect found by Beloe and Derakshan (2020) when they assessed the impact of dual *n*-back training on depression in an adolescent population. Given, that Kim et al., (2022) found depression to escalate work productivity loss and predict worse work limitations in women affected by breast cancer, this is a pertinent finding in the context of work. Specifically, the finding indicates that dual *n*-back training may enhance workability in women by improving their cognitive efficiency which strengthens their emotional resilience to depression, a well-known predictor of poorer work-related outcomes in women affected by breast cancer (Ho et al., 2018; Dorland et al., 2018, Tan et al., 2021; Kim et al., 2022). Given that depression also increases the risk of recurrence and mortality by up to 30% in women with breast cancer (Wang et al., 2020; see **Chapter 1 section 1.4.2.3**), cognitive interventions using dual *n*-back training can protect against the effect of depression on clinical outcomes such as survival.

In contrast to earlier research conducted by Swainston & Derakshan (2018, 2021), the current findings revealed that both dual 1-back and dual *n*-back training resulted in significant sustained reductions in anxiety, with marginally greater effects found for the dual 1-back group. One possible explanation for the inconsistency in findings between our study and Swainston & Derakshan (2018) is

the difference in the measure used. Whilst we elected to use the anxiety subscale from the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) their study reported on a composite score formed of anxious arousal, general distress and hyperarousal, indicating that the two questionnaires may have captured different physiological and psychological components of anxiety. Another reason may simply be linked to the individual differences and motivation between participants recruited (Jaeggi et al., 2014), for example, our study specifically recruited women who were experiencing a decline in workability as a result of cognitive difficulties, implying that the intrinsic motivation to engage with training would be very high amongst our participants. Reduced workability has been linked to greater anxiety in women with breast cancer (Carlsen et al., 2013; Kim et al 2022). Similar, to the finding in this study, Swainston & Derakshan (2021) found women with a history of breast cancer report a better quality of life (as measured by Quality of Life in Breast Cancer Patient Scale) following mindfulness training, mindfulness combined with dual *n*-back training, dual *n*-back training or dual 1-back training.

Similar to Li et al's., (2020) finding, dual *n*-back training diminished post-error slowing which did not come at the cost of accuracy, confirming that women were not experiencing a speed-accuracy trade-off. Post-error slowing refers to the slowing of subsequent responses following the commission of an error (Rabbitt, 1966). According to the bottleneck error monitoring account (Dudschig & Jentzsch, 2009; Jentzsch & Dudschig, 2009), error monitoring after an error requires time and engagement of central information processors, leading to a bottleneck effect (i.e., slower response) on subsequent trials. Li et al., (2020) delineate that both dual *n*-back training (*(1)* storing and manipulation of '*n*' trial and *(2)* current trial information) and post-error slowing (*(1)* error from previous trial and *(2)* current trial information) entail parallel processing of two separate streams of information for optimal performance, requiring the division of central resources into two-parts to process information. Accordingly, *n*-back training functions to strengthen this skill and enables parallel processing to become more automated. Taken together, it can, therefore, be speculated that this finding was driven by the elimination of the bottleneck effect in error monitoring as a result of dual *n*-back training. Interestingly, the diminishment of post-error slowing occurred in the absence of changes in the ERN and Pe. The current study is the

first to explore the impact of dual *n*-back training on neural indices of error processing and working memory that may be implicated in workability in women affected by primary breast cancer. In contrast to the earlier prediction, findings showed that neither dual *n*-back or dual 1-back training resulted in significant changes in the amplitude of the ERN or Pe, indicating that working memory training does not have a significant impact on neural indices of error processing in women living with a history of primary breast cancer. Similar findings have been reported in adolescents (Beloe & Derakshan, unpublished).

In line with cognitive training studies (Gajewshki & Falkenstien, 2012, 2018; Tusch et al., 2016; Lotfi et al., 2020), the current findings revealed that dual *n*-back training resulted in a significant increase in the amplitude of the early (250-450ms) P3. Such findings suggest that dual *n*-back training enhances the general allocation of cognitive resources to task-relevant information regardless of trial type. This change in early P3 was accompanied by a decrease in reaction time on both congruent and incongruent correct trials for the dual *n*-back training group, indicating that greater ability to allocate cognitive resources (as reflected by the enhanced P3 amplitude) may underlie improvements in performance efficiency. Further, findings showed neither dual *n*-back or dual 1-back training led to significant changes in the late (450-600ms) P3, however, differential effects were found for congruent trials, with dual *n*-back training showing an increase in P3 amplitude and dual 1-back showing a decrease. It can be speculated that this could show that dual *n*-back training elicits a sustained allocation of cognitive resources over time. Future research is however required to corroborate this claim.

Of focal importance, the additional exploration analysis revealed that change in the amplitude of early P3 from baseline to post-training significantly correlated with change in self-reported psychopathology and workability (one-year – baseline), such that a greater increase in P3 met with a greater reduction in rumination, depression and work output difficulty from baseline to one-year. In a series of recent studies, it was shown that a blunted P3 amplitude on the flanker task was associated with depression in non-cancer populations (Klawohn et al., 2020; Santopetro et al., 2020, 2021). In particular, Santopetro et al., (2020) found that reduced P3 amplitude at baseline predicted greater depression at a two-year follow-up, demonstrating the link between P3 and risk of escalating levels of

depression. Such research affirms that our novel finding warrants more investigation, as it provides an important proof of principle that change in P3 following dual *n*-back training can be utilised as a predictor of training efficacy in working women affected by primary breast cancer.

### 5.6.1. **Limitations**

**Chapter 5** presents some limitations that should be considered when interpreting the findings. Firstly, participants were recruited from online advertisements placed on social media platforms including Facebook, Twitter and Instagram, and therefore may not be fully representative of the wider population. The sample size was also relatively small ($n$ =31 per group), indicating that individual differences may have impacted the findings in this chapter at the group level. This may also explain some of the differences found in the baseline measures between the two training groups, for example, finding show worse perceived cognitive ability and workability in women randomly allocated to the dual *n*-back training group at baseline, despite there being no significant difference in demographic, clinical and work-related characteristics. Due to the small sample, the study presented in **Chapter 5** may not have been sufficiently powered to detect differences between the two training groups on self-report, behavioural and neural measures, highlighting the importance of replicating this research with a much larger sample to substantiate the proof-of-principle findings reported.

It is important to note, that findings in this chapter showed that women in the dual 1-back group also experienced an improvement in their perceived cognitive ability, workability, quality of life and depression when comparing their baseline scores to one-year post-training; although the differences indicate that this was to a lesser degree than in the dual *n*-back group. It is feasible that these improvements were associated with test-retest effects or more general placebo effects, as well as women's expectancy of the training (i.e., women's belief in the training effectiveness was driving their self-reported improvement as opposed to the genuine effectiveness of the training). Women are also likely to experience a degree of natural recovery as they continue to move away from the treatment period which may explain some of the improvements found. Future research should consider including

a third waiting list group alongside the active control, as this will enable a better understanding of the true efficacy of the training. As the 'BRiCatWork' study recruited women who were struggling with their workability as a result of cognitive difficulties, it was decided that assigning women to a waiting list condition for a year could be highly detrimental to their emotional health. Finally, the 'BRiCatWork' study reported in **Chapter 5** was conducted during the outbreak of COVID-19 in the UK which may influence some of the findings reported.

### 5.6.2. **Conclusion**

To conclude, **Chapter 5** is the first to examine whether dual *n*-back training can help women affected by primary breast cancer sustain work across time by enhancing workability via targeting impaired cognitive function. In line with the predictions, the findings in this chapter show that dual *n*-back training elicited greater improvements in perceived cognitive ability and workability, as well as in depression, with effects sustained up to one-year. Further, findings revealed that *n*-back training also significantly increased WMC on CDT, evidencing that training leads to generalisation or cognitive transfer effects. Significant increases in P3 amplitude coupled with better performance on the flanker task, notably the elimination of post-error slowing was found indicating improvements in processing efficiency. Taken together, the findings suggest that dual *n*-back training could play a crucial role in supporting women affected by breast cancer to sustain work across time and therefore should be routinely offered by health care and occupational services.

# **Chapter 6**: Exploring the impact of quality of working life on cognitive and emotional vulnerability in women living with a diagnosis of metastatic breast cancer in the UK

## 6.1. **Chapter Overview**

As outlined in **Chapter 1** studies have shown that work-related factors and workability play a key role in promoting quality of life and emotional resilience in women living with a diagnosis of primary breast cancer, however, research concentrating on the cognitive and emotional health of women living with metastatic breast cancer (MBC) is limited, despite approximately 35,000 women living with this diagnosis in the UK. The main aim of the cross-sectional study presented in **Chapter 6** was to examine how self-reported quality of working life related to global health, perceived cognitive function, anxiety and depression in women with MBC. Furthermore, the study also aimed to explore women's experience with their employers following their MBC diagnosis and its relationships with perceived quality of working life.

## 6.2. **Introduction**

To date, only a very limited amount of research has explored the cognitive and emotional health of women living with a diagnosis of MBC. It is estimated that at present, around 35,000 women are living with MBC in the UK (Breast Cancer Now, 2021). According to recent figures, approximately 26% of women with stage 4 breast cancer will survive at least five years, a figure that is expected to continuously increase over the coming years as diagnostic techniques and available treatments advance (Cancer Research UK, 2020). Johnson and Swanton (2006) outlined that some women diagnosed with MBC can survive up to 15 years. MBC survival rate is affected by a host of factors including the region of metastatic spread (e.g., brain, liver, lungs or bones), number of metastatic sites, tumour

characteristics (e.g., oestrogen-receptor positive) and "*de novo"* or metastases after primary breast cancer (Largillier et al., 2008; McKenzie et al., 2020). Given, these survival rates it is crucial that research is dedicated to identifying factors that can improve the quality of life and emotional wellbeing of women living with MBC.

Women with MBC are highly susceptible to experiencing emotional distress, including anxiety and depression (Fulton et al., 1998; Caplette-Gingras & Savard, 2008; Grabsch et al., 2006; Park et al., 2018) as well as cognitive problems (Carreira et al., 2020). This is partly due to the adverse side effects of treatment, poor social support and risk of disease (tumour) progression (Caplette-Gingras & Savard., 2008; Jehn et al., 2012). Depression has been associated with poorer health-related quality of life, medical comorbidities, activity disruption and sleep problems in women with MBC (Palesh et al., 2007; Mosher & DuHamel, 2012; Low & Stanton, 2015). In a recent meta-analysis by Wang et al., (2020; see **Chapter 1 section 1.4.2.3**), it was shown that anxiety and depression independently increased the risk of all-cause mortality and cancer-related mortality in women with breast cancer by up to 30% respectively, showing the urgent need for accessible interventions that can target cognitive and emotional health and improve the quality of life (QoL) in MBC. In a recent study by Dobrestsova and Derakshan (2021), it was found that good cognitive functioning and its interaction with social support protected against escalating levels of depression in women living with MBC such that those with high levels of cognitive functioning and high social support had the lowest levels of depression. Such a finding implies that good social support is important to protect against depression. Depression has also been shown to negatively correlate with employment status, such that being unemployed is significantly associated with worse depression in cancer survivors (Inhestern et al. 2017). An earlier study found that a reduction in depression over the first year of a randomised control trial increased the duration of survival time in MBC by approximately 28.5 months (median survival time for decrease = 53.6 months and increase = 25.1 months) (Giese-Davis et al., 2011).

Research shows that work plays a central role in providing a sense of value and meaning in everyday life and substantially contributes to re-affirming identity after a breast cancer diagnosis. Most often women with earlier-stage cancer report returning to work gave them a sense of normality and

distraction away from their cancer patient identity, as well as helped with financial concerns (Kennedy et al., 2007; van Maarschalkerweerd., 2020; MacLennan et al., 2021). Financial worries and economic burden (i.e., reduction in the number of working hours) created by a cancer diagnosis are significantly associated with a poorer quality of life (Meneses et al., 2012; Keim-Malpass et al., 2016) and higher levels of anxiety (Park et al., 2018) and depression (Perry et al., 2020).

In a study by Verrill et al., (2020), it was found that approximately one in four (25%) women with MBC are unable to continue working following their diagnosis. Factors such as pain, nausea, fatigue, sadness, drowsiness, memory difficulties and numbness/tingling have been linked to poor sustainment of work in individuals living with metastatic cancer (Tevaarwerk et al., 2016). For some women, however, the decision to discontinue work may not be due to physical or cognitive difficulties but rather is a personal choice driven by a re-evaluation of work importance in everyday life and a greater desire to spend time engaging in other activities such as spending time with family and friends. Similarly, to women with earlier-stage breast cancer, women with MBC have been shown to experience reduced workability and work productivity (Cleeland et al., 2014; Lyons et al., 2019; Verrill et al., 2020). In women with earlier-stage cancer, employer and co-worker support and flexibility have been linked to better workability, confidence, retention of work and an earlier return to work (Munir et al., 2010; Mehnert et al., 2013; Blinder et al., 2017). Lyons et al., (2019) revealed that over two-thirds of women living with advanced breast cancer reported that they were restricted in the types of work they can perform (68%), had to reduce their work (71%) or needed to take frequent rest breaks at work to manage their adverse side effects (71%). Such figures indicate that women living with MBC require a high level of employer understanding, support, and flexibility in the workplace.

In the 'BRiCatWork' study presented in **Chapter 3 (**Chapman et al., 2021), it was found that many working women living with a history of primary breast cancer experience a lack of understanding from their employers when it comes to their cancer-related fatigue and cognitive impairment. Factors such as social support, job stress and fatigue have been shown to significantly influence quality of working life amongst cancer survivors (Jin & Lee, 2018, 2020). Quality of working life is defined as 'the experiences and perceptions of cancer survivors in their work life' (de Jong et al., 2016). At present,

the effects of workplace experiences with employers (e.g., understanding of required adjustments) and quality of working life on cognitive and emotional health are understudied in women living with a diagnosis of MBC.

### 6.2.1. **Aims**

Considering studies have shown that continued work has a plethora of benefits including better quality of life and lower emotional distress in non-metastatic breast cancer, it was crucial to extend this research and explore the relationships between quality of working life and workplace experiences (e.g., understanding) with cognitive and emotional vulnerability (anxiety and depression), as well as global health in women living with a diagnosis of MBC. The main aim of the study presented in this chapter was to investigate how quality of working life was related to self-reported anxiety and depression, as well as perceived cognitive function and global health. To this end, women's experiences with their employers (MBC-EE) after MBC diagnosis and its relationship with quality of working life was explored. Given, studies have evinced that younger age is predictive of psychological (emotional) distress including anxiety and depression in MBC (see Kissane et al., 2004; Mosher & Duhamel, 2012) and its interaction with cognitive functioning in predicting traumatic stress has recently been established in MBC (Dobrestsova & Derakshan, 2021) the role(s) of age, and other demographic factors such as education and time since diagnosis were examined.

It was predicted that self-reported quality of working life would be associated with global quality of life measures, as well as negatively related to emotional vulnerability to anxiety and depression and cognitive vulnerability. It was also predicted that women's experience with their employers after MBC diagnosis would correlate positively with self-reported quality of working life.

## 6.3. **Method**

### 6.3.1. **Design**

The design was cross-sectional. Women were asked to complete online questionnaires assessing their perceived cognitive function and emotional wellbeing, as well as their work experiences following their MBC diagnosis. Ethical approval was obtained from the local research committees (see **Chapter 2 section 2.2** for a more comprehensive description of ethical procedures).

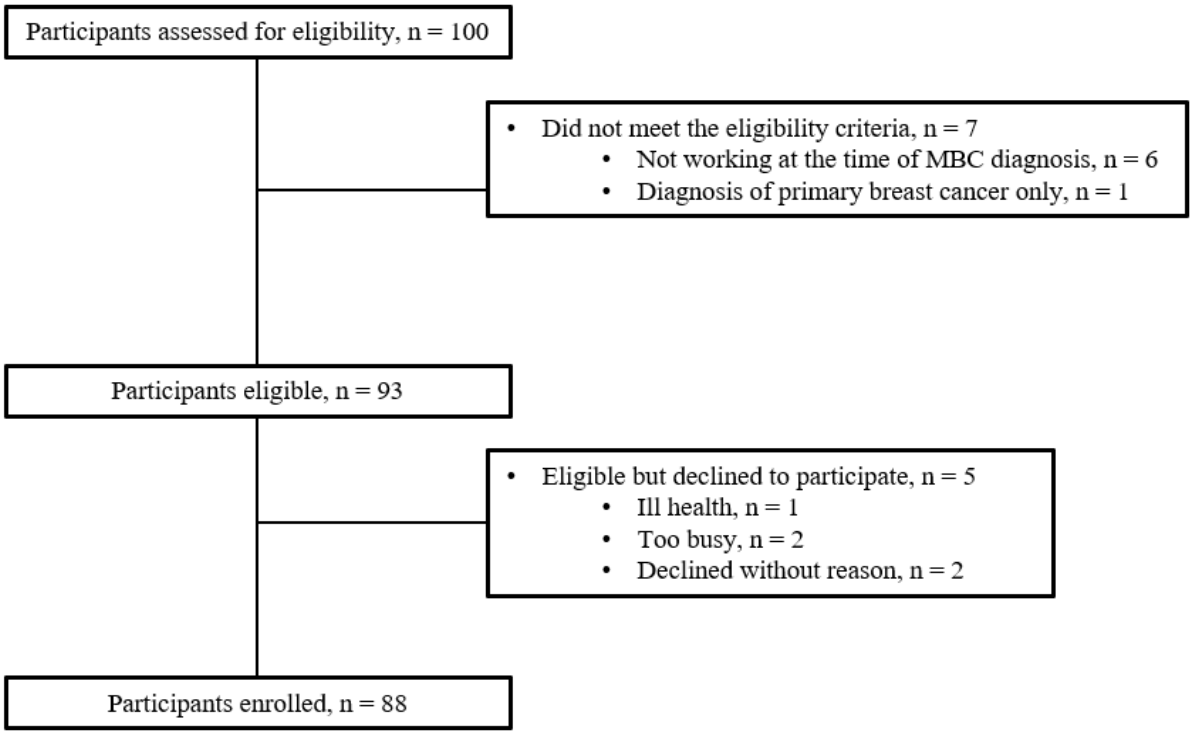
### 6.3.2. **Participants**

Women living with an MBC diagnosis (*N* = 88) in the United Kingdom were recruited via voluntary sampling using online advertisements placed on social media platforms including Facebook, Twitter and Instagram between 1st March 2021 and 4th June 2021.

Inclusion criteria included: (1) living with a diagnosis of MBC, (2) over the age of 18 years, (3) receiving treatment including hormone therapy, target therapy, chemotherapy and radiotherapy or not receiving any treatment, (4) women must have been working (employed, self-employed or volunteering) at the time of MBC diagnosis but they did not have to be working at the time of enrolment onto the study. Reasons given for not taking part in the study included not working at the time of MBC diagnosis (*n* = 6), diagnosis of primary breast cancer (*n* =1), being too busy to complete the questionnaires (*n* = 2) and unexpected ill health (*n* =1) (see **figure 6.1** for the flowchart of participants).

**Figure 6.1**

*Flowchart of participants*




## 6.3.3. **Materials**

Sociodemographic and clinical information (i.e., region of cancer metastasis) was self-reported by participants using the ***MBC Demographics Questionnaire*** (***MDQ***; Dobrestsova and Derakshan, 2021). The MDQ comprises of 26-items relating to MBC history, sociodemographic factors and work-related characteristics.

Perceived cognitive function was assessed by the 37-item ***Functional Assessment of Cancer Therapy-Cognitive Scale*** (***FACT-Cog, version 3;*** Wagner et al., 2009). Higher subscale scores and a total score demonstrate a better perceived cognitive function. Excellent reliability was found for the FACT-Cog total score in the current study: Cronbach's α = .96. The FACT-Cog total score[12] was

[12] In line with the recommendation from FACIT.org individual item-total score correlation coefficients were explored for PCI, PCA and FACT-Cog total. Results showed that all 37-items should be included in the total score.

selected as the variable of interest to increase power in the analyses (see **Chapter 2 section 2.4.2** for more detail).

Anxiety and depression were measured using the ***Hospital Anxiety and Depression Scale*** (***HADS***; Zigmond & Snaith, 1983). Higher scores represent a greater level of (trait) anxiety and depression. High reliability scores were found for the current study: HADS-A Cronbach's α = .85; HADS-D Cronbach's α = .78; HADS-total Cronbach's α = .86 (see **Chapter 2 section 2.4.4 and 2.4.5** for more detail).

Global health status was assessed using the ***European Organisation for Research and Treatment of Cancer Quality of Life*** (***EORTC-QLQ-Q30, Version 3***; Aaronson et al., 1993). A higher score for global health status indicates a better health-related quality of life and ability to function in everyday life. Good reliability was shown for the current study: Cronbach's α = .88 (see **Chapter 2 section 2.4.6** for more detail).

Financial difficulty was measured using the single item (financial impact score) on the ***European Organisation for Research and Treatment of Cancer Quality of Life*** (***EORTC-QLQ-Q30, Version 3;*** Aaronson et al., 1993). A higher score demonstrates more severe financial difficulty (see **Chapter 2 section 2.4.6** for more detail).

Quality of working life was assessed by the 23-item ***Quality of Working Life for Cancer Survivors*** (***QWLQ-CS***, de Jong et al., 2018). Higher scores for each of the subscales and overall score represent a greater quality of working life in cancer survivors. Excellent reliability was found for the overall QWLQ-CS score in the current study: Cronbach's α = .91. The overall QWLQ-CS score was used as the variable of interest to increase power in the analyses (see **Chapter 2 section 2.4.11** for more detail).

Work and activity impairment due to metastatic breast cancer (MBC) was assessed with the ***Work Productivity and Activity Impairment Questionnaire: Specific Health Problem*** (***WPAI: SHP***, ***version, 2***; Reilly et al., 1993). Higher scores reflect greater activity impairment and productivity loss as a result of MBC (see **Chapter 2 section 2.4.10** for more detail).

Women's experience with employers after metastatic breast cancer diagnosis and personal views of work were assessed using the ***Workplace Experience Questions*** (***WPEQ***; developed by BC). Two composite mean scores were formed and referred to as 'women's experience with employers score' (MBC-EE score and 'women's personal views of work score' (MBC-PVW score) (see **appendix 3** for item reliability and factor analysis). Higher scores demonstrate a better experience with employers and more positive views of work. Good reliability was found in the current study: MBC-EE Cronbach's α = .88 and MBC-PVW score Cronbach's α = .85. Both the experience with employers score (MBC-EE) and personal views of work score (MBC-PVW) were selected as variables of interest in the current study (see **Chapter 2 section 2.4.12** for more detail).

### 6.3.4. **Procedure**[13]

Women who voiced an interest in participating in the study were sent an email containing the study information, participant inclusion criteria and a secure URL link to access the battery of online questionnaires presented on Gorilla Experimental Builder (www.gorilla.sc). Women were first asked to provide online consent before completing the MDQ followed by the perceived cognitive and emotional health questionnaires and WPEQ. Women who reported being employed, self-employed or volunteering at the time of the study were asked to additionally complete the work-related questionnaires (QWLQ-CS, WPAI: SHP). Women were instructed to complete the questionnaires during a single session to ensure consistency although were told they could take short breaks as required. Upon completion, a £6 amazon e-gift voucher was sent via email.

## 6.4. **Statistical Analysis**

Statistical analyses were performed using the IBM Statistical Packages for the Social Sciences (IBM SPSS, version 28). Outliers were assessed using histograms and box plots and dealt with using

[13] Data for this study was collected during the COVID-19 outbreak in the UK.

Winsorization prior to analysis (Reifman & Keyton, 2010). Descriptive statistics were produced for the sociodemographic information, breast cancer history and work-related characteristics as well as self-reported questionnaire scores (see **table 6.1** for participant demographics and **table 6.2** for summaries for questionnaire scores).

Using Shapiro-Wilk normality was assessed. Bootstrapped Pearson's correlation analysis was performed between experience with employers (MBC-EE score) and quality of working life for cancer survivors (QWLQ-CS) to explore whether women's experience with their employer after their MBC diagnosis related to their perceived quality of working life. Furthermore, analysis was also conducted between personal views of work (MBC-PVW score) and QWLQ-CS to investigate whether women's views of work correlated with their perceived quality of working life.

Hierarchical regression analyses were then conducted to explore the relationship of self-reported quality of working life in women working (employed, self-employed or volunteering) at the time of the study to four dependent variables including perceived cognitive function, anxiety, depression and global health status after allowing for sociodemographic factors. In step 1, education, time since MBC diagnosis and current age were included. Overall quality of working life (as measured by QWLQ-CS) was then added as the final predictor in step 2. Assessing analysis of standardised residual, no outliers were found for **depression** (Cooks distance = 0.2, std Residual Min = -1.9, std Residual Max = 2.9), **anxiety** (Cooks distance = 0.2, std Residual Min = -2.0, std Residual Max = 2.2), **global health status** (Cooks distance = 0.1, std Residual Min = -2.0, std Residual Max = 2.6) and **perceived cognitive function** (Cooks distance = 0.2, std Residual Min = -2.2, std Residual Max = 1.9). Checks for violations of the assumptions of collinearity, independent error, normality, homoscedasticity and linearity were also performed using histogram and normal P-P plots. Each of the assumptions was met for the regression analyses performed in the current study. Cohen's $f^2$ was calculated.

Additional exploratory bootstrapped Pearson's correlation analysis was carried out to examine whether financial difficulty related to perceived cognitive function, anxiety, depression and global health in women attending paid work (employed or self-employed) or not in paid work (volunteering or not undertaking any form of work) at the time of completing the study.

## 6.5 **Results**

### 6.5.1. **Sample characteristics**

**Table 6.1** displays the sociodemographic, breast cancer history and work-related characteristics of the 88 women who completed the study. Women had a mean age of 46 years (*SD* = 7.5, *range* 33-65) at the time of MBC diagnosis and a mean time of approximately 32 (*SD* = 24.3, *range* 0-115) months since their MBC diagnosis. Approximately 74% of women were employed, self-employed or undertaking volunteering at the time of the study.

**Table 6.1**

*Participant sociodemographic information, breast cancer history and work-related characteristics*

| | ***N* = 88** | **(%)** |
|---|---|---|
| ***Sociodemographic*** | | |
| Age | Mean 49.5 (SD = 7.2, Range 36-68) | |
| *Education* [a] | | |
| Secondary education | 9 | 10.2 |
| Further education | 19 | 21.6 |
| Higher education | 58 | 65.9 |
| *Ethnicity* | | |
| White | 83 | 94.3 |
| Asian | 2 | 2.3 |
| Multi-ethnic | 2 | 2.3 |
| Middle Eastern | 1 | 1.1 |
| *Civil Status* | | |
| Married/Civil Partnership/Cohabiting | 67 | 76.1 |
| Divorced/Separated | 7 | 7.9 |
| Single/Widowed | 14 | 15.9 |
| Psychiatric Condition | 10 | 11.4 |

| | | |
|---|---|---|
| Neurological Condition | 8 | 9.1 |
| ***Clinical Breast Cancer History*** | | |
| Age at MBC diagnosis [b] | Mean 46.7 (SD = 7.5, Range 33–65) | |
| Time since MBC diagnosis (months) [c] | Mean 31.6 (SD = 24.3, Range 0-115) | |
| *Region of cancer metastasises* | | |
| Bone | 66 | 75.0 |
| Lungs | 25 | 28.4 |
| Brain | 6 | 6.8 |
| Liver | 23 | 26.1 |
| Other | 12 | 13.6 |
| *Current treatment regimen* | | |
| Surgery | 1 | 1.1 |
| Chemotherapy | 26 | 29.5 |
| Radiotherapy | 1 | 1.1 |
| Hormone therapy | 55 | 62.5 |
| Target therapy | 49 | 55.7 |
| Other | 7 | 8.0 |
| None | 1 | 1.1 |
| ***Work*** | | |
| *Current work* | | |
| Employed | 56 | 64.4 |
| Self-employed | 6 | 6.9 |
| Undertaking volunteering work | 3 | 3.4 |
| Not undertaking any form of work | 23 | 26.4 |

*Note.* [a] Two participants did not report their highest level of education, [b] One participant did not report their age at the time of their MBC diagnosis, [b] Six participants did not state the number of months since their MBC diagnosis

**Table 6.2** shows the mean scores for self-reported cognitive and emotional health (anxiety and depression), as well as global health status and experience with employers (MBC-EE) following MBC diagnosis for the entire sample. The personal views of work score (MBC-PVW) for women working (employed, self-employed or volunteering) at the time of the study is also included.

**Table 6.2**

*Mean scores for each of the self-reported questionnaires*

| | *Mean (SD)* | *Range (Minimum – Maximum)* |
|---|---|---|
| Perceived cognitive function (FACT-Cog total score) [a] | 93.1 (27.1) | 34-144 |
| Anxiety (HADS-A) | 9.2 (4.2) | 2-19 |
| Depression (HADS-D) | 6.3 (3.5) | 0-16 |
| Global health status (EORTC-QLQ-C30) | 60.3 (19.2) | 8.33-100 |
| Experience of employers (MBC-EE)[14] | 3.7 (1.1) | 1-5 |
| Personal views of work (MBC-PVW) | 2.9 (1.2) | 0-5 |

*Note.* [a] Perceived cognitive function (FACT-Cog): higher score = better perceived cognitive function; Anxiety and depression (HADS): higher scores = worse symptomology; Global health status (EORTC-QLQ-C30): higher score = better perceived global health; MBC-EE: higher score = better experience with employers after MBC diagnosis; MBC-PVW: higher score = more positive view of work

[14] An independent (bootstrapped) *t*-test found no significant difference in MBC-EE scores (0.32, BCa 95% CI [0.64, 4.26], $t$ (84) = 2.61, $p$ =.26) between women who were working (employed, self-employed or volunteering) at the time of the study ($M$ = 3.82, $SD$ = 1.11) and those who were not working ($M$ = 3.49, $SD$ = 1.17) at the time of the study.

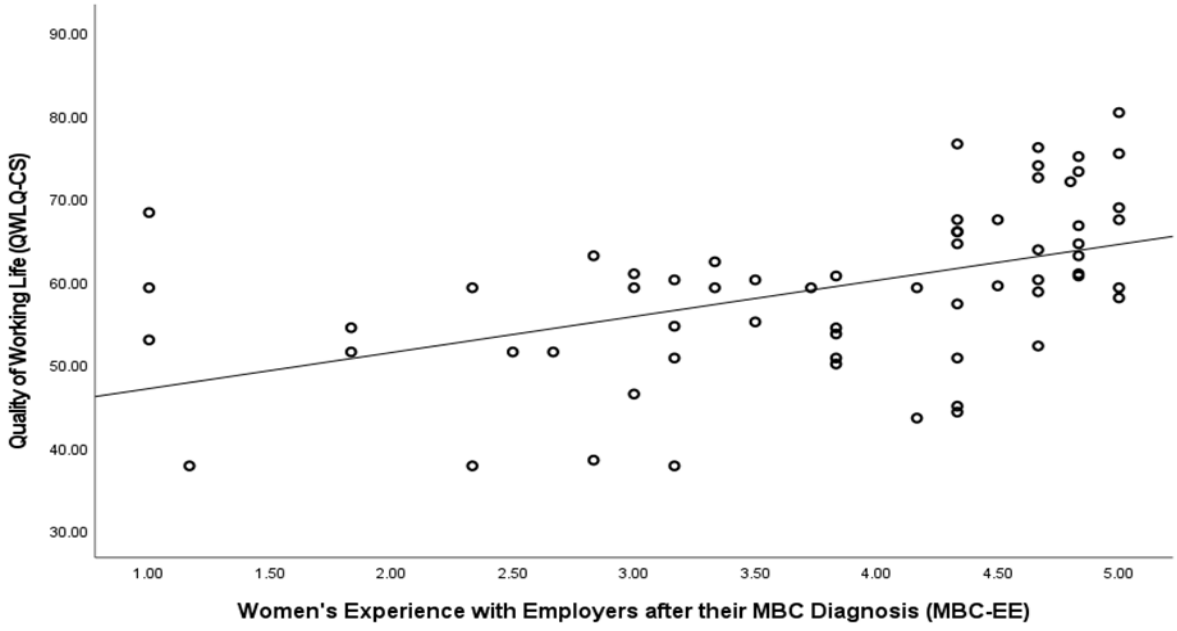
### 6.5.2. **Relationship between women's experience with employers and self-reported quality of working life**

As **figure 6.2** shows, experience with employers after MBC diagnosis (MBC-EE score) positively correlated with perceived quality of working life in working (employed, self-employed or volunteering) women (QWLQ-CS), $r$ (61) = .48, Bca 95% CI [.25, .68], $p$ <.001. Such a finding suggests that better experience with employers (e.g., greater understanding) following MBC diagnosis was associated with a greater perceived quality of working life (see **figure 6.2** for scatterplot of the relationship between MBC-EE score and quality of working life).

Similarly, **figure 6.3** shows that women's personal views of work (MBC-PVW score) positively correlated with QWLQ-CS, $r$ (61) = .60, Bca 95% CI [.46, .74], $p$ <.001, suggesting that more positive views of work met with a greater perceived quality of working life (see **figure 6.3** for scatterplot of the relationship between MBC-PVW score and quality of working life).

**Figure 6.2**

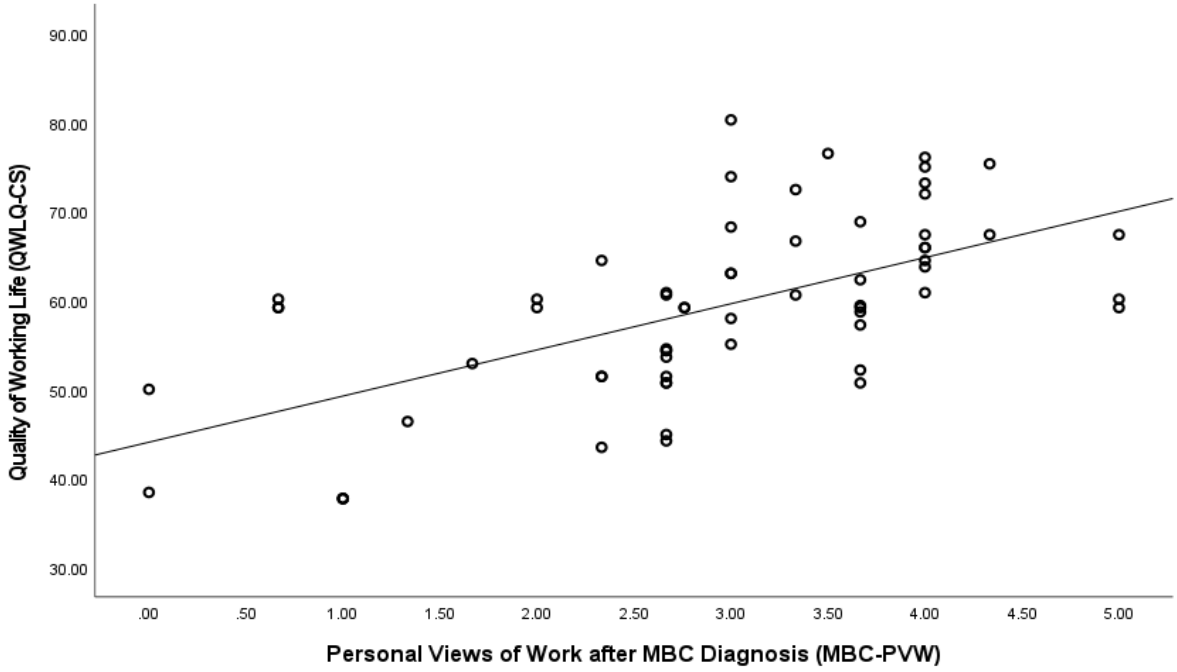
*A scatterplot showing the relationship between women's experience with their employers (MBC-EE score) and quality of working life (QWLQ-CS)*



*Note*. $R^2 = 0.23$

**Figure 6.3**

*A scatterplot showing the relationship between women's personal views of work (MBC-PVW score) and quality of working life (QWLQ-CS)*




*Note*. $R^2 = 0.37$

## 6.5.3. **Relationships between self-reported quality of working life with perceived cognitive impairment, emotional distress and global health in working women with MBC**

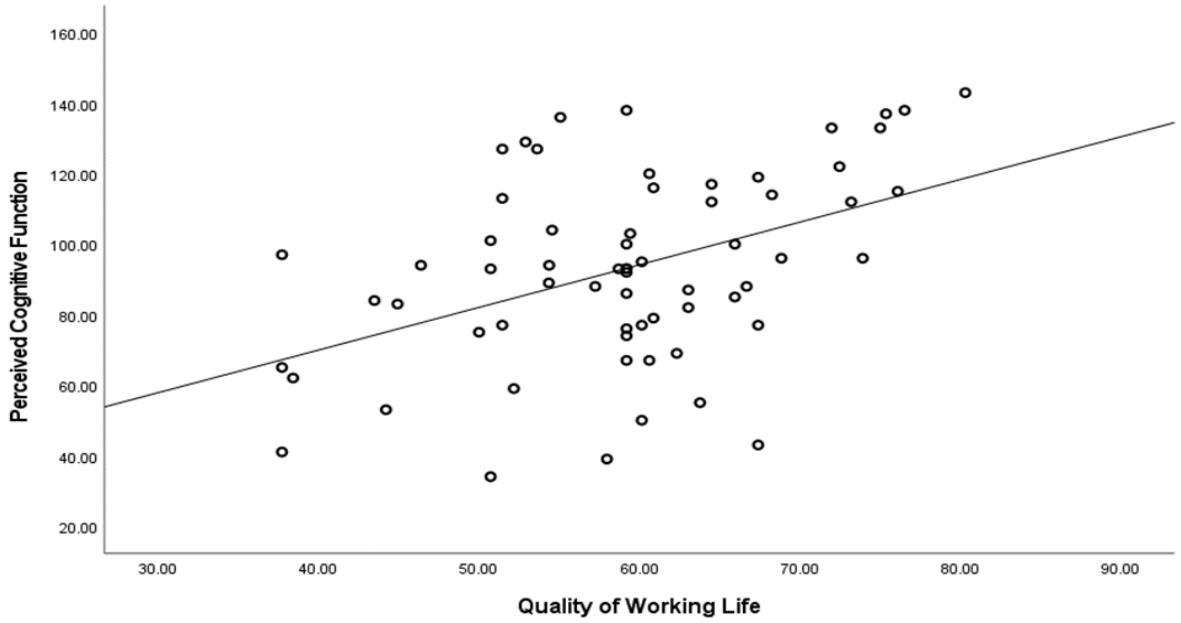
**Perceived cognitive function**[15] – As **table 6.3** shows, step 1including education, time since MBC diagnosis and current age accounted for approximately 5% of the variance in perceived cognitive

[15] Quality of working life (QWLQ-CS) was a significant predictor of the FACT sub-scales: perceived cognitive impairment (PCI) ($t$ (60) = 3.12, $p$ <.005), perceived cognitive ability (PCA) ($t$ (60) = 3.31, $p$ <.005) and impact on quality of life (QoL) ($t$ (60) = 4.67, $p$ <.001).

function. When quality of working life (QWLQ-CS) was added in step 2, the model explained an additional 18% of the variance, with perceived quality of working life acting as a significant predictor ($t$ (60) = 3.75, $p$ <.001) (Cohen's $f^2$ = 0.23). Greater quality of working life met with better perceived cognitive function (see **figure 6.4** for the relationship between quality of working life and perceived cognitive function).

**Figure 6.4**

*A scatterplot showing the relationship between quality of working life (QWLQ-CS) and perceived cognitive function*




*Note.* $R^2$ = 0.20

**Depression – Table 6.3** shows step 1 including the demographic factors, accounted for approximately 8% of the variance in depression, with education acting as a significant predictor ($t$ (60) = -2.00, $p$ = .05). Lower education levels (secondary/further education) were met with greater depression ($M$ = 7.33, $SD$ = 2.94) compared with those who had higher education degrees who had lower depression scores ($M$ = 5.68, $SD$ = 3.68). In step 2, quality of working life significantly predicted depression ($t$ (60) = -3.23, $p$ <.005), with greater perceived quality of working life meeting a lower level

of depression. Education remained a significant predictor ($p < .05$). Overall, the model explained around 21% of the variance in depression scores. Cohen's $f^2 = 0.17$ (see **figure 6.5** for the relationship between quality of working life and self-reported depression).

**Figure 6.5**

*A scatterplot showing the relationship between quality of working life (QWLQ-CS) and depression*

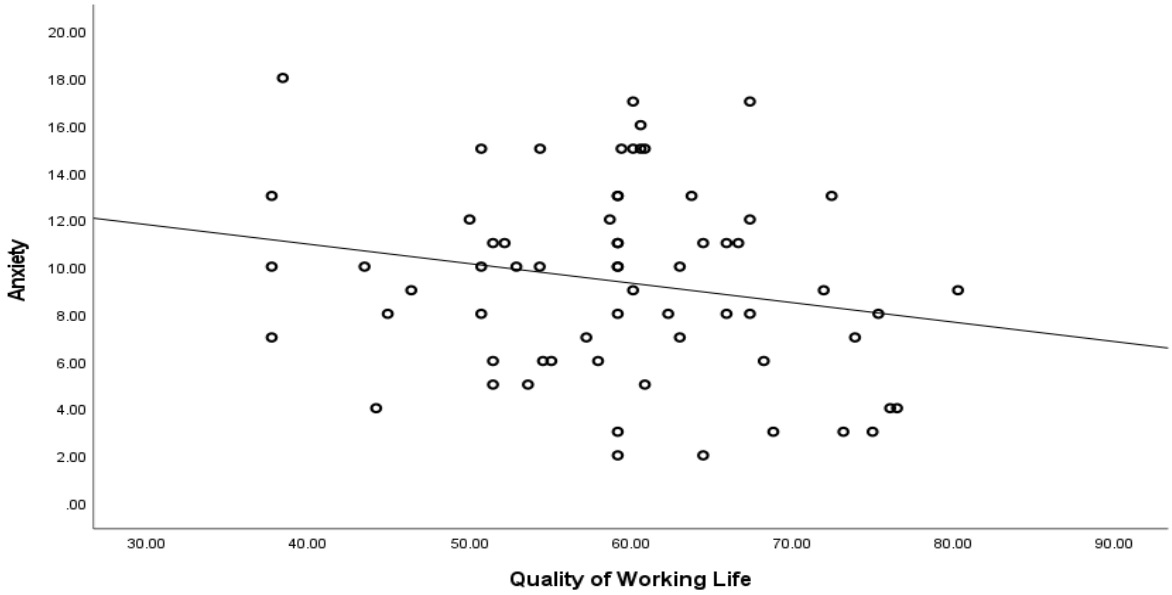

*Note.* $R^2 = 0.16$

**Anxiety –** Step 1 accounted for a moderate 16% of the variance in anxiety. As **table 6.3** shows, the only variables significant in predicting anxiety scores on both steps 1 and 2 were education and current age, both *t*'s >-2.5, both *p*'s = .01. Lower education levels (secondary/further education) were met with worse anxiety ($M = 10.67$, $SD = 3.89$) compared with those who had higher education degrees ($M = 8.75$, $SD = 3.99$). Younger (current) age was also met with greater anxiety (younger: $M = 10.11$, $SD = 4.27$; older: $M = 8.33$, $SD = 3.50$). Quality of working life did not significantly predict anxiety on step 2 ($t(60) = -1.22$, $p > .05$). Overall, approximately 18% of the variance was explained by the models

in predicting anxiety (see **table 6.3** for hierarchical regression; see **figure 6.6** for the relationship between quality of working life and anxiety).

**Figure 6.6**

*A scatterplot showing the relationship between quality of working life (QWLQ-CS) and anxiety*

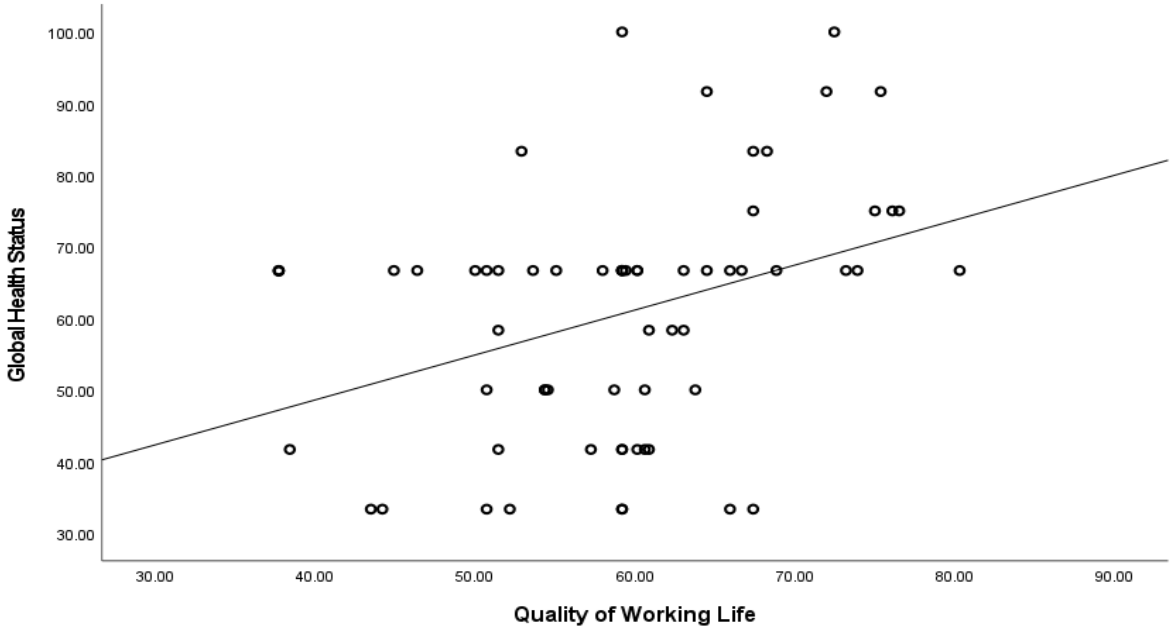



*Note.* $R^2 = 0.04$

**Global health status** – In step 1 the three demographic predictors (education, time since MBC diagnosis, current age) accounted for a small 0.3% of the variance in global health scores. The only significant predictor of global health was quality of working life ($t$ (60) = 3.26, $p < .005$), with an overall 15% of variance explained. Greater self-reported quality of working life met with better global health status. Cohen's $f^2 = 0.18$ (see **table 6.3** for hierarchal regression; see **figure 6.7** for the relationship between quality of working life and global health status).

**Figure 6.7**

*A scatterplot showing the relationship between quality of working life (QWLQ-CS) and global health status*




*Note.* $R^2 = 0.13$

**Table 6.3**

*Hierarchical regression analyses for perceived cognitive function, depression, anxiety and global health status*

| | *b* | *SE B* | ß | *t* | *p* |
|---|---|---|---|---|---|
| ***Perceived cognitive function*** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 62.90 (3.06, 122.73) | 29.92 | | 2.10 | .04 |
| Education | 11.16 (-4.27, 26.59) | 7.72 | .20 | 1.45 | .15 |
| Time since MBC diagnosis | -0.07 (-0.39, 0.26) | 0.16 | -.05 | -0.42 | .67 |
| Current age | 0.50 (-0.58, 1.58) | 0.54 | .12 | 0.93 | .36 |
| $R^2 = .05$<br>$F$ (3,61) = .96<br>$p = .42$ | | | | | |
| ***Step 2*** | | | | | |
| Constant | -2.20 (-66.66, 62.27) | 32.23 | | -0.07 | .95 |
| Education | 10.43 (-3.58, 24.44) | 7.01 | .18 | 1.49 | .14 |

| | | | | | |
|---|---|---|---|---|---|
| Time since MBC diagnosis | 0.07 (-0.23, 0.37) | 0.15 | .05 | 0.45 | .65 |
| Current age | 0.31(-0.68, 1.29) | 0.49 | .08 | 0.62 | .54 |
| Quality of working life | 1.21 (0.56, 1.85) | 0.32 | .44 | 3.75 | .00 |
| $R^2$ = .23 | | | | | |
| $\Delta R^2$ = .18 | | | | | |
| $\Delta F$ (1,60) = 14.07 | | | | | |
| $p$ <.001 | | | | | |
| ***Depression*** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 11.48 (3.81, 19.15) | 3.84 | | 2.99 | .00 |
| Education | -1.98 (-3.96, -0.00) | 0.99 | -.27 | -2.00 | .05 |
| Time since MBC diagnosis | 0.01 (-0.03, 0.05) | 0.02 | .06 | 0.43 | .67 |
| Current age | -0.09 (-0.22, 0.05) | 0.07 | -.16 | -1.23 | .22 |
| $R^2$ = .08 | | | | | |
| $F$ (3,61) = 1.72 | | | | | |
| $p$ =.17 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 18.84 (10.37, 27.32) | 4.24 | | 4.45 | .00 |
| Education | -1.90 (-3.74, -0.06) | 0.92 | -.25 | -2.06 | .04 |
| Time since MBC diagnosis | -0.01 (-0.05, 0.03) | 0.02 | -.04 | -0.33 | .75 |
| Current age | -0.06 (-0.19, 0.07) | 0.07 | -.12 | -0.97 | .34 |
| Quality of working life | -0.14 (-0.22, -0.05) | 0.04 | -.39 | -3.23 | .00 |
| $R^2$ = .21 | | | | | |
| $\Delta R^2$ = .14 | | | | | |
| $\Delta F$ (1,60) = 10.41 | | | | | |
| $p$ =.002 | | | | | |
| ***Anxiety*** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 20.80 (12.42, 29.19) | 4.19 | | 4.96 | .00 |
| Education | -2.77 (-4.93, -0.60) | 1.08 | -.32 | -2.56 | .01 |
| Time since MBC diagnosis | 0.01 (-0.04, 0.06) | 0.02 | .06 | 0.45 | .65 |
| Current age | -0.20 (-0.35, -0.05) | 0.08 | -.33 | -2.65 | .01 |
| $R^2$ = .16 | | | | | |
| $F$ (3,61) = 3.83 | | | | | |
| $p$ = .01 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 24.07 (14.16, 33.98) | 4.96 | | 4.86 | .00 |
| Education | -2.73 (-4.88, -0.58) | 1.08 | -.32 | -2.53 | .01 |
| Time since MBC diagnosis | 0.00 (-0.04, 0.05) | 0.02 | .02 | 0.15 | .88 |

| | | | | | |
|---|---|---|---|---|---|
| Current age | -0.19 (-0.34, -0.04) | 0.08 | -.32 | -2.52 | .01 |
| Quality of working life | -0.06 (-0.16, 0.04) | 0.05 | -.15 | -1.22 | .23 |
| $R^2$ = .18<br>$\Delta R^2$ = .02<br>$\Delta F$ (1,60) = 1.50<br>$p$ = .23 | | | | | |
| ***Global health status*** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 56.96 (18.01, 95.90) | 19.48 | | 2.92 | .01 |
| Education | 0.93 (-9.12, 10.97) | 5.02 | 0.03 | 0.19 | .85 |
| Time since MBC diagnosis | 0.04 (-0.17, 0.25) | 0.11 | 0.05 | 0.38 | .71 |
| Current age | 0.04 (-0.66, 0.74) | 0.35 | 0.02 | 0.12 | .91 |
| $R^2$ =.003<br>$F$ (3,61) = .05<br>$p$ = *.98* | | | | | |
| ***Step 2*** | | | | | |
| Constant | 19.25 (-23.73, 62.22) | 21.48 | | 0.90 | .37 |
| Education | 0.51 (-8.84 9.85) | 4.67 | 0.01 | 0.11 | .91 |
| Time since MBC diagnosis | 0.12 (-0.08, 0.32) | 0.10 | 0.15 | 1.18 | .24 |
| Current age | -0.07 (-0.73, 0.58) | 0.33 | -0.03 | -0.22 | .83 |
| Quality of working life | 0.70 (0.27, 1.13) | 0.22 | 0.40 | 3.26 | .00 |
| $R^2$ = .15<br>$\Delta R^2$ = .15<br>$\Delta F$ (1,60) =10.62<br>$p$ = .002 | | | | | |

*Note*. (95% Confidence Intervals)

Checks for violation of assumptions using residuals showed that assumptions of collinearity (Tolerance > .01, VIF < 10), independent error (**Perceived cognitive function**: Durbin-Watson = 1.8, **Depression**: Durbin-Watson = 1.9, **Anxiety**: Durbin-Watson = 2.2, **Global health status**: Durbin-Watson = 2.0), normality and homogeneity of variance and linearity were met for perceived cognitive function, anxiety, depression and global health status.

### 6.5.4. **Additional analyses:**

#### Relationships between financial difficulty and perceived cognitive and emotional vulnerability depending on work status at the time of the study

Pearsons (bootstrapped) correlation analysis revealed that financial difficulty significantly correlated with self-reported quality of working life (QWLQ-CS) ($r$ (60) = -.50, Bca 95% CI [-.68, -.27], $p$ <.001), depression ($r$ (62) = .28, Bca 95% CI [.06, .48], $p$ =.02) and perceived cognitive function ($r$ (62) = -.37, Bca 95% CI [-.55, -.12], $p$ =.01) in working women in paid work (employed, self-employed). Such findings suggest that greater financial difficulty was associated with a poorer quality of working life, greater depression and worse perceived cognitive function. No significant relationship was found with anxiety ($p$ > .05).

Furthermore, the analysis showed that financial difficulty significantly correlated with anxiety, $r$ (22) = .46, Bca 95% CI [.05, .74], $p$ =.02 in women not attending paid work (volunteering or not undertaking any form of work) at the time of the study, indicating greater financial difficulty was related to worse anxiety. No significant relationships were found with depression or perceived cognitive function ($p$ > .05).

## 6.6. **Discussion**

The main aim of the study presented in **Chapter 6** was to investigate the relationship between self-reported quality of working life and perceived cognitive function, anxiety, depression and global health status in women living with a diagnosis of MBC in the UK, in addition to exploring women's experience with employers (MBC-EE) and its relationship with self-reported quality of working life. As predicted, the study found that women's experience with employers following MBC diagnosis positively correlated with self-reported quality of working life, such that having a better experience with employers met with a greater quality of working life. Similarly, findings showed that a more positive view of work (MBC-PVW score) met with a better quality of working life. Much like primary breast

cancer, women living with MBC experience a series of debilitating treatment-related sequelae such as fatigue (Mosher et al., 2013) and pain (Reed et al., 2012) that affect their ability to function in everyday life. Women also attend regular oncology appointments and treatment sessions that can adversely impact their workability and work presenteeism. In a recent study by Lyons et al., (2019), it was shown that more than two-thirds of women with MBC report being restricted in work and require a series of work-based adaptions highlighting, the importance of social support and understanding in the workplace. Furthermore, studies by Jin & Lee (2018, 2020) have shown that greater social support, as well as lower job stress and fatigue, predicts a better quality of working life in cancer survivors. It is plausible that the finding presented in this chapter could therefore be underpinned by greater experience with employers reducing levels of job stress, increasing work engagement and promoting a sense of value and worthiness in the workplace, subsequently improving perceptions of quality of working life. Supporting the needs of women living with MBC in the workplace is, however, highly complex and many employers may not feel adequately equipped to give the level of support required. Further qualitative research is needed to comprehensively understand women's experiences with employers and explore the factors influencing quality of working life in women living with a diagnosis of MBC. Research also urgently needs to better understand employers' experiences of supporting an employee with MBC.

In line with the prediction, the current study also found that greater self-reported quality of working life met with better perceived cognitive function and global health, as well as lower levels of depression. Such findings suggest that quality of working life may play a crucial role in protecting against escalating levels of pre-existing cognitive vulnerability and emotional vulnerability to depression in working women living with MBC. Substantiating evidence has shown that emotional distress (anxiety and depression) (Grabsch et al., 2006), cognitive impairment (Carreira et al., 2020) and reduced quality of life (Reed et al., 2012) are common amongst women with MBC. Depression has been associated with poor adherence to treatment (DiMatteo & Haskard-Zolnierek, 2011), health-related quality of life, and sleep problems (Mosher et al., 2012), as well as increased suicidal ideations (Akechi et al., 2000) in cancer patients including those with breast cancer. Given, that an earlier meta-

analysis by Wang and colleagues (2020) found depression to increase the risk of mortality by up to 30% in women with breast cancer, this finding has important implications. In particular, the finding suggests that more accessible resources and educational (or support) programs should be available to employers and co-workers of women diagnosed with MBC to help improve their understanding and awareness of the common treatment-related sequelae and possible adjustments needed in the workplace. Notably, Giese-Davis et al (2011) found reductions in depression to increase MBC survival time by around 28 months. It is, therefore, possible that enhancing the quality of working life by improving experience of employers may contribute to longer-term survivorship in working women with MBC, although further longitudinal research is required to substantiate this claim.

As mentioned, the current study found that women with a greater quality of working life experienced better perceived cognitive functioning, this is an important finding as the 'BRiCatWork' study presented in **Chapter 3** found impaired cognitive function adversely affects workability, general emotional health and work-related confidence in women living with a history of primary breast cancer (Chapman et al., 2021). Collectively the findings, indicate that greater quality of working life may play an influential role in enhancing workability by increasing perceived cognitive function in working women with MBC. Reduced workability and work productivity are common amongst women with MBC (Cleeland et al., 2014; Lyons et al., 2019; Verrill et al., 2020). Subsequent research needs to be conducted to investigate the moderating role of quality of working life in the relationship between perceived cognitive function and workability. It is feasible that women with a better quality of working life experience less job stress, which has been associated with self-reported cognitive function in cancer survivors (Ottati & Feuerstein, 2013). Stress has been shown to adversely affect key brain regions including, the prefrontal cortex and hippocampus (Jay et al., 2004). Similar, to the finding presented in this chapter, Mehnert and Koch (2013) found greater work satisfaction correlated with better health-related quality of life amongst cancer survivors. More research is needed to develop a better understanding of the factors underpinning the relationships between quality of working life with perceived cognitive function and health-related quality of life.

Interestingly, the study presented in this chapter found that perceived quality of working life was not associated with anxiety in women with MBC, however, in line with existing research, both current age and level of education were significantly associated with anxiety (Mosher et al., 2012; Tsaras et al., 2018). In particular, the findings showed that younger age and lower education (secondary/further) met with more severe anxiety. Education was also predictive of depression, with lower education associated with worse levels of depression. These findings have vital implications as they evince that younger working women with MBC and those with a lower level of education are more vulnerable to developing anxiety and depression, escalating their risk of premature mortality and a poorer quality of life (Rustøen et al., 2005). Health care professionals including occupational health should account for these sociodemographic factors when determining the support provided, as women in these high-risk groups may benefit from receiving early or more continuous access to e-health apps, counselling services or cognitive interventions that promote emotional resilience. One possible reason for this non-significant finding in the current study is that the anxiety experienced by women with MBC is driven by factors such as treatment uncertainty, fear of disease progression and death, which are not impacted by quality of working life. In a recent study by Verduzco-Aguirre et al., (2021), it was shown that uncertainty is met with high levels of anxiety in individuals living with advanced cancer. Although age and education have also been shown to influence risk for cognitive impairment and poorer QoL (Boscher et al., 2020; Carreira et al., 2020), this study did not replicate these findings in working women with MBC.

Finally, the additional exploration analyses presented in this chapter showed that financial difficulty was associated with elevated levels of anxiety in women not undertaking any form of paid work at the time of the study. In an earlier study by Park et al., (2018), it was shown that financial instability was predictive of anxiety in young women diagnosed with *de novo* breast cancer. The current finding may be explained by the fact that women in this sample were younger (current age: $M = 50.08$) increasing the likelihood that they will be affected by family responsibilities (i.e., supporting a dependent) and financial obligations such as a mortgage. In addition, findings showed greater financial difficulty to be related to poorer quality of working life as well as worse depression and perceived

cognitive function in women attending paid work (employed or self-employed). Perry et al., (2020) reported a similar relationship between financial strain and depression in women with breast cancer and de Jong et al., (2017) found poorer perceived quality of working life to be associated with lower income in cancer survivors. It is plausible that these findings in working women may be connected to reduced career progression and work opportunities following MBC diagnosis. The findings from the 'BRiCatWork' study presented in **Chapter 3** showed that career progression is at a standstill for many primary breast cancer survivors as a result of the effects from post-treatment sequelae (Chapman et al., 2021). Similar research should be replicated to explore career development and opportunities in working women living with a diagnosis of MBC.

### 6.6.1. **Limitations**

The study presented in **Chapter 6** has some limitations that need to be taken into consideration. Firstly, women were recruited from online advertisements placed on public and private support groups on social media platforms including, Facebook, Twitter and Instagram and, therefore, may not be fully representative of the wider population. The sample was also well-educated (65.9%) and Caucasian (94.3%), indicating women from BAME backgrounds are underrepresented in this study. Furthermore, women were asked to self-report their demographic and clinical information. Medical records should be obtained and checked to ensure the reliability of the information reported in future studies. Finally, the current study was cross-sectional meaning that it only provides a single snapshot of women's experiences at the time of completing the questionnaires and therefore could be impacted by current mood or situational events (e.g., an upcoming scan or hospital appointment). It is recommended that future research includes longitudinal studies with multiple follow-ups as well as qualitative studies to provide a more in-depth understanding of women's experiences at work and the factors affecting perceived cognitive impairment and emotional vulnerability to depression in women living with MBC. Research should also investigate the relationship between objective cognitive function and work-related outcomes including perceived quality of working life.

### 6.6.2. **Conclusion**

To conclude, the study presented in **Chapter 6** aimed to investigate how self-reported quality of working life was related to perceived cognitive function, anxiety, depression and global health in women living with MBC, in addition to exploring women's experience with their employers following MBC diagnosis and its association with quality of working life. The findings presented in this chapter show that experience with employers after MBC diagnosis positively relates to women's perceived quality of working life. Further, the findings also show that quality of working life significantly relates to global health and cognitive and emotional vulnerability, with results indicating women with a greater quality of working life are at a reduced risk of developing a poorer quality of life, cognitive vulnerability and emotional vulnerability to depression. Taken together, the findings presented in **Chapter 6** emphasise the importance of good employer experience and quality of working life for women living with a diagnosis of MBC.

## **Published paper associated with this chapter**:

Chapman, B., Grunfeld, E. A., Derakshan, N. (2022). Quality of working life can protect against cognitive and emotional vulnerability in women living with metastatic breast cancer: A cross-sectional study. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-022-01169-0

# **Chapter 7**: Exploring the impact of the COVID-19 outbreak in the UK on women living with a diagnosis of primary breast cancer

## 7.1. **Chapter Overview**

As outlined in **Chapter 1**, women living with a history of breast cancer are at an increased risk for experiencing cancer-related cognitive impairment (CRCI), anxiety and depression compared to the wider population (Inhestern et al., 2017; Janelsins et al., 2017, 2018; Carreira et al., 2018, 2020, 2021). Considering, the novelty of the Coronavirus disease 2019 (COVID-19) pandemic and the known vulnerabilities of women living with breast cancer, the principal aim of the study presented in **Chapter 7** was to investigate the impact of the COVID-19 outbreak and its restrictive measures on the cognitive and emotional health of women living with a history of primary breast cancer in the United Kingdom (UK). In the UK the outbreak of COVID-19 caused severe disruption to oncology services and employment and resulted in many women receiving a UK Government shielding letter advising them to isolate for a minimum of 12-weeks during the peak of the pandemic (Lai et al., 2020; Riera et al., 2021).

The aim of this study was two-fold. First, the study aimed to investigate the impact of the UK Government shielding letter and disruption to scheduled oncology appointments on self-reported cognitive function and emotional distress (anxiety and depression), in addition to exploring the relationship between COVID-19-related emotional vulnerability (COVID-EMV) and perceived cognitive function, anxiety and depression across the entire sample. Considering women's existing predispositions to emotional distress and the value placed on work after diagnosis and treatment, women may be at an increased risk for experiencing escalating levels of emotional vulnerability and poorer mental health outcomes as a result of the distress and trauma caused by threats to job loss and job security induced by the COVID-19 outbreak. The study, therefore, aimed to then explore the relationship between job insecurity created by the COVID-19 outbreak and perceived cognitive and emotional vulnerability in working women. To this end, the impact of changes in employment status

(i.e., furloughed) on perceived cognitive and emotional health, as well as on perceptions of work was explored. Work plays an important part in the recovery process and return to a more 'normal' day-to-day life for many women affected by breast cancer.

## 7.2. **Introduction**

The Coronavirus disease 2019 (COVID-19) outbreak, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) generated a new set of unprecedented challenges for populations worldwide, significantly escalating levels of worry and distress, particularly amongst individuals living with pre-existing health conditions such as breast cancer. The debilitating effects of cancer and anti-cancer treatment (i.e., chemotherapy) on the immune system (Verma et al., 2016) together with the comorbidity or multi-comorbidity frequently experienced by cancer patients (Renzi et al., 2019), indicate that women living with a diagnosis of breast cancer may be at a higher risk for experiencing life-threatening complications as a result of contracting COVID-19 compared to the wider population (Zhang et al., 2020).

In the United Kingdom (UK), the pandemic had a serious disruptive impact on the oncology services available, with many services being reassigned to help provide vital treatment and care for patients diagnosed with COVID-19. To reduce the risk of spreading and to protect vulnerable individuals most scheduled face-to-face appointments were postponed, shortened (i.e., reduced number of planned cycles) or cancelled. In a recent study by Lai et al (2020), it was found that at the peak of the pandemic in the UK attendance to chemotherapy sessions and critical referrals sent for early diagnosis dropped by approximately 60% and 76%, respectively. As a result of the delay in early diagnosis and access to anti-cancer treatment(s), many women face worse cancer-related outcomes including, more advanced cancer, a poorer prognosis and a lower chance of long-term survival (Richards et al., 1999; Bleicher et al., 2016). Ho et al., (2020) found that women diagnosed with invasive non-metastatic or metastatic breast cancer (MBC) have a much lower chance of survival when treatment is delayed by at least 90 days or when there is a gap between surgery and the start of adjuvant treatment

(i.e., chemotherapy). It has been predicted that there will be an additional 6,270 deaths from newly diagnosed cancer in the UK in the year following the COVID-19 outbreak, an increase of around 20% (Lai et al., 2020).

In addition to delays and disruption in early breast cancer diagnosis and active treatment (i.e., chemotherapy or radiotherapy), women in survivorship may also be adversely affected by the disruption to available oncology services, as most are offered regular check-ups, scans and mammograms to monitor for possible recurrence or metastasising of the original breast cancer tumour (Breast Cancer Now, 2019). Women diagnosed with oestrogen receptor-positive (ER+) breast cancer are prescribed hormone (or endocrine) therapy medications such as tamoxifen or aromatase inhibitors (AIs) for up to 10 years to reduce the risk of recurrence (Cancer Research UK, 2020). Despite, these advances in routine screening and treatment approximately 30% of women will still go on to develop metastatic breast cancer (MBC) (Johnston et al., 2010; Breast Cancer Org., 2022). Although recurrence risk is highest in the first couple of years after the primary diagnosis recurrence can still occur many years later (i.e., +10/15 years) (Breast Cancer Now, 2019), showing the importance of accessible oncology services for women living with a diagnosis of breast cancer. Emotional distress particularly, anxiety has been associated with fear of disease progression or recurrence and risk of premature mortality (Baqutayan, 2012; Sun et al., 2019; Berry-Stoelzle et al., 2020), suggesting that the impact of the disruption to oncology services as a result of the COVID-19 outbreak may further increase vulnerability to anxiety and depression in women living with a diagnosis of breast cancer.

As well as the reprioritising of health care services, the UK government also executed a 12-week social restriction and shielding plan for any individual considered to be at high risk of experiencing life-threatening or life-ending complications from contracting the virus (Gov.UK, n.d), this included many women living with a diagnosis of breast cancer. Recipients of the letter included those receiving active treatment, for example, chemotherapy, radiotherapy, immunotherapy, as well as targeted cancer treatments such as protein kinase inhibitors or PARP inhibitors that suppress the functioning of the immune system (Kang et al., 2009). Some women longer into survivorship also received the letter at the discretion of their general practitioner (GP) or oncologist as a result of their

ongoing sequelae (i.e., shortness of breath). The restrictions imposed by the shielding letter may be associated with increased levels of social isolation and loneliness (Holmes et al., 2020). Studies have shown that both social isolation and loneliness (i.e., living alone) are linked to greater anxiety and depression, as well as worse self-harm in cancer patients (Suppli et al., 2014; Elovainio et al., 2017; Carreria et al., 2018). In a meta-analysis conducted by Carreria et al., (2021), it was shown that women with breast cancer are more at risk of fatal and nonfatal self-harm compared to a non-cancer reference group, suggesting that the ramifications of the COVID-19 outbreak may be severe for women with breast cancer.

Furthermore, the outbreak of Coronavirus disease 2019 (COVID-19) has also had a substantial impact on global economies and individual employment (Qualtrics, 2020). The national lockdown imposed by the UK government on 23rd March 2020 included the closure of the majority of non-essential businesses, with many workforces instructed to work from home (if feasible). When working from home was not possible, employers had to either issue redundancies or furlough their staff under the government Job Retention Scheme. It is estimated that over eight million jobs were furloughed in the UK, during which time the Government paid up to 80% of the UK median salary, to a maximum of £2,500 (Bell et al., 2020). In a recent study by Qualtrics (2020), it was shown that being furloughed by an employer was associated with poorer mental health, with higher levels of stress and anxiety recorded. Studies have shown that work is instrumental in promoting cognitive and emotional recovery, as well as a better quality of life for women after a breast cancer diagnosis and treatment (Timperi et al., 2013; Keim-Malpss et al., 2016). Studies suggest that the beneficial effects of work on cognitive function may occur through exercising and strengthening neuroplasticity (or cognitive reserve) of the brain via consistent positive stimulation (e.g., processing of new or complex information through social interaction), as well as by reducing anxiety, depression and financial burden, as a consequence of receiving a wage (Vance et al., 2016; Perry et al., 2020). Further, being in work has significant psychological benefits including providing a sense of purpose, social value, identity and normality for many women living with a diagnosis of cancer (Rasmussen & Elverdam, 2008; Johnsson et al., 2010; Blinder et al., 2012; Nilsson et al., 2013).

Conversely, involuntary job loss and unemployment have consistently been shown to have a significant and long-term impact on mental health (Gallo et al., 2000; Inhestern et al., 2017). Compounding this, the emergence of depression following job loss increases the risk of continued unemployment (Stolove et al., 2017). In the same way, job insecurity is considered to be a stressor that is detrimental to wellbeing and mental health (Llosa et al., 2018), and is associated with increasing levels of depression (Blom et al., 2015). Such adverse outcomes are of additional concern for vulnerable populations already experiencing high levels of emotional distress (anxiety and depression). It is well documented that women living with breast cancer are at a greater risk for developing emotional distress, including long-term anxiety and depression, as well as maladaptive levels of worry (see Carreira et al., 2018, 2020, 2021, for reviews) compared to the wider population. Evidence also suggests that they are at a higher risk for experiencing suicidal ideations and suicide up to 25 years after their diagnosis (Schairer et al., 2006; Gaitanidis et al., 2018; see Carreira et al., 2018, for a review). This is of significance as it is estimated that a rise in unemployment in the general population from 4.94% to 5.64% (24.7 million job losses, worldwide) as a result of COVID-19 could be accompanied by an additional 9,570 suicides each year (Kawohl & Nordt, 2020).

### 7.2.1. **Aims**

Given the uncertain nature of the COVID-19 outbreak in the UK and its effects on oncology services and employment, it was crucial to investigate the impact of COVID-19 on the general cognitive and emotional health of women living with a diagnosis of primary breast cancer. Short- and long-term sequelae including emotional distress (anxiety and depression), cancer-related cognitive impairment (CRCI) and physical side effects such as fatigue are highly common amongst women diagnosed and treated for breast cancer (See Joly et al., 2019; Carreria et al., 2020, for reviews). In a study by Burgess et al., (2005), it was shown that up to 50% of women with breast cancer experience emotional distress (anxiety and/or depression) in the first year after diagnosis, with approximately 15% still experiencing symptoms five years into survivorship. Anxiety and depression are significantly associated with poorer quality of life (Zeng et al., 2016), reduced workability (Carlsen et al., 2013; Zeng et al., 2016; Ho et al.,

2018) and worse clinical outcomes (Wang et al., 2020) in women affected by breast cancer. A recent meta-review by Wang et al., (2020) found that anxiety and depression increase the risk of cancer recurrence, all-cause mortality and breast cancer-specific mortality by up to 24%, 30% and 29%, respectively, further highlighting the urgent need to understanding the impact of the COVID-19 outbreak on anxiety and depression in women with a diagnosis of breast cancer (see **Chapter 1 section 1.4.2.3** for more comprehensive description of Wang et al., 2020).

In a study conducted by Soo and Sherman (2015), it was shown that rumination which is defined as the repetition of negative thoughts and feelings (Nolen-Hoeksema et al., 2008) was predictive of higher levels of anxiety and depression in breast cancer patients. Worry which is defined as uncontrollable negative thoughts about the future (Borkovec, et al., 1983) has also been shown to be predictive of anxiety and depression in older cancer survivors (Deimling et al., 2006). Both rumination and worry are core cognitive components of clinical anxiety and depression (Beckwé et al., 2014). In cancer patients, rumination and worry are predominately associated with health-related concerns including, the fear of cancer recurrence or disease progression (i.e., repetitive thoughts that cancer may have spread to other regions of the body), early mortality and the adverse post-treatment sequelae (Steiner et al., 2014; Thewes et al., 2016). High worry is thought to create an internal distraction that reduces the cognitive resources available for cognitive functions such as working memory and attentional control (Hirsch & Mathews, 2012). One study found that higher worry in women with breast cancer was associated with poorer perceived cognitive function and greater objective cognitive impairment (Berman et al.,2014), indicating that worry and rumination provoked by COVID-19 may also contribute to greater emotional distress and poorer cognitive function.

It is plausible that the outbreak of COVID-19 in the UK may further exacerbate the severity of pre-existing emotional distress (anxiety and depression) and perceived cognitive impairment, as well as reduce quality of life amongst women living with a diagnosis of breast cancer. The aim of the current study was two-fold. The study first aimed to explore the impact of disruption to scheduled oncology services (i.e., delayed treatment or cancelled scans) and the UK Government shielding letter on the cognitive and emotional health of women living with a diagnosis of primary breast cancer, in addition

to examining the relationship between COVID-19 related emotional vulnerability (COVID-EMV) and anxiety, depression and perceived cognitive function whilst allowing for the effects of rumination, worry and key clinical and sociodemographic variables. As worry and rumination have been shown to be significant predictors of anxiety and depression (Nolen-Hoeksema, 2000; Deimling et al., 2006; Soo & Sherman, 2015; see Koster et al., 2017, for a review) and cognitive impairment (Berman et al., 2014) in cancer patients, it was important to allow for their predictive value whilst assessing the impact of COVID-EMV on self-reported anxiety, depression and perceived cognitive function. The study then aimed to explore how threats to job security would relate to levels of emotional distress including anxiety and depression, as well as perceived cognitive function. To this end, the effects of COVID-19 generated employment status (i.e., 'continued' working or being furloughed) on perceptions of job security, work importance and employer support in response to the COVID-19 pandemic was examined.

Accordingly, it was predicted that women experiencing disruption to their scheduled oncology services (e.g.., telephone appointments in place of face-to-face) as a result of the pandemic or who received the UK Government shielding letter would report worse anxiety, depression and COVID-EMV, as well as greater perceived cognitive impairment compared to those who were unaffected. It was also predicted that both worry and rumination would significantly predict anxiety and depression, as well as self-reported cognitive function. Furthermore, it was predicted that after allowing for the effects of worry, rumination and key clinical and sociodemographic variables, COVID-EMV would significantly predict worse levels of anxiety and depression and a poorer perceived cognitive function in women living with a diagnosis of primary breast cancer. It was similarly predicted that the threat and uncertainty induced by COVID-19 to job security would predict worse perceived cognitive function and increased vulnerability to anxiety and depression. Finally, it was predicted that there would be significant differences in women's perceptions of work depending on their COVID-19-generated employment status (i.e., 'continued' working or furloughed).

## 7.3. **Method**

### 7.3.1. **Design**

A cross-sectional survey design was utilised. The study was approved by the Research Ethics Committee of the Department of Psychological Sciences, the College Research Ethics Committee at Birkbeck College, University of London, and the Economic and Social Research Council (see **Chapter 2 section 2.2** for a more comprehensive description of ethical procedures).

### 7.3.2. **Participants**

Participants were recruited using voluntary sampling via advertisements placed on social media platforms including Facebook and Twitter during the peak of the COVID-19 outbreak in the UK. Participants completed the online questionnaires between the 9th of April and the 26th of May 2020.

Inclusion criteria for this study included: (1) aged 18 years or older, (2) a diagnosis of breast cancer, (3) at any stage of active treatment, hormone blocker therapy or target therapy and (4) employed, self-employed, undertaking voluntary work or not undertaking any work at the time of recruitment.

### 7.3.3. **Materials**

Sociodemographic and clinical information was self-reported using the ***Demographic and Clinical Questionnaire*** (***GDQ***). The GDQ comprises of 29-items relating to breast cancer history, sociodemographic factors, psychiatric history and employment.

Perceived cognitive function was measured using the ***Functional Assessment of Cancer Therapy-Cognitive Scale*** (***FACT-Cog,*** *Version 3;* Wagner et al., 2009**)**. Higher scores indicate a better perceived cognitive function. Excellent reliability was found in the current study: Cronbach's α =.97.

The FACT-Cog total score was selected as the variable of interest to increase power in the analysis [16](see **Chapter 2 section 2.4.2** for more detail).

Rumination was measured by the ***Rumination Response Scale*** (***RRS****;* Treynor et al., 2003). A greater score indicates a higher level of rumination. The RRS showed excellent reliability in the current study: Cronbach's α = .94 (see **Chapter 2 section 2.4.3** for more detail).

Anxiety and depression were assessed using the ***Hospital Anxiety and Depression Scale*** (***HADS****;* Zigmond & Snaith, 1983). Greater scores on each of the subscales reflect a worse severity of symptomology. Good reliability was found in the current study: total score: Cronbach's α = .89, anxiety: Cronbach's α = .86, depression: Cronbach's α = .82 (see **Chapter 2 section 2.4.4** and **section 2.4.5** for more detail).

Worry was assessed using the ***Penn State Worry Questionnaire*** (***PSWQ****;* Meyer et al., 1990). A higher score reflects greater pathological worry. The PSWQ had excellent reliability in the current study: Cronbach's α = .94 (see **Chapter 2 section 2.4.7** for more detail).

Comorbidity was measured by the ***Modified Self-Report-Generated Charlson Comorbidity*** (***CCI****;* Charlson et al. 1987). A greater score indicates worse comorbidity (see **Chapter 2 section 2.4.8** for more detail).

The impact of COVID-19 was measured by 24 individual items referred to as the ***COVID-19 Impact Questions.*** A composite score derived from the five emotional vulnerability items was formed and referred to as COVID-EMV. Higher scores indicate a higher level of COVID-19-generated emotional vulnerability. Good reliability was shown for the current study: Cronbach's α = .89 (see **appendix 3** for item reliability, factor analysis and COVID-EMV correlations; see **Chapter 2 section 2.4.13** for more detail).

The impact of COVID-19 on work was assessed by eight individual questions referred to as the ***COVID-19 Work Items***. Higher scores indicate more positive views of work and greater employer

[16] In line with the recommendation from FACIT.org individual item-total score correlation coefficients were explored for PCI, PCA and FACT-Cog total. Results confirmed that all 37-items should be included in the total score and analysis.

support. Good reliability was found in the current study: Cronbach's α = .74. Individual items were used in the analysis (see **Chapter 2 section 2.4.13** for more detail).

Work productivity loss was assessed using the ***Work Limitations Questionnaire*** (***WLQ***; Lerner et al, 2001; 2003). A higher score reflects a greater loss of work productivity in the last 14 days. The WLQ showed excellent reliability in the current study: Cronbach's α = .97 (see **Chapter 2 section 2.4.9** for more detail).

### 7.3.4. **Procedure**

Participants who responded by email to one of the study advertisements placed on social media platforms including Facebook, Twitter and Instagram were sent a return email containing the study information and a secure URL link to access the series of online questionnaires presented on Gorilla Experimental Builder (www.gorilla.sc). All participants were asked to provide online consent before being redirected to the GDQ followed by the cognitive and emotional health questionnaires, as well as the COVID-19 impact questions. Participants who reported being employed, self-employed or undertaking volunteering work at the time of the study were asked to additionally complete the work-related questions (WLQ, COVID-19 work items). A £5 gift voucher and debrief document were emailed upon completion.

## 7.4. **Statistical Analysis**

Statistical analyses were conducted with IBM Statistical Package for the Social Sciences (IBM SPSS, version 25). Descriptive statistics were produced for participants' sociodemographic characteristics, breast cancer and treatment characteristics, work-related characteristics and history of psychological disorders (see **table 7.1** for participant demographic information).

To address the first aim of the study, a series of 2x2 analysis of variance (ANOVAs) were performed to investigate the main effects of the UK Government shielding letter and disruption to

scheduled oncology services and its interaction effect on women's self-reported COVID-19-related emotional vulnerability (COVID-EMV), anxiety, depression and perceived cognitive function. Hierarchical regression analyses were then performed to investigate the relationships between COVID-EMV and three dependent variables including anxiety, depression and perceived cognitive function after allowing for the effects of key sociodemographic and clinical factors. Step 1 included grade, active treatment status, time since diagnosis, age at diagnosis, education and health co-morbidities (as measured by CCI). Measures of rumination and pathological worry were then added in step 2 and COVID-EMV was added as the final predictor on step 3.

Using analysis of standardised residual, no outliers were identified (**Anxiety**: std Residual Min = -2.3, std Residual Max = 2.5, std deviation = .98; **Depression**: std Residual Min = -2.6, std Residual Max = 3.1, std deviation = .98; **Perceived cognitive function**: std Residual Min = -2.7, std Residual Max = 2.6, std deviation = .98). Checks for violations of the assumptions of collinearity, independent error, normality, homoscedasticity and linearity were also conducted and all assumptions were met. Post hoc achieved power calculations using Cohen's $f^2$ and a significance of .05 were performed using G*Power software (Faul et al., 2007, 2009).

To address the second aim of the study, a series of one-way ANOVAs were then performed to explore the impact of employment status (i.e., working, not working due to COVID-19 or never working) on perceived cognitive function, anxiety and depression, as well as COVID-EMV. Partial eta squared effect sizes were calculated. Independent t-tests were performed to examine the effects of employment type (employed vs. self-employed) on levels of anxiety and depression during this outbreak. Furthermore, independent t-tests were also conducted to explore the effects of COVID-19 generated work status (i.e., continued working or furloughed) on employer support, the importance of work and job security. Cohen's *d* effect sizes were calculated. Post hoc analyses were conducted using G*Power software (Faul et al., 2007, 2009). Following this, hierarchical regression analyses were performed to explore the relationship of women's job security to four dependent variables including, perceived cognitive function, anxiety, depression and emotional distress after allowing for clinical and sociodemographic predictors, as well as employment type (i.e., employed, self-employed or

volunteering). On the first step, seven predictors including education, age at diagnosis, time since diagnosis (months), treatment status, grade, pre-existing co-morbidities (as assessed by the CCI) and employment type were added. Rumination, worry and COVID-19-EMV were then entered on step 2. Finally, job security was included in step 3. Cohen's $f^2$ effect sizes were calculated for each of the regressions.

Assessing standardised residuals, no outliers were found in the four regression analyses: **anxiety** (std Residual Min = -2.4, std Residual Max = 2.6), **depression** (std Residual Min = -2.3, std Residual Max = 2.9), **emotional distress** (std Residual Min = -2.2, std Residual Max = 2.7) and **perceived cognitive function** (std Residual Min = -2.6, std Residual Max = 2.4). In addition, no violations of the assumptions of collinearity, independent error, normality, homoscedasticity and linearity were found. Post hoc achieved power calculations were carried out with G*Power software (Faul et al., 2007, 2009) using Cohen's $f^2$ and a significance of .05.

Finally, moderation analyses were conducted to explore the moderating role of perceived cognitive function on job security in predicting anxiety and depression. Perceived cognitive function and self-reported job security were mean-centred. Checks for violations of the assumption of heteroscedasticity were performed and all standard errors in the model were based on the Heteroscedasticity Consistent Standard Error (HC1).

No missing questionnaire data was found for the FACT-Cog, HADS, RRS, PSWQ, CCI and COVID-EMV. Scores for the four subscales of the WLQ were calculated if half or more of the scale's questions had been answered (see **Chapter 2 section 2.4.9** for more detail). Missing data in the WLQ was likely due to the COVID-19-induced work changes. Only 13 participants who were employed but furloughed or unable to work as a result of the COVID-19 outbreak failed to complete the individual COVID-19 work items. These participants were excluded from the analysis examining these items as scale and person-specific means were unable to be computed and substituted for the missing items.

## 7.5. **Results**

### 7.5.1. **Sample characteristics**

**Table 7.1** presents the demographic, clinical and work-related characteristics of the 234 women recruited. Women had a mean age of 51 years (*SD* = 7.9, *range* = 27-78) at the time of the study and a mean age of 47 years (*SD* = 7.7, *range* = 24-77) at the time of diagnosis. Approximately 23% (54 women) had received a UK Government shielding letter, 32% (74 women) had been affected by disruptions to scheduled oncology services (i.e., cancelled or delayed appointments) and 10% (24 women) had received the shielding letter ***and*** experienced disruption to scheduled oncology services or appointments. Only 15% (35 out of 234) reported that they had shown COVID-19-related symptoms. Approximately 10% of symptoms reported were fever and/or cough. None of these participants reported that they had received an official diagnosis of COVID-19.

Most of the women reported that they were employed (147, 63%), self-employed (25, 11%) or volunteering (14, 6%) before the outbreak of COVID-19. As a result of the outbreak, 50 (21%) participants reported they were no longer working or had been furloughed, whilst 127 (54%) had continued to work, but with appropriate adaptations to meet the restrictive or protective measures put in place by the UK Government. In women who had continued to work a work productivity loss of approximately 8% was found (measured by the WLQ).

**Table 7.1**

*Participant sociodemographic, clinical and work-related characteristics*

| | ***N = 234 (%)*** |
|---|---|
| ***Sociodemographic*** | |
| Age | Mean = 51 (Range 27-78) |
| | |
| *Education* | |
| Secondary education | 26 (11.1) |
| Further education | 50 (21.4) |
| Higher education | 152 (65.0) |
| Other | 6 (2.6) |

| | |
|---|---|
| *Ethnicity* [a] | |
| White | 222 (94.9) |
| Black | 3 (1.3) |
| Asian | 5 (2.1) |
| Multi-ethnic | 3 (1.3) |
| | |
| *Civil Status*[b] | |
| Married/Civil Partnership/Cohabiting | 173 (73.9) |
| Divorced/Separated | 19 (8.1) |
| Single/Widowed | 38 (16.2) |
| | |
| ***Work*** | |
| *Employment status* | |
| Employed | 147 (62.8) |
| Self-employed | 25 (10.7) |
| Undertaking volunteering work | 14 (6.0) |
| Not undertaking any form of work | 48 (20.5) |
| | |
| ***Clinical - Breast Cancer History*** | |
| Age at diagnosis | Mean = 47 (Range 24-77) |
| | |
| Time since diagnosis (months) | Mean = 51.46 (Range 0-177) |
| | |
| *Grade*[c] | |
| Grade 1 | 28 (12.0) |
| Grade 2 | 86 (36.8) |
| Grade 3 | 117 (50.0) |
| | |
| *Active Treatment* | |
| Yes | 15 (6.4) |
| No | 215 (91.9) |
| Due to Start | 2 (0.9) |
| Other | 2 (0.9) |
| | |
| *Type of Treatment Received*[d] | |

| | |
|---|---|
| Chemotherapy | 171 (73.1) |
| Radiotherapy | 186 (79.5) |
| Surgery | |
| Mastectomy | 97 (41.5) |
| Lumpectomy | 98 (41.9) |
| Mastectomy & Lumpectomy | 23 (9.8) |
| | |
| *Endocrine Therapy* | |
| Yes | 161 (68.8) |
| No | 63 (26.9) |
| Other (i.e., Prescribed but decided not to take it) | 10 (4.3) |
| | |
| Time since completion of treatment (months) | Mean = 38 (Range 0-140) |
| | |
| History of Psychological Condition | 100 (42.7) |
| | |
| Prescribed medication for conditions other than cancer | 49 (20.9) |

*Note.* [a] One participant did not disclose their ethnicity, [b] Four participants did not disclose their civil status, [c]Three participants did not state the grade of their breast cancer, [d]One participant did not disclose the treatment they received

### 7.5.2. **Effect of oncology service disruptions and the UK government shielding letter**

A series of 2x2 ANOVAs were performed to examine the main effects of the UK Government shielding letter and disruption to oncology services, as well as the interaction effect between the shielding letter and disruption to oncology services on women's self-reported COVID-EMV, anxiety, depression and cognitive function. Results show that disruption to scheduled oncology services had a significant main effect on women's COVID-EMV ($F$ (1, 230) = 9.68, $p$ = .002), anxiety ($F$ (1, 230) = 5.69, $p$ = .02) and depression ($F$ (1, 230) = 7.22, $p$ =.01), with women who experienced a service disruption showing greater general emotional vulnerability and COVID-EMV (see **table 7.2** for

questionnaire scores). They also perceived having a poorer cognitive function, however, the effect was non-significant *(p* = .10). No main effect of the UK Government shielding letter on COVID-EMV, anxiety or depression was found, however, there was a significant effect with self-reported cognitive function (*F* (1, 230) = 6.69, *p* =.01), with those who received the shielding letter reporting a worse perceived cognitive function (see **table 7.2** for questionnaire scores). The interaction effect between disruption to scheduled oncology services and the UK Government shielding letter was not significant for any of the dependent variables of interest (all *p*'s > .05) (see **table 7.3** for ANOVA main effects and interaction effects).

**Table 7.2**

*Means and standard deviations for self-reported cognitive and emotional health as well as COVID-EMV*

| | Disruption to oncology services | | No disruption to oncology services | | Received shielding letter | | No shielding letter | |
|---|---|---|---|---|---|---|---|---|
| | M | SD | M | SD | M | SD | M | SD |
| Perceived cognitive function (FACT-Cog-Total) | 82.1 | 29.8 | 90.5 | 28.7 | 78.1 | 29.3 | 90.8 | 28.7 |
| Anxiety (HADS-A) | 10.4 | 4.6 | 9.1 | 4.4 | 10.3 | 5.0 | 9.3 | 4.3 |
| Depression (HADS-D) | 7.8 | 4.4 | 6.4 | 3.8 | 7.7 | 4.3 | 6.6 | 3.9 |
| COVID-Generated Emotional Vulnerability (COVID-EMV) | 16.4 | 6.2 | 13.7 | 6.6 | 15.6 | 7.2 | 14.2 | 6.4 |
| Rumination (RRS) | 49.5 | 14.2 | 45.5 | 14.2 | 49.5 | 15.6 | 45.9 | 13.8 |
| Pathological worry (Pen State Worry) | 54.6 | 14.6 | 50.0 | 14.8 | 52.9 | 15.6 | 51.0 | 14.7 |

*Note.* [a] Perceived cognitive function (FACT-Cog total): higher score = better perceived cognitive function; Anxiety and depression (HADS): higher score = worse anxiety and depression; COVID-related emotional vulnerability (COVID-EMV): higher score = greater level of COVID-EMV: Rumination (RRS): higher score = greater rumination; Pathological worry (PSWQ): higher score = greater level of pathological worry

**Table 7.3**

*ANOVA results using disruption to oncology services and UK Government shielding letter as predictors*

| | Sum of Squares | *df* | Mean Square | *F* | *P* |
|---|---|---|---|---|---|
| ***Anxiety*** | | | | | |
| Intercept | 15314.11 | 1 | 15314.11 | 774.31 | 0.00 |
| Disruption to oncology services | 112.58 | 1 | 112.58 | 5.69 | 0.02 |
| Government shielding letter | 27.93 | 1 | 27.93 | 1.41 | 0.24 |
| Disruption to oncology Services x government shielding letter | 42.26 | 1 | 42.26 | 2.14 | 0.15 |
| Error | 4548.91 | 230 | 19.78 | | |
| ***Depression*** | | | | | |
| Intercept | 8344.03 | 1 | 8344.03 | 528.22 | 0.00 |
| Disruption to oncology services | 113.97 | 1 | 113.97 | 7.22 | 0.01 |
| Government shielding letter | 44.08 | 1 | 44.08 | 2.79 | 0.10 |
| Disruption to oncology Services x government shielding letter | 33.17 | 1 | 33.17 | 2.10 | 0.15 |
| Error | 3633.17 | 230 | 15.80 | | |
| ***COVID-EMV*** | | | | | |
| Intercept | 36269.65 | 1 | 36269.65 | 863.77 | 0.00 |
| Disruption to oncology services | 406.42 | 1 | 406.42 | 9.68 | 0.00 |
| Government shielding letter | 57.05 | 1 | 57.05 | 1.36 | 0.25 |
| Disruption to oncology Services x government shielding letter | 65.3 | 1 | 65.30 | 1.56 | 0.21 |
| Error | 9657.67 | 230 | 41.99 | | |

| | | | | | |
|---|---|---|---|---|---|
| ***Perceived cognitive function*** | | | | | |
| Intercept | 1086389.00 | 1 | 1086389.00 | 1314.69 | 0.00 |
| Disruption to oncology services | 2305.93 | 1 | 2305.93 | 2.79 | 0.10 |
| Government shielding letter | 5529.04 | 1 | 5529.04 | 6.69 | 0.01 |
| Disruption to oncology Services x government shielding letter | 128.20 | 1 | 128.20 | 0.16 | 0.69 |
| Error | 190059.94 | 230 | 826.35 | | |

### 7.5.3. **Impact of COVID-19-related emotional vulnerability on general cognitive and emotional health** [17]

***Anxiety*** - On step 1, demographic and clinical factors (education, grade, active treatment status, age at diagnosis, time since diagnosis and health co-morbidity) accounted for 3.6% of the variance in anxiety (see **table 7.4** for hierarchical regression). When rumination and pathological worry were added in step 2 an additional 52.4% of the variance was explained, with both rumination and worry acting as significant predictors ($p$ <.001). On the final step, COVID-EMV predicted significant variance in anxiety with an $R^2$ (change) of 8.9% ($t$ (221) = 7.50, $p$ <.001). Higher COVID-EMV met with greater anxiety. Cohen's $f^2$ = 1.44 and achieved statistical power (1-ß err prob) = 0.99.

***Depression*** – Analysis shows that the six demographic and clinical predictors entered on step 1 accounted for a moderate 6.6% of the variance in depression (see **table 7.4** for hierarchical regression). When measures of worry and rumination were entered, step 2 explained a further 33.5% of the variance, with both rumination and worry acting as significant predictors ($p$ <.05). In the final step, COVID-EMV

[17] Analysis showed that excluding women who reported experiencing a COVID-19 related symptom(s) had no effect on the significance of predictors included in the three regression models. Thus, it was decided to include all participants in the analyses.

added a further 3.1% in explaining depression after allowing for the other variables ($t$ (221) = 3.50, $p$ = .001). Greater COVID-EMV met with worse depression. Comorbidity was also a significant predictor on the third step ($p$ =.01). Cohen's $f^2$ = 0.59 and achieved statistical power (1-ß err prob) = 0.99.

***Perceived cognitive function*** – As **table 7.4** shows, demographic and clinical predictors explained 5.4% of the variance in perceived cognitive function. When rumination and worry were then entered in step 2 an extra 21.9% of the variance was explained, with rumination acting as a significant predictor ($p$ <.001). On the third step, COVID-EMV predicted significant variance in perceived cognitive function with an $R^2$ (change) of 3.3% ($t$ (221) = -3.25, $p$ =.001). Poorer self-reported cognitive function met a higher level of COVID-EMV. Cohen's $f^2$ = 0.33 and achieved statistical power (1-ß err prob) = 0.99.

**Table 7.4**

*Hierarchical regression analyses for the predictors of anxiety, depression and perceived cognitive function*

| | ***b*** | ***SE B*** | **β** | ***t*** | ***p*** |
|---|---|---|---|---|---|
| **Anxiety** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 12.15 (5.68, 18.63) | 3.29 | | 3.70 | .00 |
| Education | -0.70 (-1.52, 0.13) | 0.42 | -.11 | -1.67 | .10 |
| Grade | 0.22 (-0.63, 1.06) | 0.43 | .03 | 0.50 | .62 |
| Active treatment status | 1.23 (-0.58, 3.03) | 0.92 | .09 | 1.34 | .18 |
| Age at diagnosis | -0.05 (-0.13, 0.03) | 0.04 | -.08 | -1.25 | .21 |
| Time since diagnosis (months) | -0.02 (-0.04, 0.00) | 0.01 | -.12 | -1.76 | .08 |
| Charlson Co-morbidity Index | 0.15( -0.49, 0.79) | 0.32 | .03 | 0.46 | .65 |
| $R^2$ = .04 | | | | | |
| $\Delta F$ (6, 224) = 1.38 | | | | | |
| $p$ = .23 | | | | | |
| ***Step 2*** | | | | | |
| Constant | -1.27 (-5.97, 3.44) | 2.39 | | -0.53 | .60 |
| Education | -0.43 (-0.99, 0.13) | 0.28 | -.07 | -1.5 | .14 |

| | | | | | |
|---|---|---|---|---|---|
| Grade | -0.1 (-0.68, 0.48) | 0.29 | .06 | -0.35 | .73 |
| Active treatment status | 0.02 (-1.23,1.26) | 0.63 | .00 | 0.02 | .98 |
| Age at diagnosis | -0.01 (-0.07, 0.04) | 0.03 | -.03 | -0.53 | .59 |
| Time since diagnosis (months) | 0.01 (-0.01, 0.02) | 0.01 | .04 | 0.84 | .40 |
| Charlson Co-morbidity Index | 0.08 (-0.36, 0.51) | 0.22 | .02 | 0.34 | .74 |
| Rumination (RRS) | 0.13 (0.10, 0.16) | 0.02 | .42 | 7.6 | .00 |
| Pathological worry | 0.13 (0.10, 0.16) | 0.02 | .44 | 8.31 | .00 |
| $\Delta R^2$ =.52 | | | | | |
| $\Delta F$ (2, 222) = 132.12 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | -2.15 (-6.37, 2.07) | 2.41 | | -1.01 | .32 |
| Education | -0.40(-0.90, 0.10) | 0.25 | -.06 | -1.57 | .12 |
| Grade | -0.11 (-0.62, 0.41) | 0.26 | -.02 | -0.4 | .69 |
| Active treatment status | 0.62 (-0.51, 1.74) | 0.57 | .05 | 1.08 | .28 |
| Age at diagnosis | -0.02 (-0.07, 0.03) | 0.02 | -.03 | -0.76 | .45 |
| Time since diagnosis (months) | 0.01 (0.00, 0.02) | 0.01 | .08 | 1.89 | .06 |
| Charlson Co-morbidity Index | 0.16 (-0.23, 0.55) | 0.20 | .03 | 0.83 | .41 |
| Rumination (RRS) | 0.09 (0.06, 0.12) | 0.02 | .28 | 5.35 | .00 |
| Pathological worry | 0.08 (0.05, 0.11) | 0.02 | .27 | 5.24 | .00 |
| COVID-EMV | 0.28 (0.20, 0.35) | 0.04 | .41 | 7.50 | .00 |
| $\Delta R^2$ =.09 | | | | | |
| $\Delta F$ (1, 221) = 56.22 | | | | | |
| $p$ <.001 | | | | | |
| | | | | | |
| **Depression** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 10.83 (5.08, 16.59) | 2.92 | | 3.71 | .00 |
| Education | -0.42 (-1.15, 0.31) | 0.37 | -.07 | -1.13 | .26 |
| Grade | 0.65 (-0.10, 1.40) | 0.38 | .11 | 1.70 | .09 |
| Active treatment status | -0.13 (-1.73, 1.48) | 0.81 | -.01 | -0.16 | .88 |
| Age at diagnosis | -0.07 (-0.14, 0.00) | 0.04 | -.12 | -1.87 | .06 |
| Time since diagnosis (months) | -0.02 (-0.04, -0.00) | 0.01 | -.17 | -2.51 | .01 |
| Charlson Co-morbidity Index | 0.65 (0.08, 1.21) | 0.29 | .15 | 2.24 | .03 |
| $R^2$ = .07 | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| $\Delta F$ (6, 224) =2.63 | | | | | |
| $p$ =.02 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 2.18 (-2.78 7.13) | 2.51 | | 0.87 | .39 |
| Education | -0.25 (-0.84, 0.34) | 0.30 | -.04 | -0.82 | .41 |
| Grade | 0.33 (-0.28, 0.94) | 0.31 | .06 | 1.07 | .29 |
| Active treatment status | -1.23 (-2.54, 0.08) | 0.67 | -.10 | -1.85 | .07 |
| Age at diagnosis | -0.04 (-0.10, 0.01) | 0.03 | -.08 | -1.48 | .14 |
| Time since diagnosis (months) | -0.00 (-0.02, 0.01) | 0.01 | -.02 | -0.32 | .75 |
| Charlson Co-morbidity Index | 0.53 (0.08, 0.99) | 0.23 | .12 | 2.30 | .02 |
| Rumination (RRS) | 0.14 (0.10, 0.18) | 0.02 | .49 | 7.72 | .00 |
| Pathological worry | 0.05 (0.01, 0.08) | 0.02 | .18 | 2.84 | .01 |
| $\Delta R^2$ = .36 | | | | | |
| $\Delta F$ (2, 222) = 62.03 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | 1.70 (-3.14, 6.54) | 2.46 | | 0.69 | .49 |
| Education | -0.23 (-0.81, 0.36) | 0.29 | -.04 | -0.79 | .43 |
| Grade | 0.33 (-0.27, 0.92) | 0.30 | .06 | 1.09 | .28 |
| Active treatment status | -0.91 (-2.20, 0.38) | 0.66 | -.07 | -1.39 | .17 |
| Age at diagnosis | -0.04 (-0.10, 0.01) | 0.03 | -.08 | -1.59 | .11 |
| Time since diagnosis (months) | 0.00 (-0.01, 0.01) | 0.01 | .01 | 0.13 | .90 |
| Charlson Co-morbidity Index | 0.58 (0.14, 1.03) | 0.23 | .14 | 2.56 | .01 |
| Rumination (RRS) | 0.12 (0.08, 0.15) | 0.02 | .41 | 6.20 | .00 |
| Pathological worry | 0.02 (-0.02, 0.06) | 0.02 | .08 | 1.16 | .25 |
| COVID-EMV | 0.15 (0.07, 0.23) | 0.04 | .24 | 3.50 | .00 |
| $\Delta R^2$ =.03 | | | | | |
| $\Delta F$ (1, 221) = 12.24 | | | | | |
| $p$ <.001 | | | | | |
| **Perceived cognitive function** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 93.04 (51.05,135.04) | 21.31 | | 4.37 | .00 |
| Education | 2.38 (-2.96, 7.72) | 2.71 | .06 | 0.88 | .38 |
| Grade | -5.66 (-11.15, -0.18) | 2.78 | -.13 | -2.04 | .04 |

| | | | | | |
|---|---|---|---|---|---|
| Active treatment status | -8.83 (-20.55, 2.88) | 5.95 | -.10 | -1.49 | .14 |
| Age at diagnosis | 0.31 (-0.20, 0.82) | 0.26 | .08 | 1.21 | .23 |
| Time since diagnosis (months) | 0.10 (-0.02, 0.22) | 0.06 | .11 | 1.65 | .10 |
| Charlson Co-morbidity Index | -3.87 ( -8.01, 0.27) | 2.10 | -.12 | -1.84 | .07 |
| $R^2$ = .05 | | | | | |
| $\Delta F$ (6,224) = 2.13 | | | | | |
| $p$ =.05 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 138.18 (98.62, 177.74) | 20.08 | | 6.88 | .00 |
| Education | 1.46 (-3.25, 6.17) | 2.39 | .04 | 0.61 | .54 |
| Grade | -3.55 (-8.41, 1.32) | 2.47 | -.08 | -1.44 | .15 |
| Active treatment status | -1.78 (-12.26, 8.70) | 5.32 | -.02 | -0.34 | .74 |
| Age at diagnosis | 0.18 (-0.27, 0.63) | 0.23 | .05 | 0.80 | .43 |
| Time since diagnosis (months) | -0.02 (-0.12, 0.09) | 0.06 | -.02 | -0.28 | .78 |
| Charlson Co-morbidity Index | -3.04 (-6.69, 0.62) | 1.86 | -.01 | -1.64 | .10 |
| Rumination (RRS) | -0.95 (-1.24, -0.67) | 0.14 | -.46 | -6.60 | .00 |
| Pathological worry | -0.09 (-0.36, 0.17) | 0.13 | -.05 | -0.70 | .48 |
| $\Delta R^2$ =.22 | | | | | |
| $\Delta F$ (2, 222) =33.52 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | 141.70 (102.91, 180.50) | 19.69 | | 7.20 | .00 |
| Education | 1.35 (-3.26, 5.97) | 2.34 | .03 | 0.58 | .56 |
| Grade | -3.53 (-8.30, 1.23) | 2.42 | -.08 | -1.46 | .15 |
| Active treatment status | -4.17(-14.53, 6.19) | 5.26 | -.05 | -0.79 | .43 |
| Age at diagnosis | 0.20 (-0.24, 0.64) | 0.22 | .05 | 0.89 | .38 |
| Time since diagnosis (months) | -0.04 (-0.15, 0.07) | 0.05 | -.04 | -0.70 | .48 |
| Charlson Co-morbidity Index | -3.39 (-6.98, 0.20) | 1.82 | -.11 | -1.86 | .06 |
| Rumination (RRS) | -0.78 (-1.08, -0.49) | 0.15 | -.38 | -5.19 | .00 |
| Pathological worry | 0.10 (-0.8, 0.40) | 0.14 | .05 | 0.73 | .47 |
| COVID-EMV | -1.10 (-1.77, -0.43) | 0.34 | -.25 | -3.25 | .00 |
| $\Delta R^2$ = .03 | | | | | |
| $\Delta F$ (1, 221) =10.53 | | | | | |
| $p$ =.001 | - | | | | |

*Note.* (95% Confidence Intervals)

Checks for violation of assumptions using residuals revealed that assumptions of collinearity (Tolerance > 0.1, VIF < 10), independent error (**General anxiety**: Durbin-Watson = 2.0; **General depression**: Durbin-Watson = 2.1; **Perceived cognitive function**: Durbin-Watson= 2.1), normality and homogeneity of variance and linearity were met for anxiety, depression and perceived cognitive function.

### 7.5.4. **Impact of employment status on emotional vulnerability and perceived cognitive function**

One-way ANOVAs were carried out to explore the effect of employment status (i.e., 'continued' working, not working as a result of COVID-19 or not working before the outbreak) on levels of anxiety, depression, perceived cognitive function and COVID-EMV. Results show a non-significant effect of employment status on women's level of anxiety ($F<1$, *ns*), depression ($F$ (2, 231) = 1.39, *ns,* $\eta^2$ *partial* = 0.01) and perceived cognitive function ($F$ (2, 231) = 1.57, *ns,* $\eta^2$ *partial = 0.01*). There was, however, a trend towards significance for COVID-EMV (Working: $M$ = 14.58, $SD$ = 6.90; Furloughed or unable to work: $M$ = 12.96, $SD$ =5.61; Never working: $M$= 15.84, $SD$ = 6.60, $F$ (2, 231) = 2.58, $p$ = .08, $\eta^2$ *partial* = 0.02), with women who were never working showing the worse COVID-EMV. Post hoc analyses show that the achieved statistical power (1-ß err prob) was greater than 0.95 for all of the one-way ANOVAs performed.

Moreover, independent t-tests examining the effects of employment type show non-significant differences in the level of anxiety and depression ($t$ < 1, *ns*) experienced by employed or self-employed women living with breast cancer (see **table 7.5** for descriptive statistics).

**Table 7.5**

*Means and standard deviations for symptomology measured*

| | Employed | | Self-Employed | |
|---|---|---|---|---|
| | *M* | *SD* | *M* | *SD* |
| Anxiety[a] | 9.4 | 4.7 | 9.5 | 4.1 |
| Depression | 6.7 | 4.0 | 6.9 | 4.2 |
| Perceived cognitive function | 88.5 | 29.4 | 86.5 | 26.6 |
| Rumination | 47.6 | 14.4 | 44.2 | 14.6 |
| Pathological worry | 52.1 | 14.6 | 51.2 | 17.1 |

*Note.* [a] Perceived cognitive function (FACT-Cog total): higher score = better perceived cognitive function; Anxiety and depression (HADS): higher score = worse anxiety and depression; Rumination (RRS): higher score = greater rumination; Pathological worry (PSWQ): higher score = greater level of pathological worry

### 7.5.5. **Impact of COVID-19 generated work status on perceptions of work**

There was a significant difference in the view of the importance of work ($t$ (54.27) = 2.01, $p$ = .05, $d$ = .38) between women who 'continued' to work ($M$ = 2.83, $SD$ = 1.39) during the COVID-19 outbreak and those who had been furloughed or unable to work ($M$ = 2.27, $SD$ = 1.54). Women who 'continued' to work reported having a higher view of the importance of work. Similarly, there was a significant difference ($t$ (54.35) = 3.44, p <.01, $d$ = .66) found for the level of job security, with women who 'continued' to work ($M$ = 2.54, $SD$ = 1.44) reporting a greater job security compared to those unable to work or furloughed *(*$M$ = 1.54, $SD$ = 1.59) as a consequence of the COVID-19 outbreak.

### 7.5.6. **Impact of COVID-19 induced job insecurity on general emotional and cognitive functioning**

***Depression*** -As **table 8.6** shows, clinical, sociodemographic and employment type predictors entered on step 1 explained a modest 5.1% of the variance in depression scores. When measures of

worry, rumination and COVID-EMV were then added on step 2, the model explained an additional 35.9% of the variance, with both rumination ($p$ <.001) and COVID-EMV ($p$ <.05) acting as significant predictors. On step 3, job security significantly predicted depression ($t$ (157) = 2.20, $p$ =.03) after allowing for the effects of the other predictors, with the overall model predicting approximately 43% of the variance in depression. A higher level of job security met with a lower level of depression. Cohen's $f^2$ = 0.63 and achieved statistical power (1-ß err prob) = 0.99.

***Anxiety -*** Analysis shows that the seven demographic variables included in step 1 accounted for a moderate 6.6% of the variance in anxiety scores (see **table 7.6** for the hierarchical regression). After worry, rumination and COVID-EMV were entered on step 2, an additional 59.5% of the variance was explained, with all three acting as significant predictors ($p$ <.001). On the final step, women's job security fell short of explaining anxiety ($t$ (157) = 1.35, $p$ = .18). Overall, approximately 66% of the variance was explained by the models in predicting anxiety Cohen's $f^2$ = 1.78 and achieved statistical power (1-ß err prob) = 0.99.

***Emotional distress*** **- Table 7.6** shows that when the clinical, sociodemographic and employment type predictors were entered on step 1, they accounted for a modest 6.1% of the variance in emotional distress (as measured by the HADS-total). When worry, rumination and COVID-EMV were added on step 2, the model explained an additional 57.8% of the variance, with all three acting as significant predictors ($p$ <.05). On step 3, job security significantly predicted emotional distress ($t$ (157) = 2.24, $p$ =.03) after allowing for the effects of the other predictors, with the overall model predicting 65% of the variance in emotional distress. Greater job security met with a lower level of emotional distress. Cohen's $f^2$ = 1.66 and achieved statistical power (1-ß err prob) = 0.99.

***Perceived cognitive function*** – As **table 7.6** shows, the seven demographic variables added in step 1 account for a small 4.5% of the variance in perceived cognitive function. After worry, rumination and COVID-EMV were entered in step 2, the explained variance increased by 23.2%, with both rumination and COVID-EMV acting as significant predictors ($p$. <.05). In step 3, job security was a

significant predictor of perceived cognitive function ($t$ (157) = 2.16, $p$ =.03) after allowing for the effects of the clinical, sociodemographic and employment type predictors. Overall, approximately 30% of the variance was explained. Higher job security was associated with better perceived cognitive function. Cohen's $f^2$ = 0.33 and achieved statistical power (1-ß err prob) = 0.99.

**Table 7.6**

*Hierarchical regression analyses for anxiety, depression, emotional distress, and perceived cognitive function*

| | *b* | *SE B* | β | *t* | *p* |
|---|---|---|---|---|---|
| **Depression** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 12.58 (5.32, 19.85) | 3.68 | | 3.42 | .00 |
| Education | -0.41 (-1.34, 0.53) | 0.47 | -.07 | -0.86 | .39 |
| Grade | 0.45 (-0.47, 1.37) | 0.47 | .08 | 0.96 | .34 |
| Active treatment status | -0.68 (-2.78, 1.42) | 1.06 | -.05 | -0.64 | .52 |
| Age at diagnosis | -0.06 (-0.15, 0.03) | 0.05 | -.10 | -1.23 | .22 |
| Time since diagnosis (in months) | -0.02 (-0.04, 0.01) | 0.01 | -.13 | -1.51 | .13 |
| Charlson Co-morbidity Index | -0.11 (-0.92, 0.70) | 0.41 | -.02 | -0.27 | .79 |
| Employment type | -0.62 (-1.73, 0.49) | 0.56 | -.09 | -1.10 | .27 |
| $R^2$ = .05 | | | | | |
| $\Delta F$ (7,161) = 1.24 | | | | | |
| $p$ = .28 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 1.59 (-4.78, 7.96) | 3.22 | | 0.49 | .62 |
| Education | -0.04 (-0.80, 0.71) | 0.38 | -.01 | -0.11 | .91 |
| Grade | 0.15 (-0.59, 0.89) | 0.38 | .03 | 0.40 | .69 |
| Active treatment status | -1.32 (-3.02, 0.39) | 0.87 | -.10 | -1.52 | .13 |
| Age at diagnosis | -0.02 (-0.09, 0.05) | 0.04 | -.04 | -0.53 | .60 |
| Time since diagnosis (in months) | 0.01 (-0.01, 0.02) | 0.01 | .04 | 0.63 | .53 |
| Charlson Co-morbidity Index | 0.21 (-0.44, 0.86) | 0.33 | .04 | 0.63 | .53 |
| Employment type | -0.36 (-1.25, 0.53) | 0.45 | -.05 | -0.80 | .43 |
| Pathological worry | 0.02 (-0.03, 0.06) | 0.02 | .06 | 0.69 | .49 |
| Rumination (RRS) | 0.12 (0.08, 0.17) | 0.02 | .44 | 5.39 | .00 |
| COVID-EMV | 0.13 (0.03, 0.24) | 0.05 | .22 | 2.50 | .01 |

| | | | | | |
|---|---|---|---|---|---|
| $\Delta R^2$ = .36 | | | | | |
| $\Delta F$ (3, 158) = 32.07 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | 2.54 (-3.81, 8.89) | 3.21 | | 0.79 | .43 |
| Education | -0.01 (-0.76, 0.74) | 0.38 | .00 | -0.03 | .98 |
| Grade | 0.20 (-0.53, 0.93) | 0.37 | .03 | 0.54 | .59 |
| Active treatment status | -1.30 (-2.99, 0.39) | 0.86 | -.10 | -1.52 | .13 |
| Age at diagnosis | -0.02 (-0.09, 0.05) | 0.04 | -.04 | -0.57 | .57 |
| Time since diagnosis (in months) | 0.01 (-0.01, 0.02) | 0.01 | .06 | 0.83 | .41 |
| Charlson Co-morbidity Index | 0.19 (-0.46, 0.83) | 0.33 | .04 | 0.57 | .57 |
| Employment type | -0.45 (-1.33, 0.43) | 0.45 | -.07 | -1.00 | .32 |
| Pathological worry | 0.01 (-0.03, 0.06) | 0.02 | .05 | 0.60 | .55 |
| Rumination (RRS) | 0.12 (0.08, 0.16) | 0.02 | .43 | 5.37 | .00 |
| COVID-EMV | 0.13 (0.02, 0.23) | 0.05 | .21 | 2.40 | .02 |
| Job security | -0.36 (-0.67, -0.04) | 0.16 | -.14 | -2.20 | .03 |
| $\Delta R^2$ = .02 | | | | | |
| $\Delta F$ (1,157) = 4.86 | | | | | |
| $p$ =.03 | | | | | |
| | | | | | |
| **Anxiety** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 16.31 (8.08, 24.54) | 4.17 | | 3.91 | .00 |
| Education | -1.09 (-2.15, -0.03) | 0.54 | -.16 | -2.03 | .04 |
| Grade | -0.15 (-1.19, 0.90) | 0.53 | -.02 | -0.28 | .78 |
| Active treatment status | 1.40 (-0.98, 3.78) | 1.21 | .09 | 1.16 | .25 |
| Age at diagnosis | -0.08 (-0.19, 0.02) | 0.05 | -.13 | -1.56 | .12 |
| Time since diagnosis (in months) | -0.02 (-0.04, 0.00) | 0.01 | -.13 | -1.63 | .11 |
| Charlson Co-morbidity Index | -0.36 (-1.28, 0.56) | 0.47 | -.06 | -0.78 | .44 |
| Employment type | -0.33 (-1.58, 0.56) | 0.64 | -.04 | -0.51 | .61 |
| $R^2$ =.07 | | | | | |
| $\Delta F$ (3, 161) = 1.63 | | | | | |
| $p$ =.13 | | | | | |
| ***Step 2*** | | | | | |
| Constant | -2.40 (-7.91, 3.12) | 2.79 | | -0.86 | .39 |
| Education | -0.38 (-1.03, 0.27) | 0.33 | -.06 | -1.15 | .25 |

| | | | | | |
|---|---|---|---|---|---|
| Grade | -0.40 (-1.04, 0.25) | 0.33 | -.06 | -1.22 | .23 |
| Active treatment status | 1.03 (-0.45, 2.51) | 0.75 | .07 | 1.38 | .17 |
| Age at diagnosis | -0.02 (-0.09, 0.04) | 0.03 | -.03 | -0.67 | .51 |
| Time since diagnosis (in months) | 0.01 (-0.01, 0.02) | 0.01 | .06 | 1.08 | .28 |
| Charlson Co-morbidity Index | 0.21 (-0.36, 0.77) | 0.29 | .04 | 0.73 | .47 |
| Employment type | 0.16 (-0.61, 0.93) | 0.39 | .02 | 0.41 | .69 |
| Pathological worry | 0.09 (0.05, 0.13) | 0.02 | .30 | 4.61 | .00 |
| Rumination (RRS) | 0.09 (0.05, 0.13) | 0.02 | .28 | 4.52 | .00 |
| COVID-EMV | 0.26 (0.17, 0.35) | 0.05 | .38 | 5.66 | .00 |
| $\Delta R^2 = .59$ | | | | | |
| $\Delta F$ (3, 158) = 92.38 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | -1.89 (-7.44, 3.66) | 2.81 | | -0.67 | .50 |
| Education | -0.36 (-1.01, 0.29) | 0.33 | -.05 | -1.1 | .28 |
| Grade | -0.37 (-1.01, 0.27) | 0.32 | -.05 | -1.13 | .26 |
| Active treatment status | 1.04 (-0.43, 2.52) | 0.75 | .07 | 1.4 | .17 |
| Age at diagnosis | -0.02 (-0.09, 0.04) | 0.03 | -.04 | -0.69 | .49 |
| Time since diagnosis (in months) | 0.01 (-0.01, 0.02) | 0.01 | .06 | 1.2 | .23 |
| Charlson Co-morbidity Index | 0.20 (-0.37, 0.76) | 0.29 | .03 | 0.68 | .50 |
| Employment type | 0.11 (-0.66, 0.88) | 0.39 | .01 | 0.28 | .78 |
| Pathological worry | 0.09 (0.05, 0.12) | 0.02 | .29 | 4.56 | .00 |
| Rumination (RRS) | 0.09 (0.05, 0.13) | 0.02 | .28 | 4.48 | .00 |
| COVID-EMV | 0.26 (0.17, 0.35) | 0.05 | .38 | 5.59 | .00 |
| Job security | -0.19 (-0.47, 0.09) | 0.14 | -.06 | -1.35 | .18 |
| $\Delta R^2 = .004$ | | | | | |
| $\Delta F$ (1, 157) =1.83 | | | | | |
| $p$ =.18 | | | | | |
| | | | | | |
| **Emotional distress** | | | | | |
| ***Step 1*** | | | | | |
| Constant | 29.13 (15.18, 43.07) | 7.06 | | 4.13 | .00 |
| Education | -1.47 (-3.27, 0.32) | 0.91 | -.13 | -1.62 | .11 |
| Grade | 0.18 (-1.59, 1.95) | 0.9 | .02 | 0.2 | .84 |
| Active Treatment status | 0.76 (-3.27, 4.79) | 2.04 | .03 | 0.37 | .71 |
| Age at diagnosis | -0.14 (-0.31, 0.04) | 0.09 | -.13 | -1.55 | .12 |

| | | | | | |
|---|---|---|---|---|---|
| Time since diagnosis (in months) | -0.04 (-0.08, 0.00) | 0.02 | -.15 | -1.81 | .07 |
| Charlson Co-morbidity Index | -0.50 (-2.06, 1.06) | 0.79 | -.05 | -0.64 | .52 |
| Employment type | -0.99 (-3.12, 1.13) | 1.08 | -.07 | -0.92 | .36 |
| $R^2$ = .06 | | | | | |
| $\Delta$ (7, 161) = 1.50 | | | | | |
| $p$ =.17 | | | | | |
| ***Step 2*** | | | | | |
| Constant | -0.61 (-10.21, 8.99) | 4.86 | | -0.13 | .90 |
| Education | -0.39 (-1.53, 0.75) | 0.58 | -.03 | -0.67 | .50 |
| Grade | -0.37 (-1.49, 0.75) | 0.57 | -.03 | -0.65 | .52 |
| Active treatment status | -0.22 (-2.80, 2.35) | 1.31 | -.01 | -0.17 | .86 |
| Age at diagnosis | -0.04 (-0.15, 0.07) | 0.06 | -.04 | -0.71 | .48 |
| Time since diagnosis (in months) | 0.01 (-0.01, 0.04) | 0.01 | .05 | 1 | .32 |
| Charlson Co-morbidity Index | 3.96 (-0.59, 1.38) | 0.5 | .04 | 0.79 | .43 |
| Employment type | -0.26 (-1.60, 1.08) | 0.68 | -.02 | -0.39 | .70 |
| Pathological worry | 0.10(0.03, 0.16) | 0.03 | .19 | 2.94 | .00 |
| Rumination (RRS) | 0.21 (0.14, 0.28) | 0.03 | .39 | 6.19 | .00 |
| COVID-EMV | 0.41 (0.25, 0.57) | 0.08 | .35 | 5.08 | .00 |
| $\Delta R^2$ = .58 | | | | | |
| $\Delta F$ (3, 158) = 84.53 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | 0.84 (-8.73, 10.41) | 4.85 | | 0.17 | .86 |
| Education | -0.34 (-1.47, 0.78) | 0.57 | -.03 | -0.6 | .55 |
| Grade | -0.29 (-1.40, 0.81) | 0.56 | -.03 | -0.52 | .60 |
| Active treatment status | -0.20 (-2.75, 2.35) | 1.29 | -.01 | -0.16 | .88 |
| Age at diagnosis | -0.04 (-0.15, 0.07) | 0.06 | -.04 | -0.76 | .45 |
| Time since diagnosis (in months) | 0.02 (-0.01, 0.04) | 0.01 | .06 | 1.20 | .23 |
| Charlson Co-morbidity Index | 0.36 (-0.61, 1.33) | 0.49 | .04 | 0.73 | .47 |
| Employment type | -0.39 (-1.73, 0.93) | 0.67 | -.03 | -0.59 | .56 |
| Pathological worry | 0.09 (0.03, 0.16) | 0.03 | .19 | 2.88 | .01 |
| Rumination (RRS) | 0.21 (0.14, 0.27) | 0.03 | .39 | 6.19 | .00 |
| COVID-EMV | 0.40 (0.24, 0.56) | 0.08 | .34 | 5.01 | .00 |
| Job security | -0.54 (-1.03, -0.06) | 0.24 | -.11 | -2.24 | .03 |
| $\Delta R^2$ = .01 | | | | | |

$\Delta F$ (1, 157) = 5.01

$p$ =.03

***Perceived cognitive function***

| | | | | | |
|---|---|---|---|---|---|
| ***Step 1*** | | | | | |
| Constant | 83.56 (31.79, 135.33) | 26.22 | | 3.19 | .00 |
| Education | 2.88 (-3.79, 9.55) | 3.38 | .07 | 0.85 | .40 |
| Grade | -4.63 (-11.19, 1.94) | 3.32 | -.11 | -1.39 | .17 |
| Active treatment status | -9.93 (-24.91, 5.04) | 7.58 | -.11 | -1.31 | .19 |
| Age at diagnosis | 0.50 (-0.16, 1.15) | 0.33 | .13 | 1.5 | .14 |
| Time since diagnosis (in months) | 0.10 (-0.05, 0.25) | 0.07 | .11 | 1.36 | .18 |
| Charlson Co-morbidity Index | -1.67 (-7.45, 4.12) | 2.93 | -.05 | -0.57 | .57 |
| Employment type | -0.93 (-8.82, 6.95) | 3.99 | -.02 | -0.23 | .82 |
| $R^2$ =.04 | | | | | |
| $\Delta F$ (7, 161) = 1.07 | | | | | |
| $p$ =.38 | | | | | |
| ***Step 2*** | | | | | |
| Constant | 140.11 (90.03, 190.19) | 25.35 | | 5.53 | .00 |
| Education | 0.94 (-5.00, 6.88) | 3.01 | .02 | 0.31 | .76 |
| Grade | -2.85 (-8.67, 2.98) | 2.95 | -.07 | -0.97 | .34 |
| Active treatment status | -6.54 (-19.98, 6.90) | 6.81 | -.07 | -0.96 | .34 |
| Age at diagnosis | 0.30 (-0.27, 0.88) | 0.29 | .08 | 1.04 | .30 |
| Time since diagnosis (in months) | -0.03 (-0.17, 0.10) | 0.07 | -.03 | -0.44 | .66 |
| Charlson Co-morbidity Index | -3.49 (-8.63, 1.65) | 2.6 | -.10 | -1.34 | .18 |
| Employment type | -1.88 (-8.87, 5.12) | 3.54 | -.04 | -0.53 | .60 |
| Pathological worry | 0.12 (-0.22, 0.46) | 0.17 | .07 | 0.71 | .48 |
| Rumination (RRS) | -0.74 (-1.09, -0.40) | 0.18 | -.38 | -4.21 | .00 |
| COVID-EMV | -1.01 (-1.84, -0.18) | 0.42 | -.24 | -2.4 | .02 |
| $\Delta R^2$ =.23 | | | | | |
| $\Delta F$ (3,158) =16.87 | | | | | |
| $p$ <.001 | | | | | |
| ***Step 3*** | | | | | |
| Constant | 132.81 (82.85, 182.77) | 25.29 | | 5.25 | .00 |
| Education | 0.69 (-5.18, 6.57) | 2.97 | .02 | 0.23 | .82 |
| Grade | -3.24 (-9.00, 2.53) | 2.92 | -.08 | -1.11 | .27 |
| Active treatment status | -6.65 (-19.94, 6.64) | 6.73 | -.07 | -0.99 | .32 |

| | | | | | |
|---|---|---|---|---|---|
| Age at diagnosis | 0.31 (-0.26, 0.88) | 0.29 | .08 | 1.08 | .28 |
| Time since diagnosis (in months) | -0.04 (-0.18, 0.09) | 0.07 | -.05 | -0.63 | .53 |
| Charlson Co-morbidity Index | -3.31 (-8.40, 1.77) | 2.57 | -.09 | -1.29 | .20 |
| Employment type | -1.19 (-8.13, 5.75) | 3.52 | -.02 | -0.34 | .74 |
| Pathological worry | 0.14 (-0.20, 0.48) | 0.17 | .08 | 0.81 | .42 |
| Rumination (RRS) | -0.73 (-1.08, -0.39) | 0.18 | -.37 | -4.18 | .00 |
| COVID-EMV | -0.96 (-1.78, -0.13) | 0.42 | -.22 | -2.30 | .02 |
| Job security | 2.74 (0.23, 5.25) | 1.27 | .15 | 2.16 | .03 |
| $\Delta R^2 = .02$ | | | | | |
| $\Delta F\text{-}Change$ (1, 157) = 4.67 | | | | | |
| $p = .03$ | | | | | |

*Note.* (95% Confidence Intervals)

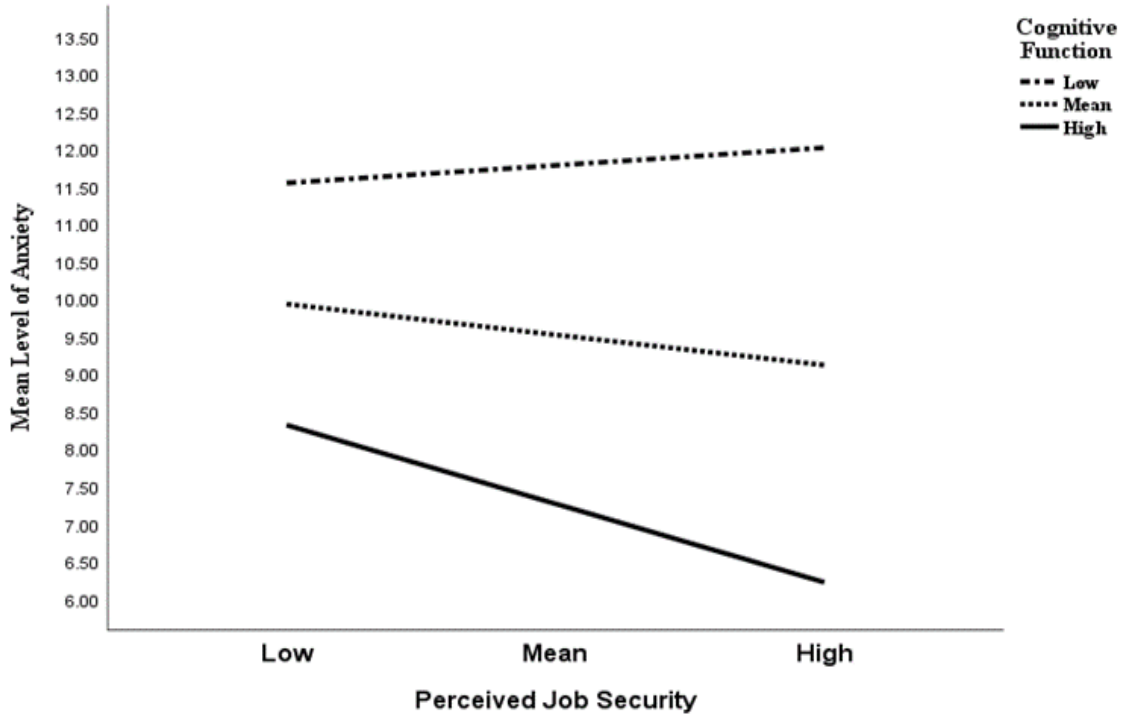
Checks for violation of assumptions showed that the assumption of collinearity (Tolerance > 0.1, VIF <10), independent error (**Depression**: Durbin-Watson = 2.0; **Anxiety**: Durbin-Watson = 1.9; Emotional Distress Durbin-Watson = 2.0; **Perceived cognitive function**: Durbin-Watson = 2.1), normality and homogeneity of variance and linearity were met for all four regression analyses performed.

### 7.5.7. **Moderating role of perceived cognitive function in the relationship between self-reported job security and emotional symptomatology**

As **figure 7.1** shows, perceived cognitive function significantly moderates the relationship between self-reported job security and anxiety ($b$ = -0.01, 95% CI [-0.03, -0.00], $t$ = 2.15, $p$ =.03). Such that at higher levels of perceived cognitive function, job security was met with lower levels of anxiety ($b$ = - 0.71, 95% CI [-1.19, -0.22], $t$ = 2.86, $p$ < .01), indicating that the relationship between job security and anxiety is affected by perceived cognitive function. Women with better perceived cognitive functioning and high job security report lower levels of anxiety. There was no significant moderation found for depression.

**Figure 7.1**

*Simple slope equations for the regression of anxiety on job security at three levels of perceived cognitive function*




## 7.6. **Discussion**

The aim of the current study was two-fold. First, the study aimed to explore the impact of the COVID-19 outbreak and its associated restrictive measures (i.e., UK Government shielding letter), as well as COVID-19-related emotional vulnerability (COVID-EMV) on the general cognitive and emotional health of women affected by primary breast cancer. The study then aimed to examine the effects of COVID-19-induced job insecurity and employment status (i.e., working or furloughed) on perceived cognitive function, anxiety and depression, in addition to exploring the impact of COVID-19-generated employment status on perceptions of work, job security and employer support. Women living with breast cancer are at a high risk of developing emotional disorders such as anxiety and depression as a result of diagnosis, treatment and the post-treatment sequelae endured (Tsaras et al.,2018; Carreira et al., 2018, 2021). In the UK the outbreak of COVID-19 caused significant disruption

to available oncology services, with many services cancelled or delayed. In addition, it also resulted in many women receiving the UK Government shielding letter advising them to isolate for 12-weeks to reduce their risk of contracting the virus. Given, the uncertain nature of the COVID-19-induced disruptions to oncology services and the restrictive measures it is plausible that women living with breast cancer may be at an increased risk for developing more severe and debilitating emotional distress.

As predicted, the current study found that women who encountered disruptions to their oncology services (e.g., cancelled or postponed appointments) experienced higher levels of anxiety and depression, as well as greater COVID-19 EMV compared to those who were not affected. In addition, the study found that women who received a UK Government shielding letter had a worse perceived cognitive function, however, no association was found with anxiety or depression. One plausible explanation for this finding is that receiving the shielding letter provoked symptoms of Post-Traumatic Stress Disorder (PTSD), as many women are advised to shield by their oncologist during their active treatment period. In a recent study by Boscher et al., (2020), it was found that breast cancer survivors with PTSD symptoms had a greater likelihood of experiencing cognitive impairment. Further research should be conducted to explore this association. Taken together such findings indicate that the indirect effects of the COVID-19 outbreak in the UK (i.e., on oncology service disruption and social isolation) may further escalate pre-existing levels of cognitive and emotional vulnerability in women living with a diagnosis of primary breast cancer.

Furthermore, significant differences in women's work perceptions depending on their current work status were found, with women who had been furloughed, or were unable to work, as a result of the COVID-19 outbreak reporting lower levels of work importance compared to those who had 'continued' to work. Such a finding indicates that the outbreak of COVID-19 provoked a re-evaluation of work importance, with a more detrimental effect noted for women who had been left unable to work. It is plausible that this reduction in work importance could be part of a coping mechanism used by women who had been furloughed or left unable to work. In line with the predictions, women who were unable to work as a result of COVID-19 perceived a greater level of threat or uncertainty surrounding their long-term job security. It is predicted that the global economic recession triggered by the outbreak

of COVID-19 could result in 24.7 million job losses worldwide, approximately two million more than the 2008-2009 global financial crisis (International Labor Organization, 2020). Given that unplanned loss of employment is associated with worse mental health outcomes (Gallo et al., 2000), and that women with a history of breast cancer have a pre-existing vulnerability for developing anxiety and depression (Burgess et al., 2005; Avis et al., 2015; Cvetković & Nenadović, 2016; Carreira et al., 2018), this finding has important implications. In particular, the results suggest that women furloughed by employers or who are unable to work as a result of the pandemic could benefit from the early implementation of interventions and support services that aim to improve emotional resilience.

In line with the findings from previous research studies (Deimling et al., 2006; Soo &Sherman, 2015), the exploratory analyses revealed that pathological worry and rumination were predictors of anxiety and depression, respectively, with higher worry and rumination meeting with worse levels of anxiety and depression. In early research by Nolen-Hoeksema (2000), it was shown that rumination and worry were key cognitive predictors of heightened levels of depression, anxiety and mixed anxiety and depression symptomology due to their intrusive and persistent nature. Studies have also shown that they are significantly associated with cognitive impairment (Beckwé et al., 2014; see Koster et al., 2017, for a review). One study by Berman et al., (2014) found that higher pre-treatment worry was associated with poorer self-reported cognitive complaints and objective cognitive impairment in cancer patients. Supporting this earlier work, the current findings showed that greater rumination was predictive of worse perceived cognitive function, however, there was no association with self-reported pathological worry. One possible explanation for the non-significant finding with worry is the specificity of worry symptoms that were assessed by the PSWQ. It is also plausible that the current findings differ from Berman et al., (2014) as most of the women were post-active treatment, potentially suggesting that the impact of worry on perceived cognitive function reduces after the completion of active treatment.

Corroborating recent studies demonstrating a significant association between comorbidity and emotional wellbeing in cancer patients (Yang et al., 2017; Read et al., 2017; Carreria et al., 2018), findings from the hierarchical regression analyses exploring the role of COVID-EMV showed comorbidity with other health conditions (i.e., heart disease or liver disease) to be a significant predictor

of greater emotional vulnerability to depression and worse perceived cognitive function. In a study by Read et al., (2017), it was shown that depression was two to three times more likely in individuals living with multiple health conditions. Similarly, Mandelblatt et al., (2014) found that high comorbidity was associated with worse cognitive function before the initiation of breast cancer treatment. It is feasible that the findings in this current study were underpinned by the elevated cytokines caused by comorbidity (Alfano et al., 2017). It is well documented that both depression (Boyle et al., 2017) and cognitive function (Patel et al., 2015; van der Willik et al., 2018) are associated with greater levels of inflammatory markers (i.e., IL-6) in women affected by breast cancer.

Of critical importance, after allowing for the predictive value of sociodemographic and clinical factors, comorbidity, pathological worry and rumination, greater (or worse) COVID-EMV was a significant predictor of more severe anxiety and depression, as well as poorer perceived cognitive function. Compounding this, the findings also showed that job insecurity induced by the COVID-19 outbreak was a significant predictor of greater emotional vulnerability to depression and poorer perceived cognitive function. In a study by Blom et al., (2018), it was shown that threat to job security was significantly associated with increased depressive symptoms including, loss of interest, lack of energy and lower mood. Such findings further substantiate the notion that the outbreak of COVID-19 and its effects on everyday life in the UK may contribute to escalating levels of cognitive and emotional vulnerability in women living with a diagnosis of primary breast cancer beyond the pre-existing level. Importantly, the regression analyses performed allowed for the potential confounding effects of clinical variables including, active treatment status, grade, age of diagnosis and time since diagnosis, suggesting that these findings can be applied across the entire sample of women recruited, and not only those with more severe cancer characteristics. Given, that previous research has shown worry and rumination to be significant predictors of both anxiety and depression (Nolen-Hoeksema, 2000; Ryum et al., 2017; S. L. Brown et al., 2020; Beckwé et al., 2014; Spinhoven et al., 2018) in cancer survivors (Deimling et al., 2006; Soo & Sherman, 2015), the analyses also allowed for the effects of these two factors. After the predictive value of worry and rumination have been accounted for, COVID-EMV was a significant predictor of anxiety and depression. Greater threat to job security was a significant predictor of worse

emotional vulnerability to depression. As studies have already established that emotional distress (anxiety and depression) is highly prevalent in women affected by breast cancer (Avis et al., 2015; Yang et al., 2017; Carreira et al., 2018, 2020, 2021), these findings have important implications. In particular, the findings indicate that women with breast cancer might benefit from the early implementation of interventions and support services that promote emotional resilience. Emotional distress in women with breast cancer has been associated with worse clinical outcomes (Wang et al., 2020; see **Chapter 1 section 1.4.2.3**), poorer quality of life (Zeng et al., 2016) and reduced treatment adherence. This, in turn, has been linked to greater disease progression and possible premature mortality (Greer et al., 2008; Satin et al., 2009; Linden et al., 2012, Wang et al., 2020), any additional distress brought about by the COVID-19 pandemic is, therefore, a concern for long-term health and survivorship and needs to be addressed early to minimise its long-term impact.

Although previous research has shown that threat to job security in nurses was associated with greater depression ***and*** anxiety (Boya et al., 2008), the current study found no association with anxiety in women living with a diagnosis of primary breast cancer. One possible explanation for this non-significant finding is that the anxiety experienced by women during the peak of the COVID-19 pandemic, when this study was conducted, was associated more with persistent negative thinking and fear of the possible implications if they were to contract this novel virus (e.g., high risk of health complications and premature mortality), as opposed to job insecurity. It is, therefore, important that research continues to assess the effect(s) of threat to job security and possible COVID-19-related job loss on anxiety after the peak of the COVID-19 outbreak and the lifting of restrictive measures, as this will provide greater insight into the specific factors triggering the symptoms of anxiety experienced by women living with breast cancer.

CRCI is a common complaint reported by women living with a diagnosis of breast cancer (see Ahles and Root, 2018 and Joly et al., 2019, for reviews), which can greatly impact quality of life (Chapman et al., 2019) and reduce workability (Calvio et al., 2010; Zeng et al., 2016; Von Ah et al., 2018), potentially resulting in fewer work opportunities and financial hardship. It is important that women who have been left unable to work or furloughed as a result of the COVID-19 outbreak have

good emotional and cognitive resilience on their return to work as this will improve their work efficiency, potentially reducing the risk of them being selected for redundancy against other candidates. Taken together, the findings indicate that women experiencing greater COVID-EMV or threat to job security as a result of the COVID-19 outbreak would likely benefit from receiving adaptive cognitive training to improve their cognitive function. Whilst the current study found that greater COVID-EMV and job insecurity predicts worse levels of anxiety and/or depression, as well as poorer perceived cognitive function, the relationships may be bidirectional and therefore, must be interpreted with caution. Besides, it is possible that a third variable not allowed for in the current analyses may also influence the results.

Importantly the current study found that perceived cognitive function significantly moderates the relationship between self-reported job security and anxiety. That is, women with better perceived cognitive function were less vulnerable to anxiety when job security was less of a concern. Previous studies indicate that cognitive function has a protective effect in attenuating emotional vulnerability (anxiety and depression) in women living with breast cancer. In a large cross-sectional study carried out by Chapman et al., (2019), it was found that self-reported cognitive function (as measured by the FACT-Cog) significantly predicted emotional vulnerability and quality of life, such that better perceived cognitive function was coupled with greater emotional wellbeing and quality of life. In addition, a cognitive training study by Swainston and Derakshan (2018) found that women who received 12 sessions of adaptive cognitive training (i.e., dual *n*-back training) had greater sustained reductions in (trait) anxiety symptomology compared to the active control group who completed dual 1-back training. The moderating effect of perceived cognitive function found in this study further corroborates the notion that in women living with a diagnosis of breast cancer, perceived cognitive function protects against the development of emotional vulnerability to anxiety. As such, these findings suggest that women with a lower perceived cognitive function may benefit more extensively from receiving adaptive cognitive training interventions (such as dual *n*-back training) that boost cognitive efficiency particularly when there is a threat to their job security.

Collectively, the findings corroborate and advance recent research suggesting that vulnerable groups living with pre-existing health conditions such as breast cancer are at a greater risk of suffering from worse outcomes as a result of the COVID-19 pandemic (Zhang et al., 2020; Lai et al., 2020). The findings from this study suggest that the impact of the COVID-19 outbreak and its associated restrictive measures (i.e., disruption to oncology services and UK shielding letter) may heighten the anxiety, depression and perceived cognitive impairment experienced by women living with primary breast cancer. Importantly, the findings also demonstrate that greater COVID-19-related emotional vulnerability (COVID-EMV) and COVID-19-induced job insecurity predict worse levels of anxiety and/or depression, as well as poorer perceived cognitive function. Longitudinal research should be conducted to explore the extent of the ongoing distress induced by the COVID-19 disruptions. In addition, research should also be conducted to explore the impact of the COVID-19 disruptions on women living with metastatic breast cancer (MBC). Taken together the findings suggest that future government preparedness plans consider the cognitive and emotional health of women living with a diagnosis of breast cancer. They also highlight the importance of developing and delivering appropriate remote eHealth interventions that promote cognitive and emotional resilience (Penedo et al., 2020). Based on the findings, it could also be advocated that where possible; employers offer women the opportunity to vocalise their concerns about possible job insecurity, as such open discussions may alleviate distress and depression or allow better preparation in the eventuality of job loss.

### 7.6.1. **Limitations**

**Chapter 7** presents some limitations that need to be considered when interpreting the findings. Firstly, the study was cross-sectional and therefore provides only a snapshot of women's experiences at the time of completing the questionnaires. The study's design also limits explanations around cause and effect. In a study conducted by Chapman et al. (2019), evidence for a bi-directional relationship between self-reported cognitive function and emotional wellbeing in women with breast cancer was found. It is advocated that future research includes longitudinal studies with multiple follow-up sessions, as this will provide vital information on the trends of how COVID-19 impacts the cognitive

and emotional health of women with breast cancer across the pandemic. By assessing the trends and the specific predictors associated with anxiety and depression, as well as poorer perceived cognitive function, more targeted support and interventions could be provided to reduce the risk of developing clinical affective disorders.

A second limitation of the study is that participants were asked to self-report their demographic information including, breast cancer history and pre-existing psychological or affective disorders. In future studies, medical records should be obtained and assessed to ensure the reliability of the information reported. Finally, all participants were recruited using voluntary sampling via online advertisements placed on social media platforms including Facebook and Twitter due to the social restrictions and shielding guidelines imposed by the UK Government during the peak of the COVID-19 outbreak. As a consequence, this sample of women may not be representative of the much wider breast cancer population. It should be noted, that the sample was also well-educated and primarily Caucasian (95%), indicating that women living with a breast cancer diagnosis from BAME backgrounds are underrepresented in this study. Emerging data suggest that individuals from BAME backgrounds are at a greater risk of contracting COVID-19 and experiencing worse clinical outcomes (Pan et al., 2020), implying that the adverse effects on emotional distress and perceived cognitive function found in this study may be even further emphasised in BAME populations. Future research should recruit women from multiple sources including, a referral from oncologists or other health care professionals.

### 7.6.2. **Conclusion**

To conclude, the findings from the study presented in **Chapter 7** indicate that women living with a diagnosis of primary breast cancer may be at a greater risk for developing more severe emotional distress (anxiety and depression) and poorer perceived cognitive function as a result of the adverse effects of the COVID-19 outbreak in the UK. The current findings have important implications for pandemic preparedness plans, which should consider such adverse effects. Further, the findings highlight the importance of delivering cognitive and emotional health interventions for women affected by primary breast cancer. Future longitudinal research should continue to monitor the longer-term

effects of the COVID-19 outbreak on the cognitive and emotional health of women living with a diagnosis of breast cancer.

## Published papers associated with this chapter:

Chapman, B., Swainston, J., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 outbreak effects on job security and emotional functioning amongst women living with breast cancer. *Frontiers in Psychol.* 11:582014. doi: 10.3389/fpsyg.2020.582014.

Swainston, J*., Chapman, B*., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 Lockdown and its adverse impact on psychological health in breast cancer. *Frontiers in Psychol.* 11:2033. http://doi:10.3389/fpsyg.2020.02033.

*Joint first authorship

# **Chapter 8:** General Discussion

## 8.1. **Chapter Overview**

In **Chapter 8** the main findings presented throughout this PhD thesis (see **Chapters 3**, **4**, **5**, **6**, and **7**) will be summarised and discussed. First, this chapter will provide a general overview of the thesis including the aims of this PhD programme (see **section 8.2**), which is followed by the summary and discussion of the main findings for each of the chapters (see **section 8.3**). Implications of the findings and suggestions for future direction are outlined in **section 8.4**. The limitations are reviewed in **section 8.5** followed by concluding remarks in **section 8.6**.

## 8.2. **General Overview of the Thesis**

As of 2020, breast cancer is the most common form of cancer diagnosed in women worldwide (World Health Organization, 2020). In the last 40 years improvements in early detection and screening, as well as treatments available have resulted in survival rates doubling, with approximately 8 out 10 women now surviving beyond 10 years (Breast Cancer Now, 2020). Substantiating evidence has, however, shown that women affected by breast cancer are at a greater risk for developing impaired cognitive functioning and emotional vulnerability to anxiety and depression (Joly et al., 2020; Carreira et al., 2018, 2021), adversely affecting their quality of life and work-related outcomes (Zeng et al., 2016; Von Ah et al., 2018; Ho et al., 2018; Chapman et al., 2019). In a recent meta-analysis conducted on findings from nearly 300,000 women, it was reported that anxiety and depression increased women's risk of cancer recurrence and mortality by up to 30% (Wang et al., 2020; see **Chapter 1 section 1.4.2.3**), and a recent study by Kim et al., (2022) found that depression and anxiety were both independently associated with greater work output difficulty in women affected by breast cancer. Existing studies indicate a bidirectional relationship between cancer-related sequelae and work-related outcomes in

women affected by breast cancer, where work-related factors and cancer-related impairments affect each other interchangeably escalating emotional vulnerability to anxiety and depression.

While current work-related interventions have focused on supporting the initial return-to-work (RTW) process following diagnosis and active treatment (i.e., chemotherapy or radiotherapy) (see de Boer et al., 2015; Lamore et al., 2019, for reviews), no research to date has explored the implementation of cognitive training interventions to target the cognitive impairment experienced at work, especially beyond the initial RTW period. This is surprising given that cancer-related cognitive impairment is one of the most common and debilitating complaints experienced, with evidence indicating deficits can be ongoing for up to 20 years (Boykoff et al., 2009; Koppelmans et al., 2012). Concerningly, there is also little-to-no research investigating the cognitive and emotional health, as well as work experiences of women living with a diagnosis of metastatic breast cancer (MBC), despite figures showing that 30% of women diagnosed with primary breast cancer will go on to develop MBC (Breast Cancer Org., 2022).

To address these gaps in the existing literature and to find ways to empower women's workability which is known to be instrumental in promoting good cognitive and emotional health the ideas and methods of the current PhD thesis were developed. Using a mixed-methods approach this PhD thesis set out to better understand how cognitive functioning and emotional vulnerability relate to workability and work-related factors in women living with a diagnosis of breast cancer, as well as to ascertain the longer-term effectiveness of online adaptive cognitive training in supporting women experiencing cognitive difficulties improve and sustain their workability and work over time.

The aim of the current PhD thesis was two-fold. First, this thesis presented the longitudinal 'BRiCatWork' randomised control trial (RCT) study (see **Chapters 3**,**4**, and **5**) which aimed to explore the longer-term efficacy of adaptive dual *n*-back training as an intervention for helping women affected by primary breast cancer sustain workability over time by targeting impaired cognitive function. To this end, the study also explored women's experiences with sustained cancer-related cognitive impairment and its impact on their work and workability before receiving the intervention (see **Chapter 3**). To date, there are no other studies which have utilised objective measures of cognitive function, ERPs, self-report questionnaires and semi-structured interviews in such an integrative matter to provide a more

comprehensive understanding of the issues that women with breast cancer face in the workplace and how they can be remediated using adaptive cognitive training via dual *n*-back training and assessed the effectiveness in the longer-term.

Following on, **Chapter 6** explored how perceived quality of working life related to perceived cognitive function and emotional vulnerability to anxiety and depression, as well as quality of life in women with MBC. Women's experience with their employers following their MBC diagnosis and its relationship with quality of working life was also explored. It is well acknowledged by women with MBC that their experiences following diagnosis have been minimised both in everyday society and within the field of research, with many women reporting that MBC is considered second-rate compared to primary breast cancer, especially also when it comes to treatment development. As a result of the unexpected Coronavirus (COVID-19) outbreak in the UK during this PhD programme, the final study presented in **Chapter 7** focused on exploring the impact of COVID-19-related emotional vulnerability (COVID-EMV) and COVID-19-induced job insecurity on the cognitive and emotional health of women affected by primary breast cancer, an area of research previously unstudied.

All the studies presented in this thesis provide new and novel insight into challenges that women living with a diagnosis of primary or metastatic breast cancer have to deal with in their everyday life, particularly within the workplace. It is hoped that the findings can provide a pathway for developing new policies and strategies that can be implemented by occupational health and wider hospital settings to promote a better quality of life and longer-term survivorship.

## 8.3. **Summary and discussion of the main findings**

### 8.3.1. **Empowering workability in women with breast cancer beyond the return-to-work period**

The longitudinal study presented in this thesis is the first to utilise a series of objective measures of cognitive function, self-report questionnaires, and neural indices assessed using a multimodal

assessment of electrophysiology, as well as semi-structured telephone interviews to provide a comprehensive understanding of how adaptive dual *n*-back training can be utilised to empower workability beyond return to work (RTW). This is important as recent figures have confirmed that the unemployment rate is more than double in women with a diagnosis of breast cancer compared with non-cancer populations (35.6% vs. 15.2%) (The Economist Intelligence Unit, 2017), costing the UK economy an estimated £1.4 billion each year (Hilhorst & Lockey, 2019). The findings presented in this thesis provide initial promise that dual *n*-back training, a low-cost and easy-to-administer online intervention has high efficacy for improving workability and work-related outcomes such as career development in women struggling with cognitive difficulties. Specifically, the findings evidenced that 12 sessions of dual *n*-back training can improve women's workability by eliciting longer-term improvements in perceived cognitive function and reducing emotional vulnerability to anxiety and depression; well-known risk factors for limiting workability and quality of life (Von Ah et al., 2018; Ho et al., 2018; Chapman et al., 2019; Kim et al., 2022). Accordingly, perceived improvements in cognitive function were promoting women's confidence in the workplace and in their workability, undermining greater emotional wellbeing and self-esteem.

Of focal importance, the findings provide new insight that targeting impaired cognitive function via adaptive dual *n*-back training can empower workability by boosting career developments and progressions, with women reporting increases in their workload or working hours (in a paid or voluntary capacity) as soon as one-month after training. Importantly career developments continued at the longer-term follow-ups of six months and one year, affirming dual *n*-back training can help women with breast cancer sustain work and workability over time by targeting impaired cognitive function. Adding to this finding, women also reported significant reductions in dependency on work-related support methods for cognitive impairment. The positive experiences described by women during the three post-training telephone interviews were strikingly different from the experiences outlined at baseline. Before training, women outlined how their cognitive impairment had adversely impacted their ability to engage in work-related tasks, and induced a series of negative emotions such as feelings of being "stupid" and "embarrassed", as well as depleted their self-confidence in their ability to function adequately in the

workplace, provoking questions about sustainment of work longer-term. Further, many women outlined that their perceived cognitive impairment and its consequences on confidence and fatigue had limited their career development and progression, causing their careers to come to a complete standstill beyond the RTW period. To date, there is no other study that has shown such promise for empowering the workability of women with a history of primary breast cancer. These findings are pertinent given that accumulating evidence points to an association between unemployment and escalating levels of emotional vulnerability to depression (Inhestern et al., 2017) as well as an increased risk of mortality (Maruthappu al., 2015) in women diagnosed with breast cancer.

Extending on these findings, the study found dual *n*-back training to be described as "challenging", "enjoyable" and "fun", with many women stating that they would like to continue the training because of its profound effects on their workability and overall quality of life. These experiences are in stark contrast to the active control group who described their training as "tedious" and a "chore". It is important to note, that this was despite women showing good accuracy across the 12 training sessions. Taken together, the findings suggest that adaptive dual *n*-back training can be offered as part of a post-active treatment support package by oncology services, occupational health services and employers to ensure a good quality of working life and consequently a good quality of life.

### 8.3.2. T**ransfer effects on physiology and objective measures of cognitive function**

Uniquely this thesis used a multimodal assessment of cognitive function which included using electrophysiological measures to establish an understanding of the transfer effects of dual *n*-back training on neurocognitive functioning which may be implicated in workability. Strikingly the findings showed that change in the amplitude of early P3 (post-training – pre-training) following dual *n*-back training predicted change in psychopathology and workability (one-year post-training – pre-training), such that a greater increase in P3 amplitude met with a greater reduction in levels of self-reported rumination and depression, as well as work output difficulty (an index measure of workability). No significant correlations were found for the active control group. Of crucial importance, no other study to date has established the potential role of P3 ERP in predicting the longer-term efficacy of dual *n*-

back training in clinical or non-clinical populations. Previous research has, however, shown a significant relationship between blunted P3 amplitude and escalating levels of depression in non-cancer populations (Klawohn et al., 2020; Santopetro et al., 2020, 2021), highlighting the importance of these findings for clinical outcomes of depression. These novel findings provide a good ground for researchers to continue investigating how adaptive dual *n*-back training can normalise the amplitude of the P3 in other populations to protect against escalating levels of depression and rumination (a hallmark of anxiety) and poor workability, as well as determine whether the change in P3 amplitude following *n*-back training can be used to predict those individuals who will respond best in the long-term to receiving adaptive cognitive training and those who may benefit from receiving an alternative intervention. In addition, research should extend on these current findings to identify whether the change in P3 following adaptive *n*-back training can be used to predict long-term reductions in cancer-specific fears such as fear of cancer recurrence and fear of mortality amongst women with breast cancer which are known to disrupt functioning in everyday life and escalate levels of emotional vulnerability, particularly to anxiety (Berry-Stoelzle et al., 2020). Fear of cancer recurrence is the most common and persistent concern reported by women diagnosed with breast cancer, with a prevalence ranging from 47% to 99% (Johnson, 2001; Koch et al., 2014; Tewari & Chagpar, 2014; Befort & Klemp, 2011).

Extending previous research conducted by Owens et al., (2013) with an emotionally vulnerable population, findings evidenced that adaptive dual *n*-back training elicited significant near transfer-related gains in working memory capacity (WMC) when measured by the reliable and valid change detection task (CDT) (Vogel et al, 2005; Owens et al., 2012, 2013). This finding is the first to confirm that adaptive dual *n*-back training results in generalisation or cognitive transfer-related gains in the WM functioning of women affected by primary breast cancer using independent measures of WM. This is a significant finding as working memory is inherent to supporting higher-order cognitive processes which are essential to workability and protecting against vulnerability to anxiety and depression. In a large meta-analysis by Moran (2016), for example, it was shown that greater trait anxiety met with worse performance on tasks assessing WM functioning. It is proposed that increasing WMC via adaptive cognitive training leads to greater attentional control over attending to ruminative or worrying

information that escalates vulnerability to symptoms of anxiety and depression and reduces cognitive performance on emotionally neutral tasks. In earlier studies conducted by Swainston and Derakshan (2018; 2021) in our lab, it was shown that improvements in working memory functioning, as measured by the increase in '*n*' on the dual *n*-back training task elicited sustained reductions in rumination and anxiety up to 15 months after the completion of training. The findings in this thesis build upon this earlier work by evidencing the existence of near-transfer gains in the WMC of women with primary breast cancer, in addition to increases in the level of '*n*' achieved across the 12 sessions of online training.

Another novel finding that provides new insight into the efficacy of dual *n*-back training is the finding that dual *n*-back training diminishes women's post-error slowing on the flanker task which does not come at the cost of performance accuracy, suggestive of greater cognitive efficiency. A similar finding was reported by Li e al., (2020) in a healthy population who received 15 sessions of dual *n*-back training when they were compared to a group who completed a simple visual search task. In common dual *n*-back training and post-error slowing both require the division of central resources into two parts to enable the successful processing of two separate streams of information at the same time (i.e., *(1)* processing the error produced on the previous trial and *(2)* processing the current trial information or *(1)* storing and manipulation of '*n*' trial and *(2)* processing of current trial information) for optimal performance. It is proposed that practising dual *n*-back training causes this skill to become more efficient and automated. The current finding implies that the ability to split central resources is transferable to other tasks or situations where parallel processing of information is required by women experiencing cognitive impairment as a result of breast cancer diagnosis and treatment. This finding warrants further investigation to determine its impact in real-world situations outside of experimental settings.

### 8.3.3. **Discovering flaws in self-management coping strategies to support work-related performance**

Interestingly, the findings in this thesis provide new information regarding potential flaws in the self-management coping strategies used by women living with a history of primary breast cancer in the workplace to aid their work-related performance. In particular, the findings uncovered that some women find cognitive support methods such as notetaking or calendar alerts to be ineffective (or problematic) and of little benefit in the workplace because of their impairment in memory and concentration which limits their ability, for example, to remember that they have made the notes. This novel finding highlights the need for adaptive cognitive training interventions such as adaptive dual *n*-back training or alternative interventions that target impaired cognitive function to be provided as part of an accessible support package by services giving work-based survivorship care. Importantly, the current thesis provides promising evidence that receiving 12 sessions of adaptive dual *n*-back training results in sustained reductions in the level of dependency on cognitive support methods which were previously described by many women as "safety nets" and "parachutes" due to a lack of "trust" and "confidence" in their cognitive ability in the workplace. Further, findings showed that *n*-back training led to visible improvements in the effectiveness and efficiency of cognitive support methods, boosting emotional wellbeing and confidence and empowering workability. This is important as baseline (pre-training) findings revealed that some women have negative feelings and views of using the self-management methods in the workplace as they further highlight the true extent of their cognitive impairment and changes in workability, provoking feelings of distress.

### 8.3.4. **Beyond workability**

Importantly the findings presented in this thesis extend beyond workability and work-related outcomes, with implications for influencing clinical outcomes such as cancer recurrence and mortality risk. In a recent meta-analysis performed by Wang et al., (2020) which included data from more than 280,000 women living with a diagnosis of breast cancer, it was shown that anxiety and depression

increased the risk of recurrence and mortality by up to 24% and 30%, respectively, with depression revealed as the strongest predictor. Extending this, Wang et al., also found substantiating evidence that these risks were highest during the first five years of survivorship (see **Chapter 1 section 1.4.2.3** for more comprehensive explanation). This thesis presents a plethora of robust and consistent findings affirming that adaptive dual *n*-back training induces longer-term improvements in general emotional well-being and can offer protection against escalating vulnerability to trait anxiety and depression, with significant reductions noted for self-reported depression in the current study. In line with Swainston and Derakshan (2018, 2021) the current findings suggest that dual *n*-back training may protect against increasing levels of depression and anxiety in women with a history of primary breast cancer by improving their WMC (i.e, efficiency of the WM system) (as evidenced in the current study by significant gains in the level of '*n*' and on the CDT) and thus their attentional control over attending to depression-inducing or anxiety-inducing information or thoughts. Such findings significantly contribute to extending the Attentional Control Theory which proposes that attentional control is a key vulnerability mechanism (or moderator) in anxiety and depression (DeRaedt & Koster, 2010). In addition, they also provide initial support for a relationship between working memory capacity, attentional control and vulnerability to depression in women living with a diagnosis of primary breast cancer. In a series of studies conducted by DiMatteo et al., (2000; 2011), it was shown that depression and anxiety profoundly reduce adherence to planned treatment in individuals diagnosed with cancer. Studies have also shown that women living with a diagnosis of breast cancer who experience anxiety and/or depression are at an increased risk of suicide (Akechi et al., 2000; Kim et al., 2013). These findings, therefore, imply that receiving *n*-back training could play a central role in promoting longer-term survivorship in women affected by primary breast cancer by improving adherence to anticancer treatment(s) and reducing suicide, further research is needed to ascertain this claim.

Concerningly figures estimate that one in every three women diagnosed with primary breast cancer will go on to develop MBC (Breast Cancer Org, 2022), costing approximately £26 million per year (Remák & Brazil, 2004). This thesis provides good grounds to advocate that more research should be conducted to investigate the relationship(s) between adaptive dual *n*-back training and depression

and the rate of recurrence amongst women diagnosed with breast cancer. It is important to acknowledge that adaptive dual *n*-back training can be administered at a very low financial cost to the NHS or wider healthcare services, therefore, if it is found to successfully reduce the rate of recurrence has the potential to deplete some of the current financial burdens reported, in addition, to increasing the rate of longer-term survival. The findings could also have beneficial implications for decreasing the fear of cancer recurrence which has been associated with excessive body monitoring and medical appointment apprehension, occupying women's attention and lowering their quality of life (Koch et al., 2014).

### 8.3.5. **Enrichment of future research using qualitative measures**

Implementing qualitative measures this thesis was able to gain some rich information and guidance from women with a history of primary breast cancer on when dual *n*-back training should be administered by oncology services. Although views were mixed amongst women depending on their experiences with diagnosis and treatment, many reported that they felt six to 12 months after active treatment (i.e., chemotherapy or radiotherapy) would be an optimal time to be offered the training. Indeed, it was suggested that dual *n*-back training should be incorporated as part of post-active treatment recovery and support programs that are available to all women following treatment. This patient-led work can be used to inform future policy and change in healthcare services that provide post-active treatment survivorship care. Listening to the recommendations of women in this study who stated that they felt it could also be beneficial to receive the 12 sessions of dual *n*-back training during the active treatment period this research will be carried forward. These patient-led recommendations provide a good ground for examining the efficacy of adaptive cognitive training administered to women (who wish to receive the training) whilst they receive chemotherapy and/or radiotherapy.

### 8.3.6. **Resilience during the COVID-19 trauma?**

The study presented in this thesis was the first to investigate the impact of the novel COVID-19 outbreak on the general cognitive and emotional health of women diagnosed with primary breast

cancer during the peak of the pandemic in the UK. The findings imply that women living with a diagnosis of primary breast cancer may be at greater risk for developing more severe emotional distress (anxiety and depression) and poorer perceived cognitive function as a result of the adverse effects of the COVID-19 outbreak in the UK. Specifically, the findings evidenced that COVID-19-induced disruptions (i.e., postponed oncology appointments) were associated with higher levels of anxiety and depression, as well as greater COVID-EMV compared to those not affected. Whilst receiving the UK Government shielding letter was associated with a poorer perceived cognitive function. It is well-acknowledged that women diagnosed and treated for breast cancer are more susceptible to developing anxiety and depression compared to the wider population (Carreira et al., 2018, 2021). The findings in this thesis are not unexpected given women's fear of cancer recurrence and its relationship with escalating levels of anxiety and distress. Further, the finding revealed that COVID-EMV and job insecurity were predictive of anxiety and depression, as well as self-reported cognitive function, with higher COVID-EMV and greater job insecurity predicting worse emotional distress and perceived cognitive function in women living with a diagnosis of primary breast cancer regardless of their specific cancer history (i.e., grade). The findings highlight the need for future UK Government preparedness plans to consider the cognitive and emotional health implications of pandemics for women living with breast cancer.

Interestingly, the findings from the longitudinal training study seem to indicate that dual *n*-back training may have protected women against escalating levels of cognitive and emotional vulnerability induced by the trauma of the COVID-19 outbreak, as continuous improvements in perceived cognitive ability, rumination, depression and quality of life, as well as workability were recorded. Further, anxiety remained relatively unchanged between six months and one-year coinciding with the peak of the pandemic in the UK. The findings provide initial insight that dual *n*-back training may be an effective intervention to protect against the impact of traumatic or distressing events. Based on these findings more research should be conducted to examine the efficacy of adaptive dual *n*-back training in protecting against impaired cognitive function, anxiety and depression, as well as possible suboptimal workability induced by distressing events such as pandemics, job insecurity or more specific cancer-

related events like attending check-ups scans to monitor cancer for recurrence or progression. 'Scanxiety' is a common and important clinical problem for women living with a diagnosis of breast cancer (Feiler, 2011; See Bui et al., 2021, for a review), with a prevalence of up to 83%. In a study by Cho et al., (2015), it was found that 'scanxiety' can impede workability and concentration amongst women with breast cancer. Such a finding indicates that targeting 'scanxiety' via adaptive dual *n*-back training could result in a beneficial transfer effect on workability and quality of life, particularly during these distressing periods which typically span over many weeks.

### 8.3.7. **Secondary breast cancer not second rate**

Of crucial importance, the work presented in this thesis extends beyond just understanding the experiences of women living with a diagnosis of primary breast cancer by including women diagnosed with MBC (also commonly known as secondary breast cancer), who are largely overlooked and minimised in the existing literature and much wider society. Indeed, far less is known about the cognitive and emotional health, as well as work experiences of women diagnosed with MBC compared with primary breast cancer. This is worrying as estimates predict that one in three women with primary breast cancer will go on to receive a diagnosis of MBC in their lifetime (Breast Cancer Org., 2022). It is probable that the issues with equality between primary and secondary breast cancer are due to the misperception that MBC is incurable and thus all about dying which is not at all the case. In fact, most women with MBC, with the right support, may be able to continue everyday life in survivorship which may include attending work. The advances in the anticancer treatments and screening programs available to women with MBC in the UK mean that more women with this diagnosis are living longer. This, suggests that research should focus on the experiences of women with MBC which are distinctively different from women with primary breast cancer. Workability is an essential part of day-to-day life for many women with breast cancer providing not only greater financial stability but also protection against depression, which of course has been found to increase the risk of premature mortality (Giese-Davis et al., 2011; Wang et al., 2020). High levels of anxiety and depression and poorer

perceived cognitive function have been associated with reduced workability among women with breast cancer (Carlsen et al., 2013; Von Ah et al., 2018; Ho et al., 2018). The findings in this thesis provide new insight into the importance of having a good quality of working life and positive experiences with employers after a diagnosis of MBC diagnosis for cognitive and emotional health, as well as overall quality of life. Specifically, the findings evidenced that having a more positive experience with employers (i.e., greater support and understanding) was associated with a greater perceived quality of working life. This novel finding supplements previous research studies showing that greater social support in the workplace predicts better quality of working life in cancer survivors (Jin & Lee, 2018, 2020). Extending this, the findings affirmed that greater quality of working life predicts better perceived cognitive function and global quality of life and lower levels of self-reported depression. Such findings contribute initial evidence that employer experience and perceived quality of working life may play a pivotal role in protecting against escalating levels of pre-existing cognitive impairment and emotional vulnerability to depression in working women with MBC, potentially reducing the risk of premature mortality and empowering workability and overall quality of life. This thesis demonstrates the importance of studying the experiences of women living with a diagnosis of MBC, in addition to primary breast cancer. The findings provide a good ground for encouraging greater societal awareness of MBC, particularly amongst employers and work-based policymakers.

## 8.4. **Implications of the findings and future directions**

### 8.4.1. **Implications for work policies and change**

The findings presented in this thesis provide a pathway for implementing new policies and guidelines that consider the cognitive and emotional health of women diagnosed with breast cancer to empower workability and good quality of working life. Specifically, the findings provide new insight that can be used by occupational health services that provide guidance to employers and women with breast cancer in the workplace beyond the initial RTW period. This is important as in a recent study by Klaver et al., (2020), it was acknowledged that CRCI in the workplace is poorly understood by

occupational healthcare services, supervisors and colleagues, leading to escalating levels of psychological distress. In this thesis, for example, it was found that fear of judgement and discrimination were key concerns amongst women experiencing cognitive impairment and who were using cognitive support methods to aid their work-related performance. Such a finding highlights the need for occupational health services to implement new strategies and rules that support open communication between employers and employees around addressing these issues. The findings presented in this thesis provide a good ground for recommending that occupational health services and hospital services can package dual *n*-back training as part of an open access tool that is available for all women diagnosed with breast cancer. It is estimated that cancer-related unemployment and productivity loss (i.e., reduced working hours) cost the UK economy £1.4 billion each year (Hilhorst & Lockey, 2019), indicating that empowering women's workability via adaptive dual *n*-back training may have positive societal implications by reducing the financial burden incurred.

### 8.4.2. **Implications for the MBC community and workability**

Crucially, this thesis has implications for empowering the workability and overall quality of life of women in the MBC community who are largely ignored in the current literature and broader society. Specifically, the findings provide new information about how experience with employers following MBC influences women's perceived quality of working life, which in turn, predicts the severity of depression and perceived cognitive function, as well as the global quality of life. These findings call for the urgent need to develop and implement new rules and strategies designed with the needs of women with MBC in mind. The needs of women with MBC in the workplace are distinctively different from the needs of women with primary breast cancer, with the former requiring much higher levels of flexibility and understanding from their employers to balance workability with receiving essential treatments that ensure their long-term survival. Many women with MBC strive to maintain a high level of normalcy and ordinariness in their everyday life (see Willis et al., 2015, for a review). Introducing new rules that promote greater quality of working life by improving employer support and

understanding could lead to more women in the MBC community returning to work or sustaining longer-term employment, beneficially reducing financial concerns, feelings of social isolation, loss of independence and control, as well as feelings of being a social "outsider". Enabling independence and control via workability may also contribute to reducing the negative feelings of distress, fear, guilt and worthlessness often encountered when depending on family members or friends for social or financial support. Greater financial difficulty has been associated with escalating levels of anxiety and depression (Park et al., 2018; Perry et al., 2020), which significantly increases mortality risk (Wang et al., 2020) and places strain on personal relationships (i.e., marital or parental). The findings in this thesis, therefore, have several implications for improving the longer-term survivorship of women in the MBC community, empowering workability and overall quality of life by promoting independence and control, in addition to helping maintain good personal relationships.

The findings in this thesis also have implications for improving career opportunities for women with MBC by empowering workability and reducing symptoms of depression and perceived cognitive impairment. Greater career prospects may positively boost women's confidence and self-esteem, as well as improve their sense of worthiness in society which is known to be adversely impacted by a diagnosis of breast cancer.

### 8.4.3. **Implications for future research targeting fear of recurrence**

The findings from this thesis also have important implications for targeting the fear of cancer recurrence which may prevent some women from returning to work. Fear of cancer recurrence or cancer progression has been considered one of the most common unmet needs by cancer patients diagnosed with localised or metastatic disease (see Bergerot et al., 2022, for a review). It is well-acknowledged that fear of cancer recurrence causes a series of adverse emotions and distresses, limiting quality of life. As mentioned throughout this thesis substantiating evidence has shown that both depression and anxiety significantly escalate the risk of cancer recurrence and mortality amongst women with breast cancer (Wang et al., 2020; see **Chapter 1 section 1.4.2.3**). The novel findings provide insight into the

importance of having a good quality of working life, positive experiences with employers and high job security, as well as access to adaptive dual *n*-back training for lowering levels of anxiety and depression and promoting better cognitive functioning, known risk factors for recurrence and cancer progression. For most women, the loss of confidence and self-esteem in the workplace due to poorer experiences with employers or cancer-related sequelae such as cognitive impairment induces a series of negative feelings of distress and heightens exhaustion which could lead to concern that being in the workplace is increasing the chance of recurrence or further progression of cancer. Remediating the fear of cancer recurrence by improving women's experiences in the workplace and providing adaptive cognitive training which has shown such promise in this thesis may encourage more women to return to work or sustain longer-term work without fearing the consequence on their health. Future research should examine the efficacy of adaptive dual *n*-back training on fear of cancer recurrence.

### 8.3.4. I**mplications for improving employer's understanding of the needs of women with breast cancer**

Furthermore, the findings also have implications for improving relationships with employers and co-workers by developing a greater understanding of the needs and experiences of women with breast cancer in the workplace, particularly beyond the return-to-work (RTW) period. The findings in this thesis evidence the urgent need for more open communication around the long-term post-treatment cancer-related sequelae experienced by women in everyday life following diagnosis and treatment to improve the relationship between employers and employees with breast cancer. By improving, relationships and understanding women may feel more inclined to approach their employer with concerns they have about work in the absence of fear of judgement and discrimination, reducing escalating levels of distress that may contribute to greater recurrence or mortality risk. Future research needs to work directly with employers to change the misperception that cancer-related sequelae such as cognitive impairment and fatigue disappear after the completion of active treatment.

### 8.4.5. **Recommendations for future research**

The findings in this thesis encourage the use of multi-modal assessment in breast cancer research to comprehensively understand women's experiences of cancer-related cognitive impairment. Neuroimaging evidence has shown when there are structural and functional alterations as a result of diagnosis and treatment, there is evidence of compensatory activation and recruitment from a wider network in task performance. Most recently, Swainston et al., (2021) found no significant difference in task performance on a modified flanker between women treated for breast cancer and a non-cancer reference control, however, their neural findings showed that women with breast cancer expressed a greater ΔERN and Pe amplitude after producing an error response. Such findings support the notion that women treated for primary breast cancer are using greater neural compensatory activation to maintain their performance accuracy. Importantly, the findings in this thesis seem to show a strong correlation between women's self-reported experiences and their physiological and behavioural changes following training increasing their credibility; however, future research should include more sensitive measures of cognitive performance that can be assessed outside of the laboratory settings. Laboratory settings are designed to minimise the impact of distractibility on performance and thus are likely to escalate the level of compensatory activation experienced. Future research should look at recording lapses in everyday attention and memory to gain a more realistic understanding of cancer-related impairment in women's everyday life, for example, women could be asked to keep a daily record of each time they experience a memory lapse in a specific period of time (i.e., six-weeks). The findings from this data would provide a comprehensive understanding of the true impact of cancer-related cognitive impairment in everyday life. This form of assessment should also be used to assess the efficacy of adaptive cognitive training on cognitive functioning in the real world including in the workplace.

Whilst adaptive dual *n*-back training is not the only way to empower workability and cognitive and emotional health in women with breast cancer the efficacy of adaptive cognitive training has been understudied compared to other forms of cognitive rehabilitation methods such as cognitive behavioural therapy. Although the findings in this thesis provide initial promise for the efficacy of dual *n*-back

training as an intervention for improving workability by targeting impaired cognitive function, in addition to improving emotional health and quality of life beyond work it is important to acknowledge that there are variations in its effectiveness across women. Future research should move towards implementing machine learning processes to personalise cognitive training to maximise training's effectiveness (Shani et al., 2021). Machine learning algorithms can be used to identify the specific demographic (i.e., age, race), personality and lifestyle, as well as treatment (i.e., time since treatment) characteristics of women with breast cancer who will benefit most from receiving certain forms of cognitive training (i.e., adaptive dual *n*-back training) or alternative interventions. Using machine learning will enable us to provide the most effective treatment or cognitive training at the right time for each woman diagnosed with breast cancer, enhancing the intervention's effectiveness.

## 8.5. **Limitations**

Several general limitations should be taken into consideration when interpreting the findings reported in this thesis. Firstly, all women participating in the studies were recruited via advertisements placed on private and public support groups (i.e., Centre for Building Resilience in Breast Cancer (BRiC)) available on social media platforms including Facebook, Twitter and Instagram, and therefore the findings may not be fully representative of the wider breast cancer population. Whilst online social media recruitment methods have been shown to elicit a greater enrolment rate in studies compared with hospital-based recruitment methods, findings have suggested that online social media advertisements can sometimes lead to a less demographically diverse population participating in the study (Benedict et al., 2019). In **Chapter 7**, for example, demographic information revealed that around 95% of the women were Caucasian, suggesting that women from BAME backgrounds were underrepresented in this COVID-19 study. These women must be represented in future research as studies have shown that race is significantly associated with the severity of cognitive impairment, with women from BAME backgrounds experiencing greater impairment (Janelsins et al., 2017; Ahles & Hurria, 2018). Given that the advertisements were placed on private and public breast cancer support groups the studies may have

only attracted women who are motivated to gain research-led support for their cancer-related issues and not those who prefer to seek out private support. It may also restrict women without access to the internet and more specifically these online support groups from taking part in the study unless it is recommended to them by a member of the group. Recent figures have shown that 92% of adults in the UK are internet users, with almost all adults aged 16 to 44 years (99%) reporting that they have access to the internet (Office for National Statistics, 2021). Future research should use both social media recruitment and hospital-based recruitment (i.e., using waiting room poster advertisements or databases to contact potential participants).

Another limitation of the longitudinal study was that participants needed to have access to a computer or laptop to complete their 12 sessions of dual *n*-back training or dual 1-back training. Future research should compare and contrast the efficacy of adaptive cognitive training administered using different forms of devices such as tablets and smartphones to overcome this limitation. In a recent report it was found that smartphone ownership was considerably greater than computer/laptop in the UK, with approximately 96% of respondents having a smartphone compared to 77% with a computer/laptop (eMarketer, 2021). If no significant differences are found in the outcome measures offering participants the opportunity to complete their training sessions on different smart devices will increase inclusion and promote more equal opportunities for women living with a diagnosis of breast cancer. Participants in the studies presented in **Chapters 6** and **7** were able to complete the series of questionnaires on either a smartphone, tablet or computer/laptop increasing the accessibility of the study. The studies were conducted online via Gorilla Experimenter Builder (www.gorilla.sc) enabling women from anywhere in the UK to participate. Indeed, one of the main strengths of the study presented in **Chapter 7** was its large sample of 234 women with a diagnosis of primary breast cancer in the UK, who were recruited during the first national lockdown. Whilst it was not the aim of these novel studies included in this thesis recent evidence has shown that Gorilla Experimental Builder can be utilised to collect reliable data from objective measures of cognitive function (Anwyl-Irvine et al., 2020) this is an important next step, considering there is no published research exploring the relationship between objective cognitive functioning and work-related outcomes in women with MBC.

A limitation which has not previously been discussed and which significantly impacted participant recruitment was the requirement that participants had to travel to the MERLiN laboratory (Birkbeck, University of London) in central London to complete the computerised working memory tasks and an EEG to assess neural indices. The cost associated with travel, as well as the travel time may have prevented some participants who wanted to receive the online training from enrolling or even enquiring about the study, in addition to concerns about the possible impact of this travel on their fatigue. Fatigue is one of the most debilitating cancer-related sequelae experienced by women long into survivorship (see Joly et al., 2019, for a review). Future studies would benefit from using portable (or mobile) EEG systems that can be transported by the researcher to the participant's homes to collect neural data. Emerging evidence has shown that mobile EEG systems yield reliable data comparable to data obtained in laboratory settings (Ries et al., 2014; Mikkelsen et al., 2021).

A further limitation which should also be considered when interpreting the findings presented in this PhD thesis is the same researcher (BC) delivered the adaptive cognitive training intervention to participants, conducted their in-person testing session in the MERLiN laboratory and conducted their telephone interviews. Whilst women were asked to talk openly and honestly about their experiences with the online cognitive training it is plausible that meeting and/or discussing the training with BC may have biased some women's reports of their training experience, with them (un)consciously focusing on the positive outcomes and the benefits as opposed to giving a more objective review. In future studies, independent researchers should be assigned to delivering the intervention and collecting the interview data to minimise participant (friendliness bias) bias.

It is important to mention that the longitudinal study presented in this thesis was significantly impacted by the sudden outbreak of COVID-19 in the UK. The study had planned to collect follow-up data from objective measures of WM and neural indices which may be implicated in workability at six-months and one-year alongside the self-report questionnaires and telephone interviews, however, due to the ongoing closure of the MERLiN laboratory at Birkbeck University for around 18 months this data was unable to be collected in the timeframe of this PhD. The outbreak also increased the dropout rate (22.5% from enrolment to baseline questionnaires) because of job uncertainty and reduced access

to computers/laptops needed to complete the online adaptive cognitive training and questionnaires. Future research should replicate this study with a larger sample size to corroborate the novel findings reported throughout this PhD thesis, in addition to collecting data from objective measures of cognitive function and electrophysiological measures at six-months and one-year.

An overarching limitation is that recruitment was restricted to women diagnosed with primary or metastatic breast cancer. Although it is much rarer for men to receive a diagnosis of breast cancer compared to women (approx. 56,000 cases per year) figures have shown that there are still around 390 cases diagnosed in the UK each year (Macmillan, 2018c). Future research should extend its recruitment criteria to include men diagnosed and treated for breast cancer, a currently understudied population. In fact, to date, there is almost no published research investigating the workability and work experiences of men affected by breast cancer.

## 8.6. **Concluding remarks**

Taken together the studies in this thesis provide new and novel insight into the experiences of women living with a diagnosis of breast cancer in the UK, particularly in the workplace. Importantly, the findings provide promising evidence that online adaptive dual *n*-back training can be used to help women affected by breast cancer sustain their workability over time by targeting their impaired cognitive function, in addition to remediating their emotional vulnerability to anxiety and depression; known risk factors for reducing workability and increasing mortality. The findings showed that dual *n*-back training can elicit improvements in women's career development and progression, as well as reduce their dependency on work-related self-management methods for cognitive impairment. Furthermore, the findings in this thesis supply new information highlighting the importance of good quality of working life and experiences with employers for the cognitive and emotional health of women living with a diagnosis of MBC, a population who are largely overlooked and minimised in existing research and wider society and deserve far more attention in future research. Finally, the findings in this thesis contribute novel evidence showing that women affected by breast cancer may be at an increased risk for developing escalating levels of emotional distress (anxiety and depression) and worse perceived

cognitive functioning as a result of the unexpected COVID-19 outbreak and its impact on oncology services and shielding, as well as on job security, highlighting the importance of considering women with breast cancer in future UK Government preparedness plans. The findings in this thesis provide hope for women living with breast cancer who are struggling as a result of their diagnosis and treatment.

The work from this thesis has been discussed with Breast Cancer Now and breast cancer now nurses who are very keen to implement the findings to devise better regulatory strategies to improve quality of life, quality of working life and workability, particularly amongst women with MBC who are often overlooked and minimised in society.

## References


Aaronson, N. K., Ahmedzai, S., Bergman, B., Bullinger, M., Cull, A., Duez, N. J., Filiberti, A., Flechtner, H., Fleishman, S. B., & de Haes, J. C. (1993). The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute*, *85*(5), 365–376. https://doi.org/10.1093/jnci/85.5.365

Ahles T. A. (2012). Brain vulnerability to chemotherapy toxicities. *Psycho-Oncology*, *21*(11), 1141–1148. https://doi.org/10.1002/pon.3196

Ahles, T. A., Saykin, A. J., Noll, W. W., Furstenberg, C. T., Guerin, S., Cole, B., & Mott, L. A. (2003). The relationship of APOE genotype to neuropsychological performance in long-term cancer survivors treated with standard dose chemotherapy. *Psycho-Oncology*, *12*(6), 612–619. https://doi.org/10.1002/pon.742

Ahles, T. A., & Saykin, A. J. (2007). Candidate mechanisms for chemotherapy-induced cognitive changes. *Nature reviews. Cancer*, *7*(3), 192–201.

Ahles, T. A., Root, J. C., & Ryan, E. L. (2012). Cancer- and cancer treatment-associated cognitive change: an update on the state of the science. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *30*(30), 3675–3686.

Ahles, T. A., Li, Y., McDonald, B. C., Schwartz, G. N., Kaufman, P. A., Tsongalis, G. J., Moore, J. H., & Saykin, A. J. (2014). Longitudinal assessment of cognitive changes associated with adjuvant treatment for breast cancer: the impact of APOE and smoking. *Psycho-Oncology*, *23*(12), 1382–1390. https://doi.org/10.1002/pon.3545

Ahles, T. A., & Root, J. C. (2018). Cognitive effects of cancer and cancer treatments. *Annual Review of Clinical Psychology*, *14* (1), 425-451. https://doi:10.1146/annurev-clinpsy-050817-084903

Ahles, T. A., & Hurria, A. (2018). New Challenges in Psycho-Oncology Research IV: Cognition and cancer: Conceptual and methodological issues and future directions. *Psycho-Oncology*, *27*(1), 3–9. https://doi.org/10.1002/pon.4564

Akechi, T., Okamura, H., Kugaya, A., Nakano, T., Nakanishi, T., Akizuki, N., Yamawaki, S., & Uchitomi, Y. (2000). Suicidal ideation in cancer patients with major depression. *Japanese Journal of Clinical Oncology*, *30*(5), 221-224.

Alatawi, Y., Hansen, R. A., Chou, C., Qian, J., Suppiramaniam, V., & Cao, G. (2021). The impact of cognitive impairment on survival and medication adherence among older women with breast cancer. *Breast Cancer (Tokyo, Japan)*, *28*(2), 277–288. https://doi.org/10.1007/s12282-020-01155-3

Alfano, C. M., Peng, J., Andridge, R. R., Lindgren, M. E., Povoski, S. P., Lipari, A. M., Agnese, D. M., Farrar, W. B., Yee, L. D., Carson, W. E., 3rd, & Kiecolt-Glaser, J. K. (2017). Inflammatory cytokines and comorbidity development in breast cancer survivors versus noncancer controls: evidence for accelerated aging?. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *35*(2), 149–156. https://doi.org/10.1200/JCO.2016.67.1883

Amir, Z., Neary, D., & Luker, K. (2008). Cancer survivors' views of work 3 years post diagnosis: A UK perspective. *European Journal of Oncology Nursing*, *12*(3), 190-197.

Andryszak, P., Wiłkość, M., Izdebski, P., & Żurawski, B. (2017). A systemic literature review of neuroimaging studies in women with breast cancer treated with adjuvant chemotherapy. *Contemporary Oncology (Poznan, Poland)*, *21*(1), 6–15. https://doi.org/10.5114/wo.2017.66652

Anwyl-Irvine, A., Massonnié, J., Flitton, A., Kirkham, N., & Evershed, J. K. (2020). Gorilla in our midst: An online behavioral experiment builder. *Behaviour Research Methods, 52,* 388-407.

Au, J., Sheehan, E., Tsai, N., Duncan, G. J., Buschkuehl, M., & Jaeggi, S. M. (2015). Improving fluid intelligence with training on working memory: a meta-analysis. *Psychonomic Bulletin & Review, 22*(2), 366–377. https://doi.org/10.3758/s13423-014-0699-x

Avis, N. E., Levine, B. J., Case, L. D., Naftalis, E. Z., & Van Zee, K. J. (2015). Trajectories of depressive symptoms following breast cancer diagnosis. *Cancer Epidemiology Biomarkers & Prevention, 24*(11), 1789-1795. https://doi:10.1158/1055-9965.

Baddeley, A. (1986). *Working memory*. Clarendon Press/Oxford University Press

Bai, L., & Yu, E. (2021). A narrative review of risk factors and interventions for cancer-related cognitive impairment. *Annals of Translational Medicine*, *9*(1), 72. https://doi.org/10.21037/atm-20-6443

Bajaj, P.S., Sussman, M., Yu, J., Reyes, C.M., Stein, A., Lai, C., Mayer, M., Hurvitz, S.A., & Tripathy, D. (2017). How are quality of life and work productivity associated with living longer with HER2+ metastatic breast cancer? *Psychosocial Issues, 35*(5).

Baqutayan S. M. (2012). The effect of anxiety on breast cancer patients. *Indian Journal of Psychological Medicine*, *34*(2), 119–123. https://doi.org/10.4103/0253-7176.101774

Bayer, S. J., Yang, G. S., & Lyon, D. E. (2022). Genetic variation associated with depressive symptoms in breast cancer patients: A systematic review. *Cancer Nursing, 45*(1), E197–E205. https://doi.org/10.1097/NCC.0000000000000903

Beckwé, M., Deroost, N., Koster, E. H. W., De Lissnyder, E., & De Raedt. R. (2014). Worrying and rumination are both associated with reduced cognitive control. *Psychological Research, 78*(5), 651-660. https://doi:10.1007/s00426-013-0517-5.

Befort, C. A., & Klemp, J. (2011). Sequelae of breast cancer and the influence of menopausal status at diagnosis among rural breast cancer survivors. *Journal of Women's Health (2002)*, *20*(9), 1307–1313. https://doi.org/10.1089/jwh.2010.2308

Beloe, P., & Derakshan, N. (2020). Adaptive working memory training can reduce anxiety and depression vulnerability in adolescents. *Developmental Science*, *23*(4), e12831. https://doi.org/10.1111/desc.12831

Bell, T., Gardiner, L., & Tomlinson, D. (2020). 'Getting Britain Working (Safely) Again: The Next Phase of the Coronavirus Job Retention Scheme'. *Resolution Foundation.* https://www.resolutionfoundation.org/publications/.

Benedict, C., Hahn, A. L., Diefenbach, M. A., & Ford, J. S. (2019). Recruitment via social media: advantages and potential biases. *Digital Health*, *5*, 2055207619867223. https://doi.org/10.1177/2055207619867223

Bergerot, C. D., Philip, E. J., Bergerot, P. G., Siddiq, N., Tinianov, S., & Lustberg, M. (2022). Fear of Cancer Recurrence or Progression: What Is It and What Can We Do About It?. *American Society of Clinical Oncology educational book. American Society of Clinical Oncology. Annual Meeting*, *42*, 1–10. https://doi.org/10.1200/EDBK_100031

Berman, M. G., Askren, M. K., Jung, M., Therrien, B., Peltier, S., Noll, D. C., Zhang, M., Ossher, L., Hayes, D. F., Reuter-Lorenz, P. A., & Cimprich, B. (2014). Pretreatment worry and neurocognitive responses in women with breast cancer. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, *33*(3), 222–231. https://doi.org/10.1037/a0033425

Berry-Stoelzle, M. A., Mark, A. C., Kim, P., & Daly, J. M. (2020). Anxiety-related issues in cancer survivorship. *Journal of Patient-Centered Research and Reviews*, *7*(1), 31-38.

Bjerkeset, E., Röhrl, K., & Schou-Bredal, I. (2020). Symptom cluster of pain, fatigue, and psychological distress in breast cancer survivors: prevalence and characteristics. *Breast Cancer Research and Treatment*, *180*(1), 63–71. https://doi.org/10.1007/s10549-020-05522-8

Biering, K., Frydenberg, M., Pappot, H., & Hjollund, N. H. (2020). The long-term course of fatigue following breast cancer diagnosis. *Journal of Patient-reported Outcomes*, *4*(1), 37. https://doi.org/10.1186/s41687-020-00187-9

Bidstrup, P. E., Christensen, J., Mertz, B. G., Rottmann, N., Dalton, S. O., & Johansen, C. (2015). Trajectories of distress, anxiety, and depression among women with breast cancer: Looking beyond the mean. *Acta oncologica (Stockholm, Sweden)*, *54*(5), 789–796. https://doi.org/10.3109/0284186X.2014.1002571

Bilodeau, K., Tremblay, D., & Durand, M. J. (2017). Exploration of return-to-work interventions for breast cancer patients: a scoping review. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *25*(6), 1993–2007. https://doi.org/10.1007/s00520-016-3526-2

Blacker, K. J., Negoita, S., Ewen, J. B., & Courtney, S. M. (2017). N-back versus complex span working memory training. *Journal of Cognitive Enhancement*, *1*, 434-454.

Bleicher, R. J., Ruth, K., Sigurdson, E. R., Beck, J. R., Ross, E., Wong, Y. N., Patel, S. A., Boraas, M., Chang, E. I., Topham, N. S., & Egleston, B. L. (2016). Time to surgery and breast cancer survival in the United States. *JAMA Oncology*, *2*(3), 330-339.

Blinder, V.S., M. M. Murphy, L. T. Vahdat, H.T. Gold, I de Melo-Martin, M. K. Hayes, R. J. Scheff, E Chuang, A. Moore, and M. Mazumdar. (2012). Employment after a breast cancer diagnosis: A qualitative study of ethnically diverse urban women'. *Journal of Community Health*, *37*(4), 763-772.

Blinder, V., Eberle, C., Patil, S., Gany, F. M., & Bradley, C. J. (2017). Women with breast cancer who work for accommodating employers more likely to return jobs after treatment. *Health Affairs, 36(2).* https://doi.org/10.1377/hlthaff.2016.1196

Blom, V., Richter, A., Hallsten, L., & Svedberg, P. (2015). The associations between job insecurity, depressive symptoms and burnout: The role of performance-based self-esteem. *Econ Ind Democr*, 9, 48-63. https:// doi: 10.1177/0143831X1560911

Boelhouwer, I. G., Vermeer, W., & van Vuuren, T. (2021). Late effects of cancer (treatment) and work ability: guidance by managers and professionals. *BMC Public Health, 21*(1), 1255. https://doi.org/10.1186/s12889-021-11261-2

Bolton, G., & Isaacs, A. (2018). Women's experiences of cancer-related cognitive impairment, its impact on daily life and care received for it following treatment for breast cancer. *Psychology, Health & Medicine, 23*(10), 1261-1274. https://doi.org/10.1080/13548506.2018.1500023

Borkovec, T. D., Robinson, E., Pruzinsky, T., and DePree, J. A. (1983). Preliminary exploration of worry: some characteristics and processes. *Behaviour Research and Therapy*, *21*(1), 9–16. https://doi.org/10.1016/0005-7967(83)90121-3.

Boscher, C., Joly, F., Clarisse, B., Humbert, X., Grellard, J-M., Binarelli, G., Tron, L., Licaj, I., & Lange, M. (2020). Perceived cognitive impairment in breast cancer survivors and its relationship with psychological factors. *Cancer*, *12*(10), 3000. https://doi.org/10.3390/cancers12103000

Boot, W. R., Simons, D. J., Stothart, C., & Stutts, C. (2013). The pervasive problem with placebos in psychology: Why active control groups are not sufficient to rule out placebo effects. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, *8*(4), 445–454. https://doi.org/10.1177/1745691613491271

Bower, J. E., Ganz, P. A., Aziz, N., & Fahey, J. L. (2002). Fatigue and proinflammatory cytokine activity in breast cancer survivors. *Psychosomatic Medicine*, *64*(4), 604–611. https://doi.org/10.1097/00006842-200207000-00010

Bower, J. E., Ganz, P. A., Desmond, K. A., Bernaards, C., Rowland, J. H., Meyerowitz, B. E., & Belin, T. R. (2006). Fatigue in long-term breast carcinoma survivors: a longitudinal investigation. *Cancer*, *106*(4), 751–758. https://doi.org/10.1002/cncr.21671

Bower J. E. (2007). Cancer-related fatigue: links with inflammation in cancer patients and survivors. *Brain, Behavior, and Immunity*, *21*(7), 863–871. https://doi.org/10.1016/j.bbi.2007.03.013

Bower J. E. (2008). Behavioral symptoms in patients with breast cancer and survivors. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *26*(5), 768–777. https://doi.org/10.1200/JCO.2007.14.3248

Bower, J. E., Partridge, A. H., Wolff, A. C., Thorner, E. D., Irwin, M. R., Joffe, H., Petersen, L., Crespi, C. M., & Ganz, P. A. (2021). Targeting Depressive Symptoms in Younger Breast Cancer Survivors: The Pathways to Wellness Randomized Controlled Trial of Mindfulness Meditation and Survivorship Education. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *39*(31), 3473–3484. https://doi.org/10.1200/JCO.21.00279

Boya, F. Ö., Demiral, Y., Ergör, A., Akvardar, Y, & De Witte, H. (2008). Effects of perceived job insecurity on perceived anxiety and depression in nurses. *Industrial Health, 46*, 613-619. https://doi:10.2486/indhealth.46.613.

Boykoff, N., Moieni, M., & Subramanian, S. K. (2009). Confronting chemobrain: an in-depth look at survivors' reports of impact on work, social networks, and health care response. *Journal of Cancer Survivorship: Research and Practice*, *3*(4), 223–232. https://doi.org/10.1007/s11764-009-0098-x

Boyle, C. C., Ganz, P. A., Van Dyk, K. M., & Bower, J. E. (2017). Inflammation and attentional bias in breast cancer survivors. *Brain, Behavior, and Immunity*, *66*, 85–88. https://doi.org/10.1016/j.bbi.2017.05.016

Bradley, C.J., & Bednarek, H.L. (2002). Employment patterns of long-term cancer survivors. *Psycho-Oncology*, *11*, 188-198. https://doi.org/10.1002/pon.544

Bradley, C.J., Neumark, D., Luo, Z., & Schenk, M. (2007). Employment and cancer: Findings from a longitudinal study of breast and prostate cancer survivors. *Cancer Investigation*, *25*, 47–54. doi:10.1080/07357900601130664

BrainVision Analyzer (Version 2.2. 0) [Software]. (2019). Gilching, Germany: Brain Products GmbH

Bray, V. J., Dhillon, H. M., Bell, M. L., Kabourakis, M., Fiero, M. H., Yip, D., Boyle, F., Price, M. A., & Vardy, J. L. (2017). Evaluation of a Web-Based Cognitive Rehabilitation Program in Cancer Survivors Reporting Cognitive Symptoms After Chemotherapy. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *35*(2), 217–225. https://doi.org/10.1200/JCO.2016.67.8201

Breast Cancer Now. 2019. "Follow-up after treatment". Accessed May 10, 2020. https://breastcancernow.org/information-support/facing-breast-cancer/going-through-breast-cancer-treatment/follow-after-treatment#:~:text=4.-,Mammograms%20after%20breast%20cancer,mastectomy%20(with%20or%20without%20reconstruction)

Breast Cancer Now. n.d. "Facts and Statistics 2020". Accessed May 10, 2020. https://www.breastcancernow.org/about-us/media/facts-statistics.

Breast Cancer Now. 2021. "Facts and Statistics 2021". Accessed August 10, 2021. https://breastcancernow.org/about-us/media/facts-statistics

Breast Cancer Now. 2021. "Finanical support and benefits when you have breast cancer". Accessed August 19, 2022. https://breastcancernow.org/information-support/facing-breast-cancer/living-beyond-breast-cancer/life-after-breast-cancer-treatment/financial-support-benefits-when-you-have-breast-cancer

Breast Cancer.Org. 2022. "Metastatic Breast Cancer". Accessed July 28, 2022. https://www.breastcancer.org/types/metastatic

Breckenridge, L. M., Bruns, G. L., Todd, B. L., & Feuerstein, M. (2010). Cognitive limitations associated with tamoxifen and aromatase inhibitors in employed breast cancer survivors. *Psycho-Oncology, 21*(1), 43-53. https://doi.org/10.1002/pon.1860

British Psychology Society. 2018. "Code of ethics and conduct". Accessed May, 10, 2020. https://www.bps.org.uk/news-and-policy/bps-code-ethics-and-conduct

Brown, L. C., Murphy, A. R., Lalonde, C. S., Subhedar, P. D., Miller, A. H., & Stevens, J. S. (2020). Posttraumatic stress disorder and breast cancer: Risk factors and the role of inflammation and endocrine function. *Cancer, 126*(14), 3181–3191. https://doi.org/10.1002/cncr.32934

Brown, S. L., Hughes, M., Campbell, S., & Cherry M. G. (2020). Could worry and rumination mediate relationship between self-compassion and psychological distress in breast cancer survivors?. *Clinical Psychology Psychotherapy*, *27*(1), 1-10.

Buchanan, N. D., Dasari, S., Rodriguez, J. L., Lee Smith, J., Hodgson, M. E., Weinberg, C. R., & Sandler, D. P. (2015). Post-treatment neurocognition and psychosocial care among breast cancer survivors. *American Journal of Preventive Medicine*, *49*(6 Suppl 5), S498–S508. https://doi.org/10.1016/j.amepre.2015.08.013

Bui, K. T., Liang, R., Kiely, B. E., Brown, C., Dhillon, H. M., & Blinman, P. (2021). Scanxiety: a scoping review about scan-associated anxiety. *BMJ open*, *11*(5), e043215. https://doi.org/10.1136/bmjopen-2020-043215

Burgess, C., Cornelius, V., Sharon Love, S., Graham, J., Richards, M., & Ramirez, A. (2005). Depression and anxiety in women with early breast cancer: five year observational cohort study. *BMJ Clinical research ed.*, *330*(7493), 702. https://doi:10.1136/bmj.38343.670868.D3.

Calvio, L., Peugeot, M., Bruns, G. L., Todd, B. L., & Feuerstein, M. (2010). Measures of cognitive function and work in occupationally active breast cancer survivors. *Journal of Occupational and Environmental Medicine, 52*(2), 219-227.

Cancer Research UK. 2020a. "Invasive lobular breast cancer". Accessed August, 2021. https://www.cancerresearchuk.org/about-cancer/breast-cancer/stages-types-grades/types/invasive-lobular-breast-cancer

Cancer Research UK. 2020a. “Breast Cancer Survival Statistics”. Accessed August, 2021. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer#heading-Three

Cancer Research UK. 2020b. “Risk Factors”. Accessed May, 2020.

Cancer Research UK. 2020c. “Hormone Therapy”. Accessed May, 2021.

Cancer Research UK. 2020e. “Targeted Cancer Drugs”. Accessed May, 2021. www.cancerresearchuk.org/about-cancer/breast-cancer/treatment/breast-targeted-cancer-drugs

Cancer Research UK. n.d. “Breast cancer statistics”. Accessed August, 2020

Cancer Research UK. (2020, January). “Survival”. Accessed April 2021. https://www.cancerresearchuk.org/about-cancer/breast-cancer/survival

Caplette-Gingras, A., & Savard, J. (2008). Depression in women with metastatic breast cancer: A review of the literature. *Palliative and Supportive Care*, *6*(4), 377–387. https://doi.org/10.1017/s1478951508000606

Carlsen, K., Jensen, A. J., Rugulies, R., Christensen, J., Bidstrup, P. E., Johansen, C., Huitfeldt Madsen, I. E., & Dalton, S. O. (2013). Self-reported work ability in long-term breast cancer survivors. A population-based questionnaire study in Denmark. *Acta oncologica (Stockholm, Sweden)*, *52*(2), 423–429. https://doi.org/10.3109/0284186X.2012.744877

Carreira, H., Williams, R., Müller, M., Harewood, R., Stanway, S., & Bhaskaran, K. (2018). Associations between breast cancer survivorship and adverse mental health outcomes: A systematic review. *Journal of the National Cancer Institute*, *110*(12), 1311-1327. https://doi:10.1093/jnci/djy177.

Carreira, H., Williams, R., Dempsey, H., Stanway, S., Smeeth, L., & Bhaskaran, K. (2020). Quality of life and mental health in breast cancer survivors compared with non-cancer controls: a study of patient-reported outcomes in the United Kingdom. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-020-00950-3

Carreira, H., Williams, R., Funston, G., Stanway, S., & Bhaskaran, K. (2021) Associations between breast cancer survivorship and adverse mental health outcomes: A matched population-based cohort study in the United Kingdom. *PLOS Medicine, 18*(1), e1003504. https://doi.org/10.1371/journal.pmed.1003504

Castellon, S. A., Ganz, P. A., Bower, J. E., Petersen, L., Abraham, L., & Greendale, G. A. (2004). Neurocognitive performance in breast cancer survivors exposed to adjuvant chemotherapy and tamoxifen. *Journal of Clinical and Experimental Neuropsychology*, *26*(7), 955–969. https://doi.org/10.1080/13803390490510905

Centre for Mental Health. (2020). *Covid-19 and the nation's mental health. Forecasting needs and risks in the UK: October 2020. https://www.centreformentalhealth.org.uk/sites/default/files/publication/download/CentreforMentalHealth_COVID_MH_Forecasting3_Oct20_0.pdf*

Chapman, B., Helmrath, S., & Derakshan, N. (2019). Perceived cognitive functioning and its influence on emotional vulnerability in breast cancer. *Health Psychology Open, 6*(2), 2055102919871661.

Chapman, B., Derakshan, N., & Grunfeld, E.A. (2021). Exploring primary breast cancer survivors' self-management of sustained cancer-related cognitive impairment in the workplace. *Psycho-Oncology*. https://doi.org/10.1002/pon.5844

Chapman, B., Swainston, J., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 outbreak effects on job security and emotional functioning amongst women living with breast cancer. *Front. Psychol*. https://doi.org/10.3389/fpsyg.2020.582014

Charlson, M. E., Pompei, P., Ales, K. L., & Mackenzie, C. R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases, 40* (5), 373-83.

Cho, J., Kang, D., Park, S., & Lee, J. E. (2015). Scanxiety and quality of life among breast cancer survivors. Journal of Clinical Oncology, 33 (15_suppl): e20569-e20569

Cibeira, G. H., Giacomazzi, J., Aguiar, E., Schneider, S., Ettrich, B., DE Souza, C. I., Camey, S., Caleffi, M., Weber, B., Ashton-Prolla, P., & Moriguchi, E. H. (2014). Apolipoprotein E genetic polymorphism, serum lipoprotein levels and breast cancer risk: A case-control study. *Molecular and Clinical Oncology*, *2*(6), 1009–1015. https://doi.org/10.3892/mco.2014.369

Cimprich B, Janz NK, Northouse L, Wren PA, Given B, Given CW (2005) Taking charge: a self-management program for women following breast cancer treatment. *Psycho-Oncology*, *14*(9), 704–717. doi:10.1002/pon.891

Ciobotaru, D., Jefferies, R., Lispi, L., & Derakshan, N. (2021). Rethinking cognitive training: The moderating roles of emotional vulnerability and perceived cognitive impact of training in high worriers. *Behaviour Research and Therapy*, *144*, 103926.

Claus, E. B., Petruzella, S., Carter, D., & Kasl, S. (2006). Quality of life for women diagnosed with breast carcinoma in situ. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *24*(30), 4875–4881. https://doi.org/10.1200/JCO.2005.05.2290

Cleeland, C. S., Mayer, M., Dreyer, N. A., Yim, Y. M., Yu, E., Su, Z., Mun, Y., Sloan, J. A., & Kaufman, P. A. (2014). Impact of symptom burden on work-related abilities in patients with locally recurrent or metastatic breast cancer: Results from a substudy of the VIRGO observational cohort study. *Breast (Edinburgh, Scotland)*, *23*(6), 763–769. https://doi.org/10.1016/j.breast.2014.08.004

Colom, R., Martínez, K., Burgaleta, M., Román, F. J., García-García, D., Gunter, J. L., Hua X., Jaeggi, S. M., Thompson, P. M. (2016). Gray matter volumetric changes with a challenging adaptive cognitive training program based on the dual n-back task. *Personality and Individual Differences*, *98*, 127-132.

Conroy, S. K., McDonald, B. C., Smith, D. J., Moser, L. R., West, J. D., Kamendulis, L. M., Klaunig, J. E., Champion, V. L., Unverzagt, F. W., & Saykin, A. J. (2013). Alterations in brain structure and function in breast cancer survivors: effect of post-chemotherapy interval and relation to

oxidative DNA damage. *Breast Cancer Research and Treatment*, *137*(2), 493–502. https://doi.org/10.1007/s10549-012-2385-x

Costa, W. A., Monteiro, M. N., Queiroz, J. F., & Gonçalves, A. K. (2017). Pain and quality of life in breast cancer patients. *Clinics (Sao Paulo, Brazil)*, *72*(12), 758–763. https://doi.org/10.6061/clinics/2017(12)07

Course-Choi, J., Saville, H., & Derakshan, N. (2017). The effects of adaptive working memory training and mindfulness meditation training on processing efficiency and worry in high worriers. *Behaviour Research and Therapy*, *89*, 1–13. https://doi.org/10.1016/j.brat.2016.11.002

Cribb, J., Emmerson, C., & Tetlow, G. (2013, April 17). *Women working in their sixties: why have employment rates been rising?* Institute for fiscal studies. https://www.ifs.org.uk/publications/6662

Cribb, J., & Emmerson, C. (2018, March 5). *Retiring at 65 no more? The increase in the state pension age to 66 for men and women*. Institute for Fiscal Studies. https://www.ifs.org.uk/publications/13949

Crouch, A., & Von Ah, D. (2017). Addressing cognitive impairment after breast cancer. What do women want? *Clinical Nurse Specialist*, *31*(2), 82-88.

Cui, B., Luo, Y., Tian, P., Peng, F., Lu, J., Yang, Y., Su, Q., Liu, B., Yu, J., Luo, X., Yin, L., Cheng, W., An, F., He, B., Liang, D., Wu, S., Chu, P., Song, L., Liu, X., Luo, H., … Liu, Q. (2019). Stress-induced epinephrine enhances lactate dehydrogenase A and promotes breast cancer stem-like cells. *The Journal of clinical investigation*, *129*(3), 1030–1046. https://doi.org/10.1172/JCI121685

Cvetković, J., and Nenadović, M. (2016). Depression in breast cancer patients. *Psychiatry Research, 240*, 343-347. https://doi:10.1016/j.psychres.2016.04.048.

Dahl, A. A., Fosså, S. D., Lie, H. C., Loge, J. H., Reinertsen, K. V., Ruud, E., & Kiserud, C. E. (2019). Employment status and work ability in long-term young adult cancer survivors. *Journal of Adolescent and Young Adult Oncology*, *8*(3), 304–311. https://doi.org/10.1089/jayao.2018.0109

Damholdt, M. F., Mehlsen, M., O'Toole, M. S., Andreasen, R. K., Pedersen, A. D., & Zachariae, R. (2016). Web-based cognitive training for breast cancer survivors with cognitive complaints-a randomized controlled trial. *Psycho-Oncology*, *25*(11), 1293–1300. https://doi.org/10.1002/pon.4058

Debener, S., Ullsperger, M., Siegel, M., Fiehler, K., von Cramon, D. Y., & Engel, A. K. (2005). Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *25*(50), 11730–11737. https://doi.org/10.1523/JNEUROSCI.3286-05.2005

de Boer, A. G., Verbeek, J. H., Spelten, E. R., Uitterhoeve, A. L., Ansink, A. C., de Reijke, T. M., Kammeijer, M., Sprangers, M. A., & van Dijk, F. J. (2008). Work ability and return-to-work in cancer patients. *British Journal of Cancer*, *98*(8), 1342–1347. https://doi.org/10.1038/sj.bjc.6604302

de Boer, A. G., Taskila, T., Ojajärvi, A., van Dijk, F. J., & Verbeek, J. H. (2009). Cancer survivors and unemployment: a meta-analysis and meta-regression. *JAMA*, *301*(7), 753–762. https://doi.org/10.1001/jama.2009.187

de Boer, A. G., Taskila, T. K., Tamminga, S. J., Feuerstein, M., Frings-Dresen, M. H., & Verbeek, J. H. (2015). Interventions to enhance return-to-work for cancer patients. *The Cochrane Database of Systematic Reviews*, *2015*(9), CD007569. https://doi.org/10.1002/14651858.CD007569.pub3

de Boer, A. G., Torp, S., Popa, A., Horsboel, T., Zadnik, V., Rottenberg, Y., Bardi, E., Bultmann, U., & Sharp, L. (2020). Long-term work retention after treatment for cancer: a systematic review

and meta-analysis. *Journal of Cancer Survivorship: Research and Practice*, *14*(2), 135–150. https://doi.org/10.1007/s11764-020-00862-2

de Jong, M., Tamminga, S. J., de Boer, A. G. E. M., & Frings-Dresen, M. H. W. (2016). The quality of working life questionnaire for cancer survivors (QWLQ-CS): a pre-test study. *BMC Health Serv Res*, *16*. https://doi.org/10.1186/s12913-016-1440-4

de Jong, M., Tamminga, S. J., van Es, R., Frings-Dresen, M., & de Boer, A. (2018). The quality of working life questionnaire for cancer survivors (QWLQ-CS): factorial structure, internal consistency, construct validity and reproducibility. *BMC Cancer*, *18*(1), 66. https://doi.org/10.1186/s12885-017-3966-1

de Jong, M., Tamminga, S. J., Frings-Dresen, M. H., & de Boer, A. G. (2017). Quality of Working Life of cancer survivors: associations with health- and work-related variables. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *25*(5), 1475–1484. https://doi.org/10.1007/s00520-016-3549-8

de Ruiter, M. B., Reneman, L., Boogerd, W., Veltman, D. J., van Dam, F. S., Nederveen, A. J., Boven, E., & Schagen, S. B. (2011). Cerebral hyporesponsiveness and cognitive impairment 10 years after chemotherapy for breast cancer. *Human Brain Mapping*, *32*(8), 1206–1219.

Derakhshan, N. (2020). Attentional control and cognitive biases as determinants of vulnerability and resilience in anxiety and depression. In T. Aue & H. Okon-Singer (Eds.), *Cognitive biases in health and psychiatric disorders: Neurophysiological foundations* (pp. 261–274). Elsevier Academic Press. https://doi.org/10.1016/B978-0-12-816660-4.00012-X

Dhruva, A., Dodd, M., Paul, S. M., Cooper, B. A., Lee, K., West, C., Aouizerat, B. E., Swift, P. S., Wara, W., & Miaskowski, C. (2010). Trajectories of fatigue in patients with breast cancer before, during, and after radiation therapy. *Cancer Nursing*, *33*(3), 201–212. https://doi.org/10.1097/NCC.0b013e3181c75f2a

Deimling, G. T., Bowman, K. F., Sterns, S., Wagner, L. J., & Kahana, B. (2006). Cancer-related health worries and psychological distress amongst older adult, longer-term cancer survivors. *Psycho-Oncology, 15*, 306-320. DOI: 10.1002/pon.955

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine, 160*(14), 2101–2107. https://doi.org/10.1001/archinte.160.14.2101

DiMatteo, M. R., & Haskard-Zolnierek, K. B. (2011). Impact of depression on treatment adherence and survival from cancer. In D. W. Kissane, M. Maj, & N. Sartorius (Eds.), *Depression and cancer* (pp. 101–124). Wiley-Blackwell.

Dieluweit, U., Debatin, K. M., Grabow, D., Kaatsch, P., Peter, R., Seitz, D. C., & Goldbeck, L. (2011). Educational and vocational achievement among long-term survivors of adolescent cancer in Germany. *Pediatric Blood & Cancer, 56*(3), 432–438. https://doi.org/10.1002/pbc.22806

Diamond, A., & Ling, D. S. (2019). Review of the evidence on, and fundamental questions about, efforts to improve executive functions, including working memory. Cognitive and working memory training: Perspectives from Psychology, Neuroscience, and Human Development, 145-389

Dobrestsova, A. & Derakshan, N. (2021). Cognitive function and emotional vulnerability in metastatic breast cancer: Moderating effects of age and social support. *Psycho-Oncology*, *30*(9), 1563-1571.

Dolgoy, N., Brose, J. M., Dao, T., Suderman, K., Gross, D. P., Ho, C., Culos-Reed, N., & McNeely, M. L. (2020). Functional, work-related rehabilitative programming for cancer survivors experiencing cancer-related fatigue. *British Journal of Occupational Therapy*. https://doi.org/10.1177/0308022620927351

Dorland, H. F., Abma, F. I., Van Zon, S. K. R., Stewart, R. E., Amick, B. C., Ranchor, A. V., Roelen, C. A. M., & Bültmann, U. (2018). Fatigue and depressive symptoms improve but negatively related to work functioning over 18 months after return to work in cancer patients. *Journal of Cancer Survivorship, 12*, 371-378. https://doi.org/10.1007/s11764-018-0676-x

Drijver, A. J., Oort, Q., Otten, R., Reijneveld, J. c., & Klein, M. (2022). Is poor sleep quality associated with poor neurocognitive outcome in cancer survivors? A systematic review. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-022-01213-z

Drolet, M., Maunsell, E., Mondor, M., Brisson, C., Brisson, J., Mâsse, B., & Deschênes, L. (2005). Work absence after breast cancer diagnosis: a population-based study. *CMAJ : Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne*, *173*(7), 765–771. https://doi.org/10.1503/cmaj.050178

Dudschig, C., & Jentzsch, I. (2009). Speeding before and slowing after errors: Is it all just strategy? *Brain Research, 1296*, 56–62. https://doi.org/10.1016/j.brainres.2009.08.009

Duijts, S. F., van der Beek, A. J., Boelhouwer, I. G., & Schagen, S. B. (2017a). Cancer-related cognitive impairment and patients' ability to work: a current perspective. *Current Opinion in Supportive and Palliative Care*, *11*(1), 19–23. https://doi.org/10.1097/SPC.0000000000000248

Duijts, S. F. A., van Egmond, M. P., Gits, M., van der Beek, A. J., & Bleiker, E. M. (2017b). Cancer survivors' perspectives and experiences regarding behavioral determinants of return to work and continuation of work. *Disability and Rehabilitation, 39*(21), 2164-2172. DOI: 10.1080/09638288.2016.1219924

Elovainio, M., Hakulinen, C., Pulkki-Råback, L., Virtanen, M., Josefsson, K., Jokela, M., Vahtera, J., and Kivimäki, M. (2017). Contribution of risk factors to excess mortality in isolated and lonely individuals: An analysis of data from the UK biobank cohort study'. *The Lancet. Public Health*, *2*(6), e260–66. https://doi.org/10.1016/S2468-2667(17)30075-0.

eMarketer. (2021). *Global Media Intelligence 2021: United Kingdom*. https://www.insiderintelligence.com/content/global-media-intelligence-2021-united-kingdom

Eriksen, B., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task *. *Perception & Psychophysics*, *16*(1), 143–149.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion (Washington, D.C.)*, *7*(2), 336–353. https://doi.org/10.1037/1528-3542.7.2.336

Falkenstein M., Hoorman S. C., Hohnsbein J. (2000). ERP components on reaction errors and their functional significance: a tutorial. *Biol. Psychol*. *51*, 87–107. 10.1016/S0301-0511(99)00031-9

Fallowfield, L., Ratcliffe, D., Jenkins, V., & Saul, J. (2001). Psychiatric morbidity and its recognition by doctors in patients with cancer. *British Journal of Cancer*, *84*(8), 1011–1015. https://doi.org/10.1054/bjoc.2001.1724

Faul, F., Erdfelder, E., Lang, A-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*, 175-191.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A-G. (2009). Statistical power analyses using G*Power 3.1: tests for correlation and regression Analyses. *Behavior Research Methods*, *41*, 1149-1160.

Feiler B. (2011). Scanxiety. Fear of a postcancer ritual. *Time*, *177*(24), 56.

Fenlon, D. R., & Rogers, A. E. (2007). The experience of hot flushes after breast cancer. *Cancer Nursing*, *30*(4), E19–E26. https://doi.org/10.1097/01.NCC.0000281731.95113.a3

Fenlon, D, Addington-Hall, J., O'Callaghan, A. C., Clough, J., Nicholls, P., & Simmonds, P. (2013). A survey of joint and muscle aches, pain, and stiffness comparing women with and without breast cancer. *Journal of Pain and Symptom Management*, *46*(4), 523-535.

Ferrell, B. R., Grant, M. M., Funk, B., Otis-Green, S., & Garcia, N. (1997). Quality of life in breast cancer survivors as identified by focus groups. *Psycho-Oncology*, *6*(1), 13–23. https://doi.org/10.1002/(SICI)1099-1611(199703)6:1<13::AID-PON231>3.0.CO;2-S

Foroughi, C. K., Monfort, S. S., Paczynski, M., McKnight, P. E., & Greenwood, P. M. (2016). Placebo effects in cognitive training. *Proceedings of the National Academy of Science, 113* (27): 7470-7474.

Foster, J. L., Shipstead, Z., Harrison, T. L., Hicks, K. L., Redick, T. S., & Engle, R. W. (2015). Shortened complex span tasks can reliably measure working memory capacity. *Memory and Cognition*, *43*(2), 226–236. https://doi.org/10.3758/s13421-014-0461-7

Fu, M. R., Axelrod, D., Guth, A. A., Cleland, C. M., Ryan, C. E., Weaver, K. R., Qiu, J. M., Kleinman, R., Scagliola, J., Palamar, J. J. & Melkus G. D. (2015). Comorbidities and quality of life among breast cancer survivors: A prospective study. *Journal of Personalized Medicine*, *5*(3), 229-242. https://doi.org/10/3390/jpm5030229.

Fulton, C. (1998). The prevalence and detection of psychiatric morbidity in patients with metastatic breast cancer. *European Journal of Cancer Care*, *7*, 232-239.

Gajewski, P. D., & Falkenstein, M. (2012). Training-induced improvement of response selection and error detection in aging assessed by task switching: effects of cognitive, physical, and relaxation training. *Frontiers in human neuroscience*, *6*, 130. https://doi.org/10.3389/fnhum.2012.00130

Gajewski, P. D., & Falkenstein, M. (2018). ERP and Behavioral Effects of physical and cognitive training on working memory in aging: A randomized controlled study. *Neural plasticity*, *2018*, 3454835. https://doi.org/10.1155/2018/3454835

Gaitanidis, A., Alevizakos, M., Pitiakoudis, M., & Wiggins, D. (2018). Trends in incidence and associated risk factors of suicide mortality among breast cancer patients. *Psycho-Oncology*, *27*(5), 1450-1456. https://doi:10.1002/pon.4570.

Gale, N. K., Heath, G., Cameron, E., Rashid, S., & Redwood, S. (2013). Using the framework method for the analysis of qualitative data in multi-disciplinary health research. *BMC Medical Research Methodology*, *13*(117). https://doi.org/10.1186/1471-2288-13-117

Gallo, W. T., Bradley, E. H., Siegel, M., & Kasl, S. V. (2000). Health effects of involuntary job loss amongst older workers: Findings from the health and retirement survey. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, *55*(3), S131-S140. https://doi:10.1093/geronb/55.3.s131.

Ganz, P.A., & Bower, J. E. (2007). Cancer related fatigue: A focus on breast cancer and Hodgkin's disease survivors. Acta Oncologica, *46*, 474-479.

Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin E. (1993). A neural system for error-detection and compensation. *Psychol. Sci*., *4,* 385–390. 10.1111/j.1467-9280.1993.tb00586.x

General Data Protection regulation GDPR. 2018. "GDPR". Accessed May 10, 2020. https://gdpr-info.eu/

Giese-Davis, J., Collie, K., Rancourt, K. M., Neri, E., Kraemer, H. C., & Spiegel, D. (2011). Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: a secondary analysis. *Journal of Clinical Oncology:Official Journal of the American Society of Clinical Oncology*, *29*(4), 413–420. https://doi.org/10.1200/JCO.2010.28.4455

Gilbertson, H., Fang, L., Andrzejewski, J. A., & Carlson, J. M. (2021). Dorsal anterior cingulate cortex intrinsic functional connectivity linked to electrocortical measures of error monitoring. *Psychophysiology*, e13794. https://doi.org/10.1111/psyp.13794

Glaser, B. G. (1965). The constant comparative method of qualitative analysis. *Social Problems, 12*(4), 436–445. https://doi.org/10.1525/sp.1965.12.4.03a00070

Goodwin, P. J., Ennis, M., Pritchard, K. I., Trudeau, M., & Hood, N. (1999). Risk of menopause during the first year after breast cancer diagnosis. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *17*(8), 2365–2370. https://doi.org/10.1200/JCO.1999.17.8.2365

Government UK. 2020. "Coronavirus (COVID-19)". Accessed May 10, 2020. https://www.gov.uk/coronavirus.

Government UK. n.d. "Guidance on Shielding and Protecting People Who Are Clinically Extremely Vulnerable from COVID-19". Accessed 14 May, 2020

Grabsch, B., Clarke, D. M., Love, A., McKenzie, D. P., Snyder, R. D., Bloch, S., Smith, G., & Kissane, D. W. (2006). Psychological morbidity and quality of life in women with advanced breast cancer: a cross-sectional survey. *Palliative & supportive care*, *4*(1), 47–56.

Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology*, *55*(4), 468–484. https://doi.org/10.1016/0013-4694(83)90135-9

Greer, J. A., Pirl, W. F., Park, E. R., Lynch, T. J., and Temel, J. S. (2008). Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. *Journal of Psychosomatic Research*, *65*(6), 549–52. https://doi.org/10.1016/j.jpsychores.2008.03.005.

Gregorowitsch, M. L., Ghedri, A., Young-Afat, D. A., Bijlsma, R., Baas, I. O., van Schaik-van de Mheen, C., Agterol, M. J., Göker, E., ten Bokkel Huinink, D., van den Bongard, H. J. G. D., Verkooijen, H. M., & UMBRELLA study group. (2019a). The effect of chemotherapy on subjective cognitive function in younger early-stage breast cancer survivors treated with chemotherapy compared to older patients. *Breast Cancer Research and Treatment*, *175*, 429-441. https://doi.org/10.1007/s10549-019-05149-4.

Gregorowitsch, M. L., van den Bongard, H., Couwenberg, A. M., Young-Afat, D. A., Haaring, C., Van Dalen, T., Schoenmaeckers, E., Agterof, M. J., Baas, I. O., Sier, M. F., Ernst, M. F., van Hummel, R., Verkooijen, H. M., & UMBRELLA study group (2019b). Self-reported work ability in breast cancer survivors; a prospective cohort study in the Netherlands. *Breast (Edinburgh, Scotland)*, *48*: 45–53. https://doi.org/10.1016/j.breast.2019.08.004

Grinshpun, A., & Rottenberg, Y. (2019). Unemployment following breast cancer diagnosis: A population-based study. *Breast (Edinburgh, Scotland)*, *44*, 24–28. https://doi.org/10.1016/j.breast.2018.12.013

Groenvold, M., Petersen, M. A., Idler, E., Bjorner, J. B., Fayers, P. M., & Mouridsen, H. T. (2007). Psychological distress and fatigue predicted recurrence and survival in primary breast cancer patients. *Breast Cancer Research and Treatment*, *105*(2), 209–219. https://doi.org/10.1007/s10549-006-9447-x

Grutzmann, R., Endrass, T., Kaufmann, C., Allen, E., Eichele, T., & Kathmann, N. (2016). Presupplementary motor area contributes to altered error monitoring in obsessive-compulsive disorder. *Biological Psychiatry*, *80*, 562–571.

Gullett, J. M., Cohen, R. A., Yang, G. S., Menzies, V. S., Fieo, R. A., Kelly, D. L., Starkweather, A. R., Jackson-Cook, C. K., & Lyon, D. E. (2019). Relationship of fatigue with cognitive performance in women with early-stage breast cancer over 2 years. *Psycho-Oncology*, *28*, 997-1003. https://doi:10.1002/pon.5028.

Gupta, D., Lis, C. G., & Grutsch, J. F. (2007). Perceived cancer-related financial difficulty: implications for patient satisfaction with quality of life in advanced cancer. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, *15*(9), 1051–1056. https://doi.org/10.1007/s00520-007-0214-2

Haggstrom, L. R., Vardy, J. L., Carson, E. K., Segara, D., Lim, E., & Kiely, B. E. (2022). Effects of Endocrine Therapy on Cognitive Function in Patients with Breast Cancer: A Comprehensive Review. *Cancers*, *14*(4), 920. https://doi.org/10.3390/cancers14040920

Hajj, A., Hachem, R., Khoury, R., Hallit, S., Eijebbawi, B., Nasr, F., El Karak, F., Chahine, G., Kattan, J., & Rabbaa Khabbaz, L. (2021). Clinical and genetic factors associated with anxiety and depression in breast cancer patients: a cross-sectional study. *BMC Cancer*, *21*(1), 872. https://doi.org/10.1186/s12885-021-08615-9

Hamood, R., Hamood, H., Merhasin, I., & Keinan-Boker, L. (2019). Work transitions in breast cancer survivors and effects on quality of life. *Journal of Occupational Rehabilitation*, *29*(2), 336–349. https://doi.org/10.1007/s10926-018-9789-3

Hansen, J.A., Feuerstein, M., Calvio, L.C., & Olsen, C.H. (2008). Breast cancer survivors at work. *Journal of Occupational and Environmental Medicine, 50,* 777–784. doi:10.1097/JOM.0b013e318165159e

Hashemi, S. M., Rafiemanesh, H., Aghamohammadi, T., Badakhsh, M., Amirshahi, M., Sari, M., Behnamfar, N., & Roudini, K. (2020). Prevalence of anxiety among breast cancer patients: a

systematic review and meta-analysis. *Breast cancer (Tokyo, Japan)*, *27*(2), 166–178. https://doi.org/10.1007/s12282-019-01031-9

Henderson, F. M., Cross, A. J., & Baraniak, A. R. (2019). 'A new normal with chemobrain': Experiences of the impact of chemotherapy-related cognitive deficits in long-term breast cancer survivors. *Health Psychology Open*, *6*(1), 2055102919832234. https://doi.org/10.1177/2055102919832234

Henneghan, A. M., Carter, P., Stuifbergan, A., Parmelee, B., & Kesler, S. (2018). Relationships between self-reported sleep quality components and cognitive functioning in breast cancer survivors up to 10 years following chemotherapy. *Psycho-Oncology*, *27*, 1937-1943.

Hermelink, K., Voigt, V., Kaste, J., Neufeld, F., Wuerstlein, R., Bühner, M., Münzel, K., Rjosk-Dendorfer, D., Grandl, S., Braun, M., von Koch, F. E., Härtl, K., Hasmüller, S., Bauerfeind, I., Debus, G., Herschbach, P., & Harbeck, N. (2015). Elucidating pretreatment cognitive impairment in breast cancer patients: the impact of cancer-related post-traumatic stress. *Journal of the National Cancer Institute*, *107*(7), djv099. https://doi.org/10.1093/jnci/djv099

Hilhorst, S., & Lockey, A. (2019). *Cancer costs: A 'ripple effect' analysis of cancer's wider impact*. Pfizer. https://demos.co.uk/wp-content/uploads/2020/01/Cancer-Costs-FINAL-Jan-2020.pdf

Hirsch, C. R., & Mathews, A. (2012). A cognitive model of pathological worry. *Therapy*, *50*(10), 636-646.

Ho, P, J., Hartman, M., Gernaat, S. A. M., Cook, A. R., Lee, S. C., Hupkens, L., & Verkooijen, H. M. (2018). Associations between workability and patient-reported physical, psychological and social outcomes in breast cancer survivors: A cross-sectional study. *Supportive Care in Cancer*, *26*, 2815-2824. https://doi.org/10.1007/s00520-018-4132-2

Ho, P. J., Cook, A. R., Binte Mohamed Ri, N. K., Liu, J., & Hartman, M. (2020). Impact of delayed treatment in women diagnosed with breast cancer: A population-based study'. *Cancer Medicine*, *9*(7), 2435-2444. https://doi.org/10.1002/cam4.2830.

Hoffmann, T. C., Glasziou, P. P., Boutron, I., Milne, R., Perera, R., Moher, D., Altman, D. G., Barbour, V., Macdonald, H., Johnston, M., Lamb, S. E., Dixon-Woods, M., McCulloch, P., Wyatt, J. C.,

Chan, A. W., & Michie, S. (2014). Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ (Clinical Research ed.)*, *348*, g1687. https://doi.org/10.1136/bmj.g1687

Holmes, J., Gathercole, S. E., & Dunning, D. L. (2009). Adaptive training leads to sustained enhancement of poor working memory in children. *Developmental Science*, *12*(4), F9–F15. https://doi.org/10.1111/j.1467-7687.2009.00848.x

Holmes, E. A., O'Connor, R. C., Perry, V. H., Tracey, I., Wessely, S., Arseneault, L., Ballard, C., Christensen, H., Cohen Silver, R., Everall, I., Ford, T., John, A., Kabir, T., King, K., Madan, I., Michie, S., Przybylski, A. K., Shafran, R., Sweeney, A., Worthman, C. M., … Bullmore, E. (2020). Multidisciplinary research priorities for the COVID-19 pandemic: a call for action for mental health science. *The lancet. Psychiatry*, *7*(6), 547–560. https://doi.org/10.1016/S2215-0366(20)30168-1

Hotton, M., Derakshan, N., & Fox, E. (2018). A randomised controlled trial investigating the benefits of adaptive working memory training for work memory capacity and attentional control in high worriers. *Behaviour Research and Therapy*, *100*, 67-77.

Hughes, G., & Yeung, N. (2011). Dissociable correlates of response conflict and error awareness in error-related brain activity. *Neuropsychologia*, *49*(3), 405–415. https://doi.org/10.1016/j.neuropsychologia.2010.11.03

Hurria, A., Somlo, G., & Ahles, T. (2007). Renaming "chemo brain". *Cancer Invest*, *25*, 388-394.

Ilmarinen, J., Tuomi, K., & Seitsamo, J. (2005). New dimensions of work ability. *International Congress Series*, *1280*, 3-7. https://doi.org/10.1016/j.ics.2005.02.060

Inhestern, L., Beierlein, V., Bultmann, J. C., Möller, B., Romer, G., Koch, U., & Bergelt, C. (2017). Anxiety and depression in working-age cancer survivors: a register-based study. *BMC Cancer*, *17*(1), 347. https://doi.org/10.1186/s12885-017-3347-9

IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY: IMB Corp

IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0, Armonk, NY: IMB Corp

International Labor Organization. 2020. Almost 25 million jobs could be lost worldwide as a result of COVID-19, say ILO. Accessed May 20, 2020. https://www.ilo.org/global/about-the-ilo/newsroom/news/WCMS 738742/lang-en/index.htm.

Irvine, D. M., Vincent, L., Graydon, J. E., & Bubela, N. (1998). Fatigue in women with breast cancer receiving radiation therapy. *Cancer Nursing*, *21*(2), 127–135. https://doi.org/10.1097/00002820-199804000-00006

Islam, T., Dahlui, M., Majid, H. A., Nahar, A. M., Mohd Taib, N. A., Su, T. T., & MyBCC study group (2014). Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health*, *14 Suppl 3*(Suppl 3), S8. https://doi.org/10.1186/1471-2458-14-S3-S8

Jaeggi, S. M., Seewer, R., Nirkko, A. C., Eckstein, D., Schroth, G., Groner, R., & Gutbrod, K. (2003). Does excessive memory load attenuate activation in the prefrontal cortex? Load-dependent processing in single and dual tasks: functional magnetic resonance imaging study. *NeuroImage*, *19*(2 Pt 1), 210–225. https://doi.org/10.1016/s1053-8119(03)00098-3

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(19), 6829–6833. https://doi.org/10.1073/pnas.0801268105

Jaeggi, S. M., Studer-Luethi, B., Buschkuehl, M., Su, Y-F., Jonides, J., & Perrig, W. J. (2010). The relationship between n-back performance and matrix reasoning – implications for training and transfer. *Intelligence*, *38*(6), 625-635.

Jaeggi, S. M., Buschkuehl, M., Shah, P., & Jonides, J. (2014). The role of individual differences in cognitive training and transfer. *Memory & Cognition*, *43*, 464-480.

Janelsins, M. C., Kohli, S., Mohile, S. G., Usuki, K., Ahles, T. A., & Morrow, G. R. (2011). An update on cancer- and chemotherapy-related cognitive dysfunction: current status. *Seminars in Oncology*, *38*(3), 431–438. https://doi.org/10.1053/j.seminoncol.2011.03.014

Janelsins, M. C., Heckler, C. E., Peppone, L. J., Kamen, C., Mustian, K. M., Mohile, S. G., Magnuson, A., Kleckner, I. R. Guido, J. J., Young, K. L., Conlin, A. K., Weiselberg, L. R., Mitchell, J. W., Ambrosone, C. A., Ahles, T. A., & Morrow, G. R. (2017). Cognitive complaints in survivors of breast cancer after chemotherapy compared with age-matched controls: An analysis from a nationwide, multicenter, prospective longitudinal study. *Journal of Clinical Oncology*, *35*(5), 506-514.

Janelsins, M. C., Heckler, C. E., Peppone, L. J., Ahles, T. A., Mohile, S. G., Mustian, K. M., Palesh, O., O'Mara, A. M., Minasian, L. M., Williams, A. M., Magnuson, A., Geer, J., Dakhil, S. R., Hopkins, J. O., & Morrow, G. R. (2018). Longitudinal trajectory and characterization of cancer-related cognitive impairment in a nationwide cohort study. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *36*(32), JCO2018786624. https://doi.org/10.1200/JCO.2018.78.6624

Jasper, H. H. (1958). The ten-twenty electrode system of the interactional federation. *Electroencephalography and Clinical Neurophysiology*, *10*, 371-375.

Jay, T. M., Rocher, C., Hotte, M., Naudon, L., Gurden, H., & Spedding, M. (2004). Plasticity at hippocampal to prefrontal cortex synapses is impaired by loss of dopamine and stress: importance for psychiatric diseases. *Neurotoxicity Research*, *6*(3), 233–244. https://doi.org/10.1007/BF03033225

Jehn, C. F., Flath, B., Strux, A., Krebs, M., Possinger, K., Pezzutto, A., & Lüftner, D. (2012). Influence of age, performance status, cancer activity, and IL-6 on anxiety and depression in patients with metastatic breast cancer. *Breast Cancer Research and Treatment*, *136*(3), 789–794. https://doi.org/10.1007/s10549-012-2311-2

Jenkins, V., Shilling, V., Fallowfield, L., Howell, A., & Hutton, S. (2004). Does hormone therapy for the treatment of breast cancer have a detrimental effect on memory and cognition? A pilot study. *Psycho-Oncology*, *13*(1): 61–66. https://doi.org/10.1002/pon.709

Jentzsch, I., & Dudschig, C. (2009). Why do we slow down after an error? Mechanisms underlying the effects of posterror slowing. *The Quarterly Journal of Experimental Psychology, 62*(2), 209–218

Jin, J.H., & Lee, E.J. (2018). Factors influencing quality of working life of cancer survivors after return to the workplace. *Korean Journal of Occupational Health Nursing*, *27*(4), 203-214.

Jin, J.H., & Lee, E.J. (2020). Factors affecting quality of work life in a sample of cancer survivor female nurses. *Medicina (Kaunas).* doi: 10.3390/medicina56120721

Jin J. (2021). Factors associated with the quality of work life among working breast cancer survivors. *Asia-Pacific Journal of Oncology Nursing*, *9*(2), 97–104. https://doi.org/10.1016/j.apjon.2021.11.005

Johnsson, A., Fornander, T., Rutqvist, L. E., & Olsson, M. (2010). Factors influencing return to work: A narrative study of women treated for breast cancer. *European Journal of Cancer Care*, *19*(3), 317-323. https://doi:10.1111/j.1365-2354.2008.01043.x.

Johnson Vickberg, S. M. (2001). Fears about breast cancer recurrence: Interviews with a diverse sample. *Cancer Practice*, *9*(5), 237–243. https://doi.org/10.1046/j.1523-5394.2001.009005237.x

Johnston, S.R.D. (2010). Living with secondary breast cancer: coping with an uncertain future with unmet needs. *European Journal of Cancer Care, 19*(5), 561-563.

Johnson, S. R. D., & Swanton, C. (2006). *Handbook of metastatic breast cancer*. Informa Healthcare.

Joly F, Giffard B, Rigal O, De Ruiter MB, Small BJ, Dubois M, LeFel J, Schagen SB, Ahles TA, Wefel JS, Vardy JL, Pancré V, Lange M, Castel H. (2015). Impact of cancer and its treatments on cognitive function: Advances in research from the Paris international cognition and cancer task force symposium and ipdate Since 2012. *J Pain Symptom Manage*, *50* 6), 830-41.

Joly, F., Lange, M., Dos Santos, M., Vaz-Luis, I., & Di Meglio, A. (2019). Long-term fatigue and cognitive disorders in breast cancer survivors. *Cancers*, *11*(12), 1896. https://doi.org/10.3390/cancers11121896

Kam, J. W. Y., Brenner, C.A., Handy, T. C., Boyd, L. A., Liu-Ambrose, T., Lim, H. J., Hayden, S., & Campbell, K. L. (2016). Sustained attention abnormalities in breast cancer survivors with cognitive deficits post chemotherapy: An electrophysiological study. *Clinical Neurophysiology*, *127*, 369-378.

Kamiya, A., Hayama, Y., Kato, S., Shimomura, A., Shimomura, T., Irie, K., Kaneko, R., Yanagawa, Y., Kobayashi, K., & Ochiya, T. (2019). Genetic manipulation of autonomic nerve fiber innervation and activity and its effect on breast cancer progression. *Nature neuroscience*, *22*(8), 1289–1305

Kang, D., Weaver, M. T., Park, N., Smith, B., McArdle, T., and Carpenter, J. (2009). Significant impairment in immune recovery following cancer treatment. *Nursing Research, 58*(2), 105–14. https://doi.org/10.1097/NNR.0b013e31818fcecd.

Kawohl, W., and Nordt, C. (2020). COVID-19, unemployment, and suicide. *The Lancet Psychiatry, 7*(5), 289-390.

Keim-Malpass, J., Levine, B., Danhauer, S. C., & Avis, N. E. (2016). Work-related perception and quality of life among breast cancer survivors. *Psycho-Oncology*, *25*(7), 873-876.

Kennedy, F., Haslam, C., Munir, F., & Pryce, J. (2007). Returning to work following cancer: a qualitative exploratory study into the experience of returning to work following cancer. *Eur J Cancer Care (Engl), 16*(1), 17-25. doi:10.1111/j.1365-2354.2007.00729.x

Kesler, S., Janelsins, M., Koovakkattu, D., Palesh, O., Mustian, K., Morrow, G., & Dhabhar, F. S. (2013a). Reduced hippocampal volume and verbal memory performance associated with interleukin-6 and tumor necrosis factor-alpha levels in chemotherapy-treated breast cancer survivors. *Brain, Behavior, and Immunity*, *30 Suppl* (0), S109–S116. https://doi.org/10.1016/j.bbi.2012.05.017

Kesler, S., Hadi Hosseini, S. M., Heckler, C., Janelsins, M., Palesh, O., Mustian, K., & Morrow, G. (2013b). Cognitive training for improving executive function in chemotherapy-treated breast

cancer survivors. *Clinical Breast Cancer*, *13*(4), 299–306. https://doi.org/10.1016/j.clbc.2013.02.004

Kesler, S. R., Rao, V., Ray, W. J., Rao, A., & Alzheimer's Disease Neuroimaging Initiative (2017). Probability of Alzheimer's disease in breast cancer survivors based on gray-matter structural network efficiency. *Alzheimer's & Dementia (Amsterdam, Netherlands)*, *9*, 67–75. https://doi.org/10.1016/j.dadm.2017.10.002

Kim, J-M., Jang, J-E., Stewart, R., Kim, S-Y., Kim, S-W., Kang, J-J., Shin, I-S., Park, M-H., Yoon, J-H., & Yoon, J-S. (2013). Determinants of suicidal ideation in patients with breast cancer. *Psycho-Oncology, 22*(12), 2848-2856.

Kim, S-Y., Kissane, D. W., Richardson, G., Senior, J., Morgan, J., Gregory, P., Birks, S., Ooi, C., Lipton, L., Antill, Y., Vereker, M., Michael, N., & Bobevski, I. (2022). The role of depression and other psychological factors in work ability among breast cancer in survivors in Australia. *Psycho-Oncology, 31*(2), 167-175. https://doi.org/10.1002/pon.5802

Kim, S. Y., Kissane, D. W., Richardson, G., Senior, J., Morgan, J., Gregory, P., Birks, S., Ooi, C., Lipton, L., Antill, Y., Vereker, M., Michael, N., & Bobevski, I. (2022). The role of depression and other psychological factors in work ability among breast cancer survivors in Australia. *Psycho-Oncology*, *31*(2), 167–175. https://doi.org/10.1002/pon.5802

Kissane, D. W., Grabsch, B., Love, A., Clarke, D. M., Bloch, S., & Smith, G. C. (2004). Psychiatric disorder in women with early stage and advanced breast cancer: a comparative analysis. *The Australian and New Zealand Journal of Psychiatry*, *38*(5), 320–326. https://doi.org/10.1080/j.1440

Klaver, K. M., Duijts, S. F. A., Engelhardt, E. G., Geusgens, C. A. V., Aarts, M. J. B., Ponds, R. W. H. M., van der Beek, A. J., & Schagen, S. B. (2020). Cancer-related cognitive problems at work: experiences of survivors and professionals. *Journal of Cancer Survivorship, 14*, 168-178. https://doi.org/10.1007/s11764-019-00830-5

Klawohn, J., Santopetro, N. J., Meyer, A., & Hajcak, G. (2020). Reduced P300 in depression: Evidence from a flanker task and impact on ERN, CRN, and Pe. *Psychophysiology*, *57*(4), e13520. https://doi.org/10.1111/psyp.13520

Koch, L., Bertram, H., Eberle, A., Holleczek, B., Schmid-Höpfner, S., Waldmann, A., Zeissig, S. R., Brenner, H., & Arndt, V. (2014). Fear of recurrence in long-term breast cancer survivors-still an issue. Results on prevalence, determinants, and the association with quality of life and depression from the cancer survivorship--a multi-regional population-based study. *Psycho-Oncology*, *23*(5), 547–554. https://doi.org/10.1002/pon.3452

Kohli, S., Fisher, S. G., Tra, Y., Adams, M. J., Mapstone, M. E., Wesnes, K. A., Roscoe, J. A., & Morrow, G. R. (2009). The effect of modafinil on cognitive function in breast cancer survivors. *Cancer*, *115*(12), 2605–2616. https://doi.org/10.1002/cncr.24287

Koppelmans, V., de Ruiter, M. B., van der Lijn, F., Boogerd, W., Seynaeve, C., van der Lugt, A., Vrooman, H., Niessen, W. J., Breteler, M. M., & Schagen, S. B. (2012a). Global and focal brain volume in long-term breast cancer survivors exposed to adjuvant chemotherapy. *Breast Cancer Research and Treatment*, *132*(3), 1099–1106. https://doi.org/10.1007/s10549-011-1888-1

Koppelmans, V., Breteler, M. M. B., Boogerd, W., Seynaeve, C., Gundy, C., & Schagen, S. B. (2012b). Neuropsychological performance in survivors of breast cancer more than 20 years after adjuvant chemotherapy. *Journal of Clinical Oncology*, *30*(10), 1080-1086. https://doi:10.1200/JCO.2011.37.0189.

Koopman, C., Nouriani, B., Erickson, V., Anupindi, R., Butler, L. D., Bachmann, M. H., Sephton, S. E., & Spiegel, D. (2002). Sleep disturbances in women with metastatic breast cancer. *The Breast Journal*, *8*(6), 362–370. https://doi.org/10.1046/j.1524-4741.2002.08606.x

Koster, E. H. W., Hoorelbeke, K., Onraedt, T., Owens, M., & Derakshan, N. (2017). Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review*, *53* (April), 79–92. https://doi.org/10.1016/j.cpr.2017.02.002.

Knobf, M. T., & Sun, Y. (2005). A longitudinal study of symptoms and self-care activities in women treated with primary radiotherapy for breast cancer. *Cancer Nursing*, *28*(3), 210–218. https://doi.org/10.1097/00002820-200505000-00010

Kreukels, B. P., Schagen, S. B., Ridderinkhof, K. R., Boogerd, W., Hamburger, H. L., & van Dam, F. S. (2005). Electrophysiological correlates of information processing in breast-cancer patients treated with adjuvant chemotherapy. *Breast Cancer Research and Treatment*, *94*(1), 53–61. https://doi.org/10.1007/s10549-005-7093-3

Kreukels, B. P., Schagen, S. B., Ridderinkhof, K. R., Boogerd, W., Hamburger, H. L., Muller, M. J., & van Dam, F. S. A. M. (2006). Effects of high-dose and conventional-dose adjuvant chemotherapy on long-term cognitive sequelae in patients with breast cancer: An electrophysiological study. *Clinical Breast Cancer*, *7*(1), 67-78.

Kreukels, B. P. C., Hamburger, H. L., de Ruiter, M., van Dam, F. S. A. M., Ridderinkhof, K. R., Boogerd, W., Schagen, S. B. (2008). ERP amplitude and latency in breast cancer survivors treated with adjuvant chemotherapy. *Clinical Neurophysiology*, *119*(3), 533-541. Lai, A. G., Pasea, L., Banerjee, A., Denaxas, S., Katsoulis, M., Chang, W. H., Williams, B., Pillay, D., Noursadeghi, M., Linch, D., Hughes, D., Forster, M. D., Turnbull, C., Fitzpatrick, N. K., Boyd, K., Foster, G.R., Cooper, M., Jones, M., Pritchard-Jones, K., Sullivan, R., Hall, G., Davie, C., Lawler, M., & Hemingway, H. (2020). Estimating excess mortality in people with cancer and multimorbidity in the COVID-19 emergency. *medRxiv*. DOI: 10.1101/2020.05.27.20083287

Lamore, K., Dubois, T., Rothe, U., Leonardi, M., Girard, I., Manuwald, U., Nazarov, S., Silvaggi, F., Guastafierro, E., Scaratti, C., Breton, T., & Foucaud, J. (2019). Return to Work Interventions for Cancer Survivors: A Systematic Review and a Methodological Critique. *International Journal of Environmental Research and Public Health*, *16*(8), 1343. https://doi.org/10.3390/ijerph16081343

Landeiro, L., Gagliato, D. M., Fêde, A. B., Fraile, N. M., Lopez, R. M., da Fonseca, L. G., Petry, V., Testa, L., Hoff, P. M., & Mano, M. S. (2018). Return to work after breast cancer diagnosis: An

observational prospective study in Brazil. *Cancer*, *124*(24), 4700–4710. https://doi.org/10.1002/cncr.31735

Lange, M., Joly, F., Vardy, J., Ahles, T., Dubois, M., Tron, L., Winocur, G., De Ruiter, M. B., & Castel, H. (2019a). Cancer-related cognitive impairment: an update on state of the art, detection, and management strategies in cancer survivors. *Annals of oncology: official journal of the European Society for Medical Oncology*, *30*(12), 1925–1940. https://doi.org/10.1093/annonc/mdz410

Lange, M., Licaj, I., Clarisse, B., Humbert, X., Grellard, J. M., Tron, L., & Joly, F. (2019b). Cognitive complaints in cancer survivors and expectations for support: Results from a web-based survey. *Cancer Medicine*, *8*(5), 2654–2663. https://doi.org/10.1002/cam4.2069

Largillier, R., Ferrero, J. M., Doyen, J., Barriere, J., Namer, M., Mari, V., Courdi, A., Hannoun-Levi, J. M., Ettore, F., Birtwisle-Peyrottes, I., Balu-Maestro, C., Marcy, P. Y., Raoust, I., Lallement, M., & Chamorey, E. (2008). Prognostic factors in 1,038 women with metastatic breast cancer. *Annals of Oncology: Official Journal of the European Society for Medical Oncology*, *19*(12), 2012–2019. https://doi.org/10.1093/annonc/mdn424

Lavigne, J. E., Griggs, J. J., Tu, X. M., & Lerner, D. J. 2008. Hot flashes, fatigue, treatment exposures and work productivity in breast cancer survivors. *Journal of Cancer Survivorship*, *2*, 296-302. https://doi.org/10.1007/s11764-008-0072-zLee, M. K., Kang, H. S., Lee, K. S., & Lee, E. S. (2017). Three-year prospective cohort study of factors associated with return to work after breast cancer diagnosis. *Journal of Occupational Rehabilitation*, *27*(4), 547–558. https://doi.org/10.1007/s10926-016-9685-7

Leensen, M., Groeneveld, I. F., van der Heide, I., Rejda, T., van Veldhoven, P., Berkel, S. V., Snoek, A., Harten, W. V., Frings-Dresen, M., & de Boer, A. (2017). Return to work of cancer patients after a multidisciplinary intervention including occupational counselling and physical exercise in cancer patients: a prospective study in the Netherlands. *BMJ open*, *7*(6), e014746. https://doi.org/10.1136/bmjopen-2016-014746

Lerner, D., Amick 3rd, B. C., Rogers, W. H., Malspeis, S., Bungay, K., & Cynn, D. (2001). The work limitations questionnaire. *Med Care*, *39*(1), 72-85. https://doi:10.1097/00005650-200101000-00009.

Lerner, D., Rogers, W. H., & Chang, H. (2002). The work limitations questionnaire. *Qual Life*, *28*, 9-10.

Lerner, D., Amick 3rd, B. C., Lee, J. C., Rooney, T., Rogers, W. H., Chang, H., & Berndt, E. R. (2003). Relationship of employee-reported work limitations to work productivity. *Medical Care*, *41*(5), 649-659. http://doi:10.1097/01.MLR.0000062551.76504.A9.

Li, Q., Long, Q., Hu, N., Tang, Y., & Chen, A. (2020). N-back Task training helps to improve post-error performance. *Frontiers in Psychology*, *11*, 370. https://doi.org/10.3389/fpsyg.2020.00370

Linden, W., Vodermaier, A., Mackenzie, R., & Greig, D. (2012). Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender and age. *Journal Affective Disorders, 141*, 343-351.

Liou, K. T., Ahles, T. A., Garland, S. N., Li, Q. S., Bao, T., Li, Y., Root, J. C., & Mao, J. J. (2019). The relationship between insomnia and cognitive impairment in breast cancer survivors. *JNCI cancer spectrum*, *3*(3). pkz041. https://doi.org/10.1093/jncics/pkz041

Liu, S., Wang, F., Yang, Q., Feng, D., Chen, Y., & Cheng, A.S. K. (2021). Work productivity loss in breast cancer survivors and its effects on quality of life. *Work*, *70*(1), 199-207. https://doi.org/10.3233/WOR-213565

Lloret, A., Fuchsberger, T., Giraldo, E., & Viña, J. (2015). Molecular mechanisms linking amyloid β toxicity and Tau hyperphosphorylation in Alzheimer′s disease. *Free Radical Biology & Medicine, 83*, 186–191. https://doi.org/10.1016/j.freeradbiomed.2015.02.028

Llosa, J. A., Menéndez-Espina, S., Agulló-Tomás, E., & Julio Rodríguez-Suárez. (2018). Job insecurity and mental health: a meta-analytical review of the consequences of precarious work in clinical disorders. *Anales de Psicol*ogia, *34*(2), 211-221.

Lotfi, S., Rostami, R., Shokoohi-Yekta, M., Ward, R. T., Motamed-Yeganeh, N., Mathew, A. S., & Lee, H-J. (2020). Effects of computerized cognitive training for children with dyslexia: An ERP study. *Journal of Neurolinguistics, 55*, 100904.

Lotfi, S., Ward, R. T., Ayazi, M., & Bennett, K. P. (2021). The effects of emotional working memory training on symptoms and error-related negativity of individuals with high trait anxiety: A randomized controlled study. *Cognitive Therapy and Research, 45*, 969-985.

Low, C.A., & Stanton, A. L. (2015). Activity disruption and depressive symptoms in women living with metastatic breast cancer. *Health Psychology, 34*, 89-92.

Lyons, K. D., Newman, R. M., Sullivan, M., Pergolotti, M., Braveman, B., & Cheville, A. L. (2019). Employment concerns and associated impairments of women living with advanced breast cancer. *Archives of Rehabilitation Research and Clinical Translation, 1*(1-2), 100004.

Maass, S., Brandenbarg, D., Boerman, L. M., Verhaak, P., de Bock, G. H., & Berendsen, A. J. (2021). Fatigue among long-term breast cancer survivors: A controlled cross-sectional study. *Cancers, 13*(6), 1301. https://doi.org/10.3390/cancers13061301

Mackereth, P., Farrell, C., Bardy, J., Molassiotis, A., & Finnegan-John, J. (2015). Legitimising fatigue after breast-cancer treatment. *British Journal of Nursing (Mark Allen Publishing), 24*(4), S4–S12. https://doi.org/10.12968/bjon.2015.24.Sup4.S4

MacLennan, S., Cox, T., Murdoch, S., & Eatough, V. (2021). An interpretative phenomenological analysis of the meaning of work to women living with breast cancer. *Chronic Illness*. https://doi.org/10.1177/1742395320987883

Macmillan. 2018a. "Ductal Carcinoma In Situ (DCIS)". Accessed May 10, 2020.

Macmillan. 2018b. "Staging and Grading of Breast Cancer". Accessed May, 2020

Macmillan. 2018c. "Breast Cancer in Men". Accessed June, 2022.

Macmillan. 2019. "Triple Negative Breast". Accessed June, 2022.

Mackereth, P., Farrell, C., Bardy, J., Molassiotis, A., & Finnegan-John, J. (2015). Legitimising fatigue after breast-cancer treatment. *British Journal of Nursing*, *24*(4). https://doi.org/10.12968/bjon.2015.24.Sup4.S4

Mandelblatt, J. S., Stern, R. A., Luta, G., McGuckin, M., Clapp, J. D., Hurria, A., Jacobsen, P. B., Faul, L. A., Isaacs, C., Denduluri, N., Gavett, B., Traina, T. A., Johnson, P., Silliman, R. A., Turner, R. S., Howard, D., Van Meter, J. W., Saykin, A., & Ahles, T. (2014). Cognitive impairment in older patients with breast cancer before systemic therapy: is there an interaction between cancer and comorbidity?. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology*, *32*(18), 1909–1918. https://doi.org/10.1200/JCO.2013.54.2050

Maruthappu, M., Watkins, J. A., Waqar, M., Williams, C., Ali, R., Atun, R., Faiz, O., & Zeltner, T. (2015). Unemployment, public-sector health-care spending and breast cancer mortality in the European Union: 1990-2009. *European Journal of Public Health*, *25*(2), 330–335. https://doi.org/10.1093/eurpub/cku167

Masood S. (2016). Neoadjuvant chemotherapy in breast cancers. *Women's Health (London, England)*, *12*(5), 480–491. https://doi.org/10.1177/1745505716677139

Maunsell, E., Brisson, C., Dubois, L., Lauzier, S., & Fraser, A. (1999). Work problems after breast cancer: an exploratory qualitative study. *Psycho-Oncology*, *8*(6), 467–473. https://doi.org/10.1002/(sici)1099-1611(199911/12)8:6<467::aid-pon400>3.0.co;2-p

McDonald, B. C., Conroy, S. K., Ahles, T. A., West, J. D., & Saykin, A. J. (2012). Alterations in brain activation during working memory processing associated with breast cancer and treatment: a prospective functional magnetic resonance imaging study. *Journal of clinical oncology: Official Journal of the American Society of Clinical Oncology*, *30*(20), 2500–2508. https://doi.org/10.1200/JCO.2011.38.5674

McDonald, B. C., & Saykin, A. J. (2013). Alterations in brain structure related to breast cancer and its treatment: chemotherapy and other considerations. *Brain Imaging and Behavior*, *7*(4), 374–387. https://doi.org/10.1007/s11682-013-9256-x

McKenzie, H. S., Maishman, T., Simmonds, P., Durcan, L., POSH Steering Group., Eccles, D., & Copson, E. (2020). Survival and disease characteristics of de novo verse recurrent metastatic breast cancer in a cohort of young patients. *Br J Cancer*, *122*, 1618-1629. https://doi.org/10.1038/s41416-020-0784-z

McLachlan, S. A., Devins, G. M., & Goodwin, P. J. (1999). Factor analysis of the psychosocial items of the EORTC QLQ-C30 in metastatic breast cancer patients participating in a psychosocial intervention study. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *8*(4), 311–317. https://doi.org/10.1023/a:1008939818096

Mehnert A. (2011). Employment and work-related issues in cancer survivors. *Critical Reviews in Oncology/Hematology*, *77*(2), 109–130. https://doi.org/10.1016/j.critrevonc.2010.01.00

Mehnert, A., de Boer, A., & Feuerstein, M. (2013). Employment challenges for cancer survivors. *Cancer*, *119(*Suppl 11), 2151–2159. https://doi.org/10.1002/cncr.28067

Mehnert, A., & Koch, U. (2013). Work satisfaction and quality of life in cancer survivors in the first year after oncological rehabilitation. *Work (Reading, Mass.)*, *46*(4), 407–415. https://doi.org/10.3233/WOR-131676

Meneses, K., Azuero, A., Hassey, L., McNees, P., & Pisu, M. (2012). Does economic burden influence quality of life in breast cancer survivors? *Gynecologic Oncology*, *124*(3), 437–443. https://doi.org/10.1016/j.ygyno.2011.11.038

Menning, S., de Ruiter, M. B., Kieffer, J. M., van Rentergem, J. A., Veltman, D. J., Fruijtier, A., Oldenburg, H. S. A., Boven, E., van der Meij, S., Lustig, V., Bos, M. E. M., Boogerd, W., Reneman, L., & Schagen, S. B. (2016). Cognitive impairment in a subset of breast cancer patients after systemic therapy – results from longitudinal study. *Journal of Pain and Symptom Management*, *52*(4), 560-569.

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the penn state worry questionnaire'. *Behaviour Research and Therapy*, *28*(6), 487–95. https://doi.org/10.1016/0005-7967(90)90135-6.

Mierzynska, J., Taye, M., Pe, M., Coens, C., Martinelli, F., Pogoda, K., Velikova, G., Bjelic-Radisic, V., Cardoso, F., Brain, E., Ignatiadis, M., Piccart, M., Van Tienhoven. G., Manse,l R., Wildiers, H., Bottomley, A., & EORTC and EORTC Breast Cancer Group. (2020). Reference values for the EORTC QLQ-C30 in early and metastatic breast cancer. *European Journal of Cancer (Oxford, England: 1990), 125*, 69-82. https://doi.org/10.1016/j.ejca.2019.10.031

Mikkelsen, K. B., Tabar, Y. R., Christensen, C. B., & Kidmose, P. (2021). EEG vary less between lab and home locations than they do between people. *Front. Comput. Neurosci*.. https://doi.org/10.3389/fncom.2021.565244

Miyake, A., & Shah, P. (1999). *Models of working memory: Mechanisms of active maintenance and executive control* (Eds.). Cambridge University Press.

Moran T. P. (2016). Anxiety and working memory capacity: A meta-analysis and narrative review. *Psychological Bulletin*, *142*(8), 831–864. https://doi.org/10.1037/bul0000051

Moser, J. S., Schroder, H. S., Heeter, C., Moran, T. P., & Lee, Y. H. (2011). Mind your errors: evidence for a neural mechanism linking growth mind-set to adaptive posterror adjustments. *Psychological Science*, *22*(12), 1484–1489. https://doi.org/10.1177/0956797611419520

Moser, J. S., Moran, T. P., Schroder, H. S., Donnellan, M. B., & Yeung, N. (2013). On the relationship between anxiety and error monitoring: a meta-analysis and conceptual framework. *Frontiers in Human Neuroscience*, *7*, 466. https://doi.org/10.3389/fnhum.2013.00466

Mosher, C. E., & Duhamel, K. N. (2012). An examination of distress, sleep, and fatigue in metastatic breast cancer patients. *Psycho-Oncology*, *21*(1), 100–107. https://doi.org/10.1002/pon.1873

Mosher, C. E., Johnson, C., Dickler, M., Norton, L., Massie, M. J., & DuHamel, K. (2013). Living with metastatic breast cancer: a qualitative analysis of physical, psychological, and social sequelae. *The Breast Journal*, *19*(3), 285–292. https://doi.org/10.1111/tbj.12107

Munir, F., Burrows, J., Yarker, J., Kalawsky, K., & Bains, M. (2010). Women's perceptions of chemotherapy-induced cognitive side affects on work ability: a focus group study. *Journal of Clinical Nursing*, *19*(9-10), 1362–1370. https://doi.org/10.1111/j.1365-2702.2009.03006.x

Munir, F., Kalawsky, K., Lawrence, C., Yarker, J., Haslam, C., & Ahmed, S. (2011). Cognitive intervention for breast cancer patients undergoing adjuvant chemotherapy: A needs analysis. *Cancer Nursing*, *34*, 385–392. https://dx.doi.org/10.1097/NCC.0b013e31820254f3

Musti, M. A., Collina, N., Stivanello, E., Bonfiglioli, R., Giordani, S., Morelli, C., & Pandolfi, P. (2018). Perceived work ability at return to work in women treated for breast cancer: a questionnaire-based study. *La Medicina del lavoro*, *109*(6), 407–419. https://doi.org/10.23749/mdl.v110i6.7241

Myers, J. S. (2012). Chemotherapy-related cognitive impairment: the breast cancer experience. *Oncology Nursing Forum*, *39* (1), E31-E40.

National Cancer Institute. 2020. "BRCA Gene Mutations: Cancer Risk and Genetic Testing". Accessed August 1, 2021.

National Health Service (NHS). 2021. "Mastectomy". Accessed 10th April 2021. https://www.nhs.uk/conditions/mastectomy/

National Institute for Health and Care Excellence (NICE). 2018. Early and locally advanced breast cancer: diagnosis and management NICE guideline. Accessed 18th January 2019.

Newport, D. J., & Nemeroff, C. B. (1998). Assessment and treatment of depression in the cancer patient. *Journal of Psychosomatic Research*, *45*(3), 215–237. https://doi.org/10.1016/s0022-3999(98)00011-7

Nilsson, M. I., Olsson, M., Wennman-Larsen, A., Petersson, L-M., & Alexanderson, K. (2013). Women's reflections and actions regarding working after breast cancer surgery – a focus group study. *Psycho-Oncology*, *22*, 1639-1644.

Nolen-Hoeksema, S. (2000). The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *Journal of Abnormal Psychology*, *109*(3), 504-511.

Nolen-Hoeksema, S., Wisco, B. E., and Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science*, *3*(5), 400–424. https://doi.org/10.1111/j.1745-6924.2008.00088.x

Norredam, M., Meara, E., Landrum, M. B., Huskamp, H. A., & Keating, N. L. (2009). Financial status, employment, and insurance among older cancer survivors. *Journal of General Internal Medicine*, *24 Suppl 2*(Suppl 2), S438–S445. https://doi.org/10.1007/s11606-009-1034-5

Oberst, K., Bradley, C. J., Gardiner, J. C., Schenk, M., & Given, C. W. (2010). Work task disability in employed breast and prostate cancer patients. *Journal of Cancer Survivorship: Research and Practice*, *4*(4), 322–330. https://doi.org/10.1007/s11764-010-0128-8

Office for National Statistic. 2019. "Cancer survival in England: national estimates for patients followed up to 2017". Accessed February, 2021. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/cancersurvivalinengland/nationalestimatesforpatientsfollowedupto2017

Office for National Statistics. 2021. "Internet users, UK: 2020". Accessed August, 2021. https://www.ons.gov.uk/businessindustryandtrade/itandinternetindustry/bulletins/internetusers/2020#:~:text=92%25%20of%20adults%20in%20the,aged%2075%20years%20and%20over.

Ong, W. L., Schouwenburg, M. G., van Bommel, A., Stowell, C., Allison, K. H., Benn, K. E., Browne, J. P., Cooter, R. D., Delaney, G. P., Duhoux, F. P., Ganz, P. A., Hancock, P., Jagsi, R., Knaul, F. M., Knip, A. M., Koppert, L. B., Kuerer, H. M., McLaughin, S., Mureau, M., Partridge, A. H., … Saunders, C. (2017). A Standard Set of Value-Based Patient-Centered Outcomes for Breast Cancer: The International Consortium for Health Outcomes Measurement (ICHOM) Initiative. *JAMA oncology*, *3*(5), 677–685. https://doi.org/10.1001/jamaoncol.2016.4851

Orre, I. J., Reinertsen, K. V., Aukrust, P., Dahl, A. A., Fosså, S. D., Ueland, T., & Murison, R. (2011). Higher levels of fatigue are associated with higher CRP levels in disease-free breast cancer

survivors. *Journal of Psychosomatic Research*, *71*(3), 136–141. https://doi.org/10.1016/j.jpsychores.2011.04.003

Osborne, R.H., Elsworth, G. R., Sprangers, M. A., Oort, F. J., & Hopper, J. L. (2004). The value of the hospital anxiety and depression scale (HADS) for comparing women with early onset breast cancer with population-based reference women. *Quality of Life Research*: *An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, *13*(1), 191-206.

Ottati, A., & Feuerstein, M. (2013). Brief self-report measure of work-related cognitive limitations in breast cancer survivors. *Journal of Cancer Survivorship: Research and Practice*, *7*(2), 262–273. https://doi.org/10.1007/s11764-013-0275-9

Overbeek, T.J.M., Nieuwenhuis, S., & Ridderinkhof, K. R. (2005) Dissociable components of error processing: on the functional significance of the Pe vis-à-vis the ERN/Ne. *J Psychophysiol 19,* 319–329.

Owens, M., Koster, E. H., & Derakshan, N. (2012). Impaired filtering of irrelevant information in dysphoria: an ERP study. *Social Cognitive and Affective Neuroscience*, *7*(7), 752–763. https://doi.org/10.1093/scan/nsr050

Owens, N., Koster, E. H. W., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on work memory capacity and filtering efficiency. Psychophysiology, *50*(3), 297-307.

Paalman, C. H., van Leeuwen, F. E., Aaronson, N. K., de Boer, A. G., van de Poll-Franse, L., Oldenburg, H. S., & Schaapveld, M. (2016). Employment and social benefits up to 10 years after breast cancer diagnosis: a population-based study. *British Journal of Cancer*, *114*(1): 81–87. https://doi.org/10.1038/bjc.2015.431

Padgett, L. S., Van Dyk, K., Kelly, N. C., Newman, R., Hite, S., & Asher, A. (2020). Addressing cancer-related cognitive impairment in cancer survivorship. *Oncology Issues*, *35*(1), 52-57. DOI: 10.1080/10463356.2020.1692601

Palesh, O. G., Collie, K., Batiuchok, D., Tilston, J., Koopman, C., Perlis, M. L., Butler, L. D., Carlson, R., & Spiegel, D. (2007). A longitudinal study of depression, pain, and stress as predictors of sleep disturbance among women with metastatic breast cancer. *Biological Psychology*, *75*(1), 37–44. https://doi.org/10.1016/j.biopsycho.2006.11.002

Pan, D., Sze, S., Minhas, J. S., Bangash, M. N., Pareek, N., Divall, P., Williams, C. M., Oggioni, M. R., Squire, I. B., Nellums, L. B., Hanif, W., Khunti, K., & Pareek, M. (2020). The impact of ethnicity on clinical outcomes in COVID-19: A systematic review. *EClinicalMedicine*, *23*, 100404. https://doi.org/10.1016/j.eclinm.2020.100404

Park, E. M., Gelber, S., Rosenberg, S. M., Seah, D., Schapira, L., Come, S. E., & Partridge, A. H. (2018). Anxiety and depression in young women with metastatic breast cancer: A cross-sectional study. *Psychosomatics*, *59*(3), 251–258. https://doi.org/10.1016/j.psym.2018.01.007

Pashler, H. (1988). Familiarity and visual change detection. *Perception & Psychophysics*, *44*, 369-378.

Patel, S. K., Wong, A. L., Wong, F. L., Breen, E. C., Hurria, A., Smith, M., Kinjo, C., Paz, I. B., Kruper, L., Somlo, G., Mortimer, J. E., Palomares, M. R., Irwin, M. R., & Bhatia, S. (2015). Inflammatory biomarkers, comorbidity, and neurocognition in women with newly diagnosed breast cancer. *Journal of the National Cancer Institute*, *107*(8), djv131. https://doi.org/10.1093/jnci/djv131

Peipins, L. A., Dasari, S., Rodriguez, J. L., White, M. C., Hodgson, M. E., & Sandler, D. P. (2021). Employment after breast cancer diagnosis and treatment among women in the sister and the two sister studies. *Journal of Occupational Rehabilitation*, *31*, 543-551.

Penedo, F. J., Oswald, L. B., Kronenfeld, J. P., Garcia, S. F., Cella, D., and Yanez., B. (2020). The increasing value of eHealth in the delivery of patient-centred cancer care. *The Lancet Oncology*, *21*(5), e240–51. https://doi.org/10.1016/S1470-2045(20)30021-8

Pergher, V., Shalchy, M. A., Pahor, A., Van Hulle, M. M., Jaeggi, S. M., & Seitz, A. R. (2019). Divergent research methods limit understanding of working memory training. *Journal of Cognitive Enhancement*, *4*, 100-120.

Perrin, F., Pernier, J., Bertrand, O., & Echallier, J. F. (1989). Spherical splines for scalp potential and current density mapping. *Electroencephalography and Clinical Neurophysiology*, *72*(2), 184–187. https://doi.org/10.1016/0013-4694(89)90180-6

Perry, L. M., Hoerger, M., Seibert, K., Gerhart, J. I., O'Mahony, S., & Duberstein, P. R. (2020). Financial Strain and Physical and Emotional Quality of Life in Breast Cancer. *Journal of Pain and Symptom Management*, *58*(3), 454–459. https://doi.org/10.1016/j.jpainsymman.2019.05.011

Phillips, K. M., Jim, H. S., Small, B. J., Laronga, C., Andrykowski, M. A., & Jacobsen, P. B. (2012), Cognitive functioning after cancer treatment. *Cancer*, *118*(7), 1925-1932. https://doi.org/10.1002/cncr.26432

Pilevarzadeh, M., Amirshahi, M., Afsargharehbagh, R., Rafiemanesh, H., Hashemi, S. M., & Balouchi, A. (2019). Global prevalence of depression among breast cancer patients: a systematic review and meta-analysis. *Breast Cancer Research and Treatment*, *176*(3), 519–533. https://doi.org/10.1007/s10549-019-05271-3

Plym, A., Johansson, A., Bower, H., Voss, M., Holmberg, L., Fredriksson, I., & Lambe, M. (2019). Causes of sick leave, disability pension, and death following a breast cancer diagnosis in women of working age. *Breast (Edinburgh, Scotland)*, *45*, 48–55. https://doi.org/10.1016/j.breast.2019.02.012

Polich J. (2007). Updating P300: an integrative theory of P3a and P3b. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, *118*(10), 2128–2148. https://doi.org/10.1016/j.clinph.2007.04.019

Polich, J. (2012). Neuropsychology of P300. In S. J. Luck, & E. S. Kappenman (Eds.), *Oxford library of psychology. The Oxford Handbook of Event-Related Potential Components* (pp. 159–188). Oxford University Press. https://doi.org/10.1093/ oxfordhb/9780195374148.013.0089

Poulson M. J. (2001). Not just tired. *Journal of clinical oncology: Official Journal of the American Society of Clinical Oncology*, *19*(21), 4180–4181. https://doi.org/10.1200/JCO.2001.19.21.4180

Pryce, J., Munir, F., & Haslam, C. (2007). Cancer survivorship and work: symptoms, supervisor response, co-worker disclosure and work adjustment. *Journal of Occupational Rehabilitation*, *17*(1), 83–92. https://doi.org/10.1007/s10926-006-9040-5Putman, P., Verkuil, B., Arias-Garcia, E., Pantazi, I., & van Schie, C. (2014). Erratum to "EEG theta/beta ratio as a potential biomarker for attentional control and resilience against deleterious effects of stress on attention". *Cognitive, Affective & Behavioral Neuroscience*, *14*(3), 1165. https://doi.org/10.3758/s13415-014-0264-0

Purcell, A., Fleming, J., Burmeister, B., Bennett, S., & Haines, T. (2011). Is education an effective management strategy for reducing cancer-related fatigue? *Supportive Care in Cancer*, *19*, 1429-1439.

Qualtrics XM. 2020. "The Other COVID-19 Crisis: Mental Health." Accessed May 28, 2020. https://www.qualtrics.com/blog/confronting-mental-health/.

Quinlan, E., Thomas-MacLean, R., Hack, T., Kwan, W., Miedema, B., Tatemichi, S., Towers, A., & Tilley, A. (2009). The impact of breast cancer among Canadian women: disability and productivity. *Work (Reading, Mass.)*, *34*(3), 285–296. https://doi.org/10.3233/WOR-2009-0926

Quinlan, E., MacLean, R., Hack, T., Tatemichi, S., Towers, A., Kwan, W., Miedema, B., & Tilley, A. (2011). Breast cancer survivorship and work disability. *Journal of Disability Policy Studies*, *22*(1), 18-27. https://doi.org/10.1177/1044207310394439

QSR International Pty Ltd. (2018) NVivo (Version 12), https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home

Rabbitt, P. M. (1966). Errors and error correction in choice-response task. *Journal of Experimental Psychology*, *71*(2), 264-272.

Radloff, L. S. (1977). The CESD-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*(3), 385-401.

Rasmussen, D. M., & Elverdam, B. (2008). The meaning of work and working life after cancer: An interview study. *Psycho-Oncology*, *17*(12), 1232-1238. https://doi:10/1002/pon.1354.

Raque-Bogdan, T. L., Hoffman, M. A., Ginter, A. C., Piontkowski, S., Schexnayder, K., & White, R. (2015). The work life and career development of young breast cancer survivors. *Journal of Counseling Psychology, 62*(4), 655–669. https://doi.org/10.1037/cou0000068

Read, J. R., Sharpe, L., Modini, M., and Dear, B. F. (2017). Multimorbidity and depression: A systematic review and meta-analysis. *Journal of Affective Disorders*, *221*(October), 36–46. https://doi.org/10.1016/j.jad.2017.06.009.

Reed, E., Simmonds, P., Haviland, J., & Corner, J. (2012). Quality of life and experience of care in women with metastatic breast cancer: a cross-sectional survey. *Journal of Pain and Symptom Management*, *43*(4), 747–758. https://doi.org/10.1016/j.jpainsymman.2011.05.005

Reifman, A., & Keyton, K. (2010). Winsorize. In: Salkind, N. J. (Eds.), *Encyclopedia of Research Design* (pp. 1636–1638). Sage.

Reilly, M. C., Zbrozek, A. S., & Dukes, E. M. (1993). The validity and reproducibility of a work productivity and activity impairment instrument. *PharmacoEconomics*, *4*(5), 353–365. https://doi.org/10.2165/00019053-199304050-00006

Remák, E., & Brazil, L. (2004). Cost of managing women presenting with stage IV breast cancer in the United Kingdom. *British Journal of Cancer*, *91*(1), 77–83. https://doi.org/10.1038/sj.bjc.6601890

Renna, M. E., Rosie Shrout, M., Madison, A. A., Lustberg, M., Povoski, S. P., Agnese, D. M., Reinbolt, R. E., Wesolowski, R., Williams, N. O., Ramaswamy, B., Sardesai, S. D., Noonan, A. M., VanDeusen, J. B., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2021). Worry and rumination in breast cancer patients: perseveration worsens self-rated health. *Journal of Behavioral Medicine*, *44*(2), 253–259. https://doi.org/10.1007/s10865-020-00192-9

Renzi, C., Kaushal, A., Emery, J., Hamilton, W., Neal, R. D., Rachet, B., Rubin, G., et al. (2019). Comorbid chronic diseases and cancer diagnosis: Disease-specific effects and underlying mechanisms. *Nature Reviews. Clinical Oncology*, *16*(12), 746–61. https://doi.org/10.1038/s41571-019-0249-6.

Richards, M.A., Westcombe, A. M., Love, S. B., Littlejohns, P., & Ramirez, A. J. (1999). Influence of delay on survival in patients with breast cancer: A systematic review. *Lancet*, *353*(9159), 1119-1126.

Riera, R., Bagattini, Â. M., Pacheco, R. L., Pachito, D. V., Roitberg, F., & Ilbawi, A. (2021). Delays and disruptions in cancer health care due to COVID-19 pandemic: Systematic review. *JCO Global Oncology*, *7*, 311–323. https://doi.org/10.1200/GO.20.00639

Ries, A., J., Touryan J., Vettel, J., McDowell, K., & Hairston, D. H. (2014). A comparison of electroencephalography signals acquired from conventional and mobile systems. *Journal of Neuroscience and Neuroenginerring*, *3*, 10-20.

Ritchie, J. & Spencer, L. (1994). Qualitative data analysis for applied policy research. In A. Bryman & R.G. Burgess (Eds.), *Analysing qualitative data* (pp.173-194). London: Routledge.

Ritchie J., Spencer L., O'Connor W. (2003). Carrying out qualitative analysis. In J. Ritchie & J. Lewis (Eds), *Qualitative research practice; a guide for social science students and researchers* (pp. 219-26). SAGE Publications.

Rosenberg, S. M., & Partridge, A. H. (2013). Premature menopause in young breast cancer: effects on quality of life and treatment interventions. *Journal of thoracic disease*, *5 Suppl 1*(Suppl 1), S55–S61. https://doi.org/10.3978/j.issn.2072-1439.2013.06.20

Ruiz-Casado, A., Álvarez-Bustos, A., de Pedro, C. G., Méndez-Otero, M., & Romero-Elías, M. (2021). Cancer-related Fatigue in Breast Cancer Survivors: A Review. *Clinical Breast Cancer*, *21*(1), 10–25. https://doi.org/10.1016/j.clbc.2020.07.011

Rustøen, T., Moum, T., Padilla, G., Paul, S., & Miaskowski, C. (2005). Predictors of quality of life in oncology outpatients with pain from bone metastasis. *Journal of Pain and Symptom Management*, *30*(3), 234–242. https://doi.org/10.1016/j.jpainsymman.2005.04.002

Ryum, T., Kennair, L. E. O., Hjemdal, O., Hagen, R., Halvorsen, J. Ø., & Solem, S. (2017). Worry and metacognitions as predictors of anxiety symptoms: A prospective study'. *Front Psychol*, *8*, 924. https://doi.org/10.3389/fpsyg.2017.00924.

Salminen, T., Mårtensson, J., Schubert, T., & Kühn, S. (2016). Increased integrity of white matter pathways after dual n-back training. *NeuroImage*, *133*, 244–250. https://doi.org/10.1016/j.neuroimage.2016.03.028

Salminen, T., Forlim, C. G., Schubert, T., & Kühn, S. (2020). Dual n-back training improves functional connectivity of the right inferior frontal gyrus at rest. *Scientific Reports*, *10*(1), 20379. https://doi.org/10.1038/s41598-020-77310-9

Sandberg, J. C., Strom, C., & Arcury, T. A. (2014). Strategies used by breast cancer survivors to address work-related limitations during and after treatment. *Women's Health Issues: Official Publication of the Jacobs Institute of Women's Health*, *24*(2), e197–e204. https://doi.org/10.1016/j.whi.2013.12.007

Santopetro, N. J., Kallen, A. M., Threadgill, A. H., & Hajcak, G. (2020). Reduced flanker P300 prospectively predicts increases in depression in female adolescents. *Biological Psychology*, *156*, 107967.

Santopetro, N. J., Brush, C. J., Bruchnak, A., Klawohn, J., & Hajcak, G. (2021). A reduced P300 prospectively predicts increased depressive severity in adults with clinical depression. *Psychophysiology*, *58* (4), e13767.

Sari, B. A., Koster, E. H., Pourtois, G., & Derakshan, N. (2016). Training working memory to improve attentional control in anxiety: A proof-of-principle study using behavioral and electrophysiological measures. *Biological Psychology*, *121*(Pt B), 203–212. https://doi.org/10.1016/j.biopsycho.2015.09.008

Satin, J. R., Linden, W., and Phillips, M. J. (2009). Depression as a predictor of disease progression and mortality in cancer patients: A meta-analysis. *Cancer*, *115*(22), 5349–61. https://doi.org/10.1002/cncr.24561.

Schairer, C., Brown, L. M., Chen, B. E., Howard, R., Lynch, C. F., Hall, P., Storm, H., Pukkala, E., Anderson, A., Kaijser, M., Andersson, M., Joensuu, H., Fosså, S. D., Ganz, P. A., & Travis, L. B. (2006). Suicide after breast cancer: An international population-based study of 723,810 women. *JNCI*, *98*(19),1416-1419. https://doi.org/10.1093/jnci/djj377.

Schilder, C. M., Seynaeve, C., Beex, L. V., Boogerd, W., Linn, S. C., Gundy, C. M., Huizenga, H. M., Nortier, J. W., van de Velde, C. J., van Dam, F. S., & Schagen, S. B. (2010). Effects of tamoxifen and exemestane on cognitive functioning of postmenopausal patients with breast cancer: results from the neuropsychological side study of the tamoxifen and exemestane adjuvant multinational trial. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *28*(8), 1294–1300. https://doi.org/10.1200/JCO.2008.21.3553

Schmidt, M. E., Chang-Claude, J., Vrieling, A., Heinz, J., Flesch-Janys, D., & Steindorf, K. (2011). Fatigue and quality of life in breast cancer survivors: temporal courses and long-term pattern. *Journal of Cancer Survivorship*, *6*, 11-19.

Schmidt, M. E., Chang-Claude, J., Vrieling, A., Heinz, J., Flesch-Janys, D., & Steindorf, K. (2012). Fatigue and quality of life in breast cancer survivors: temporal courses and long-term pattern. *Journal of Cancer Survivorship: Research and Practice*, *6*(1), 11–19. https://doi.org/10.1007/s11764-011-0197-3

Schmidt, J. E., Beckjord, E., Bovbjerg, D. H., Low, C. A., Posluszny, D. M., Lowery, A. E., Dew, M. A., Nutt, S., Arvey, S. R., & Rechis, R. (2016). Prevalence of perceived cognitive dysfunction in survivors of a wide range of cancers: Results from the 2010 LIVESTRONG survey. *Journal of Cancer Survivorship: Research and Practice*, *10*(2), 302-311. https://doi.org/10.1007/s11764-015-0476-5.

Schmidt, M. E., Scherer, S., Wiskemann, J., & Steindorf, K. (2019). Return to work after breast cancer: The role of treatment-related side effects and potential impact on quality of life. *European Journal of Cancer Care*, *28*(4), e13051. https://doi.org/10.1111/ecc.13051

Schneider, W., Eschman, A., & Zuccolotto, A. (2012). E-prime user's guide. Pittsburg: Psychology Software Tools

Schoemaker, M. J., Jones, M. E., Wright, L. B., Griffin, J., McFadden, E., Ashworth, A., & Swerdlow, A. J. (2016). Psychological stress, adverse life events and breast cancer incidence: a cohort investigation in 106,000 women in the United Kingdom. *Breast Cancer Research: BCR*, *18*(1), 72. https://doi.org/10.1186/s13058-016-0733-1

Schroder, H. S., Moran, T. P., & Moser, J. S. (2018). The effect of expressive writing on the error-related negativity among individuals with chronic worry. *Psychophysiology*, *55*(2), 10.1111/psyp.12990. https://doi.org/10.1111/psyp.12990

Sealed Envelope Ltd. (2017). Simple randomisation service [Online]. Retrieved from https://www.sealedenvelope.com/simple-randomiser/v1/

Shani, R., Tal, S., Derakshan, N., Cohen, N., Enock, P. M., McNally, R. J., Mor, N., Daches, S., Williams, A. D., Yiend, J., Carlbring, P., Kuckertz, J. M., Yang, W., Reinecke, A., Beevers, C. G., Bunnell, B. E., Koster, E., Zilcha-Mano, S., & Okon-Singer, H. (2021). Personalized cognitive training: Protocol for individual-level meta-analysis implementing machine learning methods. *Journal of Psychiatric Research*, *138*, 342–348. https://doi.org/10.1016/j.jpsychires.2021.03.043

Sherwin, B. B. (1996). Hormones, mood, and cognition functioning in postmenopausal women. *Obstetrics and Gynecology*, *87*(2 Suppl), 20S-26S.

Shim, E. J., Lee, J. W., Cho, J., Jung, H. K., Kim, N. H., Lee, J. E., Min, J., Noh, W. C., Park, S. H., & Kim, Y. S. (2020). Association of depression and anxiety disorder with the risk of mortality in breast cancer: A National Health Insurance Service study in Korea. *Breast Cancer Research and Treatment*, *179*(2), 491–498. https://doi.org/10.1007/s10549-019-05479-3

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. (2016). Do "Brain-Training" Programs Work?. *Psychological Science in the*

*Public Interest: A Journal of the American Psychological Society*, *17*(3), 103–186. https://doi.org/10.1177/1529100616661983

Simó, M., Rifà-Ros, X., Rodriguez-Fornells, A., & Bruna, J. (2013). Chemobrain: a systematic review of structural and functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews*, *37*(8), 1311–1321. https://doi.org/10.1016/j.neubiorev.2013.04.015

Simó, M., Gurtubay-Antolin, A., Vaquero, L., Bruna, J., & Rodríguez-Fornells, A. (2018). Performance monitoring in lung cancer patients pre- and post-chemotherapy using fine-gained electrophysiological measures. *NeuroImage: Clinical*, *18*, 86-96. https://doi.org/10.1016/j.nicl.2017.12.032

Singh, S.K., Pradhan, R.K., Panigrahy, N.P., & Jena, L.K. (2019). Self-efficacy and workplace well-being: moderating role of sustainability practices. *Benchmarking: An International Journal*, *26*(6), 1692-1708. https://doi.org/10.1108/BIJ-07-2018-0219

Small, B. J., Rawson, K. S., Walsh, E., Jim, H. S., Hughes, T. F., Iser, L., Andrykowski, M. A., & Jacobsen, P. B. (2011). Catechol-O-methyltransferase genotype modulates cancer treatment-related cognitive deficits in breast cancer survivors. *Cancer*, *117*(7), 1369–1376. https://doi.org/10.1002/cncr.25685

Smidt, K., Mackenzie, L., Dhillon, H., Vardy, J., Lewis, J., & Loh, S.Y. (2016). The perceptions of Australian oncologists about cognitive changes in cancer patients. *Supportive Cancer Care*, *24*, 4679-4687.

Smith H. R. (2015). Depression in cancer patients: Pathogenesis, implications and treatment (Review). *Oncology Letters*, *9*(4), 1509–1514. https://doi.org/10.3892/ol.2015.2944

Soo, H., & Sherman, K. A. (2015). Rumination, psychological distress and post-traumatic growth in women diagnosed with breast cancer. *Psycho-Oncology*, *24*(1), 70–79. https://doi.org/10.1002/pon.3596

Soveri, A., Antfolk, J., Karlsson, L., Salo, B., & Laine, M. (2017). Working memory training revisited: A multi-level meta-analysis of n-back training studies. *Psychonomic Bulletin & Review*, *24*(4), 1077–1096. https://doi.org/10.3758/s13423-016-1217-0

Spinhoven, P., van Hemert, A. M., & Penninx, B. W. (2018). Repetitive negative thinking as a predictor of depression and anxiety: A longitudinal cohort study. *Journal of Affective Disorders*, *241*, 216-225.

Stajkovic, A. D., & Luthans, F. (1998). Self-efficacy and work-related performance: A meta-analysis. *Psychological Bulletin, 124*(2), 240–261. https://doi.org/10.1037/0033-2909.124.2.240

Stagl, J. M., Lechner, S. C., Carver, C. S., Bouchard, L. C., Gudenkauf, L. M., Jutagir, D. R., Diaz, A., Yu, Q., Blomberg, B. B., Ironson, G., Glück, S., & Antoni, M. H. (2015). A randomized controlled trial of cognitive-behavioral stress management in breast cancer: survival and recurrence at 11-year follow-up. *Breast Cancer Research and Treatment*, *154*(2), 319–328. https://doi.org/10.1007/s10549-015-3626-6

Stajkovic, A. D., & Luthans, F. (1998). Self-Efficacy and work-related performance: A meta-analysis. *Psychological Bulletin*, *124*(2), 240-261.

Steiner, J. L., Wagner, C. D., Bigatti, S. M., & Storniolo, A. M. (2014). Depressive rumination and cognitive processes associated with depression in breast cancer patients and their spouses. *Fam Syst Health*, *32*(4), 378-388.

Stilley, C. S., Bender, C. M., Dunbar-Jacob, J., Sereika, S., & Ryan, C. M. (2010). The impact of cognitive function on medication management: three studies. *Health Psychology: Official Journal of the Division of Health Psychology, American Psychological Association*, *29*(1), 50–55. https://doi.org/10.1037/a0016940

Stolove, C. A., Galatzer, I.R., & Bonanno, G. A. (2017). Emergence of depression following job loss prospectively predicts lower rates of reemployment. *Psychiatry Research, 253*, 79-83. https://doi:10.1016/j.psychres.2017.03.036.

Sun, Y., Shigaki, C. L., & Armer, J. M. (2017). Return to work among breast cancer survivors: A literature review. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *25*(3), 709–718. https://doi.org/10.1007/s00520-016-3446-1

Sun, H., Yang, Y., Zhang, J., Liu, T., Wang, H., Garg, S., & Zhang, B. (2019). Fear of cancer recurrence, anxiety and depressive symptoms in adolescent and young adult cancer patients. *Neuropsychiatric Disease and Treatment*, *15*, 857–865. https://doi.org/10.2147/NDT.S202432

Suppli, N. P., Johansen, C., Christensen, J., Kessing, L. V., Kroman, N., & Dalton, S. O. (2014). Increased risk for depression after breast cancer: A nationwide population-based cohort study of associated factors in Denmark, 1998-2011. *Journal of Clinical Oncology*, *32*(34), 3831-3838. https://doi:10.1200/JCO.2013.54.0419.

Swainston, J., and Derakshan, N. (2018). Training cognitive control to reduce emotional vulnerability in breast cancer. *Psycho-Oncology*, *27*(7), 1780–86. https://doi.org/10.1002/pon.4727

Swainston, J., Chapman, B., Grunfeld, E. A., & Derakshan, N. (2020). COVID-19 lockdown and its adverse impact on psychological health in breast cancer. *Front. Pyschol.* https://doi.org/10.3389/fpsyg.2020.02033

Swainston, J., Louis, C., Moser, J., Derakshan, N. (2021). Neurocognitive efficiency in breast cancer survivorship: A performance monitoring ERP study. *International Journal of Psychophysiology*, *168*, 9-20. https://doi.org/10.1016/j.ijpsycho.2021.06.013

Swainston, J., & Derakshan, N. (2021). Reduced anxiety following mindfulness and adaptive working memory training in women with breast cancer. *Mindfulness*. https://doi.org/10.1007/s12671-021-01651-3

Szmalec, A., Verbruggen, F., Vandierendonck, A., & Kemps, E. (2011). Control of interference during working memory updating. *Journal of Experimental Psychology Human Perception & Performance*, *37*(1), 137–151. doi:10.1037/a0020365

Tamminga, S.J., Verbeek, J.H.A.M., Bos, M.M.E.M., Fons G., Kitzen, J.J.E.M., Plaisier, P.W., Frings-Dresen, M.H.W., de Boer, A.G.E.M. (2013). Effectiveness of a hospital-based work support intervention for female cancer patients—a multi-Centre randomised controlled trial. *PLoS One*, *8*(5).

Tan, C. J., Yin ChIng Yip, S., Chan, R. J., Chew, L., & Chan, A. (2021). Investigating how cancer-related symptoms influence work outcomes among cancer survivors: a systematic review. *Journal of Cancer Survivorship*. https://doi.org/10.1007/s11764-021-01097-5

Taskila, T., Martikainen, R., Hietanen, P., & Lindbohm, M. L. (2007). Comparative study of work ability between cancer survivors and their referents. *European Journal of Cancer (Oxford, England: 1990)*, *43*(5), 914–920. https://doi.org/10.1016/j.ejca.2007.01.012

Tevaarwerk, A. J., Lee, J. W., Terhaar, A., Sesto, M. E., Smith, M. L., Cleeland, C. S., & Fisch, M. J. (2016). Working after a metastatic cancer diagnosis: Factors affecting employment in the metastatic setting from ECOG-ACRIN's Symptom Outcomes and Practice Patterns study. *Cancer*, *122*(3), 438–446. https://doi.org/10.1002/cncr.29656

Tewari, A., & Chagpar, A. B. (2014). Worry about breast cancer recurrence: a population-based analysis. *The American Surgeon*, *80*(7), 640–645.

Thaker, P. H., Han, L. Y., Kamat, A. A., Arevalo, J. M., Takahashi, R., Lu, C., Jennings, N. B., Armaiz-Pena, G., Bankson, J. A., Ravoori, M., Merritt, W. M., Lin, Y. G., Mangala, L. S., Kim, T. J., Coleman, R. L., Landen, C. N., Li, Y., Felix, E., Sanguino, A. M., Newman, R. A., … Sood, A. K. (2006). Chronic stress promotes tumor growth and angiogenesis in a mouse model of ovarian carcinoma. *Nature medicine*, *12*(8), 939–944. https://doi.org/10.1038/nm1447

The Economist Intelligence Unit. (2017). *The road to a better normal: Breast cancer patients and survivors in the EU workforce*. https://www.workingwithcancer.co.uk/wp-content/uploads/2017/11/EIU-Reports.pdf

Thewes, B., Lebel, S., Leclair, C. S., and Butow, P. (2016). A qualitative exploration of fear of cancer recurrence (FCR) amongst Australian and Canadian breast cancer survivors. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *24*(5), 2269–76.

Tiedtke, C., Dierckx de Casterlé, B., de Rijk, A., Christiaens, M. R., & Donceel, P. (2011). Breast cancer treatment and work disability: Patient perspective. *Breast*, *20*(6), 534-538. https://doi.org/10.1016/j.breast.2011.06.002

Timperi A. W., Ergas, I. J., Rehkopf, D. H., Roh, J. M., Kwan, M. L., & Kushi, L. H. (2013). Employment status and quality of life in recently diagnosed breast cancer survivors. *Psycho-Oncology*, *22*(6), 1411-1420.

Todd, B. L., Feuerstein, E. L., & Feuerstein, M. (2011). When breast cancer survivors report cognitive problems at work. *The International Journal of Psychiatry in Medicine*, *42*(3), 279-294.

Toh, Y. L., Wang, C., Ho, H. K., & Chan, A. (2020). Distinct cytokine profiles across trajectories of self-perceived cognitive impairment among early-stage breast cancer survivors. *Journal of Neuroimmunology*, *342*, 577196. Advance online publication. https://doi.org/10.1016/j.jneuroim.2020.577196

Torp, S., Nielsen, R. A., Gudbergsson, S. B., & Dahl, A. A. (2012). Worksite adjustments and work ability among employed cancer survivors. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *20*(9), 2149–2156. https://doi.org/10.1007/s00520-011-1325-3

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research*, *27*(3), 247-259. https://doi.org/10.1023/A:1023910315561.

Tsaras, K., Papathanasiou, I. V., Mitsi, D., Veneti, A., Kelesi, M., Zyga, S., and Fradelos, E. C. (2018). Assessment of depression and anxiety in breast cancer patients: Prevalence and associated factors. *Asian Pacific Journal of Cancer Prevention: APJCP*, *19*(6), 1661–69. https://doi.org/10.22034/APJCP.2018.19.6.1661.

Turner, M. L., & Engle, R. W. (1989). Is working memory capacity task dependent ? *Journal of Memory and Language, 28*, 127–154

Tusch, E. S., Alperin, B. R., Ryan, E., Holcomb, P. J., Mohammed, A. H., & Daffner, K. R. (2016). Changes in neural activity underlying working memory after computerized cognitive training in older adults. *Frontiers in Aging Neuroscience, 8*, 255. https://doi.org/10.3389/fnagi.2016.00255

Unsworth, N., Heitz, R. P., Schrock, J. C., & Engle, R. W. (2005). An automated version of the operation span task. *Behavior Research Methods, 37*(3), 498–505. https://doi.org/10.3758/bf03192720

Vahdaninia, M., Omidvari, S., & Montazeri, A. (2010). What do predict anxiety and depression in breast cancer patients? A follow-up study. *Social Psychiatry and Psychiatric Epidemiology, 45*(3), 355–361. https://doi.org/10.1007/s00127-009-0068-7

Vance, D. E., Bail, J., Enah, C. C., Palmer, J. J., & Hoenig, A. K. (2016). The impact of employment on cognition and cognitive reserve: Implications across diseases and aging. *Nursing: Research and Reviews, 6*, 61-67.

van der Willik, K. D., Koppelmans, V., Hauptmann, M., Compter, A., Ikram, M. A., & Schagen, S. B. (2018). Inflammation markers and cognitive performance in breast cancer survivors 20 years after completion of chemotherapy: a cohort study. *Breast Cancer Research: BCR, 20*(1), 135. https://doi.org/10.1186/s13058-018-1062-3

Van Dyk, K., Bower, J. E., Crespi, C. M., Petersen, L., & Ganz, P. A. (2018). Cognitive function following breast cancer treatment and associations with concurrent symptoms. *npj Breast Cancer*, 4 (25). https://doi.org/10.1038/s41523-018-0076-4

Van Maarschalkerweerd, P. E. A., Schaapveld, M., Paalman, C. H., Aaronson, N. K., & Duijts, S. F. A. (2020). Changes in employment status, barriers to, and facilitators of (return to) work in breast cancer survivors 5-10 years after diagnosis'. *Disability and Rehabilitation, 42*(21), 3052-3058. https://doi:10.1080/09638288.2019.1583779

Vardy, J.L., Booth, C., Pond, G.R., Zhang, H., Dhillon, S., Clarke, S.J., & Tannock, I. F. (2007). Cytokine levels in patients with colorectal cancer and breast cancer and their relationship to fatigue and cognitive function. *Supplement to Journal of Clinical Oncology*, 18S:9070.

Vega, J. N., Dumas, J., & Newhouse, P. A. (2018). Self-reported chemotherapy-related cognitive impairment compared with cognitive complaints following menopause'. *Psycho-Oncology*, *27*, 2198-2205.

Verdecchia, A., Guzzinati, S., Francisci, S., De Angelis, R., Bray, F., Allemani, C., Tavilla, A., Santaquilani, M., Sant, M., & EUROCARE Working Group (2009). Survival trends in European cancer patients diagnosed from 1988 to 1999. *European Journal of Cancer (Oxford, England: 1990)*, *45*(6), 1042–1066. https://doi.org/10.1016/j.ejca.2008.11.029

Verduzco-Aguirre, H.C,, Babu, D., Mohile, S.G., Bautista, J., Xu, H., Culakova, E., Canin, B., Zhang, Y., Wells, M., Epstein, R.M., Duberstein, P., McHugh, C., Dale, W., Conlin, A., Bearden, J 3rd., Berenberg, J., Tejani, M., & Loh, K.P.(2021). Associations of uncertainty with psychological health and quality of life in older adults with advanced cancer. *J Pain Symptom Manage*. doi: 10.1016/j.jpainsymman.2020.08.012.

Verma, R., Foster, R. E., Horgan, K., Mounsey, K., Nixon, H., Smalle, N., Hughes, T. A., and Carter, C. R. D. (2016). Lymphocyte depletion and repopulation after chemotherapy for primary breast cancer. *Breast Cancer Research*, *18*(1), 10. https://doi.org/10.1186/s13058-015-0669-x

Verrill, M., Wardley, A. M., Retzler, J., Smith, A. B., Bottomley, C., Ní Dhochartaigh, S., Tran, I., Leslie, I., & Schmid, P. (2020). Health-related quality of life and work productivity in UK paitners with HER2-positive breast cancer: a cross-sectional study evaluating the relationships between disease and treatment stage. *Health and Quality of Life Outcomes, 18(353)*. https://doi.org/10.1186/s12955-020-01603-w

Villarreal, G., Hamilton, D. A., Petropoulos, H., Driscoll, I., Rowland, L. M., Griego, J. A., Kodituwakku, P. W., Hart, B. L., Escalona, R., & Brooks, W. M. (2002). Reduced hippocampal volume and total white matter volume in posttraumatic stress disorder. *Biological psychiatry*, *52*(2), 119–125. https://doi.org/10.1016/s0006-3223(02)01359-8

Vogel, E. K., McCollough, A. W., & Machizawa, M. G. (2005). Neural measures reveal individual differences in controlling access to working memory. *Nature*, *438*(December 2005). https://doi.org/10.1038/nature04171

Von Ah, D. M., Kang, D.-H., & Carpenter, J. S. (2008). Predictors of cancer-related fatigue in women with breast cancer before, during, and after adjuvant therapy. *Cancer Nursing*, *31*(2), 134–144. https://doi.org/10.1097/01.NCC.0000305704.84164.54

Von Ah, D., Carpenter, J. S., Saykin, A., Monahan, P., Wu, J., Yu, M., Rebok, G., Ball, K., Schneider, B., Weaver, M., Tallman, E., & Unverzagt, F. (2012). Advanced cognitive training for breast cancer survivors: a randomized controlled trial. *Breast Cancer Research and Treatment*, *135*(3), 799–809. https://doi.org/10.1007/s10549-012-2210-6

Von Ah, D., Habermann, B., Carpenter, J. S., & Schneider, B. L. (2013a). Impact of perceived cognitive impairment in breast cancer survivors. *European Journal of Oncology Nursing*, *17*, 236-241.

Von Ah, D. & Tallman, E. F. (2015). Perceived cognitive function in breast cancer survivors: Evaluating relationships with objective cognitive performance and other symptoms using the functional assessment of cancer therapy-cognitive function instrument. *Journal of Pain and Symptom Management*, *49*(4), 697-706.

Von Ah, D, Storey, S., Jansen, C. E., & Allen, D. H., (2013b). Coping strategies and interventions for cognitive changes in patients with cancer. *Seminars in Oncology Nursing*, *29*(4), 288-299.

Von Ah, D., Storey, S., Tallman, E., Nielsen, A., Johns, S. A., & Pressler, S. (2016). Cancer, Cognitive Impairment, and Work-Related Outcomes: An Integrative Review. *Oncology Nursing Forum*, *43*(5), 602–616. https://doi.org/10.1188/16.ONF.602-616

Von Ah, D., Storey, S., Crouch, A., Johns, S. A., Dodson, J., & Dutkevitch, S. (2017). Relationship of self-reported attentional fatigue to perceived work ability in breast cancer survivors. *Cancer Nursing*, *40*(6), 464-470.

Von Ah, D., Storey, S., & Crouch, A. (2018). Relationship between self-reported cognitive function and work-related outcomes in breast cancer survivors. *J Cancer Survivor*, *12*(2), 246-255.

Von Ah, D., & Crouch, A. (2021). Relationship of perceived everyday cognitive function and work engagement in breast cancer survivors. *Supportive Care in Cancer: Official Journal of the Multinational Association of Supportive Care in Cancer*, *29*(8), 4303–4309. https://doi.org/10.1007/s00520-020-05950-8

Voute, M., Morel, V., Joly, D., Villatte, C., Martin, E., Durando, X., Pereira, B., & Pickering, G. (2020). Predicting Pain Trajectories in the One Year Following Breast Cancer Diagnosis-An Observational Study. *Journal of Clinical Medicine*, *9*(6), 1907. https://doi.org/10.3390/jcm9061907

Waddell, G., & Burton, A. K. (2006). Is work good for your health and well-being? London (UK): The Stationery Office.

Wagner, L. Lai, J-S., Cella, D., Sweet, J., & Forrestal, S. (2004). Chemotherapy-related cognitive deficits: Development of the FACT-Cog instrument. *Ann Behav Med*. *27,* S010.

Wagner, L. I., Sweet, J., Butt, Z., Lai, J. S., & Cella, D. (2009). Measuring patient self-reported cognitive function: development of the functional assessment of cancer therapy-cognitive function instrument. *Journal of Supportive Oncology*, *7*(6), W32-W39.

Wagner, L. I., Gray, R. J., Sparano, J. A., Whelan, T. J., Garcia, S. F., Yanez, B., Tevaarwerk, A. J., Carlos, R. C., Albain, K. S., Olson, J. A., Jr, Goetz, M. P., Pritchard, K. I., Hayes, D. F., Geyer, C. E., Dees, E. C., McCaskill-Stevens, W. J., Minasian, L. M., Sledge, G. W., Jr, & Cella, D. (2020). Patient-reported cognitive impairment among women with early breast cancer randomly assigned to endocrine therapy alone versus chemoendocrine therapy: Results from TAILORx. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *38*(17), 1875–1886. https://doi.org/10.1200/JCO.19.01866

Wang, L., Hong, B. Y., Kennedy, S. A., Chang, Y., Hong, C. J., Craigie, S., Kwon, H. Y., Romerosa, B., Couban, R. J., Reid, S., Khan, J. S., McGillion, M., Blinder, V., & Busse, J. W. (2018). Predictors of unemployment after breast cancer surgery: A systematic review and meta-analysis of observational studies. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, *36*(18), 1868–1879. https://doi.org/10.1200/JCO.2017.77.3663

Wang, X., Wang, N., Zhong, L., Wang, S., Zheng, Y., Yang, B., Zhang, J., Lin, Y., & Wang, Z. (2020). Prognostic value of depression and anxiety on breast cancer recurrence and mortality: a systematic review and meta-analysis of 282,203 patients. *Molecular Psychiatry*, *25*(12), 3186–3197. https://doi.org/10.1038/s41380-020-00865-6

Wefel, J. S., Lenzi, R., Theriault, R. L., Davis, R. N., & Meyers, C. A. (2004). The cognitive sequelae of standard-dose adjuvant chemotherapy in women with breast carcinoma: results of a prospective, randomized, longitudinal trial. *Cancer*, *100*(11), 2292–2299.

Wefel, J. S., Saleeba, A. K., Buzdar, A. U., & Meyers, C. A. (2010). Acute and late onset cognitive dysfunction associated with chemotherapy in women with breast cancer. *Cancer*, *116*(14), 3348–3356. https://doi.org/10.1002/cncr.25098

Whittaker, A. L., George, R. P., & O'Malley, L. (2022). Prevalence of cognitive impairment following chemotherapy treatment for breast cancer: a systematic review and meta-analysis. S*cientific Reports*, *12*, 2135. doi.org/10.1038/s41598-022-05682-1

Whisenant, M., Wong, B., Mitchell, S. A., Beck, S. L., & Mooney, K. (2020). Trajectories of depressed mood and anxiety during chemotherapy for breast cancer. *Cancer Nursing*, *43*(1), 22–31. https://doi.org/10.1097/NCC.0000000000000670

Wolvers, M., Leensen, M., Groeneveld, I. F., Frings-Dresen, M., & De Boer, A. (2018). Predictors for earlier return to work of cancer patients. *Journal of Cancer Survivorship: Research and Practice*, *12*(2), 169–177. https://doi.org/10.1007/s11764-017-0655-7

Wolvers, M., Leensen, M., Groeneveld, I. F., Frings-Dresen, M., & De Boer, A. (2019). Longitudinal Associations Between Fatigue and Perceived Work Ability in Cancer Survivors. *Journal of Occupational Rehabilitation*, *29*(3), 540–549. https://doi.org/10.1007/s10926-018-9814-6

World Health Organization. 2019. "Naming the coronavirus disease (COVID-19) and the virus that causes it". Accessed May 16, 2020. https://www.who.int/emergencies/diseases/novel-

coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it.

World Health Organization. 2020. "Breast cancer fact sheet". Accessed May, 2021. https://gco.iarc.fr/today/data/factsheets/cancers/20-Breast-fact-sheet.pdf

Yang, H., Brand, J. S., Fang, F., Chiesa, F., Johansson, A. L. V., Hall, P., Czene, K. (2017). Time-dependent risk of depression, anxiety, and stress-related disorders in patients with invasive and *In Situ* breast cancer. *International Journal of Cancer*, *140*(4), 841-852.

Yang, Y., & Hendrix, C. C. (2018). Cancer-related cognitive impairment in breast cancer patients: Influences of psychological variables. *Asia-Pacific Journal of Oncology Nursing*, *5*(3), 296–306. https://doi.org/10.4103/apjon.apjon_16_18

Yeung, N., & Cohen, J. D. (2006). The impact of cognitive deficits on conflict monitoring: Predictable dissociations between error-related negativity and N2. *Psychological Scinece*, *17* (2), 164-171.

Zeng, Y., Cheng, A. S. K., Liu, X., & Feuerstein, M. (2016). Symptom profiles, work productivity and quality of life among Chinese female cancer survivors. *Gynaecology & Obstetrics*, *6*(2),1000357. http://dx.doi.org/10.4172/2161-0932.1000357 .

Zhang, L., Zhu, F., Xie, L., Wang, C., Wang, J., Chen, R., Jia, P., Guan, H, Q., Peng, L., Chen, Y., Peng, P., Zhang, P., Chu, Q., Shen, Q., Wang, Y., Xu, S. Y., Zhao, J. P., & Zhou, M. (2020). 'Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China'. *Annals of Oncology*, *31*(7), 894-901. https://doi.org/10.1016/j.annonc.2020.03.296

Zigmond, A. S. and Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatri*ca *Scandinavica*, *67*(6), 361–370. https://doi.org/10.1111/j.1600-0447.1983.tb09716.x.

# Appendix

## Appendix 1

**DEPARTMENT OF PSYCHOLOGICAL SCIENCES**
**BIRKBECK UNIVERSITY OF LONDON**

**INFORMATION SHEET FOR:** Neurocognitive intervention for improving and sustaining workability in women with a breast cancer diagnosis

**Researchers**: Miss Bethany Chapman, Professor Nazanin Derakhshan and Professor Beth Grunfeld

Before agreeing to participate in this study, it is important for you to understand why the research is being done and what it will involve. **Please take the time to read the following information carefully**. If you have any questions/queries or would like any further information please do not hesitate to contact Bethany Chapman (BRiCatWork@bbk.ac.uk).

Please note that in order to participate in the present research you must have a diagnosis of **primary cancer** and **must be between 6-months to 60-months post-active treatment** (i.e. no longer receiving chemotherapy and/or radiotherapy). You **can,** however, be taking hormone therapy (i.e. Tamoxifen or Aromatase Inhibitors) or target therapy (i.e. Herceptin) medications. This research also requires you to be **attending regular paid work** (please note, there is no limit to the number of hours worked per week or the type of work) and be **between the age of 18 to 65-years old**. Moreover, you must be experiencing a decline in workability that is directly associated with cognitive difficulties noticed since completing treatment.

**AIM** -The current research primarily aims to explore the efficacy of neurocognitive training as an intervention for helping women with a breast cancer diagnosis improve and sustain workability upon returning to work following the completion of active treatment. This study is **longitudinal**.

If you agree to participate you will be required to complete **12 consecutive sessions of computerised online training** at home as well as **four sessions of testing** including, **pre-training**, **immediately post-training**, a **6-month follow-up** and a **1-year follow-up.** The tasks involved in these sessions will need to be completed either at home **or** in the MERLiN laboratory at Birkbeck College.

**Each of the sessions will involve you completing:**

1. **A series of online questionnaires -** lasting approximately **30 minutes** at home.
2. **A short telephone interview** with the researcher – lasting **1 hour** at home.
3. **Three short computerised memory tasks** and a **non-invasive EEG** – lasting approximately **3 hours** at Birkbeck College, University of London, Malet Street.

Individual instructions on how to complete each of the tasks will be provided.

On completion of the fourth session or at the point of withdrawal you will receive a **single cash payment of £100.**

Please note that if you agree to participate in the current research you will be provided with a randomised participant number which you will be asked to write in place of your name on all of the material/measures collected, this is to ensure that you remain totally anonymous throughout the research and in any publications that may occur. All of the data collected will be treated with the utmost confidentiality.

You are able to withdraw from the study at any time without reason by simply emailing the researcher.

The results from this research will be written up as part of a PhD thesis as well as for publication and conferences. At your request, the researcher will be able to provide you with information regarding the overall findings. However, please note that individual results will not be available.

The present study has received ethical approval from the Department of Psychological Sciences Research Ethics Committee of Birkbeck University of London

Please contact Bethany Chapman (BRiCatWork@bbk.ac.uk), if you wish to take part in the present research study or if you have any questions/queries regarding any element of the research.

**DEPARTMENT OF PSYCHOLOGICAL SCIENCES**
**BIRKBECK UNIVERSITY OF LONDON**

**INFORMATION SHEET FOR:** Neurocognitive intervention for improving and sustaining workability in women with a breast cancer diagnosis

**Researchers**: Miss Bethany Chapman, Professor Nazanin Derakhshan and Professor Beth Grunfeld

Before agreeing to participate in this study, it is important for you to understand why the research is being done and what it will involve. **Please take the time to read the following information carefully**. If you have any questions/queries or would like any further information please do not hesitate to contact Bethany Chapman (BRiCatWork@bbk.ac.uk).

Please note that in order to participate in the present research you must have a diagnosis of **primary cancer** and **must be between 6-months to 60-months post-active treatment** (i.e., no longer receiving chemotherapy and/or radiotherapy). You **can,** however, be taking hormone therapy (i.e., Tamoxifen or Aromatase Inhibitors) or target therapy (i.e. Herceptin) medications. This research also requires you to be **attending regular paid work** (please note, there is no limit to the number of hours worked per week or the type of work) and be between the **age of 18 to 65-years old**. Moreover, you must also be experiencing a decline in workability that is directly associated with cognitive difficulties noticed since completing treatment.

**AIM** - The current research primarily aims to explore the efficacy of neurocognitive training as an intervention for helping women with a breast cancer diagnosis improve and sustain workability upon returning to work following the completion of active treatment. This study is **longitudinal**.

If you agree to participate you will be required to complete **12 consecutive sessions of computerised online training** at home as well as **four sessions of testing** including, **pre-training**, **immediately post-training**, **6-month follow-up** and a **1-year follow-up.** The tasks involved in these sessions will need to be completed either at home **or** in the MERLiN laboratory at Birkbeck College.

**Each of the sessions will involve you completing:**

1. **A series of online questionnaires -** lasting approximately **30 minutes** at home.
2. **Three short computerised memory tasks** and a **non-invasive EEG** – lasting approximately **3 hours** at Birkbeck College, University of London, Malet Street.

Individual instructions on how to complete each of the tasks will be provided.

On completion of the fourth session or at the point of withdrawal you will receive a **single cash payment of £100.**

Please note that if you agree to participate in the current research, you will be provided with a randomised participant number which you will be asked to write in place of your name on all of the material/measures collected, this is to ensure that you remain totally anonymous throughout the research and in any publications that may occur. All of the data collected will be treated with the utmost confidentiality.

You are able to withdraw from the study at any time without reason by simply emailing the researcher.

The results from this research will be written up as part of a PhD thesis as well as for publication and conferences. At your request, the researcher will be able to provide you with information regarding the overall findings. However, please note that individual results will not be available.

The present study has received ethical approval from the Department of Psychological Sciences Research Ethics Committee of Birkbeck University of London

Please contact Bethany Chapman (BRiCatWork@bbk.ac.uk), if you wish to take part in the present research study or if you have any questions/queries regarding any element of the research.

**DEPARTMENT OF PSYCHOLOGICAL SCIENCES**

**BIRKBECK UNIVERSITY OF LONDON**

**INFORMATION SHEET FOR:** Effects of Coronavirus (COVID-19) Outbreak Restrictions on Anxiety and Work Ability in Women with a Diagnosis of Breast Cancer

Before you decide to take part in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of the research team can be contacted if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

**Aim**: The current research primarily aims to explore women's experiences of the Coronavirus (COVID-19) outbreak on their cognitive and emotional health as well as workability.

If you agree to participate in the present study, you will be asked to complete a **single online session lasting approximately 30 to 40 minutes.** This session will involve you answering a series of multi-choice questions as well as a few short answer questions about various aspects of your cognitive and emotional health as well as your current work adaptations.

Please note, that in order to participate in the present research you must have **a diagnosis of breast cancer** and **must be over the age of 18.** You **can** be pre-treatment, receiving active treatment or post-treatment for chemotherapy and/or radiotherapy. You **can** be pre-treatment, receiving active treatment or post-treatment for chemotherapy and/or radiotherapy. You **can** also be taking hormone therapies medications such as Tamoxifen or Aromatase Inhibitors or receiving target therapies such as Herceptin.

**On completion of the online session, you will receive an amazon voucher worth £5.**

Please note, that if you agree to participate in the current research, you will be asked to provide a preferred email address at the end of the online session so that amazon e-gift voucher can be sent. All data collected will be treated with the utmost confidentiality.

You have the right to withdraw participation at any point up until the point that the anonymised data can no longer be identified.

The results from this research will be written up as part of a PhD thesis as well as for publication and conferences. At your request, the researcher will be able to provide you with information regarding the overall findings. However, please note that individual results will not be available.

The project has received ethical approval from the Department of Psychological Sciences Research Ethics Committee of Birkbeck University of London

Please contact Dr Jessica Swainston (jswain01@mail.bbk.ac.uk) or Bethany Chapman (bchapm02@mail.bbk.ac.uk), if you wish to take part in the present research study or if you have any questions/queries regarding any element of the research.

For information about Birkbeck's data protection policy please visit:

http://www.bbk.ac.uk/about-us/policies/privacy#7

If you have concerns about this study, please contact the School's Ethics Officer at: ethics@psychology.bbk.ac.uk

School Research Officer

School of Science, Department of Psychological Sciences

Birkbeck, University of London

London WC1E 7HX

You also have the right to submit a complaint to the Information Commissioner's Office

https://ico.org.uk/

**DEPARTMENT OF PSYCHOLOGICAL SCIENCES**
**BIRKBECK UNIVERSITY OF LONDON**

**INFORMATION SHEET FOR:** Understanding the role of work and work flexibility in the mental well-being of women with secondary breast cancer.

Before you decide to take part in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of the research team can be contacted if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

**Aim:** The current research primarily aims to investigate the cognitive and emotional health of women living with a diagnosis of secondary breast cancer in the UK and their experiences with work and with their employers.

If you agree to participate in the present study, you will be asked to complete a **single online session lasting approximately 35 minutes.** This session will involve you answering a series of multi-choice questions about various aspects of your cognitive and emotional health as well as your experience with your employer and their flexibility around required work adaptations after your secondary diagnosis.

Please note, that to participate in the present research you must have **a diagnosis of secondary breast cancer** and **must be over the ages of 18.**

You **can have finished receiving** or **actively still be receiving** treatment(s) including chemotherapy and/or radiotherapy at the time of enrolment. You can also be employed, self-employed, volunteering or not currently working although **you must have been attending some form of work at the time of your secondary breast cancer diagnosis.**

**On completion of the online session, you will receive an amazon voucher worth £6.**

Please note, that if you agree to participate in the current research, you will be asked to provide a preferred email address at the end of the online session so that amazon e-gift voucher can be sent. All data collected will be treated with the utmost confidentiality.
You have the right to withdraw participation at any point up until the point that the anonymised data can no longer be identified.

The results from this research will be written up as part of Bethany Chapman's PhD thesis as well as for publication and conferences. At your request, the researcher will be able to provide you with information regarding the overall findings. However, please note that individual results will not be available.

The project has received ethical approval from the Department of Psychological Sciences Research Ethics Committee of Birkbeck University of London

Please contact Bethany Chapman (bchapm02@mail.bbk.ac.uk), Professor Beth Grunfeld and Professor Naz Derakshan's PhD student if you wish to take part in the present research study or if you have any questions/queries regarding any element of the research.

For information about Birkbeck's data protection policy please visit:
http://www.bbk.ac.uk/about-us/policies/privacy#7

If you have concerns about this study, please contact the School's Ethics Officer at: ethics@psychology.bbk.ac.uk

School Research Officer
School of Science, Department of Psychological Sciences
Birkbeck, University of London
London WC1E 7HX

You also have the right to submit a complaint to the Information Commissioner's Office
https://ico.org.uk/

## Appendix 2

**COVID-19 Impact Questions:**

1. Have you personally experienced any COVID-19 symptoms?

   Yes ☐

   No ☐

2. Please indicate which of the following symptoms you have experienced

   High Temperate/Fever ☐

   A new, continuous cough ☐

   Shortness of breath ☐

   Persistent pain, tightness or pressure in the chest ☐

   New confusion or inability to arouse (associated with high fever) ☐

   Bluish lips or face ☐

   Sore throat ☐

   Sneezing or runny nose ☐

   Loss of smell and/or taste ☐

   Other (please specify) ☐

3. Has anyone in your household experienced COVID-19 symptoms?

   Yes ☐

   No ☐

4. Have you been self-isolating?

   Yes ☐

   No ☐

   Other (please specify) ☐

5. What prompted your decision to self-isolate? (50-word limit)

6. Have you received a text message or letter from the government advising you to self-isolate/shield due to your cancer diagnosis or other condition?

Yes ☐

No ☐

7. What concerns do you have about the restrictions listed in the letter? (50-word limit)

8. Do you think the restrictions from the letter will impact your wider family or social group?

Not at all 0 1 2 3 4 5 Extremely

9. Has the COVD-19 Outbreak had any impact on your scheduled treatment?

Yes ☐

No ☐

10. Can you please explain what impact it has had? (50-word limit)

11. Has the COVID-19 outbreak made you feel more anxious than usual?

Not at all 0 1 2 3 4 5 Extremely

12. Has the COVID-19 outbreak made you feel more upset than usual?

Not at all 0 1 2 3 4 5 Extremely

13. Has the COVID-19 outbreak made you feel more fearful about cancer than usual?

Not at all 0 1 2 3 4 5Extremely

14. Has the COVID-19 outbreak made you feel less in control of your health than usual?

Not at all 0 1 2 3 4 5 Extremely

15. Has the COVID-19 outbreak made you feel more socially withdrawn than usual?

Not at all 0 1 2 3 4 5 Extremely

16. Has the COVID-19 outbreak made you less confident than usual?

Not at all 0 1 2 3 4 5 Extremely

17. Are you currently:

Employed ☐

Self-employed ☐

Undertaking volunteering work ☐

Not undertaking any form of work ☐

**Please, select the answer that is closest to your experience at work:**

18. How has COVID-19 impacted your typical working day/working duties? (50-word limit)

19. Have your employers supported your required work adaptations (particularly if you are in a job that cannot typically be carried out remotely from home)?

Yes ☐

No ☑

20. Please rate your employer's support in response to the COVID-19 impact on work

Not at all supportive0 1 2 3 4 5 Extremely supportive

21. Has the COVID-19 outbreak changed your view on the importance of your work?

Much less important0 1 2 3 4 5 Much more important

22. How has the COVID-19 outbreak impacted on your job satisfaction?

Much less satisfied 0 1 2 3 4 5 Much more satisfied

23. Has the COVID-19 outbreak changed how confident you feel at work?

Much less Confident 0 1 2 3 4 5 Much more Confident

24. Has the COVID-19 outbreak changed your view on how secure your job is?

Much less secure 0 1 2 3 4 5 Much more secure

**Workplace Experience Questions (WPEQ):**

**Please answer the questions below in relation to your experience before the COVID-19 outbreak.**

1. Are you still employed or self-employed, volunteering? If no, please go to Q3

   Yes ☐

   No ☐

   Other (please specify) ☐

2. Are you still with the same employer? If yes, please go to Q7

   Yes ☐

   No ☐

   Other (please specify) ☐

3. Please indicate how long (in months) after your secondary diagnosis you left the workforce?

4. Please, indicate if your decision to leave the workforce personally driven or employer-driven?

   Personally ☐

   Employer ☐

   Combination of the two ☐

   Other (please specify) ☐

5. What factor(s) prompted you to leave the workforce? (tick, the boxes that apply)

   Lack of employer support or understanding ☐

   Lack of employer flexibility (i.e., not adaptable) ☐

   Re-evaluation of work importance ☐

   Health and function (i.e., mobility) ☐

   Advice from health care professionals ☐

   Other (please specify) ☐

6. Do you feel like you would have been able to continue working under different circumstances (i.e., better employer support)?

   Yes ☐

   No ☐

   Other (please specify) ☐

7. Has the impact of your secondary diagnosis on work created a financial burden?

   Yes ☐

   No ☐

   Other (Please specify) ☐

8. Please, indicate the gender of your line manager(s) or direct report(s) (tick, the box that applies)

   Male ☐

   Female ☐

   Mix team of males and females ☐

   Other (please specify) ☐

9. Did you disclose your secondary diagnosis to your employer?

   Yes ☐

   No ☐

   Other (please specify) ☐

10. If yes, how soon after your secondary diagnosis did you disclose this to your employers?

11. Please indicate which of the following adaptations you needed/need to manage your work and the side effects (i.e., fatigue) experienced (tick all of the boxes, that apply)

Reduced hours ☐

Flexible hours ☐

Reduced workload (i.e., physical or mental) ☐

Change in the type of work duties ☐

Ability to flexibly work from home or away from the office, if required ☐

Access to memory aids or prompts (i.e., planning software) ☐

More flexible work deadlines or targets ☐

N/A ☐

12. After your secondary diagnosis, how comfortable did you feel about having open discussions with your employer about the work adjustments (i.e., flexible hours) you need?

    Not at all comfortable 0 1 2 3 4 5 Extremely comfortable

13. If you had meetings, who drove those discussions or meetings?

Human resources (HR) ☐

Occupational health ☐

Line manager or direct report ☐

Myself ☐

Combination ☐

Other (please specify) ☐

14. How receptive were your employers to your required adjustments?

    Not at all receptive 0 1 2 3 4 5 Extremely receptive

15. How supportive were your employers' following your secondary diagnosis?

Not at all supportive 0 1 2 3 4 5 Extremely supportive

16. How understanding were the employers of your needs following your secondary diagnosis?

No understanding 0 1 2 3 4 5 Extremely understanding

17. Was your employer aware of the challenges you experienced in everyday life due to secondary breast cancer (i.e., fatigue, cognitive complaints, anxiety and/or depression or pain)?

No awareness 0 1 2 3 4 5 Extremely aware

18. Did you experience discrimination at work following your secondary diagnosis?

Very discriminated 0 1 2 3 4 5 No discrimination

19. How confident did you feel at work following your secondary diagnosis?

Much less confident 0 1 2 3 4 5 Much more confident

20. How did your employer's response to your secondary diagnosis affect your confidence at work?

Severely affected 0 1 2 3 4 5 Not affect at all

21. How satisfied are you in your job following your secondary diagnosis?

Much less satisfied 0 1 2 3 4 5 Much more satisfied

22. How protected do you feel in your job after your secondary diagnosis?

Much less secure 0 1 2 3 4 5 Much more secure

## Appendix 3

Reliability analysis showed that COVID-EMV had excellent reliability, α = .89.

Table 1. Inter-item correlation for COVID-EMV

| | COVID-19 Anxiousness | COVID-19 Upset | COVID-19 Fearful | COVID-19 Control | COVID-19 Confidence |
|---|---|---|---|---|---|
| COVID-19 Anxiousness | 1.00 | .79 | .62 | .72 | .63 |
| COVID-19 Upset | | 1.00 | .56 | .65 | .60 |
| COVID-19 Fearful | | | 1.00 | .63 | .56 |
| COVID-19 Control | | | | 1.00 | .62 |
| COVID-19 Confidence | | | | | 1.00 |

Table 2. Item-Total Statistics

| | Scale Mean if Item Deleted | Scale Variance if Item Deleted | Corrected Item-Total Correlation | Squared Multiple Correlation | Cronbach's Alpha if Item Deleted |
|---|---|---|---|---|---|
| COVID-19 Anxiousness | 11.16 | 29.82 | .81 | .71 | .86 |
| COVID-19 Upset | 11.56 | 28.90 | .76 | .65 | .86 |
| COVID-19 Fearful | 12.22 | 28.08 | .68 | .48 | .88 |
| COVID-19 Control | 11.37 | 28.60 | .77 | .60 | .86 |
| COVID-19 Confidence | 11.85 | 27.72 | .70 | .49 | .88 |

Item-total statistics show that all five items should be retained in COVID-EMV as removal of items would result in a decrease in the Cronbach's α value.

KMO = .87 (Meritorious Value)

Table 3. Factor Analysis for COVID-EMV

| | Loading onto Factor One | Communalities |
|---|---|---|
| COVID-19 Anxiousness | .89 | .78 |
| COVID-19 Upset | .83 | .68 |
| COVID-19 Fearful | .82 | .52 |
| COVID-19 Control | .74 | .68 |
| COVID-19 Confidence | .72 | .54 |
| Eigenvalue | 3.55 | |

| | |
|---|---|
| % of Total Variance | 71.05 |

Table 4. Correlations between COVID-EMV and cognitive and emotional health questionnaires

| | COVID-EMV | HADS-Anxiety | HADS-Depression | Penn State Worry | Rumination Response Scale | FACT-Cog |
|---|---|---|---|---|---|---|
| COVID-EMV | 1.00 | .70** | .51** | .59** | .56** | -.41** |

**Correlation is significant at the 0.01 level

Employer Experience Questions:

Kaiser-Meyer-Olkin Measure (KMO) of Sampling Adequacy = .87 (Meritorious Value)

KMO values for individual variables were greater than .0.80.

Two factors had eigenvalues over Kaiser's criteria of 1 and explained 69.72% of the variance.

Multicollinearity determinant = 0.001

Table 1. Pattern Matrix

| | Factor One | Factor Two |
|---|---|---|
| MBC-Understanding | .99 | |
| MBC-Receptive | .91 | |
| MBC-Supportive | .89 | |
| MBC-Awareness | .58 | |
| MBC-Comfortable | .51 | |
| MBC-Response | .50 | |
| MBC-Protected | | .88 |
| MBC-Satisfied | | .84 |
| MBC-Confident | | .71 |

Reliability analysis revealed that the six-items composing Experience of Employers Score (MBC-EE) had a high reliability, α = .88 and Personal Views of Work Score (MBC-PVW) had a reliability, α =.85.

Table 2. Inter-item correlation for MBC-EE

| | MBC-Receptive | MBC-Supportive | MBC-Understanding | MBC-Comfortable | MBC-Awareness | MBC-Response |
|---|---|---|---|---|---|---|
| MBC- Receptive | 1.00 | .77 | .83 | .53 | .55 | .55 |
| MBC-Supportive | | 1.00 | .81 | .55 | .50 | .50 |
| MBC-Understanding | | | 1.00 | .55 | .58 | .54 |

| | | | |
|---|---|---|---|
| MBC- Comfortable | 1.00 | .39 | .60 |
| MBC-Awareness | | 1.00 | .31 |
| MBC-Response | | | 1.00 |

Table 3. Item-Total Statistics for MBC-EE

| | Scale Mean if Item Deleted | Scale Variance if Item Deleted | Corrected Item-Total Correlation | Squared Multiple Correlation | Cronbach's Alpha if Item Deleted |
|---|---|---|---|---|---|
| MBC-Receptive | 18.67 | 26.26 | .81 | .73 | .84 |
| MBC-Supportive | 18.50 | 27.46 | .78 | .70 | .85 |
| MBC-Understanding | 18.91 | 24.20 | .82 | .79 | .83 |
| MBC-Comfortable | 19.12 | 24.97 | .64 | .46 | .86 |
| MBC-Awareness | 19.70 | 25.92 | .55 | .36 | .88 |
| MBC-Response | 18.94 | 26.19 | .61 | .44 | .87 |

Item-total statistics reveal that no items should be removed from the MBC-EE score

Table 4. Inter-item correlation for MBC-PVW

| | MBC-Protected | MBC-Satisfied | MBC-Confident |
|---|---|---|---|
| MBC-Protected | 1.00 | .75 | .67 |
| MBC-Satisfied | | 1.00 | .60 |
| MBC-Confident | | | 1.00 |

Table 5. Item-Total Statistics for MBC-PVW

| | Scale Mean if Item Deleted | Scale Variance if Item Deleted | Corrected Item-Total Correlation | Squared Multiple Correlation | Cronbach's Alpha if Item Deleted |
|---|---|---|---|---|---|
| MBC-Protected | 5.61 | 7.20 | .68 | .47 | .85 |
| MBC-Satisfied | 5.69 | 5.25 | .75 | .58 | .77 |
| MBC-Confident | 5.29 | 4.61 | .79 | .64 | .73 |

Item-total statistics reveal that no items should be removed from the MBC-PVW score

## Appendix 4

Structured Telephone Interview – Baseline

Thank you for agreeing to this interview. During the interview, I will be asking you a series of questions that relate to the thinking difficulties (for example, memory difficulties, difficulties) you may be experiencing as consequence of your diagnosis and treatment. I will also be asking about how you think these thinking difficulties are affecting aspects of your life, for example, your personal relationships and work ability.

There are no right or wrong answers to my questions and everything you say will be treated in the confidence. I will guide you through the interview so that we finish in approximately one hour. I would like to record our conversation as I will not be able to write everything down.

Please do not hesitate to ask any questions you have during the interview.

**Participant Number (as provided to participant in first email):**

**Date of Interview:**

**Study Phase:**

*** Questions

1. General Introductory Questions

A. Firstly, I would like to ask you a few general questions relating to your breast cancer diagnosis and the treatment you received.

When were you first diagnosed (time since)?

And what treatment(s) did you receive?

Whilst receiving this treatment(s) did you notice any changes in your physical ability, social life, workability, or mood (emotional functioning/wellbeing)?

You said you noticed changes in **X** can you please give me an example or describe a time when you experienced **X**?

How did this make you feel? Did you use any coping methods (covered more in Q5)?

Have you or are you still receiving any hormone therapies (AI or tamoxifen) or target therapies?

Did/Do you experience any effects from taking **X**? (Prompt: What did you experience? Did you notice any changes in your cognitive skills?)

2. At this moment in time, what would you describe as your main job role?

   What does your job involve on a typical day?

   Did you work during your treatment? (How did this differ from your usual working day (prior to receiving your diagnosis)? (i.e., duties, hours or location)

   If time was taken off – When did you return to work?

   What factors that influenced your decision to return to work at that point?

.

   How have you found work since you've returned?

   Are there any changes in the type of work or the way that you approach work?

   Do you feel supported? (Prompt: Why do you feel support? What makes you feel support?)

   Do you feel there are any ongoing challenges since returning to work?

3. Cognitive Symptoms

After receiving a breast cancer diagnosis and undergoing treatments including chemotherapy and/or hormone therapy (aromatase inhibitors or tamoxifen) some women report experiencing changes in their cognitive skills (or thinking skills), this can include poor memory, difficulty making decisions and planning as well as difficulties with attention or concentration.

A. Have you experienced any difficulties with any cognitive skills (thinking skills) since completing active treatment?

If they appear unsure of the terminology outline some examples of various cognitive domains.

Can you tell me something about how experiencing these changes in cognitive (thinking) skills make you feel?

| |
|---|
| |

B. Which of these difficulties (if any, or could be more than one) would you say was the most important or had the most impact on you (both in a personal and work capacity)? (Prompt: Why would you say **X**?)

| |
|---|
| |

C. Do you feel that changes or difficulties have improved or worsened over time?
   Can you give me an example?

D. Since first noticing these changes in your cognitive skills (thinking skills) do you feel you have experienced any level of improvement?
   If so, which thinking skill(s) have improved?
   Can you describe this improvement or give an example of when you notice this improvement (what were you doing)? How has this improvement made you feel?
   Have people around you noticed or commented?

| |
|---|
| |

A. Can you talk me through any changes in the way you carry out or approach your work compared with before you received cancer treatment(s) (i.e., chemotherapy)?
How do these changes in your thinking make you feel?
Do you feel that the changes are noticeable to your colleagues (if yes how do you manage that)?

B. You mentioned before that you have noticed changes in **X**, which change(s) do you feel is/are most disruptive, or has/have the greatest impact on your work, to your work, to your workability/performance (i.e., If you said memory, attention, decision making – it would indicate that memory is most problematic to your job performance)?
In what way(s) are these changes in cognition (or thinking) affecting or impacting you at work (for example, not being able to follow a conversation, forgetting names of things, forgetting things you have planned to do, etc)?

Have these changes in cognitive skills (or thinking skills changed the way you approach your work)?

C. Do you feel like the level of stress you experience at work currently is different when compared with before your treatment?
If YES- In what way does this stress differ?

Is there any particular aspect of your daily life (personal & work) that you find to be more stressful?

Would you say this stress is significantly affecting you?

D. Since completing treatment have you made any adaptations to your work commitments (i.e., reduced/increased the number of hours, changed job/job role, etc)?
If YES – Was this decision primarily driven by your cognitive difficulties? And/or What other factors contributed to your decision (i.e., re-evaluation of the importance of work, etc)?

How did this make you feel?

Would you say you are content in your work?

5. Coping

A. How do you cope with, or manage, the impact of changes in **X** (for example, not being able to follow a conversation, forgetting names of things, forgetting things you have planned to do, etc) or your difficulties (i.e., written lists, using a diary, etc)?
Do you have any tips for others in your situation about how to cope with changes in thinking skills?

If nothing is offered outline some examples of methods to see if that helps.

You mentioned that you use **Y** as a method(s) for coping with **X**, how does using this/these method(s) make you feel (i.e., angry, embarrassed, etc)? Why?

6. Impact of these symptoms on personal life (quality of life)

A. To what extent do you feel these difficulties (i.e., memory difficulties) are currently affecting your relationships or interactions with partners/parents/siblings/friends?
How do these changes make you feel?

Do you feel like your partners/parents/friends understand why you experience changes in thinking skills?

Are there any other factors that have influenced your relationships or interactions (i.e., physical changes)?

| |
|---|
| |

B. Are the difficulties you previously identified affecting your social life or social role (i.e., going out with friends or work colleagues)?
How much would you say this is due to the thinking changes/difficulties alone?

Have any other factors such as anxiety/stress, change to body imagine affected your desire to socialise with family/friends?

| |
|---|
| |

**Intervention group only**

7. Expectations of the training intervention

A. What changes would you like to see as a result of completing the training (on physical, social relationships, emotional function/wellbeing and thinking (cognitive) skills?

| |
|---|
| |

B. How would you like this training to impact your functioning or work or your work performance?

Are there any specific changes/difficulties you would like improved by this intervention?

Can you give an example of how you would like **X** to improve?

| |
|---|
| |

Do you have anything else that you would like to mention/ask before we conclude our interview?

| |
|---|
| |

TURN OFF RECORDER

Thank you very much for your time today it is very much appreciated. If you have any questions/ concerns between now and our next session please do not hesitate to contact me.

Structured Telephone Interview – **Schedule for Post-training**

Thank you for agreeing to this interview. During the interview, I will be asking you a series of questions that relate to changes in thinking skills (for example, memory difficulties, difficulties) you feel you may have experienced following the training intervention. I will also be asking about how you think these changes in thinking skills affect key aspects of your life for example your, personal relationships and work ability.

In today's interview I will also ask you a few questions about your views of the training intervention you took part in. For example, I would like to know how you think this training has had an impact on you.

There are no right or wrong answers to my questions and everything you say will be treated in the strictest confidence. I will guide you through the interview so that we finish in approximately one hour. If it is okay, I would like to record our conversation as I will not be able to write everything down.

Please do not hesitate to stop and ask any questions you have during the interview.

**Participant Number (as provided to participant in first email):**

**Date of Interview:**

**Study Phase:**

*** Questions

1. Please can you describe your current job role?

What does your job involve on a typical day?

How did this differ from your usual working day (prior to receiving the training)? (i.e., duties, hours or location)

2. Cognitive Symptoms

After receiving a breast cancer diagnosis and undergoing treatments including chemotherapy and/or hormone therapy (aromatase inhibitors or tamoxifen) some women report experiencing changes in their thinking skills, this can include poor memory, difficulty making decisions and planning as well as difficulties with attention or concentration.

A. Have you experienced any difficulties with thinking skills and activities since completing the training?

If they appear unsure of the terminology outline some examples of various cognitive domains.

Can you tell me something about how experiencing these changes in thinking skills makes you feel?

B. Which of these difficulties (if any, or could be more than one) would you say was the most important or had the most impact on you (in either a personal and work capacity)? What? Why?

C. Do you feel that changes /difficulties have improved or worsened over time?

Can you give me an example? If you feel that there has been no improvement or the changes have worsened, can you give me an example?

D. Since completing the training do you feel you have experienced any level of improvement in your thinking skills?

If so, which thinking skill(s) have improved?

Can you describe this improvement or give an example of when you notice this improvement (what were you doing)?

How has this improvement made you feel?

Have people around you noticed or commented?

3. Impact of these symptoms on work ability

   A. Can you talk me through any changes in the way you carry out or approach your work compared with before you received the training?

   Can you give me an example of when you noticed **X**? what were you doing at time?
   How do these changes in your thinking make you feel?
   Do you feel that the changes are noticeable to your colleagues (if yes how do you manage that?)

| |
|---|
| |

   B. You mentioned before that you have noticed changes in (thinking skills) **X**, which change(s) do you feel is/are most disruptive, or has/have the greatest impact on your work, to your work, to your work ability/performance (i.e., If you said memory, attention, decision making – it would indicate that memory is most problematic to your job performance)?

   C. In what way(s) do these changes in thinking affect or impact you at work (for example, not being able to follow a conversation, forgetting names of things, forgetting things you have planned to do, etc)

   D. Have these changes in thinking skills changed the way that you approach your work?

| |
|---|
| |

   E. Do you feel like the level of stress you experience at work currently is different when compared with before the training?

If YES- In what way does this stress differ?

Is there any particular aspect of your daily life (personal & work) that you find to be more stressful?

Would you say this stress is significantly affecting you?

F. Since completing the training have you made any adaptations to you work commitments (i.e., reduced/increased the number of hours, changed job/job role, etc)?

If YES – Was this decision primarily driven by your cognitive difficulties? And/Or What other factors contributed to your decision (i.e., re-evaluation of the importance of work, etc)?

How did this make you feel? Why?

Would you say you are content in your work? Why?

4. Coping

A. How do you cope with, or manage, the impact of changes in thinking (for example, not being able to follow a conversation, forgetting names of things, forgetting things you have planned to do, etc) or your difficulties (i.e., written lists, using a diary, etc)?

Do you have any tips for others in your situation about how to cope with changes in thinking skills? What? Why?

(If nothing is offered outline some examples of methods to see if that helps.)

You mentioned that you use **Y** as a method(s) for coping with **X**, how does using this/these method(s) make you feel (i.e., angry, embarrassed, etc)? Why?

Since completing the training intervention a few months ago have you noticed any changes with the way you use the mechanism/methods (i.e., are you less dependent on the method)?

| |
|---|
| |

Quality of life questions

5. Impact of these symptoms on personal life (quality of life)

    A. To what extent do you feel these difficulties (i.e., memory difficulties) are currently affecting your relationships or interactions with partners/parents/siblings/friends?
    How do these changes make you feel?
    Do you feel like your partners/parents/friends understand why you experience changes in thinking skill?
    Are there any other factors that have influenced your relationships or interactions (i.e., physical changes)?

| |
|---|
| |

    B. Are the difficulties you previously identified affecting your social life or social roles (i.e., going out with friends or work colleagues)?

How much would you say this is due to the thinking changes/difficulties alone?

Have any other factors such as anxiety/stress, change to body imagine affected your desire to socialise with family/friends?

6. Perceived effects of the training intervention

A. Since the training intervention you did a few months ago, have you noticed any changes in your thinking skills?

Do you feel like you can see the benefits from receiving the training program (relationships, work, etc)?

If YES -can you elaborate? Or given an example of when you noticed this improvement?

How have these changes made you feel (probe anxiety, stress, confidence)?

Have other people (colleagues, friends/family) around you commented on any changes?

Would you say that this intervention has had a positive impact (probe QoL)?

B. Would you recommend this training program to others? Why?

C. Did you feel like you were able to engage with the training program (sessions/time required)?

Were there any challenges in taking part in the intervention?

Did the timing of the training work for you or would it have been more useful at a different stage? (i.e., during treatment or immediately on return to work)

Did the program meet your earlier expectations?

D. Finally, I would like to ask you if there is anything else you would have liked to have seen after receiving this intervention (i.e., different improvements)

Do you have anything else that you would like to mention/ask before we conclude our interview?

TURN OFF RECORDER

Thank you very much for your time today it is very much appreciated. If you have any questions/ concerns between now and our next session please do not hesitate to contact me.