Understanding psychosocial factors that are associated with distress and symptom experience in breast cancer survivors on hormone therapy

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by

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Abstract

Background: Seventy-five percent of breast cancers are hormone receptor positive meaning hormone therapy is prescribed for up to 10 years to reduce the risk of recurrence. In addition to the general physical and psychological survivorship issues including experiencing distress that cancer patients need to manage, hormone therapy itself has side effects, and this burden is often correlated with distress. However, the symptom-distress relationship is not well understood, and they are often treated separately without acknowledgement of the potential interaction. Theoretical models provide potential frameworks for understanding distress in physical illness and give an indication for the variables that may be associated with the symptom-distress relationship. Evidence for two models, the common-sense model of illness representations (CSM) and acceptance and commitment therapy (ACT), is varied in cancer. There are several reviews of the CSM illness perceptions providing an indication of the beliefs and cognitions about illness in understanding distress in cancer which may contribute to intervention development. Despite no systematic review of ACT processes and distress in cancer, ACT interventions are common after a cancer diagnosis. ACT proposes that inflexible processes such as experiential avoidance and cognitive fusion may lead to distress, whilst interventions aim to increase psychologically flexible skills such as acceptance and present moment awareness to encourage meaningful, values-driven behaviour. Longitudinal data for both models in cancer is scarce, particularly in this population, limiting the conclusions that can be drawn regarding their contribution to explaining distress. Understanding these models and variables will provide targets for future interventions to better manage the symptoms and distress experienced by these women.

Aims and objectives: The primary aim of the PhD was to determine the relationship between psychosocial factors including cognitive behavioural and acceptance and commitment therapy (ACT) processes and symptom experience and distress in female breast cancer survivors on adjuvant hormone therapy. A pragmatic multi-methods approach was used to provide a thorough understanding of symptoms and distress, drawing on the strengths of both qualitative and quantitative methodology. The PhD objectives were to:

- conduct a systematic review and meta-analysis of the association of ACT processes with distress in people with cancer.
- conduct a qualitative study to explore symptoms and distress to understand the emotional impact of taking hormone therapy in breast cancer survivors.
- conduct a longitudinal observational study to understand the psychosocial correlates of symptoms and distress, and the potential mediators and moderators of the symptom-distress relationship for breast cancer survivors on hormone therapy.

Methods: A systematic review and meta-analysis (Chapter 4, *paper published in Health Psychology Review, 2023*) was conducted to identify the strength and direction of relationships between ACT processes and distress across all cancer groups. For the qualitative study (Chapter 5), semi-structured interviews were conducted with breast cancer survivors on hormone therapy to explore distress and experience of symptoms. Finally, a longitudinal observational study (Chapters 6 and 7) tested psychological variables, including ACT processes and CSM illness perceptions, to predict distress and tested hypothesised third variables in the symptom-distress pathway as mediators and moderators.

Results: For the systematic review, 108 studies were included, with 77 meta-analysed. Flexible processes were associated with lower distress whilst inflexible processes were

associated with higher distress. This comprehensive review supports elements of ACT being associated with distress in the context of cancer, highlighting potential key processes for further investigation. For the qualitative study, an inductive reflexive thematic analysis of 23 patient interviews generated themes around why symptoms are distressing for breast cancer survivors on hormone therapy. Themes focused on helplessness around symptoms, living with and managing difficult feelings around loss and change, living with fear, worry and uncertainty around side effects and the internal conflict when making treatment decisions which goes beyond previous research which focuses on adherence to this medication. This study identifies specific areas to target in clinical communication as well as content for intervention development; including providing clearer information about side effect expectations, helping manage the helplessness around symptoms and supporting the acceptance of the loss and change associated with the impact of side effects. The longitudinal observational study recruited 269 breast cancer survivors in the first 2 years of taking hormone therapy with a 90% retention rate at 6 months and 83% at 12 months. ACT processes explained a greater amount of variance in distress in this population than the CSM illness perceptions, although an integrated model consisting of several cognitive-behavioural processes across models predicted more variance in 12-month distress than any model alone. Several psychological processes including cognitive fusion, values obstruction, symptom focusing, breast cancer consequences and embarrassment avoidance mediated the symptom-distress pathway, indicating that an increase in symptom burden at baseline resulted in a change in the psychological process at 6 months which in turn, resulted in increased distress at 12 months. Treatment coherence and damage beliefs moderated the symptom-distress pathway whereby those who displayed greater understanding of their

treatment had less impact of symptoms on distress and those who felt that symptom indicated damage to the body had a larger impact on distress.

Conclusions: This PhD has contributed to understanding distress and symptom burden in breast cancer survivors on hormone therapy whilst understanding *why* symptoms might be distressing as well as *how* and *for whom* symptoms may lead to distress. ACT is a useful model for understanding distress in this population and interventions should be developed from the evidence base. Additionally, an integrated model may be more useful to understand distress in this population as variables from several cognitive-behavioural models were identified as significant mediators and moderators in the symptom-distress pathway. These findings provide targets for interventions that may help mitigate the negative impact of symptoms on these women. This PhD has the potential to inform clinical practice and intervention development and ultimately improve outcomes for this population.

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COVID-19 Impact Statement

The COVID-19 pandemic started approximately six months into the PhD. Unfortunately, the work completed to prepare for NHS ethics, including collaborating with NHS clinicians and clinics had to be halted due to non-COVID related research being paused nationwide. The observational studies were then redesigned to suit online community recruitment, university ethics was sought and granted, and recruitment was conducted solely online. This pivot away from NHS recruitment took a substantial amount of time to complete and online recruitment during a pandemic took substantially longer than originally anticipated in NHS clinics. In order to achieve sufficient power, recruitment went beyond the initial planned timetable. Students supported to help mitigate the impact and manage the online recruitment. Despite these mitigations, this combination of effects caused delays to data analysis for both the qualitative and observational studies. Furthermore, enforced off campus working due to lockdowns delayed access to some papers for the systematic review and meta-analysis.

At the PhD upgrade, it was decided in conjunction with internal expert reviewers to remove the final pilot study due to the expected delays from the COVID-19 pandemic and after assessment decided there was substantial content to the PhD without this study, with meta-analysis and advanced statistical analysis of longitudinal data planned. The thesis includes two additional student publications (one under review and one in the appendix) that were supported using the data collected in the PhD. Although some of the originally planned methods for the PhD had to be adjusted to account for lack of access and delays during COVID-19 lockdowns, the overall aims have been achieved with substantial contribution made to the understanding of distress in breast cancer survivors on hormone therapy.

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List of Abbreviations and Acronyms

AAQ: Acceptance and action questionnaire

ACT: Acceptance and commitment therapy

AI's: Aromatase inhibitors

ALND: Axillary lymph node dissection

BCPT: Breast cancer prevention trial

BEAQ: Brief experiential avoidance questionnaire

BNF: British National Formulary

CAQ: Committed action questionnaire

CBRQ: Cognitive behavioural responses questionnaire

CBT: Cognitive behavioural therapy

CFQ: Cognitive fusion questionnaire

CI: Confidence interval

CSM: Common sense model of illness representations

DBT: Dialectal behaviour therapy

DCIS: Ductal carcinoma in situ

DSM: Diagnosis statistical manual

DV: Dependent variable

ER+/-: Oestrogen receptor positive/negative

FCR: Fear of cancer recurrence

GAD: Generalised anxiety disorder

HER2+/-: Human epidermal growth factor receptor 2 positive/negative

HR+/-: Hormone receptor positive/negative

HT: Hormone therapy

IBD: Inflammatory Bowel Disease

IPQ: Illness perception questionnaire (variations)

IV: Independent variable

LCIS: Lobular carcinoma in situ

LTC: Long term condition

MAAS: Mindful attention awareness scale

MBCT: Mindfulness based cognitive therapy

MEAQ: Multidimensional experiential avoidance questionnaire

MRC: Medical research council

MS: Multiple Sclerosis

NCCN: National comprehensive cancer network

NHS: National health service

NICE: The national institute for health and care excellence

NIHR: National institute for health and care research

NST: No special type (invasive ductal carcinoma)

PBT: Process based therapy

PHQ: Patient health questionnaire (-ADS: Anxiety and depression scale)

PPI: Patient and public involvement

PR+/-: Progesterone receptor positive/negative

PTSD: Post traumatic stress disorder

QoL: Quality of life

RCT: Randomised controlled trial

REML: Restricted maximum likelihood

RFT: Relational frame theory

RR: Relative risk

SACS: Self-as-context scale

SCS: Self-compassion scale

SD: Standard deviation

SERMS: Selective oestrogen receptor modulators

SE: Standard error

SES: Socioeconomic status

SQRQ: Standards for reporting qualitative research

TMA-LTC: Transdiagnostic theoretical model of adjustment to LTCs

VIF: Variance inflation factor

VQ: Valuing questionnaire

Chapter 1 Breast Cancer

1.1 Chapter overview

This chapter will provide an introduction to breast cancer in terms of its clinical characteristics, stages, epidemiology, and treatment. In addition, the psychosocial impact of a diagnosis of breast cancer and challenges to survivorship with a specific focus on adjuvant hormone therapy will be discussed with relevant literature. For context, the timing of the studies will be discussed with consideration of the COVID-19 pandemic.

1.2 Breast cancer

1.2.1 Clinical characteristics of breast cancer

When abnormal cells grow and divide uncontrollably to form a malignant growth or tumour in the breast tissue, this is known as invasive breast cancer. Tumours can grow in the milk ducts of the breast or the lobes. Lobes and lobules are glandular tissue which connect to the ducts and then to the nipple. Most commonly, breast cancer starts in the milk ducts with around 70-80% of breast cancers now known as invasive breast cancer no special type (NST; previously known as invasive ductal carcinoma; Cancer Research UK, 2020b; Sinn & Kreipe, 2013). This means the cancer does not have any special characteristics and has started in the milk ducts and spread into the surrounding tissue with the tumour most likely appearing as a lump. Around 15% of breast cancers are known as invasive lobular carcinomas, which mean the cancer starts in the lobules of the breast and spreads to the surrounding tissue (Cancer Research UK, 2020c). Lobular breast cancer can appear differently to the common lump seen in invasive breast cancer NST, as there can be skin thickening, webbing or rippling as the tumour is more likely spread throughout the lobules (Cancer Research UK, 2020c).

Approximately five percent of invasive breast cancers are special types meaning they have particular features (more than 12 varieties) and considered rarer forms of breast cancer (Yerushalmi, Hayes, & Gelmon, 2009). Invasive breast cancers are different to ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS), as these are classified as early forms of breast cancer that have not spread to other breast tissue, and therefore non-invasive. However, if left untreated these can turn into invasive breast cancer. For the purpose of this thesis, the term breast cancer will refer to invasive breast cancers.

1.2.2 Breast cancer stages

Primary breast cancer (also referred to as early stage, stage I-III or invasive) is a first diagnosis which effects a primary breast site and may or may not include the lymph nodes under the armpit. In invasive primary breast cancer, there are three separate stages depending on the size of the tumour, number of lymph nodes effected and how far the tumour has spread away from the breast. Number staging is often used to determine the extent of the invasive breast cancer (see Table 1.1 for a detailed description of the number staging). Stage 0 would refer to DCIS and LCIS as they are non-invasive. Early-stage breast cancer, stages I-III, means the cancer has not spread further than the breast. Stage I and II describe tumours that are smaller and/or have spread to fewer lymph nodes. Stage III breast cancers are sometimes referred to as locally advanced as the tumour may have spread to the skin of the breast or the chest wall. This breast cancer has not spread further than the breast area and if it had, would be referred to as metastatic, advanced or stage IV breast cancer.

Table 1.1.

Breast cancer number staging

Number stage		Description
Stage I	Ia	The tumour is 2cm or smaller and has not spread outside the breast.
	Ib	Either there is no tumour in the breast, or the tumour is smaller than 2cm but has spread to the lymph nodes very near the breast.
Stage II	IIa	Either there is no tumour, or the tumour is less than 2cm and cells are found in 1-3 lymph nodes in the armpit or breastbone; or the tumour is larger than 2cm but less than 5cm and there are no cancer cells in the lymph nodes.
	IIb	The tumour is 2-5cm and has spread to the lymph nodes near the breast or the tumour is between 2-5cm and has spread to 1-3 lymph nodes in the armpit or breastbone; or the tumour is greater than 5cm but not in the lymph nodes.
Stage III	IIIa	Either there is no tumour or a tumour of any size and is found in 4-9 lymph nodes in the armpit or breastbone; or the tumour is larger than 5cm and there are cells in nearby lymph nodes; or the tumour is more than 5cm and has spread to 1-3 lymph nodes in the armpit or breastbone.
	IIIb	The tumour has spread to the skin of the breast or the chest wall and may have spread to up to 9 lymph nodes in the armpit or breastbone.
	IIIc	There is no tumour, or a tumour of any size is found and has spread to 10 or more lymph nodes in the armpit, the collar bone and/or breastbone. In addition, there is cancer in the skin of the breast.

Information retrieved from (Cancer Research UK, 2023)

1.2.3 Breast cancer types

There are several types of breast cancer that differ in how they develop and therefore how they are treated. Hormone receptor positive (HR+) breast cancers mean cancer cells are stimulated to grow and divide by the hormone's oestrogen and/or progesterone which are produced by the ovaries. Around 75% percent of breast cancers are HR+ (Harrell et al., 2007). Around one in five breast cancers are HER2+ which means they have a higher-than-normal level of the HER2 protein (human epidermal growth factor receptor 2) on their surface which stimulates the cancer cells (Wolff et al., 2014). Alternatively, the cancer may be known as triple negative breast cancer whereby neither the hormones nor the protein stimulates the cancer cells to grow as there are no hormone receptors or HER2 protein

receptors. Although triple negative breast cancer impacts fewer women, with around 15% of breast cancers of this type, it is associated with poorer outcomes due to its aggressive nature and limited treatment options (Sharma, 2016).

1.3 Breast cancer statistics

1.3.1 Breast cancer incidence

Worldwide, breast cancer incidence was 2.3million in 2020 (Sung et al., 2021) with approximately 56,000 new diagnoses each year in the UK (Cancer Research UK, 2018). It is the UK's most common cancer, and the world's most prevalent cancer, with 7.8million women living with breast cancer having been diagnosed in the last 5 years (World Health Organisation, 2021). Incidence rates are rising which could be due to earlier detection from screening programs but may also be due to over diagnosis of precancerous tumours such as DCIS (Bleyer & Welch, 2012). However, increased incidence may also be due to lifestyle factors including alcohol consumption, diet (being overweight and a lack of good nutrition and physical activity) and stress (Martin-Moreno, Soerjomataram, & Magnusson, 2008). In addition, hormones contribute, whereby early first occurrence of menstruation, late age of menopause and late age of first pregnancy can increase the risk of breast cancer (Martin-Moreno, Soerjomataram, & Magnusson, 2008).

1.3.2 Breast cancer survival

Although there was an average of 11,499 deaths per year from breast cancer in the UK between 2017 and 2019, UK breast cancer survival rates have doubled in the last 40 years with women living longer and surviving their disease (Cancer Research UK, 2018). In England, between 90 and 98% of women with stage I-II breast cancer and 70% of stage III will survive more than 5 years after diagnosis (Office for National Statistics, 2019). However,

there are inequalities in breast cancer deaths as 9 out of 10 women may survive in high income countries, but as low as 4 to 6 out of 10 will survive in low- and middle-income countries (World Health Organization, 2023). This may be due to inadequate services for diagnosis and treatment, late diagnosis, access and cost issues, and low coverage of health services (World Health Organization, 2023). However, even within higher income countries, low socio-economic status (SES) can add to inequalities as there is increased mortality compared to those with higher SES (Lundqvist et al., 2016). Breast cancer was the leading cause of years of life lived with disability in 119 of 184 countries worldwide in 2008 (Soerjomataram et al., 2012).

1.3.3 Breast cancer recurrence

There is a risk that after treatment, the breast cancer might return. If the cancer comes back in the same breast, it is known as a local recurrence whereas a breast cancer that has spread further than the breast into the lymph nodes, skin or chest wall is known as a locally advanced recurrence. Although the risk of recurrence varies, there is a greater risk of recurrence in the first 2-5 years after diagnosis (Geurts et al., 2017; Saphner, Tormey, & Gray, 1996). This can vary from 0.6 to 17.9% in the first year, to 4.6 to 45.5% in the fifth year after diagnosis, depending on stage and receptor status (Neuman et al., 2023). If the breast cancer has spread to other parts of the body such as the bones, lungs, liver or brain, this is known as secondary, metastatic or advanced breast cancer.

1.3.4 Breast cancer and ethnicity

Overall, the prevalence of breast cancer in the UK is higher in White women (Gathani et al., 2021b). For example, in a study of 24,022 women aged 30-46 years old at diagnosis, 92% were White and, in the older category (53-70 years old) of 92,555 women, 96% were White

(Gathani et al., 2021b). Although data from the US suggests incidence rates are equal for non-Hispanic White and non-Hispanic Black younger women (<50 years old; DeSantis et al., 2014). Additionally, it has been found that White women are more likely to have HR+ breast cancer, whilst Indian, Pakistani, Black Caribbean, Black African and African American women are more likely to have oestrogen receptor-negative (ER−), progesterone receptor-negative (PR−), and triple-negative (ER−, PR−, HER2−) breast cancer than White women (Cui et al., 2014; DeSantis et al., 2014; Gathani et al., 2021b). These women are also more likely to present with a higher stage tumour at diagnosis (Gathani et al., 2021b). These breast cancer characteristics are regarded as less favourable due to the severity of cancers at diagnosis and the more limited treatment options (Gathani et al., 2021b) and therefore these groups of women can have worse prognosis and outcomes (Møller et al., 2016).

1.4 Treatment

Breast cancer can be found during routine screening such as the UK national breast screening programme or from self-checking. Upon examination of the breast, an ultrasound scan and mammogram (breast x-ray) will be conducted. If abnormalities are found, a biopsy will be taken to test for cancer cells. To check for cancer cells in the lymph nodes, an axilla lymph node ultrasound will be completed, and a biopsy taken if anything looks abnormal. Treatment will vary depending on the stage and type of breast cancer with the aim to remove the tumour (from both the breast and the lymph nodes) and additionally to prevent recurrence (Waks & Winer, 2019). Primary (first line) treatment will typically involve surgery (lumpectomy and mastectomy), chemotherapy and/or radiotherapy. Preoperative treatment is known as neo-adjuvant treatment, whilst treatment post-surgery is known as adjuvant treatment. Treatment guidelines in the UK follow the early and locally advanced

breast cancer: diagnosis and management guidelines (NG101; National Institute for Clinical Excellence, 2023) which are explained in the next sections.

1.4.1 Neoadjuvant treatment

Chemotherapy is a systemic therapy involving drugs to destroy cancer cells and prevent them from dividing and growing. In some cases, chemotherapy may be given as a neoadjuvant treatment to reduce tumour size before surgery but is more commonly given after surgery. Chemotherapy is more common for triple negative and HER2+ breast cancers than ER+ and is usually administered for 12-24 weeks (Cardoso et al., 2019). In trials, chemotherapy has been found to reduce mortality by 38% for women under 50 with breast cancer (Early Breast Cancer Trialists' Collaborative Group, 2005). Chemotherapy is associated with many side effects including nausea, neuropathy, hair loss, pain, fatigue, sleep and cognitive issues (Byar et al., 2006; Cancer Research UK, 2020a). Chemotherapy can also have a detrimental impact on the ovaries as it brings about an early menopause in pre-menopausal women and although this can recover, it can result in permanent infertility (Tao, Visvanathan, & Wolff, 2015). For those with HER2+ breast cancers, targeted therapy such as trastuzumab (Herceptin) can be prescribed before surgery or in 3-week intervals for 1 year in conjunction with other primary treatment. One year on trastuzumab has been found to significantly increase disease-free survival however, approximately 20% will still experience a recurrence (Cameron et al., 2017; Yang et al., 2022). Targeted and immunotherapy drugs which may include monoclonal antibodies, target specific proteins such as HER2, by attaching to proteins on cancer cells (Cancer Research UK, 2020d). Due to the nature of the drugs, targeted and immunotherapy drugs for breast cancer may cause serious side effects but the most common are fatigue, anaemia, nausea and flu-like symptoms (Cancer Research UK, 2020d). Immunotherapy drugs may be particularly useful

for triple negative breast cancer and advancements are being made at a promising rate (Ye et al., 2023).

1.4.2 Primary treatment

Depending on the size and spread of the tumour, different surgeries may be planned. A lumpectomy (also known as breast conserving surgery or wide local excision) will only remove the area of cancer tumour in the breast, whereas a total mastectomy will remove the whole breast. After mastectomy, there is the option to have immediate or delayed breast reconstruction by removing skin and muscle from the stomach to reconstruct the breast. There has been controversy regarding the comparability of breast conserving surgery and mastectomy but research suggests that outcomes (including survival at 10 years and recurrence at 10 years) for stage I-II women having a lumpectomy with radiotherapy is equal to those having a mastectomy (Jacobson et al., 1995). If a patient had an abnormal biopsy of the lymph nodes, then they will have an additional surgery called an axillary lymph node dissection (ALND) at the same time as their other surgery to remove the lymph nodes under the arm. If the lymph nodes looked normal on the ultrasounds at diagnosis, the patient will have a sentinel biopsy at the time of surgery. If abnormal lymph nodes are found, it could mean another operation or further treatment. Improvements over the years means the cosmetic and functional impact of surgery have been reduced (Waks & Winer, 2019). However, a common complication from surgery, which can also be from chemotherapy and/or radiotherapy, is lymphedema, with 20% of women experiencing this in the arm after breast cancer treatment (DiSipio et al., 2013). Lymphedema is the build-up of lymph fluid, causing swelling and pain and occurs due to the disruption to lymph flow from damage caused by treatment (Stanton & Bower, 2015).

Radiotherapy involves targeting high energy x-rays to kill cancer cells and is usually given post-surgery. Radiotherapy is offered after breast conserving surgery, but if there is a low risk of recurrence, some won't receive it or only have partial breast radiotherapy. The NICE guidelines report that local recurrence without radiotherapy occurs in 50 per 1000 women at 5 years but with radiotherapy is 10 per 1000 at 5 years (National Institute for Clinical Excellence, 2023). Side effects of radiotherapy include skin soreness and limitations to movement in the arm. Radiotherapy is administered in doses called fractions, consisting of 15 fractions, 5 days a week for 3 weeks, however this changed due to new evidence, to only 5 fractions at the start of the COVID-19 pandemic (Dave et al., 2021).

1.4.3 Adjuvant treatment: hormone therapy

In addition to going through primary cancer treatment, women with HR+ breast cancer will be prescribed adjuvant hormone therapy for up to 10 years (Davies et al., 2013). This medication reduces the level of oestrogen and/or progesterone or stops it from stimulating the cancer cells to grow and divide, reducing the risk of the cancer recurring (Harrell et al., 2007). Depending on the age and menopausal status of a woman with breast cancer, different hormone therapy medication may be prescribed. In pre-menopausal women, oestrogen is mainly produced by the ovaries but this production decreases in postmenopausal women. Tamoxifen, often prescribed to pre-menopausal women with HR+ breast cancer, works by blocking oestrogen receptors, stopping the oestrogen attaching to the cancer cell, and therefore preventing oestrogen from stimulating the cancer cells. This is known as a selective oestrogen receptor modulator (SERMs).

For post-menopausal women, aromatase inhibitors (AIs) are prescribed to stop an enzyme called aromatase which is naturally found in fatty tissue, from converting other hormones

into oestrogen (Chumsri et al., 2011). Common examples of AI's are anastrozole, letrozole and exemestane. Taking AIs for a long period of time can affect bone health so those at risk of osteoporosis often take bisphosphonates such as zoledronic acid or clodronate in conjunction with AIs (Chumsri et al., 2011). Ovarian suppression treatment such as goserelin (Zoladex) may also be given with hormone therapy medication for pre-menopausal women, which induces a temporary menopause which can be reversed. Some women opt for an oophorectomy, also known as ovarian ablation, which is the removal of the ovaries causing a permanent menopause. In these instances, women would then be prescribed an AI.

Hormone therapy is effective at reducing cancer recurrence and mortality risk over 5-10 years of taking the medication (Cuzick et al., 2015; Early Breast Cancer Trialists' Collaborative Group, 2011). In a meta-analysis, the Early Breast Cancer Trialists' Collaborative Group (2011) report that over five years, tamoxifen significantly reduced the risk of recurrence by a third (Relative Risk; RR = 0.53 in years 0-4 and RR = 0.68 in years 5-9). Whilst tamoxifen reduced mortality by a third over the first 0-4 years (RR = 0.77). In addition, the Arimidex, Tamoxifen Alone or in Combination Trial, ATAC Trialists' Group (2005) compared tamoxifen and anastrozole for 5 years in 9366 postmenopausal women with early stage breast cancer. They found anastrozole was superior to tamoxifen in prolonging disease-free survival, time to recurrence and reducing distant metastases.

The Early Breast Cancer Trialists' Collaborative Group (2015) meta-analysis explored data that compared taking tamoxifen or AIs for postmenopausal breast cancer 5 years after diagnosis and found reduction in risk of recurrence rates was stronger in years 0-1 and 2-4 for aromatase inhibitors than tamoxifen. Hormone therapy has recently been extended to 10 years as it has been reported that 50% of breast cancer recurrence occurs more than 5

years after initial diagnosis and improved outcomes have been reported (Dowling et al., 2019). The ATLAS trial (Davies et al., 2013) randomly allocated women with early-stage breast cancer who had completed 5 years of tamoxifen, to either continue for another 5 years or stop taking the medication. They found for those who continued for 10 years, there was a significant reduction of recurrence risk and reduced mortality risk, with a 21.4% vs 25.1% recurrence risk for those on 10 years vs 5 years respectively (Davies et al., 2013).

1.4.3.1 Hormone therapy side effects

Due to the medications' impact on oestrogen in the body, physical side effects and adverse events have been reported in drug trials and are listed by the manufacturers. Side effects are defined as unintended effects of a drug (Due, 2023). Some definitions include adverse reactions in the definition of side effects however these are not interchangeable terms (Due, 2023). In the UK, the British National Formulary (BNF), which lists information about drugs, report a long list of common or very common side effects of hormone therapy medication with almost the same side effects listed for tamoxifen and AIs (anastrozole/letrozole). These include hot flushes, fluid retention/weight gain, vaginal bleeding/discharge, fatigue, bone pain, joint disorders, osteoporosis, headaches and nausea (British National Formulary, 2023a, 2023b, 2023c).

Trials, such as by the ATAC Trialists' Group (2006), report that adverse events in postmenopausal women, such as bone fractures, osteopenia or osteoporosis, are more likely in those receiving anastrozole than tamoxifen. Gynaecological events and diagnoses of treatment-related endometrial cancer were more common for those on tamoxifen. Anastrozole was associated with significantly fewer overall treatment-related serious adverse events. From a sub study of the ATAC trial (Fallowfield et al., 2004), there was no

difference in quality of life for those on anastrozole vs tamoxifen, and endocrine symptoms increased between baseline and three months and then became stable. Those receiving anastrozole reported fewer other side effects including cold sweats and vaginal discharge, but more vaginal dryness, painful intercourse and loss of sexual interest. The symptoms were relatively stable for the 2 years with only a slight improvement reported. Whelan and Pritchard (2006) report that in trials of AIs in postmenopausal women, there are no differences in measures of quality of life between medications, but symptoms are reported differently such as bone/muscle aches are more common with exemestane compared to tamoxifen.

Hot flushes and night sweats are common in both AIs and tamoxifen (Garreau et al., 2006). Cuzick et al. (2008) report in a retrospective study of the ATAC trial, that symptoms may be a useful biomarker for a greater response to hormone therapy working as they found that those who reported new vasomotor (e.g., hot flushes or night sweats) or joint symptoms, had a decrease in breast cancer recurrence compared to those who did not report these symptoms. Additionally in another study, around 78% reported hot flushes and hot flushes were found to be a strong negative predictor of breast cancer recurrence (Mortimer et al., 2008). There is less information on the cognitive impact as much research has focused on chemotherapy or 'chemo brain', and cognitive dysfunction is potentially under diagnosed in those taking endocrine therapy (Haggstrom et al., 2022). However, oestrogen signalling can be directly impacted by endocrine therapy, causing direct effects on cognition (Haggstrom et al., 2022). Other side effects such as fatigue, sleep and mood problems can also indirectly impact on cognition. One study (Castellon et al., 2004) found that breast cancer survivors who received chemotherapy and tamoxifen scored worse in neurocognitive performance

than those receiving local therapy (surgery and radiotherapy), although a group with only tamoxifen was not compared against.

1.5 Breast cancer survivorship

Women who complete primary treatment for early-stage breast cancer with curative intent are often termed breast cancer survivors and the term survivorship depicts the move from active treatment to follow up care. It is also sometimes known as the re-entry phase as cancer patients are trying to go back to their pre-cancer lives (Stanton et al., 2005).

1.5.1 Psychological impact of breast cancer and breast cancer survivorship

A breast cancer diagnosis can be a stressful and threatening experience (Stanton & Bower, 2015). Women often describe diagnosis as a shock, overwhelming and a blur which continues through treatment (Lethborg et al., 2000). Women report that during primary treatment they are in survival mode, focusing on and powering through their treatment, which implies a potential neglect of the more psychological aspects (Lethborg et al., 2000; Stanton et al., 2005). It is often not until after primary treatment has finished, that the emotional impact is more apparent and there is time for reality to hit (Lethborg et al., 2000). Even though women are considered disease free after primary treatment, the impact of treatment and medical support coming to an end can result in continued distress and physical and psychological difficulties (Lethborg et al., 2000). There are various estimates of the percentage of breast cancer survivors experiencing distress as some reviews combine all stages of diagnosis, but it has been reported up to 40% experience distress (Bjerkeset, Röhrl, & Schou-Bredal, 2020; Fann et al., 2008; Hashemi et al., 2020; Syrowatka et al., 2017). Depression and anxiety are frequently reported as moderate to severe unmet needs and survivorship issues (Vuksanovic et al., 2021).

Few studies have explored the persistence of distress over time for breast cancer survivors although research indicates that distress can persist for up to 5 years (Saleeba, Weitzner, & Meyers, 1996). In a review of long term breast cancer survivors (Mols et al., 2005) and in a 10 year population based study of 387 female breast cancer patients (Koch et al., 2013), quality of life (QoL) was generally reported to be good, however there are reported limits to functioning and reported symptoms restricting certain elements of quality of life. In some of the studies in the review, they found longer term survivors had poorer psychological and emotional wellbeing than non-cancer control groups (Mols et al., 2005).

Stanton et al. (2005) explain that there are myths or preconceptions about the move to survivorship. For example, there is an expectation that women should celebrate, that recovery should be quick, that other peoples' perceptions are that women are cured and therefore okay, that women should return to their pre-cancer self, and that they no longer need support. However, contrary to these expectations, this period of time has often been reported to be particularly difficult. In a qualitative study of early-stage breast cancer survivors, some of the specific concerns that women report are that there is less frequent medical contact, uncertainty around the future, fears of recurrence and having difficult thoughts around reintegration to their pre-cancer lives (Lethborg et al., 2000). Fear of cancer recurrence is estimated to be experienced by the majority of cancer survivors across diagnoses with reports of up to 60% in a recent meta-analysis (Luigjes-Huizer et al., 2022) and in breast cancer survivors, up to 56% reported moderate to high fear of recurrence (Ellegaard et al., 2017; van den Beuken-van Everdingen et al., 2008) and is often reported to be the most common unmet need (Vuksanovic et al., 2021). As previously mentioned, elements of QoL may be restricted in the long term of breast cancer survivorship. Both Mols et al. (2005) and Koch et al. (2013) report limits to sexual functioning, physical and social

functioning, pain and financial difficulties persisting for up to 10 years into breast cancer survivorship.

Women also have to manage possible appearance changes after recovery from surgery and chemotherapy and/or radiotherapy. One study has shown that body image concerns are associated with distress, fatigue and poorer quality of life in breast cancer survivors, although prevalence of poor body image did not differ compared to controls without cancer (Falk Dahl et al., 2010). Into the course of survivorship, women often still report significant pain, fatigue and sleep problems as well as anxiety and depression (Burgess et al., 2005; Marino et al., 2014; Schreier et al., 2019). Fatigue and sleep have been reported as frequent moderate or severe survivorship issues (Vuksanovic et al., 2021). In addition, it has been reported that around 15% of women experience lymphoedema, although some reports have been up to 60% (Stanton & Bower, 2015; Vuksanovic et al., 2021). However, studies have suggested lymphoedema is less often rated as a moderate or severe issue compared to other symptoms (Vuksanovic et al., 2021). Fertility concerns have also been reported in breast cancer survivors, in particular those who are younger (Howard-Anderson et al., 2012).

However, research has shown that some women survivors of breast cancer show good adjustment with positive outcomes. Bellizzi and Blank (2006) found in a sample of 224 breast cancer survivors, that they reported growth of relationships with others, a sense of new possibilities and appreciation for life. Factors such as age at diagnosis, marital status, employment, education, perceived intensity of disease and active coping accounted for a proportion of the variance in those outcomes. Additionally, Ruini, Vescovelli and Albieri (2013) found that breast cancer survivors reported significantly higher levels of post-

traumatic growth and distress and lower psychological wellbeing than healthy women experiencing other stressful events.

1.5.2 Survivorship and adjuvant hormone therapy

As well as the generic impact a breast cancer diagnosis and survivorship have on a woman, taking adjuvant hormone therapy can add an additional layer of difficulties. As previously described, trials and guidelines list a number of common side effects of taking hormone therapy medication. Side effects are assumed to be temporary and charity support pages state that after a few weeks or months they will settle down (Cancer Research UK, 2021). However, women have reported feeling their health care professionals do not adequately prepare them for the experience and severity of side effects (Clancy et al., 2020), or the timeframe.

1.5.2.1 Impact and persistence of side effects

In two qualitative systematic reviews of breast cancer survivors taking hormone therapy, side effects are reported to be as bad or worse than having the cancer itself and have a severe, disabling daily impact (Clancy et al., 2020; Peddie et al., 2021). In a sample comparing those on hormone therapy and those not on hormone therapy, researchers found that those on hormone therapy had less positive outcomes in terms of quality of life and wellbeing over time, than those who were not on the medication (Andreu et al., 2022). Several studies have reported side effects persisting throughout breast cancer survivorship. In a sample where 80% were on hormone therapy (Cheng, Wong, & Koh, 2016), the most common symptoms reported were physical including lack of energy, numbness, tingling, pain and difficulty sleeping in survivors less than 2 years after diagnosis. Similar symptoms

were reported for survivors who were 2-5 years into survivorship, indicating symptoms persist throughout survivorship.

Hunter et al. (2004) report that those taking tamoxifen still experience hot flushes and night sweats 3 years post diagnosis with prevalence of 80% and 72% respectively. In addition, the hot flushes and night sweats were associated with greater anxiety, poorer emotional functioning and more sleep issues. Furthermore two longitudinal studies of women taking hormone therapy, by Ganz et al. (2016b) and Moon et al. (2019b) reported that over 12 months, side effect intensity significantly increased. Updated NICE guidelines report that the common side effects will continue during extended endocrine therapy (National Institute for Clinical Excellence, 2023). Therefore, these women live with not only the ongoing effects and bodily changes from primary treatment, but also the addition of ongoing physical symptoms and medical management of taking hormone therapy which can have a significant personal impact. Breast cancer survivors report feeling unprepared for side effects or having the assumption that they will not last long (Peddie et al., 2021). However, as reported through the research presented in this section, there seems to be a mismatch between the clinical communication that survivors receive, and the patient reported experience of side effects persisting. Due to the issue with defining side effects presented in Section 1.4.3.1, and the variation in physical symptoms reported at different stages of survivorship, for the purpose of this PhD, physical symptoms (in relation to or attributed to hormone therapy) and side effects will be used interchangeably.

1.5.2.2 Managing side effects

Despite the high prevalence of physical symptoms, management and treatment for these side effects is limited (Cella & Fallowfield, 2008; Hall et al., 2022). Women are often

prescribed bisphosphonates for bone issues (e.g. osteoporosis) associated with oestrogen deficiency, but this doesn't manage the bone and joint pain and stiffness that women report (Cella & Fallowfield, 2008). Management for sexual issues, hot flushes, loss of libido and cognitive impairment is limited and it is advised against using oestrogen medications which may be beneficial as they have been found to be associated with an increased risk of a new breast cancer event (Cella & Fallowfield, 2008; Holmberg & Anderson, 2004). Vitamin E is also not recommended for women with breast cancer who experience hot flushes due to interfering with the therapeutic effects of hormone therapy (National Institute for Clinical Excellence, 2023; Peralta et al., 2009). More recently, an umbrella review of literature and guidelines by Hall et al. (2022) found there was consensus for gels and lubricants to manage vaginal symptoms, but despite being effective, may not be offered due to barriers around discussing sexual problems with clinicians (Reese et al., 2017). Hall et al. (2022) report little evidence and research on other management strategies apart from yoga and aerobic exercise to manage fatigue which had support from two high quality reviews (Cramer et al., 2017; Cramp & Byron-Daniel, 2012).

Garreau et al. (2006) found that there is a personal cost for managing side effects on hormone therapy as women reported spending nearly $70 per month with many using non-evidence-based products. As there are limited appropriate or safe pharmacological treatments for side effects and/or access is limited, other methods of intervening need to be explored. Psychological treatments that aim to change the way in which people respond to the symptoms, may be able to reduce the impact of those symptoms. For example, Ayers et al. (2012) found cognitive behavioural therapy (CBT) was effective at reducing the burden of hot flushes and night sweats and the frequency of night sweats in menopausal women. In another CBT based trial, it was found that this therapy was effective at reducing hot flush

and night sweat problems as well as the frequency of them in women who had treatment for breast cancer (MENOS4 trial; Fenlon et al., 2020). In addition, anxiety and depression also significantly improved. The authors report that the MENOS4 trial had significant and lasting improvements compared to medications for hot flushes such as serotonin and norepinephrine reuptake inhibitors (Fenlon et al., 2020). This intervention was a nurse-led group therapy, which may be more accessible for some women and therefore reach a wider proportion of women in need. However, therapist or professional supported interventions can be more costly than self-management interventions (Chatterton et al., 2016) and in-person groups may not be accessible for some people (Renn et al., 2019). It may therefore be useful for further research to be conducted on designing evidence based self-management or digital interventions that could not only reach a wider proportion of women but also help how people respond and psychologically manage these difficult side effects to reduce the impact of them.

1.5.2.3 Adherence to hormone therapy

Even though hormone therapy is reported to be effective at reducing recurrence risk, many women stop adhering to their medication often due to the side effects impacting negatively on their quality of life (Nestoriuc et al., 2016). Barron et al. (2013) reports that non-adherence to hormone therapy in early-stage breast cancer patients was associated with a significant increase in the odds of a breast cancer recurrence. Hershman et al. (2011) also report from using pharmacy records, that both early discontinuation and non-adherence were independent predictors of mortality. The adherence literature often reports side effects as key factors involved in non-adherence to hormone therapy, with women reporting having to weigh up their quality of life with the potential reduction in recurrence risk (Moon et al., 2017c; Peddie et al., 2021). As discussed, the experience of side effects has

been associated with distress and poorer quality of life in both quantitative and qualitative research (Jacobs et al., 2020). However, the majority of research on breast cancer survivors prescribed hormone therapy focuses on the exploration of medication taking behaviour such as the barriers and facilitators of adherence. This limits our understanding of factors such as quality of life and distress, particularly in those women who persist with their medication despite experiencing side effects.

1.6 Context of COVID-19 and breast cancer

The COVID-19 pandemic led to changes in usual treatment pathways for breast cancer management (Dave et al., 2021). One study reports that almost 60% of women with early-stage breast cancer had treatment altered (Dave et al., 2021). For example, hormone therapy was initiated before surgery, rather than after which is the more common treatment pathway. This was to postpone surgery when it was anticipated that theatre capacity was reduced (Dave et al., 2021). There was a quick uptake of a lower dose of radiotherapy whereby women received 5 fractions instead of 15. This particular change had been trialled for a number of years and was evaluated and published as safe, routine practice at the start of the pandemic (Brunt et al., 2020). These changes were in line with evidence-based guidelines from before the pandemic and therefore it is estimated that survival outcomes were not negatively impacted. Additionally, immediate breast reconstruction was often avoided, and breast screening was suspended. It was reported that there were 28% less referrals in the first 6 months of 2020 than the year before (Gathani et al., 2021a), meaning some women may not have been attending GPs for symptoms or signs of potential breast cancer.

Research suggests that the disruption to breast cancer services during the pandemic had a significant impact on the emotional health of women, increasing anxiety and depression (Swainston et al., 2020). Women felt neglected and worried about these treatment changes as, for example, their follow-up mammograms were postponed (Hughes et al., 2020b). Those on treatment (immunosuppressed from chemotherapy or immunotherapy) were told they were at greater risk of catching COVID-19 and experiencing worse effects of the virus, leading to concerns and requests to shield at home by staying indoors and minimising contact with others (Savard et al., 2021). Women reported feeling trapped, socially isolated and upset at not seeing their family (Hughes et al., 2020b). Also, young women who would usually have received immediate breast reconstruction after total mastectomy were offered delayed reconstruction which could have psychological implications (Dave et al., 2021). On the other hand, one study reported little difference in psychological wellbeing during this time in a small mixed cancer sample compared to a sample from before the pandemic, although they did report there was confusion about the long-term implications of treatment changes (Hulbert-Williams et al., 2021). Rapid research studies were published early in the pandemic, however upon scoping searches, the majority of the data in UK based studies has focused on the impact to screening, treatment and clinical outcomes such as deaths. Due to the recency of the COVID-19 pandemic, longer term effects of the disruption during this period of time are unknown. This makes it difficult to draw concrete conclusions about the potential impact of the pandemic on breast cancer survivors. The research in this thesis was carried out during the COVID-19 pandemic and therefore will add some understanding to the experience of survivorship during this time. The potential impact or implications of this period of time will also be referred to when discussing the various results.

1.7 Summary

Seventy-five per cent of women are diagnosed with HR+ breast cancer and therefore a significant proportion of breast cancer survivors are prescribed adjuvant hormone therapy treatment for up to 10 years. A diagnosis of breast cancer and the move to survivorship can have a significant psychological impact, and on top of this there is an additional stressor of taking hormone therapy and living with and manging side effects. Distress is a prevalent and persistent outcome for breast cancer survivors and therefore needs to be explored and examined to effectively support this population through interventions. In addition, the experience and impact of the side effects and symptoms on breast cancer survivors has been suggested to be difficult and distressing but the exact pathway between physical symptoms and distress is relatively unexplored. Understanding theoretical models of distress will provide a framework for exploring and investigating the potential predictors of distress in breast cancer survivors on hormone therapy to address this important patient outcome.

Chapter 2 Theoretical approaches to understanding distress in cancer

2.1 Chapter overview

Distress is experienced by breast cancer survivors taking hormone therapy. An understanding of distress in the context of physical illness is needed to provide avenues for future research to appropriately support breast cancer survivors. Various theoretical cognitive-behavioural models have been proposed to understand the correlates, potential determinants and protective factors for distress in physical illness, providing insights into the variability in distress experiences. These factors may be modifiable, meaning interventions can be developed to target distress through these mechanisms. Theoretical models can also offer a framework for understanding the experience and conceptualisation of the relationships between physical symptoms and distress, which are two crucial aspects for breast cancer survivors on hormone therapy.

2.2 Understanding and conceptualising distress in cancer

2.2.1 Definition of distress

Distress is hard to conceptualise, operationalise and define, as many studies either fail to conceptualise or define distress, or do so without adequate justification, often basing it solely on an assessment measure (Mitchell, 2013; Wasteson et al., 2009). In addition, in the literature, the terms psychological, psychosocial and emotional distress appear to be used interchangeably. One definition of distress is the emotional reaction to a situation or memory that results in a mood disturbance or state of negative mood or affect (e.g., Vodermaier, Linden, & Siu, 2009). Similarly, in sociology, distress is described as an

emotional state with emotional suffering characterised often by symptoms of anxiety and depression (Mirowsky & Ross, 1986, 2002). Emotional distress in the context of cancer can be formulated as an emotional reaction to a cancer-related event, where that stressor may be the diagnosis itself, the stage of cancer, treatment or experience of physical symptoms (Pearlin, 1989; Pearlin et al., 1981). If the stressor exceeds the perceived coping efficacy of the individual, they will experience distress (Horwitz, 2007; Ridner, 2004).

Emotional distress is also defined by the National Comprehensive Cancer Network (NCCN; National Comprehensive Cancer Network, 2020), as 'a multifactorial unpleasant experience of a psychological (i.e. cognitive, behavioural, emotional), social, spiritual, and/or physical nature, that may interfere with one's ability to cope effectively with cancer, its physical symptoms, and its treatment (p.6).' The NCCN emphasises using the term distress as it is less stigmatising and more acceptable than using the terms anxiety or depression. Throughout the definitions presented, the emotional element of distress is highlighted. Specifically, in some of these definitions, anxiety and depression are emphasised.

Anxiety is characterised by feelings of worry or apprehension regarding future events or activities, whilst depression is characterised by persistent low mood and a loss of interest or enjoyment in everyday activities (American Psychiatric Association, 2013). The collective term for distress including anxiety and depression can be based on a continuum from minor symptoms that may have a small impact on daily life, to more severe symptoms that may impact functioning but not necessarily be classified as a disorder (Wasteson et al., 2009). Vodermaier, Linden and Siu (2009) further adds to the definition that the state of negative affect may be suggestive of an affective disorder, anxiety disorder or adjustment disorder.

The *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5; American Psychiatric Association, 2013) describes an emotional disorder as referring to either an affective disorder which includes major depressive disorder and bipolar disorder or an anxiety disorder, which includes generalised anxiety disorder, obsessive compulsive disorder and post-traumatic stress disorder (PTSD). Each disorder has criteria that need to be met for a diagnosis. This conceptualisation is categorical as a presence or absence of a disorder, rather than on a continuum of distress (Wasteson et al., 2009). This is not aligned with the previous definitions presented which describe distress as an emotional state rather than a presence or absence of distress. The DSM-5 criteria for major depressive disorder includes severe impact to daily functioning, a specific length of time for the symptoms to be present and certain other characteristics such as suicidal ideation (American Psychiatric Association, 2013). These are strict criteria that do not include the general state-like feeling of distress and emotion that does not necessarily severely impact daily functioning. However, these emotional states can still impact an individual and disrupt functioning, without meeting the criteria and are therefore important to consider (Bultz & Johansen, 2011).

Measures such as the distress thermometer (National Comprehensive Cancer Network, 2020), patient health questionnaire for depression (PHQ-9; Kroenke, Spitzer, & Williams, 2001) and the generalised anxiety disorder measure for anxiety (GAD-7; Spitzer et al., 2006) allow distress to be measured as a dimension or continuum. These continuous scales allow individuals to report varying levels of distress, more suited to the definitions presented that describe distress as a state of distress, rather than classifying as an absence or presence of a disorder. For example, if an absence of a disorder was reported, it may mean that a person is not offered support for experiencing below threshold levels of distress. The measures do also indicate cut offs for depressive and anxious symptoms, for example the GAD-7 and

PHQ-9 describe scores over 10 indicating clinical levels of distress and therefore a possible disorder which would need to be diagnosed and potentially treated with psychological intervention (Kroenke, Spitzer, & Williams, 2001). This could create a categorical outcome more in line with the DSM definition. However, as presented, it is not just diagnosed disorders that are problematic for individuals, as clinical and nonclinical levels, particularly those ongoing, can also be disruptive (Bultz & Johansen, 2011). Patients could also be just below the threshold on both anxiety and depression, and therefore overall be quite distressed, despite not reaching a level for diagnosis. Therefore, measuring this on a continuum, not only supports the definition presented that considers distress as an emotional state, but also measures the problematic emotional suffering that may not be as severe or fit strict criteria as in the DSM. Distress measurement will be further discussed in Chapter 6.

Fear of cancer recurrence (FCR) is a different but related construct to distress. FCR is defined as the fear or worry about the cancer returning or progressing (Lebel et al., 2016) and has been described as a form of anxiety (Butow et al., 2015; Humphris et al., 2018). FCR can be seen as anxiety or distress specific to cancer survivorship and therefore, a different concept to generalised emotional distress. Measures of FCR vary but generally include questions specifically around fears or concerns of the potential recurrence or progression of cancer and intrusive thoughts about this (Humphris et al., 2018). FCR is found to be moderately positively associated with distress, anxiety and depression (Butow et al., 2015; Custers et al., 2016) providing some confirmation that while related, they are also different constructs. Cancer related distress is a term also used in the cancer literature but often alludes to the definitions of distress already described. However, some studies separate ‘general distress’ to include anxiety and depression measures, to specific ‘cancer related distress’ by using

measures such as the impact of event scale which asks about experiences of intrusions and avoidance in relation to the stressful cancer experience (Horowitz, Wilner, & Alvarez, 1979). These cancer related measures could be broader than the specific element of FCR as they could relate to the wider cancer experience including terminal diagnoses of cancer or the impact of stressful medical procedures.

As presented in this chapter, distress is conceptualised and defined in different ways, which has led to several distinct but related concepts, grouped under the category of distress. The terms anxiety, depression and fear of cancer recurrence seem to be more clearly defined than the concept of distress. The definition of distress that studies use should determine the measures used, as well as targets of intervention, and therefore it is recommended that it should be described clearly. Throughout this thesis, the term distress is used to indicate a negative emotional state, characterised by symptoms such as anxiety and depression. This will be explored in the context of breast cancer. In line with this definition, measures of distress on a continuum will be used for the observational study in this thesis. However, research data will be presented on any use of the term distress due to the variation in conceptualisation throughout the cancer literature.

2.2.2 Prevalence and impact of distress in cancer

There are multiple systematic reviews that estimate the prevalence of distress in cancer patients at diagnosis, end of primary treatment and into longer term survivorship. In a general cancer sample, one review found a clinical diagnosis of depression had a prevalence rate of 5-16% in outpatients, 4-14% of inpatients and this increased to 49% for those receiving palliative care (Walker et al., 2013). Linden et al. (2012) found in a large sample of over 10,000 cancer patients before treatment, that prevalence of clinical levels of anxiety

was 19% whilst subclinical symptoms was 22.6%. For depression, 12.9% reported clinical symptoms whilst a further 16.5% reported subclinical symptoms. This study found that women and those younger than 50 had either clinical or subclinical anxiety in over 50% of cases.

Distress also persists over time. In a systematic review of long-term cancer survivors (two years after diagnosis) prevalence for a clinical diagnosis of depression was reported as 11.6% and anxiety as 17.9% (Mitchell et al., 2013). The prevalence of anxiety in cancer survivors was significantly higher than healthy controls (Mitchell et al., 2013). In another systematic review of long-term cancer survivors five or more years after diagnosis, prevalence rates for depressive symptoms ranged from 5.4-49% and for anxiety symptoms this ranged from 3.4-43% (Brandenbarg et al., 2019).

In breast cancer specifically, it is estimated between 15 and 36% experience distress after primary treatment has finished, up to 1 year after diagnosis (Burgess et al., 2005; Ploos van Amstel et al., 2013). Ploos van Amstel et al. (2013) report significantly more distress in the first two years than between 2-5 years after surgery. In a systematic review of 42 studies, Syrowatka et al. (2017) report the median prevalence of distress in breast cancer survivors was 26%. Prevalence estimates for breast cancer survivors specifically on hormone therapy can be harder to estimate due to samples consisting of women with breast cancer both prescribed and not prescribed hormone therapy. A study involving 350 long term breast cancer survivors where nearly 42% were on anti-hormonal treatment, and 350 age and GP matched controls, found the odds of experiencing mild symptoms of depression and severe symptoms of anxiety were 2.3 times and 2.1 times higher respectively, for breast cancer survivors vs controls (Maass et al., 2019). These results were present whilst controlling for

depressive history and antidepressant usage. In this particular sample, 10.6% experienced mild depression and 3.7% severe depression (4.9% and 1.1% respectively, for controls), and 18.6% experienced mild symptoms of anxiety and 8% severe anxiety (16.3% and 4% respectively, for controls). The median time since diagnosis was 10 years, suggesting distress may persist for a significant period after primary treatment for some women.

The NCCN proposes that managing distress is just as important as medical care and therefore should be addressed in cancer care (National Comprehensive Cancer Network, 2020). Emotional distress is therefore identified as the sixth vital sign in cancer after pulse, respiration, blood pressure, temperature and pain (NCCN; National Comprehensive Cancer Network, 2020). Although distress may be a normal, understandable reaction to a diagnosis of cancer, prolonged distress may be problematic, resulting in negative personal as well as clinical outcomes.

Distress is associated with multiple domains of quality of life including poor physical functioning and emotional wellbeing (Fang & Schnoll, 2002). Emotional wellbeing is a positive affective state compared to distress being a negative affective state, and therefore has overlap (Stewart et al., 1992). In a large mixed cancer sample, Skarstein et al. (2000) found distress, as measured by anxiety and depression subscales, was associated with poorer quality of life dimensions including physical functioning, social functioning, cognitive functioning, pain, fatigue and overall quality of life. In a cross-sectional study of breast cancer survivors, anxiety and depressive symptoms were correlated with different dimensions of quality of life including social avoidance, appearance concerns, financial problems, family distress and sexual problems (Perez-Tejada et al., 2021).

Distress has been directly associated with poorer immune functioning in cancer (Fang & Schnoll, 2002). Perez-Tejada et al. (2021) found that depressive symptoms were correlated with the pro-inflammatory cytokine TNF-α which moderated the negative effect of distress on quality of life, whereby increased levels of TNF-α strengthened the negative association between depressive symptoms and quality of life. The immune system is vital for cancer detection and to monitor cell changes, and lower immunity may result in infections, impacting daily living and may even contribute to the progression of cancer (Finn, 2012; Reiche, Nunes, & Morimoto, 2004). Receiving chemotherapy may be a confounder when investigating distress and immunity as chemotherapy itself is associated with reduced immune cell counts (Wijayahadi et al., 2007) meaning it may be difficult to isolate the findings. Chemotherapy is a standard part of cancer treatment; however, distress is something that can be reduced, meaning any additive effect or impact of distress on immunity could potentially be mitigated.

Biological processes such as lowered immunity and increased stress may contribute to the poorer outcomes in recurrence and survival found in cancer patients who are distressed (Antoni et al., 2017). However, there may also be an indirect effect through behaviours such as treatment non-adherence. Studies report that anxiety and depression are risk factors for non-adherence to medical treatment (DiMatteo, Lepper, & Croghan, 2000), which in turn can reduce the effectiveness of the medication, leading to poor clinical outcomes. This may be particularly important for women on hormone therapy as this is prescribed for up to 10 years post treatment in order to reduce the risk of recurrence and therefore reduce the risk of mortality (Cuzick et al., 2015; Early Breast Cancer Trialists' Collaborative Group, 2005). It has been estimated that those women with adherence rates less than 80% over a year had

an increased risk of death than those whose adherence rates were over 80% (Winn & Dusetzina, 2016).

Poorer health outcomes will have wider healthcare and economic implications as distress has also been associated with increased healthcare costs such as increased attendance to GPs or hospitals (Deckx et al., 2021). A study in Canada conducted over 12 months with a sample of mixed cancer patients, found people who accessed healthcare services (e.g. counselling, symptom support, nutritionist and advocacy) had significantly higher scores on distress, anxiety and depression with a high percentage above clinical cut off scores (Waller et al., 2013). However, not everyone who had high distress accessed services. Distressed patients who were older, female and had lower education were less likely to access services. This suggests these factors may protect the negative impact of distress or alternatively, these individuals may not be able to or felt able to access services. This study was conducted in Canada so may not be applicable to the UK context and availability of services. Only tertiary (specialist) care referral was recorded meaning attendance to outpatients or nurse and GP appointments were not monitored. There is likely higher resource utilisation for distressed individuals, but these data are not definitive.

As outlined above, distress is an important patient reported outcome with potentially serious implications for the individual and society. Therefore, there is a need to understand the correlates and determinants of distress to develop effective interventions.

2.2.3 Correlates of distress

Due to the significant impact of distress on both physical and mental health outcomes, there is a large body of research exploring the potential determinants of distress in people with breast cancer. The research is largely correlational, however there are longitudinal studies

which allow for the predictors of distress to be explored. Categories of determinants include sociodemographic factors, clinical factors, social, psychological and physical factors.

In terms of sociodemographic factors, younger age is consistently found to be associated with distress in breast cancer (Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017). Costanzo et al. (2007) found in a sample of 89 breast cancer patients with 77% on hormone therapy, that younger age predicted greater distress at 3 months post treatment. In addition, a systematic review of 42 studies in breast cancer survivors (Syrowatka et al., 2017) found that being non-Caucasian, having a lower socio-economic status (SES) and not being married were associated with distress; however only 14-35% of studies reported that these relationships were significant. In terms of clinical characteristics, having advanced cancer (Syrowatka et al., 2017), recently transitioning to survivorship (Syrowatka et al., 2017), having a mastectomy (Lo-Fo-Wong et al., 2016) and having received chemotherapy (Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017) are associated with distress in breast cancer. In addition, having more extensive treatment has been found to be associated with increased anxiety (Costanzo et al., 2007). However, despite studies reporting significant findings, in the review by Syrowatka et al. (2017), they report that a large proportion of studies found non-significant associations for socio-demographic and breast cancer characteristics and treatment. These mixed results limit the confidence that sociodemographic and clinical factors may be important in understanding distress and therefore other factors may be important to investigate.

Research has explored social and psychological factors that are associated with distress in breast cancer. Several studies have found lower levels of social support are associated with distress (Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017). Cancer worry, low social support,

lack of physical fitness and low life satisfaction also predict distress over time (Lo-Fo-Wong et al., 2016). Costanzo et al. (2007) found that trying to get back to normal life was a significant source of distress as well as creating a 'new normal', however these were not validated measures and were identified as potential stressors through interviews. Trying to get back to what life was like pre-cancer may not be easy or realistic for some women, as their diagnosis and treatment may have resulted in new challenges that need to be adapted to. Distress is likely to occur if someone's appraisal of their situation does not match reality, for example trying to control an uncontrollable situation (reality-matching hypothesis; Folkman, 1984; Sharpe & Curran, 2006). Alternatively, if a stressor is appraised as threatening and exceeds the coping beliefs or capacity of an individual (Lazarus & Folkman, 1984). Self-efficacy in coping with cancer has been found to be strongly inversely correlated with distress in a systematic review and meta-analysis (Chirico et al., 2017). However, there were few longitudinal studies, limiting the conclusions that can be drawn about the direction of association between these factors.

In a large sample of 746 women with breast cancer, Lo-Fo-Wong et al. (2016) found the personality trait neuroticism measured at 6 months post-diagnosis, predicted clinical distress at 15 months post-diagnosis. In the multivariate model where they included sociodemographic and clinical factors (e.g. age, living situation, employment status, surgery, radio/chemotherapy), they found that only neuroticism, lack of muscle strength, low satisfaction with life and more frequent cancer worry were significant predictors of distress at 15 months post-diagnosis. Including the psychological factors in the model meant sociodemographic and clinical factors became non-significant predictors, highlighting the fact that these psychological factors may be more important predictors of distress. However, the model only explained 30% of the variance in distress. In a sample of South

African breast cancer patients, Kagee, Roomaney and Knoll (2018) found once social and physical factors were added to a multivariate model (such as perceived social support and stress around body changes), demographic and clinical factors including income, age, education, stage of cancer and time since diagnosis became non-significant predictors of distress. The models accounted for 39% and 30% of the variance in psychological distress and depressive symptoms respectively.

The research demonstrates that once psychological factors are incorporated into a model predicting distress, sociodemographic and clinical factors become non-significant predictors, suggesting psychological factors may be more important in understanding distress in this population. However, these factors still only explain a limited amount of variance in distress outcomes suggesting there are other factors that might contribute to this unexplained variance. Research indicates that some physiological measures such as lower muscle strength and stress around body changes may be important predictors, so exploring the physical experience may be critical.

2.2.3.1 Symptoms and distress

As outlined in Chapter 1, primary treatment for breast cancer can leave women with ongoing physical effects such as pain and lymphoedema from surgery. Additionally, due to the direct physiological impact of adjuvant hormone therapy, women taking this medication report further ongoing side effects and physical symptoms (Moon et al., 2019b; Peddie et al., 2021). Physical symptoms have found to be consistently associated with distress in women survivors of breast cancer. In the systematic review by Syrowatka et al. (2017), approximately 70% of studies that reported menopausal symptoms (hot flushes and night sweats), pain, fatigue and sleep disturbance found significant associations between these

symptoms and distress, although the review did not report the effect sizes. Jim et al. (2007) report that greater physical symptoms/side effects predicted greater levels of distress four months after treatment completion in 151 early-stage breast cancer patients. However, although physical symptoms as measured by the presence and severity of symptoms was a significant independent predictor, this variable only added an additional 5% of the variance in distress after controlling for marital status and diagnosis of a mental disorder. Bleiker et al. (2000) found that almost two years after diagnosis of early-stage breast cancer, 16% of the women reported a high level of psychological distress and the best predictors were health complaints such as headaches and back pain, problems with sleeping and other psychological variables such as intrusive thoughts about the disease and trait-anxiety. This suggests there may be an interplay between distress and physical symptoms, as all physical factors presented were significant predictors of distress.

Although hormone therapy has associated side effects, it is important to allude to the bidirectional nature of symptoms and distress that has been reported in the literature. Moon et al. (2016) found depression was associated with increased odds of more severe hot flushes and night sweats in women prescribed tamoxifen. Across a general cancer sample, Baker, Krok-Schoen and McMillan (2016) found feeling irritable was associated with increased odds of experiencing pain. Distress may impact indirectly on symptoms, whereby depression may lead to poor physical and social lifestyle behaviours such as inactivity and poor diet which in turn may lead to experience of symptoms such as pain (Gold et al., 2020). Although there does appear to be a bidirectional relationship, the first two studies report cross-sectional data, limiting the conclusions that can be drawn. On the other hand, both Jim et al. (2007) and Bleiker et al. (2000) report physical symptoms predict distress in longitudinal data suggesting the direction of relationship. However, these relationships need

to be replicated in longitudinal studies to understand the direction of relationship in this population of cancer survivors.

Studies have reported that the actual impact, rather than just the presence of symptoms, has been associated with distress. Syrowatka et al. (2017) report physical, role, social and cognitive functioning limitations, which could be related to physical side effects or symptoms, were associated with the presence of distress in approximately 50-75% of studies that reported these relationships. The impact of symptoms has been replicated in qualitative research specifically for breast cancer survivors taking hormone therapy. In a systematic review of qualitative studies, Peddie et al. (2021) found that across 16 studies, it was reported that side effects are distressing and impact quality of daily life including socially, with relationships, at work and mentally. This varied impact may then lead to distress due to the disruptions of daily living. In addition, rather than the direct impact of the presence of symptoms, Lo-Fo-Wong et al. (2016) reported that lack of physical fitness and muscle strength, as well as fatigue, were associated with distress. However, in the multivariate model, muscle strength was the only significant physiological predictor of distress 15 months post-diagnosis. Physical fitness and muscle strength may be the result of reduced activity due to symptoms such as pain and fatigue.

Henselmans et al. (2010) found that groups of breast cancer survivors who showed a 'no-distress' trajectory a year after diagnosis, reported the least number of physical complaints due to treatment. The authors report that this group had the strongest personal resources including being high in optimism and mastery and low in neuroticism. These personality and cognitive factors may have moderated the impact of physical symptoms on distress, but interaction effects were not formally tested. This study poses an important question for

understanding the relationship and pathway between symptoms and distress which may guide essential targets for interventions. Studies that explore mediation and moderation analysis may help to understand this relationship. Mediation studies classically aim to give an indication of the causal pathway, identifying the mechanism between an X and Y variable (Maxwell, Cole, & Mitchell, 2011), whereby the X variable (symptoms or symptom burden) will predict the mediator variable which in turn predicts Y (distress). Moderators on the other hand, may modify a causal effect by altering the magnitude or direction of the relationship between X and Y, sometimes referred to as an interaction (Wu & Zumbo, 2008).

Some studies have explored possible moderators and mediators of distress. In a sample of 100 women with breast cancer, Manning-Walsh (2005) found the perception of social support partially mediated the effect of symptom distress on quality of life. However, they describe social support as acting as a 'buffer', reducing the negative effect on quality of life which implies a moderator effect. Liang et al. (2016) found in 201 women who had received chemotherapy for breast cancer that symptom self-management self-efficacy (belief about how much they can manage adverse effects from chemotherapy treatment) mediated the effect of symptom distress on quality of life. Furthermore, in a study of 250 breast cancer survivors at different stages of survivorship (Cheng, Wong, & Koh, 2016), unmet needs were found to partially mediate the effect of symptom burden on quality of life. The authors in this paper attempt to argue that symptom burden would 'cause' or predict a perception of greater unmet need or a response that they have a greater unmet need, and this in turn is related to reduced quality of life. Finally, in a large breast cancer survivor sample of 1127 participants, Cohee et al. (2021) explored mediation specifically on distress outcomes. They found avoidance coping mediated the effect of a specific physical symptom, fatigue, on

depression and anxiety outcomes. This indirect effect explained 19% and 24% respectively of the total effect.

The first two studies (Liang et al., 2016; Manning-Walsh, 2005) conceptualise social support and self-efficacy as mediators, however according to the definition of moderators and mediators presented above, these variables would be better conceptualised as moderators as different levels of them may buffer the negative effect of symptom distress on quality of life. This highlights a limitation in this area where studies fail to conceptualise mediators and moderators correctly or fail to do so *a priori* with a clear rationale for this conceptualisation. Wu and Zumbo (2008) explain that the nature of a third variable (mediator or moderator) should be appropriately operationalised, and variables should not be used interchangeably (i.e., a variable has a null result as a mediator, so it is then tested as a moderator). They go on to explain how a mediator should be conceptualised as a variable that is responsive to another variable, making it a more situational or state-like (*vs* trait) variable. Whilst a more trait-like concept or personal attribute such as gender, which is likely to be more stable would not fit the mediator concept but instead suit a moderator conceptualisation. Even if a variable may fit either definition, it is the author's responsibility to clearly state the conceptualisation, whether based on previous literature or exploratory, whilst also checking the basic assumptions such as the predictor variable not being highly correlated with a moderator (Wu & Zumbo, 2008). Additionally, as mediators and moderators are looking at understanding causal pathways, longitudinal studies should be used as temporality is vital to understand the direction of relationships (Maxwell & Cole, 2007; Wu & Zumbo, 2008). All studies presented above were conducted on cross-sectional data, meaning the core assumption of direction needed for causality is not met.

The current literature on exploring the relationship between symptoms and distress has limitations due to the poor conceptualisation of third variables and cross-sectional data and this needs to be addressed in future research. The specific relationship between symptoms and distress has also not been adequately investigated in breast cancer as the majority of studies report quality of life outcomes rather than distress. Identifying the mediators will help to understand *how* symptoms might lead to distress and therefore highlight a process of change to target in future interventions. In addition, exploring the variation in experiences by conducting moderation analysis on trait or characteristic variables, will give an indication of *who* might be more susceptible to experiencing the negative effects of symptoms. This in turn may also contribute to understanding the key targets of an intervention to support these women as some of these factors may be modifiable. Models of distress in cancer survivorship can provide a theoretical understanding and identification of some of the potential mechanisms that might be involved in the symptom-distress relationship, whilst also considering the potential moderators.

2.3 Models of distress in relation to illness

Traditional medical models conceptualise distress (and mental illness) by the presence or absence of physiology (brain dysfunction) whereby medical treatment would fix the problem and cure a person of the illness (Diefenbach & Leventhal, 1996; Engel, 1977; Moss-Morris, 2013). However, many disorders are present without a physiological cause or dysfunction, and many are due to problems or challenges within someone's daily life (Engel, 1977). The medical or biomedical model therefore is reductionist by explaining mental illness as arising from a physiological problem, and also separates the mind from the body (Engel, 1977). Engel (1977) proposes that biopsychosocial factors are involved with illness

where a person's biological, social, behavioural and psychological dimensions should be taken into account beyond that of the presence of disease. These dimensions interplay in the context of illness and should be considered in treatment. Despite the contributions the model has made in considering the wider patient experience, it fails to define how to implement the model and therefore how to intervene (Álvarez, Pagani, & Meucci, 2012). Early cognitive models took a similar approach to the biopsychosocial model whereby a patient's cognitions, emotions and behaviours were taken into consideration, but addressed some of the previous limitations by providing a framework for intervention by identifying the relationships between these elements (Beck & Dozois, 2014). This model represents one of the earliest cognitive behavioural theories that describes how individuals process information, develop and sustain dysfunctional beliefs, and subsequently how identifying and transforming these beliefs into more adaptive ones can be achieved through cognitive restructuring and behavioural strategies (Beck & Dozois, 2014). This approach is commonly referred to as cognitive behavioural therapy (CBT). A CBT formulation, which is a description and understanding of an individual's problem, will identify the five P's: presenting issues, precipitating, perpetuating, predisposing and protective factors (Dudley & Kuyken, 2006). The five P's are a systemic approach which overlaps with the biopsychosocial model. The biological and environmental predisposing factors, as well as proximal factors precipitating an area of concern or something that is difficult to manage is taken into consideration. The CBT formulation specifically highlights that identifying the perpetuating factors, the cognitions and behaviours that maintain problems, will provide essential information for intervention as these may be the process mechanisms needing to be targeted (Dudley & Kuyken, 2006). The earlier cognitive-behavioural models were largely used to explain various psychological outcomes, whereas other models are more specific to physical illness.

The common sense model of illness representation (Diefenbach & Leventhal, 1996) is a model that considers the biopsychosocial approach, the five P's for formulation and cognitive-behavioural (and emotional) processes in the specific context of physical illness. Models that identify specific factors that should be considered when understanding distress in physical illness can provide specific guidance for treatment in this context (Carroll et al., 2022). Although the common-sense model does not specifically relate to cancer, long term conditions (LTC) and physical illness have overlaps with cancer survivorship such as the potentially limiting physical symptoms, ongoing treatment and attendance to medical appointments and uncertainty around illness progress and the future (Dennison et al., 2011). Specifically, those taking hormone therapy may have limiting physical symptoms, must self-manage taking medication for up to 10 years and may have ongoing fears around cancer recurrence. Although there is overlap in these experiences, the key difference is that survivors are arguably disease free, which is different to those with a chronic physical illness.

2.3.1 The common-sense model of illness representation: overview

The common-sense model of illness representation (CSM; Leventhal, Diefenbach, & Leventhal, 1992; Leventhal, Phillips, & Burns, 2016) identifies illness related beliefs and emotional processes that determine health behaviour in response to physical illness including self-managing that illness. The self-regulatory model is a parallel processing model, whereby both cognitive and emotional representations of illness occur (see Figure 2.1; Diefenbach & Leventhal, 1996). Illness representations or *illness perceptions* are beliefs about illness identity, the causes of illness, the consequences of illness, the duration or timeline of illness and personal or treatment control. Identity refers to the illness or symptom label; the cause of illness refers to the beliefs around what may have caused the

illness e.g., stress or genes; the consequences of illness might refer to anticipated outcomes of the illness; the timeline refers to whether the illness is acute, chronic or cyclical; the controllability aspect includes both personal and treatment control which is whether a person feels they can control their illness themselves and how much they believe their treatment can control their illness. Illness coherence was later added by Moss-Morris et al. (2002) to a measure of CSM illness perceptions to measure someone's understanding of their illness. These beliefs, along with the emotional representations, lead to coping behaviour which is then appraised to evaluate the outcome of coping, demonstrating the self-regulatory nature of the model. As it is a dynamic process model, there is ongoing feedback. The appraisal will deem the coping behaviour as effective or ineffective which will in turn determine whether the behaviour is maintained or changed and may go back to informing or altering the initial illness or emotional representations (Auyeung, Hughes, & Weinman, 2020). The coping element of the model has similarities to the transactional theory of stress and coping which explains how a stressor which is challenging or threatening is appraised by the perceived ability to handle its demands, initiating coping strategies to manage distress (Kvillemo & Bränström, 2014; Lazarus & Folkman, 1984). Coping strategies may consist of problem-focused coping such as planning and seeking informational support, and emotion-focused such as acceptance or denial (Carver, Scheier, & Weintraub, 1989; Lazarus & Folkman, 1984).

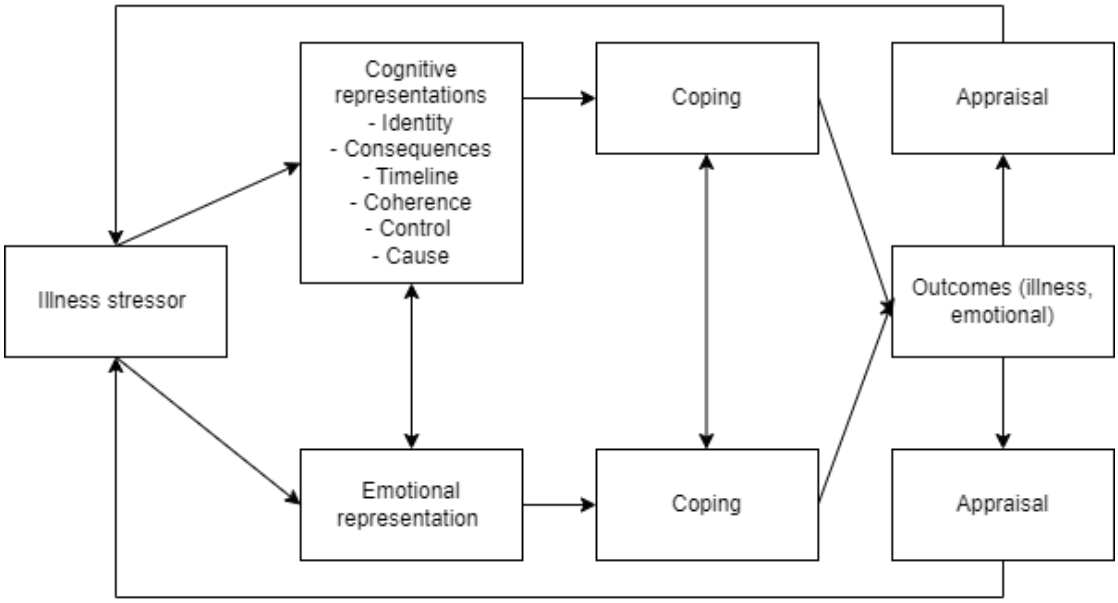
However, the CSM focuses on illness related coping behaviour or procedures rather than strategies (Diefenbach & Leventhal, 1996). The coping behaviour will result in an outcome which would lead to an appraisal to see if the behaviour worked or whether further changes in behaviour are needed (Biggs, Brough, & Drummond, 2017). For example, if cold symptoms are identified as a controllable, acute cold, the coping behaviour may be to get

some over the counter cold and flu medicine (Diefenbach & Leventhal, 1996). However, if these were appraised to not have alleviated the symptoms, the identity of a cold may be changed, leading to a new set of coping behaviour such as going to the doctors. The CSM does not outline the specific coping behaviours as these are in response to and specific to the illness, however they do refer to Lazarus and Folkman (1984) for the distinction between behaviours that may be emotion focused vs problem focused. Due to the extent of different coping behaviours and the limited information in the model, a wide variety of coping strategies have been tested in the literature leading to disparate conclusions to be drawn regarding the coping element of the model.

As applied to cancer, perceptions of the cancer diagnosis or experience will lead to specific coping mechanisms which will impact outcomes including distress (Gibbons, Groarke, & Sweeney, 2016). A specific example conceptualised from the model in the context of breast cancer survivors on hormone therapy could start with physical symptoms as the illness stressor. Someone may perceive more consequences of their breast cancer or treatment, perceive symptoms to be chronic or perceive not being able to control symptoms. In conjunction with these illness perceptions, coping behaviour may be initiated such as reducing or avoiding physical activity. This behaviour may result in distress due to the avoidance of social situations and this behaviour in turn is unlikely to improve symptoms, and therefore reinforce the chronic, uncontrollable nature of the illness beliefs.

Figure 2.1.

The common-sense model of illness representation adapted from (Hagger et al., 2017; Leventhal, Diefenbach, & Leventhal, 1992)



There are a number of related measurements now developed to measure illness perceptions including the illness perceptions questionnaire (IPQ; Weinman et al., 1996) and the illness perception questionnaire-revised (IPQ-R) which added the emotional representations and coherence subscales and separated the control dimension into personal and treatment control (Moss-Morris et al., 2002). The IPQ-R showed good psychometric properties in a variety of illness samples including asthma, diabetes and multiple sclerosis (MS). In addition, a short version of the IPQ-R was developed, with one item per perception also showing good psychometric properties (Broadbent et al., 2006). The IPQ-BCS was developed specifically for breast cancer survivors on hormone therapy (Moon et al., 2017a). The emotional representations of this subscale refer to fears and emotions specifically around cancer recurrence so has a different conceptualisation to the broader definition of distress presented earlier in this chapter. These measures allow illness

perceptions to be adequately investigated in research to understand and provide evidence for the CSM. A disease specific measure enables items to be directly related to the disease specific experiences or treatments, however, responses cannot be compared to those of other long-term conditions, which the more general measures allow.

Several studies have investigated illness perceptions and coping variables in explaining variance in distress in breast cancer patients cross-sectionally. In a sample of breast cancer patients before primary treatment, Gibbons, Groarke and Sweeney (2016) found illness perceptions added a significant proportion of variance for distress outcomes (32%-40%). A significant negative predictor was greater illness coherence, and a significant positive predictor was stronger illness identity. The coping variables (fighting spirit and anxious preoccupation) added 10% of the variance in the models.

In breast cancer females within 2 years of diagnosis Rozema, Völlink and Lechner (2009) found that illness identity, a chronic timeline and negative consequences were significantly correlated with worse perceived mental health as measured by the mental health subscale of the RAND-36 (Hays, Sherbourne, & Mazel, 1993). In addition, treatment control was associated with better perceived mental health and emotional representations were associated with poorer perceived mental health whilst controlling for other CSM variables and demographic and illness related variables. The emotional representations and perceived mental health measures may have some overlap so there could be an issue of confounding in these results although the correlation was moderate. Illness perceptions added significant variance in mental health (R^2_{change} = 35%). Adding coping approaches after illness perceptions were added, did not add significant variance (R^2_{change} = 1%).

These studies have tested the CSM in a linear way using hierarchical regression analysis, stipulating that the illness perceptions come before the coping strategies. However, the CSM is proposed as a self-regulatory model, with continual appraisal and adjustment of illness perceptions and coping based on an individual's lived experience. Therefore, imposing a linear relationship between illness perceptions and coping strategies and outcomes may prevent the full contribution on outcomes to be explored. This is further restricted by using cross-sectional data.

McCorry et al. (2013) conducted a longitudinal study over six months with recently diagnosed breast cancer patients. They split the sample into two clusters, one with more negative cognitions about their cancer on the different illness perception dimensions, the other with more positive cognitions. In regressions, the negative illness representations cluster was a significant predictor of both anxiety and depression at 6 months. Illness perceptions contributed 21-25% of the variance in distress outcomes at baseline (10%-12% at 6 months). Coping (reflection/relaxation, positive focus, diversion, planning) added an additional 10-13% of the variance in distress at diagnosis and 4.4-13% at 6 months over and above the illness cognitions cluster. This study has attempted to address previous limitations by testing the model in longitudinal data and found coping variables predict more variance over and above illness perceptions, however regression analyses still do not allow the self-regulatory/process-based nature of the model to be tested.

Gibbons, Groarke and Sweeney (2016) conducted mediation analysis to determine if the effect of illness perceptions on an unvalidated measure of cancer-related distress was mediated by anxious preoccupation. This coping variable partially mediated the effect of illness coherence, chronic timeline, consequences and identity on cancer-related distress.

Illness perceptions with a negatively valence were therefore associated with more maladaptive coping, which in turn predicted increased distress, providing support for the process based CSM. However, McCorry et al. (2013) additionally reports there was no evidence for coping mediating the relationship presented, but these data were not reported in the paper. This type of analysis represents a better way of testing the process model although inconsistent results are reported, and is still limited in fully understanding the ongoing self-regulatory process.

These studies conducted specifically in breast cancer have small sample sizes (*n* = 90-119) especially in relation to the number of predictors included in the models, suggesting a lack of statistical power. Additionally, cross-sectional findings limit the conclusions that can be drawn from the data. A narrative systematic review of studies of illness perceptions specifically in breast cancer (Kaptein et al., 2015) reported illness perceptions are associated with outcomes such as distress and quality of life. However, the majority of studies were cross-sectional, and the review itself is limited as the data are not reported, and there is no indication of effect sizes or directions of effects. A meta-analysis in cancer (Richardson et al., 2017) found all illness perceptions had significant pooled positive correlations with anxiety, depression and psychological distress. Only identity, consequences and emotional representations had moderate pooled correlations with these outcomes whilst the others had weak associations. The authors also report a majority of correlational research. Hagger et al. (2017) conducted a systematic review and meta-analysis on 250 studies with a range of illnesses including cancer, and found when people had more 'negative' illness perceptions, these were significantly positively correlated with distress. In addition, to provide evidence for the process model, they also report significant small indirect effects of illness perceptions on distress mediated by coping. This review suggests illness perceptions

independently predict outcomes as well as predict outcomes via coping as a mediator (e.g., avoidance, emotion venting, seeking social support and cognitive reappraisal) suggesting the potential utility of the model in understanding outcomes such as distress in physical illness.

The coping variables presented in the different studies have substantial variation and this has been reported throughout the literature before with many coping measures demonstrating poor psychometric properties and predicting a limited proportion of variance in outcomes (Moss-Morris, 2013; Oakland & Ostell, 1996). The CSM proposed illness related coping behaviour in response to illness perceptions as part of the model, however studies have used measures of general coping strategies to represent this section of the model. In addition, whilst associations have been found between coping measures and wellbeing in breast cancer, coping-based interventions are less well supported (Kvillemo & Bränström, 2014). Self-management interventions that incorporate psycho-education and coping skills training in cancer survivors have been found to be limited with null effects on patient reported outcomes and are not always based on a theory (Cuthbert et al., 2019). In addition, coping strategies that try to eliminate or reduce the stressor might not be appropriate in the context of illness where illness related stressors are ongoing (Kvillemo & Bränström, 2014).

Although there is less validation of the broader coping part of the CSM, a benefit of the model is that it identifies illness perceptions as potentially modifiable factors to target in interventions. Interventions show that illness perceptions themselves are amenable to change and have effects on outcomes (Auyeung, Hughes, & Weinman, 2020). Fischer et al. (2013) report a longitudinal investigation of 57 breast cancer patients who took part in a psycho-educational group intervention. Distress decreased over time and changes in illness

perceptions were associated with decreases in follow up distress. There have been further illness perception related interventions in other conditions including diabetes and cardiovascular disease although studies focus more on behavioural outcomes such as adherence (Jones, Smith, & Llewellyn, 2016). These interventions do report changing illness perceptions (rather than focusing on coping) so suggest the perceptions themselves are a mechanism of action for intervention which is proposed by the dynamic, process-based model. The self-regulatory nature of the model implies that illness perceptions are themselves influenced by the appraisal process, suggesting an ongoing relationship.

The data presented highlight the potential utility of the CSM in understanding distress in physical illness and breast cancer specifically. However, the limitations of these data have been highlighted including studies consisting of small sample sizes and multiple cross-sectional papers. There is also unexplained variance in distress outcomes in breast cancer studies and this is demonstrated in other cancer populations as well (e.g., Dempster et al., 2011). There is some difficulty in understanding the key significant illness perceptions in relation to distress and cancer as studies report varied results. Studies employ different ways of measuring coping, resulting in varied estimates and difficulties evaluating the behaviours or strategies. Additionally, there is limited understanding of the emotional processing arm of the model which is often only measured by the emotional representations subscale of the IPQ measures and is an often-ignored part of the model (Karekla, Karademas, & Gloster, 2019). Finally, there are few interventions based on this approach within the context of cancer. This could be due to the descriptive, explanatory nature of the model as it explains how illness perceptions may lead to coping and outcomes. However, as it is not a treatment intervention model, it does not show how to change illness perceptions and therefore which dimensions might be more important to target for more

favourable outcomes. Therefore, the mechanisms of change for interventions need to be inferred from the model. The CSM provides more physical illness related information about potential beliefs about illness and their relationship to outcomes, which builds on the general cognitive-behavioural model presented at the beginning of the chapter.

Third-wave cognitive-behavioural models are an extension of the traditional cognitive-behavioural models and extremely prevalent in cancer interventions. Third wave approaches such as acceptance and commitment therapy (ACT) highlight mechanisms of change, in the form of flexible and inflexible processes, to improve psychological wellbeing (Hayes et al., 2006). These flexible and inflexible processes may be variables that explain distress and therefore provide an indication of the unexplained variance reported. The ACT model concentrates on expanding an individual's psychological resources and skills to enhance their coping responses to challenging stressors, rather than focusing on the content or form of cognitions (Hulbert-Williams, Storey, & Wilson, 2015). Due to the mechanisms proposed by the model, these approaches can directly guide intervention development and help guide research to identify additional important predictors of distress.

2.3.2 Acceptance and commitment therapy: overview

Third wave approaches focus on the context and functions of thoughts or emotions, rather than the form, and therefore the treatments tend to include more flexible, contextual and experiential strategies (Hayes, 2004). The third wave approaches include acceptance and commitment therapy (ACT; Hayes et al., 2006), mindfulness based cognitive therapy (MBCT; Teasdale et al., 2000) and dialectical behaviour therapy (DBT; Linehan, 1993). Third wave approaches in cancer have increased in recent years particularly for ACT, as systematic reviews report increasing numbers of trials in various LTCs and cancer populations (e.g.,

Graham et al., 2016). Although some effects are small, there is an indication that these interventions could be effective for patient reported outcomes but need to be better understood in the context of cancer. This includes understanding the processes in relation to distress, as currently, unlike for the CSM illness perceptions, there are no systematic reviews of all the processes identified in the model.

ACT is based on relational frame theory (RFT), which posits that cognition and language is based on the ability to relate to events in a context (Hayes, 2004). ACT aims to increase psychological flexibility, which promotes the willingness to experience thoughts, emotions and sensations, whilst participating in meaningful, value consistent behaviours or actions (Feros et al., 2011; Graham et al., 2016; Hayes et al., 2006). The concept of psychological flexibility encompasses six core processes or psychological skills. The aim to develop psychological flexibility is so that difficult internal experiences interfere less with meaningful activities (Mosher et al., 2021).

The six core flexible processes are known as the ACT hexaflex, labelled as mindfulness and acceptance processes and commitment and behaviour change processes (Hayes et al., 2006; see Figure 2.2). In addition, the hexaflex can be broken down into the triflex of open, aware and engaged as also seen in Figure 2.2. The processes of psychological flexibility have corresponding inflexible processes. Psychological inflexibility, as it is collectively known, contributes to psychopathology and suffering (Hayes et al., 2013; Hayes et al., 2006). *Acceptance* is the awareness of and willingness to experience thoughts, feelings and sensations, without attempting to change them (particularly their frequency or form). Whilst *experiential avoidance* refers to the attempts to alter or avoid difficult thoughts, feelings or sensations. *Cognitive defusion* on the other hand refers to changing the

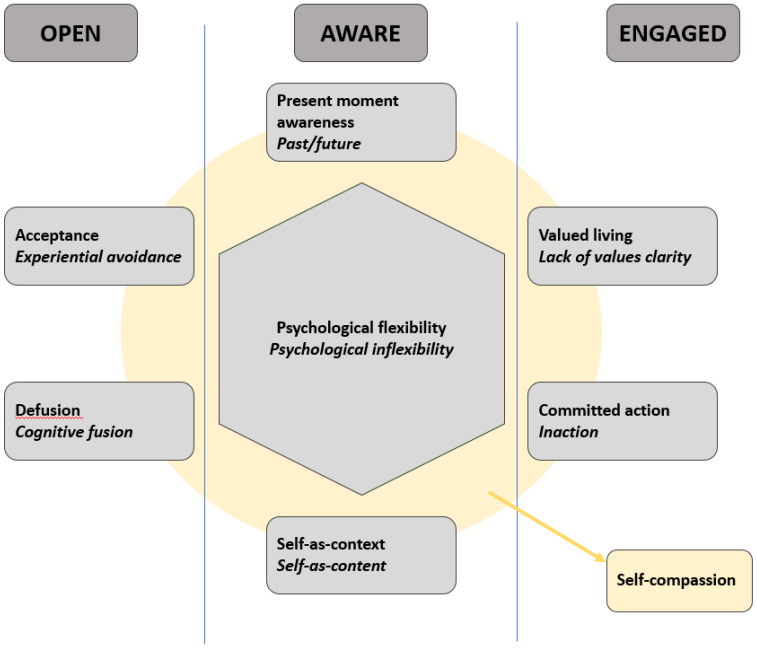
relationship with thoughts and memories, in order to change their function (rather than the form or frequency). This aims to reduce their literal quality and help recognise thoughts as thoughts rather than as the content the thought refers to. Whilst *cognitive fusion* refers to understanding thoughts as truth, fact or as a direct reflection of reality. Seeing thoughts this way can dominate awareness and therefore influence subsequent behaviour. *Present moment awareness* refers to the ongoing non-judgemental contact with the internal (psychological) and external (environmental) world. The individual can connect and engage with whatever is happening in their present world directly. Again, present moment awareness is an ongoing process or skill, whilst the term dispositional mindfulness is often used to describe the trait version of this. *Loss of contact with the present moment* indicates where someone cannot connect with the present moment and therefore may be stuck in their mind, rather than engaging with the world.

Self-as-context is having an awareness of one's experiences without attachment. It refers to an element of perspective taking whereby one has a recognition of the self as the context from which we can observe our thoughts, emotions and memories. *Self-as-content* on the other hand refers to being attached to our internal experience as well as stuck with the stories we have about ourselves. *Values* are qualities of action based on what is important and what matters to an individual. A *remoteness from values* refers to a lack of awareness or clarity of one's values. *Committed action* refers to effective action that is driven by values. Goals must be values-consistent and workable. *Inaction* however refers to unworkable action, not driven by values. The concept of workable and unworkable action suggests if a behaviour is working and moving someone towards a valued direction, this should be built on (Dindo, Van Liew, & Arch, 2017).

Self-compassion is a concept closely interwoven throughout the ACT model and in practice (Neff & Tirch, 2013). Self-compassion is the process of being open, aware, kind and understanding towards oneself in difficult situations or when suffering (Neff, 2003). This includes a non-judgemental view to one's difficulties and as part of a wider human experience (Neff, 2003). Therefore, the three core components to self-compassion are self-kindness, common humanity and mindfulness (Neff, 2003). The lack of formal inclusion in the model, despite it being assumed throughout, makes it difficult to test and understand this process in the context of ACT.

Figure 2.2.

The psychological flexibility model, with inflexible processes in italics, incorporating self-compassion. Adapted from the Hexaflex by (Hayes et al., 2006)



ACT focuses on changing the responses to thoughts and emotions rather than changing the content of thoughts with the view to altering emotions as some research suggests that focusing on trying to change thoughts has been found to increase distress (Harris, 2019;

Hayes et al., 2006; Ruiz, 2010). Additionally, it may not be appropriate to change or alter some thoughts particularly those that may be realistic, such as that symptoms might last a long time throughout treatment. ACT proposes that distress and suffering are all part of a normal universal human experience, so rather than trying to change these stressors, the model proposes the importance of addressing how one responds to these experiences. ACT is a particularly adaptive model as it proposes these processes are universal and therefore transdiagnostic (Dindo, Van Liew, & Arch, 2017). The psychological flexibility components exist across specific contexts, i.e., for people with cancer or other physical health conditions.

The ACT approach may be particularly useful in the context of cancer, due to the rational and realistic responses someone may have to a cancer diagnosis. Individuals with a cancer diagnosis may have valid thoughts around recurrence and it therefore may not be appropriate to try and challenge or change that realistic thought. However according to the model, avoiding or fusing with this thought may lead to distress; whilst acknowledging, experiencing and being present with these thoughts, is less likely to lead to distress. Therefore, changing the response to the thought, rather than the content of the thought, may be beneficial. Additionally, avoiding physical symptoms may exacerbate them, or result in negative psychological outcomes through avoiding medical attention or avoiding meaningful activity in order to manage the symptom (Mosher et al., 2021). In relation to the symptom-distress relationship, the ACT model proposes that fusion of symptom-related thoughts, or not being present with the symptoms and/or trying to avoid them, could result in distress. ACT encourages a focus on valued living, to engage in and pursue activity that is meaningful to the person and values driven, in the presence of difficulties. A cancer diagnosis may interfere with this focus when there is disruption to daily living caused by

treatment, medical appointments and recovery time (González-Fernández & Fernández-Rodríguez, 2019).

Aiming to reduce physical symptoms, distress or suffering is not the main aim of ACT as this could lead to increases in these outcomes through focusing attention on symptoms. Rather, ACT aims to increase psychologically flexible skills to engage in a meaningful, valued life. Often, reductions in distress or symptoms are secondary outcomes. The ACT model proposes inflexible processes that may result in psychopathology and suffering so the model can be applied to distress to understand the processes that may be involved in this emotional state of suffering. A benefit of the ACT model is that it identifies the modifiable processes to be targeted in interventions, aiming to increase flexible skills and decrease inflexible responses.

Hayes et al. (2006) suggests looking at a variety of study types including component observational studies and intervention mediation studies to help identify the strength of ACT processes for patient outcomes which forms part of an 'inductive, technique-building' approach (p. 14). This helps to develop evidence-based, theory-matched and driven treatments (Hayes et al., 2006). For example, experiential avoidance has been found to predict distress over time. In a sample of 40 breast cancer patients receiving radiotherapy, when controlling for baseline depression and follow up experiential avoidance, baseline experiential avoidance significantly predicted depressive symptoms at 6 months and added an additional 6% explained variance (R2 = 57%; Trindade et al., 2020). Greater mindfulness (a measure used for present moment awareness) has been found to be moderately associated with wellbeing and lower distress in breast cancer (Liu et al., 2021a; Liu et al., 2018). Mindfulness has also been found to account for 27% of the variance in mood

(controlling for age, repression and suppression) in women with breast cancer and 35% of variance in stress-symptoms (Tamagawa et al., 2013).

A limitation to this area of research in the context of cancer compared to the evidence base for the CSM and illness perceptions is a lack of comprehensive systematic reviews and meta-analyses on the processes in the ACT model. However, at the current time of writing, there are two reviews that focus on specific processes, one on acceptance and one for self-compassion. In meta-analyses, Secinti et al. (2019) found small to moderate pooled effects for acceptance and distress outcomes (r = -0.31 to -0.22). The definition of acceptance the authors used was a broad integrated definition encapsulating coping theory and the ACT process-based definition, however they included a variety of measures that do not all necessarily meet this definition. In addition, Hughes et al. (2021) conducted a narrative systematic review of studies on self-compassion and distress in LTCs where half the studies were in cancer. This review reported moderate to large correlations for self-compassion with anxiety and depression (r = -0.37 to -0.66). Many studies were correlational in nature, a limit to the overall field; and grey literature was not searched which is a limitation of this particular review.

Despite limits to the evidence base for ACT process-based observational studies, ACT is frequently used in clinical practice and there are a number of reviews of ACT interventions specifically in cancer. In the most recent systematic review upon writing, Salari et al. (2023) found a total of 15 studies of ACT interventions for distress (anxiety and depression) in cancer. The review narratively reports that in all studies, ACT reduced anxiety and depression, however not all studies reported significant findings and there were a range of small to large effect sizes. In a review specifically of breast cancer samples (mixed stages; Li

et al., 2021), a meta-analysis of 13 RCTs was completed for anxiety, depression and stress outcomes and pooled effect sizes favoured the intervention with moderate to large effect sizes. However, there were some limitations to the findings which limits the interpretation and generalisability of these findings as there were only four studies for anxiety and only two for stress, and studies were only conducted in two countries: Iran and USA. RCTs were also poorly described meaning there was insufficient detail for a thorough risk of bias assessment. In a meta-analysis of 23 studies in all cancer types and various stages (Zhao et al., 2021), ACT significantly reduced psychological distress, anxiety and depression with large effect sizes. The review conducted trial sequential analysis to determine that more studies would not be needed to establish ACT's effectiveness on reducing psychological distress. However, eight studies were not RCTs, and a quarter of studies were low quality. Despite this, trial type (non-RCT vs RCT) was not a significant moderator, and neither was study quality indicating the effects did not vary based on these factors. The heterogeneity in included studies and the proportion of low-quality studies does limit the confidence in conclusions drawn from this review. In a systematic review of 13 ACT trials specifically for cancer survivors, Mathew et al. (2020) found only small positive effects for anxiety, depression, fear of recurrence, and improved psychological flexibility and QoL. Despite a similar percentage of higher quality interventions included, the effects are smaller for survivors than in the review that incorporated all cancer types and all stages. These findings could be attributed to the methodological differences between the reviews. For example, Mathew et al. (2020) included fewer studies and multiple different outcomes and did not combine outcome measures for meta-analysis.

In summary, there are consistent issues emerging with these trial results as there are small sample sizes, poor methodological quality and issues with design meaning results need to

be interpreted with caution (Fashler et al., 2018; González-Fernández & Fernández-Rodríguez, 2019; Hulbert-Williams, Storey, & Wilson, 2015; Salari et al., 2023). Despite these limitations, there is an indication that ACT interventions may have some effects in reducing distress in cancer. However, RCTs have not conducted mediation analysis to establish how the ACT intervention results in change in outcomes by identifying the effective processes. Alongside this, the observational research is also limited with many cross-sectional studies and currently no comprehensive systematic review has been conducted for the ACT processes and distress in cancer. In contrast, the CSM illness perception literature has few interventions or RCTs designed specifically around the CSM to provide an indication of effects of interventions on distress. This is unsurprising due to the CSM being an explanatory model rather than a treatment model. It does however have a stronger evidence base in terms of multiple systematic reviews indicating associations between illness representations and cancer distress although this is limited by a prevalence of cross-sectional studies. Both the CSM and ACT model only report a limited amount of the variance in distress. However, there may be specific processes within each model that are particularly useful and relevant in understanding distress in breast cancer survivors and when combined may explain a greater proportion of variance in an outcome. Integrated theoretical models incorporate the pertinent processes or factors from across theories and the evidence base that may have important associations with outcomes in different contexts. Therefore, these integrated models may provide a more comprehensive understanding of particular outcomes and provide a foundation for testing proposed relationships.

2.4 Integration of models

The transdiagnostic model of adjustment to long term conditions (TMA-LTC; Carroll et al., 2022) is a model that brings elements of both the CSM and ACT models together to provide a conceptual understanding of the factors involved in adjustment to illness. Both CSM illness perceptions and ACT processes appear in this model as well as other cognitive-behavioural processes.

2.4.1 TMA-LTCs: overview

The TMA-LTC (see Figure 2.3) draws on the CSM which proposes, as mentioned, that a physical illness or ongoing physical health stressor disrupts an individual's emotional equilibrium. Returning to a state of equilibrium requires developing accurate or more adaptive cognitive, behavioural and emotional responses to illness. In addition, the model considers the environmental and illness specific context that may impact the ability to return to equilibrium and achieve good psychological adjustment. The TMA-LTC differs to the CSM in that it proposes an outcome, whereby these factors precipitate and perpetuate illness related distress which would result in poor psychological adjustment. Good psychological adjustment is represented as a state of equilibrium being reached. The precipitating factors included in the model may include the acute events (such as diagnosis and initial treatment) as well as ongoing illness stressors (such as experience of side effects).

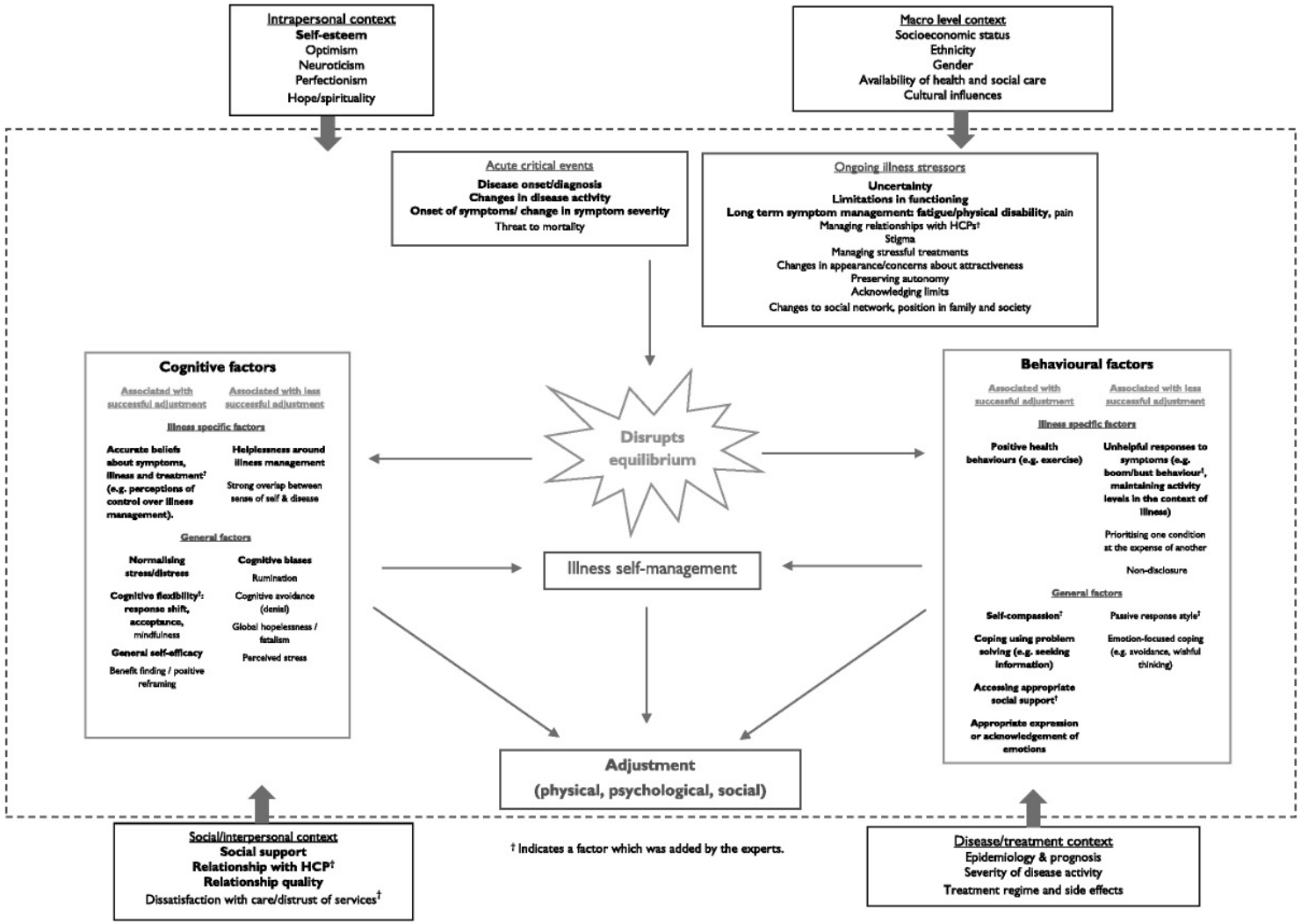
Similarly to ACT, the TMA-LTC highlights that distress is an expected and typical response to illness, however if distress is prolonged and/or excessive, this can negatively impact the adjustment to a physical illness (Moss-Morris, 2013). The factors included in the model are drawn from the empirical evidence. The ACT processes as depicted by the model have not all been added to the TMA-LTC, which is likely due to the lack of observational evidence for

ACT. However, theorised processes such as cognitive flexibility, acceptance, mindfulness, cognitive avoidance and self-compassion are included. The illness perceptions are also not fully outlined in the model and the emotional processing element is limited and more related to the stressors and outcomes. The TMA-LTC also proposes several other cognitive and behavioural processes that may help or hinder the adjustment to an LTC which have also been drawn from the evidence base.

A benefit of the TMA-LTC as a model of distress and adjustment is the focus on physical illness as it outlines multiple areas that may be involved in the adjustment to the illness itself. The model outlines specific illness stressors, such as symptoms, and how factors may then help or hinder adjustment and distress. Therefore, the model proposes the symptom-distress pathway, with potentially testable mediators and moderators. Although the TMA-LTC does not draw directly from the cancer literature, it is a transdiagnostic model just as the CSM and ACT model are.

Figure 2.3.

The transdiagnostic model of adjustment to long term conditions (TMA-LTC; Carroll et al., 2022), used with permission



The cognitive-behavioural responses to symptoms questionnaire (CBRQ) is a measure that has been developed for the specific responses to and interpretations of symptoms (Picariello et al., 2023). This questionnaire particularly contributes to being able to measure the more behavioural responses outlined in the TMA-LTC. Whilst measures such as the IPQ-R or IPQ-BCS focus more on the illness perceptions part of the CSM, the CBRQ proposes that the day-to-day specific symptom responses may be useful to consider and may determine coping behaviours (Picariello et al., 2023). This may be particularly useful for the context of breast cancer survivors on hormone therapy due to the ongoing experience of side effects and requirement to manage long term treatment.

The TMA-LTC starts to address the limitations of singular models such as the CSM or ACT model which do not adequately explain distress, by incorporating factors from several models. This has the benefit of drawing attention to all of the factors that could be useful. However, as the TMA-LTC is transdiagnostic, there may be less utility for specific groups such as those with cancer. There are two examples of integrated models specifically in cancer, one for anxiety and one for fear of cancer recurrence (Curran, Sharpe, & Butow, 2017; Fardell et al., 2016). These models aimed to integrate several theoretical approaches to explain these outcomes in cancer, in order to inform interventions and address some of the current literatures' limitations. Although the anxiety and fear of recurrence models have since been pilot tested and used for interventions and found to be effective, the models themselves were based on a review of relevant theories, rather than empirical evidence (Curran, Sharpe, & Butow, 2021; Sharpe et al., 2019). However, none of the integrated models presented focus on general distress. An integrated model for distress which is based on empirical evidence as well as theory will provide a framework for intervention development.

Although the integration of theory into models represents a significant step forward in understanding anxiety and fear of recurrence in cancer and adjustment to physical illness, the models are designed to be applicable across a range of cancers and stages and LTCs respectively. The utility to understand distress and the specific experiences of breast cancer survivors on hormone therapy is therefore limited. There are potential benefits of integrating evidence-based processes from different theoretical approaches in order to understand an outcome more thoroughly. This may have positive impacts on intervention development and is therefore a promising rationale for integrating theoretical models in understanding distress for this population.

2.5 Summary

Distress is a prevalent and significant patient reported outcome in breast cancer. Theoretical models of distress in the context of physical illness offer a framework for understanding predictors of distress and, consequently, potential intervention targets. Whilst neither the CSM nor the ACT model provides a comprehensive explanation of distress in physical illness, both models identify factors that could be of importance. However, there is currently no systematic review for all ACT processes and distress in cancer, and a shortage of longitudinal studies for both models. The TMA-LTC and other integrated models aim to bring together cognitive-behavioural factors across theoretical models to understand adjustment, including distress, in physical illness and cancer. Combining important processes from the different models (CSM and ACT) into an integrated model, may help to explain distress in breast cancer more thoroughly. Although cancer survivorship has overlap with the experiences someone may have with an LTC, there are some differences, so the proposed factors need to be evidenced in breast cancer survivors to fully understand the relationships. The TMA-

LTC does provide an example of an integrated theoretical framework for understanding the psychological processes from the CSM and ACT models that could be significant in the relationship between symptoms and distress. This framework can lead to the formulation of hypotheses that require testing in the context of breast cancer survivors.

Chapter 3 Thesis rationale and overview

3.1 Chapter overview

Studies based on theoretical models of distress in physical illness have presented potential correlates and predictors of distress that could be useful in the context of breast cancer survivors on hormone therapy. However, data specifically in this population is limited. In addition, studies exploring potential correlates are often conducted on small, cross-sectional samples. Furthermore, physical symptoms have been proposed throughout the thesis as not only an important experience for breast cancer survivors on hormone therapy but as a possible predictor of distress. There is a dearth of research on the relationship between symptoms and distress in breast cancer survivors on hormone therapy and studies are limited to cross-sectional findings and poor conceptualisation of third variables that may be involved in the relationship. Models such as the CSM, ACT and TMA-LTC provide an appropriate framework for testing hypotheses, as they indicate the processes, or potential third variables, that may be involved in pathways such as the symptom-distress relationship.

To investigate these relationships, studies need to be conducted in the specific context of breast cancer survivors on hormone therapy. As discussed in Chapter 1, adherence is an often-explored outcome in this population due to ongoing prescribed adjuvant hormone therapy medication. Therefore, many qualitative studies have focused on understanding how symptoms impact medication-taking behaviour and fail to interrogate the symptom-distress relationship. Given the heterogeneity of emotional, psychological and behavioural responses to symptom burden, understanding the relationship between symptoms and distress in targeted qualitative research may provide new avenues for investigation or confirm theorised ones as presented throughout the chapters. Quantitative research using

longitudinal observational methods will address some of the limitations presented such as indicating direction of effects and incorporating temporality when testing third variables in a potential causal pathway.

Identifying evidence-based processes from proposed theoretical models, will provide potential targets for intervention. Hormone receptor positive breast cancer accounts for a significant proportion of breast cancer survivors (75%) implying there are potential benefits for a large proportion of female breast cancer patients. Treating and improving distress may in turn result in improvements in other outcomes such as quality of life, recurrence and mortality and personal and healthcare costs.

In order to gather information regarding the symptom-distress relationship in this population and identify variables that may inform interventions, a multi-methods approach was used.

3.2 Rationale for a multi-methods approach

A multi-methods approach refers to the use of both qualitative and quantitative research (Schutz, Chambless, & DeCuir, 2003). This combined approach can be utilised rather than that of qualitative or quantitative research conducted in isolation as both approaches can provide different and synergistic benefits (Johnson & Onwuegbuzie, 2004). This approach allows a researcher to *identify and understand,* as more common in qualitative research, but also *test and examine relationships,* as more common in quantitative research (Dures et al., 2011). The combination of these approaches can provide a more comprehensive understanding of constructs from different perspectives, contextualise information and provide a deeper understanding of a problem (Creswell et al., 2011). Given the real-world application of health psychology research covering concerns and health experiences, Dures

et al. (2011) suggests there is an apparent benefit of the flexibility of using multiple methods.

However, there are inconsistencies in the definitions of a mixed- vs multi-method approach and the terms are often used interchangeably (Anguera et al., 2018). Both approaches propose combining qualitative and quantitative data to answer a research question or problem. However, *how* the methods are used and analysed have differences. A mixed-methods approach depicts both qualitative and quantitative methodology within a single study, whilst a multi-methods approach uses both approaches in separate but linked studies in order to address a wider research problem and is the approach used in this thesis. The methods used in this thesis answer separate research questions within their respective studies, whilst the results from each will be integrated in the discussion in relation to the wider research question of the thesis.

Quantitative research aims to examine variables that may vary in quantity, for example, over time, in size or in magnitude (Gravetter & Forzano, 2009). The results of these data are typically collected in or transformed into numerical form, enabling the application of statistical methods for analysis and interpretation (Gravetter & Forzano, 2009). A fundamental assumption behind quantitative approaches is that of nomothetic science, which involves explaining concepts that are generalisable and universally applicable (Gelo, Braakmann, & Benetka, 2008). Quantitative approaches are formed on positivism and objectivity (verification and replication of observable findings) and due to this are perceived as a more reliable and valid approach (Park, Konge, & Artino Jr, 2020). Hypotheses can be tested empirically in large samples, producing data that may be generalisable to a wider population depending on the recruitment method. Collecting a vast amount of data from

short questionnaires can be significantly less resource intensive than interviewing people but therefore may be less detailed. Predictions can also be made, and causal pathways tested (Gelo, Braakmann, & Benetka, 2008). However this approach may not fully reflect participants perspectives, as measures may be limited in the construct they aim to capture and therefore important information may be missed (Gelo, Braakmann, & Benetka, 2008; Johnson & Onwuegbuzie, 2004). In addition, there may be limitations to specific quantitative methods such as participant attrition in longitudinal studies, potentially leading to issues with generalisability and statistical power (Gustavson et al., 2012).

A qualitative approach, one that uses observation and a narrative approach to analyse and interpret, has its strengths in understanding participants' experiences in depth (Gravetter & Forzano, 2009). The main assumption here is that of ideographic science, which involves intensive focus on individual cases and where reality is socially and psychologically constructed (Gelo, Braakmann, & Benetka, 2008). A more complex description and contextualisation with rich detail can be achieved, as opposed to being constrained by items in a scale, as in quantitative research. Qualitative research can be conducted in an inductive approach to allow for data-driven exploration, or from a deductive, theory driven perspective. Qualitative methods can include semi-structured interviews which have the benefit of being flexible in order to explore and ask relevant probing questions (Adeoye-Olatunde & Olenik, 2021). This approach may also highlight previously unconsidered areas, leading to the identification of new research directions and generating hypotheses (Gelo, Braakmann, & Benetka, 2008). However, in-depth qualitative methods are limited in sample size, to a specific group, are time consuming and resource intensive. This implies the data might not be generalisable; however, this is not the aim of qualitative research (Gelo,

Braakmann, & Benetka, 2008). In addition, quantitative predictions cannot be tested (Johnson & Onwuegbuzie, 2004).

Historically, these approaches have been identified as being incompatible due to technical restrictions and also to the assumptions that underlie each method (Morgan, 1998) with purists suggesting research should use one approach or the other (Johnson & Onwuegbuzie, 2004). A pragmatic approach, which does not fall under one assumption, asserts that both quantitative and qualitative data can be effectively utilised to allow for a thorough understanding of the research problem and best address the requirements and objectives of the research (Dures et al., 2011; Johnson & Onwuegbuzie, 2004). Johnson and Onwuegbuzie (2004) also suggest that an interdisciplinary approach can utilise the strengths of both approaches and address some of the limitations for each, in a complimentary way. For example, a small qualitative study may uncover detail about individual variables in a relationship, which can lead to quantitative hypotheses investigating these variables in a larger, generalisable sample. Patient insights might be missed in quantitative research so including a qualitative element may help to address this limitation. For example, in qualitative research, a key variable can be investigated beyond that of items on a measure, and a flexible interview can allow for probing around the topic. This can ensure suitable measures are being used in quantitative methods, or if additional constructs need to be measured.

Additionally, qualitative research may help to generate hypotheses, choose measurement instruments and ensure contexts are considered. Combining these methods can assist in ensuring that research is not only generalisable to different contexts but also that it has a meaningful impact on patients by providing a more comprehensive knowledge base to

inform practice (Johnson & Onwuegbuzie, 2004). Both methods can bring different elements of validity. Quantitative methods provide external validity through generalisability and internal validity through construct and causal validity (Gelo, Braakmann, & Benetka, 2008). Whilst qualitative methods provide internal validity in forms of description, interpretation and transferability as a form of generalisability (Gelo, Braakmann, & Benetka, 2008).

Despite the potential utility of a mixed- or multi-methods approach, there are some practical challenges which need to be considered. Firstly, there may be a need to learn multiple methods and require larger budgets for training and conducting more expensive and time-consuming methods (Park, Konge, & Artino Jr, 2020). However, these barriers are uncommon in health psychology as researchers are often trained in multiple methods in interdisciplinary teams at early stages of their careers, especially in order to comply with standards of training (The British Psychological Society, 2015) and there are opportunities for funding to support research. In addition, multi-methods approaches need to have a clear aim and rationale (Creswell et al., 2011). This is particularly important to ensure that the methodology aligns with the aims and does not contradict them, taking into account the potential integration of findings. A broader aim may be needed in order to allow for the various methods; whilst on the other hand, having a more targeted research question that could be answered with either qualitative or quantitative methods, could be more focused and easier to interpret.

Triangulation of methods means findings from both approaches can be corroborated to address research questions and to inform further studies. A sequential mixed-methods design suits an exploratory project and can help methods complement one another

whereby results from a qualitative study can inform a quantitative study and then be interpreted (Creswell et al., 2011). Johnson and Onwuegbuzie (2004) describes this as a mixed-model design as it is across stages of a research process. A sequential design was followed throughout this thesis, whereby findings could be used to inform subsequent studies. For example, both meta-analysis and qualitative findings could identify pertinent variables within a context and generate hypotheses for quantitative observational research to test and investigate in a larger sample, in order to improve understanding of symptoms and distress in breast cancer survivors.

3.3 Methods and thesis overview

The overarching aim of the thesis was to explore psychosocial factors that explain distress in breast cancer survivors on hormone therapy and specifically identify the psychological factors that explain the relationship between symptoms and distress. Chapter 1 provided a context for breast cancer survivors experiences, whilst Chapter 2 identified limitations with existing literature and models in explaining distress in physical illness. Both the CSM and ACT models have only demonstrated a proportion of the variance in distress in breast cancer and the majority of previous studies are cross-sectional. In addition, there is no comprehensive review of ACT processes in the cancer literature on distress, limiting the understanding of this model in this context. Finally, although some studies have investigated the relationship between symptoms and quality of life in breast cancer, there is little evidence for the relationship between symptoms and distress in this population. This represents a noteworthy limitation in the current evidence base as symptoms are a significant part of the experience for breast cancer survivors on hormone therapy as demonstrated so far in this thesis. Before large scale time and resource intensive

interventions and randomised controlled trials (RCTs) are conducted, it is imperative that observational research is conducted to gather evidence and provide a detailed understanding of potential targets of interventions. This includes testing the theories that underlie interventions.

A pragmatic assumption underpins this thesis where use of multiple methods was deemed the most appropriate to address the research aims. Quantitative methods were selected to evaluate the evidence base for ACT processes and distress in cancer, systematically and comprehensively, whilst providing estimates of the effects. Qualitative methods were used to enhance the understanding of the symptom-distress relationship and inform generation of hypotheses to be tested in a quantitative study. Additionally, longitudinal quantitative methods were also utilised to test the psychological processes (from both the CSM and ACT models) in a large, generalisable sample as well as identifying the variables in the symptom-distress causal pathway. Together, this multi-methods approach provides context and patient insight and allows for testable hypotheses to be generated and examined. This approach allows the use of methods that best align with individual objectives in order to contribute to a wider programme of research.

Therefore, to achieve the broader aim of this PhD to understand the distress and the symptom-distress relationship in hormone receptor positive breast cancer, and to address some of the gaps in the literature, the following specific objectives were answered:

Objective A: To systematically review the literature on the associations between ACT processes and distress in cancer (Chapter 4), which will provide preliminary data to inform PhD objective C.

Objective B: To use qualitative methods to explore the emotional impact of being on hormone therapy from the perspective of breast cancer survivors, specifically exploring why symptoms/side effects may be distressing (Chapter 5, informing objective C).

Objective C: To carry out a longitudinal observational study to identify psychosocial variables including those specifically from the CSM and ACT model that predict distress, compare variables from the different models in their ability to predict distress (Chapter 6) and finally, to explore the psychological variables that explain the relationship between symptoms and distress by using mediation and moderation analysis (Chapter 7).

Each study is analysed and reported independently throughout the thesis. A detailed rationale and justification for the methods used in each study is provided in each respective chapter, along with a summary of how each stage of research built on the previous stages. An overview of the pragmatic multi-methods used for the thesis is discussed below.

In order to address objective A, a systematic review and meta-analysis was conducted (Chapter 4). This method is the gold standard of research evidence, providing a comprehensive evidence base of a particular area of research and identifying areas that require further investigation (Page et al., 2021; Parums, 2021). There was no previous review of all ACT processes and distress in cancer, whilst there are several for the CSM illness perceptions as presented in Chapter 2 (Hagger et al., 2017; Kaptein et al., 2015; Richardson et al., 2017). A high-quality review of the literature identified a group of potential psychological processes that may be essential to understanding distress in cancer. The review aimed to demonstrate the transdiagnostic universal processes of ACT in the specific context of cancer, with the potential to inform future research and effective interventions. Where possible, a meta-analysis was conducted on the correlations, providing

a pooled effect size and evaluation of the data (Parums, 2021). In addition, meta-analysis also allowed investigation of potential moderators such as type of cancer which explored variables that may alter the strength or direction of the relationship between two variables (in this instance, between the ACT process and distress).

The second study (Chapter 5) used a qualitative approach to address objective B to gain insights into the distress experienced by women in the context of being prescribed and taking hormone therapy by uncovering a more nuanced understanding of why symptoms are distressing. The use of semi-structured interviews allows detailed explorations of a topic as well as flexibility to explore potentially new avenues of research which may not have been identified so far in the literature. Identifying important variables and confounders directly from women with breast cancer, can lead to the generation of testable hypotheses, which can subsequently be examined in a larger, more representative group. Therefore, as part of the sequential approach of the overall thesis, the qualitative study informed some of the hypotheses in the quantitative study in Chapter 7. An inductive approach was taken for the qualitative study to ensure the results were driven from the data with some researcher interpretation and this is described further in Chapter 5. This approach allows the results to be assessed after initial analysis to see how they align with existing theories or models. A subsequent, deductive secondary analysis was conducted on the interviews with these women to identify any ACT universal processes in action, in this specific context. This was an MSc student project that was supervised throughout the PhD. Using ACT theory as a lens allowed specific experiences and examples to be identified that directly support the processes of ACT theory and how they may relate to distress in this context, whilst providing potential insights to develop content for future interventions, based on real life experience. This secondary analysis is discussed at the end of Chapter 5.

The third study, with an observational longitudinal design, is presented across two chapters, each aligned with specific objectives (Chapters 6 and 7). In Chapter 6, the proposed predictors of distress from the CSM, ACT and an integrated model were tested to compare how much variance in distress the models can predict. The TMA-LTC had not been published at the start of this study so was not formally tested as the integrated model, however, will be discussed in relation to the results at the end of the thesis. Testing an integrated model allowed a more parsimonious and effective model to be proposed. In addition, the relationship between symptoms and distress was tested (Chapter 7). The qualitative study built on understanding *why* being on hormone therapy is distressing and more specifically *what* it is about symptoms that is distressing. Observational quantitative studies allow for observing these relationships, the strength and direction, and potential causal pathways without intervention. Therefore, it can help to understand *how* symptoms might lead to distress as well as *for whom* this relationship might be stronger, by using mediation and moderation methods. This type of study also allows for covarying factors to be controlled for, meaning the contribution of the variables of interest can be identified. Testing these hypotheses in a longitudinal study helped to address some of the limitations of previous cross-sectional research presented in the previous chapters.

Chapter 2 highlighted that current definitions and conceptualisations of distress are varied and sometimes unclear. A related study undertaken as part of the longitudinal observational study aimed to determine a suitable outcome measure for distress in this population, which is both acceptable, methodologically valid and in line with the definition and conceptualisation of emotional distress as presented in Chapter 2. This was another MSc student project supervised as part of the PhD. In Chapter 6, the psychometric characteristics of the measure are outlined.

Finally, in Chapter 8, the findings are combined and summarised to discuss the contribution of knowledge to the field and theoretical implications, to inform future recommendations, strengths and limitations, and conclusions that can be drawn.

Chapter 4 Acceptance and commitment therapy processes and their association with distress in cancer: a systematic review and meta-analysis

4.1 Chapter overview

Chapter 2 outlined two models that may be useful in understanding distress in cancer, the common-sense model (CSM) and acceptance and commitment therapy (ACT). Several systematic reviews of illness perceptions based on the CSM have already been conducted with distress as an outcome in cancer (Hagger et al., 2017; Kaptein et al., 2015; Richardson et al., 2017). As discussed in Section 2.3, negative illness perceptions are associated with increased distress in cancer populations. No such review currently exists for all ACT processes and distress in cancer; however, two reviews have been published for specific processes including acceptance (Secinti et al., 2019) and self-compassion (Hughes et al., 2021). Chapter 2 also outlined the potential utility of ACT in cancer, due to its perspective that distress is a normal response to difficulties and how changing responses to, rather than the content of thoughts and emotions, may lead to better outcomes. Observational studies also indicate associations between processes and distress. Despite there not being a published systematic review of all ACT processes and distress in cancer, there is increasing development of ACT based interventions in this context, but limitations to methodology and small effects are often reported. It is imperative to understand the evidence-based processes associated with distress to inform effective interventions. Identifying ACT processes in a systematic review will help to build effective interventions before large scale RCTs are conducted, and either support the theory or identify potential limitations of this theory in a particular context. The present review aimed to achieve this and is presented in

this chapter as a published article: *'Acceptance and commitment therapy processes and their association with distress in cancer: a systematic review and meta-analysis'* (Fawson et al., 2023). Published supplementary materials are presented in Appendix A.

This chapter also provides further rationale for the review that could not be incorporated into the published journal article, including for the process and outcome measures included. The published paper included studies that recruited all cancer types and cancer type was not differentiated in the published meta-analysis. However, exploring these ACT processes in breast cancer specifically was of interest to this thesis. Therefore, this chapter presents additional analyses which use the percentage of breast cancer patients in the sample as an additional moderator.

This chapter has been published in the following article:

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Co-author contributions: SF designed and planned the review, conducted the searches, data extraction, all analysis, risk of bias assessment and wrote the report. ZM, LDH and RMM contributed to the planning of the review and gave feedback on drafts. LDH supervised the analysis and interpretation of the data. KN, FM, IT and KF contributed to second screening. CJ contributed to the inclusion and exclusion criteria of ACT processes and gave feedback on earlier drafts.

4.2 Published article

Article title: Acceptance and commitment therapy processes and their association with distress in cancer: a systematic review and meta-analysis

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Keywords: cancer, oncology, meta-analysis, distress, Acceptance and Commitment Therapy, self-compassion

Acceptance and commitment therapy processes and their association with distress in cancer: a systematic review and meta-analysis

Abstract

Around 42% of individuals with cancer experience distress. Acceptance and commitment therapy (ACT) can reduce distress, but effects are small, and mechanisms unclear. This review aimed to identify associations between ACT processes and distress in cancer. Search terms included cancer, ACT processes, self-compassion, and distress. Six online databases and grey literature were searched until March 2022. Of 6555 papers screened, 108 studies were included with 17195 participants. Five meta-analyses of 77 studies were conducted. Random effects meta-analyses of correlations revealed higher scores on flexible processes (acceptance, present moment awareness, self-compassion) were associated with lower distress (r_{pooled} = -0.24, -0.39, -0.48, respectively); whilst higher scores on inflexible processes (experiential avoidance, cognitive fusion) were associated with higher distress (r_{pooled} = 0.58, 0.57, respectively). Meta-analyses displayed moderate-to-high heterogeneity with most studies assessed as low risk of bias. Meta-regressions revealed no significant moderators (stage, time since diagnosis, gender and age). This review provides a theoretically aligned evidence base for associations between ACT processes and distress in cancer, supporting elements of ACT theory and providing targeted directions for intervention development. Due to limited evidence, future research should focus on self-as-context, values, and committed action and conduct mediation analysis in controlled trials of ACT processes on distress in cancer.

1. Introduction

Cancer poses a significant emotional, financial and social burden on individuals. Incidence is rising worldwide with 19.3 million new cases in 2020 and annual economic costs estimated at US$1.16 trillion (Sung et al., 2021; *World Cancer Report: Cancer Research for Cancer Prevention*, 2020; World Health Organization, 2021). There are many challenges associated with cancer diagnosis and treatment which can cause significant distress to patients, including increased medical appointments and unpleasant procedures, psychological and physical symptoms and fears around recurrence, spread and the future (Mathew et al., 2020; Niedzwiedz et al., 2019). Psychological or emotional distress, often characterised by symptoms of anxiety and depression, can be defined as an emotional state of suffering (Drapeau, Marchand, & Beaulieu-Prévost, 2012). Distress is up to twice as prevalent in cancer populations than in the general population, with estimates of 17-42% for anxiety symptoms and 4-24% for depressive symptoms, persisting throughout diagnosis, primary treatment, palliative treatment and long-term survivorship (Brandenbarg et al., 2019; Brunckhorst et al., 2020; Hashemi et al., 2020; Hinz et al., 2010; Krebber et al., 2014; Linden et al., 2012; Mitchell et al., 2013; Niedzwiedz et al., 2019; Walker et al., 2013).

High levels of distress in individuals with cancer can result in higher personal and healthcare costs and poorer health outcomes in terms of reduced quality of life, treatment non-adherence, poorer rates of recurrence and survival (DiMatteo & Haskard-Zolnierek, 2011; Fang & Schnoll, 2002; Onitilo, Nietert, & Egede, 2006). Guidelines worldwide recommend that distress is routinely measured based on the premise that identifying, evaluating, and managing distress in patients with cancer is as important as physical health care (National

Comprehensive Cancer Network, NCCN, Holland & Bultz, 2007; CSG4, National Institute for Clinical Excellence, 2004).

Research exploring Acceptance and Commitment Therapy (ACT) as an approach to managing distress in cancer has increased over the last 10 years. ACT is a third-wave cognitive behavioural approach aiming to increase psychological flexibility; defined as the ability to be open and aware in the present moment whilst engaging in meaningful, valued activity (Graham et al., 2016; Hayes et al., 2006). ACT is an approach that evolved from but differs to conventional Cognitive Behavioural Therapy (CBT). ACT focuses on our relationship with or responses to thoughts and emotions rather than on disrupting or changing unhelpful thoughts and emotions, which can exacerbate distress (Harris, 2019; Hayes et al., 2006; Ruiz, 2010). ACT is proposed to work through increasing psychological flexibility, which is the ability to fully connect with the present moment in order to engage behavioural patterns supporting movement towards valued ends (Hayes et al., 2006). ACT encompasses six core flexible processes or psychological skills (Bennett & Oliver, 2019; Graham et al., 2016; Harris, 2019; Hayes et al., 2013; Hayes et al., 2006; Hayes, Strosahl, & Wilson, 2011). *Acceptance* is the awareness and willingness to experience private thoughts, feelings and emotions without trying to change or control them. *Defusion* refers to changing the relationship with, or detaching from thoughts, images and memories in order to alter their function and reduce their literal quality; and developing the ability to recognise thoughts as thoughts and not fact. *Present moment awareness* is the non-judgemental contact with the internal and external world such that an individual can consciously connect with and engage in whatever is happening in the present moment. *Self-as-context* is the awareness of one's own internal experience without attachment and the recognition of the self as the context from which thoughts, beliefs, emotions and memories can be observed. *Values* are qualities

of ongoing action based on knowing what matters to an individual. Lastly, *committed action* refers to workable values driven goals and action. The six flexible processes have corresponding inflexible processes (collectively termed as psychological inflexibility) contributing to psychopathology and suffering (Hayes et al., 2013; Hayes et al., 2006). These are *experiential avoidance,* which refers to the attempts to change or avoid uncomfortable thoughts or emotions; *cognitive fusion*, which is seeing the thought as an absolute reflection of reality such that it dominates awareness and influences behaviour; *loss of contact with the present moment,* whereby individuals cannot connect with and engage in the present moment; *self-as-content*, which refers to being attached to our internal experience and stuck with stories we have about ourselves; *lack of awareness of one's values* or remoteness from values; and *inaction*, which is unworkable action that is not guided by values (Hayes et al., 2013; Hayes et al., 2006). Self-compassion is implied throughout the model and, although not an explicit process, is a close concept and key feature of ACT in practice (Neff & Tirch, 2013). Self-compassion is the process of being kind and understanding towards oneself in difficult situations, whilst holding thoughts and feelings non-judgementally and mindfully, as though part of a wider human experience (Neff, 2003).

ACT may be a particularly useful approach for patients with cancer. ACT views distress and suffering as normal parts of the universal human experience and sees difficult thoughts and emotions as common and realistic responses to a cancer diagnosis. ACT seeks to encourage the development of psychological flexibility through processes such as valued living, enabling individuals to pursue meaningful activity even in the presence of difficulties such as distress and disruptions to daily living caused by treatment, medical appointments and recovery time whilst living with cancer (González-Fernández & Fernández-Rodríguez, 2019). ACT has also been shown to effectively support those with chronic pain and sleep

difficulties, symptoms commonly associated with cancer treatment (Mosher et al., 2018; NG193, National Institute for Clinical Excellence, 2021) and although not the main aim of ACT, symptom or distress reduction is often found to be a secondary benefit (Graham et al., 2016). Whilst there are a number of techniques associated with ACT, it can be delivered in a protocolised format, and this is commonly undertaken in research trials to ensure fidelity. However, ACT is a process-oriented psychological intervention and experienced clinicians will conduct sessions in a process-focussed manner, basing their intervention on dynamic assessments of a client's presentation and moving between ACT processes as indicated (Bennett & Oliver, 2019). Therefore, understanding the relevant impact and contribution of the processes can aid the formulation of this dynamic assessment.

Several reviews have sought to determine the effectiveness of ACT interventions in cancer with different outcomes, although the results were only narratively synthesised. In a systematic review, Mathew et al. (2020) found small positive effects in terms of anxiety and depression in 13 trials evaluating ACT for cancer survivors. Furthermore, a review of 19 trials of all cancer types and stages by González-Fernández and Fernández-Rodríguez (2019) reported significant improvements in emotional states (anxiety, depression, emotional distress) and quality of life following ACT intervention, including up to 12 months later. Similar conclusions have been reported in systematic reviews and meta-analyses of ACT-based interventions for other long term physical conditions with some large effects found for reductions in distress (Graham et al., 2016; Ngan, Chong, & Chien, 2021).

Although these reviews provide promising evidence for the potential effectiveness of ACT interventions for reducing distress, the included trials are often small, low quality, and with limitations to study design (Fashler et al., 2018; González-Fernández & Fernández-

Rodríguez, 2019; Hulbert-Williams, Storey, & Wilson, 2015; Salari et al., 2023). The impact and contribution of these reviews is therefore limited as meta-analyses could not be conducted due to variation in study designs (i.e., limited randomised controlled trials) and outcome measures, meaning pooled effect sizes are not reported. In addition, the included trials do not evaluate processes of change. ACT identifies likely mechanisms of action, however ideally, mediation analysis of ACT trials in cancer is needed to provide empirical support for the proposal of the key mechanisms of change through which interventions act on distress. A theoretical understanding of these processes of change in relation to context, is a vital part of the updated Medical Research Council (MRC) framework for developing complex interventions (Skivington et al., 2021) and may improve the efficacy of future interventions by building support for which of the ACT processes are amenable to change, and which are needed to change to improve a specific outcome. Identifying the change in processes which elicits a change in outcomes from the intervention will help identify the key mechanisms for those with cancer. Exploring the evidence-base for specific ACT processes may also improve accessibility and cost-effectiveness as there is potential for them to be used in briefer more targeted interventions for patients who do not necessarily need specialist interventions delivered by an experienced clinician (Dindo, Van Liew, & Arch, 2017; Richards, 2012). Alternatively, processes could be flexibly incorporated into other theoretically consistent interventions. In the absence of published mediation studies of randomised controlled trials which would be the strongest level of evidence, associations between ACT processes and distress in observational studies in cancer can be explored and meta-analysed. This provides a first step in highlighting the ACT model in the context of cancer distress and the processes which may be key to target in future interventions.

To ensure the validity of a theory underlying an intervention, the theory needs to be tested and supported with a solid evidence base and the components of models should also be tested in studies, in different contexts, before interventions are conducted (Hayes et al., 2013; Levin et al., 2012). Data in the context of ACT in cancer is less well established than in mental health and pain (Dindo, Van Liew, & Arch, 2017), so this review aims to provide the first step to a thorough understanding of ACT processes in this context. This will add to the theoretical evidence base, facilitating the development of effective, parsimonious and appropriate interventions that maximise the potential of therapy.

To our knowledge, this is the first review to consolidate evidence for the relationship between each ACT process, including the ACT-adjunct process of self-compassion, and distress in patients with cancer, providing a theoretical grounding of the mechanistic processes of ACT as applied to cancer. Previous reviews have investigated individual ACT constructs in cancer. A meta-analysis by Secinti et al. (2019) found acceptance had a small to moderate, significant negative association with distress (r = -0.31). In addition, a narrative systematic review on self-compassion in chronic physical illness (half of the samples with cancer patients), found moderate to large negative associations with anxiety and depression (Hughes et al., 2021). The current review addresses limitations to these previous reviews by including all ACT processes and self-compassion, reviewing grey literature to reduce publication bias and conducting robust meta-analysis. Conducting meta-analyses may also allow for moderators to be tested. Previous research is inconclusive for the clinical and demographic factors that may be associated with distress, however these results give an indication of the moderators to test (Secinti et al., 2019). To understand if experiences are similar across cancer diagnoses (transdiagnostic), type of diagnosis would need to be tested as a moderator. However, individual research studies often recruit and combine a variety of

cancer types in their analysis, with some consisting of very small samples of each cancer. Therefore, completing subgroup or moderator analysis based on cancer type may not be possible or appropriate. Moreover, as cancer samples are often split between early or advanced stage and extent of disease has been found to be associated with distress (Strong et al., 2007) it may be more appropriate to explore cancer stage as a moderator. In addition, exploring whether relationships between ACT processes and distress differ for age, time since diagnosis and gender, may be useful to help target interventions incorporating ACT processes. It has been found that women, younger age at diagnosis and those with a more recent diagnosis experience greater distress, although as previously suggested, results are often mixed (e.g., Carlson et al., 2019; Secinti et al., 2019).

Therefore, the primary objective of this review is to: identify the strength of associations between ACT processes (including the ACT adjunct process of self-compassion) and distress (e.g., depression, anxiety, emotional wellbeing) in patients with cancer using meta-analyses where possible and narrative review where there are insufficient studies for meta-analysis. The secondary objective is to: identify which ACT processes mediate distress outcomes in ACT interventions for patients with cancer. The review will also explore stage of cancer, time since diagnosis, gender and age as moderators of the relationship between ACT processes and distress.

2. Methods

This systematic review and meta-analysis have been conducted in line with PRISMA 2020 (Page et al., 2021) and JARS-Quant for reporting meta-analysis guidelines (Appelbaum et al., 2018). The review is registered on PROSPERO, CRD42020166458 version 4.

2.1 Eligibility criteria

Studies were included if they conducted research with adults diagnosed with cancer, not at end of life, and reported associations between at least one ACT-related process and a distress outcome. Outcomes and processes must have been measured using validated measures that score the whole process (subscales of constructs of processes were not included, e.g., facets of present moment awareness measures; see supplementary materials, Table S1). Observational designs were eligible, as well as clinical trials that either analysed baseline data or reported mediation analysis of an ACT process on a distress outcome in a Randomised Controlled Trial (RCT). See Table 4.1 for further details on eligibility criteria.

Table 4.1.

Inclusion and exclusion criteria for the studies in the review

	Inclusion criteria	Exclusion criteria
Population	Adult patients (18+) with an adult diagnosis of cancer (any type/stage), treated with curative intent or palliative care (not end of life).	Patients under 18 years old, those without a diagnosis of cancer or adults who received a diagnosis as a child and/or those receiving end of life care (life expectancy <6 months).
Exposure/ intervention (predictor variables)	Studies presenting statistical tests of associations between validated measures of processes of ACT (see eligible processes outlined in Table S1) and the outcome.	Measures not validated. See Table S1 for further information regarding definitions of ACT processes included/excluded.
Outcome	Validated measures of distress (anxiety, depression, psychological/emotional distress, mood).	Measures of distress not validated. Studies that do not measure distress.
Study Design	Observational designs (i.e., cross sectional, prospective, cohort, baseline RCT) reporting bivariate relationships or multivariate models between the intervention variables and outcomes above. Additionally, RCTs for ACT based interventions if they explore ACT mediators on distress outcomes.	ACT RCTs that do not analyse mediators/processes of change, or do not analyse baseline data. Qualitative studies.
Other	Studies can use primary or secondary data, be conducted in any country, but must be published in English.	Studies not in English and where full texts cannot be accessed.

Note: ACT = Acceptance and Commitment Therapy; RCT = Randomised Control Trial

2.2 Information sources

Six electronic databases were searched: OVID (PsychInfo, MedLine & Embase), CINAHL, Web of Science and Cochrane library (CENTRAL); as well as five grey literature sources: SSRN, OpenGrey, WorldCat Dissertations and Theses, EThOS, Health Management Information Centre (HMIC) Ovid; with no date restrictions. The search was run between 28/02/2022 and 02/03/2022. The reference lists of included studies and other relevant reviews were hand searched.

2.3 Search strategy and selection process

The search strategy for all databases is available in supplementary materials (Table S2). Author SF managed records using EndNote version X9.3. The selection of eligible studies followed the PRISMA methodology (Page et al., 2021). Duplicates were removed using the deduplication tool on EndNote and then by hand reviewing. Author SF independently screened all titles and abstracts using the PICOS criteria (stage one). KN and FM independently screened 100% between them. Studies deemed ineligible at this stage were removed, and the remainder moved to stage two screening. In stage two, full-text versions of all papers were retrieved and screened by SF using a predefined screening table in MS Excel. Two independent reviewers (KF and FM) also screened 79% of full-text papers. Cohen's Kappa scores were calculated to determine interrater reliability and showed substantial agreement at stage one (k=0.65 to 0.73) and almost perfect agreement at stage 2 (k=0.71 to 0.84). Disagreements were discussed and resolved with the supervising corresponding author (LH).

2.4 Data items and collection process

A predefined data extraction table in MS Excel was piloted on three papers, and study location and ethnicity were added. Data extraction followed the PICOS criteria and included: study location, sample size, the proportion of males/females, mean age of the sample, ethnicity, diagnosis, time since diagnosis, treatment, study design, ACT process and measurement, outcome and measurement, means and standard deviations of our primary outcomes, type of analysis conducted and results (effect estimates and precision where reported). Data were grouped into each ACT process in the data extraction table (*note*: some studies tested more than one process). Author SF extracted the data, and two independent reviewers (IT and FM) cross-checked 70% of papers for extraction errors, including all meta-analysis data. Four authors were contacted to correct errors in published papers or to provide data where missing (i.e., from supplementary materials not publicly accessible), and two replied (see * on Table S5 and S6).

2.5 Risk of bias assessments

Risk of bias was assessed in all studies using a checklist adapted from ROBINS-E (Morgan et al., 2017) and a checklist used by Pasma et al. (2013) following guidelines on areas of bias (Dekkers et al., 2019; Sanderson, Tatt, & Higgins, 2007). This assessment was developed as it is recommended that a risk of bias assessment checklist is suitable for the specific studies included in the review (Dekkers et al., 2019), in this case observational. No RCTs were included so an additional risk of bias tool was not needed. Author SF assessed each study using a checklist of up to 11 elements including the assessment of selection bias, response bias, attrition bias for longitudinal studies, bias due to missing data and analysis of confounders. Low, moderate or high risk and overall bias was stated (see Table S8). Author

FM independently assessed 50% with moderate agreement (k=0.55) and discrepancies were discussed until agreement. The GRADE tool (Guyatt et al., 2008) to assess bias across studies was used, providing an overall quality of evidence rating per process and outcome, considering the consistency of results, precision, publication and reporting bias. This was based on each meta-analysis. Outcomes for each process started at 'low quality of evidence' due to their observational nature and were downgraded if they scored 'serious' for any criteria. Quality could be upgraded if they had a large effect (Guyatt et al., 2008). Indirectness was not assessed as all papers were of the population of interest. Publication bias was assessed using funnel plots if there was a minimum of 10 studies (Page, Higgins, & Sterne, 2021).

2.6 Effect measures

Correlations and regression coefficients were the most reported measures of effect size. Three studies reported tests of mean difference, whilst another reported a Mann Whitney U test. No other effect measures were used. In narrative synthesis, effect estimates are presented with the direction of effect and summarised based on how many studies show estimates in the same direction. Due to the lack of studies reporting regression analyses and high heterogeneity between those that did, all regression data are narratively synthesised. No relevant RCTs were found reporting mediation or process analysis.

2.7 Synthesis methods

Strong correlations are generally found between distress measures in cancer implying a similar construct is being measured (Pandey et al., 2007; Rabkin et al., 2009). Therefore as in similar meta-analyses of distress outcomes (e.g., Winger, Adams, & Mosher, 2016), measures including anxiety, depression, distress, negative affect and emotional stress were

combined where possible and average correlations calculated if they were comparable in terms of definition of measurement and where correlations with measures of individual ACT processes in each study were similar. Correlations were Fisher's Z-transformed, the mean calculated and then back transformed to an *r* correlation using R studio code (R Core Team., 2020). ACT process measures were also synthesised where measurements were comparable in definition (e.g., values importance and values success were not considered comparable definitions of values). A meta-analysis was run for each process (or the overall process of psychological flexibility) and distress if at least $k = 5$ studies used the same type of correlations e.g., Pearson's *r* (recommendations range from 2-8 as minimum; Jackson & Turner, 2017; Rhodes & Smith, 2006; Ryan, 2016). The random effects model considered between-study differences and sampling variation and was used with the Restricted Maximum Likelihood (REML) estimator for tau squared (variance between studies) due to the continuous outcome data (Harrer et al., 2021; Langan et al., 2019). The 'metacor' package on R Studio (Laliberte, 2019) used Fisher's Z-transformation to estimate pooled correlations and reports 95% confidence intervals (CI; see code in supplementary materials S3). In line with Cohen (1988), $r < 0.1$ is interpreted as a trivial effect, $r \geq 0.1$ is interpreted as a small effect, $r \geq 0.3$ is a medium effect and $r \geq 0.5$ is interpreted as a large effect. Heterogeneity was assessed using I^2, which is the percentage of the variability in effect sizes (<40% low heterogeneity, 50-100% moderate to high heterogeneity; Deeks, Higgins, & Altman, 2022). To explore heterogeneity, as decided *a-priori*, moderator analysis was conducted with stage of diagnosis, rather than by cancer type due to the mixed cancer samples being included in many studies. Moderator analysis was conducted using the meta-regression function of metacor in R studio and if the minimum number of studies was $k = 10$ (Borenstein et al., 2009). Exploratory post-hoc moderator analyses were conducted on age,

gender and time since diagnosis where there were sufficient studies, as these factors have been found to be associated with distress and ACT processes in previous research (e.g. Carlson et al., 2019; Secinti et al., 2019). Where there was insufficient data to complete meta-analysis for individual processes, the data are narratively synthesised, reporting correlations and standardised beta coefficients (or unstandardised if standardised betas were not reported). Additional data for processes that were meta-analysed but where the data could not be reasonably incorporated, have been narratively synthesised and are available in supplementary materials to provide a complete summary of available data.

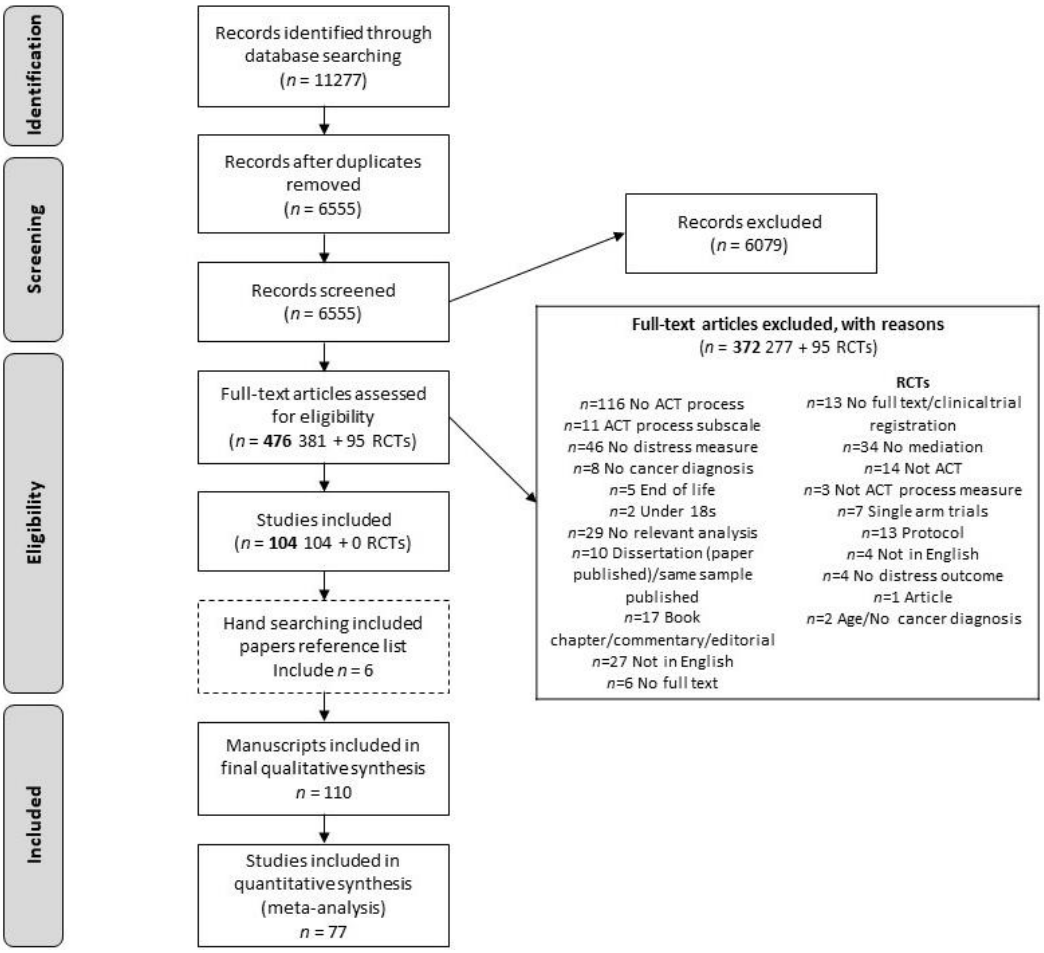
3. Results

3.1 Study selection

Figure 4.1 displays the search results and the number of papers screened at each stage. After duplicates were removed, 6555 were screened at stage one based on titles and abstracts, and 477 full texts were screened at stage two. One hundred and ten manuscripts (108 studies) were included in this systematic review, with 77 included in at least one meta-analysis. Most full texts excluded were due to studies not having distress as an outcome (*n*=46), no ACT process (*n*=116), not reporting relevant analyses (*n*=29) or not being published in English (*n*=27). The majority of RCTs excluded were due to not completing mediation analysis (*n*=34) and, if they did, not consisting of an ACT intervention or being a single-arm trial (*n*=21).

Figure 4.1.

PRISMA flow diagram of included studies.



3.2 Study characteristics

Study characteristics and a reference list of all included studies can be found in supplementary materials (Table S4). Studies are listed in alphabetical and numerical order and are therefore referenced with this corresponding number throughout this review. In the 110 studies, sample sizes ranged from 14-922 and included a total of 17195 participants (108 samples). The present review included 18 grey literature studies. The majority were carried out in the USA/Canada (*n*=44), with 30 across Europe, 11 in China and eight in

Australia/New Zealand. The remaining studies were conducted in Brazil, Jordan, Nigeria, Egypt, Japan, Taiwan, Singapore, Iran, Israel and Malaysia. The majority used either a breast cancer sample (*n*=41) or a mixed cancer sample (*n*=36). Seventy-one studies reported depression as an outcome, with 54 studies reporting anxiety, and 39 reporting distress. Some studies reported emotional/psychological wellbeing (*n*=13), emotional stress/dysfunction (*n*=12) and negative affect (*n*=6) as outcomes.

3.3 Risk of bias within studies

The risk of bias scoring is available in supplementary materials (Table S8). The methodological quality of studies was generally good, with a low risk of bias overall score for 68% of studies. Almost all studies reported *a priori* outcomes and/or hypotheses to reduce bias in reported outcomes, used validated process and outcome measures and reported significance values, scoring consistently low for risk of bias. Twenty-five per cent of studies failed to report detailed recruitment processes and received 'unclear' for risk. These details are essential to allow replication and would give a clearer indication of potential selection bias in recruitment. Response rates were also unclear, meaning risk of bias could not be assessed (53%) or were scored as moderate/high (22%), indicating potential non-response bias and difficulties with assessing representation of samples. Strategies for dealing with missing data (58%) and *a priori* sample size calculations (41%) were often not reported. Studies often failed to assess and/or control for confounders leading to potential biases in the estimates reported.

3.4 Results of meta-analyses

Syntheses are structured by ACT process. Five meta-analyses (pooled estimates are displayed in Table 4.2) were conducted between distress and experiential avoidance,

acceptance, cognitive fusion, present moment awareness, and self-compassion (raw data are available in supplementary materials, Table S5 and Figures 4.2-4.6 display all forest plots). Narrative synthesis on data that could not be incorporated into the following meta-analyses are presented in supplementary materials S7 to provide a complete overview of available data including regression data controlling for covariates.

Table 4.2.

Display of pooled estimates for random effects models

ACT process and distress	*n*	*k*	r_{pooled}	95% CI	I^2
Experiential avoidance	1822	17	0.58	0.52, 0.64	72.0%
Acceptance	2393	16	-0.24	-0.34, -0.15	78.8%
Cognitive fusion	966	8	0.57	0.47, 0.65	70.5%
Present moment awareness	5146	30	-0.39	-0.47, -0.29	92.5%
Self-compassion	3525	20	-0.48	-0.52, -0.43	65.7%

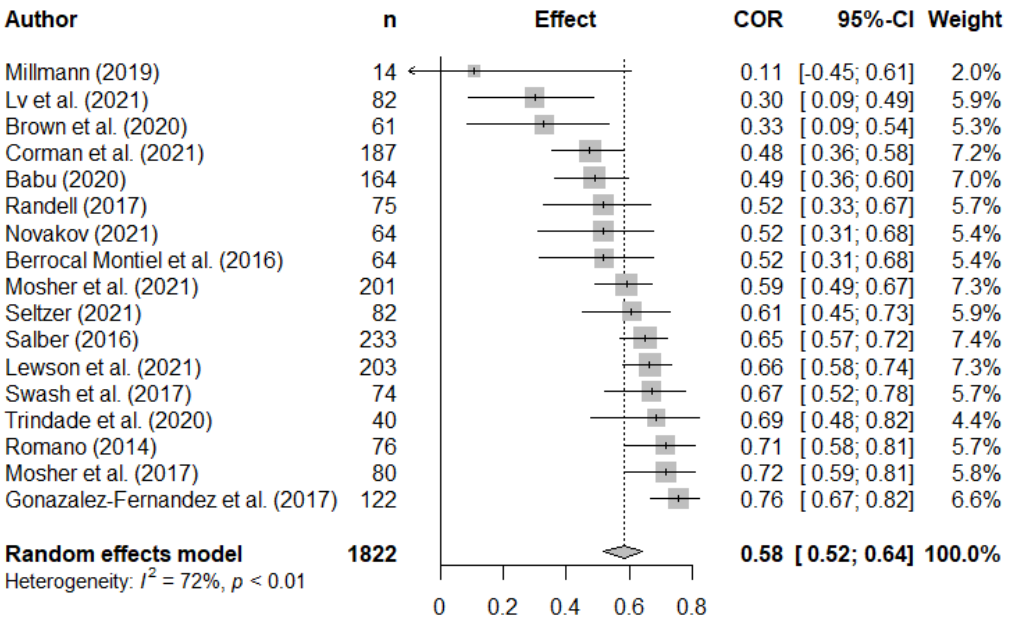
Note: n = overall sample size; k = number of effect sizes included; r_{pooled} = pooled correlation; CI = confidence interval; I^2 = test of heterogeneity

3.4.1 Experiential avoidance

Twenty-five studies explored experiential avoidance and distress outcomes: 18 cross-sectional and 7 longitudinal. Most studies were mixed cancer (*n*=10) or breast cancer (*n*=6), with five haematological, one thyroid, one prostate, one colorectal and one gynaecological sample. Sample sizes varied from 14-922. Seventeen studies were included in the meta-analysis. There was a significant pooled effect with a strong positive correlation between experiential avoidance and distress (r_{pooled} = 0.58, 95% CI 0.52, 0.64). Heterogeneity was high (I^2=72%; see Figure 4.2 for forest plot).

Figure 4.2.

Meta-analysis for experiential avoidance and distress



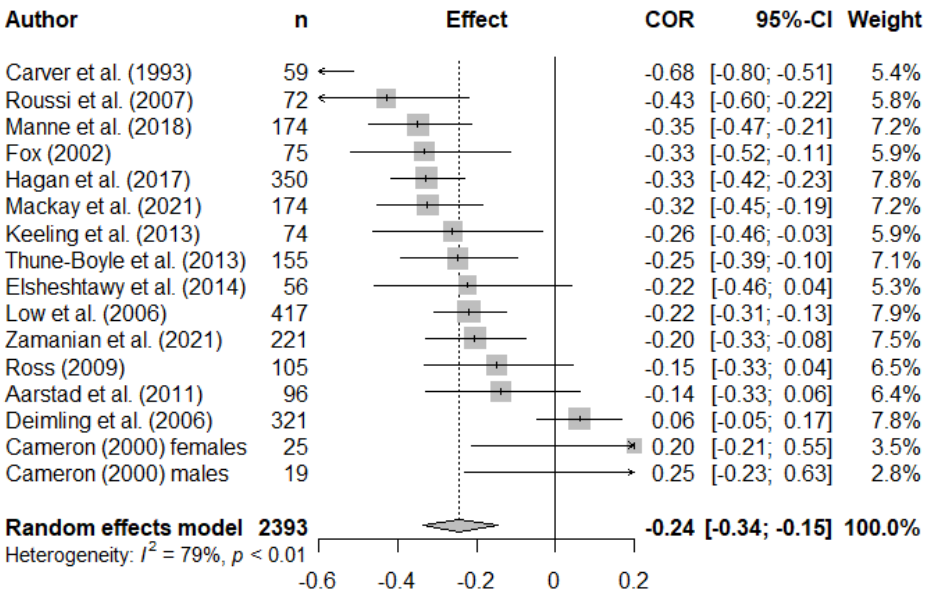
3.4.2 Acceptance

Thirty-three studies explored acceptance (measured by the COPE or brief COPE; Carver, 1997; Carver, Scheier, & Weintraub, 1989), self-acceptance, emotional acceptance and pain acceptance, in breast cancer (*n*=14), mixed cancer samples (*n*=10), gynaecological (*n*=3), and one study each in head and neck, brain, gastrointestinal, blood, colorectal and melanoma. Sample sizes ranged from 14 to 460, with 27 cross-sectional (including one baseline RCT), and six longitudinal studies. There were sufficient data to run a random effects meta-analysis for acceptance and distress. The pooled correlation was significant, although with a small effect (r_{pooled} = -0.24, 95% CI -0.34, -0.15, k = 16; see Figure 4.3. for forest plot). Only studies using the COPE measure were included in the meta-analysis. Heterogeneity was

moderately high (I^2 = 78.8%). Five studies reported non-significant, small effects, with two in the opposite direction than expected, one a grey literature study (17,26).

Figure 4.3.

Meta-analysis for acceptance and distress outcomes

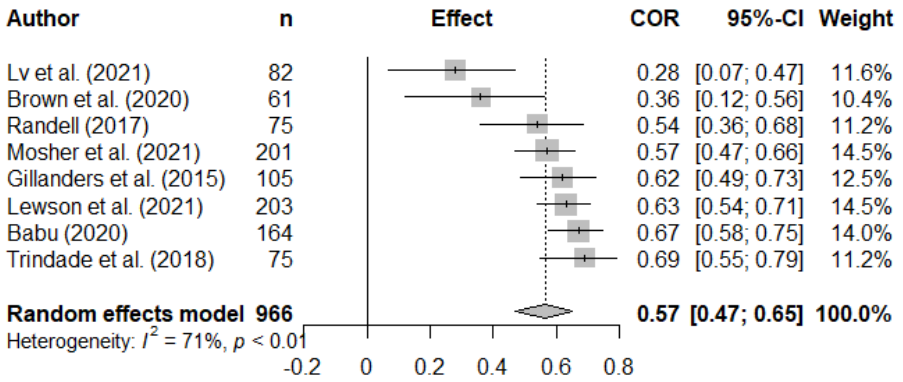


3.4.3 Cognitive fusion

Eight cross-sectional studies explored cognitive fusion with distress outcomes with samples ranging from 61 to 203. Six were mixed samples (8,15,32,52,62,75), one was a breast cancer sample (96), and one was thyroid cancer (57). There were sufficient data to run a random effects meta-analysis for cognitive fusion and distress. The pooled correlation was significant, with a large positive effect (r_{pooled} = 0.57, 95% CI 0.47, 0.65, k = 8). Heterogeneity was high (I^2 = 71%; see Figure 4.4. for forest plot).

Figure 4.4.

Meta-analysis for cognitive fusion and distress

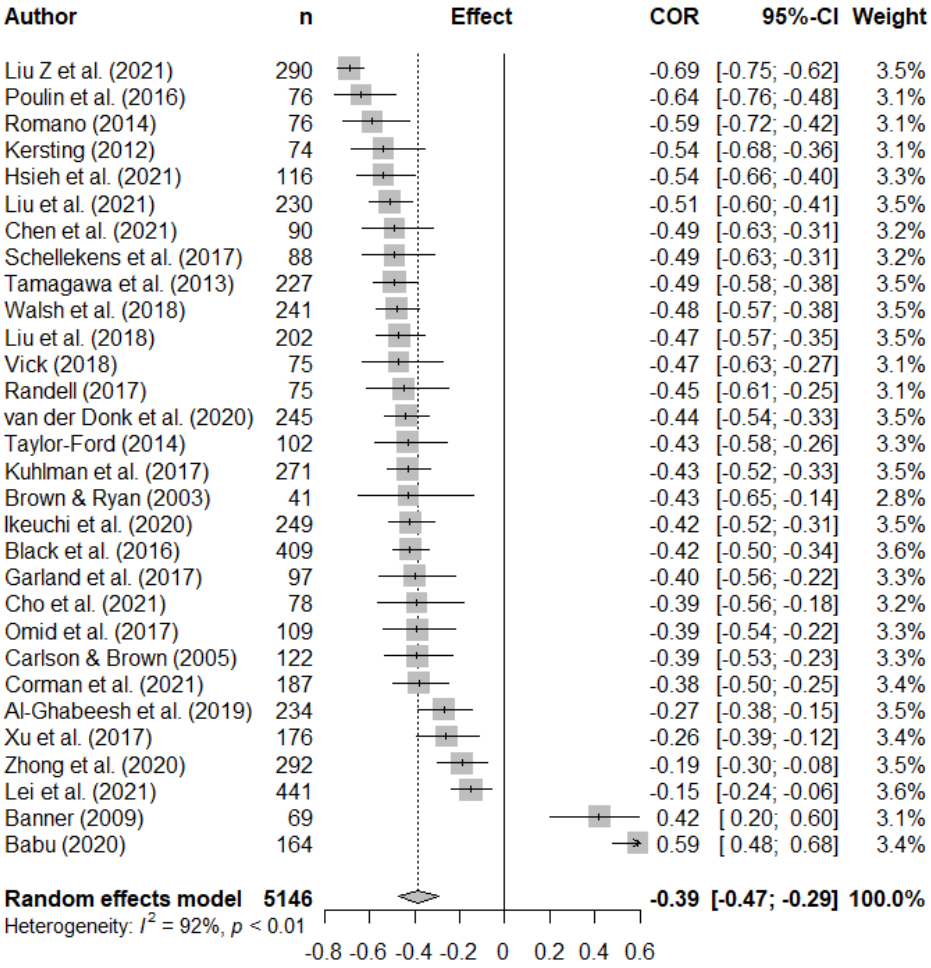


3.4.4 Present moment awareness

Thirty-four studies explored present moment awareness (using mindfulness measures) and distress in various cancer samples (mixed *n*=12, breast *n*=9, gastrointestinal *n*=6, lung *n*=4, blood *n*=2 and prostate *n*=1). Sample sizes varied from 41 to 441. Thirty-two were cross-sectional (including one baseline RCT), and two were longitudinal. There were sufficient data to run a random-effects meta-analysis using correlations for total mindfulness measure scores with distress outcomes. There was a significant medium pooled effect for present moment awareness and distress (r_{pooled} = -0.39, 95% CI -0.47, -0.29, *k* = 30). Heterogeneity was very high (I^2 92.5%; see Figure 4.5. for forest plot). Two grey literature studies report results in the opposite direction to the other studies (8,9).

Figure 4.5.

Meta-analysis for present moment awareness and distress outcomes



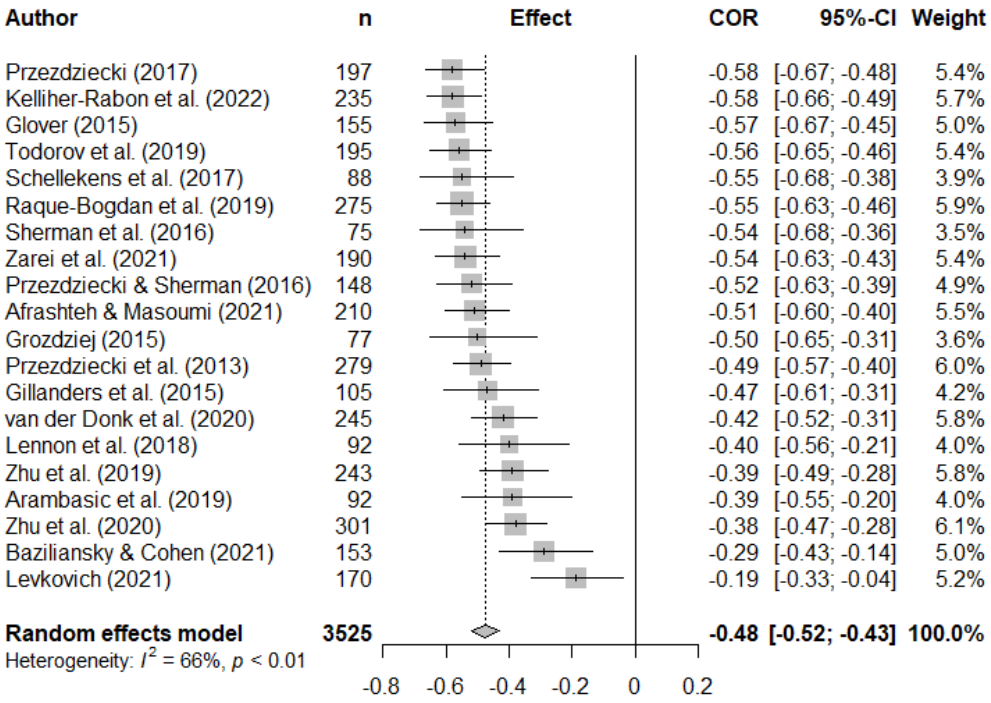
3.4.5 Self-compassion

Twenty-four studies tested self-compassion and distress outcomes in mostly breast cancer (*n* = 10) and mixed samples (*n* = 8), with two samples each for lung and colorectal cancer and one sample each for prostate and gastrointestinal cancers. Sample sizes varied from 58-301. Twenty-one studies were cross-sectional and three longitudinal. There were sufficient data from twenty studies to run a meta-analysis. The random effects meta-analyses showed there was a significant medium pooled effect with self-compassion inversely correlated with

distress (r_{pooled} = -0.48, 95% CI -0.52, -0.43, k = 20). There was moderate heterogeneity (I^2 = 65.7%; see Figure 4.6 for forest plot).

Figure 4.6.

Meta-analysis for self-compassion and distress



3.5 Moderator analysis

Heterogeneity was present in all five meta-analyses. Moderator analysis was conducted with stage of diagnosis. There were less than 10 studies for the cognitive fusion meta-analysis, so this was excluded from all further analysis. Stage of diagnosis did not significantly moderate any of the relationships between processes and distress (see Table 4.3). For exploratory moderator analysis, age, gender and time since diagnosis were analysed (there were less than 10 studies for both experiential avoidance and acceptance with the moderator 'time since diagnosis' so these were not included). There were no

moderator effects on the relationship between any of the processes and distress (see Table 4.3).

Table 4.3.

Moderator analysis

Process and distress	Moderator	*k*	*n*	i^2	R^2	B	SE	95% CI
Experiential avoidance	Stage	13	1410	62.67%	0.00%	0.000	0.001	-0.002, 0.003
	Age	17	1822	68.85%	20.94%	0.011	0.011	-0.002, 0.021
	Gender	17	1822	69.80%	17.29%	0.002	0.002	-0.001, 0.010
Acceptance	Stage	13	2025	85.47%	0.00%	-0.001	0.002	-0.005, 0.004
	Age	16	2393	79.46%	6.71%	0.011	0.011	-0.004, 0.022
	Gender	15	2172	79.68%	13.16%	-0.003	0.002	-0.011, 0.001
Present moment awareness	Stage	28	4850	93.85%	0.00%	0.000	0.002	-0.004, 0.004
	Age	26	4162	92.87%	2.29%	-0.013	0.011	-0.034, 0.010
	Gender	30	5146	93.34%	0.00%	-0.000	0.002	-0.004, 0.004
	Time since diagnosis	14	1940	87.56%	2.46%	-0.065	0.060	-0.173, 0.044
Self-compassion	Stage	13	2394	73.93%	0.00%	0.001	0.004	-0.007, 0.009
	Age	17	3035	70.56%	0.00%	0.002	0.005	-0.010, 0.011
	Gender	20	3525	66.09%	0.00%	-0.001	0.001	-0.003, 0.001
	Time since diagnosis	10	1703	58.27%	16.01%	-0.023	0.021	-0.064, 0.020

Note: n = overall sample size; k = number of effect sizes included; I^2 = residual heterogeneity; R^2 = amount of heterogeneity accounted for; B = estimate; SE = standard error; CI = confidence interval; time since diagnosis was not run as a moderator for experiential avoidance or acceptance and distress due to there being less than 10 eligible studies; no moderator analysis was run for cognitive fusion due to less than 10 studies overall.

3.6 Narrative synthesis of remaining processes

Meta-analyses could not be conducted on self-as-context, committed action, values and overall psychological flexibility due to the limited number of studies for each process, so a narrative synthesis was completed (details of extracted information and data are available in Table S6).

3.6.1 Self-as-context

One dissertation explored self-as-context in a mixed cancer sample of 164 (8). There was a significant negative correlation between self-as-context and depression (r = -0.22); however, a non-significant association was found for anxiety (r = 0.10).

3.6.2 Committed action and values

One cross-sectional study (75) was conducted with 75 mixed cancer participants. There were significant moderate-strong negative correlations between the engaged living scale (measuring committed action and values) and distress outcomes (r = -0.50 to -0.56). In regression analyses, engaged living was significantly associated with lower depression (β = -0.33), however, it was not significantly associated with lower anxiety.

3.6.3 Committed action

Two studies (8,97) explored committed action with distress outcomes. These cross-sectional studies included breast cancer and mixed cancer sample (n=82 and 164). In one study (97), there were significant, moderate negative correlations for committed action and distress outcomes (r = -0.46 to -0.53). However, in the grey literature study (8), associations in the opposite direction were found with committed action significantly positively associated with distress outcomes (r = 0.32 to 0.36).

3.6.4 Values

Five cross-sectional studies (8,22,52,62,63) and one longitudinal study (47) explored values in four mixed and two breast cancer samples, with samples from 32-203. A meta-analysis was not conducted as values measures were not comparable in definition. Value progress, success and importance was negatively correlated with anxiety, depression and distress

(8,22,52,62,63; *r* = -0.43 to -0.16), whilst value obstruction was positively associated with anxiety and depression (52,62,63; *r* = 0.61 to 0.66). In line with this, those who were anxious or depressed reported worse discrepancies between value importance and value attainment in different domains, at different time points compared to those who were not anxious or depressed (47). Another study found similar conclusions for values success in different value domains being positively correlated with emotional wellbeing (22; *r* = 0.34 to 0.50). However, greater commitment to family values was negatively correlated with emotional wellbeing (*r* = -0.29), and values success in romantic relationships was negatively associated with emotional wellbeing in females (22, β = -0.26), whilst controlling for avoidance.

3.6.5 Overall psychological flexibility

Two cross-sectional studies (60,84) measured overall psychological flexibility, with samples ranging from 144 to 286, both consisting of prostate cancer. There were strong, negative associations for psychological flexibility and distress (*r* = -0.69 and -0.67), and psychological flexibility was significantly associated with lower distress when controlling for age, self-esteem and stoicism (β = -0.41) and fear of recurrence (β = -0.56).

3.7 Risk of bias across studies

The GRADE assessment was used to assess bias across study outcomes in meta-analyses (Guyatt et al., 2008). Overall, the quality of evidence was very low for three processes and low for two processes (see Table S9 in supplementary materials). The meta-analyses for acceptance and present moment awareness scored serious or very serious in more than one domain. All meta-analyses scored serious or very serious for inconsistency as heterogeneity scores were high. However, data were relatively precise with four out of five meta-analyse

scoring not serious for imprecision and none were serious for reporting bias. For a summary of the assessment of narrative syntheses see supplementary materials S9.

4. Discussion

This review has been the first to quantify the direction and strength of relationships using meta-analysis between ACT processes, including the ACT-adjunct process of self-compassion, and distress in patients with cancer. Empirical research in this area has increased over recent years, with 26 studies published between 2020 and 2022 alone, making this systematic review and meta-analysis particularly timely to guide the direction and quality of future research. This review provides a comprehensive overview by including a total of 110 studies. Meta-analyses revealed significant associations between ACT processes and distress outcomes for people with cancer, whereby higher scores on flexible processes (present moment awareness, acceptance, and self-compassion) are associated with lower distress, and higher scores on inflexible processes (experiential avoidance, cognitive fusion) are associated with higher distress. This aligns with previous separate reviews on acceptance, self-compassion, and distress in cancer and other physical health populations (Hughes et al., 2021; Secinti et al., 2019). Narrative syntheses indicate that less investigated processes of values and overall psychological flexibility show promising moderate to strong associations with distress in the directions expected. However, only three studies explored self-as-context and committed action, with mixed results. This review provides empirical support for the theorised relationships between distress in patients with cancer and the flexible and inflexible processes depicted in the ACT model, with directions of association as suggested by the model.

Meta-analyses revealed large significant positive relationships between distress and experiential avoidance and distress and cognitive fusion indicating that greater inflexibility is associated with greater levels of distress. Self-compassion had a moderate negative pooled correlation with distress while present moment awareness had a slightly weaker, moderate negative pooled correlation with distress suggesting greater levels of these flexible processes are associated with lower levels of distress. The weakest relationship was observed between acceptance and distress. Data from the majority of cross-sectional regression analyses whilst controlling for covariates support these results, providing additional support for the relationships between these ACT processes and distress, over and above some demographic/clinical and/or psychological variables. However, these data are limited for cognitive fusion and only experiential avoidance had data from longitudinal studies to support this process predicting distress over time. Results were however across a variety of cancer samples. Similar relationships have been found in other physical health populations, such as Inflammatory Bowel Disease, Multiple Sclerosis and diabetes (Hughes et al., 2021; Jedel et al., 2013; Pagnini et al., 2019; Trindade, Ferreira, & Pinto-Gouveia, 2016; Trindade, Ferreira, & Pinto-Gouveia, 2018; Valvano et al., 2016). In line with the inflexible processes in ACT, fusing with or avoiding difficult emotions, thoughts or memories was associated with distress. It is understandable that people with cancer and other physical health conditions may have particularly difficult emotions and thoughts around future recurrence/relapse, mortality, ongoing treatment, and memories from past treatment; however, responding to these in an inflexible way may be problematic. Conversely, the flexible processes of being present and, especially being self-compassionate in facing difficulties, were associated with lower distress. The transdiagnostic evidence across different physical health conditions for these relationships, from previous research as well

as this review, supports the universal processes approach of ACT which is designed to be a unified process-driven model to reduce suffering and improve wellbeing (Hayes, 2019). The unified, process-based model can help to promote effective treatment strategies across conditions that experience similar unpleasant sensations and uncertainty. This transdiagnostic approach may broaden the access and availability of treatment, potentially improving outcomes for patients with cancer.

The smallest relationship was found between acceptance and distress, with a weak negative pooled correlation observed. Although a weak relationship was found, this is in the direction expected with greater acceptance associated with lower levels of distress. Some cross-sectional regression data controlling for covariates supported this relationship, however there was a lack of longitudinal studies conducted. According to ACT, the willingness to experience difficult emotions and thoughts should be associated with better psychological outcomes (Hayes et al., 2006). The small effect found in this review may be due to measurements of acceptance being developed from different theoretical models and definitions, such that acceptance was not adequately operationally defined to ensure consistency across participants completing the measures (McAndrews, Richardson, & Stopa, 2019). For example, the COPE inventory (Carver, 1997; Carver, Scheier, & Weintraub, 1989) was included in this review as a measure of acceptance as it has an active/process stance which ACT proposes, rather than acceptance as an end point or as resignation which is incongruent with the ACT model (Hayes et al., 2006; Hulbert-Williams, Storey, & Wilson, 2015). However, due to the variation of definitions of acceptance (McAndrews, Richardson, & Stopa, 2019), the COPE may be interpreted by participants as coping with the diagnosis label itself or another stressful life event, rather than the ongoing process of living with cancer. It may therefore fail to capture the experiential, ACT-based process like the

emotional acceptance scale (Politi, Enright, & Weihs, 2007). Whilst data were insufficient for meta-analysis using this subscale, the narrative synthesis supports this, with moderate relationships found with distress. The results are similar to a previous review (Secinti et al., 2019) which used an integrated model of acceptance, combining all coping measures, ACT measures and acceptance of illness measures, not necessarily all congruent with the ACT process model stance. The fact that small to moderate effects were found suggests neither method is adequately measuring the core ACT process of acceptance. Combining measures which are conceptually distinct from one another may also be unhelpful when deciding on definitions and models when developing interventions. Clear evidence for theories is needed to drive intervention development and specifically inclusion of processes of change. Similar to recommendations by Secinti et al. (2019), the current results suggest that the development of a measure of acceptance which encapsulates more of the cancer experience and in an ACT congruent way is needed, providing a clearer definition and conceptualisation for future research.

Although not a central tenet of the psychological flexibility model, self-compassion fits with the ACT approach in bringing awareness to suffering and distress as shared aspects of the human experience, to be acknowledged without self-criticism, a potentially pertinent process for those with cancer. Therefore, although self-compassion is interwoven throughout ACT in practice and training and seen as a potential mechanism of change, it is not adequately conceptualised within the model (Carvalho et al., 2021; Neff & Tirch, 2013). The lack of formal inclusion in the model poses the question of how this process is utilised in ACT therapy, how it is developed if there is no clear theoretical underpinning, and whether it depends on the therapists' skill. It also gives rise to uncertainty regarding the actual core processes of ACT (Arch et al., 2022). Although self-compassion is an inherent value in ACT

(Luoma & Platt, 2015), Neff and Tirch (2013) suggest explicit self-compassion exercises are needed to develop the process which can act as a mechanism of change for outcomes. The results of this review suggest that there is a moderate negative association between self-compassion and distress, such that patients with higher levels of self-compassion report less distress. This, coupled with the findings of Hughes et al. (2021) and evidence that self-compassion interventions reduce distress (Kılıç et al., 2021), suggests that a more formal description and conceptualisation of self-compassion should be incorporated into the ACT model to promote good intervention development and delivery.

Analyses revealed no significant moderators for any of these relationships between ACT processes and distress. This suggests the relationships between the processes and distress did not differ for different stages of diagnosis, age, gender or time since diagnosis. Type of cancer was not tested as a moderator due to the mixed cancer diagnoses within samples. Time since diagnosis and breakdown of stages was often poorly reported so these results should be interpreted with caution and may need further research to confirm these relationships. However, previous research is generally mixed in finding clinical and demographic factors associated with these processes and outcomes such as distress, indicating that this may remain true transdiagnostically (Secinti et al., 2019). It may be that these factors are not key moderators and therefore the relationships between processes and distress do not differ throughout the cancer journey or for individuals of different ages, stages and gender. Therefore, interventions based on these processes may be suitable for a broad population of cancer patients, potentially making implementation easier.

Few studies investigated committed action, values, self-as-context and overall psychological flexibility, so results must be interpreted with caution. A narrative synthesis of the available

data identified some associations with distress in the expected directions, with these flexible processes associated with lower distress in cross-sectional studies. It is surprising that there are so few studies providing an evidence-base for values in cancer as this is often reported as key content in ACT interventions for cancer patients (e.g. Mathew et al., 2020). However, these processes are consistently understudied in ACT literature (Arch et al., 2022). Values can be a difficult construct to measure as they are ongoing and dynamic in ACT (Barrett, O'Connor, & McHugh, 2019), and scales vary in their measurement with obstruction, progress and/or importance used and the process of values clarity rarely measured (McLoughlin & Roche, 2022). The importance of different values may understandably change over time and throughout the cancer journey, so there is potential to explore this process at different points (Lampic et al., 2002) and may be important in the development of tailored ACT interventions. Both values and self-as-context are further examples of processes that are either difficult to define or have variations in their definitions which can introduce uncertainty in how they are perceived and understood (Barrett, O'Connor, & McHugh, 2019; Zettle et al., 2018). It is, therefore, hard to determine the saliency of these constructs in the model for cancer.

The ACT theory and framework have been used to inform psychological interventions for distress in those with cancer. Still, the key mechanisms through which the intervention is hypothesised to work are often not identified in this population. Process Based Therapy (PBT), a more recent intervention approach proposed by Hayes and Hofmann (2018), suggests evidence-based processes of change should be identified and used rather than a traditional protocolised approach (Hayes, Hofmann, & Ciarrochi, 2020). They suggest this approach should be at an individual, personalised level, for a specific outcome (such as distress) and for appropriate contexts such as cancer, which could increase the efficacy and

effectiveness of interventions. The current reviews results support this approach as it provides evidence for key mechanisms associated with distress which could be developed as briefer, more targeted process-based interventions or be flexibly incorporated with other theoretically aligned interventions. In addition, where appropriate, theories themselves should be tested and refined or adapted in their application to a specific population considering the empirical evidence as it emerges (Levin et al., 2012). This review has highlighted key relationships between flexible and inflexible processes and distress in cancer providing evidence for theory development to inform more successful process-based interventions for those with cancer. However, identifying the lack of evidence for certain key processes depicted in the model, highlights a limitation to the model when applied to cancer and proposes the pathway for future research.

Implications of current findings

Understanding the key evidence-based mechanisms from the ACT model means intervention development can be guided by which variables should be targeted or emphasised. Successful psychological interventions targeting key mechanisms for managing distress in cancer have potential to reduce costs on multiple levels, including for individuals, medical systems and wider health networks (Chatterton et al., 2016). On an individual level, distress is linked to poor adherence to ongoing treatment and medical recommendations, increased recurrence and poorer survival rates, so addressing this outcome is imperative (DiMatteo & Haskard-Zolnierek, 2011; Fang & Schnoll, 2002). In addition, identifying processes that may be predictors of distress could inform screening strategies to identify those at risk of developing distress, encouraging suitable early intervention (Hulbert-Williams & Storey, 2016). It could be particularly important to identify experiential

avoidance and/or cognitive fusion at diagnosis as these processes had the strongest associations with distress across the different cancer samples.

Strengths and limitations

There are several limitations to this review which need to be considered. Firstly, most studies were cross-sectional, meaning only meta-analyses of correlations could be conducted, limiting the ability to make assumptions regarding causality. The longitudinal data available were very limited and provided mixed results. Second, the meta-analyses and GRADE assessment identified significant heterogeneity across studies. This could be due to variations in process and outcome measures used as well as limits to the number of studies and sample sizes included. Due to the nature of the GRADE assessment depicting observational studies as low-quality evidence, all meta-analyses were scored as low or very low-quality, implying that further data are likely to be substantially different from the estimated results (Guyatt et al., 2008). However, considering the number of studies included in the meta-analyses, the precision and low reporting bias, further data are likely to support the overall conclusions of the meta-analyses (particularly in the case of the directions of effects) in this review. Excluding patients facing end of life was one means by which heterogeneity was sought to be reduced. This review attempted to reduce publication bias by including grey literature, by using key terms for searching and conducting a wide search with several electronic databases. However, some relevant articles may not have been identified, and conference abstracts were not included. Some studies had non-significant results or contradictions to expected results and some of these were grey literature, studies with small sample sizes and/or those of low quality. It is important that more high-quality research is published to avoid potential publication bias. The review is also susceptible to

language bias as only English-language papers were included. Several areas of study methodology indicated an unknown or high risk of bias. Despite these limitations, the current review is the first to consolidate data on all ACT processes and the ACT-adjunct process of self-compassion and their association with distress in cancer.

There are also wider limitations associated with this field of research. The AAQ (Bond et al., 2011; Hayes et al., 2004) was used in 21 studies to measure experiential avoidance, however, the measure has been widely criticised for its strong correlations with distress due to measurement overlap (Tyndall et al., 2019). This was demonstrated in this review; however, overall results were supported by data from the alternative measures. As there were insufficient studies, formal subgroup analysis could not be conducted, which is an important consideration for future research. Findings should therefore be interpreted with some caution and alternative measures of experiential avoidance used when measuring associations with distress. Most studies in this review were cross-sectional and it is therefore recommended that more longitudinal studies are conducted to explore which processes predict distress over time as well as identifying the stability of these relationships. A diagnosis of cancer may require continual self-management and adjustment to changes in treatment and status. Understanding how the key processes are relevant to an individual's experience of living with cancer will help tailor future research and interventions (McCanney et al., 2018). Despite many trials of ACT interventions in cancer being conducted, RCTs did not complete mediation or process analysis meaning the strongest evidence for the effect of processes on distress could not be synthesised.

Future directions

Future research should look to conduct gold standard RCTs including mediation analysis to establish whether ACT-based treatment produces change in the corresponding processes such as reducing inflexibility or increasing flexible skills, which reduce distress. In addition, mediation analysis in longitudinal observational studies would provide further insight into the processes as mechanisms in relationships of independent variables and the outcome of distress. A key area of unclear bias in the included observational studies was the failure to report justification of sample size which is important to inform recruitment and determine the power and interpretation of data. Researchers publishing studies in line with guidelines such as STROBE (Cuschieri, 2019) would allow for more transparent reporting and a clearer assessment of risk of bias. Measures also need to be developed to capture the ACT process as defined. Further research on determining clearer definitions would aid stronger measurement development and consistency when responding to questionnaires. This would allow the model and potential mechanisms of change to be adequately tested to support intervention development and provide evidence of these processes translating into change (Arch et al., 2022). Additionally, work needs to ensure definitions are adequately translated and understood across different cultures, particularly in measurement development, as differences have been found (e.g. Trindade et al., 2021).

Conclusions

Overall, the present review is the first to consolidate the literature on ACT processes and distress in cancer and provides evidence from 110 manuscripts that have applied components of the ACT model to cancer. Most of the processes included in the meta-analyses had moderate to large associations with distress, supporting the use of the ACT

model to understand distress in cancer. Across cancer diagnoses, the strongest associations were found for use of the inflexible processes of experiential avoidance and cognitive fusion and increased distress, whilst the use of more flexible processes, namely present moment awareness and self-compassion, were associated with lower distress. Our search failed to identify any RCTs which explored ACT processes as mediators of change in ACT interventions for distress in cancer and should be the focus for future studies. Further research, needs to be conducted to identify relationships between distress and self-as-context, committed action, values and overall psychological flexibility. There was a paucity of longitudinal research conducted across all processes, which would allow the predictive ability of ACT processes on distress in cancer to be examined. Measures of processes also need to be developed based on clear conceptual definitions. Research developments in this area will help address and understand the maintenance and alleviation of the common experience of distress in those with cancer.

4.3 Rationale for decisions made in the systematic review

4.3.1 Conducting a systematic review and meta-analysis

Systematic reviews aim to gather all available evidence for a specific topic and a meta-analysis aims to provide an evaluation of that data (Parums, 2021). Systematic reviews have many benefits including being able to provide an overview of the state of research, include data from multiple studies rather than one in isolation, make conclusions about research and can evaluate theory (Page et al., 2021). The Medical Research Council (MRC) framework states that for intervention development, a theoretical understanding of the processes of change should be understood first, and a systematic review is one way to achieve this aim for a specific context (Skivington et al., 2021). Systematic reviews should take a methodical approach and guidelines such as registering on PROSPERO and following PRISMA try to ensure this is transparent, reproducible and of high quality (Page et al., 2021).

A systematic review was deemed essential for this thesis to, a) comprehensively synthesise the existing evidence base on ACT processes and distress in cancer to understand the extent of current research and guide future research, and b) to evaluate the existing evidence base in terms of the theory to make recommendations. This review would build on other systematic reviews that only focused on individual processes rather than considering the ACT model as a whole or included broader populations of long-term conditions (Hughes et al., 2021; Secinti et al., 2019).

4.3.2 Included search terms and PICOS criteria: cancer, process and outcomes measures

To achieve the two main aims of the review of exploring ACT processes and distress by identifying associations in observational studies and identifying potential mediators in RCTs, the following databases were chosen. PsychInfo includes studies on behavioural science and

mental health whilst Embase, MedLine and Web of Science cover biomedical research and social sciences. CINAHL was included for covering nursing and allied health literature and CENTRAL, part of the Cochrane library was also included for identification of trials. Finally, it was decided that grey literature would be searched to reduce publication bias. Many systematic reviews do not include grey literature searching due to challenges with achieving a systematic search. This is due to the limited advanced search options on the various databases. To address this, the present study created a list of combinations of the search terms outlined in the paper to identify studies. Many grey literature studies were theses and were generally not rated as high risk of bias due to the rigour in reporting for theses, suggesting study quality was not compromised by including grey literature in the search. However, some results were contrary to the expected direction and therefore need to be interpreted with caution. This may indicate some reporting bias in the published, non-grey literature studies. Therefore, inclusion of grey literature may strengthen the results and conclusions drawn from the paper as publication bias is potentially mitigated as null/weak/contrary results are included.

ACT proposes that the processes are universal for given contexts. If cancer in general is a context, we would expect to see similarities across cancer diagnoses. This could be useful to extrapolate findings to less investigated cancer groups. In addition, examining the current state of the evidence for all cancer types informs directions for future research. However, further research would need to be conducted on individual cancer groups to inform specific intervention contexts. As described in Chapter 3, all cancer diagnoses were included in this review. From scoping searches, it was estimated there were enough studies to conduct the review across cancer samples. Only 41 of the 110 studies included a breast cancer sample, meaning an inclusion criterion of only breast cancer for the review would have excluded

63% of studies, resulting in a less comprehensive review. In addition, meta-analyses would have been much smaller, limiting the conclusions that could be drawn from pooled estimates. It also would not have been possible to conduct meta-analysis on cognitive fusion due to a lack of studies in breast cancer. Rather than restrict studies, the percentage of breast cancer patients in the samples was used as a moderator in the thesis as a sensitivity analysis. This has allowed a more comprehensive contribution to the literature as well as providing specific answers for this thesis. This will give an important insight into whether, in breast cancer, ACT processes have unique relationships or if they are similar to when all cancer is included which supports the universal ACT approach.

Some ACT processes consist of multiple facets and therefore measures sometimes break down the process into these facets. It was decided for the review that only complete measures of the processes would be included for two reasons, 1) to keep the systematic review within a manageable scope for this PhD thesis and 2) the review included all ACT processes in the model, rather than focusing on individual processes. For example, the meta-analysis on acceptance and distress in cancer (Secinti et al., 2019), took a broad, integrated definition of acceptance and although still considered acceptance as a process, as in ACT, it included a wide variety of measurements, some of which considered acceptance as an end point rather than a process. As this present review focused on collecting evidence for ACT processes, acceptance was based on the ACT model definition which emphasises acceptance as ongoing, and process based. However, this means that potentially some acceptance data was not included in the review due to this screening process and the variation in acceptance definitions. In addition, there have been differing views about the measures used for experiential avoidance. In a recent review which was published whilst this paper was under review, Davis et al. (2023) completed a narrative systematic review on

experiential avoidance in advanced cancer but used different measures and a broader definition of experiential avoidance that included different facets such as cognitive, behavioural and emotional avoidance. The findings complement one another in the sense that both reviews suggest experiential avoidance may be an important process to explore with distress in cancer. Variations of the AAQ (Bond et al., 2011) were chosen for the present study alongside other overall measures of experiential avoidance (i.e., the BEAQ; Gámez et al., 2014) as the AAQ was originally designed to measure this construct. In addition, overall measures for mindfulness and self-compassion were favoured over breaking this down into the facets of these constructs. These measures create an overall score of the measure depicted in the ACT model conducive for the aims of the review. The review has established the evidence base for these concepts using global measures. Now that it has been identified that these processes are relevant, further analysis of the constructs could be explored. It may be useful to examine the individual components of definitions and their measures to ensure that interventions and techniques are targeting the full definition or component of a particular process, and that this is evidence based.

In conjunction with the definition described in Chapter 2, a broad definition of distress was used in this review incorporating anxiety, depression, mood disturbance, emotional wellbeing and negative affect as well as post-traumatic stress symptoms, due to the variation in published distress definitions. The paper provided further detail on how these were combined. This method of pooling the correlations from distress measures used in the same studies may have brought down the strength of effect for different elements of distress and means the detail is lost in terms of the specific constructs (e.g., anxiety). However, as outlined in the paper, the high correlations across distress measures are often reported (Pandey et al., 2007) and this combination aids interpretation and alignment of

analyses. In addition, specific distress measures such as those around sexual distress, death anxiety, emotional suppression and distress around loss were not included in the definition, which could be useful constructs to explore in this population. Fear of cancer recurrence was not included in this definition due to it being defined as a specific element of anxiety, which was described in Chapter 2. The relationship between fear of recurrence and ACT processes, however, would benefit from future research or a systematic review to determine this relationship. For example, cognitive fusion may be particularly pertinent in relation to thoughts around cancer recurrence and has been added to the integrated theoretical model of fear of recurrence (Fardell et al., 2016).

It was decided that mediation studies would be included if they were RCTs rather than other trials. This was due to the importance of being able to compare to a control group to understand whether the change in outcome was due to the change in the process mechanism via the intervention. In addition, as reported in the paper, many ACT trials reporting the effectiveness of interventions on distress are low quality and have small sample sizes and reviews of interventions in general have been published (Fashler et al., 2018; González-Fernández & Fernández-Rodríguez, 2019). Mediation analyses of these interventions would allow an understanding of whether changes in processes result in changes in outcomes, providing strong conclusions to be drawn about the processes on distress. Unfortunately, no studies reported mediation of an ACT process on distress in an RCT, highlighting a key suggestion for future research to investigate, as discussed in the paper.

4.4 Additional results for the systematic review and meta-analysis

4.4.1 Section overview

As described in this chapter, the percentage of breast cancer patients in samples was used as a continuous moderator to see if this type of cancer altered the relationships presented in the main paper which included all cancer types. This analysis directly applies the results to the thesis population. It was initially outlined in PROSPERO *a priori* to conduct subgroup analysis, however due to the number of mixed cancer samples, this was deemed inappropriate. Moderator analysis was chosen instead, which is a stronger methodology as all samples in existing meta-analyses could be included. The moderator analysis methodology (as used for stage, age, gender and time since diagnosis) is outlined in the published paper. See Appendix A2 for studies included in meta-analyses with the percentage of breast cancer patients reported.

4.4.2 Results

For each study included in the meta-analyses presented in the paper, the percentage of breast cancer patients in the samples was extracted (see table in Appendix A2). Almost half of the studies for each process consisted of between 50-100% of breast cancer patients. As in the main paper, there was an insufficient number of studies for cognitive fusion (including only one study in breast cancer), so moderator analysis was not run for this process. For the acceptance, present moment awareness and self-compassion meta-analyses, breast cancer was not a significant moderator of the relationships with distress. See Table 4.4 for all meta-analysis results.

Table 4.4.

Moderator analysis using % of breast cancer patients in samples as a continuous variable

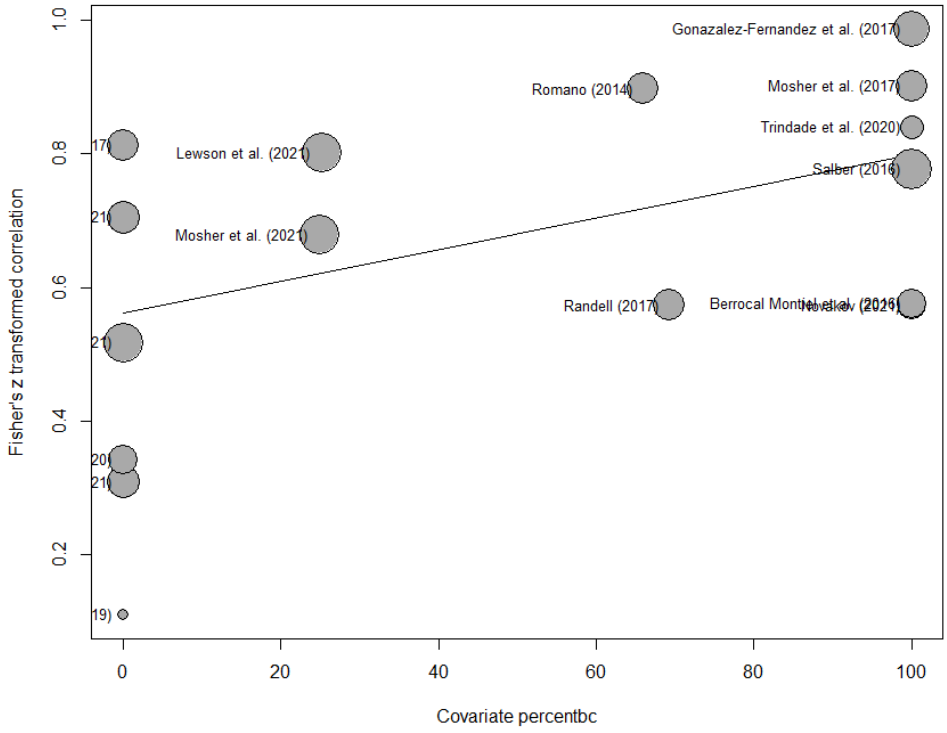
Process and distress	*k*	*n*	i^2	R^2	β	SE	95% CI
Experiential avoidance	16	1658	65.67%	31.30%	0.0024*	0.001	0.0004, 0.0044
Acceptance	16	2393	81.85%	0.00%	-0.0014	0.0012	-0.0037, 0.0009
Present moment awareness	28	4906	86.46%	0.00%	0.0005	0.0009	-0.0013, 0.0023
Self-compassion	18	3100	62.11%	0.00%	-0.0003	0.0007	-0.0017, 0.0010

*Note: k = number of studies included in meta-analysis; n = total sample size; i^2: heterogeneity; R^2: variance; B = standardised beta; SE = standard error; CI = confidence interval; *p < .05*

However, breast cancer diagnosis was a significant moderator for experiential avoidance and distress whereby a greater percentage of breast cancer survivors significantly increased the strength of the correlation. Despite this significant result, large effects were seen for the correlations across studies as shown in the bubble plot Figure 4.7. The beta estimate for experiential avoidance, although significant, was a very small effect (β = 0.0024, CI = 0.0004, 0.0044). The heterogeneity in this meta-analysis was lower than that for the main paper, demonstrating that breast cancer may account for some of the heterogeneity in the model. However, the i^2 is still in the moderate-high category.

Figure 4.7.

Bubble plot for breast cancer as a moderator for the experiential avoidance and distress meta-analysis.



4.4.3 Discussion

The additional analyses presented show that the strength of the relationships across ACT processes and distress do not differ between breast cancer and other cancer diagnoses, apart from for experiential avoidance. There was a slightly stronger correlation for studies that included more breast cancer patients for the relationship between experiential avoidance and distress. Gender was not a significant moderator, implying experiential avoidance may be particularly pertinent in breast cancer, rather than something which is more common in all female participants.

Experiential avoidance is the unwillingness to sit with or experience difficult thoughts and emotions. Whilst initially diagnosed and going through treatment, breast cancer survivors

have reported focusing on getting through and not necessarily acknowledging the distressing nature of the experience until after primary treatment has finished, avoiding the term cancer and their surgery scars, and this avoidance may be associated with distress (Aguirre-Camacho et al., 2017). For those with advanced cancer, people may feel avoidant of thoughts around the future and strong emotions about their prognosis (Davis et al., 2023). However, there is no existing evidence to explain why this process may be particularly relevant for this group over other cancers.

It is unclear why a difference in the relationship between experiential avoidance and distress was found for breast cancer. As this was an exploratory investigation, there was no predefined hypothesis to expect a difference between cancer types. No other moderators were significant, implying that stage, age, gender and time since diagnosis were not important factors in the relationships between ACT processes and distress. The findings could be influenced by methodological factors such as inclusion of heterogenous breast cancer samples across the studies or the presence of large samples of breast cancer patients in some studies. Breast cancer is a well-represented population, with many studies included in the data, making it the most common single type of cancer reported which may have skewed the results by contributing more to the effect. The correlations and information in the samples is not enough to provide us with information as to why these differences were found, however the relationship between experiential avoidance and distress warrants further investigation.

Although the results of the breast cancer moderation analysis could be extrapolated to breast cancer survivors on hormone therapy, this does pose a limitation of applying the results. Hormone therapy status was poorly reported across studies, meaning no meta-

analysis could be run in this particular group. Being able to conduct this may have reduced some of the heterogeneity in the sample and enabled direct application of the results to this thesis.

To reiterate the findings of the paper in this chapter, the AAQ, which was used by the majority of studies to measure experiential avoidance, has been criticised for being strongly correlated with distress (Tyndall et al., 2019), which was corroborated in the review findings. Looking at the items in the measure may also give an insight into the stronger correlation for breast cancer patients. The items, although mainly focusing on emotions and painful experiences or memories, do also look towards the future. At earlier stages of diagnosis or survivorship it may seem difficult to think of getting back to what life looked like before. Likewise, those with advanced cancer might also find the items looking ahead to the future may result in feelings of distress due to their prognosis. Due to the small effect found in the moderator analyses and the frequency of the AAQ used, the findings in this additional analysis therefore need to be interpreted with caution. As discussed earlier in this chapter, Davis et al. (2023) reported the cognitive, behavioural and emotional components of experiential avoidance in a narrative review in advanced cancer. It may be useful for the components of experiential avoidance to be explored more thoroughly through qualitative research and testing quantitatively in various cancer samples in future research. This may reveal further information about the importance of experiential avoidance in breast cancer such as whether it predicts distress over time.

4.5 Chapter summary

Overall, the systematic review and meta-analysis has provided a comprehensive overview of ACT processes and their association with distress in cancer. The review has highlighted that

the flexible processes of present moment awareness, acceptance and self-compassion have been widely researched and are associated with lower distress. Inflexible processes such as experiential avoidance and cognitive fusion have also been widely researched and found to be associated with an increase in distress. These findings directly support certain aspects of the ACT model, but there are several under investigated parts of the model in the cancer distress context.

Further research is needed for the less investigated processes of values, self-as-context and committed action. This is also found outside of cancer, with a systematic review on self-as-context and emotional wellbeing only identifying 20 studies, the majority of which were conducted in student samples (Godbee & Kangas, 2020). This could partly be due to measures of self-as-context only being developed in the last 5-7 years (Godbee & Kangas, 2020). Values has been more widely researched, although less so specifically in cancer, as evidenced in this review. However due to the variation in measurements and definitions of different constructs, it makes consolidating the evidence difficult, limiting our understanding of this concept in cancer. The overlap with the definition of committed action as value-directed behaviour could also contribute to the lack of studies for this process. Further research specifically on these processes in cancer would add to this evidence, enabling more confident conclusions to be drawn.

These results have found breast cancer was not a significant moderator for acceptance, self-compassion and present moment awareness. However, experiential avoidance may be particularly pertinent in breast cancer survivors. This needs to be explored further, especially in the hormone therapy population to corroborate these findings. The breast cancer samples included both early stage and advanced stage cancer and included different

times since diagnosis, including some during primary treatment. The experiences therefore might be different during survivorship. In addition, only one study exploring cognitive fusion was conducted in a breast cancer sample, further supporting the need for future investigations of this process in breast cancer.

Linking back to the models presented in Chapter 2, this first set of results from the thesis addresses a gap in the literature and provides evidence for potential important correlates of distress from the ACT model that can be applied to breast cancer. The data provides an evidence base for the model in this context which is encouraged before interventions are developed (Levin et al., 2012) to ensure targets of interventions are evidence based and effective. This, in conjunction with the previous CSM illness perceptions and distress systematic reviews (Hagger et al., 2017; Kaptein et al., 2015; Richardson et al., 2017) provides an understanding of the correlates with distress in cancer. The review identifies a lack of longitudinal studies across cancers. Further longitudinal research is needed for both the ACT processes and the CSM illness perceptions in understanding the predictive ability of these variables on distress in cancer. The results from this study directly inform the measures to be included in the quantitative study presented in Chapters 6 and 7, by using an alternative measure of experiential avoidance, and informs the development of the hypotheses to be tested in longitudinal analysis. Although the results suggest that these processes are potentially important in distress across cancers, further research is beneficial in a specific population to confirm these findings and provide data for the under investigated elements.

The results also informed secondary analysis of the qualitative data presented in Chapter 5, which was completed alongside this PhD. This study explored ACT processes qualitatively,

providing an indication of ACT processes in action, with experiences described by participants. Participants were asked how they respond to or deal with thoughts to provide detailed descriptions of the processes and how they relate to experiences. As processes such as self-as-context and values have been described to potentially be difficult to understand and measure, qualitative analysis may reveal further information about this. This study will be described further in Chapter 5 (see Appendix B6 for a copy of the paper; Moxham et al., in prep).

To conclude, this study has enabled PhD objective A to be achieved and contributes to the overall aim of the PhD by adding to the understanding of psychological correlates of distress in cancer. The observational studies can build on these data and findings and apply and test them specifically in the context of breast cancer survivors on hormone therapy.

Chapter 5 Exploring physical symptoms and distress in early-stage breast cancer survivors on hormone therapy: A qualitative study

5.1 Chapter overview

Chapter 4 has addressed a gap in the literature by providing a comprehensive overview of acceptance and commitment therapy (ACT) processes and their association with distress in cancer. In conjunction with previous reviews on the illness perceptions from the common-sense model (CSM; Hagger et al., 2017; Richardson et al., 2017), the findings give an indication of some of the variables that might be involved in distress in cancer. However, many of these studies explore samples of cancer survivors in general and do not necessarily highlight the potentially unique experience of those on hormone therapy (Fawson et al., 2023; Hagger et al., 2017). In addition, quantitative studies found various psychological predictors of distress only account for a limited amount of variance in distress (e.g., Gibbons, Groarke, & Sweeney, 2016; Trindade et al., 2020), suggesting that other important factors may be thus far unidentified.

The transdiagnostic theoretical model of adjustment to long term conditions (TMA-LTC) and the CSM provide a theoretical overview which indicates that illness related stressors can lead to distress via process mechanisms (such as through beliefs about illness/symptoms and responses to illness/symptoms). In Chapter 2, physical symptoms were proposed as potential predictors of distress as symptoms/side effects are a significant part of the experience of taking hormone therapy medication. However, there is a paucity of mediation studies exploring these relationships.

Using qualitative methods can allow for in-depth analysis of experiences in relation to distress and help identify unexplored factors that might be involved in this relationship and pathway between symptoms and distress, to inform further mediation analysis. Exploring how and why symptoms/side effects are distressing may support theory and intervention development by providing further evidence for variables as well as content for targeted support for this population of breast cancer survivors.

This approach addressed PhD objective B, by collecting data from the patient perspective to understand what is distressing about taking hormone therapy and organically explore the symptom-distress relationship. As part of the sequential multi-methods methodology of this thesis, this study may provide useful hypotheses to test in mediation analysis of the symptom-distress pathway.

5.2 Background

Breast cancer survivors prescribed hormone therapy such as tamoxifen or aromatase inhibitors (AIs) not only have to manage general survivorship burdens such as the impact of frequent medical contact ending, uncertainty around the future and fears of cancer recurrence and ongoing physical and psychological symptoms (Burgess et al., 2005; Lethborg et al., 2000; Schreier et al., 2019; van den Beuken-van Everdingen et al., 2008), but also have to take a daily medication that comes with additional challenges. The effect of hormone therapy on the reduction or interference of oestrogen can have significant physical and psychological effects (Hunter et al., 2004). Specifically, women report menopausal symptoms such as hot flushes, night sweats, vaginal dryness, joint pain and stiffness, fatigue, and headaches (Fallowfield et al., 2004; Garreau et al., 2006; Whelan & Pritchard, 2006).

Distress is prevalent in breast cancer survivors and is associated with poor health outcomes such as lower quality of life, non-adherence to hormone therapy and increased personal and health care costs (DiMatteo & Haskard-Zolnierek, 2011; Fang & Schnoll, 2002; Moon et al., 2019b; Waller et al., 2013; Wong & Fielding, 2007). Distress is therefore a key factor that should be explored to improve patient outcomes and reduce healthcare utilisation costs. Symptoms such as pain, menopausal symptoms and fatigue have been found to be associated with distress (Andreu et al., 2022; Lambert et al., 2018; Moon et al., 2016; Syrowatka et al., 2017), however quantitative studies are limited in their ability to explore the underlying reasons for and nuances of distress. Qualitative research provides a framework to explore the experiences of breast cancer survivorship in more detail as well as to understand *why* these experiences are distressing, informing intervention development.

Previous qualitative research with women prescribed hormone therapy has had a relatively narrow focus primarily exploring barriers and facilitators to adherence, distressing symptoms perceived as medication side effects and the impact of these on adherence, and strategies to manage symptoms (Harrow et al., 2014; Ibrar et al., 2022; Jacobs et al., 2020; Wen et al., 2017). A thematic synthesis of 16 qualitative studies identified themes related to the daily impact of side effects, the role of health care professionals in preparing women for side effects and supporting adherence, strategies to manage side effects and the impact on adherence and weighing up pros and cons of taking hormone therapy (Peddie et al., 2021). Although revealing important aspects of side effects and hormone therapy, this qualitative synthesis focused on how these aspects relate to medication taking and fails to acknowledge and explore the distressing experience that has been highlighted in previous quantitative research.

Where some qualitative studies have identified themes around side effects being distressing (Jacobs et al., 2020), the content does not indicate *why* these symptoms are distressing, and relates the experiences back to the influence on medication adherence, rather than recognising distress as an important outcome in its own right. It is particularly important to focus on distress as well as adherence, as some women will persist with taking the medication despite experiencing side effects. These women may continue to experience side effects and therefore continue to experience distress. This may therefore lead to lower quality of life (Moon et al., 2016) and increased healthcare utilisation (Waller et al., 2013) which is overlooked due to favourable behavioural outcomes. As the nature of hormone therapy means that symptoms are likely to persist, identifying *why* symptoms are distressing will help identify targets for future interventions to help manage distress alongside encouraging long-term adherence and providing evidence for an outcome that has been relatively poorly understood thus far.

Theoretical approaches can give some insight to the broader impact of distress in illness. The transdiagnostic model of adjustment to long term conditions including cancer survivorship, (TMA-LTC; Carroll et al., 2022) which draws on the common sense model of illness (CSM; Leventhal, Diefenbach, & Leventhal, 1992) explains that ongoing physical health stressors can disrupt a person's emotional equilibrium which can in turn impact adjustment to an illness, resulting in distress. Although this current study does not test a particular model, these theories suggest *how* and *why* illness may be distressing but has not yet been appropriately explored in women with breast cancer prescribed hormone therapy.

The overall aim of the present study was to explore the distress breast cancer survivors on hormone therapy experience with the following research question: why are physical symptoms/side effects distressing for early-stage HR+ breast cancer survivors?

5.3 Materials and methods

5.3.1 Study design

Semi-structured interviews with open questions were used to allow for an open discussion exploring experiences of distress in women on hormone therapy. Due to the COVID-19 pandemic, recruitment and interviews were conducted online through video conferencing software. A critical realist approach was adopted as this aims to report on experiences of the participants as real and true to them, not as a direct reflection but interpreted and acknowledged to inform further understanding of the data (Willig, 2013). A sample of 20-30 was estimated *a priori* to be adequate using general standards of qualitative interview analysis (Sim et al., 2018). Using the concept of information power (Malterud, Siersma, & Guassora, 2016) a sample size on the lower-to-mid end of the original estimation was determined to be sufficient as although the research question was broad and an inductive approach taken, the population was specific and the researchers were experienced in qualitative methods.

5.3.2 Participants and procedure

Breast cancer survivors were eligible for the study if they were over 18, lived in the UK, had a diagnosis of female stage I-III breast cancer and had been prescribed hormone therapy in the last two years. Ethical approval was granted by King's College London Psychiatry, Nursing and Midwifery Research Ethics Committee HR-19/20-18770 and informed consent was obtained from all participants (see Appendix B1 for ethical approval, participant

information sheet and consent form). Study adverts were posted on social media including Facebook, Instagram and Twitter as well as a university research recruitment circular. Gatekeepers of relevant charities were also contacted to share the study information. After consenting, eligible participants completed a short demographics and clinical factors questionnaire for purposive sampling (age, ethnicity, relationship status, diagnosis, treatment; see Appendix B2). Thirty-two eligible women were approached to arrange an interview with author SF or MR using Microsoft Teams. Eight women did not respond to the email to arrange an interview and one woman had a delay in starting hormone therapy so therefore was not eligible, leaving a sample of 23 women. Informed consent was confirmed over Teams and participants were fully debriefed. Interviews were conducted between October 2020 and July 2021. The interview schedule was reviewed by a patient advisory group as well as an experienced clinical psychologist (see Appendix B3 for interview schedule). Interviews were recorded, securely stored, transcribed verbatim using the Microsoft Teams software and checked for accuracy. The mean duration of interviews was just under 1 hour (57.53mins, SD 14.36, range 30mins to 89mins). A reflexive diary was kept throughout.

5.3.3 Data analysis

The interviews were analysed using inductive reflexive thematic analysis (Braun & Clarke, 2006, 2019). Reflexive thematic analysis is a theoretically flexible approach and emphasises the researcher as active in the analysis of the data (Braun & Clarke, 2019). This approach allows an in-depth exploration of the interviewee's experiences and perceptions from a data driven perspective rather than having a predefined theory or framework and acknowledges the interplay between the data, the researcher, the research question and environment and

therefore particularly suits an open purpose (Braun & Clarke, 2023). The researcher's influence when interpreting the data is considered in the reflexive report (see Section 5.3.4).

Braun and Clarke's six stages for reflexive thematic analysis were followed (see Table 5.1., Braun & Clarke, 2006, 2019). The process was iterative; moving between coding and theme generation (Braun & Clarke, 2019). NVivo 12 (QSR International Pty Ltd., 2018) was used to store and organise codes.

Table 5.1.

Phases of reflexive thematic analysis

Phase of analysis	Details from this study
Familiarising with the data	Author SF listened to all audio recordings, checked transcripts and made initial familiarisation notes.
Generating initial codes	Using NVivo 12 (QSR International Pty Ltd., 2018) author SF generated initial codes based on semantic explicit meaning. A second round of coding was completed grouping and combining codes and creating more latent, interpretive codes. The codes were discussed with the other authors and in line with the reflexive thematic analysis approach, the research question was refined.
Generating initial themes	Initial themes and subthemes were generated based on overarching concepts, shared meaning and patterns in data, rather than topics (Braun & Clarke, 2019).
Reviewing themes	Themes were then reviewed and discussed with the authors, who all have background knowledge of this area, and developed and refined multiple times using multiple thematic maps before naming final themes and subthemes.
Defining and naming themes	
Producing the report	Relevant quotes chosen and analysis related back to the research question and literature.

Some of the included quotes were edited to remove repetitions and […] indicates a skip to later content, when meaning and content is congruent. In terms of quality assessment, in line with guidance for reflexive thematic analysis, themes were conceptualised as containing

shared meaning rather than shared topics, developed through the researchers' involvement and codes were developed through ongoing interpretation and involvement with the data. Although Braun and Clarke (Braun & Clarke, 2023) recommend best practice for thematic analysis away from standardised measures, this paper reports in line with their best practice guidelines as well as generic Standards for Reporting Qualitative Research (SQRQ; O'Brien et al., 2014).

5.3.4 Reflexivity

As an insider researcher, I (SF) have prior knowledge of the experiences of women taking hormone therapy which guided the development of the research question. I made sure to develop a very open interview schedule, that although covered distress, made no assumptions about these experiences. Having this prior knowledge and understanding helped to create a good rapport with the participants, although with respect to the lived experience I am very much an outsider as I do not have personal experience of breast cancer or hormone therapy. The insider knowledge allowed participants to feel comfortable and open with their discussions and it meant the participants knew they didn't have to explain concepts in too much detail and rather respond to the questions asked. I am also female and think that helped with discussions of more intimate topics. I took a curious and interested approach. The other interviewer had a complimentary approach, as even though they were less familiar with the area, they received extensive interview training and used conversational prompts to help build rapport.

5.4 Results

Twenty-three women with a mean age of 52.57 (SD 10.94) were interviewed. See Table 5.2 for aggregate demographic and clinical characteristics. The mean time women were on

hormone therapy was 9.34 months (SD 7.45). Seventy-eight per cent were White British, and eleven were currently prescribed AIs, whilst 12 were currently taking tamoxifen.

Table 5.2.

Participant demographic and clinical characteristics

	Aggregate *n*=23
Age (M, SD, range)	52.57 (10.94; 33-81)
Ethnicity (*n*)	
White British	18
Other White background	3
Black Caribbean	1
Indian	1
Marital status (*n*)	
Married or in a civil partnership	17
Single or co-habiting	4
Separated/divorced	1
Widowed	1
Stage at diagnosis (*n*)	
Stage I	10
Stage II	8
Stage III	5
Current hormone therapy (*n*)	
Tamoxifen	12
Aromatase Inhibitors:	
Letrozole	5
Exemestane	2
Anastrozole	4
Months on hormone therapy (M, SD, range)	9.34 (7.45; 0.25-27)

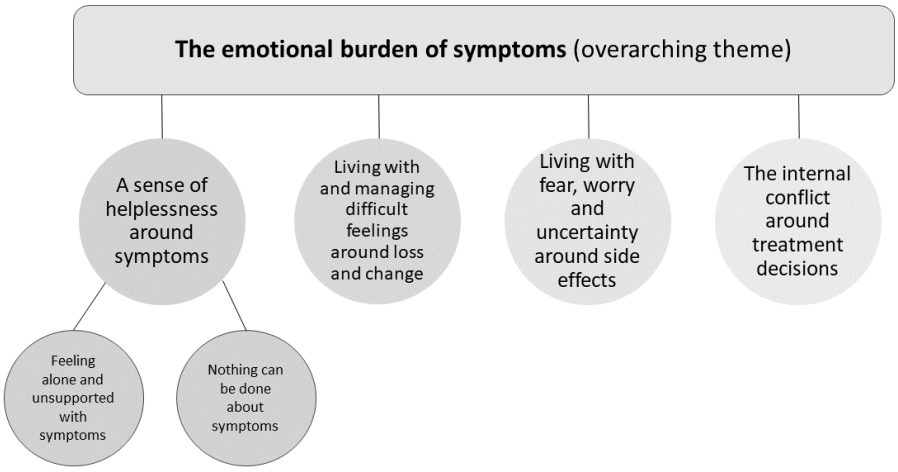
Note: M = mean, SD = standard deviation

Figure 5.1 displays the four themes and two subthemes generated from the data. Throughout the interviews, emotions were expressed in conjunction with symptom experience, which is highlighted as an overarching theme, *the emotional burden of symptoms.* However, experiences went beyond simply identifying the emotional experience of symptoms alone, and the remaining themes detail why symptoms are distressing for

women on hormone therapy. These include a *sense of helplessness around symptoms; living with and managing difficult feelings around loss and change; living with fear, worry and uncertainty around side effects;* and *internal conflict around treatment decisions.* These themes will be discussed with participant quotes (additional quotes for themes are available in Appendix B4 and a paper trail extract is available in Appendix B5).

Figure 5.1.

Thematic map



5.4.1 Overarching theme: The emotional burden of symptoms

Table 5.3 provides quotes to demonstrate and give context to the range of emotions and emotional language used to describe symptoms experienced whilst on hormone therapy, including low mood, frustration and anger. These were directly related to the experience of symptoms and described by most women regardless of their time on or type of therapy. For further context, the full range of symptoms that the women reported experiencing are also displayed in Table 5.4. Symptoms were perceived to be side effects of hormone therapy, so the terms have been used interchangeably throughout the results.

Table 5.3.

The emotional burden of symptoms quotes

*'I think **annoyance and frustration**, because even on the tamoxifen I do find I have a lot of joint pain which I didn't have before.' P20, 75, anastrozole then tamoxifen*
*'It's (sweats) horrible, it's really **horrible** […] When the hot sweats come. I think that's when, you know you think to yourself oh my God and then the **anger**, sometimes **naggy**. Really naggy, you know, and I'm like, oh why is it me and I'm sitting there sweating.' P15, 51, tamoxifen*
*'I mean I was relatively fit so it's you know, kind of it shouldn't have ached that much, you know. But yeah it, it was **horrid**.' P7, 64, anastrozole then exemestane*
*'And then you're obviously put into this accelerated menopause. So that was my **hardest** bit.' P1, 46, tamoxifen*
*'Pretty, pretty **rotten** really.' P12, 49, letrozole and goserelin*
*'So I'd say those are the **distressing** parts that the symptoms that come with taking tamoxifen is what really can take you down. I went through a period of really **low mood**.' P8, 49, tamoxifen*
*'Now, whether it was the hormone therapy's impact on my mood, or whether it was just the fact that you know my hands were getting stiffer and stiffer and stiffer and clickier by the day that was having an impact on my mood, I don't know […] But what I do find quite **galling** is it is the pain in the stiffness in the joints that is really quite um, can be quite acute at times.' P16, 47, exemestane*
*'I think I put on about half stone. Um? Since I started taking these hormone blockers, um, I'm not a very tall person. I'm only 5 foot two I think I put on half a stone when I started the menopause and then another half a stone and I thought this is, you know, this is **horrendous** […] Look putting the weight on is really **stressful**. Even though I didn't have chemotherapy, your hair thins, and all of the side effects are really **stressful**.' P11, 53, anastrozole then letrozole*
*'I had, you know I think having the sleep disruption is it's really **not fun**.' P13, 51, tamoxifen*
*'And the side effects are very very **stressful**. And I think they make you feel quite **depressed** because it just becomes **self-consuming** if you just think about them all the time.' P11, 53, anastrozole then letrozole*

Note: words related to distress/emotion are in bold font

Some women, although reporting symptoms, said their time on hormone therapy had *'not been a terribly difficult experience' (P22, 49, tamoxifen)* and that symptoms were *'manageable'*. Older age appeared to be a possible protective factor for menopausal symptoms such as hot flushes and vaginal dryness not being distressing. Another described that '*none of these problems are huge in and of themselves, but I think the distress comes from the cumulative effect of having a lot of little things' (P16, 47, exemestane)*.

Table 5.4.

Symptoms reported during the interviews

Side effect/symptom reported	*n*
Joint pain, aches, bone pain	15
Hot flushes and/or night sweats	14
Low mood	12
Insomnia and/or sleep difficulties	10
Fatigue and/or brain fog	10
Weight gain	4
Vaginal/sex issues	4
Headaches or migraines	4
Nausea on zoladex injection	1
Dizziness	1
High blood pressure	1
Bladder urgency	1

5.4.2 Theme 1: A sense of helplessness around symptoms

There was a sense of helplessness around symptoms whereby not only did women feel a lack of understanding and support around symptoms, but also felt that nothing could be done about those symptoms.

5.4.2.1 Sub theme 1.1: Feeling alone and unsupported with symptoms

Women described a heightened sense of feeling alone and unsupported after primary treatment as, in addition to the challenges of completing treatment such as surgery, chemotherapy or radiotherapy, they are being '*left with this box of tamoxifen*' which was *'more distressing' (P5, 39, tamoxifen)*.

Women described feeling unsupported by both family and friends, and healthcare professionals in terms of understanding the symptoms experienced, and the impact of these. Women felt that because their difficult side effects were not visible there was a lack of understanding from loved ones and other people. One woman described how her *'family laughs at me because they think I'm making it up' (P12, 49, letrozole and goserelin)* suggesting support and understanding may be limited.

> *And I just thinking I'm not OK though, I don't feel OK, I know I look OK but I don't feel OK.* P15, 51, tamoxifen

Women felt invalidated and '*discounted'* when oncologists seemed to *'shrug'* off their concerns *(P8, 49, tamoxifen)* or attributed symptoms to other causes which leaves women feeling they have a lot to learn themselves, and that the impact is not understood. On the other hand, women who felt listened to and were told that side effects and symptoms were normal, appreciated the validation, reassurance, and knowledge. This reassurance came from different sources such as breast care nurses, social support online groups, and personal research. One participant explained how breast cancer nurses reassured them that side effects are normal, giving them '*the ability to kind of go OK, it is what it is' (P22, 49, tamoxifen*). Another participant explained how seeing others' experiences through Facebook was reassuring '*to know that other people are going through the same thing' (P14, 45, anastrozole and goserelin).*

Some women wondered if the sense of feeling unsupported was related to the COVID-19 pandemic preventing access to support that they felt they could have benefited from, including seeing more people in clinics and more nurses. Some charities withdrew their face-to-face services during the height of the COVID-19 lockdown and women found it *'difficult to ask for things over the phone' (P14, 45, anastrozole and goserelin).* However, it seems that even those who initiated treatment before the COVID-19 pandemic still felt unsupported and alone and therefore this does not appear to be specific to the COVID-19 pandemic changes.

5.4.2.2 Sub theme 1.2: Nothing can be done about symptoms

There was a sense of helplessness that nothing can be done about side effects or symptoms; therefore, women just had to deal with, live with or suffer with them.

> *So it's a lot of, there's not a lot of help out there, you just kind of have to suffer it really. That's the only way, It's a shame.* P19, 43, tamoxifen and goserelin

One participant explained that you can't make actual symptoms better or worse, rather things improve by learning to cope with them.

Even when there is medication available to help manage symptoms and side effects, women reported *'most of the things that you can do to manage it, they say you can't have' (P1, 46, tamoxifen).* Some women were reluctant to take further medication or treatment to manage side effects of their hormone therapy in addition to the hormone therapy medication they are already taking.

In relation to this sense that there is nothing that can be done about symptoms and people must suffer it, some women felt there is no option but to be on hormone therapy itself as it is the *'blue ribbon treatment' (P11, 53).* For some, there was a desire for it to *'be a choice*

rather than a necessity' (P3, 33) as those who felt they had a choice or option to stop taking hormone therapy for a period of time or change medication, felt having this sense of control, helped their distress around symptoms.

> *Just knowing that that option was there, I think in some ways gave me something to focus on and to make a decision about rather than feeling hopeless.* P12, 49, letrozole and goserelin

5.4.3 Theme 2: Living with and managing difficult feelings around loss and change

Difficult symptoms were described in conjunction with limitations to lifestyle and losses. Women used strong emotional language to describe *'not being able to do the things I could before'* and dealing with *'loss'* to parts of their lives *(P14, 45, anastrozole and goserelin).*

> *And no you can't pick that up when you can't do this hobby and duh duh duh. It's death by all of these things* P16, 47, exemestane

Due to these limitations, one woman felt her body was '*less resilient*' which then made it harder to cope with change *(P11, 53, anastrozole then letrozole)*.

A specific area of loss which was unexpected and difficult to manage, was related to vaginal dryness and the impact of this on their sex lives. This *'loss' (P18, 48, tamoxifen)* of an important area of their lives was something they never thought they would have to deal with and *'had no idea of the impact' (P23, 49, letrozole)*.

In addition, women reported challenging disruptions to their sense of self whilst taking hormone therapy. Women referred to the physical impact of pain meaning they feel they have *'aged about 20 years' (P20, 75, anastrozole then tamoxifen)*. Women felt too young to be going through the menopause and this was described in conjunction with feelings of sadness and low mood.

> *I feel too young to be having them, so it does, it does get me down quite a lot.* P19, 43, tamoxifen and goserelin

Additionally, women commented on how these changes '*zaps some vitality for life out of you' (P11, 53, anastrozole then letrozole)* and felt that their personality and identity was being *'chipped'* away.

> *You know that your sense of self and your identity is just. It's just being chipped at you know it's had a couple of great big fucking knocks taken out of it and then it's like oh we're just gonna chipping and keep chipping.* P16, 47, exemestane

Another specific change to sense of identity was how women now felt like someone with health issues on medication when they hadn't ever taken medication before.

Women reported feelings of uncertainty around whether they would ever feel normal again. One respondent disliked the term 'new normal' that is often used after primary treatment and felt that it being described in this way implies *'you'll get back to your normal, it'll just feel different*' whereas it is actually *'abnormal'* as you '*don't ever really get a chance to feel like yourself again' (P16, 47, exemestane).*

Some women reported that life wasn't *'awful'* but *'that comes down to adapting' (P23, 49, letrozole)* to these changes and dealing with this loss. However, learning to adapt and live differently can take time:

> *It's* [physical problems] *kind of there all the time so you learn to live differently.* P21, 54, anastrozole

Managing and coping with these difficulties was done in different ways. Firstly, practical strategies were used such as *'managing my diary very carefully and I absolutely have to factor in rest time […] to just sort of function and cope' (P23, 49, letrozole).* However, accessing practical aids to manage and adapt to symptoms such as vaginal lubricants was

felt to be *'embarrassing' (P19, 43, tamoxifen and goserelin)*. One woman used practical devices to manage the impact of her symptoms however she described this as a frustrating and irritating thing to have to do, despite helping her manage:

> *As irritating as it is, I think actually some practical aids to just help take some of the difficulty out of life, I think that does help.* P16, 47, exemestane

Another strategy was a more psychological response, whereby this same participant described having to complete self-talk to not be so *'vain'* and accept help whilst also having to lose attachment to what they used to have and having to have a gradual acceptance of their situation.

> *There is a sense in which you, you lose attachment to what you used to have and there is that gradual acceptance of the fact that OK, do you know what you're, you are below par and you may never get back to the par you had, but you can adapt and you can adjust.* P16, 47, exemestane

Despite acceptance being mentioned, another participant was aware they couldn't accept their limitations:

> *I think I haven't quite accepted my limitations, and I'm not sure that I ever will if I'm honest.* P19, 43, tamoxifen and goserelin

Others described having to just *'deal with'* limitations and *'just get on with'* life *(P17, 44, anastrozole)*. They described trying to *'do things differently rather than focusing on what I can't do' (P14, 45, anastrozole and goserelin)* which involved adapting, for example; '*if you can't do your exact hobby, find a near enough or a good enough alternative' (P16, 47, exemestane).*

5.4.4 Theme 3: Living with fear, worry and uncertainty around side effects

Women reported a range of unknown and unexpected aspects related to being on hormone therapy, which resulted in fear, worry and uncertainty. Some women reported being very *'apprehensive' (P5, 39, tamoxifen)* and *'wary' (P13, 51, tamoxifen)* when first prescribed hormone therapy, particularly with reference to what they had heard about potential side effects. In addition, women initially thought side effects would be manageable, so the actual impact of the distressing symptoms was unexpected.

One woman mentioned physical symptoms persisting *'for longer than I realized that they would' (P22, 49, tamoxifen)* and other women felt the thought of experiencing side effects for a long time was unnerving, frustrating and worrying.

> *Letrozole for 10 years and it was just seemed I just didn't think I was going to be able to cope with it. It's just unbearable*. P12, 49, letrozole and goserelin

Some women worried the side effects could actually get worse, especially the impact that this could have on their lives.

> *It seems that joint pain might be an issue later on, and that's something which I'm quite worried about because of again, that's going to stop me doing the things I want to do and being active and everything, yeah (sighs).* P3, 33, tamoxifen

Another element of uncertainty was women questioning whether they would have experienced similar symptoms of a normal menopause.

> *I mean what's hard to know is if I'd gone through the menopause, would I just be experiencing very similar things to this and is it just that I'm going through an accelerated menopause?* P1, 46, tamoxifen

One participant described the experience of symptoms leads to worries and concerns of future medical conditions.

> *I remembered almost worrying and thinking, oh my gosh, could I get dementia from this drug because of the, you know the brain fog and the concentration being able to concentrate. Yeah, those things are distressing and worrying.* P8, 49, tamoxifen

Finally, some women reported fears around changing their hormone therapy and having worse side effects on an alternative medication – particularly changing from tamoxifen to AI's. When suggested she could change from tamoxifen to AI's to manage bone pain side effects, one participant expressed their concern that they could experience *'worse bone pain'* and felt it wouldn't be *'a very good idea'* (*P1, 46, tamoxifen).*

Despite the uncertainty, some women were hopeful that things might improve, especially those who had only recently started taking their medication.

> *But I'm hoping I'm just to get them for a few months with any luck.* P9, 63, anastrozole

5.4.5 Theme 4: The internal conflict around treatment decisions

Women reported an internal conflict as they weighed up whether taking hormone therapy was the right decision for them. This included the conflict between quantity vs quality of life, which women related to the experience of the difficult side effects versus the reduced risk of recurrence.

> *I'm still young. I still got children. I've got everything to live for. And yet, it's a very difficult decision to make. Do I carry on with these horrific drugs and the side effects are indescribable sometimes? Or do I say you know what I want to have quality of life, but at 54, I need both. I don't just want quality of life. I want to be around […].* P11, 53, letrozole

This internal conflict also includes struggles with questioning decisions to switch between AIs and tamoxifen. One participant's oncologist suggested changing medication which left them weighing up different symptoms over others and the potential increase in risk of recurrence. Some women felt that they didn't have the knowledge or information to make an informed personal decision about being on hormone therapy which contributed to this internal conflict. After discussions with their oncologist, one woman reported she felt the recurrence rates were not sufficient to justify the treatment and chose not to take hormone therapy initially *(P6, 56, tamoxifen)*.

Questioning decisions to stay on hormone therapy was ongoing, with some women reporting a taste of normality and improved side effects when taking a break from their medication. However, this added to the difficulties with decision making, with women stating that hearing others miss tablets and taking *'tamoxifen holidays'* made them consider changing things and questioning things as they were *'starting to feel normal again' (P4, 57, letrozole, exemestane then tamoxifen).*

It seemed that those reporting these conflicts felt a struggle, whereas other women reported a more positive focus and seemed to experience less struggle and conflict. Some women thought of hormone therapy as '*a pretty good alternative*' *(P18, 48, tamoxifen)* to a recurrence or even *'better than dying'* (*P12, 49, letrozole and goserelin*). They felt it gives them '*less chance of it [cancer] returning*' *(P3, 33, tamoxifen)* and felt this was a good thing that gives them hope. Women felt managing side effects were therefore a *'small price to pay' (P19, 43, tamoxifen, Goserelin)*. Women reported that taking hormone therapy and going through treatment *'affords you a life to live'* and means they are around for family and *'still here as a friend' (P2, 63, letrozole)*. However, women used quite strong terminology to

describe coping with and managing this internal conflict. One participant said, '*I'm trying my hardest to accept' (P3, 33, tamoxifen)* to imply that this shift of focus or reframing was a cognitive effort to try and think about taking hormone therapy and symptoms in a different way. A sense of self-imposed pressure and a forceful nature was also interpreted from the data.

> *You have to be quite strong-minded* P11, 53, letrozole
>
> *I just think well suck it up it's, it's better than alternative.* P19, 43, tamoxifen and Goserelin

5.5 Discussion

The current study provides a detailed insight into the distress experienced whilst on hormone therapy for early-stage breast cancer survivors, from the perspectives of this population. In line with previous literature (e.g., Rosedale & Fu, 2010) and the research-based and theoretically-driven hypotheses, the majority of women described the emotional burden and distressing nature of symptoms and side effects themselves which was the overarching theme throughout this study. However, the current analysis went beyond that of previous literature by describing the in-depth emotional impact of the side effects associated with being on hormone therapy and exploring the nuances of *why* physical symptoms are distressing for these women. The study has identified that it is not just the presence of the symptoms, but the impact, burden and disruption to daily lives of these symptoms that may lead to distress. This is important to consider when selecting suitable measures for testing these hypotheses quantitively, as some studies report the number of or severity of symptoms (e.g., Jim et al., 2007) rather than the burden.

The end of primary treatment is well documented to be a difficult time for people with cancer when frequent medical contact ends, alongside an expectation to get back to normal pre-cancer life (Powers, Gullifer, & Shaw, 2016). This study has highlighted the extra dimension to survivorship for those on hormone therapy, of the impact of physical symptoms associated with the medication and why they are distressing. The first theme highlighted that there is a strong sense that women feel they have been left on their own to self-manage hormone therapy and the additional experience of side effects, with limited support and knowledge from health care professionals. This study found feeling unsupported left women feeling helpless and that nothing can be done about symptoms.

Although feelings of being unsupported by health care professionals is reported across the literature (Peddie et al., 2021), this is often described in terms of lack of advice, information and being listened to with regards to side effects which then influences adherence to the medication. The women in the current study felt the lack of information made them question whether their experience was normal and felt unheard, not understood, and therefore invalidated for their experiences. Although previous literature links these experiences to decisions to stop taking medication, this present study highlights that these experiences may also lead to distress as well. As hormone therapy is prescribed for up to ten years, women may continue to feel unsupported and helpless throughout this period of time, regardless of whether or not they are adherent. Interestingly, individuals who felt they had the option to change medication reported that having this choice available helped them to cope, as they felt in control of their own decisions. Awareness of available medication options may help individuals feel a sense of control of their situation and help mitigate the experience of symptoms leading to distress. However, some women reported fears and concerns around unknown side effects from changing to a different medication, so if the

option is made available or a decision is made to change, these options will need to be provided alongside clear expectations. In addition, individuals felt limited support and understanding from their family, friends or loved ones as well which may be partly due to the invisibility of symptoms. Women often reported finding support through social media and from others who were going through the same experiences which helped with validating and normalising experiences. Previous research has reported this before in the context of adherence (Peddie et al., 2021), but it is also evident in the context of managing symptoms and distress as demonstrated in the present study.

There was also a sense of helplessness around what to do about symptoms. Previous literature has highlighted a lack of self-management options for side effects (Hall et al., 2022), however the women in this study felt a sense of helplessness about this, feeling they need to suffer with them. This finding further supports the exploration of why symptoms might lead to distress. Rather than directly targeting management of symptoms, interventions could target self-efficacy in managing symptoms (Hoffman, 2013) or coping with experience of symptoms which might be beneficial for mental health outcomes by alleviating some of the distress expressed about lack of control and helplessness.

A separate theme around uncertainty and worry around symptoms describes worries and uncertainty continuing throughout survivorship with regards to side effects getting worse in the future and going on for longer than expected which they felt could have longer detrimental health impacts. Feeling unprepared and experiencing surprising side effects has been reported previously as these factors are related to an individual's decision to stop taking their medication (Peddie et al., 2021). However, this current study highlights the ongoing nature of these feelings, with an emphasis on the different distressing thoughts

associated with this such as the fear of the unknown and concerns about changing medications leading to experiencing different or worse symptoms. This may link to the feeling of being unsupported as some of these expectations and information giving could be provided in more detail in health care professional interactions, relieving some of the worry and concern.

Previous research reports the daily impact of symptoms and how this leads to non-adherence through the impact to quality of life and someone's social life (e.g., Clancy et al., 2020; Lambert et al., 2018). This current study highlights specific psychological and emotional impact from experiencing symptoms whereby women reported feelings of loss with their sense of self changing and feeling older than they should because of pain and stiffness. Women often reported feeling helpless and resigning to these outcomes. Others reported frustration and embarrassment with the physical changes and having to adapt to them. Accepting limitations or persisting with difficulties was challenging as some could not see past their limitations. In previous literature women have reported struggling with reintegrating into their pre-cancer lives (Costanzo et al., 2007), and in this study women also identified that the often-public narrative around the 'new normal' was not helpful as the continued physical and psychological changes from continuing hormone therapy are very different experiences to how the women were before the diagnosis. It may be that psychological support could help promote acceptance to help women cope with the impact of the symptoms and help come to terms with the distressing concepts of loss and change.

Although previous research has commonly identified themes around weighing up the pros (reduction in risk of recurrence) and cons (side effects impacting quality of life) of taking hormone therapy this is usually linked to the outcome of treatment adherence (Ibrar et al.,

2022; Moon et al., 2017c). The current study highlights that the actual process of this decision making is a burden and an ongoing source of distress and internal conflict for women on hormone therapy, which is an important consideration. Those who tried to shift to a more positive stance about taking hormone therapy, described this as requiring cognitive effort with a sense of self-imposed pressure to take the medication and having to endure symptoms to be around for their family. Several studies in the qualitative review (Peddie et al., 2021) reported feeling an obligation or duty to continue taking medication. This could be a challenging concept to come to terms with whilst being adherent. It may be that individuals also need support with accepting the decision they make regarding hormone therapy to help manage the ongoing difficult thoughts around this.

The data also support the theories described in the introduction and other chapters in this thesis that propose the ongoing physical health stressors of illness disrupt a person's emotional equilibrium, impacting their adjustment. Although an inductive approach to the analysis was taken, some of the themes and experiences fit with psychological approaches which may guide clinical support and future intervention development. Although not tested quantitatively, participants reported these psychological processes in relation to symptoms, and were talked about in conjunction with distress and other outcomes. This provides rich patient data to additionally support the theory-driven hypotheses from the TMA-LTC and CSM that symptoms lead to distress via psychological processes. Acceptance and the relationship to the self were discussed by participants, providing further justification for exploring the ACT model in this population as these are related to the flexible processes of the model. These processes were discussed as part of the open interview schedule, demonstrating that these were concepts that the participants naturally associated with, rather than being directed through structured questioning, further supporting the inclusion

of these models in future research. These findings also support the results from the systematic review in Chapter 4 that acceptance and self-as-context could be important processes to consider as they were discussed by participants alongside distress.

Although not a specific aim of the qualitative study, there seemed to be no differences between the distress experienced from those taking AIs compared to those on tamoxifen. A range of quotes from women on different medications contributed to the themes. This distinction is often not explored in qualitative research (e.g., Clancy et al., 2020; Lambert et al., 2018; Peddie et al., 2021), but quantitative research suggests that there are no differences in the magnitude of emotional distress between the two types (Ates et al., 2016). This is despite research suggesting that menopausal symptoms are more common for those on tamoxifen, whilst joint pain is more common with AIs, due to the different medications' impact on oestrogen (Garreau et al., 2006; Morales et al., 2004). If experiences are common between those on tamoxifen and AI's, this provides opportunities to inform clinical practice and interventions to treat women on either medication. This would be particularly useful as switching between the different types of hormone therapy is common whether due to side effects or menopausal status change (Kwan et al., 2017), meaning a potential intervention would be transferable through the switching process.

Overall, the themes presented provide an indication of *why* symptoms are distressing for this population of breast cancer survivors. The participants discussed the themes around hormone therapy and symptoms presented in relation to them feeling unhappy, sad and distressed, rather than in relation to stopping medication. Focusing on the facilitators and barriers to adherence as the existing body of research has done, may miss this important outcome, particularly if the outcome of adherence is the main goal and the continued

experience of taking hormone therapy is ignored. For example, those who are adherent may keep experiencing side effects and therefore distress. In addition, those who stop taking medication, may still experience physical symptoms from previous treatment but also the ongoing conflict of the decision of whether to continue the medication. Therefore, this study has provided a unique focus towards the outcome of distress and how physical symptoms, or side effects of hormone therapy may lead to distress. Highlighting distress as a meaningful outcome in this population is important, given its potential cost-related and personal implications (Fang & Schnoll, 2002; Waller et al., 2013).

5.5.1 Clinical implications and future directions

Although previous research identifies that communication around hormone therapy initiation could be improved, for example by providing more information about side effect expectations (e.g., Clancy et al., 2020; Lambert et al., 2018), this study highlights some specific opportunities for addressing additional concerns whilst on hormone therapy. Women felt alone, with a sense of helplessness around symptoms. Knowing this information can help guide clinical communication as a more empathetic approach is needed. This will provide emotional support for the wide range of distressing symptoms and the ongoing burden of the decision to persist with hormone therapy. It will also ensure information is conveyed in a meaningful way, rather than just providing more information about symptoms. Interactions should empathise and validate, acknowledge and normalise experiences and the potential length of experiencing side effects, as this may help prevent the sense of abandonment, helplessness and uncertainty. It has been previously reported in the literature that poor trust, poor communication, poor perceived empathy from healthcare professionals and lack of discussing emotional concerns can lead to worse outcomes, particularly in women from minority ethnic backgrounds (Moon et al., 2020;

Tompkins et al., 2016). In other literature, trust in health care professional relationships is associated with better outcomes (e.g., Birkhäuer et al., 2017), so the impact of these interactions should be tested in future research. However, patients are often discharged from frequent medical support after their hormone therapy initiation appointment, which highlights an opportunity for self-management support interventions to address these sources of emotional difficulties. Digital self-management interventions have the potential to be cost-effective, accessible and tailorable to participants' needs (Ebert et al., 2018; Krebs, Prochaska, & Rossi, 2010).

A traditional cognitive behavioural approach may be beneficial for altering or reframing any difficult thoughts such as catastrophic or black and white thinking around potential future side effects or issues. The themes presented have some links to the CSM illness perceptions such as control whereby participants reporting a sense of control when provided with the option to change or stop medication. In addition, being given more information about treatment may relate to treatment coherence, however understanding of treatment wasn't explicitly mentioned, rather around expectations of treatment and side effects. Whilst a more third wave cognitive behavioural approach such as ACT, promoting more flexible, accepting and compassionate responses, may be more appropriate for the experiences around losing attachment to a previous sense of self and accepting loss of ability and physical limitations and decisions to be on hormone therapy. Addressing these factors could improve emotional burden, decrease distress and therefore improve quality of life, as has been found in other cancer samples and in long term conditions (Graham et al., 2016). These will be useful to be tested quantitatively to provide further support for the use of these models in understanding symptoms and distress and therefore inform interventions. As explained in Chapter 2, distress has been found to be associated with non-adherence to

medication as well as having potential important negative clinical outcomes (Fang & Schnoll, 2002; Winn & Dusetzina, 2016). Treating distress therefore has the potential to improve medication adherence, reduce cancer recurrence and reduce healthcare costs (DiMatteo & Haskard-Zolnierek, 2011; Early Breast Cancer Trialists' Collaborative Group, 2011; Moon et al., 2019b; Waller et al., 2013).

Differences of experiences have implications for future support. Stage of life was a potential protective factor as older women mentioned being less emotionally distressed, particularly by menopausal symptoms. Younger women may need increased support to manage symptoms and their associated impacts such as reduced vitality, sexual difficulties and stiffness. Other than differences in symptoms experienced, there was no clear pattern of differences between the emotional experiences of women on tamoxifen and AIs which supports quantitative research finding no differences in distress between these groups (Ates et al., 2016). It may be that the collective experience of managing the helplessness, change and loss linked to the symptoms and the ongoing decision making, is where the distress is coming from. Future communication and interventions could be the same for those on different medications, reducing costs and increasing accessibility by having one single intervention which addresses the underlying processes. Successful cognitive behavioural interventions have been developed for specific symptoms such as hot flushes and night sweats (Fenlon et al., 2020; Mann et al., 2012), but it may be that more support for the global burden of ongoing symptoms in survivorship is also important.

5.5.2 Strengths and limitations

There are several limitations to this current research. Firstly, people with distress may be less likely to respond to online research advertisements, however the current online sample

did appear to experience distress. Equally, it could be that those experiencing symptoms and greater distress were more likely to respond as an opportunity to share their experience. Despite this, there does appear to be variations in the symptoms reported and their associated impact, suggesting a varied sample. The sample only included those who had been on hormone therapy for around two years. Future research could focus on those continuing to take hormone therapy for longer as medication is prescribed for up to 10 years, to see if these emotional experiences continue after the first two years. Most women in the sample were of White ethnicity; however, as online methods were used, this allowed women to be able to be recruited from all over the UK to include different healthcare experiences.

The current research also has some key strengths. Using qualitative interviews bring richness to the data and provides in-depth patient perspectives which has enabled a deeper understanding of the experiences of hormone therapy that could not be explored in quantitative studies. The current study follows best practice recommendations for thematic analysis (Braun & Clarke, 2023). A critical realist approach was adopted in the study whereby a participant's experience is reported with researcher interpretation (Willig, 2013). Reflective thematic analysis fits with the critical realist approach as it allows in-depth exploration of the interviewer's experiences whilst acknowledging the role of the researcher in the interpretation of the data (Braun & Clarke, 2023). This method encourages researcher reflexivity throughout the analytic process. As described in the reflexivity section, I had pre-existing knowledge of experiences of this population and developed the research question. However, I aimed to structure the interview schedule very openly, taking an open and curious stance, and only exploring the relationship between symptoms and distress if this came up organically. The realist position entails that methods need to match the approach

to facilitate this understanding, which is why individual interviews were chosen. Building rapport with participants was important to enable truthful and non-judgemental discussion of participants' lives and allowed the participant to lead the conversation.

A further strength of the current study was the use of the concept of information power (Malterud, Siersma, & Guassora, 2016) over the concept of data saturation. Data saturation has been criticised and is incongruent with an inductive thematic analysis approach (Braun & Clarke, 2021). The concept that no new themes emerge does not consider the involvement of researcher interpretation in the construction of themes. Therefore, reaching the end of data collection will be based on the subjective experience of the researcher as there could always be potential for new insights to be interpreted (Braun & Clarke, 2021). For this study, a target of 20-30 interviews was estimated due to previous literature and sample sizes to provide some initial direction. However, the information power of the data was reflected on by considering the five areas proposed by Malterud, Siersma and Guassora (2016); study aim, sample specificity, established theory, quality of dialogue and analysis strategy. The research question was relatively broad, although still a specific part of the wider hormone therapy experience and the population was a specific group of breast cancer survivors, suggesting higher information power and therefore a smaller sample size. An inductive, non-theory driven approach was taken, however, strong dialogue was estimated due to the previous experience and knowledge of the researchers and as case analysis rather than cross-case analysis was the main focus, information power is assumed. As discussed in Chapter 3, qualitative research involves smaller sample sizes as the aim is to explore rather than generalise (Gelo, Braakmann, & Benetka, 2008). Hormone receptor positive breast cancer is more common in White women (Cui et al., 2014) and the majority of the current sample were of White ethnicity, so the data could be used to inform future

research that may be applicable to these women. However, further research would be useful to focus on breast cancer survivors from other ethnicities to ensure data informing research is applicable and relevant.

5.5.3 Secondary analysis of the data

Secondary deductive analysis was conducted on the interviews (Moxham et al., in prep; see Appendix B6), whereby the data were examined through the lens of ACT theory to understand experiences in relation to ACT processes which has not yet been explored in the literature. This study found examples of ACT processes in action, whereby individuals reported responses to thoughts and feelings in various flexible and inflexible ways. This not only provides useful data for developing interventions, but also confirms the universal assumption of ACT processes as these women had not received an intervention but were describing their experiences organically. ACT understands the processes in terms of whether they are workable or unworkable, for example, if someone was engaging in a process-based behaviour that is moving them in their valued direction, it would be considered workable (Dindo, Van Liew, & Arch, 2017). Generally, the inflexible processes are deemed unworkable potentially leading to distress or poorer outcomes, however they can also be considered workable if they are moving someone towards their values and therefore have more positive outcomes.

Experiential avoidance was interpreted in the data as being both a workable and unworkable process that in some situations helped 'control' thoughts which participants saw as beneficial, preventing them from spiralling into their negative thoughts. However, some women also described unworkable avoidance, whereby distracting themselves from thoughts, which is a form of avoidance, in turn led to more negative thoughts at nighttime.

This supports the results in Chapter 4 which highlighted that general experiential avoidance of thoughts and emotions was associated with distress. The secondary analysis on the qualitative data has drawn out some aspects of experiential avoidance that may be useful to understand in this specific context that is potentially lost in quantitative measures such as a more adaptive use of avoidance. This understanding may be important for interventions that focus on targeting experiential avoidance, as it may be necessary for participants to assess whether their avoidance is workable for them in their context first. This assessment is likely conducted during face-to-face psychology support but may be missed in digital or self-management interventions and therefore could be useful assessment to incorporate into self-management interventions.

In addition, in line with the systematic review presented in Chapter 4, certain processes were not brought up or well understood by participants which may be due to a difficulty of understanding and defining the processes. The concept of self-as-context for example is poorly understood and consists of several different aspects such as perspective taking and fusing with a self-story (Zettle et al., 2018) and may be why research has steered away from exploring this process. In the study presented in this chapter, the self was discussed whereby symptoms disrupted perceptions someone had of themselves which indicates a form of self-as-context. Whereas in the secondary analysis (Moxham et al., in prep), it was interpreted that some participants reported how others see them and how they see themselves in relation to the identity of a cancer patient. This is more of a perspective taking form of self-as-context as well as the self-stories someone might have about themselves. Additionally, it was interpreted through the analysis that some could step away from their experiences as a form of perspective taking, demonstrating the different concepts of self-as-context. These different elements of the self are insightful for content

development. Self-as-context is often not reported as a process used in ACT interventions (unpublished scoping review) potentially due to the reasons presented. Exploring these elements could provide useful avenues to include in interventions that have so far been missing.

5.5.4 Summary and conclusions

Women on hormone therapy experience distressing physical symptoms. This study contributes to the understanding of *why* these symptoms are distressing for this population of breast cancer survivors. This includes feelings of helplessness around symptoms and managing difficult feelings of loss and change. Understanding and managing the distress related to the side effects from taking hormone therapy provides clear targets to improve clinical communication in terms of expectations, validation and acknowledgement, and normalising and compassion which could help manage some of the uncertainty and worry experienced. In addition, the data provides information to contribute to intervention development to support these women. Third wave or more traditional cognitive behavioural approaches could be beneficial to help target some of these factors in future interventions. The secondary analysis (Moxham et al., in prep) has contributed to how third wave ACT processes may be used and understood in this population and therefore directly informs intervention content and other factors to consider. Improving outcomes can have implications for individual and systemic healthcare costs. In addition, there may be implications for patient outcomes both clinically in terms of adherence and recurrence risk, and psychologically in terms of reducing distress and improving quality of life for these women.

This study has enabled PhD objective B to be achieved and contributed to the overall aim of the thesis by uncovering rich data from the patient perspective about the experience of being on hormone therapy and the distressing nature of the medications' side effects. The results support the research presented in the thesis from the systematic review and meta-analysis, the previous research on CSM illness perceptions and the integrated theoretical models, as psychological processes were described from the data in relation to experiences of distress and symptoms. The combination of studies can contribute to the generation of testable hypotheses which will be explored and tested in the next chapter. Specifically, this study highlights psychological processes such as acceptance and self-beliefs which the CSM and ACT outline. Therefore, the processes of the models can be tested and compared to see how they predict distress in this particular population and to see how they may be involved in the relationship between symptoms and distress. The impact of symptoms, rather than just the presence of symptoms, was a strong theme throughout which can inform the measure used in the next study to cover symptom burden rather than just the number or severity of symptoms. As a wider implication of the two qualitative studies presented in this chapter, the detail provided can directly inform intervention content. Both studies provide direct experiences and examples that can be addressed and utilised in interventions to provide examples that directly relate to this population.

Chapter 6 Comparing acceptance and commitment therapy and the common-sense model of illness representation in explaining distress in breast cancer survivors on hormone therapy: A longitudinal study

6.1 Chapter overview

Chapters 4 and 5 have addressed the first two objectives of this PhD thesis to understand the associations of ACT processes and distress in cancer and to qualitatively explore why symptoms are distressing on hormone therapy for breast cancer survivors. Chapters 6 and 7 present the observational study to address PhD objective C. Chapter 6 has investigated the cognitive-behavioural processes including ACT processes associated with distress in this population. Chapter 7 investigated the mediators and moderators of the proposed key relationship between symptoms and distress. These two chapters cover the same study but due to the different aims, have been split to aid reading and interpretation.

6.2 Background

Distress is prevalent in breast cancer survivors with estimates of up to 49% for symptoms of anxiety and depression (Brandenbarg et al., 2019) and is an important patient reported outcome with potentially harmful implications (e.g., Winn & Dusetzina, 2016). Breast cancer survivors on hormone therapy face challenges as they contend with living with the medication's side effects in addition to the general survivorship experience. Symptoms/side effects of hormone therapy have been reported to have a severe impact on individuals' daily lives (Peddie et al., 2021) and may be one contributor of distress. Chapter 2 defined distress for this thesis as a negative emotional state often characterised by anxious and depressive

symptoms. In order to measure emotional distress that incorporates anxiety and depressive symptoms, the PHQ-ADS was chosen for the outcome measure in this study as this is a composite measure of emotional distress consisting of anxiety and depression measures (Kroenke et al., 2016). Previous literature has found inconclusive evidence for the socio-demographic and clinical factors that might predict distress in breast cancer (Syrowatka et al., 2017). However, younger age, not being married, having a more advanced stage of cancer and receiving chemotherapy have been identified as possible variables that predict distress (Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017). The application of these results is limited as these variables are not modifiable through intervention however may provide useful screening tools.

Chapter 2 presented theoretical models which could be useful in understanding distress in physical illness and can be applied to breast cancer. Firstly, acceptance and commitment therapy (ACT) proposes that how we respond to thoughts, emotions or physical sensations, determines whether we move in a valued direction (psychologically flexible), or experience poorer outcomes such as distress (psychological inflexibility; Hayes et al., 2006). The model proposes six flexible and six inflexible processes which are described in full in Chapters 2 and 4. The systematic review and meta-analysis presented in Chapter 4 revealed that across cancer, flexible processes are associated with lower distress and inflexible processes are associated with greater distress (Fawson et al., 2023). This review highlighted some limitations with the current literature including few studies measuring cognitive fusion, self-as-context, values and committed action, limiting the understanding for the whole ACT model and distress in cancer. In addition, in studies that include breast cancer patients, hormone therapy status is often not reported. This limits the understanding of the association between psychological variables and distress in this particular context. It is

therefore difficult to compare against the more general cancer or breast cancer samples to see if there are any differences that may be attributable to hormone therapy. This review also revealed that previous studies have focused on individual processes and that there are no studies exploring the contributions of all of the processes in the ACT model to distress in cancer.

The common-sense model of illness representations (CSM) is another model presented in the earlier chapters that may help to explain distress in physical illnesses such as cancer. The CSM proposes that beliefs about illness lead to coping behaviour which in turn is appraised and may result in reinforcement of or changes in beliefs as well as outcomes such as distress (Leventhal, Diefenbach, & Leventhal, 1992; Leventhal, Phillips, & Burns, 2016). There are systematic reviews suggesting illness perceptions are associated with distress in cancer (Hagger et al., 2017; Kaptein et al., 2015; Richardson et al., 2017). The findings reveal that the strongest relationships are for more negative beliefs about the consequences of illness and a stronger illness identity and poorer outcomes (distress, anxiety, depression), whilst greater perceived control is associated with better outcomes, albeit with weaker correlations (Hagger et al., 2017; Richardson et al., 2017).

Both models present variables that may contribute to explaining distress, however, only the CSM has been tested as whole theory-based model in cancer (Gibbons, Groarke, & Sweeney, 2016; Rozema, Völlink, & Lechner, 2009). Although as discussed in Chapter 2, these studies do not use longitudinal data and are not specific to breast cancer survivors on hormone therapy. Although the CSM is transdiagnostic across illnesses, illness perceptions are also context dependent as they are illness related. Therefore, there might be circumstances for this population that warrant further investigation, as these survivors

manage both concerns around the cancer recurring and concerns around ongoing treatment. For ACT, almost all research in cancer to date has tested the model in a data-driven way rather than a theory-driven way, with individual processes being tested based on their statistical relationship with the outcome rather than testing the theory in its entirety to identify its contribution to distress in cancer (Fawson et al., 2023). It is therefore difficult to understand the utility of the model in its proposed form due to the lack of a complete evidence base, limiting the potential of theory-based interventions.

It has been presented throughout the thesis that breast cancer survivors report experiencing physical symptoms related to hormone therapy medication and this may be one predictor of distress in this population (Bleiker et al., 2000; Jim et al., 2007; Peddie et al., 2021). In the qualitative study in Chapter 5, it was particularly highlighted that the impact of symptoms rather than the presence was important. The cognitive-behavioural responses to symptoms questionnaire (CBRQ; Picariello et al., 2023) is a measure that includes both cognitive and behavioural responses specifically to physical symptoms and therefore allow these constructs to be measured and tested, to further understand how psychological processes may contribute to the experience of distress. All or nothing behaviour, avoidance behaviours and more maladaptive cognitions in response to or related to symptoms have been found to be associated with worse symptoms, poor functioning and distress in a variety of physical health conditions including breast cancer, atrial fibrillation and those with persistent physical symptoms (Barends et al., 2023; Hughes et al., 2020a; Taylor et al., 2021). The symptoms breast cancer survivors on adjuvant hormone therapy contend with may lead women to engage in avoidant behaviour or avoid certain situations and therefore result in further distress. In addition, as presented in the systematic review in Chapter 4 (Fawson et al., 2023), self-compassion is not an explicit process in the ACT model

however it closely aligns with the principles and key features of ACT in practice (Neff & Tirch, 2013). Correlations between self-compassion and distress in cancer were moderate and significant in pooled data analysis. This may be another important variable to consider when explaining distress in cancer.

Both the CSM and ACT models are process-based, meaning the factors they propose may be predictors of distress and therefore suggestive of mechanisms of change to target in interventions. However, there is still a substantial amount of variance in distress that is not explained by the processes from either model alone (McCorry et al., 2013; Rozema, Völlink, & Lechner, 2009; Tamagawa et al., 2013; Trindade et al., 2020) suggesting unmeasured explanatory factors. Both models come from slightly different perspectives. The CSM proposes that illness cognitions/beliefs and emotional responses to the illness may be predictors of ways in which people cope with their illness or illness behaviour. These illness specific cognitions and behaviours may in turn impact outcomes. The ACT model proposes that general responses to thoughts/emotions/sensations predict outcomes. The CBRQ, although not directly incorporated into either of these models provide the symptom specific responses and cognitions that may predict outcomes. It may be that a combination of processes from the models, alongside other factors shown to be related to distress such as symptom burden, the reaction to symptoms and self-compassion complement each other and explain more variance in distress, offering a stronger explanatory model.

A further limitation of the research thus far is that it is dominated by cross-sectional studies, which although suggest there is an association between variables, cannot infer causality nor determine the direction of the relationships. Longitudinal studies are needed to investigate

these relationships and test the proposed explanatory and predictive utility of the models, which is particularly important as hormone therapy is prescribed for up to ten years.

The present study aims to address some of the limitations of previous research by testing the theoretical models concurrently in both cross-sectional and longitudinal data, incorporating other relevant evidence based cognitive and behavioural processes whilst controlling for symptom burden. This may allow for a more parsimonious, integrated model to then be tested to see if it can explain more variance in distress. This may help with intervention design and effectiveness (Corda et al., 2010). Illness perceptions may be amenable to change (Fischer et al., 2013) and despite the limited observational evidence, the popularity of ACT interventions in cancer is still increasing and reviews of interventions report some promising effects (e.g., Mathew et al., 2020). Therefore, this study has the potential to inform interventions by identifying the important evidence-based theoretical processes that should be addressed and targeted to reduce distress in this population over time.

6.2.1 Aims, objectives and hypotheses

The specific aims of this study of women survivors of breast cancer on adjuvant hormone therapy were:

1) To explore demographic, clinical and psychosocial correlates of distress.
2) To explore associations between distress (outcome) and ACT processes and CSM illness perceptions at baseline and follow up whilst controlling for symptom burden and other sociodemographic factors related to distress.
3) To explore associations between other cognitive-behavioural variables linked to the models presented and distress.

The specific objectives were:

1) To run correlations and other bivariate analyses of distress to identify possible demographic, clinical and psychosocial covariates to provide an indication of variables suitable for later analyses.
2) To identify the best explanatory model of distress by running hierarchical linear regressions controlling for covariates both cross-sectionally and longitudinally.

Specific hypotheses can be made based on previous research and theoretical assumptions:

a) Based on previous research it is hypothesised that younger women, women with no partner, those with stage 3 cancer at diagnosis and those who received chemotherapy will have increased distress.
b) It is expected that flexible ACT processes (including self-compassion) will be associated with lower distress, whilst inflexible processes will be associated with greater distress.
c) CSM illness perceptions including cure beliefs, personal control, treatment control and coherence will be negatively associated with distress. Breast cancer consequences, hormone therapy consequences, identity, risk of recurrence and emotional representations will be positively associated with distress.
d) CBRQ variables will be positively associated with distress.
e) It is expected that a combined model of significant ACT and CSM processes, as well as specific cognitive-behavioural responses to symptoms, will account for a greater proportion of variance in distress than either of the models alone.

6.3 Methods

6.3.1 Study design and setting

This study was a longitudinal observational design with 3 time points (T0 = baseline, T1 = 6 months follow up, T2 = 12 months follow up). The online recruitment period was from December 2020 to June 2021 with final 12 month follow up data collected by July 2022.

6.3.2 Participants and procedure

Women were eligible for the study if they were over 18, prescribed hormone therapy for stage I-III breast cancer in the last 2 years and lived in the UK. Ethical approval was granted by King's College London Psychiatry, Nursing and Midwifery Research Ethics Committee (HR-19/20-18770) and informed consent was obtained from all participants (see Appendix B1.1 for ethical approval and Appendix C1.1 and 1.2 for participant information sheet and informed consent form). Participants were recruited via online methods including posts and paid adverts on social media as well as the King's College London university recruitment circular. Gatekeepers of relevant charities were contacted to post study information on their newsletters, social media and/or on their mailing lists. Upon clicking on the study link, participants were shown a patient information sheet on Qualtrics (Qualtrics, 2020), participants completed a screening questionnaire and if eligible, completed a consent form. After consenting, participants were directed to the baseline questionnaire (T1). Six months (T2) and 12 months later (T3), participants were emailed a link to the follow up questionnaires.

6.3.3 Measures

Demographics/clinical characteristics: Age, ethnicity, relationship status, number of children, stage at diagnosis, time since diagnosis, type of breast cancer (lobular/ductal),

treatment, hormone therapy medication and time on hormone therapy were self-reported in the baseline questionnaire (see Appendix C1.3 for questions).

Distress: The PHQ-ADS is a composite measure of distress incorporating both the patient health questionnaire-8 depression scale (PHQ-8; Kroenke et al., 2009) and the generalised anxiety disorder-7 anxiety scale (GAD-7; Spitzer et al., 2006). The PHQ-8 consists of the first eight items of the original PHQ-9 (Kroenke, Spitzer, & Williams, 2001) as the ninth question, which assesses suicidal thoughts cannot ethically be used in this type of distance study where timely intervention and support cannot be guaranteed. Each scale measures symptoms over the past two weeks with items scored from '0 not at all' to '3 nearly every day'. The total scores range from 0-24 for depression and 0-21 for anxiety. Higher scores indicate greater depression and anxiety, with scores of 10 and above meaning moderate to severe depression or anxiety. Due to high coexistence and correlations between constructs of anxiety and depression it was argued that a composite score could be beneficial, not only to avoid multicollinearity but also for clinical use, research analysis and interventions that target both outcomes, reducing the number of measures and analyses needed (Chilcot et al., 2018; Kroenke et al., 2016).

The 16-item scale has been validated in chronic pain, oncology and a dialysis patient sample with good structural validity and a unidimensional scale of distress (Chilcot et al., 2018; Kroenke et al., 2016). The 15-item scale (not including the suicide item) was validated in this sample of breast cancer survivors and is being published elsewhere (Ibrahimi et al., under review). The psychometric properties revealed a bi-factor model had the best fit, confirming a sufficient unidimensional construct (Ibrahimi et al., under review). Strong correlations were reported between the GAD-7 and PHQ-8 in the current study, further supporting the

decision to use the PHQ-ADS as a composite score for the outcome. The McDonalds omega in the current sample was 0.92.

Symptom burden: The Breast Cancer Prevention Trial (BCPT) symptom checklist was initially developed as a 43-item tool to measure tamoxifen side effects (Day et al., 1999; Ganz et al., 1995). In this study, a shorter scale was used of 19 items that represented the most relevant symptoms for women on hormone therapy as used in other studies (Alfano et al., 2006; Ganz et al., 2016a). The measure gives an indication of symptom bother, with scores from '0 not at all' to '4 extremely'. There are eight subscales covering symptoms of vasomotor (hot flushes and night sweats), musculoskeletal pain (joint pain, muscle stiffness, general aches and pains), vaginal (dryness and pain with intercourse), fatigue (tiredness, difficulties getting to sleep or staying asleep), bladder control (difficulty when laughing or crying, difficulty at other times), cognitive (forgetfulness, difficulty concentrating, easily distracted), weight (weight gain, unhappy with appearance of body) and gynaecological symptoms (vaginal discharge, bleeding or spotting, genital itching or irritation). The total subscale scores were calculated if at least 1 out of 2 or 2 out of 3 items were answered with the mean score imputed for the missing item (Ganz et al., 2016a). If more items were missing, the subscale was scored as missing. The total symptom bother score was then calculated based on the total of the subscale scores. The McDonald's omega reliability coefficient (ω) was 0.84 for the whole scale.

Experiential avoidance (ACT): The brief experiential avoidance questionnaire (BEAQ; Gámez et al., 2014) was used to measure experiential avoidance. This was chosen over the AAQ and AAQ-II due to the high correlations with distress and criticism of the AAQ/AAQ-II (Fawson et al., 2023; Tyndall et al., 2019). The BEAQ is a shortened version of the 62-item

multidimensional experiential avoidance questionnaire (MEAQ; Gámez et al., 2011) and consists of 15-items covering avoidance of pain, emotions and difficult situations. Each item is scored on a scale of '1 strongly disagree' to '6 strongly agree'. One item is reversed scored and the total summed. Higher scores indicate greater experiential avoidance. The initial validation paper reported good psychometrics in three samples (students, psychiatric outpatients and community adults) including strong convergence with the MEAQ and discriminant validity with negative affect and neuroticism (Gámez et al., 2014). The reliability in the current sample was ω = 0.87.

Cognitive fusion (ACT): The cognitive fusion questionnaire (CFQ; Gillanders et al., 2014) is a 7-item measure with questions around getting stuck with thoughts someone might have. Items are scored '1 never true' to '7 always true'. Higher scores indicate greater cognitive fusion. The initial psychometric paper reported good construct validity, concurrent validity, internal consistency and test-retest reliability in a variety of samples including physical health populations (Gillanders et al., 2014). In a general cancer sample, the Cronbach's alpha was 0.93 (Gillanders et al., 2015) and in this sample the McDonalds omega was 0.95.

Mindfulness (ACT): The mindful attention awareness scale (MAAS; Brown & Ryan, 2003b) was used to measure dispositional mindfulness. The measure was validated in a cancer sample (50% breast cancer) and reported good construct validity and internal consistency (α = 0.87; Carlson & Brown, 2005), which was also excellent in the current sample (ω = 0.92). The measure consists of 15-items about noticing and attentiveness in everyday experiences. The scale ranges from '1 almost always' to '6 almost never'. The scale is scored by computing a mean of the 15 items. Higher scores indicate higher dispositional mindfulness.

Self-as-context (ACT): The self-as-context scale (SACS; Zettle et al., 2018) is a 10-item measure consisting of centering and transcending subscales. Scale items range from '1 very poor' to '5 very good'. The total score was used, with higher scores representing higher use of the flexible process of self-as-context. The measure was validated in a number of samples (including students and community adults receiving psychotherapy) and had good internal consistency, and good concurrent and discriminant validity (Zettle et al., 2018). There is no published study of the scale used in cancer samples other than one thesis (Babu, 2020; Fawson et al., 2023). The omega for this sample was 0.93.

Committed action (ACT): The committed action questionnaire (CAQ-8; McCracken, Chilcot, & Norton, 2015) is an 8-item measure initially validated in a chronic pain sample. The items ask about plans and barriers to reaching goals, scored from '0 never true' to '6 always true'. Four items are reverse scored and then summed to create a total score. Higher scores represent greater committed action. The measure has been validated in breast cancer patients with good psychometric properties (Trindade et al., 2018b). In the current sample the omega was 0.84.

Values (ACT): The valuing questionnaire (VQ; Smout et al., 2014), is a two factor 10-item measure of progress in valued living and obstruction to valued living. Items are scored from '0 not at all true' to '6 completely true'. Each subscale consists of five items. The development paper tested the measure in a student sample and clinical adult sample and found good internal consistency and convergent validity (Smout et al., 2014). Lewson et al. (2021) used the measure in a sample of cancer survivors and reported good internal consistency for both subscales. In the current sample reliability was very good (values progress $\omega = 0.84$; values obstruction $\omega = 0.82$).

Self-compassion (ACT): The self-compassion scale (SCS; Neff, 2003) is a 26-item scale which measures how someone acts towards themselves during difficult times. There are six subscales scored from '1 almost never' to '5 almost always': self-kindness, self-judgement, common humanity, isolation, mindfulness and over-identification. The negative subscale items are reverse scored (self-judgment, isolation, and over-identification) and the total mean is computed. Higher scores indicate greater self-compassion. The measure has been used extensively in cancer with excellent item reliability in a breast cancer survivors' sample (Przezdziecki et al., 2013) as in this current sample (ω = 0.94).

Illness perceptions (CSM): The illness perception questionnaire for breast cancer survivors (IPQ-BCS; Moon et al., 2017a) is an adapted version of the revised illness perception questionnaire (IPQ-R; Moss-Morris et al., 2002) and looks at beliefs specific to the breast cancer survivorship experience including beliefs and representations around taking tamoxifen. Tamoxifen was replaced with 'hormone therapy'. The measure validation paper showed it had good construct validity (Moon et al., 2017a). The measure covers the identity component of the model and for this study, the number of symptoms attributed to hormone therapy was used to represent this. The views about my illness section has eight subscales: cure beliefs (instead of timeline), breast cancer consequences, hormone therapy consequences, recurrence beliefs, personal control, treatment control, coherence and emotional representations. The 'causes' section was not analysed. Higher scores for consequences, recurrence and emotional representations represent more negative beliefs. Whilst control, coherence, and cure beliefs represent more positive beliefs. All subscales showed good reliability (ω = 0.75-0.93), with treatment control and cure beliefs scoring the lowest.

Cognitive and behavioural responses questionnaire (CSM-related): The CBRQ-Short form (SF; Picariello et al., 2023; Ryan et al., 2018) is an 18-item measure with higher scores indicating more unhelpful symptoms specific cognitions and behaviours based on six subscales: fear avoidance, damage beliefs, embarrassment avoidance, symptom focusing, all-or-nothing behaviour and avoidance/resting. Items are scored on a 5-point Likert scale from '0 strongly disagree' to '4 strongly agree'. This is a truncated form of the original CBRQ which had 40 items (Picariello et al., 2023). The CBRQ-SF was validated in multiple health samples including chronic fatigue syndrome, multiple sclerosis (MS), haemodialysis, inflammatory bowel disease (IBD) and chronic dizziness and performed well although the fear avoidance scale had the lowest reliability coefficients (ω = 0.59 to 0.79; Picariello et al., 2023). In this current sample, the omegas for subscales varied from 0.65 to 0.93, with fear avoidance and damage belief subscales scoring the lowest.

Covid-related distress: Due to recruitment throughout the COVID-19 pandemic, a bespoke measure based on the distress thermometer (National Comprehensive Cancer Network, 2024) was used, as at the time there were no validated measures developed. The question asked, 'how distressed do you feel about the impact COVID-19 has had on your life?' The scale was from '0 no distress' to '100 extremely distressed'.

6.3.4 Sample size calculation

G*Power version 3.1.9.2 (Faul, 2014) was used to determine the sample size using previous literature (Hughes, 2018). A medium effect size for side effects predicting distress with 0.05 alpha level and 80% power, would require a sample of 102-165 (anxiety, depression respectively). However, a typical rule for hierarchical regression analysis is for a minimum of 10 observations per variable, assuming up to 20 variables are used, a minimum of 200 will

be required (VanVoorhis & Morgan, 2007). In a study with the same type of breast cancer population, Moon et al. (2019b) reported a 75% retention rate at 12 months from in person/clinic recruitment. As this study relies on online recruitment, a more conservative estimate of attrition with a 65% retention rate is estimated. In addition, for the third aim of the study which is presented in Chapter 7, Fritz and MacKinnon (2007) suggest for a medium (β = 0.26) α path and *b* path, sample sizes should range from 150-200 for a variety of mediation tests. Therefore, a baseline sample of 400 was desired to provide a final 12-month sample of *n*=260.

6.3.5 Analysis/statistical methods

SPSS version 29 was used for the analysis. A significance level of $p < .05$ was set for all analyses. Across baseline data collection, missing data for scale items was approximately 0.75%. Therefore, missing data for individual scales was dealt with by imputing the mean as long as a minimum number of items were answered as outlined by the developers of the respective measures and other literature. Mplus version 8.10 (Muthén & Muthén, 1998-2017) was used to estimate the change over time for distress using latent growth modelling with missing data imputed. The intercept loadings were fixed to 1 and the linear slope factors were fixed to 1 for 6-month distress and 2 for 12 months. The variance in intercept and slope is reported to see individual variability.

Due to attrition of participants at 6 months and 12 months follow up, sensitivity analyses were run using multiple imputation based on 50 datasets which are reported in the appendices. Age, number of children and months on hormone therapy were included in the imputation models to aim to reduce bias by predicting data based on these other variables.

Minimal differences were noted so the results of the collected data are presented in this chapter and the imputed data as sensitivity analysis in the appendices.

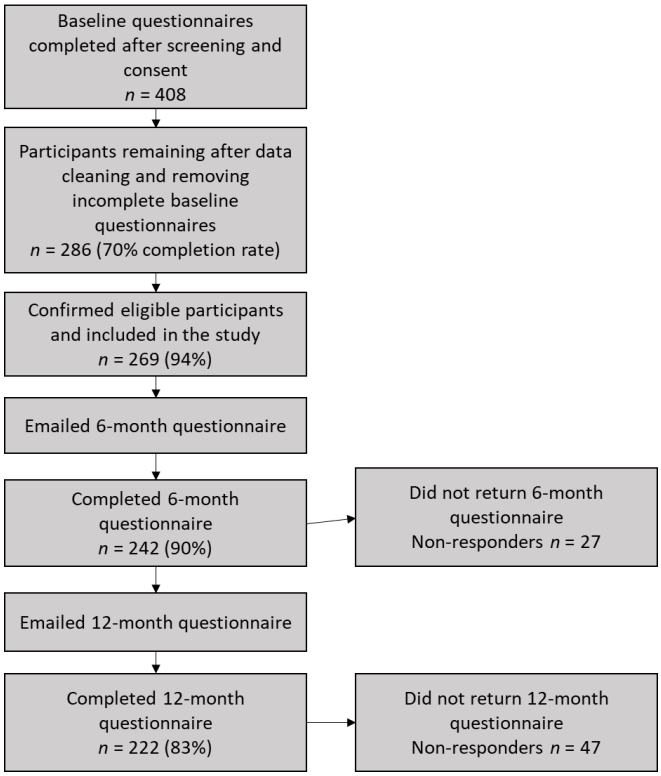
Upon checking for normality, distress and months on hormone therapy appeared skewed on visual inspection of histograms, however after checking the skewness and kurtosis statistics, both variables remained in the boundary of between -2 and 2 (George & Mallery, 2018). For bivariate analyses, Pearsons' correlations were used with point biserial for binary variables. Separate hierarchical linear regressions were run to assess the relationships between distress and processes from the CSM, ACT and integrated models. Clinical and demographic variables that showed a significant bivariate relationship with distress were entered in step 1 of the hierarchical regression models. Step 2 included covariates such as COVID-19 distress and symptom burden. In step 3, the component processes of ACT and CSM were included. For hierarchical regressions, assumptions were met for linearity, normality of residuals and homoscedasticity. R^2 is reported to assess the variance to explain distress. To check for multicollinearity, variance inflation factor (VIF) scores were checked across all regression models. Values between 1 and 5 indicate variables are moderately correlated with each and multicollinearity is not a concern (Shrestha, 2020).

6.4 Results

The completion rate after screening and consent was 70%. There was a 90% retention rate at 6 months and an 83% retention rate at 12 months follow up. Figure 6.1 displays the recruitment flow diagram.

Figure 6.1.

Recruitment flow diagram



6.4.1 Sample characteristics

Demographics and clinical characteristics are presented in Table 6.1. Two hundred and sixty-nine eligible women completed baseline questionnaires. The mean age of the sample was 58 (SD 9, range 25-81). Participants were mostly White (98%), with a partner (76%) and had children (79%). The mean time from diagnosis was 15 months and the mean time on hormone therapy was 10 months. Sixty-six per cent of the sample had been on hormone therapy for less than 1 year. Most women had stage 1 (32%) or stage 2 (48%) breast cancer. Seventy percent were prescribed aromatase inhibitors and 29% were prescribed tamoxifen.

Table 6.1.

Demographic and clinical characteristics (n = 269)

Age *(M, SD, range)*	57.8 (9.2, 25-81)
Ethnicity *(%)*	
White	98.1
Mixed	0.7
Asian	0.7
Black	0.4
Other	0.0
Partner status *(%)*	
Partner	76.2
No partner	23.8
Children *(%)*	
Children	78.8
No children	20.8
Tumour stage (*n*, %)	
Stage 1	31.6
Stage 2	48.3
Stage 3	17.5
Unsure	2.6
Tumour type *(%)*	
Lobular	20.1
Ductal	66.5
Mixed/other	10.0
Treatment *(%)*	
Lumpectomy	63.6
Mastectomy (single/double)	35.7/2.6
Chemotherapy	40.1
Radiotherapy	80.7
Type of hormone therapy *(%)*	
Tamoxifen	29
AI's	69.5
Time since diagnosis, months *(M, SD)*	14.7 (10.2)
Months on hormone therapy *(M, SD)*	10.2 (8.5)
Anxiety groups *(%)*	
Minimal (0-4)	45.4
Mild (5-9)	34.2
Moderate (10-14)	9.3
Severe (15-21)	10.4
Depression groups *(%)*	
Minimal (0-4)	29.0

Mild (5-9)	37.9
Moderate (10-14)	19.0
Moderately severe (15-19)	10.0
Severe (20-24)	3.3

Note: M = mean; SD = standard deviation; AI's = aromatase inhibitors; numbers may not align due to missing data.

Means and SDs for all psychosocial variables are reported in Table 6.2. Depression levels were higher than anxiety (*M* = 8.0, *SD* = 5.2; and *M* = 6.0 *SD* = 5.1, respectively) although both means are in the mild category. The mean total distress score (PHQ-ADS) was 14 which indicates mild distress. COVID distress was moderate (*M* = 47.6, *SD* = 28.1). Mean symptom burden was 29.9 (*SD* = 12.8) with the musculoskeletal subscale scoring highest for burden (*M* = 6.7,). For QoL, lowest means were for functional wellbeing and emotional wellbeing (14.7 and 15.7 respectively), indicating worse QoL in these areas.

Table 6.2.

Means and SDs between psychosocial variables and distress and symptom burden at baseline

	Baseline	6 months	12 months
		Mean (SD)	
Demographics and clinical factors			
Age	57.8 (9.2)	/	/
Number of children	2.8 (1.2)	/	/
Months on hormone therapy	10.2 (8.5)	/	/
Outcomes			
Anxiety (GAD-7)	6.0 (5.1)	6.1 (5.2)	5.3 (4.7)
Depression (PHQ-8)	8.0 (5.2)	7.8 (5.4)	7.0 (4.9)
Distress (PHQ-ADS)	14.0 (9.6)	13.9 (9.8)	12.4 (8.9)
COVID distress (0-100)	47.6 (28.1)	39.9 (27.7)	37.5 (26.2)
Symptom burden (BCPT)	29.9 (12.8)	30.8 (11.9)	30.5 (12.7)
ACT processes			
Experiential avoidance (BEAQ)	52.8 (12.8)	52.3 (12.1)	51.4 (12.5)
Cognitive fusion (CFQ)	25.0 (9.6)	24.7 (10.)	24.4 (9.8)
Mindfulness (MAAS)	4.0 (0.9)	3.9 (1.0)	3.9 (0.9)
Self-as-context (SACS)	47.7 (12.2)	46.7 (12.5)	46.8 (12.4)
Values progress (VQ)	18.5 (6.0)	18.3 (5.9)	18.3 (5.4)
Values obstruction (VQ)	12.3 (6.5)	12.0 (6.8)	12.4 (6.7)
Committed action (CAQ)	30.0 (7.3)	30.0 (7.4)	29.6 (7.1)
Self-compassion (SCS)	3.0 (0.7)	2.9 (0.8)	3.0 (0.7)
CSM illness perceptions (IPQ-BCS)			
Identity (symptoms attributed to HT)	7.0 (5.4)	8.4 (4.3)	7.9 (4.4)
Cure beliefs	14.2 (3.1)	14.4 (3.2)	14.8 (3.2)
Breast cancer consequences	14.2 (3.6)	13.6 (3.6)	13.4 (3.9)
Hormone therapy consequences	13.0 (4.4)	13.5 (4.4)	13.3 (4.5)
Recurrence	12.5 (3.7)	12.7 (3.8)	12.3 (3.7)
Personal control	13.5 (3.2)	13.9 (3.1)	13.7 (3.2)
Treatment control	15.2 (2.5)	15.3 (2.6)	15.4 (2.6)
Coherence	15.7 (3.1)	15.5 (3.2)	15.8 (3.0)
Emotional representations	14.6 (4.1)	14.3 (4.0)	14.1 (4.1)
Cognitive behavioural responses (CBRQ)			
Fear avoidance	3.4 (2.4)	3.6 (2.6)	3.4 (2.4)
Damage beliefs	4.9 (2.1)	4.7 (2.3)	4.6 (2.3)
Embarrassment avoidance	4.9 (3.3)	4.8 (3.4)	4.9 (3.2)
Symptom focusing	6.3 (3.3)	6.2 (3.4)	6.2 (3.2)
All or nothing behaviour	6.9 (3.1)	7.1 (3.0)	7.0 (2.9)
Resting behaviour	4.5 (2.9)	4.2 (3.1)	4.1 (2.9)

Note: HT: hormone therapy; AIs: aromatase inhibitors; SD: standard deviation; GAD-7: generalised anxiety disorder scale; PHQ-8: patient health questionnaire; PHQ-ADS: patient health questionnaire anxiety and depression scale; BCPT: breast cancer prevention trial symptom list; ACT: acceptance and commitment therapy; BEAQ: brief experiential avoidance questionnaire; CFQ: cognitive fusion questionnaire; MAAS: mindful attention awareness scale; SACS: self-as-context scale; VQ: valuing

questionnaire; CAQ: committed action questionnaire; SCS: self-compassion scale; CSM: common sense model; IPQ-BCS: illness perception questionnaire for breast cancer survivors; CBRQ: cognitive behavioural responses to symptoms questionnaire

6.4.2 Responders and non-responders at follow up

T tests and chi square tests were conducted on baseline data between those who responded at 6 and 12 months, see Table 6.3. There were no significant differences between baseline characteristics of 6-month non-responders and responders. Non-responders at 12 months were more likely to be distressed (t[58.64] = 2.28, p = .013) and report greater symptom burden (t[262] = 2.37, p = .009) at baseline.

Table 6.3.

Differences between responders and non-responders on key baseline measures

	6 months		12 months	
	Responders (*n* = 242)	Non-responders (*n* = 27)	Responders (*n* = 222)	Non-responders (*n* = 47)
Age (*M, SD)*	57.6 (9.4)	59.5 (7.3)	58.0(9.3)	56.8 (8.5)
Ethnicity *(% White)*	98.3	96.3	98.6	95.7
Chemotherapy *(% had chemotherapy)*	40.1	40.7	41.0	36.2
Months on HT (*M, SD)*	10.2 (8.6)	9.8 (7.2)	10.0 (8.3)	11.0 (9.1)
Distress (*M, SD)*	13.9 (9.5)	15.0 (10.8)	13.3 (9.2) *	17.3 (11.0) *
Symptom burden (*M, SD)*	29.6 (12.6)	32.2 (15.2)	29.1 (12.7) *	34.0 (13.0) *

*Note: * indicates a statistically significant difference between responders and non-responders at p < .05; M: mean; SD: standard deviation; HT: hormone therapy*

6.4.3 Distress over time

Table 6.4 displays the means and standard deviations of distress over time. A latent growth model was run to test change over time.

Table 6.4.

Mean distress score (PHQ-ADS) over time

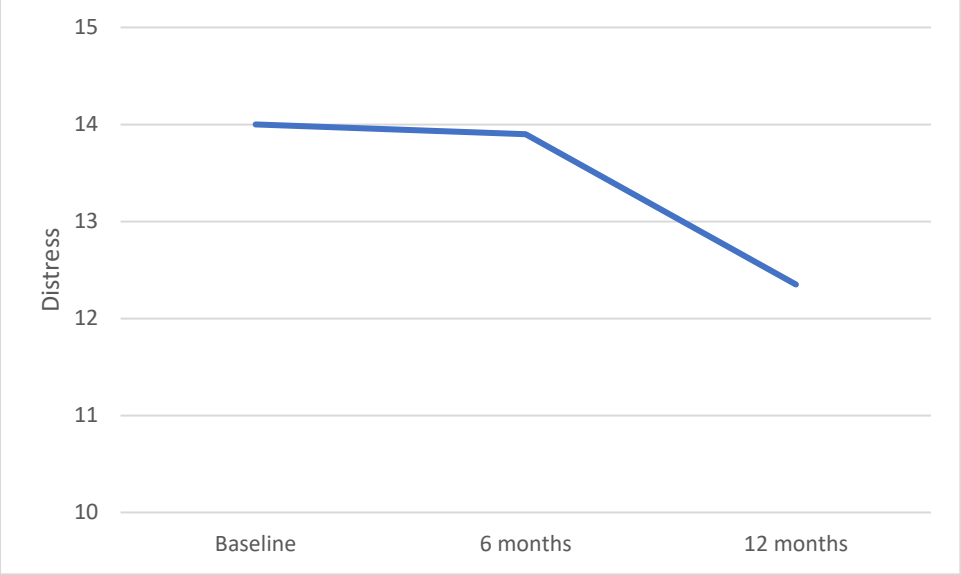
	Baseline	6 months	12 months
		Means (SD)	
Distress	14.00 (9.61)	13.90 (9.83)	12.35 (8.91)

Note: SD: standard deviation

Per unit of time there was an average decrease of 0.72 units (p = .005) in distress. There was a non-significant weak negative correlation between the intercept and slope (r = -.25, p = .08), meaning the intercept (mean distress at baseline) was not related to change over time. There was significant variance in the intercept (67.86, p < .001) but not the slope (7.30, p = .07). Change over time is depicted in Figure 6.2.

Figure 6.2.

Line graph depicting change in distress over time



6.4.4 Sociodemographic and clinical associations with distress

Correlations between all variables and baseline distress are shown in Table 6.5. The full correlation matrix is in Appendix C2. Pearsons' correlations were run on sociodemographic and clinical variables and distress (point biserial for binary). Age was the only significant

socio-demographic variable correlated with distress (r = -.16, p = .01). The number of months on hormone therapy was the only clinical variable significantly correlated with distress (r = .17, p = .01). Although the baseline mean distress score was higher for those who were stage 3 at diagnosis, a one way ANOVA revealed no significant difference between distress in each stage of diagnosis (F(2,258) = 2.22, p = .11). There were no significant differences between distress for those on tamoxifen and those on aromatase inhibitors (t[261] = 1.02, p = .155). Therefore, hormone therapy type and cancer stage were not included as covariates in later analyses with distress as the outcome.

Table 6.5.

Correlations between psychosocial variables and distress at baseline and distress at 12 months

	Distress (PHQ-ADS) at baseline	Distress (PHQ-ADS) at 12 months
Demographics and clinical factors		
Age	-.16*	-.25**
Partner (yes/no)	.00	-.05
Number of children	.09	.21**
Tumour type (lobular/ductal)	.02	-.02
HT type (AIs/tamoxifen)	-.06	.06
Months on hormone therapy	.17**	.11
Chemo (yes/no)	-.02	.02
Outcomes (baseline)		
Distress (PHQ-ADS)	-	.64**
COVID distress	.48**	.33**
Symptom burden	.51**	.47**
ACT processes (baseline)		
Experiential avoidance	.43**	.41**
Cognitive fusion	.66**	.56**
Mindfulness	-.53**	-.48**
Self-as-context	-.48**	-.43**
Values progress	-.35**	-.17**
Values obstruction	.59**	.40**
Committed action	-.50**	-.33**
Self-compassion	-.57**	-.48**
CSM illness perceptions (baseline)		
Identity (symptoms attributed to HT)	.22**	.23**
Cure beliefs	-.12*	-.11
Breast cancer consequences	.44**	.39**
Hormone therapy consequences	.33**	.21**
Recurrence	.26**	.31**
Personal control	-.22**	-.13*
Treatment control	-.23**	-.20**
Coherence	-.20**	-.15*
Emotional representations	.48**	.40**
Cognitive behavioural responses (baseline)		
Fear avoidance	.24**	.19**
Damage beliefs	.29**	.37**
Embarrassment avoidance	.43**	.43**
Symptom focusing	.39**	.37**
All or nothing behaviour	.20**	.23**
Resting behaviour	.26**	.26**

*Note: point biserial correlations are displayed for binary variables; HT: hormone therapy; AIs: aromatase inhibitors; SD: standard deviation; PHQ-ADS: patient health questionnaire anxiety and depression scale; ACT: acceptance and commitment therapy; CSM: common sense model; * = p <.05, ** = p < .01*

6.4.5 Relationship between ACT processes and distress

There were significant correlations between all ACT processes and distress in the directions predicted (see Table 6.5); whereby higher scores on flexible processes (mindfulness, self-as-context, values progress, committed action and self-compassion) were associated with lower distress (r = -0.35 to -0.57); and where higher scores on inflexible processes (experiential avoidance, cognitive fusion and values obstruction) were associated with greater distress (r = 0.43 to 0.66).

6.4.6 Relationship between CSM illness perceptions and other cognitive-behavioural processes and distress

The CSM illness perceptions as measured by the IPQ-BCS subscales were correlated with distress in the directions expected. Higher scores regarding breast cancer consequences, hormone therapy consequences, identity, recurrence and emotional representations, were significantly positively correlated with distress (r = 0.22 to 0.48). Higher scores regarding cure beliefs, personal control, treatment control and coherence, were significantly negatively correlated with distress (r = -0.12 to -0.23).

All CBRQ-SF subscales had significant positive correlations with distress, as predicted, with higher scores on unhelpful symptom responses associated with worse distress. The strongest correlations were for embarrassment avoidance and symptom focusing with distress (r = 0.43 and 0.39, respectively).

6.4.7 Psychosocial correlates of distress: hierarchical regressions using baseline data

Three hierarchal regression models were run with baseline data and baseline distress as the outcome to contribute to aim 2 (assumptions were met, see Figures C3-5 in Appendix C). Age and months on hormone therapy were added as potential covariates in step 1 of the

hierarchical regression analysis for all models due to the potential relevance of these factors highlighted in existing literature and the significant correlations in the present study. In step 2, COVID-19 distress and symptom burden were added. In the final step, model 1 shows ACT processes and model 2 shows CSM illness perceptions added to the regressions. In model 3, in this final step, all significant cognitive-behavioural processes (including ACT processes, CSM illness perceptions, CBRQ variables and self-compassion) were added based on correlations above 0.3 (Ratner, 2009) to preserve power. For ACT processes, values progress was chosen over values obstruction to represent the 'values' dimension of the model as values obstruction was highly correlated with all other ACT processes (r = -.59** to .68**; see correlation matrix in Appendix C2). For all models VIF (variance inflation factor) scores were between 1 and 3 indicating multicollinearity was not a concern.

Table 6.6 displays all hierarchical regressions. The ACT processes (model 1) explained 59% of the variance in distress (R^2 = 0.59, R^2_{adj} = 0.57, F(10) = 29.36, p < .001). Adding the ACT processes into the final step of the model added a significant proportion of variance (R^2_{change} = 13%) over and above the covariates. Whilst COVID-19 distress and symptom burden remained significant predictors, cognitive fusion was the only significant ACT process to independently predict distress (β = 0.34, p < .001). For a one SD increase in cognitive fusion, distress increased by 0.34 SD.

Table 6.6.

Multivariate hierarchical regression analyses for associations with distress at baseline

	Model 1 – ACT processes	Model 2 – CSM illness perceptions	Model 3 – integrated model
	β	β	β
Step 3:			
Age	0.01	-0.01	0.02
Months on hormone therapy	0.00	-0.00	0.00
COVID-19 distress	0.24***	0.33***	0.22**
Symptom burden	0.31***	0.42***	0.32***
Experiential avoidance	0.08		0.07
Cognitive fusion	0.34***		0.30***
Mindfulness	-0.08		-0.08
Self-as-context	0.03		0.05
Values progress	-0.07		-0.08
Committed action	0.02		0.02
Identity		-0.00	
Cure beliefs		-0.04	
Breast cancer consequences		0.08	0.06
Hormone therapy consequences		-0.09	-0.06
Recurrence		-0.07	
Personal control		-0.05	
Treatment control		-0.03	
Coherence		-0.05	
Emotional representations		0.22**	0.06
Embarrassment avoidance			0.03
Symptom focusing			-0.03
Self-compassion			-0.02
Model statistics			
Step 1 (age and months on HT)	*R^2 = 0.05, R^2_{adj} = 0.04, F(2) = 5.48, p = .005*	*R^2 = 0.04, R^2_{adj} = 0.03, F(2) = 4.69, p = .01*	*R^2 = 0.05, R^2_{adj} = 0.05, F(2) = 6.01, p = .003*
Step 2 (outcomes)	*R^2 = 0.46, R^2_{adj} = 0.45, F(4) = 45.44, p < .001 R^2_{change} = 0.41*	*R^2 = 0.47, R^2_{adj} = 0.46, F(4) = 46.51, p < .001 R^2_{change} = 0.42****	*R^2 = 0.46, R^2_{adj} = 0.45, F(4) = 44.59, p < .001 R^2_{change} = 0.41****
Step 3 (processes)	*R^2 = 0.59, R^2_{adj} = 0.57, F(10) = 29.36, p < .001 R^2_{change} = 0.13****	*R^2 = 0.53, R^2_{adj} = 0.49, F(13) = 17.40, p < .001 R^2_{change} = 0.06***	*R^2 = 0.59, R^2_{adj} = 0.56, F(16) = 18.05, p < .001 R^2_{change} = 0.13****

*Note: Significance levels: *** p < .001,** p < .01, * p < .05; ACT: acceptance and commitment therapy; CSM: common sense model*

Model 2 included the CSM illness perceptions variables. Adding in the nine CSM variables significantly added 6% of the variance above the covariates (R^2 = 0.53, R^2_{adj} = 0.49, F(13) = 17.40, p < .001). The only independent predictor from the CSM that was significant in the final step of this model was emotional representations (β = 0.22, p < .01), meaning a one SD increase in emotional representations increased distress by 0.22 SD.

Finally, model 3 displays the integrated model, incorporating all significant psychological variables from ACT, the CSM and the CBRQ, with a correlation of r > 0.3 to preserve power (including embarrassment avoidance, symptom focusing and self-compassion). This model accounted for 56% of the variance in distress, with the processes adding an additional 13% of variance over and above covariates (R^2 = 0.59, R^2_{adj} = 0.56, F(16) = 18.05, p < .001). Once again, COVID-19 distress, and symptom burden remained significant predictors and cognitive fusion was the only independent psychological predictor in this model.

6.4.8 Relationship between ACT and cognitive-behavioural processes and distress and symptom burden over time

Correlations between baseline psychological processes and 12-month distress are also presented in Table 6.5. Age and number of children were significantly correlated with 12-month distress. Similar strengths and directions of correlations were seen compared to the correlations with baseline distress. However, values progress had a weak correlation with 12-month distress (r = -.17), IPQ-BCS cure beliefs had a non-significant correlation (r = -.11) and CBRQ damage beliefs had a stronger correlation with 12 months distress than at baseline (r = .37). Correlations using imputed 12-month distress data are presented in Appendix C6. The strength and direction of correlations were unchanged compared to the

collected dataset. Cure beliefs became significant in the imputed data but as it is still a weak correlation ($r < 0.3$), was not included in later analysis.

6.4.9 Psychosocial predictors of distress over time: hierarchical regression

A further three hierarchical regression models were run mirroring the three conducted on baseline data with the outcome of distress at 12 months, see Table 6.7 (assumptions were met, see Figures C7-9 in Appendix C). For these regressions, age and number of children were entered at step 1 due to significant correlations. Step 2 included covariates of COVID-19 distress and symptom burden. As there was little change in distress over time and the strong correlation between distress at baseline and 12 months distress ($r = 0.64$), baseline distress was not controlled for. However, sensitivity analysis was run controlling for baseline distress for comparison and is available in Appendix C10 (assumptions are in Appendix C10, Figures C11-13). For all models VIF scores were between 1 and 3 indicating multicollinearity was not a concern.

Table 6.7.

Multivariate hierarchical regression analyses for predicting distress at 12 months – beta coefficients from step 3 are reported

	Model 4 – ACT processes	Model 5 – CSM illness perceptions	Model 6 – integrated model
	β	β	β
Step 3:			
Age	-0.09	-0.11	-0.08
Number of children	0.20***	0.18**	0.19***
COVID distress	0.08	0.15*	0.07
Symptom burden	0.22***	0.35***	0.21**
Experiential avoidance	0.06		0.05
Cognitive fusion	0.29***		0.25**
Mindfulness	-0.13		-0.14
Self-as-context	-0.07		-0.02
Values progress	0.10		
Committed action	-0.02		0.05
Identity		0.11	
Cure beliefs		0.03	
Breast cancer consequences		0.13	0.02
Hormone therapy consequences		-0.22**	
Recurrence		0.14	0.09
Personal control		-0.01	
Treatment control		-0.02	
Coherence		-0.12	
Emotional representations		0.08	-0.08
Damage beliefs			0.11
Embarrassment avoidance			0.09
Symptom focusing			-0.06
Self-compassion			-0.05
Model statistics			
Step 1	*R^2 = 0.11, R^2_{adj} = 0.10, F(2) = 12.60, p < .001*	*R^2 = 0.11, R^2_{adj} = 0.10, F(2) = 12.33, p < .001*	*R^2 = 0.12, R^2_{adj} = 0.11, F(2) = 12.98, p < .001*
Step 2	*R^2 = 0.32, R^2_{adj} = 0.31, F(4) = 23.27, p < .001 R^2_{change} = 0.21****	*R^2 = 0.32, R^2_{adj} = 0.30, F(4) = 22.67, p < .001 R^2_{change} = 0.21****	*R^2 = 0.32, R^2_{adj} = 0.31, F(4) = 22.89, p < .001 R^2_{change} = 0.20****
Step 3	*R^2 = 0.45, R^2_{adj} = 0.42, F(10) = 15.41, p < .001 R^2_{change} = 0.13****	*R^2 = 0.40, R^2_{adj} = 0.36, F(13) = 9.39, p < .001 R^2_{change} = 0.08***	*R^2 = 0.47, R^2_{adj} = 0.42, F(16) = 10.09, p < .001 R^2_{change} = 0.15****

*Note: Significance levels: *** p < .001,** p < .01, * p < .05; ACT: acceptance and commitment therapy; CSM: common sense model; R^2_{adj} = adjusted R^2*

In model 4, the final step including ACT processes and covariates explained 45% of the variance in distress at 12 months (R^2 = 0.45, R^2_{adj} = 0.42, $F(10) = 15.41$, $p < .001$). Entering the ACT processes into the final step of the model significantly added 13% of the variance over and above the covariates. Number of children and symptom burden remained significant predictors and cognitive fusion was the only ACT process to independently predict distress at 12 months (β = 0.29, $p < .001$). A one SD increase in cognitive fusion at baseline predicted distress to increase by 0.29 SD.

In model 5, the CSM illness perceptions accounted for 40% of the variance in 12-month distress, with the processes significantly adding 8% variance over covariates (R^2 = 0.40, R^2_{adj} = 0.36, $F(13) = 9.39$, $p < .001$). Hormone therapy consequences had a significant association in the opposite direction than expected. This variable had a strong correlation with symptom burden and therefore may be interacting with this in the model. As well as symptom burden and number of children, COVID-19 distress was also an independent predictor.

In model 6, psychological processes were added if they were correlated with 12-month distress ($r > 0.3$). With the exception of both values variables, all ACT processes, breast cancer consequences, recurrence beliefs, emotional representations, damage beliefs, embarrassment avoidance, symptom focusing, and self-compassion were included, significantly adding 15% variance over covariates (R^2 = 0.47, R^2_{adj} = 0.42, $F(16) = 10.09$, $p < .001$). This final integrated model predicted 47% of distress, 2% more than the model that included only ACT processes.

The models were run with baseline distress as sensitivity analysis (Appendix C10). The variance predicted by other variables is reduced when controlling for baseline distress due to the covariance and strong correlation presented for baseline distress and 12-month distress. The ACT model still adds significant variance in the final step, as does the integrated model. The main difference is that the CSM illness perceptions regression model does not add a significant proportion of variance in the final step. Data on the imputed datasets for further sensitivity analysis are available in Appendix C, Table C14 and C15.

6.4.10 Post-hoc power analysis

Post-hoc power analyses were run using G*Power on the integrated models using the longitudinal data and was approaching 1 for all, indicating the models were sufficiently powered, despite the final retained sample size (*n* = 222) being slightly lower than the sample size calculation suggested (*n* = 260).

6.5 Discussion

This study aimed to identify the association between theory-informed psychosocial variables with distress in a longitudinal sample of breast cancer survivors on adjuvant hormone therapy. Several sociodemographic variables including age and number of children were associated with distress, whilst months on hormone therapy was the only clinical variable to show an association. There was a small, significant reduction in distress over time, however as non-responders were more likely to be distressed, this may explain the reduction in distress at 12 months. As hypothesised, ACT process variables and CSM illness perceptions were significantly correlated with distress in the directions expected. The additional cognitive behavioural variables from the CBRQ and self-compassion were also significantly correlated with distress as hypothesised. Comparing the models revealed that

the ACT model predicted more variance in distress than the CSM illness perceptions alone, both cross-sectionally and longitudinally. However, the integrated model which included all ACT processes, three illness perception variables and three other cognitive-behavioural variables, predicted more variance in 12-month distress. This suggests the ACT process variables are contributing most of the variance in distress and whilst provided the best explanation of distress cross-sectionally in this sample, the integrated model provided the best explanation of 12-month distress. Symptom burden remained a significant predictor of distress in all models, apart from the sensitivity analysis controlling for baseline distress, supporting previous literature in other breast cancer populations (e.g., Bleiker et al., 2000; Jim et al., 2007). The longitudinal nature of the study provides an indication of the direction of effect of this relationship. The models including psychological processes predicted significant variance in distress over and above the covariates which included the highlighted predictor of symptom burden. This demonstrates the importance of investigating the relationship between symptoms, psychological processes and distress which will be tested in Chapter 7.

With respect to the first aim of the study, age and months on hormone therapy were the only demographic and clinical characteristics with a significant association with baseline distress. Younger age is often found to be associated with increased distress (Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017) and was supported in this current study in line with the hypothesis, although the effect was small. Longer duration on hormone therapy was also significantly correlated with distress, although a small correlation. This supports evidence presented that distress may persist throughout taking hormone therapy and is not just present for the first few months (e.g., Maass et al., 2019). Both age and months on hormone therapy were included in later analyses on the cross-sectional data. However once the

psychological variables were added in to the regression models, age and months on hormone therapy became non-significant predictors of distress in line with research presented in Chapter 2 (e.g., Kagee, Roomaney, & Knoll, 2018; Lo-Fo-Wong et al., 2016). This suggests the psychological variables are contributing more to explaining distress and therefore proposes investigating these variables for intervention development.

Although the evidence is varied, from previous literature it was hypothesised that those with stage 3 cancer and those who had received chemotherapy may experience more distress (e.g., Lo-Fo-Wong et al., 2016; Syrowatka et al., 2017). However, these clinical variables were not significantly correlated with distress, adding to the inconclusive evidence base for these variables. This further supports the investigation and awareness of other factors that may be important to consider in understanding and explaining distress. Clinical indicators appear less reliable at predicting distress than the ACT processes and CSM illness perception variables. Screening for these psychological factors may provide a better indicator of distress over time than relying on clinical indicators.

The number of children a participant had was significantly associated with increased distress at 12 months. The participants were recruited during the COVID-19 pandemic where children were impacted by not attending school for a period of time and having to be at home, which may have contributed to increased challenges and distress (Morgül, Kallitsoglou, & Essau, 2020). Alternatively, having to manage a diagnosis of cancer and the ongoing impact of this including hormone therapy side effects, may be additionally challenging alongside bringing up children. In a review of the literature of parents with cancer and young children it has been found that parents particularly struggle parenting through treatment, can feel guilty about not being a good parent and find maintaining

routine at home effortful (Semple & McCance, 2010). In addition, the concern around the impact of illness and symptoms on the child may also be distressing as it has been reported that children can be negatively impacted by having a parent with cancer (Morris, Martini, & Preen, 2016). Number of children remained a significant predictor despite other variables being added to the model. This could be particularly important in terms of planning resources to support women, providing them with tailored support.

The second aim was to explore associations between the psychological variables and distress. All correlations were in the directions hypothesised. The flexible ACT processes (including self-compassion) were negatively associated with distress whilst the inflexible processes were positively associated, supporting the results of the review in Chapter 4 (Fawson et al., 2023). The correlations were all significant and most were moderate in size, except for a strong correlation between cognitive fusion and distress. Illness perceptions were correlated with distress in the directions hypothesised and in line with previous literature (Hagger et al., 2017). Despite all being significant, the majority showed small correlations with distress apart from moderate correlations for breast cancer consequences, hormone therapy consequences and emotional representations. In terms of the CBRQ dimensions, all had correlations with distress in the expected directions (Hughes et al., 2020a; Picariello et al., 2023). Embarrassment avoidance, symptom focusing, and damage beliefs all showed significant moderate correlations with distress, whilst the others demonstrated small correlations.

To further address aim two, hierarchical regression models were run on the cross-sectional and longitudinal data to explore the associations and direction of effects between psychological variables and distress and compare the theoretical models in explaining

distress. At baseline, the best fit for explaining distress was the ACT model. The ACT model contributed the same amount of variance as the integrated model in the cross-sectional data, which was 7% more variance than the CSM illness perceptions alone. This implies that the ACT processes are the best explanation of distress in the cross-sectional data. However, in both longitudinal models (including sensitivity analysis controlling for baseline), the integrated model was the best fit for explaining distress at 12 months. Both integrated models predicted 2% more variance than the ACT process model alone, suggesting the addition of the other cognitive-behavioural variables alongside ACT processes marginally increased the explanatory power. However, as this was only a small increase in variance, it would be reasonable to conclude that the ACT processes contribute more explanatory variance in distress.

The results highlight the importance of using longitudinal data as slightly different patterns are shown compared to the cross-sectional data. The longitudinal data shows a combined explanation of psychological factors in predicting later distress which has implications for screening and intervention. The longitudinal models show that both the responses to general thoughts and/or emotions (ACT) and responses to symptoms (CBRQ), as well as the thoughts/beliefs themselves (CSM, CBRQ) are important for understanding distress in this population. The integrated model predicted a significant amount of variance despite baseline distress being included in the regression model which explained a large proportion of the variance due to the strong correlation between baseline and 12-month distress. This demonstrates the importance of the psychological variables in helping to explain distress at 12 months, as it is not just someone's baseline distress that predicts later distress. This may have important implications particularly in screening for other factors as indicators of risk of experiencing distress.

The results build on previous literature which have found that adding illness perceptions over clinical and demographic covariates contributes additional variance in distress in breast cancer samples (McCorry et al., 2013; Rozema, Völlink, & Lechner, 2009). As this study used the IPQ-BCS, the beliefs and cognitions are related specifically to the experience of breast cancer and hormone therapy treatment. These factors appear to be important even though primary treatment has finished and individuals are 'disease free'. However, the individual correlations for IPQ illness perceptions and distress were quite weak in this sample and the overall contribution of variance from the illness perceptions although significant was small compared to the ACT model. In addition, only breast cancer consequences, recurrence beliefs and emotional representations had moderate correlations with distress and therefore were included in the integrated model. One explanation might be that the beliefs around breast cancer and hormone therapy are realistic, with symptoms ongoing, and therefore may not show as strong relationships with distress. Therefore, it may be that the *responses* to these thoughts and beliefs are more important in this population, which the ACT model proposes. ACT specifically aims to explain psychopathology and suffering via the inflexible, unworkable processes (Hayes et al., 2006). For example, where experiential avoidance is stopping someone from engaging in meaningful activity and therefore deemed unworkable (Dindo, Van Liew, & Arch, 2017). Therefore, this may explain why the ACT processes contributed more variance in explaining distress. The illness perceptions may reflect realistic thoughts about breast cancer or hormone therapy, but it is *how* someone responds to those thoughts (inflexibly or flexibly) that results in different outcomes. This highlights one of the differences between traditional CBT approaches that might aim to change thoughts, whilst ACT aims to target the response to thoughts to increase

psychological flexibility and live a values-driven life (Harris, 2019; Hayes et al., 2006; Ruiz, 2010).

The CSM originally proposed illness perceptions as predictors of illness related coping behaviour rather than specific emotional outcomes. Illness perceptions may contribute more to illness related behaviours such as medication taking which has been found in previous research (Moon et al., 2017b). As the study identified support for the illness perceptions, along with previous research, the perceptions may still be important to consider for further analysis and intervention development not only for distress but other illness related outcomes. Illness perceptions are amenable to change, as demonstrated in previous interventions (Auyeung, Hughes, & Weinman, 2020; Fischer et al., 2013; Jones, Smith, & Llewellyn, 2016). In addition, the illness perceptions can provide specific examples of the types of thoughts and beliefs this population have which can contribute towards relevant content in intervention development.

There were several significant independent predictors in the regression models. Cognitive fusion was not only an independent predictor in the ACT regression model, but also the integrated models, both cross-sectionally and longitudinally. As reported in Chapter 4, there are limited studies exploring cognitive fusion specifically in breast cancer, however this finding is in line with previous literature presented in Chapter 4 which reports a strong correlation between cognitive fusion and distress (Fawson et al., 2023). In a general cancer sample, Gillanders et al. (2015) also found cognitive fusion was a significant independent predictor of anxiety whilst controlling for coping variables and self-compassion. A thesis found cognitive fusion was also a significant independent predictor of anxiety whilst controlling for other ACT variables and fear of cancer recurrence (Randell, 2017). The

cognitive fusion questionnaire measures getting stuck and caught up with thoughts and not being able to let go of difficult thoughts which can interrupt daily functioning (Gillanders et al., 2014). There may be multiple negative thoughts throughout cancer around identity, body changes, limitations to roles and functioning and other changes and if fused, may lead to negative outcomes (Trindade et al., 2018a). This poses a potential key variable not only for the next stage of analysis in Chapter 7, but also for intervention development.

Emotional representations were an independent predictor of distress in the baseline CSM regression model. There was a significant moderate correlation with distress at baseline which has also been found in previous research (Moon et al., 2017a). The IPQ-BCS measures recurrence-related emotional representations rather than representations of emotions generally and as there was a moderate correlation, was included in the model as there is less chance of confounding with distress than if it was more focused on emotions in general. However, in the integrated model, emotional representations became non-significant, suggesting other variables had shared variance. In addition, in the longitudinal models, recurrence related emotional representations were not a significant independent predictor so may not be as useful in predicting long term distress.

Beliefs about hormone therapy consequences were a significant predictor in the longitudinal model although in the opposite direction expected and to the bivariate correlation with distress. It was hypothesised that greater beliefs about the consequences of hormone therapy would be associated with increased distress which has been found in a previous study in this population (Moon et al., 2017a). However, it could be interpreted based on the results of the analysis that if someone knows their symptoms are due to hormone therapy, therefore understand the reason for them, they have less distress as they

understand the medication is reducing risk of recurrence and therefore worry less. In addition, according to the CSM, beliefs about hormone therapy consequences may be more likely to predict behaviours such as information/help seeking to manage symptoms which would be interesting to explore in future research. However, it was a small effect and therefore could be an interaction of multiple variables included in the model causing an error or suppressor effect as variables were correlated in the expected directions (Mason & Perreault Jr, 1991). However, the study was sufficiently powered, and collinearity statistics were checked. This variable warrants further analysis as part of the next aims of the study (Chapter 7).

Finally, in the longitudinal integrated model controlling for baseline distress, damage beliefs were a significant independent predictor of distress. This supports research in other physical health conditions such as haemodialysis patients, where damage beliefs were associated with distress in cross-sectional data (Chilcot et al., 2016). Perceiving symptoms as signs of damage in the body may result in increasing concern and distress (Picariello et al., 2023). This may be an important variable to test in Chapter 7, to see if different levels of these beliefs about symptoms in this population, alters the negative impact of symptoms on distress. If so, targeting these beliefs may be an important consideration in future interventions.

6.5.1 Strengths and limitations

The current study explored and tested two established models as well as a proposed integrated model to further understand and explain distress in this population of breast cancer survivors on hormone therapy. This study has addressed a limitation of previous literature by conducting analysis on a longitudinal sample as well as adding to the minimal

research on the association between distress and some of the ACT processes in cancer populations (Fawson et al., 2023). The study had a good sample size, minimal attrition and was adequately powered.

A limitation of the study was that 98% of the participants were of White ethnicity limiting its generalisability. Previous literature states that hormone receptor positive breast cancer is more common in White women (DeSantis et al., 2014; Gathani et al., 2021b) so the study may be representative of this population. However, women of other ethnicities with breast cancer may show different patterns of experiences and have been reported to experience more distress (Gonzalez et al., 2022). To understand any potential differences in experiences, this needs to be explored in the literature, specifically with women of different ethnicities.

Another important consideration of the data is the fact participants were recruited during the COVID-19 pandemic. As described in Chapter 1, many rapid studies were published about the potential impact of COVID-19 on people with a breast cancer diagnosis (Swainston et al., 2020) however the longer-term effects are still unknown. Participants were not only potentially experiencing distress related to diagnosis and survivorship of breast cancer but were also exposed to unprecedented stress from the global pandemic and changes to breast cancer care and treatment (Dave et al., 2021). This is a limitation to the study as the COVID-19 distress may have confounded the general distress measured in this study. However, the study aimed to mitigate the impact of this by measuring and controlling for COVID-19 related distress. This measure was specifically created for this study and was positively, moderately correlated with the PHQ-ADS, implying they measured related but different facets of distress. COVID-19 distress decreased over time as expected from

lockdowns finishing and life returning to near normal. All analyses controlled for COVID-19 distress, which is a strength of this study and in two of the longitudinal models, COVID-19 distress became non-significant once the psychological variables were included in the models. This suggests the impact of COVID-19 decreased over time, and the psychological variables were better predictors of distress over time. However, the incorporation of this variable into the regression models may have explained a large proportion of the variance, underinflating the contribution of the models in explaining distress.

As described in Chapter 5, people who are distressed may be less likely to respond to online adverts for research studies, however as reported, the current sample did self-report experiencing distress. Had the sample consisted of even more distressed individuals, the results are likely to be more robust as the results may be underestimated in the current sample. Overall, emotional distress does seem to be similar to previous research (e.g., Moon et al., 2017b).

In addition, although the study reported a good retention rate over time, a limitation was that non-responders reported higher distress at baseline, indicating there may be some bias as the follow up data might not be missing at random. To mitigate this, sensitivity analyses were run using imputed data. Multiple imputation was chosen over last observation carried forward as it creates different plausible data sets rather than assuming the variables have remained stable (Sterne et al., 2009). Therefore, other variables were included in the imputation models to aim to reduce the bias by predicting data based on these other variables. Overall, the results from the sensitivity analyses using the imputed data were similar to the collected data and did not lead to different interpretations of the data.

6.5.2 Clinical and theoretical implications

Although there was reduction in distress over time, this was minimal and may be due to the drop out of more distressed participants. If distress persists, this could suggest interventions for distress are needed. Distress was associated with longer time spent on hormone therapy, indicating that distress may persist whilst taking hormone therapy medication. This is important not only for clinicians when supporting these women, but also in developing suitable interventions. Clinical appointments are a useful way for distress to be identified and screened, and clinicians should also be aware of the potential persistence of distress. The PHQ-ADS has been validated in this population and therefore provides an easy and convenient screening tool (Ibrahimi et al., under review). Distress may be associated with potentially harmful patient outcomes such as non-adherence to medication leading to increased recurrence risk and mortality as well as costs for wider healthcare services (Deckx et al., 2021; Winn & Dusetzina, 2016). As discussed in Chapter 4, variables may provide strategies for screening for risk of distress encouraging early intervention (Fawson et al., 2023; Hulbert-Williams & Storey, 2016). As cognitive fusion and beliefs that symptoms are damaging significantly predicted 12-month distress despite other variables included in the model, these variables could provide a starting point of the content and therapy techniques to be included in the intervention.

As presented in Chapter 2, theories should be supported with a sound evidence base. This study contributes to the existing theoretical literature by providing additional empirical evidence to support both the ACT and CSM. In addition, the finding that an integrated model including components from both the ACT and CSM as well as other cognitive behavioural processes may explain more variance in longer term distress in this population has implications for intervention development. A combination of understanding the specific

illness cognitions and responses to these thoughts could be complementary. For example, Karekla, Karademas and Gloster (2019) proposed mapping ACT processes onto the CSM illness perceptions in order to provide a treatment framework. This would benefit from being tested empirically but poses the potential utility of combining the approaches for treatment. Mediation analysis should be conducted in RCTs of interventions to identify the mechanisms of change that result in more favourable outcomes.

The study has also identified some potential key variables that may be important to investigate in the pathway between symptoms and distress. The beliefs about illness or responses to symptoms may be mediators or moderators of this relationship and have been analysed and presented in Chapter 7.

6.5.3 Future directions

Replicating the study in samples of different ethnic groups will ensure the findings can be generalised to a wider proportion of breast cancer survivors. This would allow for a more nuanced understanding in these groups leading to tailored interventions to be developed. In addition, as reported in Chapter 4 there are some limitations with ACT measures as some constructs are difficult to define and measure (e.g., self-as-context, values) leading to differences in how they are perceived and understood (Barrett, O'Connor, & McHugh, 2019; Fawson et al., 2023; Moxham et al., in prep; Zettle et al., 2018). Trindade et al. (2021) reported differences across Portuguese and UK samples for example, so therefore specific studies will allow for this to be explored further, and more suitable measures to be designed.

As women were recruited at different stages of being prescribed hormone therapy, it is difficult to estimate distress at specific points of the survivorship journey and understand

patterns over time. Further research exploring within-person analysis may reveal different patterns and trajectories of distress over time for people at different stages of taking hormone therapy medication. This may be useful to understand the different patterns that the average may hide and therefore contribute to more tailored interventions.

6.5.4 Summary and conclusions

Overall, the study provides support for both the ACT model and the CSM illness perceptions in understanding distress in breast cancer survivors on hormone therapy. The ACT process model was shown to predict more variance in baseline distress, whilst the integrated model contributed an additional 2% variance in 12-month distress, indicating processes that should be tested further and potentially focused on in interventions.

The first stage of analysis has enabled part of the final thesis objective to be answered and has contributed to the overall PhD thesis aim of understanding the psychosocial processes associated with distress in this population. The study builds on Chapter 4 by providing evidence for under-investigated theoretical processes both cross-sectionally and longitudinally. Chapter 7 will build on these results by testing some of the theoretical processes in the symptom-distress pathway.

Chapter 7 Mediators and moderators of the symptom-distress relationship

7.1 Chapter overview

The first stage of analysis presented in Chapter 6 tested the explanatory power of acceptance and commitment therapy processes (ACT), illness perceptions from the common-sense model of illness representation (CSM) and an integrated model for explaining distress in breast cancer survivors on hormone therapy. The analysis also provided an indication of some of the potential variables that may be important to test in the symptom-distress relationship. This chapter presents the mediation and moderation analysis using the same data as the study presented in Chapter 6, to address the rest of the final PhD objective to understand and explore the symptom-distress relationship. The mediators and moderators to be tested are theoretically driven, as well as supported by the analysis in Chapter 6 and the qualitative study in Chapter 5.

7.2 Background

As presented in Chapter 2, the experience of symptoms has been found to be associated with distress (Syrowatka et al., 2017) and may be a potential predictor. Breast cancer survivors on hormone therapy contend with a number of side effects related to the medication including bone and muscle aches/pains and hot flushes and night sweats (Garreau et al., 2006; Whelan & Pritchard, 2006). In the previous literature presented in Chapter 2 and the qualitative study in Chapter 5, it has been suggested that it is not just the presence of symptoms that are distressing, but the actual impact and burden that these symptoms have on someone (e.g., Peddie et al., 2021). Therefore, measures that capture

the impact and burden, could provide a more useful and explanatory indication of survivors' experiences. In Chapter 6, symptom burden, as measured by the validated breast cancer prevention trialists' symptom burden scale (Ganz et al., 2016a), was found to be significantly moderately correlated with distress at baseline and 12 months. This relationship has also been found in other studies (Stanton, Bernaards, & Ganz, 2005) suggesting the importance of understanding this variable in contexts where side effects are prevalent, such as for breast cancer survivors on hormone therapy. Symptom burden is also found to persist over time (Ganz et al., 2016a; Moon et al., 2019b), despite support information implying physical symptoms will settle after six months (Cancer Research UK, 2021). This suggests that if symptoms are not managed, they could continue to negatively impact women over time. Further evidence for this relationship could improve treatments and support for women on hormone therapy.

Current self-management techniques are limited for managing the side effects of hormone therapy as discussed in Chapter 1 (Hall et al., 2022), and the qualitative study in Chapter 5 corroborated these findings as women reported feeling helpless about symptoms as well as reluctant about taking further medication. Cognitive behavioural therapy (CBT) has been found to reduce the impact and severity of hot flushes and night sweats with positive effects at reducing anxiety and depression (Fenlon et al., 2020). However, the exact mechanisms of action through which the intervention worked are unknown. In a previous iteration of this trial (not in breast cancer), changes in cognitions mediated changes in hot flush and night sweat problem ratings after intervention (Norton, Chilcot, & Hunter, 2014). The results from these studies do imply that there is a relationship between symptoms, psychological techniques, and distress outcomes. Whilst there are limited effective self-management options for side effects (Hall et al., 2022), the CBT trial for hot flushes and

night sweats provides an indication that psychological intervention can effectively improve management of physical symptoms. Therefore, exploring potential mechanisms from the various cognitive-behavioural models presented may provide further detail about what factors might be involved in the relationship between symptoms and distress. This will therefore provide direction for more effective interventions to support these women who experience symptom burden from multiple symptoms, rather than relying on pharmacological intervention which is often contraindicated, not offered or preferred not to take (Hall et al., 2022; see also chapter 5).

In Chapter 6, symptom burden was a significant independent predictor of distress at 12 months, whilst including the psychological variables from the CSM and ACT. These psychological variables still added additional explanatory variance in distress at 12 months over and above symptom burden, further suggesting the relationship between symptoms, distress and the psychological variables that may be important to investigate further. This study proposes that there is a third variable in between the symptom and distress relationship which is hypothesised from the theoretical models presented in Chapter 2, where the CSM and TMA-LTC highlight how illness related stressors (such as symptoms) are coped with, resulting in either positive or worse outcomes depending on the response to the symptoms/illness-related stressor. In addition, the qualitative study in Chapter 5 provided further support as some women described how they responded to symptoms with acceptance or felt their sense of self had changed in relation to symptoms and these experiences resulted in different outcomes. Therefore, this thesis provides theory- and data-driven rationale and hypotheses to test in the relationship between symptoms and distress.

Mediation and moderation analysis can allow for the symptom-distress relationship to be tested. Mediation analysis helps to explain and provides information about the causal pathway between two variables (Maxwell, Cole, & Mitchell, 2011), whereby X (symptom burden) will predict the mediator, which in turn predicts Y (distress). Moderators act by modifying the causal effect between two variables (X and Y), by altering the magnitude or direction of the effect (Wu & Zumbo, 2008). Mediators are responsive to another variable implying it is more situation or state like, whilst moderators tend to be more trait-like concepts or stable tendencies. Complete mediation, where the mediator fully accounts for the relationship between independent and dependent variables, would not be hypothesised due to the complex nature of psychological relationships (Maxwell, Cole, & Mitchell, 2011), however partial mediation may be expected and is more common (Gunzler et al., 2013). Partial mediation can reveal some of the explanation between two variables but may not account for the whole relationship, implying there is still some direct effect of X on Y (Gunzler et al., 2013). This information however can still be useful, as understanding part of what contributes to a relationship can provide information for future research to focus on, in order to develop more effective treatments and interventions (Gunzler et al., 2013). Moderators of interventions will show for whom the intervention was successful by understanding individual differences (Wang et al., 2017). This may be by a socio-demographic characteristic or set of beliefs or personality. In observational research, moderators may provide information about the beliefs or resources someone has which can provide information about what could mitigate the negative effect of symptoms on distress. Depending on the malleability of the beliefs or tendencies, these could be seen as intervention targets or help interventions be more suitable for a wide range of characteristics (Wang et al., 2017).

Existing literature on the symptom-distress relationship is scarce. Some mediation studies presented in Chapter 2 have explored the experience of symptoms and quality of life with social support and self-efficacy suggested as mediators (Liang et al., 2016; Manning-Walsh, 2005). However, there are some limitations with the research discussed. Firstly, mediators were poorly defined and conceptualised. Manning-Walsh (2005) tested social support as a mediator but conceptualised and interpreted it as a "buffer" and coping resource which is more of a moderator than a mediator as it suggests the relationship would change rather than being directly in the causal pathway. Furthermore, the analyses were all conducted on cross-sectional data. Mediation analysis on cross-sectional data almost always fails to capture true mediation, which ideally should be conducted on longitudinal data (Maxwell & Cole, 2007). For any causal pathway analysis, including both mediation and moderation, there should be three core concepts that are acknowledged which include correlation, temporality and confounders. Cross-sectional studies only address correlation and potentially some confounders, whilst the temporality aspect is not addressed or taken into consideration. The current study aims to address these limitations by conducting analysis on longitudinal data.

Based on the theory and results presented throughout this thesis, ACT and illness perceptions from the CSM provide a starting point for investigating the psychological variables that may be involved in the symptom-distress pathway. ACT processes postulate that responding to thoughts, emotions or physical sensations in a flexible or inflexible way, results in different outcomes. This *response*, rather than trying to change the initial thought or symptom, is important as you cannot necessarily change physical symptoms or side effects and it might not be appropriate to change a valid thought such as "my cancer might return". ACT conceptualises the inflexible and flexible processes as mechanisms whereby

responding inflexibly to a thought, emotion or situation, may result in psychopathology or suffering (Hayes et al., 2006). This definition aligns with the conceptualisation of inflexible processes as mediators, as they "explain" how distress may arise. Whilst increasing flexible processes or the resources or skills someone may have through intervention, may result in better outcomes (Hulbert-Williams, Storey, & Wilson, 2015). As the flexible processes are described as resources, tendencies or skills, in observational data where no change would be expected without intervention, the flexible processes can be conceptualised as moderators. Similarly, someone may have a tendency to avoid experiences and fuse with thoughts, however for this study, inflexible processes are conceptualised as mediators in explaining the relationship between symptoms and distress; whilst the flexible processes are conceptualised as moderators. Based on the studies in Chapters 4, 5 and 6, cognitive fusion and experiential avoidance would be hypothesised as particularly important mediators for this study, and mindfulness and self-compassion as potentially important moderators.

In Chapter 6, cognitive fusion was found to be an independent predictor of distress whilst controlling for covariates and the other ACT component processes demonstrating its potential utility in understanding and predicting distress. Cognitive fusion has been conceptualised as a mediator in other studies in cancer (Gillanders et al., 2015; Trindade et al., 2018a). Gillanders et al. (2015) found cognitive fusion mediated the pathway between threatening illness appraisals and anxiety, whereby fusing with the negative thoughts about illness was associated with greater anxiety. However, this analysis was conducted on a small cross-sectional sample, limiting the understanding of the direction of relationships. The study, alongside the theory and results presented in this thesis, supports the rationale for testing the mediation pathway in the context of the present study. It may be hypothesised that someone with increased symptom burden would likely respond with negative thoughts

about their symptoms and fusion with these difficult thoughts would in turn predict increased distress.

Furthermore, based on ACT and the results of Chapter 4, experiential avoidance was highlighted as a potentially key variable in understanding distress. As a mediator based on the theory (Hayes et al., 2006), it may be hypothesised that symptom burden would result in someone avoiding painful experiences, internal feelings, thoughts and symptoms, which would then result in distress. Previous research has found that experiential avoidance (along with functional impairment) mediated the effect of pain on distress in people with cancer (Brown et al., 2020). Participants were more likely to engage in attempts to avoid the painful experiences which in turn, resulted in interference with daily functioning and therefore more distress. Therefore, a similar relationship might be found in breast cancer survivors on hormone therapy. Acceptance, the corresponding flexible process to experiential avoidance, was noted as potentially important from the qualitative study in Chapter 5. However due to the difficulty of defining and measuring acceptance (Fawson et al., 2023; McAndrews, Richardson, & Stopa, 2019), experiential avoidance can provide a measure for the inflexible process as an alternative to acceptance.

Greater self-compassion and mindfulness are considered psychologically flexible resources or skills and therefore would be hypothesised to act as a buffer of the negative impact between symptom burden and distress. These variables have been shown to have negative associations with distress in cancer (Dempster et al., 2011; Fawson et al., 2023), suggesting higher reported self-compassion and/or mindfulness is associated with lower reported distress. Although these variables may be skills or tendencies someone may have, they can also be modified and enhanced in interventions (Keng et al., 2012), so can provide targets

for treatments if found to be relevant for this population. For example, mindfulness-based interventions have been found to be effective at reducing the severity of cancer-related pain (Ngamkham, Holden, & Smith, 2019).

The CSM is another model that may help explain the relationship between symptoms and distress. The CSM "explains" how an illness related stressor may result in the thoughts someone has about illness and then lead to coping behaviour, suggesting a mediation pathway. However, the description of illness perceptions as beliefs someone may hold about illness suggests that illness perceptions could also function as moderators, as they reflect beliefs or tendencies someone may have regarding illness, making conceptualisation as a mediator or moderator more difficult. From the model, emotional representations are on a parallel processing pathway, suggesting mediation. For the purposes of the present study to test the symptom-distress pathway, consequences and emotional representations are conceptualised as mediators; whilst treatment coherence, identity, recurrence and cure beliefs, and control are moderators. However, based on the previous results in Chapter 6, only consequences, emotional representations and coherence are hypothesised as important in the relationship whilst the others remain exploratory.

As theorised in the CSM, it would be expected that greater symptom burden (acting as an illness related stressor) would influence someone to believe there were more consequences of hormone therapy which could result in distress. Previous studies in breast cancer have shown that increased hormone therapy consequences is associated with increased distress (Moon et al., 2017b). However, the regression exploring CSM illness perceptions and distress in Chapter 6 showed a finding in the opposite direction with higher hormone therapy consequences being associated with *lower* distress. This may be a spurious finding

or suppressor effect, or it may imply that greater beliefs about the consequences of hormone therapy do not increase distress as someone may understand the purpose of hormone therapy in reducing risk of recurrence and how the medication works, therefore understanding why they are experiencing symptoms. Therefore, although this mediator is hypothesised, the expected direction is not clear.

Emotional representations were significantly related to distress for the CSM regression model in Chapter 6, although only at baseline. Symptom burden has been found to be a significant predictor of cancer worry (thoughts around recurrence and interrupting daily living) in breast cancer survivors (Phillips et al., 2013). The IPQ-BCS measures recurrence-related emotional representations. It may be that increased symptom burden may act as a day-to-day reminder of someone's cancer, treatment and recurrence risk, which could in turn increase distress, suggesting emotional representations may mediate the relationship.

In addition, previous research suggests illness coherence has been found to be associated with less anxiety and depression in cancer patients (Dempster et al., 2012; Gibbons, Groarke, & Sweeney, 2016). The IPQ-BCS measures coherence specifically around hormone therapy treatment. Treatment coherence is the understanding of the hormone therapy treatment rather than breast cancer itself (Moon et al., 2017a). This measure explores reasons for and how treatment works and based on previous research, would be hypothesised to act as a buffer of the negative impact between symptom burden and distress as this variable measures the knowledge or understanding a person may have.

Finally, the CBRQ variables studied in Chapter 6, propose specific "responses" to symptoms (Picariello et al., 2023) and would therefore be conceptualised as mediators due to the more state-like interpretation. However, the wording of items such as having damage beliefs, or

having different behaviour patterns, imply more trait or belief like moderators. Considering the use of observational data where no change is expected, some of these variables would be better conceptualised as moderators. Based on previous data in Chapter 6 and the present study's aims, two responses are posed as potentially important, and therefore symptom focusing is hypothesised as a mediator in the symptom-distress relationship, whilst damage beliefs may moderate that relationship.

Focusing on one's symptoms has been frequently found in the literature to increase symptoms, be associated with increased symptom severity and reduce functioning (Barends et al., 2020; Barends et al., 2023). Therefore, it would be reasonable to predict that increased symptom burden may result in symptom focusing which would in turn result in distress in this population of breast cancer survivors. On the other hand, if someone tended to have higher damage beliefs, whereby they believe symptoms are related to damage or harm in the body, it is hypothesised that this would enhance the negative impact, of symptoms on distress, whilst lower beliefs about damage would buffer this relationship. There is scarce research on both symptom focusing and damage beliefs in cancer, limiting the understanding of these constructs, but they have been found to be associated with impaired functioning (Barends et al., 2023). However, CBT techniques are used to manage focusing on symptoms in cancer (Moorey & Greer, 2011) and therefore if found to be a mediator in this population, could suggest this variable is incorporated into an integrated model and utilised in interventions.

Using mediation and moderation analysis will provide an understanding of *how* and *for whom* symptoms lead to distress. As presented, management for symptoms is limited, with few evidence-based treatments. Therefore, identifying the mediators and moderators of the

symptom-distress pathway will provide an alternative target for intervention. Focusing on the psychological factors may provide indicators of the effective mechanisms of treatment to help women cope with their symptoms and mitigate the impact of distress. The variables presented have not been tested previously as mediators or moderators to explore the relationship between symptoms and distress in this population of breast cancer survivors on hormone therapy.

7.3 Aims, objectives and hypotheses

This chapter addresses the third aim of the longitudinal study which was to investigate the symptom-distress relationship, by testing hypothesised pathways between the variables.

The objective was:

1) To test whether symptom burden persists over time.
2) To run longitudinal mediation and moderation analysis with relevant variables identified through theory and through the regression analyses presented in Chapter 6, on the symptom-distress pathway.

The following specific hypotheses were tested (depending on data checking):

3) From previous research and theoretical models, it is hypothesised that higher symptom burden at baseline will predict greater distress at 12 months whilst controlling for covariates (presented in Chapter 6).
4) Based on theory, the meta-analysis findings in Chapter 4, and the qualitative findings in Chapter 5, it is hypothesised that experiential avoidance and cognitive fusion will partially mediate the relationship between symptoms and distress; whilst higher self-

compassion and mindfulness will moderate the relationship, whereby these resources or skills will buffer the negative impact of symptom burden on distress.

Exploratory analysis will be run on the remaining ACT inflexible processes as mediators and the flexible processes as moderators.

5) Based on the CSM and results from the regression models in Chapter 6, hormone therapy consequences and emotional representations will partially mediate the relationship between symptoms and distress; whilst treatment coherence will moderate the relationship, whereby better understanding of treatment will buffer the negative impact of symptom burden on distress.

Exploratory analysis will be run on the remaining CSM illness perceptions with breast cancer consequences tested as a mediator as conceptualised previously and recurrence beliefs, identity, cure beliefs and control as moderators.

6) Based on the CBRQ and results from the regression models in Chapter 6, symptom focusing will partially mediate the relationship between symptoms and distress; whilst damage beliefs will moderate the relationship, whereby greater damage beliefs will increase the negative impact of symptom burden on distress.

Exploratory analysis will be run on the remaining CBRQ items with embarrassment avoidance tested as mediators and fear avoidance and all or nothing and resting behaviours as moderators.

7.4 Methods

As this analysis is part of the same study conducted in Chapter 6, the comprehensive methods section is outlined in Chapter 6, Section 6.2.

7.4.1 Statistical analysis

Mplus version 8.10 (Muthén & Muthén, 1998-2017) was used for mediation and moderation analysis. Due to multiple testing, a more stringent significance value of $p < .01$ was used for this study.

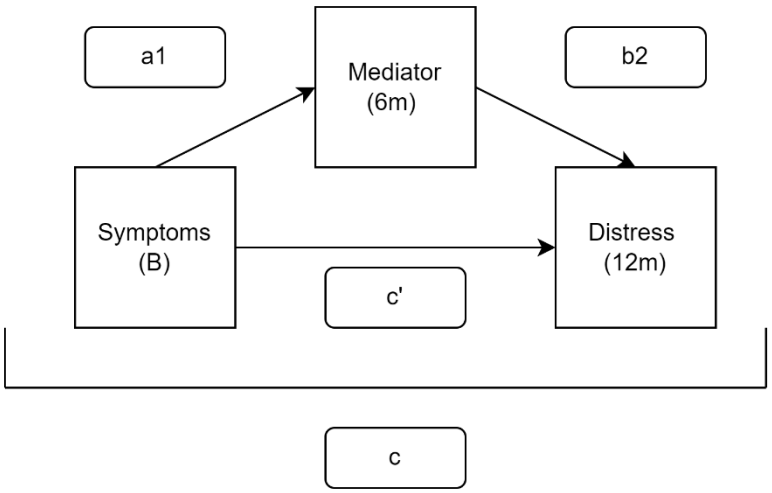
For longitudinal mediation analysis, path analysis was conducted in Mplus which tests the indirect effect rather than the *a* and *b* paths separately (Hayes, 2009). To test the suitability of hypothesised mediators, correlations were run between baseline symptom burden, 6-month psychological variables and 12-month distress as the mediator needs to be correlated with both the independent (IV; symptom burden) and dependent variables (DV; distress at 12 months). A pragmatic threshold of $r > 0.3$ was used to determine relationships between the baseline IV and 6 months mediator and 12-month DV and 6 months mediator to identify suitable variables for analysis. Mediation models were also based on the results of the regression analyses in Chapter 6 and therefore age, number of children and COVID-19 distress at baseline were included as covariates. All mediation (and moderation) models were saturated with 0 degrees of freedom so model fit is not reported. Saturated models mean the number of estimated parameters is equal to the number of means in the dataset (Ryu, 2014) and is common in less complicated structural equation models. Baseline distress was not included in the mediation models in accordance with other longitudinal studies (e.g., Philipp et al., 2021).

It is recommended that mediation models are run with bootstrapping (minimum 1000, suggested 5000), which repeatedly resamples the data improving the estimates of the indirect effect (Hayes, 2009). Bootstrapping also makes no distributional assumptions unlike other mediation tests (e.g., the Sobel test; Hayes, 2009). Mediation models were therefore

run with 5000 bootstraps. Mediation models were re-rerun with multiple imputation (50 datasets, no bootstrap) for sensitivity analysis (see Chapter 6 for rationale and Appendix D, Table D1 and D2). This method aims to reduce bias by predicting data based on other variables rather than assuming individual stability (Sterne et al., 2009), so the multiple imputation models included age, children, COVID-19 distress and then symptom burden, the mediator and distress at all time points. Figure 7.1 depicts the different pathways in the mediation models and are reported in the results tables. The percentage of effect that operates indirectly is reported (calculated by indirect/direct effect x100).

Figure 7.1.

Pathways tested and reported for mediation analysis



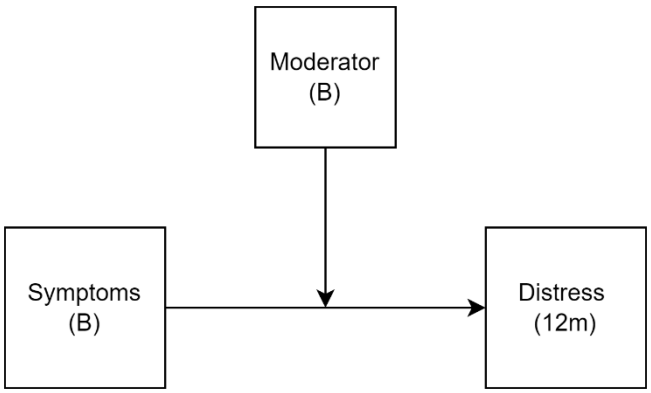
In the mediation models, *a1xb2* depicts the indirect effect, *c'* is the direct effect between the IV and DV, and *c* is the total effect (*a1xb2* + *c'*).

For moderator analysis, psychological variables at baseline were examined in correlations as they should not correlate with the independent variable (symptom burden) and if so, not highly (Kraemer et al., 2002; Wu & Zumbo, 2008). Therefore, a pragmatic threshold was applied, and moderators needed to have a correlation of $r < 0.3$ with symptom burden.

Interaction terms were created with symptom burden and the moderator at baseline and added to the model. Age, COVID-19 distress, and number of children were added into all models as covariates. Baseline distress was included as moderator analysis aims to identify factors that change the relationship between the IV and DV, rather than explain the strength of the relationship. The models were run with 5000 bootstraps and rerun on the 50 imputed datasets for sensitivity analysis (Appendix D, Table D3). Figure 7.2 demonstrates the moderator analysis tested and reported.

Figure 7.2.

Moderator analysis (B = baseline, 12m = 12 months follow up)



7.5 Results

Demographics and clinical characteristics of the 269 participants included in the sample are available in Chapter 6, Section 6.4.1.

7.5.1 Symptom burden over time

Table 7.1 displays means and standard deviations of symptom burden over time. Due to the differences in side effects experienced by each drug, to check if there were any differences in symptom burden between those participants on aromatase inhibitors (AI's) vs those on

tamoxifen, an independent samples *t* test was run. There were no significant differences between symptom burden (*t*[258] = 1.37, *p* = .086) for those on tamoxifen and those on AI's.

Table 7.1.

Symptom burden scores over time

	Baseline	6 months	12 months
		Means (SD)	
Symptom burden	29.88 (12.84)	30.78 (11.89)	30.45 (12.68)

Note: SD: standard deviation

A latent growth model was run for symptom burden. Per unit of time, there was an average increase of 0.56 units (*p* = .60) of symptom burden. However, this was non-significant, suggesting that symptom burden remained stable over time. There was a non-significant weak positive correlation between the intercept and slope (*r* = .02, *p* = .99), meaning the intercept (mean symptom burden at baseline) was not related to change over time. There was significant variance in the intercept (difference in scores at time one; 116.21, *p* < .001) but not the slope (individual difference in change over time; -2.82, *p* = .66).

7.5.2 Associations between variables

There were significant correlations between all baseline ACT processes and baseline symptom burden and 12 month distress in the directions predicted (see Table 7.2); whereby higher scores on flexible processes (mindfulness, self-as-context, values progress, committed action and self-compassion) were associated with lower symptom burden (*r* = -.15 to -.38) and lower distress (*r* = -.17 to -.48); and where higher scores on inflexible processes (experiential avoidance, cognitive fusion and values obstruction) were associated with greater symptom burden (*r* = .25 to .38) and higher distress (*r* = .40 to .56).

Table 7.2.

Correlations between baseline symptom burden, baseline psychological variables and 12-month distress

Variables at baseline	Symptom burden (baseline)	Distress (12 months)
Experiential avoidance	.25**	.41**
Cognitive fusion	.36**	.56**
Mindfulness	-.38**	-.48**
Self-as-context	**-.31****	**-.43****
Values progress	**-.15***	**-.17****
Values obstruction	.38**	.40**
Committed action	**-.31****	**-.33****
Self-compassion	-.36**	-.48**
Identity	.50**	.23**
Cure beliefs	-.04	-.11
BC consequences	.43**	.39**
HT consequences	.59**	.21**
Recurrence	**.22****	**.31****
Personal control	**-.09**	**-.13***
Treatment control	**-.16****	**-.20****
Coherence	**-.13***	**-.15***
Emotional representations	.33**	.40**
Fear avoidance	.32**	.19**
Damage beliefs	**.25****	**.37****
Embarrassment avoidance	.43**	.43**
Symptom focusing	.41**	.37**
All or nothing behaviour	**.27****	**.23****
Resting behaviour	**.25****	**.26****

*Note: BC: breast cancer; HT: hormone therapy; * = p <.05, ** = p < .01; suitable moderators are in bold*

The baseline CSM illness perceptions as measured by the IPQ-BCS subscales were correlated with symptom burden and distress in the directions expected. Higher scores regarding breast cancer consequences, hormone therapy consequences, recurrence and emotional representations, were significantly positively correlated with symptom burden (r = .22 to .59) and 12-month distress (r = .21 to .40). Coherence and treatment control were significantly negatively correlated with symptom burden (r = -.13 and -.16, respectively) and 12-month distress (r = -.15 and -.20). Cure beliefs had a non-significant correlation with both

symptom burden and distress. Personal control was significantly associated with distress (*r* = .13) but not symptom burden.

All CBRQ-SF subscales and the total score had significant positive correlations with symptom burden and distress, as predicted, with more negative responses associated with worse outcomes. The strongest correlations with symptom burden were for symptom focusing and embarrassment avoidance (*r* = .41 and .43, respectively). For 12 months distress the strongest associations were for damage beliefs, symptom focusing and embarrassment avoidance (*r* = .37, .37 and .43, respectively).

Correlations were run between 6-month psychological processes and baseline symptom burden and distress at 12 months to inform the mediation analysis. Mediators at 6 months should be correlated with both the independent variable (symptom burden at baseline) and dependent variable (distress at 12 months). All variables apart from cure beliefs and personal control had significant correlations with distress and symptom burden. See Table 7.3 for the variables in bold that met the threshold to be tested as a mediator.

Table 7.3.

Correlations between baseline symptom burden, 6-month variables and 12-month distress

Variables at 6 months	Symptom burden (baseline)	Distress (12 months)
Experiential avoidance	.25**	.49**
Cognitive fusion	**.29****	**.55****
Mindfulness	-.36**	-.48**
Self-as-context	-.23**	-.48**
Values progress	-.25**	-.22**
Values obstruction	**.33****	**.46****
Committed action	-.34**	-.44**
Self-compassion	-.24**	-.45**
Identity	.43**	.29**
Cure beliefs	-.12	-.12
BC consequences	**.38****	**.43****
HT consequences	**.53****	**.33****
Recurrence	.21**	.32**
Personal control	-.16*	-.02
Treatment control	-.21**	-.17*
Coherence	-.16*	-.25**
Emotional representations	.21**	.38**
Fear avoidance	.32**	.23**
Damage beliefs	.22**	.34**
Embarrassment avoidance	**.35****	**.44****
Symptom focusing	**.36****	**.39****
All or nothing behaviour	.29**	.28**
Resting behaviour	.26**	.24**

*Note: * = p <.05, ** = p < .01; suitable mediators in bold*

7.5.3 Mediation analysis

7.5.3.1 Hypothesised mediators

Based on the hypotheses and after checking the data, the following variables were tested as mediators: cognitive fusion, values obstruction, hormone therapy consequences, and symptom focusing. Although experiential avoidance and emotional representations were hypothesised to be mediators, mediation analysis was not carried out for these variables as their correlations with symptom burden were less than r = .30. Each mediator score at 6 months was entered into the path analysis to see if it mediated the pathway between

baseline symptoms and 12-month distress. The data reported in this section use the complete data and were run with 5000 bootstraps.

Table 7.4 shows the results of the mediation path analyses. For all mediation models, the direct, indirect and total effects are reported. Sensitivity analysis on the pooled estimates from the imputed datasets is available in Appendix D, Table D1.

Table 7.4.

Results of mediation analysis

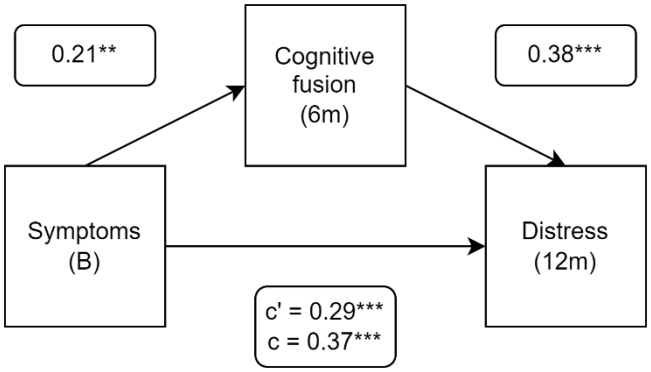
		β	SE	P value	95% CI
Cognitive fusion (CF)					
Direct effects	Symptoms to CF (a1)	0.21**	0.07	.002	0.07, 0.34
	CF to distress (b2)	0.38***	0.07	<.001	0.24, 0.51
	Symptoms to distress (c')	0.29***	0.05	<.001	0.19, 0.39
Indirect effect	a1xb2	0.08**	0.03	.005	0.03, 0.15
Total effect	(c)	0.37***	0.06	<.001	0.26, 0.48
Values obstruction (ValO)					
Direct effects	Symptoms to ValO (a1)	0.27***	0.06	<.001	0.16, 0.39
	ValO to distress (b2)	0.30***	0.08	<.001	0.14, 0.44
	Symptoms to distress (c')	0.29***	0.05	<.001	0.18, 0.39
Indirect effect	a1xb2	0.08***	0.03	.001	0.04, 0.14
Total effect	(c)	0.37***	0.06	<.001	0.26, 0.47
Hormone therapy consequences (HT)					
Direct effects	Symptoms to HT (a1)	0.50***	0.06	<.001	0.38, 0.60
	HT to distress (b2)	0.07	0.07	.346	-0.07, 0.21
	Symptoms to distress (c')	0.33***	0.06	<.001	0.20, 0.46
Indirect effect	a1xb2	0.03	0.04	.350	-0.04, 0.11
Total effect	(c)	0.37***	0.06	<.001	0.25, 0.48
Symptom focusing (SF)					
Direct effects	Symptoms to SF (a1)	0.31***	0.06	<.001	0.18, 0.43
	SF to distress (b2)	0.21**	0.07	.003	0.07, 0.33
	Symptoms to distress (c')	0.30***	0.06	<.001	0.19, 0.42
Indirect effect	a1xb2	0.06*	0.03	.012	0.02, 0.12
Total effect	(c)	0.36***	0.06	<.001	0.25, 0.47

*Note: all path models controlling for age, COVID-19 distress and number of children; bootstrapped confidence intervals; CF: cognitive fusion; ValO: values obstruction; HT: hormone therapy consequences; SF: symptom focusing; β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Cognitive fusion partially mediated the effect of symptoms on 12-month distress whilst controlling for covariates. An increase in symptom burden predicted an increase in cognitive fusion (β = 0.21, 95% CI = 0.07, 0.34) which in turn predicted increased distress (β = 0.38, 95% CI = 0.24, 0.51), resulting in an indirect effect that was significant although a small effect (β = 0.08, 95% CI = 0.03, 0.15). The indirect effect accounts for 28% of the direct effect of symptoms on distress. See Figure 7.3 for path diagram.

Figure 7.3.

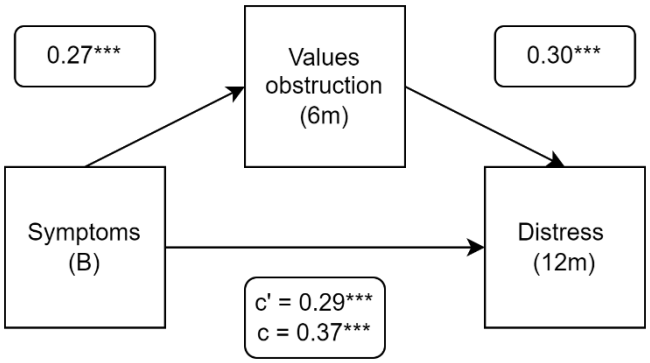
Path analysis for cognitive fusion as a mediator



Values obstruction was a partial mediator of the relationship between symptom burden and distress at 12 months, with a significant indirect effect (β = 0.08, 95% CI = 0.04, 0.14). The indirect effect accounts for 28% of the direct effect of symptoms on distress. See Figure 7.4 for path diagram.

Figure 7.4.

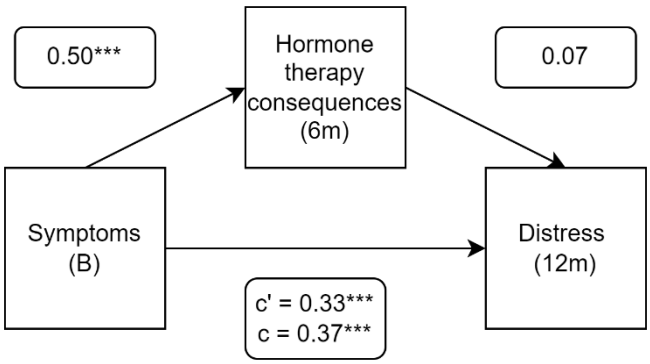
Path analysis for values obstruction as a mediator



Hormone therapy consequences did not significantly mediate the relationship between symptoms and distress. Both the direct (β = 0.33) and total effect (β = 0.37) were similar indicating that this variable does not explain the relationship, see Figure 7.5. There was a large effect of symptoms on hormone therapy consequences (*a* path; β = 0.50) implying there is a relationship between these two variables, however having stronger beliefs about the consequences of hormone therapy did not in turn increase distress.

Figure 7.5.

Path diagram for hormone therapy consequences as a mediator

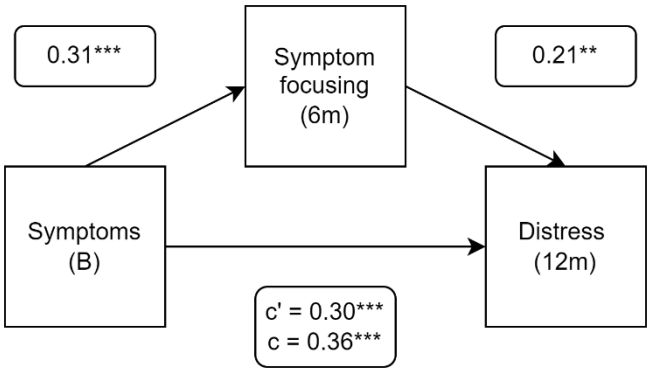


Symptom focusing significantly partially mediated the relationship between symptoms and distress. Higher symptom burden predicted greater symptom focusing (β = 0.31; 95% CI = 0.18, 0.43) which in turn predicted increased distress (β = 0.21; 95% CI = 0.07, 0.33). This

resulted in a significant, but small, indirect effect (β = 0.06; 95% CI = 0.02, 0.12). The indirect effect accounted for 20% of the direct effect of symptoms on distress. See Figure 7.6 for the path diagram.

Figure 7.6

Path diagram of symptom focusing as a mediator



7.5.3.2 Exploratory mediators

Additional analyses were run on mediators that had not been hypothesised based on previous results but where data indicated that mediation may be appropriate. After checking the correlations, embarrassment avoidance and breast cancer consequences were suitable variables to be tested and were conceptualised as mediators, see Table 7.5. Results were replicated in the imputed data (see Appendix D, Table D2).

Table 7.5.

Results of exploratory mediation analysis

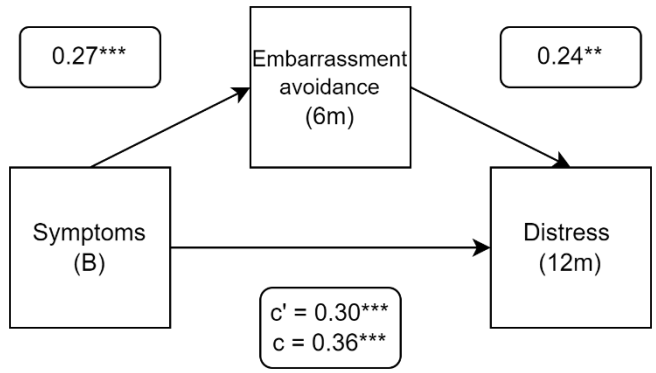
		β	SE	P value	95% CI
Embarrassment avoidance					
Direct effects	Symptoms to EA (a1)	0.27***	0.06	<.001	0.16, 0.39
	EA to distress (b2)	0.24**	0.08	.002	0.08, 0.39
	Symptoms to distress (c')	0.30***	0.06	<.001	0.18, 0.41
Indirect effect	a1xb2	0.07*	0.03	.010	0.02, 0.12
Total effect	(c)	0.36***	0.06	<.001	0.25, 0.47
Breast cancer consequences					
Direct effects	Symptoms to BC (a1)	0.31***	0.06	<.001	0.19, 0.42
	BC to distress (b2)	0.20**	0.06	.002	0.06, 0.32
	Symptoms to distress (c')	0.31***	0.06	<.001	0.19, 0.42
Indirect effect	a1xb2	0.06**	0.02	.009	0.02, 0.11
Total effect	(c)	0.37***	0.06	<.001	0.26, 0.48

*Note: all path models controlling for age, COVID distress and number of children; bootstrapped confidence intervals; EA: embarrassment avoidance; BC: breast cancer consequences; β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Embarrassment avoidance partially mediated the relationship between symptom burden and follow up distress with a significant indirect effect (β = 0.07; 95% CI = 0.02, 0.12). The indirect effect accounted for 23% of the direct effect. See Figure 7.7 for the path diagram.

Figure 7.7.

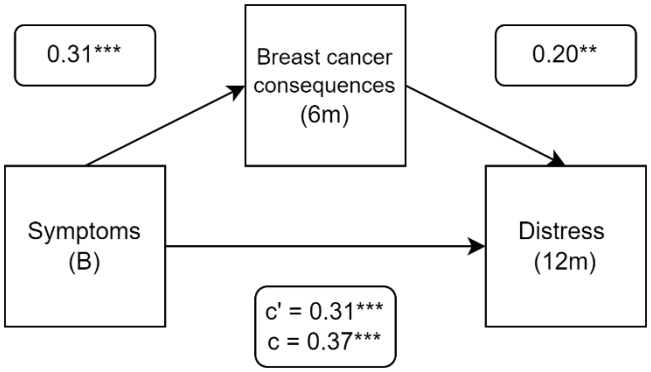
Path diagram for embarrassment avoidance as a mediator



Breast cancer consequences significantly mediated the relationship between symptom burden and distress. An increase in symptom burden predicted an increase in perceived breast cancer consequences (β = 0.31; 95% CI = 0.19, 0.42) and this in turn predicted increased distress (β = 0.20; 95% CI = 0.06, 0.32). The indirect effect was significant (β = 0.06; 95% CI = 0.02, 0.11) and accounted for 19% of the direct effect. See Figure 7.8 for the path diagram.

Figure 7.8.

Path diagram for breast cancer consequences as a mediator



7.5.4 Moderator analysis

Moderators were deemed suitable if the baseline score had a correlation of $r < .30$ with baseline symptom burden. Age, COVID-19 distress, number of children and baseline distress were included as covariates in moderator analysis. Sensitivity analysis using imputed data is available in Appendix D, Table D3. An interaction term was made between baseline symptom burden and each of the baseline moderator variables. The moderator was standardised to aid interpretation of the interaction effect at -1, 0 and +1 to represent one standard deviation above the mean, the mean and one standard deviation below the mean. The data presenting the betas at these different levels (low, average, high) are available in Appendix D, Table D4.

7.5.4.1 Hypothesised moderators

Based on the hypotheses and after checking data, treatment coherence and damage beliefs were tested as moderators. Although hypothesised, neither mindfulness nor self-compassion could be tested as a moderator due to the correlation with symptom burden being greater than +/- 0.3. Table 7.6 displays the estimates and confidence intervals for each hypothesised moderator.

Table 7.6.

Estimates and confidence intervals for hypothesised moderators

	β	SE	*p*	95% CI
Coherence (hormone treatment)				
Age	-0.12*	0.05	.013	-0.22, -0.02
Covid distress	0.01	0.05	.815	-0.09, 0.12
Child	0.12*	0.05	.021	0.02, 0.23
Baseline distress	0.52***	0.06	<.001	0.40, 0.64
Symptom burden	0.15**	0.05	.007	0.04, 0.26
Coherence	0.24*	0.11	.038	0.02, 0.47
Symptom burden X coherence	-0.33**	0.13	.009	-0.57, -0.07
Damage beliefs				
Age	-0.11*	0.05	.023	-0.22, -0.02
Covid distress	-0.01	0.05	.783	-0.12, 0.09
Child	0.14**	0.05	.006	0.04, 0.24
Baseline distress	0.49***	0.06	<.001	0.36, 0.61
Symptom burden	0.14**	0.06	.010	0.04, 0.25
Damage beliefs	-0.06	0.10	.572	-0.25, 0.15
Symptom burden X damage beliefs	0.26*	0.10	.013	0.05, 0.45

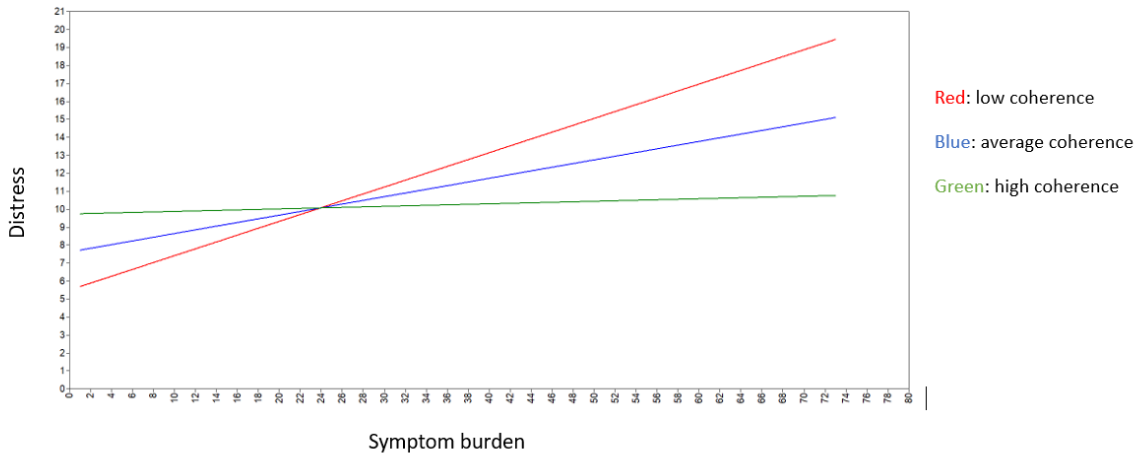
*Note: β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Treatment coherence was a significant independent predictor of distress at 12 months and there was also a significant interaction effect. The relationship between symptom burden and later distress changed, whereby a greater understanding of hormone therapy treatment at baseline, reduced the effect of symptom burden on distress at 12 months (β = -0.33, 95% CI = -0.573, -0.065). At low and average levels of treatment coherence, the relationship

between symptom burden and distress was significant despite the strength of effect changing, see Figure 7.10. However, at high levels of treatment coherence (1 SD above the mean), the relationship between symptom burden and distress became non-significant (β = 0.01, 95% CI = -0.08, 0.11), suggesting that perceiving oneself to have a good understanding of the hormone therapy was protective of the impact of symptoms on distress. Beta coefficients for the different levels of treatment coherence (low, average, high) is available in Appendix D, Table D4. In sensitivity analysis (Appendix D, Table D3), the interaction effect was non-significant using imputed data.

Figure 7.9.

The effect of low, average and high levels of treatment coherence on the relationship between symptom burden and distress.

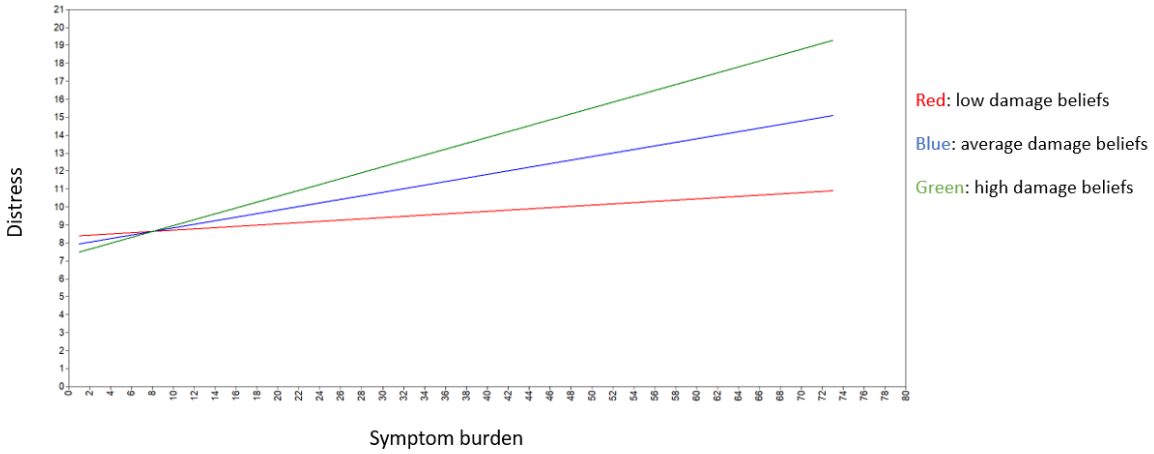


Damage beliefs were not a significant independent predictor of distress at 12 months. Greater beliefs about damage at baseline increased the strength of the effect between symptom burden and later distress (β = 0.26, 95% CI = 0.05, 0.45) however at the more stringent *p* value, the interaction effect was non-significant. At low levels of damage beliefs (1 SD below the mean), the relationship between symptom burden and distress became

non-significant see Figure 7.11 and Appendix D, Table D4. For sensitivity analysis with the imputed data set the interaction effect was also non-significant (see Appendix D, Table D3).

Figure 7.10.

The effect of low, average and high levels of damage beliefs on the relationship between symptom burden and distress.



7.5.4.2 Exploratory moderators

Based on the conceptualisations presented at the beginning of this chapter, self-as-context, values progress, recurrence beliefs, personal control, treatment control, all or nothing behaviour and resting behaviour, were tested as exploratory moderators. Cure beliefs were not tested as a moderator due to the non-significant correlation with 12-month distress. Committed action and identity could also not be tested due to strong correlations with symptom burden. See Table 7.7 for moderator analysis.

Table 7.7.

Estimates and confidence intervals for exploratory moderators

	β	SE	P value	95% CI
Self-as-context				
Age	-0.10	0.05	.053	-0.21, 0.001
Covid distress	0.00	0.06	.972	-0.11, 0.12
Child	0.13**	0.05	.014	0.03, 0.23
Baseline distress	0.51***	0.07	<.001	0.36, 0.65
Symptom burden	0.14*	0.06	.022	0.02, 0.25
Self-as-context	-0.001	0.14	.995	-0.28, 0.27
Symptom burden X self-as-context	-0.10	0.14	.474	-0.38, 0.19
Values progress				
Age	-0.12*	0.05	.023	-0.22, -0.02
Covid distress	0.01	0.06	.855	-0.10, 0.13
Child	0.13*	0.05	.016	0.03, 0.24
Baseline distress	0.55***	0.07	<.001	0.42, 0.68
Symptom burden	0.15*	0.06	.014	0.03, 0.27
Values progress	0.06	0.14	.665	-0.21, 0.32
Symptom burden X values progress	-0.03	0.14	.840	-0.29, 0.26
Committed action				
Age	-0.12	0.05	.019	-0.22, -0.02
Covid distress	0.01	0.06	.922	-0.11, 0.12
Child	0.13	0.05	.013	0.03, 0.24
Baseline distress	0.52	0.07	.000	0.39, 0.66
Symptom burden	0.15	0.06	.010	0.04, 0.27
Committed action	0.03	0.12	.811	-0.19, 0.27
Symptom burden X committed action	-0.08	0.12	.484	-0.32, 0.14
Recurrence beliefs				
Age	-0.12*	0.05	.036	-0.21, -0.01
Covid distress	0.00	0.05	.993	-0.11, 0.11
Child	0.13**	0.05	.011	0.03, 0.24
Baseline distress	0.52***	0.06	<.001	0.39, 0.64
Symptom burden	0.15**	0.06	.009	0.04, 0.26
Recurrence beliefs	0.06	0.11	.612	-0.16, 0.29
Symptom burden X recurrence beliefs	0.08	0.12	.478	-0.15, 0.31
Personal control				
Age	-0.12*	0.05	.027	-0.22, -0.01
Covid distress	0.01	0.06	.890	-0.10, 0.12
Child	0.13*	0.06	.023	0.02, 0.24
Baseline distress	0.54***	0.07	<.001	0.40, 0.67
Symptom burden	0.15**	0.06	.009	0.04, 0.27
Personal control	-0.03	0.12	.809	-0.28, 0.21
Symptom burden X personal control	0.00	0.14	.983	-0.27, 0.28
Treatment control				
Age	-0.12*	0.05	.017	-0.23, -0.02
Covid distress	0.01	0.06	.871	-0.10, 0.12

Child	0.12*	0.06	.026	0.02, 0.23
Baseline distress	0.53***	0.07	<.001	0.40, 0.66
Symptom burden	0.15**	0.06	.008	0.03, 0.26
Treatment control	-0.05	0.11	.627	-0.25, 0.16
Symptom burden X treatment control	-0.01	0.14	.929	-0.29, 0.26
All or nothing behaviour				
Age	-0.12*	0.05	.024	-0.22, -0.01
Covid distress	0.01	0.06	.878	-0.10, 0.12
Child	0.12*	0.05	.020	0.02, 0.23
Baseline distress	0.53***	0.07	<.001	0.40, 0.66
Symptom burden	0.13*	0.06	.023	0.01, 0.25
All or nothing	-0.02	0.10	.843	-0.23, 0.17
Symptom burden X all or nothing	0.11	0.10	.287	-0.10, 0.31
Resting				
Age	-0.12*	0.05	.021	-0.22, -0.01
Covid distress	0.01	0.06	.828	-0.09, 0.12
Child	0.13*	0.05	.011	0.03, 0.24
Baseline distress	0.52***	0.07	<.001	0.39, 0.66
Symptom burden	0.14*	0.06	.014	0.03, 0.25
Resting	0.03	0.12	.806	-0.19, 0.27
Symptom burden X resting	0.05	0.14	.692	-0.21, 0.32

*Note: β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

None of the exploratory variables were significant moderators of the symptom-distress relationship. See Table 7.8 for betas and significance.

7.6 Discussion

This chapter aimed to build on the results of Chapter 6 which showed symptom burden and other psychological variables were predictors of distress at 12 months, by investigating the pathway between symptoms and distress. Firstly, in this study, symptom burden was stable over time. This provides further evidence that side effects persist which is counter to the information that breast cancer survivors are being given that their side effects will decrease, as discussed in Chapter 1. A proportion of the women had been on hormone therapy for over a year at baseline data collection further providing evidence for this persistence. These results add to the existing research literature in this area (Ganz et al., 2016b; Moon et al.,

2019b) and have important implications. If symptom burden continues over time, and symptoms predict distress, this suggests distress may also continue over time, providing strong rationale for investigation these relationships. As presented in Chapter 6, although distress reduced at 12 months in this sample, this is likely due to non-responders at 12 months being significantly more distressed. Distress was stable over 6 months which may be due to less drop out and no differences in distress for those who dropped out and continued with the study, providing evidence for this potential persistence.

To explore the third variables that may be involved in the symptom-distress relationship, mediation and moderation analysis were conducted. Explanatory variables were hypothesised based on theoretical models (TMA-LTC, ACT and CSM), previous literature and the results presented in this thesis including the qualitative study and regression analysis in Chapter 6. Cognitive fusion, values obstruction, breast cancer consequences, symptom focusing, and embarrassment avoidance were all significant partial mediators of the symptom-distress relationship. Contrary to the hypothesis, beliefs about hormone therapy consequences were not a significant mediator. Damage beliefs and treatment coherence were significant moderators; whereby fewer damage beliefs and a greater understanding of hormone therapy treatment buffered the impact of symptoms on distress. Based on the data the following hypotheses could not be tested; experiential avoidance and emotional representations could not be tested as mediators and mindfulness and self-compassion could not be tested as moderators as they were too highly correlated with symptom burden at baseline.

7.6.1 Mediators

Mediation analyses were run on the longitudinal data to test the hypothesised variables in their ability to explain *how* symptoms lead to distress.

7.6.1.1 ACT mediators

ACT inflexible processes were conceptualised as mediators as they have been proposed to "explain" psychopathology and suffering (Hayes et al., 2006). Only cognitive fusion and values obstruction could be tested as mediators as the correlations for experiential avoidance with symptom burden and distress violated the assumptions of mediation analysis. Experiential avoidance could have alternatively been conceptualised as a moderator in observational data and therefore tested, as someone may have the tendency to avoid emotions, thoughts or sensations. However, the inflexible processes were conceptualised as mediators *a priori* and it is recommended not to use variables interchangeably (e.g., as a moderator if the mediator was null; Wu & Zumbo, 2008).

Cognitive fusion significantly partially mediated the relationship, whereby increased symptom burden predicted more fusion with thoughts at six months and this in turn predicted an increase in later distress. Fusion with thoughts around symptoms, emotions and experiences is hypothesised by the ACT model to result in poorer outcomes (Hayes et al., 2006) and was demonstrated by this study. The findings support previous literature which has found cognitive fusion to partially mediate the effects of body dissatisfaction and shame on depressive symptoms in breast cancer patients (Trindade et al., 2018a). The authors report that the symptoms and complications from breast cancer and treatment may lead to dissatisfaction with the body, and if this dissatisfaction and shame leads to fusion with these thoughts, this in turn results in distress. Gillanders et al. (2015) also found that

cognitive fusion mediated the impact of threat appraisals on anxiety in a cancer population whereby having more threatening appraisals of cancer was associated with increased fusion with these cognitions which in turn was associated with increased anxiety. However, this study was cross-sectional limiting the interpretation of the ordering of the variables in the model. These two studies in conjunction with the present study's results suggests that cognitive fusion may explain various relationships of cancer patients' experiences and how these might lead to distress. This process could therefore be useful for understanding how symptom burden, body dissatisfaction and threatening illness related cognitions may lead to distress and be a widely applicable process to target. In addition, the present study addressed limitations of the previous literature by testing this relationship over time, providing support for the directions of relationships.

The findings suggest targeting cognitive fusion may help to reduce the distressing impact of symptoms. The ACT model proposes cognitive defusion as the flexible skill in contrast to the inflexible nature of fusion (Hayes et al., 2006). Cognitive defusion exercises such as noticing the negative thoughts that come up around the experience of symptoms and observing them as just thoughts, may be a useful target of interventions to reduce cognitive fusion and therefore reduce the negative impact of symptoms on distress. Although data are limited in cancer, cognitive defusion has been found to be a successful mediator for outcomes such as quality of life, anxiety and depression in non-cancer samples (Stockton et al., 2019). Developing this skill could also have other positive impacts as suggested by the previous studies, as enhancing defusion skills, may also reduce the distressing impact of body dissatisfaction and threatening illness appraisals.

Values obstruction was the other significant ACT mediator and supported the hypothesis that symptom burden predicted more thoughts and feelings getting in the way of important life directions and therefore resulting in distress. Values obstruction has previously been found to be positively associated with physical symptoms and distress in metastatic breast cancer patients (Mosher et al., 2017). In Chapter 5, participants talked about having to adapt to the loss/change due to symptoms to manage daily, which may be linked to this construct. Although quantitative data in cancer is relatively limited for values and there is variation in findings due to the different measures (Fawson et al., 2023). Improvements to obstruction to values has been found in an online ACT trial for distressed college students, and these improvements mediated the effect on mental health (Levin, Krafft, & Twohig, 2020). Values progress is the corresponding flexible processes however in this trial (Levin, Krafft, & Twohig, 2020), values progress did not mediate the effect for mental health. These results may be due to the measure not picking up the improvement of the flexible process or skill. Or, as this was an ACT intervention, values obstruction may have been improved by another related ACT flexible process.

Initially, experiential avoidance was hypothesised to be a mediator of the symptom-distress relationship, however due to the low correlation with baseline symptom burden, it did not reach threshold to be tested. It may be that the measure used, the BEAQ (Gámez et al., 2014), is too focused on the avoidance of emotions, and therefore may not capture the avoidance of physical symptoms or sensations, resulting in a lower correlation with symptom burden. Previous research has found this relationship whereby experiential avoidance (along with functional impairment) mediated the effect of pain on distress in people with cancer (Brown et al., 2020). Participants were more likely to engage in attempts to avoid the painful experiences which in turn results in interference with daily functioning

and therefore more distress. Brown et al. (2020) used a measure of avoidance in pain specifically, so the avoidance was more targeted to the experience of pain symptoms rather than avoidance of more general emotions or thoughts. To understand the avoidance related to physical symptoms and how this might lead to distress, a more specific measure may be needed.

7.6.1.2 CSM and CBRQ mediators

The illness perceptions from the CSM were conceptualised as a mixture of mediators and moderators as the definitions of the perceptions differ. It was hypothesised that beliefs about hormone therapy consequences and emotional representations would mediate the pathway between symptoms and distress, as these constructs can be conceptualised as directly related to or in response to the experience of symptoms. However, emotional representations could not be tested as a mediator due to the small correlation with symptom burden. Beliefs about breast cancer consequences were conceptualised as a mediator and run as exploratory analysis.

Beliefs about hormone therapy consequences were not a significant mediator, however the *a* path, which is the direct effect between symptom burden and hormone therapy consequences had a strong effect. As hypothesised, this implies symptom burden predicts someone to have stronger beliefs around the consequences of hormone therapy that their life and functioning has been impacted by hormone therapy. However, this was not in turn predictive of increased distress. As presented in the introduction section of this chapter, it may be that individuals can make sense of their symptoms as consequences of the hormone therapy, understand their treatment is working and feel they are actively doing something to help reduce risk of recurrence and therefore not experience distress about taking the

medication. However, these beliefs were not associated with either decreased or increased distress. The interpretation of beliefs about hormone therapy consequences being a sign of treatment working is in line with research that suggests symptoms are a useful biomarker for hormone therapy working effectively as experiencing symptoms is associated with a decrease in breast cancer recurrence (Cuzick et al., 2008; Mortimer et al., 2008). However, research suggests that beliefs about tamoxifen consequences are associated with intentional non-adherence (Moon et al., 2017b), so targeting these beliefs in an intervention may not be beneficial to the wider breast cancer survivors experience due to unintended negative consequences.

Interestingly however, beliefs about breast cancer consequences were a significant mediator in exploratory analyses. Symptom burden was related to beliefs around the consequences of breast cancer itself and primary treatment which had a negative impact as this was related to increased distress. Symptom burden may act as a reminder of the impact of the breast cancer diagnosis, what life was like pre-cancer and the ongoing impact of treatment and therefore may explain an example of why symptoms can lead to distress (e.g., Rosedale & Fu, 2010). In contrast to beliefs about hormone therapy consequences, beliefs about the consequences of breast cancer have not been found to be associated with intentional non-adherence (Moon et al., 2019b; Moon et al., 2017b), suggesting targeting this variable in an intervention may not have detrimental outcomes on medication taking behaviour. This is potentially important for intervention development to focus on managing thoughts and beliefs around the ongoing general impact of treatment and symptoms after a diagnosis of breast cancer.

Emotional representations were hypothesised as a mediator due to the parallel processing definition of the CSM. However, emotional representations could not be tested as a mediator due to the small correlation with symptom burden. The IPQ-BCS does not align with the original definition of emotional representations from the CSM, rather it focuses on emotions around recurrence risk specifically which may explain the small correlation. Other research has found symptoms are related to thoughts about cancer worry (Phillips et al., 2013). Additionally, previous research has found that fear of cancer recurrence mediated the effect of somatic symptoms on perceived stress in cancer survivors (Hall et al., 2017). It may be that the emotional representations measure does not accurately reflect emotions around recurrence, and other measures of cancer worry, or fear of recurrence may be better proposed measures to investigate this relationship. Conversely, a more general emotional representations measure may confound with distress outcomes, limiting its utility in the distress literature.

Finally, several CBRQ variables were conceptualised as mediators as they explain specific responses to symptoms. It was hypothesised that symptom focusing would be important in understanding the symptom-distress relationship, and embarrassment avoidance was run as exploratory analysis due to suitable data.

Symptom focusing was a partial mediator whereby higher symptom burden resulted in increased attention to and focusing on symptoms, which in turn resulted in an increase in distress. Symptom focusing is an item measured by the CBRQ which has been used in few cancer related studies, however has been found to be associated with symptom severity, poorer mental health and impaired functioning (Barends et al., 2023; Hughes et al., 2020a). It is not a variable that appears in the models presented in Chapter 2, although techniques

used to distract from an excessive focus on somatic sensations are used in CBT for cancer (Moorey & Greer, 2011) and therefore could pose a useful technique for managing this mechanism. In addition, there are similarities between symptom focusing and cognitive fusion as both constructs relate to the focusing or attention on symptoms, other thoughts, or emotions. Cognitive defusion, as described above, could target being fused with or focused on thoughts and emotions, as used in previous ACT interventions (Feros et al., 2011; Stockton et al., 2019), and these may be specifically related to physical symptoms or sensations, meaning this technique may help with both the specific symptom focused thoughts and fusion with other thoughts. Cognitive defusion may reduce the attachment to private experiences such as thoughts or sensations rather than trying to alter their form (Hayes et al., 2006). Therefore, the mechanism of cognitive defusion in interventions may mitigate the negative effect of symptoms on distress.

Additionally, embarrassment avoidance was run as an exploratory mediator. Embarrassment avoidance, which covers feelings of shame and embarrassment about symptoms, was a significant mediator of the symptom burden-distress pathway in exploratory analysis. Previous literature has found this variable was associated with worse fatigue and impaired functioning in a breast cancer sample (Hughes et al., 2020a). In addition, qualitative research has found hot flushes are particularly embarrassing (Hunter et al., 2009). The results can also be contextualised with the findings in Chapter 5, as women reported symptoms making them feel much older than they were, discussing difficult personal symptoms and how their family would laugh at them and not understand their invisible symptoms. Embarrassment avoidance may be a modifiable target to reduce the negative effect of symptoms on distress and is a key target of CBT interventions for hot flushes which have had positive results in breast cancer (Fenlon et al., 2020). In addition, an

ACT congruent approach of acceptance and a willingness to experience these emotions (including shame) has been proposed as a possible useful approach for people with chronic conditions and disabilities although not tested as a specific intervention (Sedighimornani et al., 2019). ACT has been found to reduce shame in populations such as those with mental health difficulties (Stynes & McHugh, 2023). Embarrassment avoidance is not a construct that appears in the CSM, ACT or TMA-LTC, but is demonstrated by this study, the qualitative study and previous research and may be particularly important in understanding distress and symptom burden, supporting the utility of testing multiple models. From the literature, it seems that embarrassment avoidance may be able to be targeted by different cognitive-behavioural approaches and therefore has useful clinical applications.

7.6.2 Moderators

Moderator analyses were run on the longitudinal data to test the hypothesised variables to see if they interacted with symptom burden and therefore alter the strength or direction of the relationship between symptoms and distress. This would provide an indication of *for whom* the relationship might be stronger by understanding the beliefs or traits someone might have.

7.6.2.1 ACT moderators

ACT flexible processes were conceptualised as moderators as they can be described as skills or resources that an individual may have (Hulbert-Williams, Storey, & Wilson, 2015) and as there was no intervention to enhance these skills, it would not be appropriate to conceptualise as a mediator. Two flexible processes were hypothesised to be important moderators, however both mindfulness and self-compassion showed a moderate correlation with symptom burden which meant they were not suitable to be tested as

moderators (Wu & Zumbo, 2008). Self-as-context and values progress were run as exploratory moderators.

Both mindfulness and self-compassion were moderately negatively correlated with symptom burden and distress. This supports previous literature in cancer that has found these relationships with distress (Fawson et al., 2023) and physical symptoms (Zhu et al., 2019). Greater self-compassion and/or mindfulness may lead to someone interpreting their symptoms and experiences differently and therefore, these variables may appear in a different pathway such that these individuals experience less symptom burden to begin with. For example, one cross-sectional study found self-compassion was associated with cancer patients interpreting fewer negative consequences of their illness and more personal control, and this was associated with decreased anxiety (Zhu et al., 2020). However, this study was conducted on cross-sectional data and therefore the directions of relationships are unclear. In this present study, self-compassion was associated with fewer breast cancer and hormone therapy consequences (see full correlation matrix in Appendix C, Table C2) implying a potential different model to test. Both self-compassion and mindfulness have been investigated as the targets of interventions in breast cancer populations and have found positive outcomes in terms of emotional wellbeing, anxiety, depression and fatigue (Zhang, Zhao, & Zheng, 2019). However in a meta-analysis of 29 mindfulness based interventions, only small pooled effects were reported for cancer patients and survivors for psychological distress (Cillessen et al., 2019). Despite many interventions being conducted, effects are often small, which suggests further research may be helpful to understand how these psychological processes may be related to one another and go towards being combined in interventions to target a wider range of pertinent processes to improve outcomes.

Exploratory analysis was conducted on self-as-context, values progress and committed action as potential moderators of the symptom burden-distress relationship however these were found to be non-significant. As there is very little research on self-as-context, values and committed action in cancer (Fawson et al., 2023) no *a priori* hypotheses were outlined. The results presented in Chapter 6 provide evidence for a significant moderate correlation between self-as-context and distress and committed action and distress which the evidence base is currently missing. However, values progress had only small correlations with both symptom burden and distress. None of these three ACT variables moderated the relationship between symptoms and distress. As discussed in Chapter 4, both self-as-context and values are difficult concepts to understand, explain and measure (Fawson et al., 2023). Interventional studies have reported some change in these mechanisms through intervention (Lantheaume, Montagne, & Shankland, 2019) however in cancer, mediators of RCTs are often not measured (Fawson et al., 2023) so it is difficult to estimate the utility of these constructs.

7.6.2.2 CSM and CBRQ moderators

As previously mentioned, illness perceptions from the CSM were conceptualised as a mixture of mediators and moderators. It was hypothesised that a better understanding of treatment (treatment coherence) would buffer the impact of symptom burden on distress. Recurrence beliefs, treatment control and personal control were run as exploratory moderators due to the analysis in Chapter 6 and previous research reporting weaker correlations for these variables (Hagger et al., 2017; Richardson et al., 2017). Identity and cure beliefs could not be run due to the correlations violating the previously defined assumptions.

As hypothesised by the CSM, greater treatment coherence would be expected to be associated with better outcomes as someone understands what hormone therapy is doing and why they are taking it. Previous research in cancer has found a negative relationship between illness coherence and anxiety and depression in oesophageal cancer (Dempster et al., 2012) and greater illness coherence has been found to predict less distress in newly diagnosed breast cancer patients (Gibbons, Groarke, & Sweeney, 2016). Treatment coherence is specified in the IPQ-BCS and relates specifically to hormone therapy treatment. Therefore, although there is less research on this concept specifically, results in the same direction as illness coherence would be expected. The current study investigated treatment coherence as a moderator and found that at high levels of understanding hormone therapy medication, the effect of symptom burden on distress was reduced to a non-significant association. This has potential clinical implications, as it may be that providing patients with more information about hormone therapy treatment, its purpose and how it works, will enable them to have a better understanding of the treatment, reducing the negative impact of their symptoms. Although no studies have reported targeting this specific construct in interventions, illness coherence has been found to be increased in intervention and this has had positive effects (Broadbent et al., 2009). This means that even if the symptoms themselves aren't reduced, the psychological impact of the symptoms may be.

Recurrence beliefs, personal control and treatment control were all conceptualised as moderators based on consideration of the CSM. The exploratory analyses were data driven as the correlations were suitable to test as moderators however none of them were significant moderators of the symptom-distress relationship. An element of control was mentioned in the qualitative study, but this was around having the option to stop or change medication which might not be captured in the two control subscales. It may be that the

relationships were not strong enough to see an effect as some of the correlations were quite small with symptom burden and distress, particularly for the control variables. It may be that an overall illness representation, consisting of the negative illness perceptions is a better moderator of the symptom-distress variable, rather than looking at perceptions in isolation. McCorry et al. (2013) found a negative illness perception cluster predicted anxiety and depression at 6 months. Although this would not pinpoint the exact beliefs, it would provide an indication of targeting these potentially related perceptions overall. For example, targeting someone's understanding of hormone therapy treatment to reduce risk of recurrence may also affect their beliefs around recurrence risk and beliefs about hormone therapy consequences.

Finally, the following CBRQ variables were conceptualised as moderators; damage beliefs, fear avoidance, all or nothing behaviour and resting behaviour. Only damage beliefs were hypothesised due to the data in Chapter 6. Fear avoidance was not run due to being moderately correlated with symptom burden.

There is little research on the role of damage beliefs as a moderator. This item as measured by the CBRQ, relates symptoms to meaning something harmful is happening in someone's body (Picariello et al., 2023). This study found that greater damage beliefs strengthened the effect of symptom burden on later distress, however at the more stringent *p* value, this was non-significant. The results imply that participants who felt their symptoms are a sign of damage or harm, experienced more distress at follow up whereas low levels of damage beliefs buffered the impact of symptoms on later distress, although these were not significantly different. Damage beliefs have been previously explored as a moderator in CBT interventions for a variety of LTCs, with greater scores at baseline predicting less

improvement after CBT (de Gier et al., 2023). These results in conjunction demonstrate a potential key modifiable variable to be targeted in breast cancer survivors, to help women understand their symptoms are not a sign of damage. This also may relate to the point mentioned previously about treatment coherence and understanding the impact of hormone therapy on the body and how these beliefs may be related. However, this links to a limitation with the measure of symptom burden. The measure used for symptom burden did not specify symptoms related to hormone therapy, so we do not know what symptoms the participants may have been thinking of when answering the question, and what they have attributed the symptoms to. However, illness identity (symptoms attributed to hormone therapy) did correlate strongly with symptom burden implying the attribution of symptoms to hormone therapy.

All or nothing behaviour and resting behaviour did not moderate the symptom-distress relationship. Although the CBRQ describes them as responses to symptoms, the items also read as trait-based tendencies and behavioural patterns so therefore whilst also using observational data, they were tested as moderators. Additionally, these behaviours may be more relevant for specific symptoms such as pain and fatigue (de Gier et al., 2023), whilst the symptom burden scale incorporated a range of physical symptoms.

7.6.3 Summary of mediators and moderators

This study has contributed to the understanding of the mediators that may explain how symptom burden leads to distress in breast cancer survivors on hormone therapy. Several mediators as suggested by various theoretical models and approaches were significant. This helps to understand *how* symptoms lead to distress and therefore provides targets for intervention. In addition, the moderators suggest *for whom* symptom burden may lead to

distress, by suggesting different beliefs or tendencies someone may have that could alter the impact of symptoms on distress. Both sets of analyses contribute to the understanding that it is the experience, interpretation and response to symptoms that is impacting distress, rather than just the symptom burden itself. This is particularly important given the lack of evidence-based treatments for managing symptoms themselves in this population.

The results provide support for the processes and variables outlined by the theory and supports the rationale for the investigation of processes and variables from several key theoretical models. Both the CSM and TMA-LTC outline the pathway between illness related stressors and outcomes such as distress. All three models including ACT propose the processes or responses to stressors/experiences that may lead to these outcomes. Although not all variables proposed by the models could be tested, several from each model were found to be involved in the symptom-distress pathway. The results provide support for the integration of models. The CSM and CBRQ variables provided specific illness related beliefs and responses to symptoms that may be useful. Targeting one or two of these variables such as treatment coherence, may have an impact on other perceptions and beliefs such as damage beliefs, and breast cancer and hormone therapy consequences due to an increased understanding of treatment. Cognitive defusion techniques may help with fusion of general and illness related thoughts but also symptom specific focusing. If embarrassment avoidance leads to avoidance of activity or valued living this may be related to values obstruction and therefore targeting these areas may address these issues. The correlations between many of the variables presented in Appendix C, Table C2, demonstrate how these may be interlinked. The results in conjunction provide support for the utility of an integrated model of distress in breast cancer survivors on hormone therapy as it has found several important variables across the theoretical models.

7.6.4 Clinical implications

The moderator and mediator analysis has suggested that it is the interpretation, understanding and response to symptoms and/or hormone therapy treatment that may need to be addressed in order to improve distress outcomes. The moderators may also provide screeners for those at risk of developing distress from the experience of symptoms. Therefore, this analysis has identified some key variables that could be addressed in psychoeducation interventions in clinical practice. These 'low dose' interventions have the potential to be relatively inexpensive, easy to implement and sustainable (Schofield & Chambers, 2015), targeting a range of flexible skills and beliefs to increase the probability of a successful intervention. Clinical staff could provide further information either verbally or by leaflet regarding side effects of hormone therapy not being a sign of damage and explaining the purpose of hormone therapy and how it works. This may counter the effects of damage beliefs and low treatment coherence. For example Moon et al. (2019a) found a psychoeducation booklet for women prescribed tamoxifen was acceptable and feasible and showed initial improvements in necessity beliefs, coherence and distress. And although this intervention targeted adherence, it provides an indication of effectiveness for modifying illness or treatment related beliefs generally through a simple intervention which may also reduce distress. As reported previously, symptoms may be difficult to manage or treat, with limited self-management options, so these results provide alternative avenues for supporting women on hormone therapy.

Although psychoeducation might be able to target some of the illness or treatment related beliefs, some people may need further support. The mediation models provide evidence for processes that might be key to target in interventions to help women respond in a different way to their symptom burden. Self-management or therapist led interventions may be

developed that target the fusion around thoughts related to symptoms, breast cancer consequences, feelings of shame and embarrassment about symptoms and symptom focusing (e.g., Fenlon et al., 2020; Feros et al., 2011; Moon et al., 2019a; Stockton et al., 2019). In addition, certain responses to or beliefs about symptoms may be resulting in obstruction to daily valued living causing distress. For example, feelings of shame and embarrassment may impede on social activities (Hunter et al., 2009). These evidenced theory-driven mediators could be targeted through an integrated intervention.

7.6.5 Strengths and limitations

A strength of this study was the exploration of a potential key relationship in breast cancer survivors on hormone therapy, the pathway between symptoms and distress, which has not been studied in this population before. Although many studies have identified that increased symptom burden is related to higher distress, they have not investigated how, why or for whom this is true. This study also tests multiple cognitive-behavioural variables that have limited evidence in breast cancer. Testing variables from several models has revealed different important findings that contribute to a wider understanding of this relationship rather than testing variables from one model. This has potential implications for theory development in this population which can lead into developing effective intervention and treatment approaches. Mediation and moderation analysis has provided an indication of the potential modifiable psychological targets for intervention that may serve as an alternative to directly managing symptoms which has limited evidence-based treatments. Therefore, the study contributes to the understanding of how to reduce the negative impact of symptom burden on distress in breast cancer survivors on hormone therapy. The study addresses limitations of previous mediation and moderation analysis which failed to conceptualised variables appropriately and *a priori* and conducted analysis on cross-

sectional data. This present study outlined conceptualisations based on the theories and tested these accordingly in longitudinal data to provide support for the directions of effects.

The study used the IPQ-BCS which specifically asks about cognitions and beliefs related to the experience of being on hormone therapy for breast cancer. This ensures the illness cognitions are related to breast cancer as opposed to other co-morbid illnesses someone may have. Questions around treatment control and consequences are directly related to the hormone therapy medication during the ongoing survivorship phase. This means results can be directly related to this population's experience and therefore suggestions for enhancements to clinical communication and interventions can be specific and targeted.

As well as the limitations already discussed in Chapter 6 including the majority White British sample, COVID-19 context and recruitment of distressed participants and drop out, there are some specific limitations for this section of analysis. Despite significant partial mediators and moderators, the effects are all quite small, indicating there is still variance in the symptom burden-distress pathway that has not yet been explained by these variables. However the small effects are similar to other mediation analysis reported for psychological variables as partial mediators (Philipp et al., 2021). There are therefore other factors that might be important that this study has not tested. For example, social support has been found to buffer the negative impact of depressive symptoms on quality of life in cancer (Huang & Hsu, 2013) and intrusive thoughts on anxiety (Escalera et al., 2019).

In addition, the symptom burden scale was a general scale of bother around symptoms and did not specifically ask about hormone therapy related symptoms. However, there was a large proportion of women into the survivorship stage and had therefore been on hormone therapy for a while. This suggests these women were further away from the symptoms of

primary treatment and were therefore reporting on the ongoing experience of physical symptoms. The highest mean was for the musculoskeletal subscale of the symptom burden measure, and joint aches and pains are more commonly reported for those on AI's (Whelan & Pritchard, 2006) which 70% of the sample were on. This suggests the participants were reporting hormone therapy related side effects.

7.6.6 Future directions

Symptom specific ACT measures may help to understand the relationships of ACT processes in response to symptoms rather than more generally as suggested by the avoidance of pain measure (Brown et al., 2020). Further investigation of the role of mindfulness and self-compassion and the relationship with symptoms would be useful as these variables could not be tested in this present analysis. Further refinement of the illness perceptions in terms of their conceptualisation as mediators and moderators in observational data would be useful and help guide future research.

The next stage would be to develop interventions based on these variables. The potential mechanisms of change then need to be tested in interventions via mediation analysis to see if changes in these proposed mechanisms identified in the current study results in more favourable outcomes. Autoregressive mediation models should be used to account for previous measures of the variables to identify changes in longitudinal data (these were not used in the current analysis due to the observational nature of the data without intervention; Maxwell, Cole, & Mitchell, 2011). If the moderators in this present study were targeted in an intervention, mediation analysis would be suitable to be conducted to see if changes in the beliefs about or the understanding of hormone therapy contribute to better outcomes. Significant mediators of interventions would indicate the mechanisms of action

through which the intervention worked, providing support for the intervention and targeting these variables to improve outcomes.

7.6.7 Summary and conclusions

This study has allowed testing of hypotheses regarding the psychological variables that may be involved in the pathway between an illness related stressor, symptom burden, on the outcome of distress in breast cancer survivors on hormone therapy. This was achieved by conducting mediation and moderation analysis on longitudinal data. The hypotheses were based on theoretical models and the studies presented in this thesis (Chapter 5 and 6). This analysis of the final study has completed the third and final objective of the PhD thesis.

The study provided support for the hypothesis that symptoms predict distress over time, and that this may be explained by third variables in the causal pathway. This can help us understand *how* symptoms lead to distress and *for whom* the effect is strongest for. The study indicated that cognitive fusion, values obstruction, breast cancer consequences, embarrassment avoidance and symptom focusing may partially explain the pathway between symptom burden and distress, therefore indicating modifiable targets for interventions. Individuals with a greater understanding of their hormone therapy medication (treatment coherence) and lower damage beliefs may have the resources to buffer the negative effect of symptom burden on distress and therefore indicates further skills to increase in targeted interventions. The results of the mediation analysis have provided an indication of the variables to be addressed in interventions that may support breast cancer survivors experiencing difficult symptoms whilst on hormone therapy. Symptoms cannot necessarily be reduced or changed, so exploring the psychological processes in the symptoms-distress pathway provides informative targets for intervention.

Chapter 8 General discussion

8.1 Chapter overview

This chapter provides an overall summary of the findings from the various studies included in this thesis, with an outline of their contribution to knowledge and theoretical implications. Clinical implications will be discussed as well as strengths and limitations of the overall methodology and studies. The chapter will conclude with recommendations for future research and overall conclusions.

8.2 Summary of aims and main findings

The overarching aim of the thesis was to understand the psychosocial variables associated with distress in breast cancer survivors prescribed adjuvant hormone therapy and specifically identify the psychological factors that explain and are involved in the symptom-distress pathway. To achieve this aim, several objectives were completed over three empirical studies. A pragmatic multi-methods approach of both quantitative and qualitative studies was chosen to address the objectives.

The first objective of the PhD was to review the literature on the associations between acceptance and commitment therapy (ACT) processes and distress in cancer. To achieve this, a comprehensive systematic review with meta-analysis was conducted. One hundred and eight studies that reported associations between any ACT process and distress in cancer patients were included. Seventy-seven studies were meta-analysed, identifying that flexible ACT processes (mindfulness, acceptance, self-compassion) were associated with lower distress whilst inflexible processes (experiential avoidance, cognitive fusion) were associated with greater distress. This review was the first to bring all studies on ACT processes and distress in cancer together providing a comprehensive overview of the

current evidence base. The review provides support for the ACT model, highlighting the potential importance of experiential avoidance, cognitive fusion, mindfulness and self-compassion in the relationship with and understanding of distress in cancer. The review identified that research for distress in cancer was limited for self-as-context, values and committed action and identified directions for future research, which the third PhD study directly contributes to addressing.

The second objective of the PhD was to explore distress whilst on adjuvant hormone therapy from the perspective of breast cancer survivors, with a particular focus on why symptoms are distressing. This was achieved by conducting qualitative interviews and inductive reflexive thematic analysis with 23 breast cancer survivors. Participants not only felt unsupported and helpless about their symptoms and had difficult thoughts and feelings about the impact of them, but also found that the process of weighing up the decision to be on hormone therapy was distressing. Participants also described struggling with the thoughts around loss and change due to side effects. This study provided a context for the PhD directly from breast cancer survivors and supported the rationale for and contributed to the hypotheses to test in the symptom-distress pathway in the final PhD study. The study also provides suggestions for clinical communication to address some of the issues highlighted including providing more information about side effects to help with the fear and uncertainty of symptom experience, as well as content and targets for theory-led intervention development.

Finally, the third objective of the PhD was to test the illness perceptions from the common-sense model (CSM) and processes from the ACT model in predicting distress, and test whether an integrated model would better explain distress in a population of breast cancer

survivors. In addition, the second research question was to explore and test the symptom-distress pathway using mediation and moderation analysis. To achieve this objective, a longitudinal observational study was conducted, across three time points over 12 months. In cross-sectional data, the ACT process model seemed to contribute to explaining distress and explained more variance than either the CSM illness perceptions or an integrated model. Although in the longitudinal data, the integrated model which included all ACT processes, some CSM illness perceptions and an additional three cognitive-behavioural processes contributed slightly more variance. This demonstrates the importance of conducting longitudinal analysis, as different patterns have emerged, which should be acknowledged in later intervention development. The longitudinal nature of the study has also provided an indication of the direction of effects, highlighting potential risk factors for distress and identified that the integrated model of distress may be useful to inform intervention development.

Secondly, the mediation and moderation explored *how* symptoms may lead to distress and *for whom* this effect may be stronger. The analysis found cognitive fusion, values obstruction, breast cancer consequences, symptom focusing, and embarrassment avoidance significantly mediated the effect of symptoms on distress, contributing to explaining the symptom burden-distress pathway. The analyses indicate that responding to symptom burden inflexibly and with more negative illness cognitions or responses, can lead to distress. In addition, the moderator analyses revealed that for people with a greater understanding of hormone therapy treatment and fewer damage beliefs, having these cognitions buffered the negative effect of symptoms on later distress. There are limited studies exploring the relationship between symptoms and distress in cancer using longitudinal data and none in this specific population, so this type of analysis has provided

an understanding of what modifiable factors may be important to target in interventions, which is especially important when side effects themselves have limited treatment options.

The multi-methods design of this PhD has allowed the objectives and the overall aims of the PhD to be achieved. The systematic review and observational study provide information about the psychological variables that are associated with and predict distress in breast cancer survivors on hormone therapy. In addition, the qualitative study and observational study provide information about *why*, *how*, and *for whom* symptoms are distressing.

8.3 Contribution to knowledge and theoretical implications

The three empirical studies presented in this PhD thesis provide novel contributions to knowledge which have implications for the theories presented throughout this thesis as well as providing support for previous research.

8.3.1 Contextualising distress in breast cancer survivors on hormone therapy

Although there is considerable research in the area of distress in breast cancer survivors, this research does not always highlight the unique experiences of survivors who have been prescribed hormone therapy, which can be taken for up to 10 years after diagnosis. Where research has been conducted to explore the experiences of those taking hormone therapy, it is often focused on the medication taking behaviour and reporting of side effects (e.g., Peddie et al., 2021). This PhD aimed to provide a detailed and rich understanding of distress and physical symptoms/side effects for breast cancer survivors in relation to the experience of being on hormone therapy, with a focus on why physical symptoms are particularly distressing. This PhD therefore addresses an often-neglected area of this specific populations' experiences whilst also contributing to the wider literature that focuses on the more behavioural outcomes. As around 75% of the 2.3million new breast cancers diagnosed

annually worldwide are hormone receptor positive (HR+; Harrell et al., 2007; Sung et al., 2021), requiring adjuvant hormone therapy, this research has the potential to benefit a large number of women living with survivorship.

In particular, the qualitative study (PhD objective B) highlighted the ongoing distressing impact of symptoms/side effects and the role they play in impacting an individual's life. A key contribution of this study surrounds the unique understanding of *why* symptoms are distressing, and the study revealed that part of this was due to the ongoing conflict around weighing up the decision to take hormone therapy. It has been previously reported that women weigh up the decision to take medication based on the experience of challenging physical symptoms on their quality-of-life vs the impact of the medication on reducing risk of recurrence (quantity of life; Peddie et al., 2021). However, this thesis showed that this process of decision making in itself, also contributes to distress. This was mentioned by a variety of women, not just those at the start of taking hormone therapy medication, indicating that the pressure and conflict was ongoing. Women reported feeling helpless about what to do about their symptoms, had difficulties managing the loss and change associated with them and felt fear and uncertainty around side effects. Although there are some similarities with experiences reported related to adherence in the literature, these participants discussed these experiences in relation to distress, highlighting distress as an important and meaningful outcome. This study therefore provides a unique contribution to understanding how the ongoing experiences of survivorship for women with HR+ breast cancer may be related to the development or maintenance of distress.

As well as increasing the understanding of what breast cancer survivors prescribed hormone therapy may find distressing, the quantitative study (PhD objective C) provided further

insight into distress and symptom burden in this population. The longitudinal nature of the study provides additional evidence that distress may be relatively stable over time which suggests that without intervention, it is unlikely breast cancer survivors' distress will decrease. These results support previous literature in other cancer survivor populations (Brandenbarg et al., 2019) and further rationale for the investigation of distress in this population. In addition, symptom burden was identified as a stressor and therefore a possible predictor of distress in this population due to the experience of hormone therapy, and this was stable over time. This supports previous literature that symptoms do not seem to decrease, at least in the first few years of taking hormone therapy (e.g., Ganz et al., 2016b; Moon et al., 2019b). This goes against what breast cancer survivors are told about side effects decreasing over a few weeks or months (Cancer Research UK, 2021). Together this indicates that both symptom burden and distress may remain significant stressors for at least three years after primary treatment, highlighting the need for ongoing support for survivors.

As mentioned, there is a lot of research exploring distress in breast cancer as well as symptoms. Yet, despite some research looking at symptoms and quality of life, no studies have quantitively investigated the symptom-distress relationship in this population. This population of breast cancer survivors are likely to experience side effects for a considerable amount of time, demonstrated by the persistent nature of distress and symptom burden in the quantitative study, which is why this research is so important through contributing to interventions to support these women. A novel contribution of this PhD thesis was an exploration of this relationship by identifying *why* symptoms and taking hormone therapy is distressing (PhD objective B) and using this to inform hypothesis generation for mediation and moderation analysis to explore *how* symptoms lead to distress and *for whom.* This

relationship is particularly important to identify alternative targets for interventions when management for symptoms themselves is limited, as discussed in Chapter 1 (Hall et al., 2022) and was further supported by the feelings of helplessness about symptoms that women reported in Chapter 5. The identification of theory-based psychological factors that acted as mediators and moderators indicates that the individual's beliefs, perceptions of and reactions to symptoms are an important influence on distress, beyond the objective experience of physical symptoms. These variables also provide evidence for potential targets for intervention, opening avenues for support.

The PhD studies have added to the literature supporting persistent distress and symptoms for breast cancer survivors on hormone therapy and has contributed to understanding *why*, *how* and *for whom*, symptoms lead to distress, providing a thorough contextualisation of distress and symptoms in this population. These results aim to bring further awareness to the experience of having HR+ breast cancer, beyond the focus of adherence to the medication. As will be discussed in the next section, 8.3.2, it may be useful for the theory-driven mechanisms found in these studies to be incorporated into interventions and theory development for this specific population to help design and inform more effective treatments.

8.3.2 Theoretical models and the understanding of distress in breast cancer

Two models were presented in Chapter 2 which may help explain and understand distress and were tested in this thesis. Results from the various studies provide support and areas of consideration for the two theoretical models.

8.3.2.1 Common-sense model of self-regulation

The CSM illness perceptions were proposed as part of a model that may explain distress in breast cancer survivors on hormone therapy. Systematic reviews covering illness perceptions proposed by the CSM with distress in cancer, and in breast cancer specifically, had already been conducted before this PhD began (Hagger et al., 2017; Kaptein et al., 2015; Richardson et al., 2017). However, the data for illness perceptions are limited longitudinally and in the specific context of breast cancer survivors on hormone therapy. Therefore, this PhD has addressed these limitations by testing the CSM illness perceptions in relation to distress in this population. The study has compared the contribution of the illness perceptions from the CSM to the ACT model in explaining distress in order to provide evidence for the potential theoretical models that may explain the psychological factors that are associated with distress, to provide a framework for treatment. In addition, specific illness perceptions were tested in the symptom-distress pathway, providing novel findings.

The analysis presented in Chapter 6 found illness perceptions predicted significant variance in distress at baseline and at 12 months follow up. This demonstrates that illness related thoughts and beliefs contribute to explaining distress in this population. The findings replicate previous literature in general breast cancer samples that have found illness perceptions contribute to significant variance in mental health outcomes (McCorry et al., 2013; Rozema, Völlink, & Lechner, 2009) although with less overall variance to previous studies due to the inclusion of more covariates. However, neither of these previous studies looked at breast cancer survivors on hormone therapy specifically and neither looked at the contribution of all perceptions on a general distress outcome. The current study therefore highlights the potential utility of illness perceptions in understanding distress in this population and considering they explained a significant amount of variance in distress over

and above covariates, it provides an indication of the modifiable targets for intervention development to address distress.

However, the amount of variance explained by the illness perceptions was almost half of the variance that the ACT components explained in both cross-sectional and longitudinal data. In addition, this was up to half of what the integrated model predicted which was similar to the ACT model alone. These findings pose the question of whether the ACT model is better at explaining distress in this population. The CSM originally proposed that illness perceptions would explain or predict coping behaviours such as going to the doctor or taking medication to control the threat of illness progression or a recurrence. For example, illness perceptions have been found to significantly predict adherence to medication (Moon et al., 2019b). It may be therefore, that the illness perceptions are more limited with predicting illness outcomes such as emotional distress. This may also partly be due to the CSM identifying emotional representations about illness, as a separate, parallel pathway, indicating that an emotional reaction happens in parallel.

When looking at the CSM itself, illness related coping behaviour is also the step before appraisal and illness outcomes. Therefore, as proposed by the model, inclusion of the coping element may have enabled the regression models in Chapter 6 to have predicted more distress in this population. However, there were several reasons for not testing this. Firstly, including more variables into the regressions would have required a larger sample size. Secondly, previous studies such as Rozema, Völlink and Lechner (2009) found adding coping variables did not add significant additional variance over and above illness perceptions. A further issue with this method, as highlighted in Chapter 2, is that hierarchical regressions do not allow for the self-regulatory nature or temporality aspect of

the model to be tested. Even when using a more suitable type of analysis to test the process model Hagger et al. (2017) also found coping did not fully mediate illness perceptions on outcomes and there were direct effects for illness perceptions and distress, suggesting a direct relationship between these variables. Additionally, Hagger et al. (2017) reported that coping measures were general and may not capture illness related coping. As discussed in Chapter 2, the CSM suggests coping behaviours rather than strategies as such, and there is variation in which coping variables have been tested previously and that which may be important. For example, general coping measures such as problem focused coping, avoidant coping, seeking social support as well as relaxation and having a positive focus have been tested (McCorry et al., 2013; Rozema, Völlink, & Lechner, 2009). These measures may not pick up the illness related coping behaviours hypothesised by the model. Therefore, the disparity in results and little guidance on which ones to test, lead to inconsistent conclusions about coping.

Causal beliefs were one set of illness perceptions proposed by the CSM that were not tested, limiting the understanding of these beliefs in contributing to the variance predicted by the CSM and also within the symptom-distress pathway. Causal beliefs are the beliefs someone may have around the causes of their illness or condition (Leventhal, Diefenbach, & Leventhal, 1992). Richardson et al. (2017) found causal beliefs about illness (as one variable) had very small but significant pooled correlations with anxiety, depression and distress suggesting the variable may have limited utility in understanding distress. However the utility of a single variable is questioned as Moss-Morris et al. (2002) recommend using principal component analysis to identify groups of causes such as biological or psychological, such as stress. Causal beliefs were not included in the present study partly as a pragmatic decision as a minimum of two further variables to represent the causal beliefs would need

to be added to the model, potentially increasing the need for a larger sample size and requiring further analysis. However, the IPQ-BCS measure frames these beliefs around causes of or risk factors for a cancer recurrence. Moon et al. (2019b) found psychological attributions such as stress causing recurrence were associated with intentional non-adherence. Inclusion of this may have helped the CSM explain further distress. For example, if someone believed the cause of recurrence to be stress related or due to their emotional state, this may be more distressing for an individual. Therefore, although the omission of the causes subscale in this study somewhat limits our understanding of the impact of this illness perception on distress, this is partially mitigated by the use of an illness-specific illness perceptions measure which incorporates illness and treatment specific causal beliefs into other relevant perceptions which were included in the analyses.

An alternative interpretation to the CSM predicting less variance in distress than ACT, as discussed in Chapter 6, is that the illness perceptions and beliefs that someone with breast cancer might have, could well be realistic. This may be why a weaker effect was found with distress compared to ACT. Individuals may know that their hormone therapy has consequences by way of symptoms and know that there is a risk of recurrence as demonstrated by the way individuals describe weighing up the decision to be on the medication (chapter 5 and other qualitative studies e.g., Peddie et al., 2021). There may, therefore, be a step between the illness or treatment related belief and distress, by way of how someone responds to that belief, which in turn may result in distress. For example, despite being accurate representations, if those thoughts prevented someone doing what was important to them, or if they felt stuck with those thoughts, this may lead to distress as proposed by ACT (Hayes et al., 2006). Therefore, rather than the illness perception itself leading to distress, it may be the way people process or respond to this perception. This is

where the models may complement each other and will be discussed further in the theoretical integration section in 8.3.2.3.

A limitation highlighted in Chapter 7 is that the conceptualisation of the illness perceptions as mediators or moderators in the model is unclear. The model proposes causal links in the process model, however many of the illness perceptions are described as beliefs about illness which would suggest moderators. This makes conceptualising the illness perceptions as mediators or moderators quite difficult. A potential benefit of having an illness specific measure of illness perceptions, the IPQ-BCS, helped with the conceptualisation in this current study, as some beliefs could be interpreted as in response to symptoms (therefore mediators). Future research should consider conceptualising the illness perceptions in a clearer way which might be helped by illness and treatment specific measures.

In Chapter 7, the specific illness perceptions that were found to be involved in the symptom-distress pathway were breast cancer consequences and treatment coherence. Breast cancer consequences partially explained the relationship between symptom burden and distress, whilst individuals with a better understanding of hormone therapy medication (treatment coherence), had less negative impact from symptoms. As consequences of breast cancer were a significant mediator, this may have implications for interventions to address the wider ongoing impact from the breast cancer diagnosis and initial treatment. Ongoing symptoms could act as a reminder of the general breast cancer experience, for example related to feelings around the identity of being a cancer patient. This may relate to the findings in the qualitative study where women talked about changes to their identity and loss of self and this has also been found in previous studies (Landmark & Wahl, 2002).

Although in the qualitative study women talked about the worry and concern around future side effects and expectations of the medication, in the observational study, the negative consequences believed to be from hormone therapy medication did not mediate the relationship between symptoms and distress but did have a medium effect size with symptom burden. This links to the previous point regarding the beliefs being realistic for this population of breast cancer survivors. This warrants further testing as it may be that understanding that consequences (i.e., symptoms/side effects) are directly related to the medication taken to reduce the risk of recurrence, may not have a negative impact on distress as originally hypothesised. Instead, it may act as a reassuring factor where it helps women to contextualise the symptoms or may even act as reassurance that they are actively doing something to control their risk of recurrence, as found in the qualitative study in Chapter 5.

Treatment coherence was found to moderate the impact of symptoms and distress which suggests interventions to further increase understanding of medication may be beneficial. These findings further support the experiences reported in the qualitative study as women wanted to receive more information about side effects and the impact of hormone therapy as they felt uncertain and worried about the future. Both treatment coherence and understanding the consequences of hormone therapy are related to general understanding of treatment. Understanding illness and providing disease-specific information has been found to be amenable to change, related to having a better understanding of illness and can have potential positive outcomes on anxiety and health related quality of life (Broadbent et al., 2009; Husson et al., 2013). Therefore, clear and repeated communication about the role of physical symptoms when taking hormone therapy, acknowledgement of how this might prolong the negative experience of the breast cancer diagnosis, and intervention to

promote positive management of these beliefs may ameliorate the impact of symptom burden on distress.

Overall, the illness perceptions did seem to explain some variance in the understanding of distress and the symptom-distress relationship in breast cancer survivors. The studies provide support for the CSM, with some useful illness perceptions identified to consider for intervention. However, due to the limited explanation compared to ACT and the context of living with physical symptoms as a result of hormone therapy, as outlined above, it may be pertinent to consider how the reactions or responses to these thoughts and symptoms impact on distress, alongside the perceptions themselves.

8.3.2.2 Acceptance and commitment therapy

Acceptance and commitment therapy (ACT) was another proposed theoretical model that may help understand distress in breast cancer survivors on hormone therapy. There are many ACT-based interventions for cancer survivors which show small-medium effects (Mathew et al., 2020), however the evidence base for the processes proposed by the model had not been consolidated. Ideally, theoretical models should be supported with an evidence base before interventions are conducted (Hayes et al., 2013; Levin et al., 2012). The systematic review with meta-analysis (PhD objective A; Fawson et al., 2023) consolidates and provides an evaluation for the ACT processes and distress, in the specific context of cancer. The review highlighted some key recommendations for future studies to address. Suggestions from the review were directly addressed in the analysis conducted and presented in Chapter 6 (PhD objective C) which provides evidence both cross-sectionally and longitudinally for the under-researched areas in the specific context of breast cancer survivors.

The systematic review with meta-analysis was the first and currently only review to include all ACT processes proposed by the model and their association with distress across all cancers. This addressed a gap in the literature as previously only one meta-analysis had been completed on an integrated definition of acceptance (Secinti et al., 2019), whilst other reviews focused on narrative analysis only (Davis et al., 2023; Hughes et al., 2021). This paper contributes a broad understanding of distress which can be applied beyond breast cancer to other cancer diagnoses as there were many mixed cancer samples and other diagnoses. These findings may therefore contribute to future research and intervention development in other cancer populations. In the additional analysis, having a breast cancer diagnosis was found to be a significant moderator of the association between experiential avoidance and distress. However, this effect was very small and may be due to methodological considerations discussed in Chapter 4. Therefore, the results for processes and distress across cancers seem relatively consistent, supporting the transdiagnostic application of the model.

These findings were further tested in the observational study, and overall, the ACT model did explain variance in distress both cross-sectionally and longitudinally. The ACT model consistently predicted more variance in distress at both time points than the CSM. ACT proposes the inflexible processes, collectively psychological inflexibility, that may contribute to psychopathology and suffering (Hayes et al., 2013; Hayes et al., 2006). The model also proposes the corresponding flexible processes or psychological skills to be increased so that these difficult internal experiences have less of an impact on what people value as important in life (Mosher et al., 2021). This therefore may be why the model was better at predicting general emotional distress than the CSM as many of the constructs relate to general thoughts and/or emotions, rather than illness specific, making it potentially more

useful to explain general distress. In addition, the regression models demonstrated some key individual processes that may be important in predicting distress, which may act as indicators for those at risk to provide earlier intervention. This included cognitive fusion, which independently predicted distress at both baseline and at 12 months. However, despite significant moderate to strong correlations found across all ACT processes with distress corroborating the reviews' findings, only cognitive fusion remained an independent predictor of distress over other variables.

Based on the findings of the review, experiential avoidance was found to have a strong correlation with distress and in particular seemed to be important in breast cancer in the additional moderator analysis. The analysis in Chapter 6 and 7 used an alternative measure for experiential avoidance due to the limitations of the AAQ (Fawson et al., 2023; Tyndall et al., 2019) and supports the review findings with a moderate correlation with distress. However, in the next stages of analysis experiential avoidance was not a significant independent predictor of distress when all ACT processes were included in the regression model and experiential avoidance could not be tested as part of the symptom-distress pathway. The majority of the data in the systematic review (and all meta-analysis data) was cross-sectional. However, once this present study addressed these limitations and applied the analysis to the longitudinal data with the additional ACT processes included, the relationship was not significant.

As discussed in Chapter 7, the non-significant findings for experiential avoidance may be due to the measure being more emotionally focused rather than on the avoidance of side effect related thoughts or feelings or the experience of symptoms themselves. A significant mediation effect has been found when the scale measures the experiential avoidance of

pain specifically (Brown et al., 2020). Overall, despite initial promise of experiential avoidance in understanding distress in cancer, its importance did not emerge as strongly when explored specifically in breast cancer survivors using an alternative measure. The AAQ may have overinflated the conclusions drawn previously. Additionally, in the secondary analysis (Moxham et al., in prep), some participants described using experiential avoidance in a workable way to cope indicating that although it is conceptualised as an inflexible process in the model, it may be adaptive in certain contexts. Therefore, further investigation as suggested is needed to establish firmer conclusions.

Cognitive fusion was a process highlighted in the meta-analysis as having a significant and strong pooled association with distress in cancer (Fawson et al., 2023). However, there were considerably fewer studies researching cognitive fusion compared to the other processes included in the meta-analysis and only one of these was in breast cancer. The findings from Chapter 6 and 7 supported the review findings with a strong positive correlation found with distress and in addition found it was a significant independent predictor of distress at 12 months, whilst controlling for covariates and other ACT processes in the models. Cognitive fusion also partially mediated the pathway between symptom burden and distress. Increased symptom burden predicted fusion with thoughts and this in turn resulted in increased distress. These studies provide promising results that indicate cognitive fusion as a potentially useful variable to investigate in future research and a target for interventions to address, reducing the chance of symptom burden leading to distress. The longitudinal data suggest cognitive fusion could be used to screen patients as an early indicator of those at risk of developing distress, particularly if experiencing high symptom burden. The qualitative study in Chapter 5 described some specific difficult thoughts that breast cancer survivors might have, and the unhelpful effects of cognitive fusion and the helpful effects of

cognitive defusion were described by participants in the secondary qualitative analysis (Moxham et al., in prep) providing further support for the investigation of these processes. The data for cognitive fusion in cancer is limited, however in a review of ACT mediators in interventions for a variety of clinical samples, Stockton et al. (2019) report five studies that found that enhancing cognitive defusion, which is the corresponding flexible process or skill, mediated improvements in outcomes such as quality of life, anxiety and depression. This suggests cognitive defusion may improve outcomes and should therefore be tested in breast cancer.

Self-compassion was included in the review and discussed as a potentially useful process to incorporate more formally into the ACT model. Despite a moderate correlation with distress, self-compassion (alongside other cognitive behavioural processes) contributed only a small amount of additional variance in distress in the regression models compared to the core ACT components both cross-sectionally and longitudinally. It also could not be tested as a moderator as the correlation with symptom burden was too high for moderator analysis. It may be useful to investigate the relationship of self-compassion with physical symptoms as there may be a different explanatory pathway. It may be that people who are more compassionate to themselves, experience less burden or bother from their symptoms. Other research has explored the association between physical symptoms and self-compassion and found self-compassion is associated with fewer physical symptoms, however this is by measuring the number of symptoms rather than burden (Dunne, Sheffield, & Chilcot, 2018; Herriot & Wrosch, 2022). Further exploration of the relationships with physical symptoms could be useful. There are numerous interventions for both mindfulness and self-compassion in cancer and other physical health conditions with promising results (Kılıç et al., 2021). These studies should be using mediation analysis to see

if these constructs are increasing as a result of the intervention and whether this accounts for the changes in outcomes.

The meta-analysis in Chapter 4 revealed a small significant pooled correlation for acceptance and distress which may be due to the variation in results from included studies, with several non-significant individual findings. Most studies in the review used variations of the COPE (Carver, Scheier, & Weintraub, 1989; Fawson et al., 2023), which measures acceptance as an ongoing construct in relation to cancer, rather than viewing acceptance as an end point as in some other measures (Mack et al., 2008). This was why variations of the COPE were included in the review, to match the more process-like definition of acceptance in the ACT model. However, the COPE may not have captured the experiential element of acceptance like the emotional acceptance questionnaire which was only used by a few studies (Politi, Enright, & Weihs, 2007). There are therefore variations in the definition of acceptance and a clearer one will help measures be developed in line with theory (Arch et al., 2022; McAndrews, Richardson, & Stopa, 2019).

Nevertheless, another meta-analysis found positive results for acceptance-based studies using a broader definition of acceptance (Secinti et al., 2019), implying the potential utility of acceptance in understanding distress in cancer. These findings were further corroborated in the qualitative study in Chapter 5, where participants spontaneously discussed having to accept limitations from their symptoms and distress. Due to the limitations for measuring experiential acceptance, experiential avoidance was chosen as the corresponding inflexible process for the quantitative studies as it included avoidance of emotions and situations (Gámez et al., 2014). However, the results did not show any significant effects for this construct. Further investigation of both experiential avoidance and experiential acceptance

is needed to better understand how this inflexible process and corresponding flexible skill may be associated with distress and physical symptoms in breast cancer.

The ACT process of self-as-context was discussed in both qualitative studies (Chapter 5 and the secondary analysis; Moxham et al., in prep) with breast cancer survivors talking about the impact to the self whereby symptoms disrupted their perception of themselves. Self-as-context is a difficult construct to understand and therefore measure and may be why it seems to be relatively ignored in the cancer literature, with only one study (thesis) found in the review that measured this construct (Babu, 2020; Fawson et al., 2023). Despite a significant correlation found in Chapter 6; self-as-context was not a significant moderator of the symptom burden-distress relationship (Chapter 7). There are several possible interpretations for this. Self-as-context has a number of dimensions to its definition, including flexible perspective taking and noticing thoughts and emotions as an observer, rather than seeing them as part of the self (Zettle et al., 2018). It may be that the measure is not effectively capturing all of these parts of the construct. In Moxham et al. (in prep), individuals talked about how others see them and their identity of being a cancer patient as an element of perspective taking. The measure (Zettle et al., 2018) includes statements around perspective taking in the sense of being a witness to experiences and noticing emotions and thoughts. However, it may be that the participants were focusing more on being stuck with previous self-stories/their past self and not accepting the changes and the new self. Therefore, a more tailored measure may have captured these concepts of the self. Overall, the moderate correlation suggests that there is some relationship, but this warrants further investigation.

Components of models should be tested, and theories and interventions should be based on strong evidence which will guide the interventions better for different contexts (Hayes et al., 2013; Levin et al., 2012). Many ACT interventions have been developed and tested in cancer, so observational research needs to continue to inform these interventions as they do not always produce large effects (Mathew et al., 2020). Observational studies may be able to contribute to the intervention development stage, highlighting the key processes to target for particular populations creating more tailored and potentially effective interventions which is part of the MRC framework (Skivington et al., 2021). In addition, the ACT processes have been criticised for their definitions and measurements and may not fully capture the processes in studies (Arch et al., 2022) so it may be beneficial for research to focus on this to ensure these limitations do not limit the potential utility of ACT. Cognitive fusion and values obstruction were mediators of the symptom-distress pathway highlighting the potential importance of addressing these constructs in interventions. Currently, many ACT interventions in cancer and distress incorporate all processes (although recent scoping searches in the context of ACT for fear of recurrence interventions reveal they do not include all) whereas there is less evidence for certain processes which would benefit from further investigation. It would particularly be useful for mindfulness and self-compassion to be further researched in this specific population in relation to symptoms and distress as previously described. Rather than basing interventions solely on the ACT model, utilising the potential key variables for a population as newer approaches like process-based therapy demonstrate (Hayes & Hofmann, 2018; Hayes, Hofmann, & Ciarrochi, 2020) may be more parsimonious and effective, and will be discussed in the next section, 8.4 clinical implications.

8.3.2.3 Theoretical integration

Throughout the studies and discussion presented, both the CSM and ACT have potential utility in explaining distress in breast cancer survivors on hormone therapy. It was initially thought that an integrated model may provide a more thorough understanding of distress compared to either model alone. The integrated model predicted an additional 2% variance to that predicted by the ACT model alone in the longitudinal data, therefore implying that both the illness-related thoughts and responses to these thoughts may be important to consider, although this is only a small additional proportion of variance to the ACT processes alone. Whilst the ACT process model, CSM illness perceptions and integrated model were able to explain up to 57% of the variance in baseline distress and up to 42% in follow up distress whilst controlling for covariates, there is still unexplained variance. It may be that other variables, which were not assessed in this study, are also important.

The transdiagnostic theoretical model of adjustment to long term conditions (TMA-LTC; Carroll et al., 2022) was published during the PhD and has taken an integrated approach to understanding adjustment to long term conditions. This PhD took a similar approach by testing two well recognised models to see if integrating key concepts make a unique contribution to understanding distress. There is some overlap with the processes included in the TMA-LTC, but it was not the aim of this PhD to test this model. The results from this study do however provide support for the inclusion of the CSM illness perceptions and some ACT processes in the TMA-LTC using breast cancer as an exemplar long term condition.

Both the TMA-LTC and CSM outline the potential pathway between illness related stressors such as physical symptoms and outcomes, via psychological processes. This is what the study presented in Chapter 7 tested. Significant moderators and mediators were found

across the different theories, so had only one model been used, some key variables may have been missed. For example, symptom focusing and embarrassment avoidance which are proposed cognitive-behavioural responses to symptoms were identified and may be pertinent to this population. This is a significant benefit of integrating models, rather than relying on one. This has provided an overarching explanation of distress with a specific relationship explored, providing useful directions for future research and interventions.

The cognitions and beliefs including the CSM illness perceptions and some CBRQ items describe the specific thoughts in relation to illness and symptoms. It may be that the ACT processes act as the pathway that leads or does not lead to distress by way of how someone responds to those thoughts. As proposed by the ACT model, this would either be a flexible or inflexible response. Similarly to the CSM, it may be that there is dual processing; whereby someone has certain beliefs or cognitions in relation to their illness and then depending on how they respond to these in either an inflexible or flexible way, may lead to distress or better outcomes. This is in line with ACT as it does not propose targeting the content or form of thoughts, instead focusing on broadening psychological skills in order to cope with and respond to these thoughts related to events or stressors (Hulbert-Williams, Storey, & Wilson, 2015).

The interpretation proposed above could be tested by looking at an alternative pathway between symptom burden and distress. A serial mediation model may be able to test this, utilising processes from both models and the additional cognitive behavioural processes tested. For example, it could be hypothesised based on the theories that an increase in symptom burden means someone may have more beliefs about the consequences of their breast cancer or might be more focused on their symptoms and if they fused with those

thoughts or were experientially avoidant, that may in turn lead to distress. It would be hypothesised based on ACT that a more inflexible or negative response to the illness perception would lead to distress. The current study did not test this type of model as it completed the first step of identifying pertinent processes from the models and focused on identifying what could be used for the integration. However, it therefore poses the next steps for future research.

Recently, Karekla, Karademas and Gloster (2019) have published a paper on the potential complementary approach of using CSM and ACT in treatment for chronic illness. Karekla, Karademas and Gloster (2019) propose a pillared approach where CSM and ACT fit within chronic illness, whereby they matched ACT techniques on the concepts proposed by the CSM in a complimentary way to be used for intervention. For example, they highlight fusion of beliefs about illness and symptoms. A benefit of integrating the models is that the CSM originally aimed to explain or predict behaviour, rather than being a treatment model. Whilst ACT is a treatment model and can therefore be applied to the CSM. Within the ACT model there are treatment techniques, conceptualised by the flexible skills, which provide guidance for intervention targets, and which are missing in the other cognitive behavioural models. Testing the CSM illness perceptions and ACT responses as an explanatory model in the mediation suggested above, would further corroborate this integrative method to then further support and inform intervention development.

To summarise, using an integrative approach by investigating several psychological models in illness has provided results that have shown that both the beliefs and responses to these beliefs may help explain distress in breast cancer survivors on hormone therapy. This has important implications for future research and the design of interventions, to ensure

psychological processes from a variety of cognitive-behavioural models (including ACT), are utilised to treat distress in this population. In particular, several variables across the models may be important in treating the specific distress around physical symptoms and side effects that individuals experience with this type of breast cancer and medication.

8.4 Clinical implications

As discussed, the results from this PhD thesis have potential clinical implications. Up to 56,000 women are diagnosed with breast cancer every year and seventy-five percent are HR+ meaning medication is prescribed to reduce recurrence risk for up to 10 years (Cancer Research UK, 2018; Davies et al., 2013). Distress and experience of side effects are also prevalent in this population (Ganz et al., 2016b; Moon et al., 2019b). Therefore, there are a substantial number of individuals that these results may be relevant to. Distress is an important patient reported outcome as it has been associated with poor quality of life, non-adherence to medication and poorer health outcomes therefore highlighting the potential impact research in this area could have (Deckx et al., 2021; Skarstein et al., 2000; Winn & Dusetzina, 2016).

Demographic variables were found which may be useful to identify breast cancer survivors who may be more at risk of distress. The findings revealed that as well as age, number of children was associated with distress at follow up and was the only remaining significant predictor once psychological variables were included, as discussed in Chapter 6. It may be useful for clinics to be aware that women with children may be struggling to manage through survivorship. This could have been influenced by the environment of the COVID-19 lockdowns at the time of data collection but has also been previously reported in the literature (Semple & McCance, 2010). It may be expected that women with more children

and therefore caring responsibilities may find it particularly challenging to handle the emotional and side effect burden associated with treatment. Further research applying this directly to the experiences of breast cancer survivors on hormone therapy would allow for interventions to be designed to support this source of distress.

Chapter 6 presented psychological variables that predicted distress, including cognitive fusion and damage beliefs, and therefore suggest factors that could be screened to identify those that might be at increased risk of distress. Identifying risk factors for distress may help clinicians offer support to these women by intervening effectively earlier on. This could also be beneficial to identify those who may not be experiencing distress initially but who are at risk of developing distress later in the survivorship journey. This may be particularly important as more services move towards open access follow up whereby the patient initiates contact with the clinical care team rather than having regular routine appointments (NHS England, 2023) where signs of distress or poor management of symptoms could be identified by the breast care team. NICE guidelines state that all people with breast cancer should be offered specialist psychological support (National Institute for Clinical Excellence, 2023), however this is not something routinely offered or even available in NHS services. Previous literature had reported symptoms might be distressing (e.g., Jim et al., 2007), but it had not been previously investigated why, how or for whom symptoms may be distressing for this specific population of breast cancer survivors, which this PhD thesis has now contributed. Experience of symptoms is common for this population, but management options are limited as discussed in Chapter 1 (Hall et al., 2022). Implementing strong screening and risk factors could help triage those who are at more risk of developing distress and therefore allocate resource appropriately. However, as resource may be limited

in the NHS, the findings throughout this PhD could inform self-management interventions as discussed.

Clinical communication could also address some of the other aspects of concern for breast cancer survivors on hormone therapy revealed in the qualitative study. Some of these were around unknown length of time of side effects and which side effects to expect. These were reported to be related to distress and therefore enhancing this communication may mitigate some of the negative outcomes. In addition, women felt helpless in managing their symptoms and unsupported by their healthcare professional. The study confirmed that symptom burden is relatively stable over time which supports the other research in this area (Cheng, Wong, & Koh, 2016; Moon et al., 2019b). However, the general information given to women is that side effects will decrease after a few weeks or months (Cancer Research UK, 2021). This needs to be addressed and updated across charity support and clinical support as the results from the qualitative study as well as previous literature state that the unknown expectations of side effects is distressing (e.g., Peddie et al., 2021). The findings from the qualitative study, coupled with the mediation and moderation analysis indicates that providing realistic, ongoing information and support about the impact and management of symptoms may ameliorate the distress felt about the symptoms, even if symptoms themselves are ongoing. The need for improvements in communication regarding hormone therapy medication has been reported in the adherence literature (Moon et al., 2017c; Peddie et al., 2021), so addressing the information in clinical appointments therefore could have benefits on two important outcomes. Addressing both distress and adherence may in turn increase quality of life and improve recurrence and mortality risk which have been found to be associated with these variables (Winn & Dusetzina, 2016).

These results provide an insight into how to intervene to best support women and improve distress. The findings that cognitive fusion, values obstruction, breast cancer consequences, symptom focusing, and embarrassment avoidance partially mediated the pathway between symptoms and distress provide a starting point for interventions. These variables contribute to explaining how symptom burden leads to distress and therefore suggests that targeting these variables may have positive outcomes by way of reducing the negative impact of distress. Chapter 7 described how some of these variables could be interlinked, for example, using cognitive defusion techniques might help fusion with thoughts as well as symptom specific focusing, supporting the use of an integrated model to inform intervention development. Self-management interventions or those with minimal support could address both the cognitions and knowledge about illness and treatment, but also develop the skills to deal with the thoughts and emotions experienced, and this has been found to be effective in other physical health populations (Catella et al., 2024; Levin et al., 2020).

The results from this thesis support newer approaches such as process-based therapy (PBT) discussed in the review in Chapter 4 (Hayes & Hofmann, 2018). This approach proposes that evidence-based processes of change should be identified to inform interventions rather than following a specific protocol based on a model or theory (Hayes, Hofmann, & Ciarrochi, 2020). Identifying the essential processes for a specific outcome and context such as cancer might improve the efficacy and effectiveness of treatments as the treatment becomes more personalised to the problems of the population. This PhD supports this approach by investigating several models to determine these key variables for the population. Both therapist-supported or self-management (including digital) could focus on targeting the variables identified as long as they are theoretically aligned. Levin et al. (2012) proposed that theories need to be tested and refined for populations based on the evidence and this

PhD further supports and provides evidence for this approach. Identifying key processes may be a more economical approach and parsimonious way of developing interventions, increasing the chances of successful intervention (Corda et al., 2010; McBride et al., 2021).

One further clinical implication of the PhD is the validation and use of the PHQ-ADS as a general distress measure (Ibrahimi et al., under review). If distress is to be screened in clinic, this measure may provide a useful scale to be used to identify distress in this population. This has benefits over using two separate scales for anxiety and depression which have been found to have high correlations, reducing the number of measures and analyses needed and avoids potential multicollinearity (Chilcot et al., 2018; Kroenke et al., 2016). In addition, a measure of distress may capture the wider emotional impact of breast cancer survivors on hormone therapy rather than anxiety or depression alone, particularly for people who do not meet clinical thresholds on either construct individually, but collectively indicate low overall mood. This may include the low mood and worries about the past and future which were further evidenced in the qualitative study, enabling contribution to a more comprehensive treatment. This may have benefits regarding implementation, as a general distress intervention may be more feasible and cost-effective than specific interventions targeting different outcomes.

8.5 Strengths and limitations

Strengths and limitations of individual studies have been presented in the corresponding discussion and summary sections of relevant chapters. However, there are strengths and limitations that relate to the broader PhD thesis.

The studies presented in this thesis were conducted during the COVID-19 pandemic (March 2020-December 2021). Participants were therefore recruited online during lockdowns and

periods of uncertainty, additional distress and changes to treatment (Dave et al., 2021; Swainston et al., 2020). As presented in Chapter 5, although people reported minimal support, the level of support provided appeared to be similar to participants who had a diagnosis and treatment before the pandemic. This is therefore in line with previously reported general experiences rather than being COVID-19 specific. Levels of general distress were also similar in the longitudinal study to other samples of the same population (e.g., Moon et al., 2017b), although depression seemed to be higher than anxiety which is usually reported to be higher (Maass et al., 2019). This could be as a result of COVID-19 lockdown measures, however the thesis was exploring general distress and using a composite measure of distress mitigates the impact of this as both depression and anxiety are measured as a single outcome using the PHQ-ADS. Therefore, whilst it is important to remember the context of the studies presented in this thesis, comparisons suggest that the results are still relevant post-COVID-19.

A general limitation to the studies is generalisability as the majority of women recruited were of White ethnicity. This is fairly typical as it has been presented previously that HR+ breast cancer is more common in White women whilst women of other ethnicities are more likely to have HR- or triple negative breast cancer (Cui et al., 2014; DeSantis et al., 2014). Because of the small number of women from other ethnicities it was not possible to explore potential differences in experiences, however differences in distress have been reported elsewhere (Gonzalez et al., 2022). In either case, this poses the need for studies to focus on recruiting samples of women from different ethnic backgrounds to ensure these issues are being investigated thoroughly and women from a range of backgrounds are represented. Interventions may need to be better tailored to women's experiences, taking account of

different cultural expectations. Despite this limitation, the use of online community recruitment allowed for a broad geographical spread across the UK.

As discussed throughout Chapters 5-7, some people who are very distressed may not sign up to be involved in a research study. However, this could mean the effects found are underestimated in the current sample, and had more distressed people been recruited, the effects may have been stronger. Multiple methods were used to recruit from the community, which included different time points across the pandemic and the use of a variety of engagement methods to retain people. There was an indication of distress experienced in both the qualitative and observational study samples and the studies report similar distress to other samples of the same population (Moon et al., 2017b).

Another limitation of the study is the use of a self-reported general distress measure; the PHQ-ADS. This measure does not specify distress related to the experience of cancer or survivorship and therefore could be related to anything happening in a participant's life. However, there are several potential benefits of using a general distress measure. As mentioned in the clinical implications, measuring a combination of anxiety and depression may capture the wider experiences of this group rather than focusing on one or another. Instead of measuring a very specific element of the cancer experience like fear of recurrence or distress around treatment, a general measure allows for a broader experience to be captured and tested and therefore contribute to treatments. This may have implications for the feasibility and cost-effectiveness of treatments. In addition, using a broader distress measure may allow for the results to be compared across conditions that require illness management, a particular benefit as the models tested are proposed to be transdiagnostic.

As mentioned previously, there is still unexplained variance in distress that the included models and covariates did not account for. The experience and impact of cancer is broad and complex, and several other concepts were mentioned in the qualitative study, in previous literature and proposed by the TMA-LTC that might help explain further variance in distress. These include social support, the healthcare professional relationship, self-efficacy, resilience and optimism. For example, in Chapter 5, it was reported that hearing about other people's side effects and experiences helped women manage. In addition, one person reported their family laughed at them as they could not understand their invisible symptoms. Social support may therefore be an important variable to investigate in this population. Women who feel they have a good support network may feel less distressed and burdened by their symptoms. This may also link to the fact that women who reported having a higher number of children were more distressed, and therefore social support may interact with this. Social support has been found to be associated with distress in previous literature (Lo-Fo-Wong et al., 2016).

In addition, throughout the qualitative study women reported having little information about what to expect from side effects and felt unsupported by their healthcare professional. This is also common in the adherence literature (Peddie et al., 2021) indicating broad consequences to the perceived lack of support. In addition, the understanding of hormone therapy was found as a significant moderator in Chapter 7 and therefore both of these variables may relate to the satisfaction people have with their healthcare provider interactions. Poor trust, communication and perceived empathy by healthcare professionals have all been related to worse outcomes, particularly in women from minority ethnic backgrounds (Moon et al., 2020; Tompkins et al., 2016) whilst trust in these relationships has been associated with better outcomes (Birkhäuer et al., 2017). This may be an

important variable to consider, especially as often patients are discharged after hormone therapy initiation and since the COVID-19 pandemic, many appointments have changed to online. Digital self-management interventions may be cost-effective, accessible alternatives for support (Ebert et al., 2018; Krebs, Prochaska, & Rossi, 2010), however they would need to ensure the needs of the women are being met in terms of the satisfaction of information and whether they receive this in an empathetic way through a digital medium. Measuring relationships and support may therefore be important variables to consider in future research.

Despite these limitations, the thesis has a number of strengths. The review in Chapter 4 was the first study to systematically review and meta-analyse all ACT processes and their association with distress in cancer, addressing a gap in the literature. A notable strength was the gold standard method to systematically gather and analyse the data, following guidelines to ensure a high quality, transparent and reproducible review (Page et al., 2021).

The thesis also presents the first study in this population to compare ACT and CSM with the outcome of distress and identify potentially modifiable factors. This method allowed comparison and integration of models to explain variance in distress. A key strength of this study was that it addressed the limitations uncovered in the review in Chapter 4 by conducting both cross-sectional and longitudinal analysis of all ACT processes, use of an alternative measure to the AAQ and to combine processes to comprehensively test models. In addition, the use of both cross-sectional and longitudinal data addressed limitations highlighted in other previous research and allowed causal pathways to be tested, something that previous literature was lacking.

It was therefore the first study to explore the symptoms-distress relationship in this population in a longitudinal study providing an indication of further modifiable factors that might mitigate the negative effect of unavoidable side effects. Despite previous research suggesting symptom burden may lead to distress, these studies provide a fuller understanding of how that relationship might be formed and therefore managed. The multi-methods approach taken to the PhD thesis is a further strength as it has allowed a range of different methodologies to be brought together to build a thorough interpretation of the research aims. In particular the qualitative study provided contextualisation and an understanding of *why* symptoms are distressing, informing hypotheses to test; and the review and longitudinal analyses have built on *how* symptoms are distressing and *for whom* this effect may be stronger for.

8.6 Future directions and recommendations

There are a number of recommendations for future research that have been discussed throughout this chapter and the individual studies that would build on this existing body of research. Firstly, research should focus specifically on women of non-White ethnicities to see if these findings are replicated or whether there are individual and unique patterns of experiences in these groups related to cultural morns or expectations of cancer and its treatment (Howard, Balneaves, & Bottorff, 2007). This would enable interventions to be tailored with the aim to be more relevant and effective for these women.

Further investigation of how the presence of symptoms may lead to symptom burden in the first place could be a useful avenue for future research. This could allow for the potential individual differences to be explored to understand why symptoms might be burdensome. Further research should also consider other variables that may be relevant for this

population as have been identified in previous literature, the thesis studies and the TMA-LTC.

This thesis has provided an example of how utilising multiple theories can identify useful targets for intervention which can be further built on in future studies. The results presented could contribute to refining and adapting theories like the TMA-LTC to the specific population of breast cancer survivors on hormone therapy, in order to present a model that explains more variance in distress, informing future interventions. The TMA-LTC provides a framework of which variables may be associated with adjustment to a long-term condition. These results build on the TMA-LTC by indicating causal relationships between psychological processes to help test and design effective interventions. It is important for theories to be developed and refined based on the evidence (Levin et al., 2012), and this may provide further evidence for the variables and directions of relationships which can directly lead to intervention development. New evidence in different populations can help to build on and evolve theories to help strengthen the transdiagnostic application of these models.

The findings from this thesis can contribute to intervention development. The MRC guidance suggests context needs to be considered and theories tested (Skivington et al., 2021), which the studies from this thesis have contributed to. The review has provided a comprehensive overview of existing evidence which alongside previous evidence, supports relevant theory. The qualitative study has provided a deep contextual consideration and understanding of the needs of the population in question, whilst the quantitative study has tested core elements of processes underlying theories. The next steps would be to complete analyses recommended above and start involving patient and public involvement (PPI)

members to ensure stakeholders are engaged and involved with the research from the beginning (Hudson et al., 2020). After which the next step would be assessing feasibility with consideration of implementation (Skivington et al., 2021). An integrated model using both CSM illness perceptions and ACT processes may be worth investigating as a proposed intervention framework as presented in the theoretical integration section. Karekla, Karademas and Gloster (2019) matched features of the CSM with ACT strategies and techniques, suggesting the potential complementary nature of these two models in physical illness. Testing this as an explanatory serial mediation model would further corroborate this integrative approach to then inform intervention development.

Finally, as recommended by the review in Chapter 4, mediation analysis needs to be conducted on RCTs to understand how these evidence-based processes lead to changes in clinical outcomes in order to further refine intervention design and implementation. Network intervention analysis allows for multiple processes to be tested and may be a useful approach for this area of research (Fishbein, Haslbeck, & Arch, 2023).

8.7 Overall conclusions

This PhD thesis highlights the importance of understanding distress and physical symptoms in breast cancer survivors on hormone therapy. The results of the studies show survivorship for this group of people with breast cancer has the potential to be distressing with the experience of potentially difficult side effects. The studies make several novel contributions to the literature including the first comprehensive review and meta-analysis of ACT processes and distress and the first to explore the symptom-distress relationship in this population. The ACT processes seemed to contribute the most to explaining distress, but several other psychological variables were important third variables in the symptom-distress

pathway. Cognitive fusion, symptom focusing, embarrassment avoidance and breast cancer consequences may explain the pathway, whilst those with worse understanding of treatment and more damage beliefs are more likely to experience negative effects of symptoms. This demonstrates the utility of testing more than one model, as useful variables from several models were found.

The results of the studies have important implications both clinically and theoretically. Identifying those at risk of distress may enable earlier intervention. Future research should test how illness related cognitions may lead to inflexible or flexible responses to support an integrated approach to intervention development. Overall, the PhD thesis studies have the potential to contribute to supporting breast cancer survivors on hormone therapy and therefore improve outcomes.

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Appendices

Appendix A: Systematic review

A1) Publication supplementary materials

Supplementary materials contents:

Table S1.

Measures eligible in the review

Flexible processes *Inflexible process (in italics)*	Measures eligible in the review
Acceptance *Experiential avoidance*	Due to multiple measures for both, both are included and discussed separately Including any process-based acceptance measure (emotions, self, pain, not resignation or acceptance as an end point)
Defusion *Cognitive fusion*	Measures of cognitive fusion
Present moment awareness *Loss of contact with the present*	Measures for mindfulness (total scores)
Self-as-context *Self-as-content*	Measures of self-as-context
Values *Lack of values clarity*	Measures of personal values/valued living

Committed action *Inaction*	Measures of committed action In addition, measures combining committed action and values were included
Self-compassion *Self-judgement*	Self-compassion measures include variations of Neff (2003) measure (total scores of self-compassion or self-judgment)
Psychological flexibility *Psychological inflexibility*	Multidimensional measures of the overarching process of psychological flexibility, incorporating elements of the 6 core processes.

Table S2.

Search strategy

OVID	1. exp Neoplasms/, 2. cancer*.mp., 3. exp Metastasis/, 4. exp Oncology/, 5. oncology.mp., 6. tumo?r*.mp., 7. exp Distress/, 8. distress*.mp., 9. exp Psychological Stress/, 10. (psycho* adj stress*).mp., 11. (psycho* adj distress*).mp., 12. exp Anxiety/, 13. anxiet*.mp., 14. (anx* adj2 symptom*).mp., 15. exp "Depression (Emotion)"/, 16. depression.mp., 17. (depress* adj2 symptom*).mp. , 18. exp Emotional States/, 19. mood.mp., 20. (acceptance and commitment therapy).mp., 21. exp "Acceptance and Commitment Therapy"/, 22. acceptance.mp., 23. accept* adj5 thought*, 24. accept* adj5 feeling*, 25. accept* adj5 experience*, 26. accept* adj5 emotion*, 27. accept* adj5 cancer*, 28. accept* adj5 diagnos*, 29. accept* adj5 symptom*, 30. experiential acceptance, 31. psychological acceptance, 32. exp Experiential avoidance, 33. experiential avoidance.mp, 34. (psycho* adj flexibility).mp., 35. (psycho* adj inflexibility).mp., 36. exp Self-Compassion/, 37. self-compassion.mp., 38. self-kindness.mp., 39. (self adj compassion*).mp. , 40. (self adj kindness).mp., 41. exp Mindfulness/, 42. mindful*.mp., 43. being adj2 present, 44. present adj2 awareness, 45. present adj2 moment , 46. commit* adj2 action, 47. (cognitive adj fusion).mp. , 48. defusion.mp., 49. self-as-context.mp., 50. self adj2 context.mp., 51. contextualis* adj2 self, 52. self adj2 observer, 53. exp Personal values/, 54. personal adj value*.mp., 55. value* adj2 living, 56. value* adj2 action , 57. 1 or 2 or 3 or 4 or 5 or 6 , 58. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19, 59. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56, 60. 57 and 58 and 59.
CINAHL	1.(MH "Neoplasms+"), 2."cancer*" , 3.(MH "Oncology+"), 4."oncology" , 5.(MH "Neoplasm Metastasis+") , 6."tumor" , 7."tumour" , 8. (MH "Psycho-Oncology"), 9. "distress*", 10. (MH "Stress, Psychological+"), 11. "psych* distress*", 12. “psych* stress*”, 13. (MH "Anxiety+"), 14. "anxiet*", 15. "anxi* N2 symptom*", 16. "depression", 17. (MH "Depression+"), 18. "depress* N2 symptom*", 19. (MH "Affect"), 20. "mood", , 21. (MH "Acceptance and Commitment Therapy"), 22. "acceptance", 23. "accept* N5 thought*", 24. accept* N5 feeling*, 25. accept* N5 experience*, 26. accept* N5 emotion*, 27. accept* N5 cancer, 28. accept* N5 diagnos*, 29. accept* N5 symptom*, 30. experiential acceptance, 31. psychological acceptance, 32. experiential avoidance, 33. "psycho* flexibility", 34. "psycho* inflexibility", 35. "self-compassion", 36. "self kindness", 37. self N2 compassion*, 38. self N2 kindness, 39. (MH "Mindfulness"), 40. "mindful*", 41. being N2 present, 42.

	present N2 awareness, 43. present N2 moment, 44. “commit* N2 action” , 45. "cognitive fusion", 46. "defusion", 47. self-as-context, 48. self N2 context, 49. self N2 observer, 50. personal N2 value*.mp., 51. value* N2 living, 52. value* N2 action, 53. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8, 54. S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20, 55. S21 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR 31 OR 32 OR 34, 56. S53 AND S54 AND S55
WoS	(TS=(neoplasm* OR cancer* OR metasta* OR oncology OR tumo$r*) AND TS=(distress* OR "psych* near\2 stress" OR "psycho* near\2 distress*" OR anxious OR anxiet* OR "anx* near\2 symptoms" OR depress* OR "depress* near\2 symptoms" OR affect OR mood) AND TS=("acceptance and commitment therapy" OR "acceptance" OR "accept* near\5 thought*" OR "accept* near\5 feeling*" OR "accept* near\5 experience" OR "accept* near\5 emotion*" OR "accept* near\5 cancer*" OR "accept* near\5 diagnos*" OR "experiential acceptance" OR "psychological acceptance" OR "experiential avoidance” OR "psycho* near\1 flexibility" OR "psycho* near\1 inflexibility" OR self-compassion OR self-kindness OR "self near\1 compass*" OR "self near\1 kindness" OR mindful* OR "being near\2 present" OR "present near\2 awareness" OR "present near\2 moment” OR "commit* near\2 action" OR "cognitive near\1 fusion" OR defusion OR self-as-context OR "self near\2 context" OR "contextualis* near\2 self" OR "self near\2 observer" OR "personal values" OR "value* near\2 living" OR “value* near\2 action”))
Cochrane	1. [Neoplasms] explode all trees, 2. [Psycho-oncology] explode all trees, 3. (cancer):ti,ab,kw, 4. (oncology):ti,ab,kw, 5. (tumo?r):ti,ab,kw, 6. [Neoplasm Metastasis] explode all trees, 7. #1 OR #2 OR #3 OR #4 OR #5 OR #6, 8. [Psychological Distress] explode , 9. [Stress, Psychological] explode all trees, 10. (distress*):ti,ab,kw, 11. psycho* next distress*, 12. psycho* next stress*, 13. [Anxiety] explode, 14. (anxiet*):ti,ab,kw, 15. anx* near/2 symptom*, 16. [Depression] explode, 17.(depression):ti,ab,kw, 18. depress* near/2 symptom*, 19. Affect] explode, 20. (mood):ti,ab,kw, 21. #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 or #16 or #17 or #18 or #19 or #20, 22. Acceptance and Commitment Therapy] explode, 23. (acceptance):ti,ab,kw, 24. (accept* near/5 thought*):ti,ab,kw, 25. (accept* near/5 feeling*):ti,ab,kw, 26. (accept* near/5 experience*):ti,ab,kw, 27. (accept* near/5 emotion*):ti,ab,kw, 28. (accept* near/5 cancer*):ti,ab,kw, 29. (accept* near/5 diagnos*):ti,ab,kw, 30. (experiential next acceptance):ti,ab,kw, 31. (experiential next avoidance):ti,ab,kw, 32. (psychological next acceptance):ti,ab,kw, 33. (psychological next flexibility):ti,ab,kw, 34. psychological next inflexibility , 35. (self-compassion):ti,ab,kw, 36. (self-kindness):ti,ab,kw, 37. (self near/1 compass*):ti,ab,kw, 38. (self near/1 kindness):ti,ab,kw, 39. Mindfulness explode, 40. (mindful*):ti,ab,kw, 41. being next present , 42. present near/2 awareness, 43. present near/2 moment , 44. (commit* near/2 action):ti,ab,kw, 45. (cognitive next fusion):ti,ab,kw, 46. (defusion):ti,ab,kw, 47. (self-as-context):ti,ab,kw, 48. self near/2 context , 49. contexualis* near/2 self , 50. self near/2 observer, 51. personal next values, 52. value* near/2 living , 53. value* near/2 action , 54. #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53, 55. #7 AND #21 AND #54

S3. R code

```
Dataset1.cor <- metacor(cor,
                n,
                data = Dataset1,
                studlab = Dataset1$Author,
                sm = "ZCOR",
                comb.fixed = FALSE,
                comb.random = TRUE,
                method.tau = "REML"
                title = "Dataset1")
Dataset1.cor



m.gen.reg <- metareg(Dataset1.cor, ~moderator)
m.gen.reg
```

Table S4.

Study characteristics of included studies and reference list

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
1	Aarstad et al. (2011) Norway	96	22%	61 (11)	Not reported	Head & Neck	Lip (1%), oral cavity (29%), salivary glands (2%), pharynx (16%), larynx (42%), sinus (3%), unknown primary site (3%) Mixed stages	4 (2) years	CS
2	Afrashteh and Masoumi (2021) Iran	210	100%	38.97 (12.32)	Not reported	Breast	Breast cancer (100%)	Not reported	CS
3	Aguado Loi et al. (2013) USA	68	100%	55.4 (10.4)	Latinas: Colombian (30.9%), Puerto Rican (30.9%), Dominican (10.3%), Cuban (10.3%), Mexican (7.4%), Other (10.3%)	Breast	Breast (100%) Stages I-III	2.8 years (1.5)	CS
4	Al-Ghabeesh et al. (2019) Jordan	234	100%	46.33 (11.51)	Jordanian (100%)	Breast	Breast (100%) Mixed stages	2.86 years (2.80)	CS
5	Aldaz et al. (2019) New Zealand	31	61.30%	60.00 (14)	New Zealand, European/Pakeha (80.6%), Māori (6.5%), other European (12.9%)	Mixed	Breast (35.5%), rectum (19.4%), colon (9.7%), ovarian (9.7%), lung (6.5%), oesophageal (6.5%), prostate (6.5%), head and neck (3.2%), pancreas (3.2%) Mixed stages	Not reported	L (micro/7 days)
6	Arambasic, Sherman and Elder (2019) Australia	92	100%	58.46 (8.77)	Not reported. Place of birth: Australia (80.5%), Other (19.5%)	Breast	Breast (100%) Mixed stages	82.14 months (19.34)	CS
7	Asuzu and Elumelu (2013) Nigeria	237	84.1%	49.91 (13.48)	Yoruba (32.9%), Igbo (44.4%), Hausas (6%), other (5.5%)	Mixed	Prostate (5.5%), breast (46.4%), cervical (25.7%), other (22.4%)	Not reported	CS
8	Babu (2020) USA	164	45.5%	44.21 (9.81)	Not reported	Mixed	Mixed Mixed stages 0-IV	Not reported	CS
9	Banner (2009) USA	69	100%	59.10 (13.46)	Not reported	Breast	Breast (100%) Mixed stages	7.77 months (3.11)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
10	Baziliansky and Cohen (2021) Israel	153	47.1%	64.5 (12.1)	Not reported	Colorectal	Colon (73.9%), rectal (26.1%) Mixed stages	13.7 months (4.1)	L (T1 baseline, T2 6 months)
11	Berrocal Montiel et al. (2016) Italy	64	100%	48.14 (9.36)	Not reported	Breast	Breast (100%) Mixed stages		L (T1 baseline, T2 6 months)
12	Black et al. (2016) USA	409 (358)	47.2%	Not reported	Hispanic (100%)	Colorectal	Colorectal (100%)	3.1 years (1.7)	CS
13	Brabbins (2016) UK	72	56.9%	Not reported	Not reported	Mixed	Breast (28%), prostate (26%), bowel (13%), lung (10%), other (23%) Mixed stages	Not reported	L (T1 baseline, T2 3 months)
14	Brown and Ryan (2003a) USA	41	78%	55.31 (10.02)	Not reported	Mixed	Breast (78%), prostate (22%)	2.05 years (2.24)	CS (before RCT)
15	Brown et al. (2020) USA	61	44.3%	60.15 (11.71)	White/Caucasian (83.6%), American Indian or Alaska Native (1.6%), Asian or Asian American (3.3%), Black or African American (3.3%), Other (6.6%)	Mixed	Oral cavity and pharynx (6.6%), digestive system (26.2%), respiratory system (18.0%), skin (9.8%), genital system (9.8%), urinary system (3.3%), lymphoma (3.3%), myeloma (6.6%), brain & other nervous system (1.6%), leukaemia (3.3%), bones & joints (1.6%), other (6.6%)	Not reported	CS
16	Brunault et al. (2016) France	120	100%	56.4 (10.8)	Not reported	Breast	Breast (100%) Early stage	Not reported	CS
17	Cameron (2000) USA	44	57%	66 Males 69.1 (10.6); females 63 (12.3)	Male: White (89.5%) No response (10.5%) Female: White (60%), African American (20%), Asian American (4%), no response (16%)	Colorectal	Colorectal (100%) Mixed stages	21.6 months Males 22.4 (10.2) Females 21.2 (9.0)	L (baseline, follow up 3 months)
18	Carlson and Brown (2005) Canada/USA	122	67.21%	49.55 (12.81)	Not reported	Mixed	Breast (51.6%), prostate (17.2%)	Not reported	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
19	Carver et al. (1993) USA	59	100%	58.02 (10.83)	White (88%), Black (7%), Hispanic (5%)	Breast	Breast (100%) Early stages	Not reported	L (T0 1 day pre-surgery, T1 10 days post-surgery, T2 3 months, T3 6 months, T4 12 months)
20	Chen et al. (2021) Taiwan	90	54.4%	56.2 (10.5)	Not reported	Colorectal	Colon (58.9%), rectal (33.3%), colorectal (5.6%), anal (2.2%) Mixed stages	Not reported	CS
21	Cho et al. (2021) USA	78	50.65%	65 (10.44)	Non-Hispanic White (76%)	Lung	Non-small cell lung (100%) Stage IV	Not reported	CS
22	Ciarrochi, Fisher and Lane (2011) Australia	107	50%	62 (median)	Australian born (49%), not stated (34%), born in England (8.4%)	Mixed	Breast (29%), prostate (14%), haematological (12%), lung (8%), colorectal (7%), not stated (7%) , skin (6.5%), pancreas (4%), head & neck (3%) [ł]	6 months	CS
23	Corman et al. (2021) France *same sample as Corman et al. (2022)	187	41.9%	52.07 (13.22)	Not reported	Blood	Acute leukaemia (35.7%), myelodysplastic syndrome (17%), myeloproliferative neoplasia (10.4%), non-Hodgkin lymphoma (12.1%), others e.g., Hodgkin lymphoma, chronic leukaemia (25.1%)	Not reported	CS
24	Corman et al. (2022) France *same sample as Corman et al. (2021)	187	41.9%	52.07 (13.22)	Not reported	Blood	Acute leukaemia (35.7%), myelodysplastic syndrome (17%), myeloproliferative neoplasia (10.4%), non-Hodgkin lymphoma (12.1%), others e.g., Hodgkin lymphoma, chronic leukaemia (25.1%)	Not reported	L (T0 before transplant, T1 5 months)

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
25	Costanzo et al. (2006) USA	64	100%	62 (12.5)	Not reported	Gynae	On chemo: ovarian (72%), endometrium (14%), cervix (10%), fallopian (3%) No chemo: endometrial (69%), cervical (28%), ovarian (3%)	Not reported	CS
26	Deimling et al. (2006) * USA	321	59.2%	72.18 (7.7)	Black/African American (37.7%), White/Caucasian (62.3%)	Mixed	Breast (41.4%), prostate (28.7%), colorectal (29.9%)	10.4 years (5.5)	L (analysed data from initial interview)
27	Elsheshtawy et al. (2014) Egypt	56	100%	52 (13.3)	Not reported	Breast	Breast (100%) Early stages	Not reported	CS
28	Elumelu, Asuzu and Akin-Odanye (2015) Nigeria	110	96.4%	47.04 (10.51)	Not reported	Breast	Breast (100%)	Not reported	CS
29	Fox (2002) USA	75	67%	55.45 (15.48)	Caucasian (85.3%), Asian American (5.3%), African American (3%), others (5.3%), not identified (1%)	Mixed	Breast (33.3%), gynaecological (13.3%), urogenital (13.3%), gastrointestinal (10.6%), skin and connective tissues (9.3%), head & neck (6.6%), lymphoma (4%), haematological (2.6%), brain (2.6%), lung (1.3%), unknown (2.6%)	30.58 weeks (35.83)	CS
30	Garcia et al. (2021) Brazil	183	53.55%	62.8 (12.7)	Not reported	Mixed	Breast (23.5%), prostate (16.39%), colorectal (18.03%), others (42.08%)	1 year 10 months (2.559)	CS
31	Garland et al. (2017) USA	97	55.6%	55.8 (14.3)	White (91.7%), Latino (3.1%), Black (2.1%), other (3.1%)	Mixed	Breast (26%), prostate (9%), colon (7%), lymphoma (7%), lung cancer (7%), melanoma (6%), ovarian (3%), others including neurological cancer, haematological cancer (35%) Mixed stages	Not reported	CS
32	Gillanders et al. (2015) UK	105	45%	Mean not reported	White British (93%), missing (7%)	Mixed	Urological (37%), breast (24%), haematological (23%), lung (6%), bowel (6%), gynae (5%), throat/neck (1%)	3.59 years (4.607)	CS
33	Glover (2015) UK	204	69.5%	57.18 (11.41)	British/English/Scottish (71.3%), White/Caucasian (21%), European (2.6%),	Mixed	Breast (24.5%), genitourinary (23.5%), gynaecological (18.0%), digestive	37.67 months (50.26)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
					American (1.0%), Asian (1.0%), Others/not disclosed (3.1%)		(12.5%), other (11.5%), head, neck & brain (10%) *Those who felt personally responsible for their cancer n=155*		
34	González-Fernández et al. (2017) Spain	122	100%	52.40 (7.26)	Not reported	Breast	Breast (100%)	1 month to 8 years	CS
35	Grozdziej (2015) UK	77	100%	54 (9.7)	White (92.7%), Asian (1.8%), Black (1.8%), Mixed background (1.8%), Other (1.8%)	Breast	Breast (100%)	Not reported	CS
36	Hagan et al. (2017) USA [#] same sample as Nipp et al. (2016)	350	46%	64.86 (10.86)	White (92.3%) African American (2.9%) Asian (2.3%) American Indian or Alaskan Native (1.1%) Hispanic or Latino (2.6%) Other (1.4%)	Mixed	Non-small cell lung cancer (44%), pancreatic (24.9%), small cell lung (8.6%), oesophageal (6.9%), other (15.7%) Advanced stage	25 days (14.1)	CS
37	Ho, Fong and Wan (2022) China	127	58.3%	63.8 (8.9)	Not reported	Colorectal	Colorectal 100% Mixed stages	Not reported	L (baseline T1, 2 months later T2, 8 months T3 but only cortisol at T3
38	Hsieh et al. (2021) Taiwan	116	58.62%	54.85 (7.29)	Not reported	Lung	Non-small cell lung cancer (100%) Mixed stages IIIB or IV	32.91 months (29.28)	CS
39	Hulbert-Williams and Storey (2016) UK	129	55%	61.43 (16.8)	Not reported	Mixed	Breast (40.3%), colorectal (20.2%), prostate (19.4%), lung (18.6%), missing (1.5%)	6.8 months (3.1)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
40	Ikeuchi et al. (2020) Japan	249	100%	59.5 years (12.44)	Not reported	Breast	Breast (100%) Mixed stages I-III	Not reported	CS
41	Keeling, Bambrough and Simpson (2013) UK	74	53%	38.30 (10.67)	Not reported	Brain	Astrocytoma (58.2%), oligodendroglioma (31.3%), mixed glioma (4.5%), ependymoma (3%), other (3%) Grades 1-2	27.69 months (19.79)	CS
42	Kelliher-Rabon et al. (2022) USA	235	64.3%	61.28 (27.63)	White (91.9%), Black/African American (1.7%), Hispanic or Latino/a (2.1%), American Indian or Alaskan native (0.90%), Asian (0.4%), other race (0.4%), multiracial (1.3%) and those declined (1.3%)	Mixed	Not reported	Not reported	CS
43	Kersting (2012) USA	74 T1, 43 T2	75.7%	52.8 (12)	Caucasian (59.5%), African American (31.1%), Asian Pacific Islander (1.4%), Bi-racial (1.4%)	Mixed	Breast (45.9%), lung (9.5%), colon/rectal (6.8%)	6.2 months (4.7)	L
44	Kuba et al. (2019) Germany	922	43%	64 (13.4)	Not reported	Blood	Haematological (100%)	8.9 years (4.5)	CS
45	Kuhlman et al. (2017) USA	271	100%	56.23 (11.49)	Non-Hispanic white (71.6%), Asian (11.1%), Black (4.4%), Hispanic/Latina (3.7%), other (9.2%)	Breast	Breast (100%)	Not reported	CS
46	Lam et al. (2018) Singapore	212	68%	49.26 (9.30)	Chinese (60%), Non-Chinese - Malay, Indian, Eurasian (40%)	Mixed	Breast (35%), others (65%) (nasopharyngeal, gynaecological, pancreatic, haematological, lung, gastrointestinal, brain, renal)	Not reported	CS
47	Lampic et al. (2002) Sweden	32	100%	58 (9.6)	Not reported	Breast	Breast (100%)	Not reported	L (3 months, 1 year)
48	Larson et al. (2019) USA	111	45.9%	58 (median)	Caucasian (97.3%), African American (0.9%), Asian American (0.9%), declined to respond (.9%)	Blood	Leukaemia (34.2%), lymphoma (30.6%), multiple myeloma (28.8%), other hematologic disease (6.3%)	Not reported	L (pre transplant and 1, 3, 6 months after)

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
49	Lei et al. (2021) China	441	28.6%	60 (median)	Not reported	Lung	Lung cancer (100%) Mixed stages I-IV	Not reported	CS
50	Lennon, Hevey and Kinsella (2018) * Ireland	92	0%	68.16 (9.66)	Irish (90%), Northern Irish (5%), British (3%), Sierra Leone (1%) ǂ	Prostate	Prostate (100%)	40.63 months (38.43)	CS
51	Levkovich (2021) Israel	170	100%	51.22 (12.15)	Jewish (81.1%), Arab (18.9%)	Breast	Breast cancer (100%)	Not reported	CS
52	Lewson et al. (2021) USA	203	52.22%	63.16 (10.25)	Non-Hispanic white (75.86%), Black/African American (13.30%), Hispanic or Latino/a (3.94%), other (6.90%)	Mixed	Breast (25.12%), prostate (24.63%), gastrointestinal (25.12%), lung (25.12%) Mixed stages I-II	3.50 years (2.98)	CS
53	Liu et al. (2021a) China	230	100%	47.8 (9.1)	Not reported	Breast	Breast cancer (100%) Mixed stages 0-III	Not reported	CS
54	Liu et al. (2018) China	202	100%	47.62 (8.90)	Not reported	Breast	Breast cancer (100%) Mixed stages 0-III	Not reported	CS
55	Liu et al. (2021b) China	290	30.3%	Not reported	Not reported	Liver	Hepatocellular carcinoma (100%)	Not reported	CS
56	Low et al. (2006) USA	417	100%	58.1	White (87%)	Breast	Breast (100%) Nonmetastatic	Not reported	CS (Baseline RCT)
57	Lv et al. (2021) China	82	43.9%	37.9 (10.3)	Not reported	Thyroid	Not reported	25.4 months (8.6)	CS
58	Mackay, Burdayron and Korner (2021) Canada	174	48.9%	59.2 (13.5)	Not reported	Melanoma	Melanoma (100%) Mixed stages 0-IV	26.7 months (47.8)	CS at T3
59	Manne et al. (2018) USA	174	100%	55.32 (10.28)	Caucasian (75.9%), non-Caucasian (23.6%), 1 missing	Gynae	Ovarian (65.5%) Endometrial	3.90 months (1.90)	CS
60	McAteer and Gillanders (2019) UK	286	0%	67 (7.81)	Not reported	Prostate	Prostate (100%) Mixed stages	4.9 years (4.73)	CS
61	Millmann (2019) USA	14	100%	62.79	Caucasian/White (93%), Native/Indian American (7%)	Gynae	Ovarian (86%), fallopian (14% Stage III-IV	Not reported	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
62	Mosher et al. (2021) USA	201	49.25%	61.93 (11.93)	Non-Hispanic White (80.10%), Black (10.95%), Hispanic (2.99%), other (5.47%), missing (0.50%)	Mixed	Breast (24.88%), prostate (24.88%), lung (25.37%), gastrointestinal (24.88%) Advanced stage	3.16 years (2.93)	CS
63	Mosher et al. (2017) USA	80	100%	55.50 (11.26)	Non-Hispanic white (91.3%), other ethnicity – African American/Black, Hispanic and other (8.8%)	Breast	Breast (100%) Stage IV	3.93 years (3.64)	CS
64	Nipp et al. (2016) USA # same sample as Hagan et al. (2017)	350	46%	64.86 (10.86)	White (92.3%) African American (2.9%) Asian (2.3%) American Indian or Alaskan Native (1.1%) Hispanic or Latino (2.6%) Other (1.4%)	Mixed	Non-small cell lung cancer (44%), pancreatic (24.9%), small cell lung (8.6%), oesophageal (6.9%), other (15.7%) Advanced stage	25 days (14.1)	CS
65	Novakov (2021) Serbia	64	100%	58.36 (11.30)	Not reported	Breast	Not reported	Not reported	CS
66	Omid et al. (2017) Iran	109	70.6%	Women 49.54 (8.7) Men 50.37 (10.83)	Not reported	Mixed	Breast (36.7%), colon (25.7%), stomach (14.6%), lung (1.8%), liver (3.7%), leukaemia (8.3%), prostate (2.8%), vaginal (1.8%), ovarian (1.8%), testicular (0.9%), lymphoma (0.9%), bone marrow (0.9%)	2 years 5 months (2 years 4 months)	CS
67	Pinto-Gouveia et al. (2014) Portugal	63	82.5%	Male 55.45 (13.24) Female 52.65 (10.01)	Not reported	Mixed	Breast (73.0%), lung (6.3%), prostate (4.8%), cervix (1.6%), stomach (3.2%), intestine (1.6%), others (9.5%)	Not reported	CS
68	Ploumen (2017) Netherlands	108	69%		Not reported	Mixed	Breast (38%), other (62%)	Not reported	CS
69	Politi, Enright and Weihs (2007) USA	91 (79 complete	100%	51.5 (10.3)	Caucasian (51.9%), African American (40.5%), Hispanic (3.8%), Asian American (2.5%), other (1.3%)	Breast	Breast (100%) Early stages	13.9 months (4.9)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
		data ?							
70	Poulin et al. (2016) Canada	76	76.3%	56.53 (9.37)	Caucasian (86.8%), Asian (2.6%), African (3.9%), other (3.9%)	Mixed	Breast and gastrointestinal (% not reported)	Not reported	CS
71	Priscilla et al. (2011) Malaysia	105	52%	40	Malay (60%), non-Malay (40%)	Blood	Haematological: non-Hodgkin lymphoma (24%), acute myelogenous leukaemia (23%), acute lymphoblastic leukaemia (14%), Hodgkin lymphoma (11%) and other haematological cancers (29%)	Not reported	CS
72	Przezdziecki (2017) Australia	206	100%	56.43 (9.73)	Country of birth: Australia (79.9%), New Zealand (3.9%), UK (11.3%), Europe (0.5%), Asia and Pacific (1%), America (1.5%)	Breast	Breast (100%)	67.18 months (63.96)	CS (before RCT)
73	Przezdziecki and Sherman (2016) Australia	152	100%	54.55 (9.79)	Country of birth: Australia (80.1%), UK/Europe (13.3%), other (6.6%)	Breast	Breast (100%)	Not reported	CS
74	Przezdziecki et al. (2013) Australia	279	100%	53.4 (9.40)	Country of birth Aus/NZ (81%), Britain/Ireland (11%), Asia (1%), Europe (1%), America (4%), Africa (2%)	Breast	Breast (100%)	Not reported	CS
75	Randell (2017) UK	75	92%	51.9 (12.0)	Not reported	Mixed	Breast (69.3%), haematological (8.0%), colorectal (5.3%), brain (4.0%), upper GI (2.7%), other (10.7%) includes lung, melanoma, gynaecological, thyroid, kidney and testicular	3.5 years (4.5)	CS
76	Raque-Bogdan, Lent and Lamphere (2019) USA	275	100%	47 (11.12)	White, non-Latino (87%), African American (4%), American Indian (1%), Asian (3%), Multiracial (1%), Latino (4%)	Breast	Breast (100%)	4 years (4.22)	CS
77	Romano (2014) USA	76	92%	57 (10.22)	Caucasian (89.5%), Asian (6.6%), African American/Black (1.3%), Mixed (2%)	Mixed	Breast (66%), gynaecological (10.5%), blood, lymphatic, or bone marrow (7%), oral, head or neck (5%), colorectal (3%),	58.61 months (67.47)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
							kidney (3%), lung (1%), pancreatic (1%), unidentified (3%)		
78	Ross (2009) USA	105	62%	56 (14.70)	Latinos: Mexican (70.5%), Central American (12.4%), South American (6.7%), Cuban (2.9%), Puerto Rican (4.8%), other (2.9%)	Mixed	Breast (36.2%), prostate (16.2%), colon/rectal (10.5%) Mixed stages	Not reported	CS
79	Roussi et al. (2007) Greece	72	100%	54.13	Native Greeks (100%)	Breast	Breast (100%)	Not reported	L (pre-surgery, 2-3 days after surgery and 3 months later)
80	Salber (2016) USA	233	100%	59.50 (10.68)	Race: White (89.7%), Black (9.0%), Other (1.3%) Ethnicity: Hispanic (1.4%), non-Hispanic (98.6%)	Breast	Breast (100%) Mixed stages	5.01 years (6.41)	CS
81	Saniah and Zainal (2010) Malaysia	141	100%	50	Not reported	Breast	Breast (100%)	Not reported	CS
82	Schellekens et al. (2017) Netherlands	88	33%	62.8 (8.2)	Not reported	Lung	Lung (100%) Mixed stages	4.5 months (7.6)	CS
83	Seltzer (2021) USA	82	0%	70.4	Black (69.5%), White (29.3%), Hispanic (12%)	Prostate	Not reported	52.8 months (57.5)	CS
84	Sevier-Guy et al. (2021) UK	144	0%	68.5 (7.2)	Not reported	Prostate	Not reported	6.0 years (4.13)	CS
85	Shapiro et al. (2010) USA	283	78%	54.6 (11.7)	White (79%), African American (19%), Hispanic (2%), Asian (1%)	Mixed	Breast (42%), lung (8%), colon (7%), lymphoma (6%), prostate (5%), leukaemia (5%), ovarian (4%), myeloma (4%), pancreatic (2%), other (17%)	Not reported	CS
86	Sherman et al. (2016) Australia	75	100%	47.81 (8.86)	Country of birth: Australia (64.90%), New Zealand (4.10%), UK/Ireland (17.60%),	Breast	Breast (100%)	Not reported	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
					Asia (6.66%), Europe (4.05%), Africa (2.70%)				
87	Siwik et al. (2021) USA	58	67.2%	Not reported	Caucasian (63.8%), Black/African American (17.2%), Hispanic or Latino (1.7%), Asian/Asian American (1.7%), other (1.7%), missing (11.9%)	Lung	Non-small cell lung cancer (100%) Mixed stages	Not reported	CS
88	Stanton, Danoff-Burg and Huggins (2002) USA	70	100%	52.63 (11.94)	White (91%), African American (7%), Latina (1%)	Breast	Breast (100%) Early stages	Not reported	L
89	Stanton et al. (2018) USA	460	100%	56.4 (12.6)	Non-Latina White (67.6%), Latina (19.3%)	Breast	Breast (100%) Early stages	2.1 months (0.81)	L
90	Swash, Bramwell and Hulbert-Williams (2017) UK	91	53.2%	61 (12.4) extracted from diss	White (97.50%), Black Caribbean (1.30%), Chinese (1.30%)	Blood	Haematological	Not reported	CS
91	Tamagawa et al. (2013) Canada	272 (227)	100%	54.58 (10.32)	Not reported	Breast	Breast (100%) Mixed stages I-III	24.08 months (27.38)	CS
92	Taylor-Ford (2014) USA	102	52%	55.07 (11.24)	Non-Hispanic, White (69%), Black (3%), Hispanic (13%), Asian (12%), other (3%)	Colorectal	Colorectal (100%) Advanced stage	821 days (941)	CS
93	Thune-Boyle et al. (2013) UK	155	100%	55.7 (13.5)	Caucasian (82.6%), Black (4.5%), Asian (3.9%), Oriental (1.9%), other (7.2%)	Breast	Breast (100%) Early stages	Not reported	CS
94	Todorov, Sherman and Kilby (2019) Australia	195	100%	Mean not reported	Country of birth: Australia (68.8%), Other (67%)	Breast	Breast (100%) Mixed stages	Not reported	CS
95	Trevino et al. (2012) USA	53	66%	33.89 (5.70)	White (92.5%), African American (1.9%), Asian American (1.9%), Hispanic (3.8%)	Mixed	Breast (39.6%), brain tumour (13.2%), leukaemia/lymphoma (9.4%), colon (5.7%), soft tissue (3.8%) Advanced stages	3.72 years (3.05)	CS
96	Trindade et al. (2018a) Portugal	75	100%	57.60 (10.18)	Not reported	Breast	Breast (100%) Mixed stages	Not reported	CS
97	Trindade et al. (2018b) Portugal	82	100%	50.21 (9.76)	Not reported	Breast	Breast (100%)	Not reported	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
98	Trindade et al. (2020) Portugal	40	100%	60 (10.13)	Not reported	Breast	Breast (100%) Stages I-III	Not reported	L (T1 baseline, T2 6 months)
99	van der Donk et al. (2020) Netherlands	245	24.9%	65.35 (12.01)	Not reported	Mixed	Urological (52.8%), lung (8.5%), colorectal (6.4%), haematological (6.8%), gynaecological (8.5%), bone & soft tissue (3.0%), other (2.1%), mixed (11.9%)	2.39 years (1.39)	CS
100	van Laarhoven et al. (2011) Netherlands	151	53%	58 (13)	Not reported	Mixed	Breast (29%), prostate (12%), testis (7%), lung (10%), colon/rectum (11%), melanoma (7%), other (24%)	Not reported	CS
101	Vick (2018) USA	75	100%	51.45 (12.34)	White, non-Hispanic (84%), African American (15%), Asian American (1%)	Breast	Breast (100%) Mixed stages	6.7 months (median)	CS
102	Vickberg (2000) USA	169	100%	59 (11.41)	African American (8%), White (74%), Hispanic (10%), Multi-ethnic or other (8%)	Breast	Breast (100%) Mixed stages	3 years (1.42)	CS
103	Walsh et al. (2018) North America and Ireland	241	0%	64.02 (7.76)	North American (46.90%), European (47.7%)	Prostate	Prostate (100%) Mixed stages	Not reported	CS
104	Xu et al. (2017) China	176	46%	Not reported	Not reported	Gastro	Gastrointestinal (100%, stomach, colon, oesophageal) Mixed stages	Not reported	CS
105	Xu et al. (2019) China	156	46.8%	52.3	Not reported	Mixed	Cancer patients with chronic pain	Not reported	CS
106	Zamanian et al. (2021) Iran	221	Not reported	47.14 (9.13)	Not reported	Breast	Not reported	18.31 weeks (15.05)	CS
107	Zarei, Musarezaie and Ashouri (2021) Iran	190	42.10%	Not reported	Not reported	Gastro	Gastrointestinal (100%)	Not reported	CS
108	Zhong et al. (2020) China	292	65%	52.2 (11.8)	Not reported	Gastro	Gastrointestinal: gastric, intestinal, oesophagus (100%)	Not reported	CS
109	Zhu et al. (2020) China	301	60.40%	50.07 (13.09)	Chinese	Mixed	Breast (22.30%), lung (16.70%), gastric (10.50%), gynaecological (16.70%), colorectal (4.50%), pancreas (2.80%), liver (2.10%), lymphoma (4.9%), multiple	14.25 months (16.44)	CS

Study ID	Authors and country	*n*	Prop. females (%)	Mean age in years (SD)	Ethnicity/race	Sample	Detailed cancer sample diagnosis (%)	Mean time since diagnosis (SD)	Study design (and f/u period)
							malignant tumours (3.10%), other (16.40%)		
110	Zhu et al. (2019) China	243	65.8%	50.78 (11.61)	Not reported	Mixed	Mixed stages Breast (28.4%), lung (15.1%), gastric (3.3%), gynaecological (22.4%), colorectal (5.9%), lymph (3.9%), others (14.5%), missing (6.6%)	Not reported	L (T1 diagnosis, T2 start and T3 end of treatment)

*Note: * author contacted; # = same sample indicated; n = sample size; SD = standard deviation; f/u: follow up; CS = cross sectional study; L = longitudinal study; T1, 2 etc: time 1, time 2…); RCT: randomised controlled trial*

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Table S5.

Data included in meta-analyses

Study ID	Author (year)	*n*	Sample	Advanced stage of cancer (%)	Process Measure	Outcome Measure	Correlations	Average effect size (correlation)
Experiential avoidance								
61	Millmann (2019)	14	Gynae	18	AAQII7	POMS	0.11	0.11
57	Lv et al. (2021)	82	Thyroid	NA	AAQII7	SAS anx	0.29*	0.30
						SDS dep	0.31**	
15	Brown et al. (2020)	61	Mixed	NA	PIP avoidance scale	DT	0.33*	0.33
8	Babu (2020)	164	Mixed	0.6	BEAQ15	DASS anx	0.47**	0.49
						DASS dep	0.51**	
65	Novakov (2021)	64	Breast	0	AAQII 8 items	DASS21 anx	0.49**	0.52
						DASS21 dep	0.57**	
						DASS21 stress	0.49**	
62	Mosher et al. (2021)	201	Mixed	100	AAQII7	PROMIS anx	0.56**	0.59
						PROMIS dep	0.62**	
23	Corman et al. (2021)	187	Blood	NA	AFQ	HADS anx	0.57***	0.48
						HADS dep	0.37***	
11	Berrocal Montiel et al. (2016)	64	Breast	39	AAQII7	HADS anx	0.61***	0.52
						HADS dep	0.55***	
						PANAS	0.38*	
83	Seltzer (2021)	82	Prostate	NA	AAQII7	HADS anx	0.66**	0.61
						HADS dep	0.55**	
52	Lewson et al. (2021)	203	Mixed	0	AAQII7	PROMIS anx	0.66**	0.67
						PROMIS dep	0.67**	
75	Randell (2017)	75	Mixed	0	AAQII7	HADS anx	0.68**	0.52
						HADS dep	0.45**	
					BEAQ15	HADS anx	0.48**	
						HADS dep	0.43**	
80	Salber (2016)	233	Breast	17.6	AAQII7	HADS anx	0.72**	0.65
						HADS dep	0.65**	

						DT	0.57**	
90	Swash, Bramwell and Hulbert-Williams (2017)	74	Blood	0	AAQII7	HADS anx	0.73**	0.67
						HADS dep	0.60**	
63	Mosher et al. (2017)	80	Breast	100	AAQII7	PROMIS anx	0.75**	0.72
						PROMIS dep	0.68**	
34	González-Fernández et al. (2017)	122	Breast	0	AAQII7	HADS anx	0.77**	0.76
						HADS dep	0.79**	
						BSI/GSI	0.70**	
77	Romano (2014)	76	Mixed	14	AAQII10	HADS anx	0.77**	0.72
						HADS dep	0.65**	
98	Trindade et al. (2020)	40	Breast	0	AAQ7	DASS21 dep	0.71***	0.69
						DASS21 stress	0.66***	
Acceptance								
19	Carver et al. (1993)	59	Breast	0	COPE 3 items	POMS distress presurgery	-0.68**	-0.68
79	Roussi et al. (2007)	72	Breast	NA	bCOPE Greek	POMS distress presurgery	-0.43***	-0.43
29	Fox (2002)	75	Mixed	NA	COPE 3 items	POMS distress	-0.42***	-0.33
						IES	-0.24*	
41	Keeling, Bambrough and Simpson (2013)	74	Brain	0	bCOPE	HADS anx	-0.31(no *p* value)	-0.26
						HADS dep	-0.21(no *p* value)	
58	Mackay, Burdayron and Korner (2021)	174	Skin	2.9	bCOPE	PHQ4 anx	-0.29**	-0.33
						PHQ4 dep	-0.36**	
36	Hagan et al. (2017)	350	Mixed	100	bCOPE	HADS anx	-0.29***	-0.33
						HADS dep	-0.37***	
59	Manne et al. (2018)	174	Gynae	21.3	COPE	BDI dep	-0.35**	-0.35
93	Thune-Boyle et al. (2013)	155	Breast	0	COPE	HADS anx	-0.25**	-0.25
						HADS dep	-0.25**	
56	Low et al. (2006)	417	Breast	0	COPE	CES dep	-0.25*	-0.22
						IES	-0.19*	
27	Elsheshtawy et al. (2014)	56	Breast	0	bCOPE	HADS anx	-0.19 ns	-0.22
						HADS dep	-0.26 ns	
106	Zamanian et al. (2021)	221	Breast	NA	bCOPE	DASS21 anx	-0.18**	-0.21
						DASS21 dep	-0.23**	

17	Cameron (2000)	25	Colorectal females	0	COPE	POMS distress	0.20 ns	0.20
17	Cameron (2000)	19	Colorectal males	21.2	COPE	POMS distress	0.25 ns	0.25
78	Ross (2009)	105	Mixed	36	bCOPE	CES dep	-0.15 ns	-0.15
1	Aarstad et al. (2011)	96	Head & neck	18	COPE	BDI dep	-0.14 ns	-0.14
26	Deimling et al. (2006)	321	Mixed	0	COPE 3 items	POMS anx	0.05 ns	0.06
						CES dep	0.07 ns	
Cognitive fusion								
57	Lv et al. (2021)	82	Thyroid	-	CFQ9 Chinese	SAS anx	0.30*	0.28
						SDS dep	0.25*	
15	Brown et al. (2020)	61	Mixed	-	PIPS subscale	DT	0.36**	0.36
62	Mosher et al. (2021)	201	Mixed	-	CFQ7	PROMIS anx	0.57**	0.57
						PROMIS dep	0.57**	
52	Lewson et al. (2021)	203	Mixed	-	CFQ7	PROMIS anx	0.64**	0.63
						PROMIS dep	0.62**	
75	Randell (2017)	75	Mixed	-	CFQ7	HADS anx	0.66**	0.54
						HADS dep	0.40**	
8	Babu (2020)	164	Mixed	-	CFQ7	DASS anx	0.67**	0.67
						DASS dep	0.66**	
32	Gillanders et al. (2015)	105	Mixed	-	CFQ7	HADS anx	0.72**	0.62
						HADS dep	0.50**	
96	Trindade et al. (2018a)	75	Breast	-	CFQ CI	DASS21 dep	0.69***	0.69
Present moment awareness								
55	Liu et al. (2021b)	290	Liver	0	FFMQ	HADS distress	-0.69**	-0.69
70	Poulin et al. (2016)	76	Mixed	0	FFMQ	PHQ9 dep	-0.64***	-0.64
77	Romano (2014)	76	Mixed	14	MAAS	HADS anx	-0.64**	-0.59
						HADS dep	-0.54**	
43	Kersting (2012)	74	Mixed	9.5	MAAS	CES dep	-0.54***	-0.54
38	Hsieh et al. (2021)	116	Lung	56	FFMQ	BDI dep	-0.54***	-0.54
75	Randell (2017)	75	Mixed	0	MAAS	HADS anx	-0.53**	-0.45
						HADS dep	-0.37**	
53	Liu et al. (2021a)	230	Breast	0	MAAS	GAD7	-0.51**	-0.51
						PHQ9	-0.53**	
						PTSS	-0.50**	
20	Chen et al. (2021)	90	Colorectal	0	FFMQ	BDI dep	-0.49***	-0.49

99	van der Donk et al. (2020)	245	Mixed	0	FFMQ	CES dep	-0.47**	-0.44
						PANAS	-0.40**	
103	Walsh et al. (2018)	241	Prostate	0	Freiburg	HADS anx	-0.46**	-0.48
						HADS dep	-0.50**	
92	Taylor-Ford (2014)	102	Colorectal	100	MAAS	HADS anx	-0.45**	-0.43
						CES dep	-0.33**	
						EORTC	-0.49**	
23	Corman et al. (2021)	187	Blood	NA	FFMQ	HADS anx	-0.45***	-0.38
						HADS dep	-0.31***	
91	Tamagawa et al. (2013)	227	Breast	1.4	MAAS	POMS distress	-0.49**	-0.49
82	Schellekens et al. (2017)	88	Lung	24	FFMQ24	HADS distress	-0.49**	-0.49
14	Brown and Ryan (2003a)	41	Mixed	0	MAAS	POMS distress	-0.43**	-0.43
45	Kuhlman et al. (2017)	271	Breast	0	MAAS	CES dep	-0.43**	-0.43
40	Ikeuchi et al. (2020)	249	Breast	0	MAAS	HADS anx	-0.41**	-0.42
						HADS dep	-0.43**	
21	Cho et al. (2021)	78	Lung	100	MAAS	CES dep	-0.40***	-0.39
						IES	-0.38**	
4	Al-Ghabeesh et al. (2019)	234	Breast	5.1	MAAS	HADS anx	-0.29**	-0.27
						HADS dep	-0.25**	
31	Garland et al. (2017)	97	Mixed	49	FFMQ	DASS21 distress	-0.40***	-0.40
66	Omid et al. (2017)	109	Mixed	NA	FFMQ	DASS42 distress	-0.39**	-0.39
104	Xu et al. (2017)	176	Gastro	41.5	MAAS	GHQ distress	-0.26**	-0.26
108	Zhong et al. (2020)	292	Gastro	29	MAAS	GHQ distress	-0.19***	-0.19
9	Banner (2009)	69	Breast	0	FFMQ	TAQ anx	0.42**	0.42
						CESD short dep	0.41**	
8	Babu (2020)	164	Mixed	0.6	FFMQ	DASS anx	0.60**	0.59
						DASS dep	0.57**	
12	Black et al. (2016)	409	Colorectal	0	MAAS	DASS stress	-0.42***	-0.42
49	Lei et al. (2021)	441	Lung	74.8	FFMQ total	DT	-0.15**	-0.15
54	Liu et al. (2018)	202	Breast	0	MAAS	PTSS	-0.47**	-0.47
101	Vick (2018)	75	Breast	41	FFMQ	DT	-0.47**	-0.47
18	Carlson and Brown (2005)	122	Mixed	11	MAAS	POMS	-0.39 (no *p* value)	-0.39
Self-compassion								
33	Glover (2015)	155	Mixed	NA	SCS 26	HADS anx	-0.61**	-0.57
						HADS dep	-0.52**	

76	Raque-Bogdan, Lent and Lamphere (2019)	275	Breast	0	SCS 26	PANAS NA	-0.55**	-0.55
82	Schellekens et al. (2017)	88	Lung	24	SCS SF Dutch	HADS distress	-0.55**	-0.55
107	Zarei, Musarezaie and Ashouri (2021)	190	Gastro	NA	SCS 26	Psych MSAS distress	-0.54***	-0.54
86	Sherman et al. (2016)	75	Breast	NA	SCS SF	DASS21 anx	-0.53**	-0.54
						DASS21 dep	-0.60**	
						DASS21 stress	-0.47**	
2	Afrashteh and Masoumi (2021)	210	Breast	0	SCS 26	BAI anx	-0.53**	-0.51
						BDI dep	-0.48**	
42	Kelliher-Rabon et al. (2022)	235	Mixed	NA	SCS SF	MHP anx	-0.53**	-0.58
						MHP dep	-0.63**	
72	Przezdziecki (2017)	197	Breast	0	SCS 26	DASS21 anx	-0.52**	-0.58
						DASS21 dep	-0.58**	
						DASS21 stress	-0.63**	
						IES	-0.55**	
						PANAS NA	-0.60**	
35	Grozdziej (2015)	77	Breast	0	SCS SF	PHQ+GAD distress	-0.50***	-0.50
32	Gillanders et al. (2015)	105	Mixed	NA	SCS 26	HADS anx	-0.50**	-0.47
						HADS dep	-0.44**	
99	van der Donk et al. (2020)	245	Mixed	0	SCS 24 Dutch	CES dep	-0.47**	-0.42
						PANAS NA	-0.37**	
94	Todorov, Sherman and Kilby (2019)	195	Breast	4.1	SCS SF	DASS21 anx	-0.43***	-0.56
						DASS21 dep	-0.56***	
						DASS21 stress	-0.66***	
73	Przezdziecki and Sherman (2016)	148	Breast	0	SCS 26	DASS21 anx	-0.41**	-0.52
						DASS21 dep	-0.61**	
						DASS21 stress	-0.53**	
110	Zhu et al. (2019)	243	Mixed	11.8	SCS SF T1	STAI6 T1 anx	-0.40**	-0.39
						PHQ9 T1 dep	-0.38**	
50	Lennon, Hevey and Kinsella (2018)	92	Prostate	NA	SCS 26	DASS21 distress	-0.40**	-0.40
6	Arambasic, Sherman and Elder (2019)	92	Breast	7.3	SCS 26	DASS21 stress	-0.39*	-0.39
74	Przezdziecki et al. (2013)	279	Breast	NA	SCS 26	DASS21 anx	-0.39**	-0.49
						DASS21 dep	-0.57**	

						DASS21 stress	-0.51**	
109	Zhu et al. (2020)	301	Mixed	31.6	SCS SF	STAI anx	-0.39**	-0.38
						PHQ dep	-0.37**	
10	Baziliansky and Cohen (2021)	153		0	SCS SF	BSI distress	-0.29***	-0.29
51	Levkovich (2021)	170	Breast	0	SCS SF	BSI anx	-0.20*	-0.19
						BSI dep	-0.17*	
						BSI distress (inc somatisation)	-0.20*	

NA: Not Available; AAQ: Acceptance and Action Questionnaire; HADS: Hospital Anxiety and Depression Scale; PROMIS: Patient Reported Outcomes Measurement Information System; DASS: Distress, Anxiety and Stress Scales; SAS: Self-rating Anxiety Scale; AFQ: Avoidance and Fusion Questionnaire; BEAQ: Brief Experiential Avoidance Questionnaire; SDS: Self-rating Depression Scale; COPE: Coping Orientation to Problems Experienced Inventory; bCOPE: Brief COPE; POMS: Profile of Mood States; PHQ: Patient Health Questionnaire; BDI: Beck Depression Inventory; CES-D: Centre for Epidemiologic Studies Depression; CFQ: Cognitive Fusion Questionnaire; CFQ CI; Cognitive Fusion Questionnaire Chronic Illness; MAAS: Mindful Attention Awareness Scale; FFMQ: Five Facets of Mindfulness Scale; TAQ: Trimodal Anxiety Questionnaire; Freiburg: Freiburg Mindfulness Inventory; GAD: Generalised Anxiety Disorder Scale; GHQ: General Health Questionnaire; SCS: Self-compassion Scale (SF – Short Form); STAI: State Trait Anxiety Scale; BAI: Beck Anxiety Inventory; BSI: Brief Symptom Inventory; MHP: Multidimensional Health Profile; MSAS: Memorial Symptom Assessment Scale

Table S6.

Data included in narrative synthesis

Study ID	Author (year)	*n*	Sample	Process Measure	Outcome Measure	Correlation	Other results i.e., regression
Experiential avoidance							
75	Randell (2017)	75	Mixed	AAQII7	HADS	0.63**	
				BEAQ15	distress HADS	0.50**	Experiential avoidance was not significantly associated with anxiety whilst controlling for fear of recurrence, valued living, mindfulness and cognitive fusion β = 0.01 ns

							Experiential avoidance was not significantly associated with depression whilst controlling for fear of recurrence, valued living mindfulness and cognitive fusion β = 0.12 ns
34	González-Fernández et al. (2017)	122	Breast	AAQII7	HADS	-	Experiential avoidance was significantly associated with anxiety whilst controlling for insomnia β = 0.71***
							Experiential avoidance was significantly associated with depression whilst controlling for fatigue, social impairment and environmental reward β = 0.33***
					BSI/GSI		Experiential avoidance was significantly associated with distress whilst controlling for fatigue and insomnia β = 0.53***
11	Berrocal Montiel et al. (2016)	64	Breast	AAQII7	HADS	-	Experiential avoidance at T1 significantly predicted anxiety at T2 (6m), whilst controlling for T1 anxiety and months since diagnosis β = 0.64***
							Experiential avoidance at T1 significantly predicted depression at T2 (6m), whilst controlling for T1 depression and living with partner β = 0.37*
					PANAS		Experiential avoidance significantly predicted an increase in negative affect at T2 (6m) whilst controlling for T1 negative affect β = 0.46***
77	Romano (2014)	76	Mixed	AAQII10	HADS	-	Direct effect of experiential avoidance on anxiety in mediation analysis β = 0.60***
							Direct effect of experiential avoidance on depression in mediation analysis β = 0.50***
48	Larson et al. (2019)	111	Blood	BEAQ15	IDAS somatic anxiety	-	Experiential avoidance did not significantly predict anxiety whilst controlling for transplant graft type, age, sex and time since diagnosis β = 0.03 ns

							Experiential avoidance was not significantly associated with depression whilst controlling for transplant graft type, age, sex and time since diagnosis β = 0.11 ns
13	Brabbins (2016)	72	Mixed	AAQII7 greater acceptance	HADS anx	-0.80**	Reverse scored AAQ significantly predicted lower anxiety at T2, whilst controlling for illness perceptions, disengagement and self-blame β = -0.57*
					HADS dep	-0.60**	Reverse scored AAQ did not significantly predict reduced depression at T2 whilst controlling for illness perceptions and distraction β = -0.19 ns
					FACT-B EWB	0.73**	Reverse scored AAQ was not significantly associated with greater EWB at T2 controlling for illness perceptions β = 0.15 ns
44	Kuba et al. (2019)	922	Blood	AAQII7 greater acceptance	GAD7	-0.68**	-
					PHQ9	-0.65**	
39	Hulbert-Williams and Storey (2016)	129	Mixed	AAQII7 greater acceptance	HADS	-0.60**	Reverse scored AAQ was significantly associated with lower anxiety whilst controlling for age, time since diagnosis and treatment intent β = -0.31***
						-0.47**	Reverse scored AAQ was significantly associated with a reduction in depression whilst controlling for age, time since diagnosis and treatment intent β = -0.27***
					PANAS	-0.64***	Reverse scored AAQ was associated with reduction in negative affect whilst controlling for age, time since diagnosis and treatment intent β = -0.58***
23	Corman et al. (2021)	187	Blood	AFQ	HADS		Experiential avoidance was significantly associated with an increase in anxiety β = 0.29*** Experiential avoidance was not significantly associated with increased depression β = 0.12 ns

							Both controlling for optimism and mindfulness
				AAQII10 greater acceptance		-0.58***	Reverse scored AAQ was significantly associated with lower anxiety β = -0.21*
						-0.44***	Reverse scored AAQ was not significantly associated with lower depression β = -0.17 ns
							Both controlling for optimism and mindfulness
98	Trindade et al. (2020)	40	Breast	AAQII 7	DASS21	-	Experiential avoidance at T1 significantly predicted depression at T2, whilst controlling for T1 depression, stress and experiential avoidance at T2 β = 0.45* Experiential avoidance at T1 significantly predicted stress at T2, whilst controlling for T1 depression, stress and experiential avoidance at T2 β = 0.37*
24	Corman et al. (2022)	187	Blood	AFQ	PTSS T2	0.45*** Control for T1 anx/dep: 0.25* -0.29**	Experiential avoidance was not significantly associated with a greater risk of developing PTSD symptoms at 5 months OR = 1.67 *p* = 0.32
				AAQII10 greater acceptance		Control for T1 anx/dep: -0.02ns	
10	Baziliansky and Cohen (2021)	153	Colorectal	AAQ9	BSI	Distress at T2: 0.03 ns	Experiential avoidance was not significantly associated with distress at T1 β = 0.16 ns Experiential avoidance was not significantly associated with distress at T2 (6m) β = 0.11 ns Whilst controlling for education, marital status, chemotherapy, suppression, cognitive reappraisal, self-compassion and personal resilience
5	Aldaz et al. (2019)	31	Mixed	Experiential avoidance related to	DT	-	Daily experiential avoidance significantly predicted distress B = 1.28***

				illness uncertainty (daily measure)			
22	Ciarrochi, Fisher and Lane (2011)	107	Mixed	AAQII10	DT	-	Males: avoidance was significantly associated with higher distress β = 0.58** Females: avoidance was significantly associated with higher distress β = 0.64**
					FACT-B EWB		Males: avoidance was significantly associated with lower emotional wellbeing whilst controlling for success at health value β = -0.69** Females: avoidance was significantly associated with lower emotional wellbeing whilst controlling for success at romantic relationships β = -0.73**
Acceptance							
105	Xu et al. (2019)	156	Mixed	CPAQ pain	HADSanx HADSdep HADS distress	-0.52* -0.61* -0.63*	-
25	Costanzo et al. (2006)	64	Gynae	COPE	POMSanx POMSdep FACT EWB	-0.19 ns -0.16 ns Both control for treatment intensity 0.12 ns control for treatment intensity	-
85	Shapiro et al. (2010)	283	Mixed	bCOPE	HADSanx	-	Acceptance was significantly associated with lower anxiety, controlling for; ethnic group, recurrence, disengagement, venting, instrumental support, self-

							blame, planning, humour, cognitive functioning, insomnia, and social receptivity β = -0.80***
					HADSdep		Acceptance was significantly associated with lower depression, controlling for; behavioural disengagement, venting, self-blame, humour, religion, physical function, cognitive function, social function, appetite loss, benefit finding and hope β = -0.33*
					QLQ EWB		Acceptance was significantly associated with increased emotional wellbeing, controlling for; ethnic group, self-distraction, behavioural disengagement, venting, self-blame, emotional processing, emotion expression, role functioning, cognitive function, social functioning, nausea/vomiting and insomnia β = 2.28*
64	Nipp et al. (2016)	350	Mixed	COPE median	HADSanx	-	Acceptance was significantly associated with lower anxiety, controlling for; age, sex, marital status and cancer type β = -0.34*
					HADSdep		Acceptance was significantly associated with lower depression, controlling for; age, sex, marital status and cancer type β = -0.37*
93	Thune-Boyle et al. (2013)	155	Breast	COPE	HADS	-	Acceptance was significantly associated with reduced anxiety, controlling for; age, employment, feeling punished by god, optimism, denial, instrumental support, planning, self-blame, self-distraction and venting β = -0.23**
95	Trevino et al. (2012)	53	Mixed	bCOPE coping factor	McGillanx	-	There was a non-significant association for acceptance and lower anxiety controlling for depression, grief, proactive, distancing, negative expression, support seeking and respite seeking β = -0.16 ns
					McGilldep		Acceptance was not significantly associated with an increase in depression whilst controlling for anxiety, grief,

							proactive coping, distancing coping, negative expression coping, support seeking and respite seeking β = 0.17 ns
26	Deimling et al. (2006)	321	Mixed	COPE 3 items	POMSanx	-	There was a non-significant association for acceptance and lower anxiety controlling for race, gender, age, optimism, type of cancer, stage, years, treatment, health conditions scale, functional difficulty, coping planning, venting, denial and seeking social support B = -0.01 ns
					POMSdep		There was a non-significant association for acceptance and lower depression controlling for race, gender, age, optimism, type of cancer, stage, years, treatment, health conditions scale, functional difficulties, coping (planning, venting, denial, seeking social support) β = -0.05 ns
81	Saniah and Zainal (2010)	141	Breast	bCOPE	HADS	-	There was no difference in acceptance levels between anxious cases and non-anxious cases - Mann Whitney U Test: 0.59, *p* = 0.55
59	Manne et al. (2018)	174	Gynae	Emotional acceptance	BDI	-0.39*	-
100	van Laarhoven et al. (2011)	92	Mixed curative	COPE dutch	BDI	-0.36*	Acceptance was significantly associated with lower depression whilst controlling for age β = -0.34**
			Mixed palliative			-0.48*	Acceptance was significantly associated with lower depression whilst controlling for giving up β = -0.36**
			Mixed curative		QLQ Emotional functioning	0.25*	Acceptance was significantly associated with an increase in emotional wellbeing β = 0.24*
			Mixed palliative			0.39* All controlling for age, sex, partner, education, employment	

3	Aguado Loi et al. (2013)	68	Breast	bCOPE	PHQ9	-	Acceptance was significantly associated with lower depression β = -0.32** Acceptance was significantly associated with greater depression controlling for age, depression history, challenge, positive reframing, self-blame, body image, family and peer support β = 0.24*
89	Stanton et al. (2018)	460	Breast	COPE	CES	-	Acceptance was not significantly associated with depression controlling for age, ethnicity, marital status, income, employment, SES, cancer stage, assessment interval at which treatments ended, number of comorbidities, recruitment site, treatment, and hormone therapy Intercept = -2.19***, linear slope ns
71	Priscilla et al. (2011)	105	Blood	bCOPE	Mini MDD	-	There were no significant between-group differences between those who were not depressed M = 52.4 and those who were depressed M = 54.9; z = -0.4; *p* = 0.3
19	Carver et al. (1993)	59	Breast	COPE 3 items	POMS	-0.47* (post-surgery) -0.29* (3m) -0.43** (6m) -0.27* (12m)	For all time points acceptance was associated with a decrease in distress whilst controlling for various factors (coping, chemotherapy, preoperative distress) Pre-surgery: β = -0.27 sig Post-surgery: β = -0.33 sig 6m: β = -0.23 ns
69	Politi, Enright and Weihs (2007)	91	Breast	Emotional acceptance	POMS	-0.46*	Acceptance was significantly associated with lower distress controlling for age β = -0.49***
104	Xu et al. (2017)	176	gastro	Self-acceptance	GHQ distress	-0.39*	-
79	Roussi et al. (2007)	72	Breast	Cope short	POMS post-surgery	-0.38***	-
88	Stanton, Danoff-Burg and Huggins (2002)	70	Breast	COPE	POMS	0.03 (3m) -0.30* (12m) Both controlling for age and baseline	-

29	Fox (2002)	75	Mixed	COPE 3	POMS	-	Acceptance was significantly associated with lower distress, controlling for; religious identity, problem focused coping, social support seeking, denial, emotional approach coping, age, children, weeks since treatment initiated, perceived chance of cure and treatment side effects β = -0.25**
					IES	-	Acceptance was significantly associated with lower distress, controlling for; religious identity, problem focused coping, social support seeking, denial, emotional approach coping β = -0.28*
61	Millmann (2019)	11	Ovarian	CPAQ pain	POMS	-0.34 ns	-
7	Asuzu and Elumelu (2013)	237	Mixed	bCOPE	FACT EWB	0.07 ns	-
102	Vickberg (2000)	169	Breast	bCOPE	MHI	0.07 ns	-
16	Brunault et al. (2016)	120	Breast	bCOPE	QLQ Emotional Functioning	-	Acceptance was significantly associated with increase in emotional quality of life, controlling for; age, tumour stage, pain severity, existence of major depressive disorder, personality disorder, use of hormone therapy and self-blame B = 3.93***
28	Elumelu, Asuzu and Akin-Odanye (2015)	110	Breast	bCOPE	FACT EWB	-	There was no significant difference between those who reported 'not at all or a little bit' of acceptance coping and those who reported 'somewhat to very much' MD = -0.39 (95% CI -2.77, -1.99) *p* = 0.75
Cognitive fusion							
32	Gillanders et al. (2015)	105	Mixed	CFQ7	HADS	-	Cognitive fusion was significantly associated with anxiety whilst controlling for cognitive distress, cognitive avoidance, emotional distress, avoidance coping and self-compassion β = 0.54***

							Cognitive fusion was not significantly associated with depression whilst controlling for cognitive distress, cognitive avoidance, emotional distress, avoidance coping and self-compassion β = 0.05 ns
75	Randell (2017)	75	Mixed	CFQ7	HADS distress	0.59**	
					HADS		Cognitive fusion was significantly associated with anxiety whilst controlling for fear of recurrence, valued living, mindfulness and experiential avoidance (BEAQ) β = 0.41*** Cognitive fusion was not significantly associated with depression whilst controlling for fear of recurrence, valued living, mindfulness and experiential avoidance (BEAQ) β = 0.11 ns
Present moment awareness (PMA)							
46	Lam et al. (2018)	212	Mixed	FFMQ	HADSanx	-	The low PMA profile was significantly associated with higher anxiety compared to those who demonstrated the high PMA profile whilst controlling for sociodemographic and medical variables β = 3.28**
					HADSdep		The low PMA profile was significantly associated with higher depression compared to those who demonstrated the high PMA profile whilst controlling for sociodemographic and medical variables β = 4.06***
77	Romano (2014)	76	Mixed	MAAS	HADSanx	-	PMA was associated with lower anxiety β = -0.27** direct effect in mediation model
					HADSdep		PMA was significantly associated with reduced dep β = -0.24* direct effect in mediation model
4	Al-Ghabeesh et al. (2019)	234	Breast	MAAS	HADSanx	-	PMA was significantly associated with lower anxiety controlling for income and social support β = -0.24*
					HADSdep		PMA was significantly associated with reduced depression controlling for social support

							β = -0.20*
75	Randell (2017)	75	Mixed	MAAS	HADS distress	-0.50**	-
					HADSanx		PMA was not significantly associated with decreased anxiety controlling for experiential avoidance, psychological flexibility, cognitive fusion and valued living β = -0.18 ns
					HADSdep		PMA was not significantly associated with decreased depression controlling for experiential avoidance, psychological flexibility, cognitive fusion and valued living β = -0.06 ns
23	Corman et al. (2021)	187	Blood	FFMQ	HADSanx	-	PMA was not significantly associated with anxiety controlling for experiential avoidance, optimism and acceptance β = -0.12 *p*=0.09
					HADSdep		PMA was not significantly associated with lower depression whilst controlling for experiential avoidance, optimism and acceptance β = -0.06 *p* = 0.46
9	Banner (2009)	69	Breast	FFMQ	TAQanx	-	PMA was significantly associated with increased anxiety whilst controlling for spirituality and the spirituality x PMA interaction β = 0.4**
					CES-D short dep		PMA was significantly associated with an increase in depression controlling for spirituality and the spirituality x PMA interaction β = 0.03**
21	Cho et al. (2021)	78	Lung	MAAS	CES-Dep	-	PMA was significantly associated with lower depressive symptoms controlling for faith (mediation) B = -3.69***
					IES		PMA was significantly associated with lower distress controlling for meaning/peace B = -4.09* And controlling for faith B = -7.03***

43	Kersting (2012)	74	Mixed	MAAS	CES-Dep	-	PMA was significantly associated with lower depression whilst controlling for gender and time since diagnosis B = -0.57** However PMA did not significantly predict depression at 3 months controlling for depression T1, gender and time since diagnosis B = -0.23 ns
20	Chen et al. (2021)	90	Colorectal	FFMQ total	BDI	-	PMA was significantly associated with lower depression whilst controlling for age, history of psychological illness, cancer threat appraisal, symptoms and functions β = -0.14**
38	Hsieh et al. (2021)	116	Lung	FFMQ total	BDI-II	-	PMA was significantly associated with lower depression controlling for previous depressive illness, presence of meaning, search for meaning, global health status, quality of life (functioning, symptom distress), lung cancer specific symptom distress B = -0.08*
108	Zhong et al. (2020)	292	GI	MAAS	GHQ total	-0.20***	PMA was significantly associated with lower distress controlling for perceived stress, clinical stage, age and gender β = -0.11*
49	Lei et al. (2021)	441	Lung	FFMQ total	DT	-	PMA had a direct negative effect on psychological distress (mediation) β = -0.11**
24	Corman et al. (2022)	187	Blood	FFMQ T1	PTSS T2	-0.16 ns (controlling for anxiety and dep 0.04 ns)	-
55	Liu et al. (2021b)	290	Liver	FFMQ total	HADS	-	PMA had a direct negative effect on distress controlling for age, income, child class (mediation) β = -0.69***
68	Ploumen (2017)	108	Mixed	TFMQ	IES	-	PMA was significantly associated with lower distress controlling for gender, age, treatment phase and type of cancer B = -0.58***
					DT		PMA was significantly associated with distress controlling for gender, age, treatment phase and type of cancer

							B = -0.38***
91	Tamagawa et al. (2013)	272	Breast	MAAS	POMS	-	PMA was significantly associated with lower distress controlling for age, repression and suppression traits β = -0.40**
70	Poulin et al. (2016)	76	Mixed	FFMQ	SF12	0.64***	-
30	Garcia et al. (2021)	183	Mixed	MAAS	FACT EWB	0.34***	-
Self-as-context							
8	Babu (2020)	164	Mixed	SACS	DASS21anx DASS21dep	-0.10 ns -0.22**	-
Committed action							
97	Trindade et al. (2018b)	82	Breast	CAQ8	DASS21anx DASS21dep DASS21 stress	-0.48*** -0.53*** -0.46***	-
8	Babu (2020)	164	Mixed	CAQ8	DASS21anx DASS21dep	0.36** 0.32**	-
Values							
52	Lewson et al. (2021)	203	Mixed	VQ progress VQ obstruction VQ progress VQ obstruction	PROMIS anx PROMIS dep 	-0.36** 0.63** -0.42** 0.61**	-
63	Mosher et al. (2017)	80	Breast	VQ progress VQ obstruction VQ progress VQ obstruction	PROMIS anx PROMIS dep 	-0.36** 0.61** -0.41** 0.56**	-
62	Mosher et al. (2021)	201	Mixed	VQ progress VQ obstruction	PROMIS anx 	-0.34** 0.61**	-

				VQ progress	PROMIS dep	-0.39**	
				VQ obstruction		0.66**	
8	Babu (2020)	164	Mixed	Values importance	DASS21 anx	-0.14ns	-
					DASS21 dep	-0.21**	
47	Lampic et al. (2002)	32	Breast	Life Value	HADS anx	-	At 3 months, anxiety cases (C; M = -134, SD = 43) reported higher attainment-importance discrepancy scores for harmony values than for non-anxious cases (NC; M = -44, SD = 62); *t* = 4.00** At 1 year, anxiety cases reported significantly higher attainment-importance discrepancy scores for harmony values and positive relation values Positive relations: NC M = -24, SD = 75; C = -135, SD = 149; *t* = 2.79* Harmony: NC M = -34, SD = 43; C = -127, SD = 142; *t* = 2.75*
					HADS dep		At 3 months depression cases reported higher attainment-importance discrepancy scores for all life values except comfort Positive relations: NC M = -49, SD = 91; C M = -218, SD = 202; *t* = 3.13* Involvement: NC M = -47, SD = 87; C M = -215, SD = 175; *t* = 3.40* Responsibility: NC M = 20, SD = 53; C M = -31, SD = 46; *t* = 2.05* Harmony: NC M = -53, SD = 62; C M = -158, SD = 38; *t* = 3.63*** Health: NC M = -131, SD = 150; C M = -340, SD = 152; *t* = 2.87** Spirituality: NC M = 1, SD = 45; C M = -107, SD = 136; *t* = 3.48** At 1 year, depression cases reported higher attainment-importance discrepancy scores for all values except comfort and responsibility

							Positive relations: NC M = -33, SD = 86; C M = -240; SD = 129; *t* = 4.23*** Involvement: NC M = -48, SD = 109; C M = -225, SD = 189; *t* = 2.77** Harmony: NC M = -41, SD = 60; C M = -225, SD = 145; *t* = 4.66*** Health: NC M = -119, SD = 142; C M = -288, SD = 193; *t* = 2.13* Spirituality: NC M = -9, SD = 59; C M = -125, SD = 185; *t* = 2.63*
22	Ciarrochi, Fisher and Lane (2011)	107	Mixed	PVQ Value success:	DT		-
				Family		-0.34*	
				Leisure		-0.43*	
				Health		-0.26**	
				Spirituality		-0.16 ns	
				Greater commitment to:			
				Family values		-0.31**	
				PVQ Value success:	FACT EWB		Males: success in health was associated with greater emotional wellbeing whilst controlling for avoidance β = 0.31**
				Family		0.50*	
				Leisure		0.45*	Females: success in romantic relationships was associated with lower emotional wellbeing whilst controlling for avoidance β = -0.26**
				Health		0.34*	
				Spirituality		0.37**	
				Greater commitment to:			
				Family values		-0.29**	
Committed action and values							

75	Randell (2017)	75	Mixed	ELS	HADS anx HADS dep HADS distress	-0.50** -0.50** -0.56**	Engaged living was not significantly associated with anxiety β = -0.16 ns Engaged living was significantly associated with lower depression β = -0.33*
Self-compassion							
110	Zhu et al. (2019)	243	Mixed	SCS SF and subscales	STAI6	Positive self-compassion -0.21* Negative self-compassion -0.34* (Higher scores, lower negative self-compassion)	Overall self-compassion significantly predicted anxiety at T2 whilst controlling for T1 symptoms and education and gender but was non-significant for T3 controlling for education β = T2 -0.23**, T3 -0.16 ns Positive self-compassion significantly predicted anxiety at T2 whilst controlling for T1 symptoms, negative self-compassion, education and gender β = -0.21** Negative self-compassion did not significantly predict anxiety at T2 or T3 β = T2 -0.12, T3 -0.08 Positive self-compassion significantly predicted anxiety at T3 whilst controlling for negative self-compassion and T1 symptoms β = -0.18*
					PHQ9	Positive self-compassion -0.12 ns Negative self-compassion -0.40** (higher scores, lower negative self-compassion)	Self-compassion did not significantly predict lower depression at T2 whilst controlling for T1 symptoms β =-0.13 ns Positive self-compassion did not significantly predict depression at T2 whilst controlling for education and T1 symptoms and negative self-compassion β = -0.09 ns Positive self-compassion significantly predicted depression at T3 whilst controlling for gender, T1 symptoms and negative self-compassion β =-0.17*

							Negative self-compassion did not significantly predict depression at T2 or T3 whilst controlling for positive self-compassion and T1 symptoms β = T2 -0.13, T3 0.07
109	Zhu et al. (2020)	301	Mixed	SCS SF and subscales	STAI6	Positive self-compassion -0.14* Negative self-compassion -0.41* (Higher scores, lower negative self-compassion)	Self-compassion was significantly associated with lower anxiety whilst controlling for education and cancer recurrence -0.17**
					PHQ9	Positive self-compassion -0.06 ns Negative self-compassion -0.44* (higher scores, lower negative self-compassion)	Self-compassion total was significantly associated with lower depression, controlling for; education and cancer recurrence -0.19**
37	Ho, Fong and Wan (2022)	127	Colorectal	SCS	HADSanx	T1: Positive self-compassion 0.13 ns Negative self-compassion 0.61*, T2: Positive self-compassion 0.02 ns, Negative self-compassion 0.45*	-
					HADSdep	T1: Positive self-compassion 0.05 ns, Negative self-compassion 0.52*	

						T2: Positive self-compassion -0.11 ns Negative self-compassion 0.42*	
					PANAS	T1: Positive self-compassion 0.07 ns Negative self-compassion 0.65* T2: Positive self-compassion -0.03 ns Negative self-compassion 0.48*	
67	Pinto-Gouveia et al. (2014)	63	Mixed	SCS and subscales	DASS42anx	Positive self-compassion -0.10 ns	-
					DASS42dep	Positive self-compassion -0.59*	Positive self-compassion was significantly associated with lower depression β =-0.54***
					DASS42 stress	Positive self-compassion -0.58* 0.51 **	Positive self-compassion was significantly associated with lower stress β = -0.53 ***
					WHO-QoL-BREF psych QoL		Self-compassion significantly increased emotional wellbeing β = 0.40**
33	Glover (2015)	155 (those who felt personally responsible for cancer)	Mixed	SCS	HADSanx	-	Self-compassion was significantly associated with lower anxiety whilst controlling for gender, age, site, time since diagnosis, recurrence, recruitment source and personal responsibility B = -3.89***
					HADSdep		Self-compassion was significantly associated with lower depression whilst controlling for gender, age, site, time since diagnosis, recurrence, recruitment source and personal responsibility

							B = -3.02***
94	Todorov, Sherman and Kilby (2019)	195	Breast	SCS SF	DASS21anx	-	Self-compassion was significantly associated with lower anxiety whilst controlling for marriage status, country of birth, chemotherapy status, hormone therapy status, targeted treatment status, reconstruction status, education, employment, age and time since diagnosis β = -0.44**
					DASS21dep		Self-compassion was significantly associated with lower depression whilst controlling for covariates as above β = -0.59**
					DASS21 stress		Self-compassion was significantly associated with lower emotional stress whilst controlling for covariates as above β = -0.70**
32	Gillanders et al. (2015)	105	Mixed	SCS	HADSanx		Self-compassion was not significantly associated with lower anxiety when controlling for cognitive distress, cognitive avoidance, emotional distress, avoidance coping and cognitive fusion β = 0.01 ns
					HADSdep		Self-compassion was not significantly associated with lower depression when controlling for cognitive distress, cognitive avoidance, emotional distress, avoidance coping and cognitive fusion β = -0.17 ns
99	van der Donk et al. (2020)	245	Mixed	SCS 24 (Dutch) subscales	CES-d	Positive self-compassion -0.16* Negative self-compassion 0.42**	-
					PANAS	Positive self-compassion -0.11 ns Negative self-compassion 0.47**	

87	Siwik et al. (2021)	58	Lung	SCS SF	CES-d	-	Self-compassion was significantly associated with lower depression β = -0.64***
51	Levkovich (2021)	170	Breast	SCS SF	BSI	-	Self-compassion was significantly associated with lower distress whilst controlling for employment status, time since chemo, subjective stress and emotional control β = -0.12*
10	Baziliansky and Cohen (2021)	153	Colorectal	SCS SF	BSI	-	Self-compassion significantly predicted an increase in distress at T2 controlling for education, marital status, chemo, suppression, cognitive reappraisal, experiential avoidance and personal resilience β = 0.32 **
76	Raque-Bogdan, Lent and Lamphere (2019)	275	Breast	SCS 26	FACT EWB	0.56**	-
30	Garcia et al. (2021)	183	Mixed	SCS 26 item	Emotional wellbeing	0.36*	-
Psychological flexibility							
60	McAteer and Gillanders (2019)	286	Prostate	CompACT	DASS21	-0.69**	Psychological flexibility was significantly associated with reduced distress controlling for age, self-esteem and stoicism β = -0.41***
84	Sevier-Guy et al. (2021)	144	Prostate	CompACT	DASS21	-0.67**	Psychological flexibility was significantly associated with lower distress controlling for fear of recurrence β = -0.56***

Notes: BEAQ: Brief Experiential Avoidance Questionnaire; HADS: Hospital Anxiety and Depression Scale; AAQ: Acceptance and Action Questionnaire; IDAS: Inventory of Depression and Anxiety Symptoms; GAD: Generalised Anxiety Disorder Scale; AFQ: Avoidance and Fusion Questionnaire; PHQ: Patient Health Questionnaire; DASS: Distress, Anxiety and Stress Scales; BSI: Brief Symptom Inventory; DT: Distress Thermometer; PTSS: Post Traumatic Symptoms Scale; PIPS: Psychological Inflexibility in Pain Scale; POMS: Profile of Mood States; PANAS: Positive and Negative Affect Schedule; FACT-B EWB: Functional Assessment of Cancer Therapy Emotional Wellbeing subscale; CPAQ: Chronic Pain Acceptance Questionnaire; COPE: Coping Orientation to Problems Experienced Inventory; bCOPE: Brief COPE; McGill: McGill Quality of Life Questionnaire; BDI: Beck Depression Inventory; CES-D: Centre for Epidemiologic Studies Depression; Mini MDD: Mini International Neuropsychiatric Interview for Major Depressive Disorder; GHQ: General Health Questionnaire; IES: Impact of Events Scale; MHI: Mental Health Inventory; CFQ: Cognitive Fusion Questionnaire; FFMQ: Five Facets of Mindfulness Scale; MAAS: Mindful Attention Awareness Scale; TAQ: Trimodal Anxiety Questionnaire; EORTC QLQ: European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire; SF12: Short Form Health Survey; SACS: Self-as-context Scale; CAQ: Committed Action Questionnaire; VQ: Valuing Questionnaire; PROMIS: Patient Reported Outcomes Measurement Information System; PVQ: Personal Values Questionnaire; ELS: Engaged Living Scale; SCS: Self-compassion Scale (SF – Short Form); STAI: State Trait Anxiety Scale; WHO QoL: World Health Organisation Quality of Life Scale; CompACT: Comprehensive Assessment of Acceptance and Commitment Therapy processes.

S7. Narrative synthesis of additional data for meta-analysed processes

Experiential avoidance

Further data supported meta-analysis results, with greater experiential avoidance significantly associated with greater distress in cross-sectional regression analysis (22,23,34,39,77) and longitudinal regression analysis (5,11,13,98) whilst controlling for covariates. However, some studies found non-significant findings in cross-sectional regression analysis for experiential avoidance and depression (23,75) and distress (10). Furthermore, non-significant associations were found in longitudinal data for experiential avoidance and anxiety (48), depression (13,48) and distress (10,24). Experiential avoidance had a significant negative association with emotional wellbeing (13,22) although in this small sample it did not significantly predict emotional wellbeing at 6 months (13).

Acceptance

Data support the meta-analysis results with acceptance (pain, self and emotional) associated with lower anxiety, depression and distress in correlations (59,69,104,105). Data also supports meta-analysis results from cross-sectional regression analysis (3,29,64,69,85,93,100) and two longitudinal studies (19,88); which controlled for covariates. Data for emotional wellbeing were mixed, with three studies finding significant positive associations in cross-sectional regression analysis (16,85,100), whilst three studies found non-significant positive correlations (7,25,102). A variety of studies reported non-significant findings (25,26,61,89,95), whilst one study reported acceptance was significantly associated with an increase in depression whilst controlling for covariates (3). Three studies reported non-significant differences in between group analysis (see supplementary materials; 28,71,81).

Cognitive fusion

Studies supported the meta-analysis results with cognitive fusion associated with greater anxiety in cross-sectional regression analyses whilst controlling for covariates, but non-significant for depression (32,75).

Present moment awareness

Studies supported meta-analysis findings with present moment awareness significantly associated with lower anxiety, depression and distress in cross-sectional regression analysis whilst controlling for covariates (4,20,21,38,43,46,49,55,68,77,91,108). However, in two cross-sectional studies, present moment awareness was not significantly associated with lower anxiety or depression whilst controlling for other ACT processes (23,75) and was found to be positively associated in a small sample study (9). Longitudinal data also did not support meta-analyses, as present moment awareness was not significantly associated with lower depression or post-traumatic stress symptoms at follow ups whilst controlling for covariates (24,43). Present moment awareness was significantly positively correlated with emotional wellbeing (30,70).

Self-compassion

Twelve studies had additional data that supported the meta-analysis results with self-compassion significantly associated with lower anxiety, depression, distress, negative affect and emotional stress in cross-sectional regression analysis (33,51,67,87,94,109) and longitudinal regression analysis (110) whilst controlling for covariates. Three studies found significant positive associations with emotional wellbeing across correlations (30,67,76) and cross-sectional regression analysis (67). However, there were a few non-significant findings

for anxiety and depression in cross-sectional regression analysis (32), and in regression analysis at start (T2) and end (T3) of treatment (110), both whilst controlling for covariates. One study found self-compassion predicted an increase in distress at 6 months (10).

Table S8. *Risk of bias assessment*

Study ID	Study design	i	ii	iii	iv (L only)	v	vi	vii	viii	ix	x	xi	xii	Overall
1	CS	L	U	U	n/a	L	L	U	U	M	L	n/a	L	M
2	CS	L	M	M	n/a	L	L	U	L	M	L	n/a	L	M
3	CS	L	M	U	n/a	L	L	L	H	L	M	n/a	L	M
4	CS	L	U	L	n/a	L	L	U	L	L	M	n/a	L	L
5	L (micro)	L	L	U	L	L	L	L	L	M	n/a	M	L	M
6	CS	L	M	H	n/a	L	L	L	U	M	U	n/a	L	H
7	CS	L	L	U	n/a	L	L	U	U	M	n/a	n/a	L	M
8	CS	L	L	U	n/a	L	L	L	L	L	L	n/a	L	L
9	CS	L	L	H	n/a	L	L	U	L	L	L	n/a	L	L
10	L	L	L	L	L	M	L	U	L	L	L	M	L	L
11	L	L	L	L	L	L	L	U	L	L	L	L	L	L
12	CS	L	L	U	n/a	L	L	H	U	L	n/a	n/a	L	L
13	L	L	L	U	L	L	L	L	L	L	n/a	L	L	L
14	CS	L	L	U	n/a	L	L	U	U	L	n/a	n/a	L	L
15	CS	L	U	U	n/a	L	L	U	M	H	n/a	n/a	L	M
16	CS	L	L	M	n/a	L	L	L	L	L	L	n/a	L	L
17	L	L	L	H	L	L	L	U	H	L	L	L	L	H
18	CS	L	M	L	n/a	L	L	L	U	L	n/a	n/a	L	L
19	L	L	U	L	U	L	L	U	U	L	L	L	L	L
20	CS	L	U	L	n/a	L	L	U	L	L	U	n/a	L	L
21	CS	L	L	M	n/a	L	L	L	U	M	L	n/a	L	L
22	CS	L	U	L	n/a	L	L	L	L	L	L	n/a	L	L
23	CS	L	L	U	n/a	L	L	H	L	L	L	n/a	L	L
24	L	L	L	U	M	L	L	U	L	M	L	L	L	L
25	CS	L	U	U	n/a	L	L	U	L	M	L	n/a	L	L
26	CS	L	L	H	n/a	L	L	U	L	L	L	n/a	L	L
27	CS	L	L	U	n/a	L	L	U	U	M	n/a	n/a	L	L
28	CS	L	U	U	n/a	L	L	U	H	H	n/a	n/a	L	H
29	CS	L	L	H	n/a	L	L	U	L	L	L	n/a	L	L
30	CS	L	L	L	n/a	L	L	U	L	L	L	n/a	L	L
31	CS	L	U	U	n/a	L	L	L	U	M	n/a	n/a	L	L

Study ID	Study design	i	ii	iii	iv (L only)	v	vi	vii	viii	ix	x	xi	xii	Overall
32	CS	L	U	H	n/a	L	L	L	L	L	U	n/a	L	L
33	CS	L	L	H	n/a	L	L	L	L	L	M	n/a	L	L
34	CS	L	L	U	n/a	L	L	H	L	M	M	n/a	L	M
35	CS	L	L	U	n/a	L	L	H	L	L	L	n/a	L	L
36	CS	L	L	M	n/a	L	L	U	U	M	n/a	n/a	L	M
37	L	L	L	U	L	L	L	L	L	L	U	L	L	L
38	CS	L	U	U	n/a	L	L	U	L	L	U	n/a	L	L
39	CS	L	L	M	n/a	L	L	H	L	L	L	n/a	L	L
40	CS	L	L	L	n/a	L	L	L	U	M	n/a	n/a	L	L
41	CS	L	L	H	n/a	L	L	U	H	L	L	n/a	M	M
42	CS	L	L	U	n/a	L	L	U	U	M	M	n/a	L	M
43	L	L	U	U	L	L	L	L	L	L	L	L	L	L
44	CS	L	L	M	n/a	L	L	M	L	L	U	n/a	L	L
45	CS	L	L	U	n/a	L	L	U	U	M	M	n/a	L	M
46	CS	L	L	H	n/a	L	L	L	U	M	M	n/a	L	H
47	L	L	L	L	U	M	L	U	U	L	L	H	L	M
48	L	L	U	U	L	L	L	U	L	M	M	H	L	H
49	CS	L	L	L	n/a	L	L	U	L	U	n/a	n/a	L	L
50	CS	L	L	U	n/a	L	L	M	U	M	M	n/a	L	M
51	CS	L	L	L	n/a	L	L	U	U	L	L	n/a	L	L
52	CS	L	L	U	n/a	L	L	U	L	U	n/a	n/a	L	L
53	CS	L	U	U	n/a	L	L	L	U	M	n/a	n/a	L	L
54	CS	L	U	U	n/a	L	L	L	U	M	n/a	n/a	L	L
55	CS	L	M	L	n/a	L	L	U	U	L	L	n/a	L	L
56	L	L	L	U	L	L	L	U	L	L	L	L	L	L
57	CS	L	L	L	n/a	L	L	U	U	U	n/a	n/a	L	L
58	CS	L	L	U	n/a	L	L	U	M	M	n/a	n/a	L	M
59	CS	L	L	H	n/a	L	L	U	U	L	L	n/a	L	L
60	CS	L	L	U	n/a	L	L	L	L	L	L	n/a	L	L
61	CS	L	U	U	n/a	L	L	U	H	H	High	n/a	L	H
62	CS	L	L	U	n/a	L	L	L	L	L	L	n/a	L	L
63	CS	L	L	L	n/a	L	L	U	U	M	n/a	n/a	L	L
64	CS	L	L	U	n/a	L	L	U	U	M	L	n/a	L	L
65	CS	L	U	U	n/a	L	L	U	U	M	n/a	n/a	L	M

Study ID	Study design	i	ii	iii	iv (L only)	v	vi	vii	viii	ix	x	xi	xii	Overall
66	CS	L	U	L	n/a	L	L	U	L	H	n/a	n/a	L	M
67	CS	L	L	U	n/a	L	L	U	U	L	L	n/a	L	L
68	CS	L	U	L	n/a	L	L	U	L	M	L	n/a	L	L
69	CS	L	L	U	n/a	L	L	L	U	L	L	n/a	L	L
70	CS	L	L	H	n/a	L	L	M	L	M	L	n/a	L	M
71	CS	L	L	L	n/a	L	L	U	U	M	L	n/a	L	L
72	CS (RCT)	L	L	U	n/a	L	L	U	L	M	n/a	n/a	L	L
73	CS (RCT)	L	L	U	n/a	L	L	U	L	M	n/a	n/a	L	L
74	CS	L	L	H	n/a	L	L	U	U	L	M	n/a	L	M
75	CS	L	L	U	n/a	L	L	L	L	L	M	n/a	L	L
76	CS	L	L	U	n/a	L	L	L	U	M	n/a	n/a	L	L
77	CS	L	L	U	n/a	L	L	L	L	M	n/a	n/a	L	L
78	CS	L	L	M	n/a	L	L	U	U	L	L	n/a	L	L
79	L	L	U	U	L	L	L	U	U	M	L	L	L	M
80	CS	L	L	U	n/a	L	L	U	L	L	M	n/a	L	L
81	CS	L	M	U	n/a	L	L	U	L	M	n/a	n/a	L	M
82	CS	L	L	L	n/a	L	L	U	L	L	L	n/a	L	L
83	CS	L	M	U	n/a	L	L	U	U	L	L	n/a	L	L
84	CS	L	L	U	n/a	L	L	L	L	L	n/a	n/a	L	L
85	CS	H	M	L	n/a	L	L	U	L	H	n/a	n/a	L	H
86	CS	L	L	M	n/a	L	L	L	L	L	M	n/a	L	L
87	CS	L	U	U	n/a	L	L	M	L	M	n/a	n/a	L	M
88	L	L	U	L	L	L	L	U	H	L	L	L	L	L
89	L	L	U	U	M	L	L	L	L	L	L	L	L	L
90	CS	L	L	U	n/a	L	L	L	L	M	n/a	n/a	L	L
91	CS	L	L	U	n/a	L	L	U	L	L	L	n/a	L	L
92	CS	L	L	L	n/a	L	L	L	U	L	L	n/a	L	L
93	CS	L	L	M	n/a	L	L	U	L	L	L	n/a	L	L
94	CS	L	U	H	n/a	L	L	H	L	L	M	n/a	L	H
95	CS	L	L	U	n/a	L	L	U	H	L	L	n/a	L	L
96	CS	L	L	U	n/a	L	L	U	U	M	n/a	n/a	L	L
97	CS	L	L	U	n/a	L	L	U	U	L	L	n/a	L	L
98	L	L	U	U	U	L	L	U	U	L	L	L	L	U
99	CS (CC)	L	L	H	n/a	L	L	U	L	M	n/a	n/a	L	M

Study ID	Study design	i	ii	iii	iv (L only)	v	vi	vii	viii	ix	x	xi	xii	Overall
100	CS	L	L	L	n/a	L	L	L	L	L	L	n/a	L	L
101	CS	L	U	L	n/a	L	L	L	L	L	L	n/a	L	L
102	CS	L	L	H	n/a	L	L	L	U	L	M	n/a	L	M
103	CS	L	L	U	n/a	L	L	L	U	M	n/a	n/a	L	L
104	CS	L	U	L	n/a	L	L	L	U	M	n/a	n/a	L	L
105	CS	L	L	L	n/a	L	L	H	L	M	n/a	n/a	L	L
106	CS	L	L	U	n/a	L	L	M	U	L	M	n/a	L	M
107	CS	L	M	U	n/a	L	L	U	U	M	L	n/a	L	M
108	CS	L	U	U	n/a	L	L	U	L	M	M	n/a	L	M
109	CS	L	L	L	n/a	L	L	U	U	L	M	n/a	L	L
110	L	L	L	L	M	L	L	U	U	L	L	L	L	L

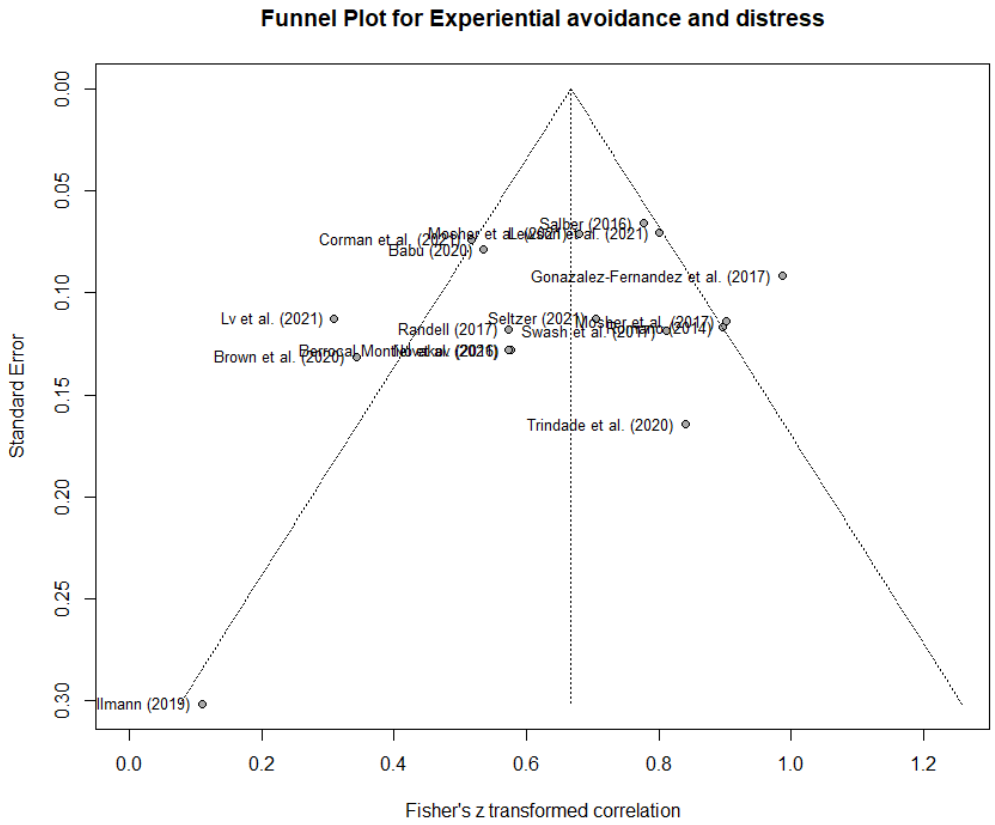
Note: CS: cross sectional; L: longitudinal; C (RCT); cross sectional/baseline analysis of an RCT; CS (CC): cohort study; i: bias in selection of reported outcomes; ii: selection bias; iii: response bias; iv: attrition bias (longitudinal only); v: valid predictor measure; vi: valid outcome measure; vii: bias due to missing data; viii: sample size a priori; ix: appropriate analysis used to control for key confounding variables; x: were confounders measured validly and reliably; xi: follow up time controlled; xii: significance levels reported; L: low risk of bias; M: moderate risk of bias; H: high risk of bias; U: unclear risk of bias; n/a: not applicable

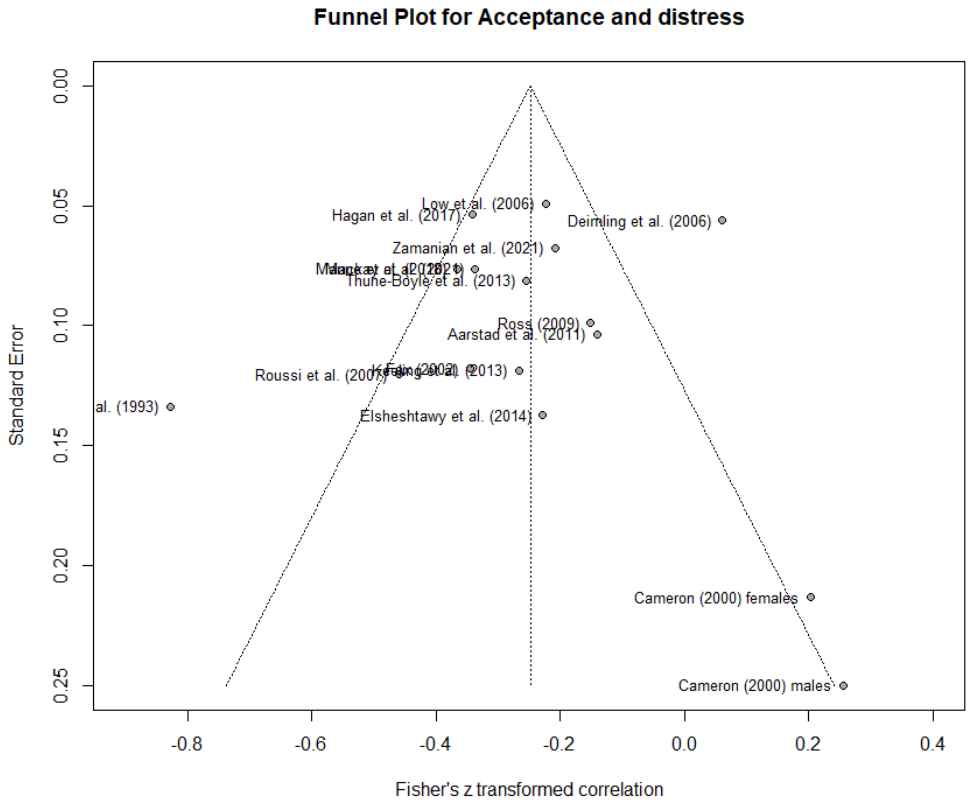
Tables S9.

GRADE quality assessment

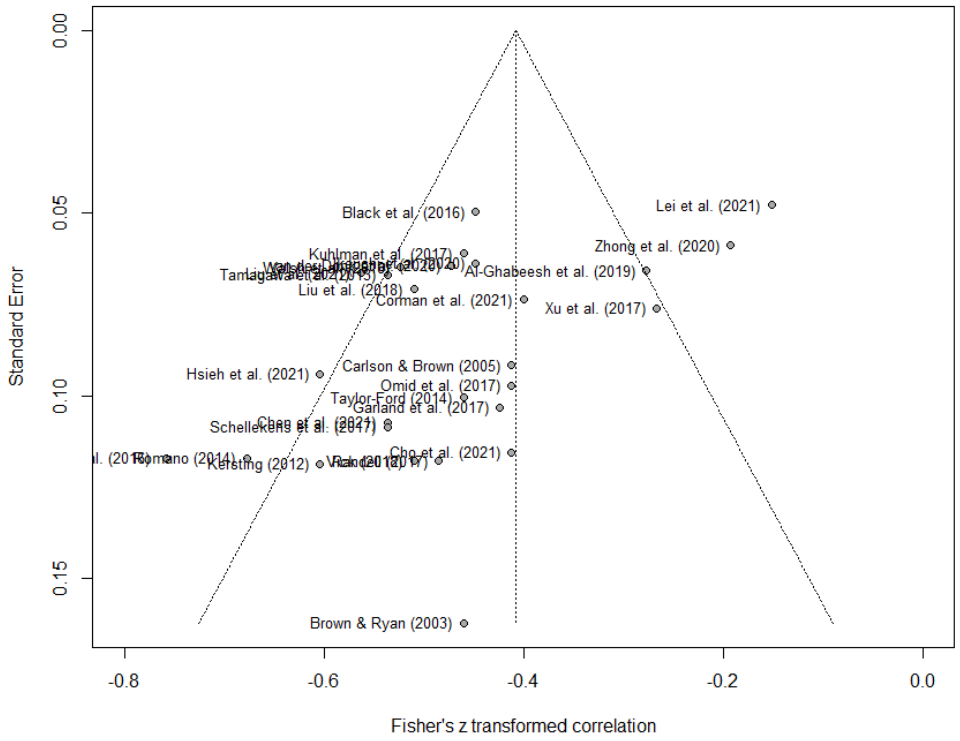
Process and distress as outcome	No. of studies	Inconsistency	Imprecision	Publication bias (see funnel plots)	Reporting bias	Quality of the evidence (GRADE)
Experiential avoidance	17	**Serious** *Heterogeneity is 72%*	**Not serious** *Narrow CI width*	**Not serious** *Relative symmetry*	**Moderate** *12 low, 3 moderate, 1 high and 1 unclear*	**Low** *Downgraded 1 for inconsistency; upgraded for large effect*
Acceptance	16	**Serious** *Heterogeneity is 79%*	**Serious** *Moderate CI width crosses small/ medium effect*	**Serious** *Substantial asymmetry*	**Moderate** *8 low, 6 moderate and 2 high*	**Very low** *Downgraded 1 for inconsistency, imprecision and publication bias*
Cognitive fusion	8	**Serious** *Heterogeneity is 71%*	**Not serious** *Narrow CI width*	**Not assessed**	**Not serious** *7 low and 1 moderate*	**Low** *Downgraded 1 for inconsistency; upgraded for large effect*
Present moment awareness	30	**Very serious** *Heterogeneity is 92.5%*	**Not serious** *Narrow CI width*	**Serious** *Substantial asymmetry*	**Not serious** *25 low and 5 moderate*	**Very low** *Downgraded 1 for inconsistency and publication bias*
Self-compassion	20	**Serious** *Heterogeneity is 65.7%*	**Not serious** *Narrow CI width*	**Moderate** *Moderate asymmetry*	**Moderate** *12 low, 6 moderate and 2 high*	**Very low** *Downgraded 1 for inconsistency*

Funnel plots to assess potential publication bias for GRADE assessment

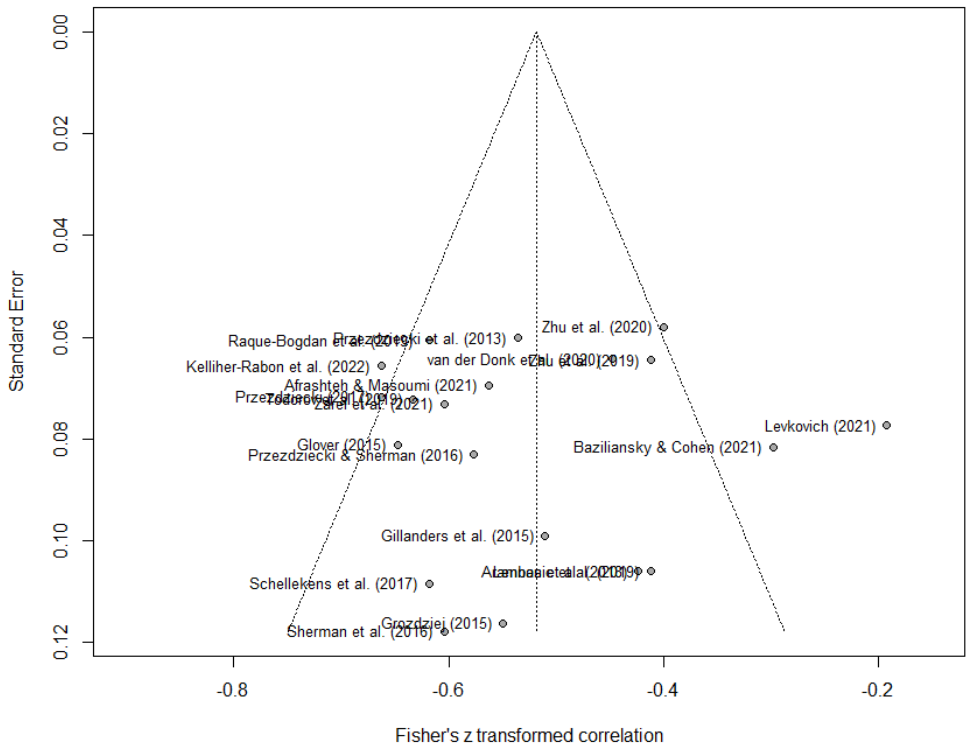




Funnel Plot for Present moment awareness and distress



Funnel Plot for Self-compassion and distress



Across study bias assessment for processes included in narrative synthesis

For narrative synthesis, the majority of findings for experiential avoidance, acceptance, present moment awareness and self-compassion were consistent with meta-analyses, with only a few inconsistent findings. Studies for present moment awareness and self-compassion were mostly low risk of bias, however for experiential avoidance and acceptance, a larger proportion of studies had moderate, high or unclear risk of bias. Data for cognitive fusion is likely to have greater heterogeneity as findings for depression were inconsistent to the meta-analysis and with limited studies. Values and psychological flexibility resulted in expected directions with a low risk of bias for all studies. Self-as-context and committed action had mixed results. All four of these processes had a very small number of studies. Fewer studies explored processes with emotional wellbeing, however most studies scored low for risk of bias, findings were generally consistent and in expected directions. Overall narrative synthesis results should be interpreted with caution.

A2) Percentage of breast cancer patients reported for each study included in meta-analyses

Study ID	Author (year)	*n*	Sample	Breast cancer stage	% of breast in sample	% on HT
Experiential avoidance						
61	Millmann (2019)	14	Gynae		0	
57	Lv et al. (2021)	82	Thyroid		0	
15	Brown et al. (2020)	61	Mixed		0	
8	Babu (2020)	164	Mixed	Mixed	NA	
65	Novakov (2021)	64	Breast	Stage I-III	100	Not reported
62	Mosher et al. (2021)	201	Mixed	Stage IV	24.88	Not provided
23	Corman et al. (2021)	187	Blood		0	
11	Berrocal Montiel et al. (2016)	64	Breast	Mixed	100	17%
83	Seltzer (2021)	82	Prostate		0	
52	Lewson et al. (2021)	203	Mixed	Stage I-II	25.12	Not reported
75	Randell (2017)	75	Mixed		69.3	46.7%
80	Salber (2016)	233	Breast	Mixed	100	Not reported
90	Swash, Bramwell and Hulbert-Williams (2017)	74	Blood		0	
63	Mosher et al. (2017)	80	Breast	Stage IV	100	85%
34	González-Fernández et al. (2017)	122	Breast	Survivors	100	70%
77	Romano (2014)	76	Mixed		66	Not reported
98	Trindade et al. (2020)	40	Breast	Stage I-III	100	Not reported
Acceptance						
19	Carver et al. (1993)	59	Breast	Stage I-III	100	36%
79	Roussi et al. (2007)	72	Breast	Not reported	100	6% HT only (others combinations)
29	Fox (2002)	75	Mixed		33.3	Not reported
41	Keeling, Bambrough and Simpson (2013)	74	Brain		0	
58	Mackay, Burdayron and Korner (2021)	174	Skin		0	
36	Hagan et al. (2017)	350	Mixed	Stage IV	0	
59	Manne et al. (2018)	174	Gynae		0	
93	Thune-Boyle et al. (2013)	155	Breast	Stage I-III (newly dx)	100	Not reported
56	Low et al. (2006)	417	Breast	Stage I-III	100	58%
27	Elsheshtawy et al. (2014)	56	Breast	Stage I-III	100	Not reported
106	Zamanian et al. (2021)	221	Breast	No brain metastases	100	Not reported
17	Cameron (2000)	25	Colorectal females		0	
17	Cameron (2000)	19	Colorectal males		0	
78	Ross (2009)	105	Mixed	Mixed	36.2	Not reported
1	Aarstad et al. (2011)	96	Head & neck		0	
26	Deimling et al. (2006)	321	Mixed		41.4	Not reported

Cognitive fusion						
57	Lv et al. (2021)	82	Thyroid		0	
15	Brown et al. (2020)	61	Mixed		0	
62	Mosher et al. (2021)	201	Mixed	Stage IV	24.88	Not provided
52	Lewson et al. (2021)	203	Mixed	Stage I-II	25.12	Not reported
75	Randell (2017)	75	Mixed		69.3	46.7%
8	Babu (2020)	164	Mixed	Mixed	NA	
32	Gillanders et al. (2015)	105	Mixed		24	19%
96	Trindade et al. (2018a)	75	Breast	Mixed	100	64%
Present moment awareness						
55	Liu et al. (2021b)	290	Liver		0	
70	Poulin et al. (2016)	76	Mixed		NA	
77	Romano (2014)	76	Mixed		66	Not reported
43	Kersting (2012)	74	Mixed		45.9	Not reported
38	Hsieh et al. (2021)	116	Lung		0	
75	Randell (2017)	75	Mixed		69.3	46.7%
53	Liu et al. (2021a)	230	Breast	Stage 0-III on chemo	100	1.7%
20	Chen et al. (2021)	90	Colorectal		0	
99	van der Donk et al. (2020)	245	Mixed		0	
103	Walsh et al. (2018)	241	Prostate		0	
92	Taylor-Ford (2014)	102	Colorectal		0	
23	Corman et al. (2021)	187	Blood		0	
91	Tamagawa et al. (2013)	227	Breast	Stage I-III	100	Not reported
82	Schellekens et al. (2017)	88	Lung		0	
14	Brown and Ryan (2003a)	41	Mixed		78	0%
45	Kuhlman et al. (2017)	271	Breast	Not reported	100	0%
40	Ikeuchi et al. (2020)	249	Breast	Stages I-III	100	84.7%
21	Cho et al. (2021)	78	Lung		0	
4	Al-Ghabeesh et al. (2019)	234	Breast	Mixed	100	3.8% HT only (others combinations)
31	Garland et al. (2017)	97	Mixed	Mixed	26	Not reported
66	Omid et al. (2017)	109	Mixed		36.7	Not reported
104	Xu et al. (2017)	176	Gastro		0	
108	Zhong et al. (2020)	292	Gastro		0	
9	Banner (2009)	69	Breast	Stage I-III	100	Not reported
8	Babu (2020)	164	Mixed	Mixed	NA	
12	Black et al. (2016)	409	Colorectal		0	
49	Lei et al. (2021)	441	Lung		0	
54	Liu et al. (2018)	202	Breast	Stage 0-III on chemo	100	2%
101	Vick (2018)	75	Breast	Mixed	100	20%
18	Carlson and Brown (2005)	122	Mixed		51.6	Not reported
Self-compassion						
33	Glover (2015)	155	Mixed		24.5	Not reported
76	Raque-Bogdan, Lent and Lamphere (2019)	275	Breast	Not reported	100	Not reported

82	Schellekens et al. (2017)	88	Lung		0	
107	Zarei, Musarezaie and Ashouri (2021)	190	Gastro		0	
86	Sherman et al. (2016)	75	Breast	Not reported	100	52.8%
2	Afrashteh and Masoumi (2021)	210	Breast	Survivors	100	Not reported
42	Kelliher-Rabon et al. (2022)	235	Mixed		NA	Not reported
72	Przezdziecki (2017)	197	Breast	Not reported	100	74%
35	Grozdziej (2015)	77	Breast	Survivors	100	Not reported
32	Gillanders et al. (2015)	105	Mixed		24	19%
99	van der Donk et al. (2020)	245	Mixed		0	Not reported
94	Todorov, Sherman and Kilby (2019)	195	Breast	Mixed	100	81.5%
73	Przezdziecki and Sherman (2016)	148	Breast	Not reported	100	67.5%
110	Zhu et al. (2019)	243	Mixed		28.4	Not reported
50	Lennon, Hevey and Kinsella (2018)	92	Prostate		0	
6	Arambasic, Sherman and Elder (2019)	92	Breast	Survivors	100	67.1%
74	Przezdziecki et al. (2013)	279	Breast	Not reported	100	60%
109	Zhu et al. (2020)	301	Mixed	Mixed	22.3	Not reported
10	Baziliansky and Cohen (2021)	153			NA	
51	Levkovich (2021)	170	Breast	Survivors early stage	100	6.5%

Appendix B: Qualitative study

B1) Study documents

B1.1) Initial ethical approval (Phase 1: Qualitative; Phase 2: Quantitative)

Research Ethics Office

Franklin Wilkins Building
5.9 Waterloo Bridge Wing
Waterloo Road
London SE1 9NH
Telephone 020 7848 4020/4070/4077
rec@kcl.ac.uk

KING'S College LONDON

Sophie Fawson

14/08/2020

Dear Sophie,

Reference Number: HR-19/20-18770
Study Title: Understanding acceptance and other psychological processes with symptoms and distress in women with breast cancer

Review Outcome: Approval with Provisos

Thank you for submitting your application for the above project. I am pleased to inform you that your application has now be approved with the proviso specified below:

1. Please note that the Committee accepts that the GAD-7 questionnaire is not a diagnostic tool. However, a high score does indicate the need for further support. Applicants are asked to complete the additional fields, generated by an affirmative response to Question 4c in Section F1, to explain their approach to dealing with disclosures. This would normally include the proposed approach to signposting.

All changes must be made before data collection commences. The Committee does not need to see evidence of these changes, however supervisors are responsible for ensuring that students implement any requested changes before data collection commences.

IMPORTANT CORONAVIRUS UPDATE: In light of the COVID-19 pandemic, the College Research Ethics Committee has temporarily suspended all primary data collection involving face to face participant interactions until further notice. **Ethical clearance for this project is granted. However, the clearance outlined in the attached letter is contingent on your adherence to the latest College measures when conducting your research.** Please do not commence data collection until you have carefully reviewed the update and made any necessary project changes:

https://internal.kcl.ac.uk/innovation/research/ethics/applications/COVID-19-Update-for-Researchers

Please ensure that you follow all relevant guidance as laid out in the King's College London Guidelines on Good Practice in Academic Research (http://www.kcl.ac.uk/college/policyzone/index.php?id=247).

For your information, ethical approval has been granted for 3 years from 14 August 2020. If you need approval beyond this point, you will need to apply for an extension at least two weeks before this. You will be required to explain the reasons for the extension. However, you will not need to submit a full re-application unless the protocol has changed. You will not be sent a reminder when it is due to lapse.

Ethical approval is required to cover the data-collection phase of the study. This will be until the date specified in this letter. However, you do not need ethical approval to cover subsequent data analysis or publication of the results.

Please ensure that you follow the guidelines for good research practice as laid out in UKRIO's Code of Practice for research: http://ukrio.org/publications/code-of-practice-for-research/.

Please note you are required to adhere to all research data/records management and storage procedures agreed to as part of your application. This will be expected even after the completion of the study.

If you do not start the project within three months of this letter please contact the Research Ethics Office.

Please note that you will be required to obtain approval to modify the study. This also encompasses extensions to periods of approval. Please refer to the URL below for further guidance about the process:

https://internal.kcl.ac.uk/innovation/research/ethics/applications/modifications.aspx

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact your panel/committee administrator in the first instance (https://internal.kcl.ac.uk/innovation/research/ethics/contact.aspx)

We wish you every success with this work.

Yours sincerely,

Mr James Patterson
Senior Research Ethics Officer

For and on behalf of

Chair

PNM Research Ethics Subcommittee

B1.2) Participant Information Sheet

NIHR | Maudsley Biomedical Research Centre

KING'S College LONDON

INFORMATION SHEET FOR PARTICIPANTS

Ethical Clearance Reference Number: HR-19/20-18770

Title of project: Understanding acceptance and other psychological processes with symptoms and distress in women with breast cancer: PHASE 1 Qualitative Interviews

I would like to invite you to participate in this research study which forms part of my PhD research project. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve.

Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information by using the contact details at the end of this document.

What is the purpose of the project?

The purpose of the project is to understand the experiences of women with breast cancer who have been prescribed hormone therapy. This is to help inform future research to support women with breast cancer.

Who is being invited to take part?

We are inviting participants into this project who have a diagnosis of stage I-III hormone receptor positive breast cancer and have been prescribed hormone therapy within the last 2 years. We are hoping to recruit 20-30 women into this part of the study, from all over the UK.

What will happen if I take part?

After reading this information sheet and answering some screening questions to confirm eligibility, if interested, you will be asked to sign a consent form electronically. This will be followed by a short demographic and clinical factors questionnaire to ensure we gather a representative sample. You will then be contacted 3-5 days later by the researcher to arrange a suitable time and date for the interview. Participation will be able to take place at your own home, using the free software, Microsoft Teams, on an internet browser on a device with audio and a microphone such as your phone, tablet or laptop. The researcher will call you at the arranged time and the interview will take up to 1 hour. You will be asked to sit in a private room and if you are interrupted by members of your household, we will pause the interview.
You will be reminded about the purpose of the interview, be given an option to withdraw and asked whether it is okay to record the phone call. You can choose if you would like to have the video on or off. You will then give verbal consent and during the phone call you will be asked questions about your experience of breast cancer, symptoms, coping and wellbeing. You can stop at any point without giving a reason. We are asking these questions to help us understand women's experiences in greater detail, in order to help develop interventions for women with breast cancer in the future. The recording will be transcribed

so that it can be analysed. You will not be identified, instead a unique code will be linked to the interview.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact us if you have any questions that will help you make a decision about taking part. If you decide to take part, we will ask you to complete some screening questions and then complete a consent form online. You will then be contacted within 3-5 working days to arrange a suitable time and date to be called for the interview.

What are the possible risks of taking part?

You may feel upset or a bit distressed when talking about your experiences. You may stop the interview or skip questions at any time. We will then give you further information for support.

What are the possible benefits of taking part?

There are no clear personal benefits to taking part in the research, however you will be contributing to important research that could ultimately benefit other patients in similar positions. We aim to use the information we collect to inform future studies and develop an intervention to manage distress and symptom burden in patients with breast cancer.

Data handling and confidentiality

Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). Your data will remain anonymous and confidential. Your data will be assigned a study ID number and the link file will only be accessed by members of the research team in order to contact you for the follow up interview.
The audio/video recording will be stored on a password protected computer and given a study ID. It will be recorded through Microsoft Teams (GDPR compliant). Once transcribed it will be deleted. The transcription will be checked for personally identifiable information and will be pseudo anonymised.
Your contact details, demographics and recording will be stored separately on the secure King's College London SharePoint server, password protected and shared only with the researchers on the project. Your research data will be kept for 7 years after the study has ended.
Direct quotes may be used in the final report and publications; however, your name and any other identifiable information will be removed.

Data Protection Statement

Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). If you would like more information about how your data will be processed in accordance with GDPR please visit the link below:

https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research

What if I change my mind about taking part?

You are free to withdraw at any point of the project, without having to give a reason. Withdrawing from the project will not affect you in any way. You can stop the interview at any point and withdraw from the study. You can also withdraw your interview data up until 2 weeks after your interview date, by contacting the researcher. After this time, the pseudo anonymised data will have been entered into the analysis. If you choose to withdraw from the project before this time, we will not retain the information you have given thus far.

How is the project being funded?

Sophie Fawson is in receipt of a PhD studentship funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

What will happen to the results of the project?

The results of the interviews may be published in a peer reviewed, scientific journal and disseminated at medical and psychological academic conferences in addition to being written up for the researchers PhD thesis. You will not be able to be identified in any publication, presentation or report. Upon request, a lay summary of results will be sent to participants.

Who should I contact for further information?

If you have any questions or require more information about this project, please contact me using the following contact details:
Sophie Fawson; sophie.fawson@kcl.ac.uk; Health Psychology Section, King's College London, 5th Floor Bermondsey Wing, Guy's Hospital, London Bridge, London, SE1 9RT

What if I have further questions, or if something goes wrong?

If this project has harmed you in any way or if you wish to make a complaint about the conduct of the project you can contact King's College London using the details below for further advice and information:
Dr Lyndsay Hughes; lyndsay.hughes@kcl.ac.uk; Health Psychology Section, King's College London, 5th Floor Bermondsey Wing, Guy's Hospital, London Bridge, London, SE1 9RT

Thank you for reading this information sheet and for considering taking part in this research.

B1.3) Participant Consent Form

CONSENT FORM ONLINE

Study Title:

Understanding acceptance and other psychological processes with symptoms and distress in women with breast cancer (Phase 1 Interviews)

Ethical Review Reference Number:

Please cross each box by clicking on the box

1. I confirm that I have read and understood the information sheet dated 16.06.2021 v4 for the above project. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I consent voluntarily to be a participant in this project and understand that I can refuse to take part and can withdraw from the project at any time, without having to give a reason, up until 2 weeks after my interview date. ☐

3. I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018. ☐

4. I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes. ☐

5. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs. ☐

6. I agree that the researcher/research team may use my data for future research and understand that no identifiable data will be included. ☐

7. I agree for my interview to be recorded (audio/video) and stored safely and pseudo anonymously (identified through a study ID number). ☐

8. I understand I will be asked questions about my breast cancer experience and will be signposted to relevant support if I feel distressed. ☐

9. I agree to take part in the above study. ☐

B2) Sociodemographic and clinical questionnaires

1. What is your age?
2. What is your ethnic group? Choose one option that best describes your ethnic group or background.

White-English/Welsh/Scottish/Northern Irish/British	White Irish
White-Gypsy or Irish Traveller	Any other White background
White and Black Caribbean	White and Black African
White and Asian	Any other Mixed/Multiple ethnic background
Indian	Pakistani
Bangladeshi	Chinese
Any other Asian background	African
Caribbean	Any other Black/African/Caribbean background
Arab	Any other ethnic group

3. What is your relationship status?
   Single, Married/in a civil partnership, Widowed, Co-habiting, Separated/Divorced
4. What stage was your breast cancer at diagnosis?
   Stage 1 (e.g. tumour was 2cm or smaller and had not spread to lymph nodes)
   Stage 2 (e.g. tumour was between 2-5cm and/or the lymph nodes in the armpit were affected)
   Stage 3 (tumour was over 5cm and may be attached to surrounding structures such as muscle or skin. The lymph nodes in the armpit were affected)
   Stage 4 (the cancer had spread to other parts of the body)
   Unsure
5. Are you currently on hormone therapy? Yes/No

B3) Interview schedule

- (rapport builder) So first of all, please could you tell me a bit about your breast cancer diagnosis?
  Prompts if needed: How long have you been on hormone therapy? Which drug?

- For the next few questions, I am going to ask you about your experiences since you've been prescribed hormone therapy.

- Have you experienced distress about your cancer or treatment? If so, can you tell me more about your experience of this? *Use 'emotions' if unsure of term distress.*

  And how did you or do you manage that distress?

- Have you experienced physical symptoms related to your cancer or treatment? If so, can you tell me about this?

  What do you do when you have these symptoms?

And how did you or do you manage those symptoms?

How do you find this? How do you feel when you respond/behave/act like that?

- *If participant indicates link between symptoms and distress, explore this:*
  E.g., You mentioned your symptoms were distressing, can you explain what you mean by that?

Table B4.

Additional quotes

Theme	Additional quotes
The emotional burden of symptoms (overarching theme)	*'Sometimes I think the mental side effects are even bigger than the physical side effects.' P11, 53, anastrozole then letrozole* *'aware that for many people they have a much greater impact' P23, 49, letrozole* *'I'm not weighed down by it every day but my cancer, you know but I still do have symptoms, I do still have side effects so it's it is still a very lived experience.' P22, 49, tamoxifen* *'Well at my age, I don't really worry much about it.' P20, 75, anastrozole then tamoxifen*
1. A sense of helplessness around symptoms	*1.1* *I think people assume that if you look normal that everything feels normal […] just because I've finished chemo and my hair's grown back doesn't mean to say that everything's a bed of roses. P21, 54, anastrozole* *'I told the oncologist this, thinking she would go oh yeah, well that just happens, some people get weird sensations in their bones, but I'm not liking my oncologist. She went, what do you want me to do?' P1, 46, tamoxifen* *'I was actually astounded that there was no support […] went up to this kind of handover meeting in the (hospital name) and they gave me a Suppository tube which I thought why don't they just hand it over to*

	everyone who's on tamoxifen? […] thought this is unnecessarily difficult.' P18, 48, tamoxifen *And I've been told by a few* [oncologists], *oh, it's not the tamoxifen, it was the chemo and I'm like, well, what about the women who didn't have chemo who were taking tamoxifen and are experiencing really bad weight gain? […] All honesty, in the medical world, the doctors, the GPs, the oncologist. I don't think they really give much um, what's the word? I don't think they really take on board fully. Um, how it impacts a person. P8, 49, tamoxifen* *[They] reassured me that these things [side effects] can go on; there isn't a timeline for them […] knowing that it's normal […] just knowing there was nothing unexpected going on, you know, just for me gives me the ability to kind of go OK, it is what it is. P22, 49, tamoxifen* *And then when I mentioned it to the, our I think breast cancer nurse, it could have been at one point, and I said about the joint pain and she goes "well that'a unusual 'cause usually you don't get joint pain, with tamoxifen". I thought well obviously you don't read that group (tamoxifen Facebook group) that I go on because there's they have had everything and everything you know, so […] 'Cause the doctor, thinks the symptoms could be menopause related. And I'm like, well I know they're not because you go on the website and tamoxifen says it's got all them symptoms so.' P15, 51, tamoxifen* *'I'm managing okay. I think a lot of people probably wouldn't know there was anything wrong with me. But I'm aware every time I'm walking, you know that I'm in pain.' P20, 75, anastrozole then tamoxifen* *I don't know if it's because I had treatment, it happened during the pandemic […] so I don't know if my experience is the same for all people […] Like having a breast cancer nurse ring me up and talk me through stuff and kind of what helps available. I think would have been better than just, they just kind of chuck the pills at you and that's it. P1, 46, tamoxifen* *1.2*

	'But yeah, the tiredness. I don't. Yeah, haven't really kind of cracked that one. And when I've asked people for suggestions, they've been like well there's not nothing you can really do for that, so.' P13, 51, tamoxifen *What you're doing is only coping, you cannot actually make it better or make it worse, but you can cope better with that kind of thing. P18, 48, tamoxifen* *'How else do I manage them? Physically, I can't really, I just have to, you just have to get on with it […] that's one of the difficulties with the hot flashes and stuff is there's nothing you really can do. You just gotta, you know, just gotta ride it out and like I say I'm trying Acupuncture hasn't really done anything yet.' P19, 43, tamoxifen and goserelin* *'And, but, and I'm not really aware of anything else, I mean the migraines, the doctors giving me some atriprarim to combat them, and it does help when I have them, but I'm I'm always a bit of the warning leaflet the info leaflet says if you use them too often it can make them worse so I try not to use it too often. But you know, when I get a migraine, it's the only thing that'll touch it paracetamol, ibuprofen just do nothing.' P12, 49, letrozole and goserelin* *It's like you're taking a tablet to take a tablet. P15, 51, tamoxifen* *Because she [oncologist] had said well I can refer you to a surgeon [for] carpal tunnel syndrome. I said I don't really want to go down that avenue. I can't go for more surgery on what this, what the letrozole was causing. P4, 57, letrozole, exemestane then tamoxifen* *'What helped with the distress level that I had there when I was thinking of coming off it was, I actually felt like I had more information, more choice and more control […] I know what my options are and I go OK, but I'm sticking with it […] I know that if I get to January and things are still intolerable, I can do something about it and I think having that sense of agency is really important […] You know that there is actually an escape clause.' P16, 47, exemestane*

	'Once all my treatment options are over and done with. I don't want to start throwing more drugs down my neck unless I've got too.' P9, 63, anastrozole
2. Difficult feelings around loss and change	*'Certainly I think, um, menopause brain. If I can call it that combined with chemo brain is literally doing my nut in because I'm um, I've always had a very good memory. I've always had a really good memory, really articulate, and now in the middle of sentences I'm like "errr" I hate that God I hate that.' P16, 47, exemestane* *'But the headaches do. But more. More cause I suppose in a way it sort of spoils things 'cause you know, like if you've got plans, then you've got a really bad headache and you can't go somewhere or do something, like I can't drive when I get them.' P17, 44, anastrozole* *Then you start feeling quite achy and lethargic and fatigued and quite depressed as well. And I think it makes your body less resilient to things that you might have ordinarily think oh, I can do that really easily, and all of a sudden you can't, so that from a mental perspective. P11, 53, anastrozole then letrozole* *But then other days it really gets me down because without getting too personal, like having sex and stuff like, you don't, you know, a vaginal dryness for want of a better word, that is something I've never experienced and it's really difficult because that has always been an important part of my life. P19, 43, tamoxifen, goserelin* *'I have definitely got it has affected me and this is where the hormone therapy, whether it's chemo or hormone therapy, that definitely an element of hormone therapy to it and a big element has affected my life and what I can do […] but the fatigue has, affected how much I can do […] no absolutely treatment and as part of that is hormone therapy has affected my lifestyle.' P23, 49, letrozole* *'I think my age, 'cause I'm still quite young, I'm so yeah, I was 44 when I was diagnosed and I'm 45 now I do feel having to go through the menopause quite early, it that's a bit, so that makes you bit, not depressed,*

	but I think I could have had another 10 years before my body starts to deteriorate.' P14, 45, anastrozole and goserelin *'It's the side effects that have been really hard to deal with, and I'm someone who is really fit. Very active. I'm only 53. It's a very hard drug to take.' (P11, 53, anastrozole then letrozole)* *Yeah, I just think because I've been someone who's never had to take tablets or never had any health issues all of a sudden being on daily medication, monthly medication and knowing that that is the way it has to be for 10 years. Is yeah, it's not very nice. P19, 43, tamoxifen and goserelin* *I should be feeling better now, so it's a kind of different, it's a different worry if you know what I mean. It's like, am I ever gonna get back to normal again? P19, 43, tamoxifen and goserelin* *'Quite down because you know it. I like to go out and about and do lots of bits and you didn't feel quite the same as you know, going out so much and I guess when you're in pain you get a little bit snappier and all of those things and it, it's just not how I like to be, if that makes sense.' P7, 64, anastrozole then exemestane* *'realise I can just focus on what I want to do another day. If I'm not able to do it that day […] It's just being something I've had to deal with and get through and deal with the loss of the things I can't do anymore.' P14, 45, anastrozole and goserelin*
3. Living with uncertainty around side effects	*'I read up a lot about tamoxifen and all the side effects, so I was really apprehensive actually before taking it' P5, 39, tamoxifen* *'I think the one that is completely unsaid out of all of the side effects that I actually had no idea is the sexual side of things. The sexual side effect. And that really is an area that is not, not. You just unaware, I had no idea. I had no idea of the impact and that is a big impact. A severe you know.' P23, 49, letrozole* *'With specifically in regards to hormone therapy, yeah, it was very, very unexpected. I think the most difficult thing was it was unexpected […] and I*

	thought that's going to be the easy bit because I'm 47. A lot of my friends have already gone through the menopause.' P18, 48, tamoxifen *'Then obviously when you go to bed as much as I enjoy lying in the bed, stretching my body out, feeling myself sinking off, but then get that hot flash turn the fan on, it's just like. Almost like Groundhog Day, you know? Chucking off the covers and it's just like when is this gonna stop? I don't know, that's the frustrating part really.' P8, 49, tamoxifen* *'And then forgetfulness […] Now, last night I left the lid off. It's not a huge catastrophe, but then you sort of look at the other areas of your life and go. Where else is this, you know? Am I going to get into the car one day and forget, you know mirror signal manoeuvre, or you know something like that. So yes, leaving the lid off the dog food, not a big thing. Potentially it could have broader implications.' P16, 47, exemestane* *'Rather than getting in touch with the hospital all the time and asking them is, is it normal? What should be happening? Is there something wrong with me?' P14, 45, anastrozole and goserelin* *'But apparently that's normal. I've been led to believe so it's kind of I just and it's just you, you know that sort of your body is not the same as it was, which is something to reconcile with.' P13, 51, tamoxifen* *'So I understand that the situation is what it is, I'm struggling with my hips, it's a normal side effect.' P21, 54, anastrozole* *'Fingers crossed, but it is, it is early days for me.' P6, 56, tamoxifen* *'And then I think the fear of coming off it and going on the other ones is even worse 'cause they say that causes joint pain.' P15, 51, tamoxifen* *'I'm hoping really, soon when the menopause maybe calms down a little bit, you know. Maybe that's when you know it may subside a bit.' P15, 51, tamoxifen* *It's a little bit harder because it's more like oh you're going to be on this for 10 years. You know it's like, oh God, is this, is this my life? […] The hot flashes, headaches […] I've gotta be on these for 10 years. It, you can't see*

	an end to it. […] is this what it's gonna be like now.' P19, 43, tamoxifen and goserelin
4. The internal conflict around treatment decisions	*'…obviously it was quality life as well. You can't spend the rest of your life 10 years absolutely racked in pain.' P4, 57, letrozole, exemestane, tamoxifen* '*It's kind of between a rock and a hard place sometimes.' P1, 46, tamoxifen* *'It's very difficult to make an informed choice, even as I said, if you're very educated and you start to understand the questions to ask, for me it's the upfront discussion [yeah]. You just don't know what to ask because I don't think you actually hear what people are telling you. It is just a blur.' P11, 53, anastrozole then Letrozole* *'So if there's two in every hundred people that possibly coming back, do you really need to take the tablet? It's like is it really needed for everybody you know, as in everything that they give to you.' P15, 51, tamoxifen* *'So I did notice patterns initially that when I missed the tamoxifen, there was it, I've kind of found my old me when I got up and I was surprised that it was just for a day, because, you know, even for a day, you wouldn't because it's a long term medication. You wouldn't think that we missed one. It's not, it shouldn't affect you that much.' P18, 48, tamoxifen* *'And when I had a six weeks holiday from the drugs, I did lose half a stone which felt really, really good. […] but now I'm back on the drugs. It's getting really hard even to lose like half not even half a pound.' P11, 53, anastrozole then Letrozole* *'I'm not perfect and I've got the aches and pains of letrozole … but I'm still around from a kids.' P2, 63, letrozole* *'But you kind of say to yourself if that's the cost of not being one of those two people* (who might get a recurrence)*.' P11, 53, anastrozole then letrozole* *Yeah, Tamoxifen is tough in that, you know you have to take it because obviously it's what's helping to stave off the oestrogen.' P8, 49, tamoxifen*

	I need to do that for myself and I need to do that for my family and friends.' P3, 33, tamoxifen *I want to see my kids grow up and that sort of thing I don't want it to come back. P12, 49, letrozole, goserelin* *'I'm kind of more grateful that the tamoxifen gives me kind of hope more than anything in the way.'P5, 39, tamoxifen* *And if it's a few side effects, but I'm here, then it don't matter. I'll cope with them.' P17, 44, anastrozole*

B5) Paper trail

Participant quote	Initial codes/ Familiarisation	Codes	Theme
So it's a lot of, there's not a lot of help out there, you just kind of have to suffer it really. That's the only way, It's a shame. P19	Limited options to manage side effects Have to suffer symptoms	No options Helplessness	Sense of helplessness around symptoms: Nothing can be done about symptoms
You know that your sense of self and your identity is just. It's just being chipped at you know it's had a couple of great big fucking knocks taken out of it and then it's like oh we're just gonna chipping and keep chipping. P16	Symptoms chip away at self and identity Identity already chipped by dx but symptoms add	Difficult/challenging changes Changes to sense of self	Living with and managing difficult feelings around loss and change
I'm still young. I still got children. I've got everything to live for. And yet, it's a very difficult decision to	Weighing up being on HT	Weighing up is a struggle Internal conflict	The internal conflict around treatment decisions

make. Do I carry on with these horrific drugs and the side effects are indescribable sometimes? P11	Weigh up side effects vs quality of life is difficult		

B6) **Moxham et al. (in prep)**

Understanding acceptance and commitment therapy processes in the context of breast cancer survivorship: a directed content analysis

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Abstract

Purpose

The purpose of this study was to gain observational evidence to support the conceptualisation, inter-relationships between and use of acceptance and commitment therapy (ACT) processes within the context of breast cancer survivors (BCS) by using directed content analysis. It aimed to identify ACT processes and overall psychological flexibility evident in experiences amongst women post- breast cancer diagnosis who had not received psychological therapy.

Method

A qualitative design utilising directed content analysis was used to complete secondary analysis on in-depth interviews from 23 respondents to gain a rich understanding of the actualisation of ACT processes in a naturalistic setting.

Results

The deductive approach meant that themes were created to reflect ACT flexible and inflexible processes. A total of nine themes were created: acceptance, experiential avoidance, cognitive defusion, cognitive fusion, being present, loss of contact with present moment, self-as-context, self-as-content and moving forward vs stuck and unfulfilled. Sub-themes were created to represent overlap between processes where respondents communicated the use of more than one process in the same instance. Participants demonstrated use of all processes, although evidence of overlap between all flexible processes was not found. Some inflexible processes were used in a workable way.

Conclusion

This research provides observational evidence for the theorised processes of ACT in the context of BCS. Relationships between processes and the expression of distress support the ACT 'Hexaflex' model. The examples of flexible and inflexible processes in action from a specific context can help to develop interventions for BCS.

Introduction

Acceptance and commitment therapy is a third-wave cognitive behavioural approach which emphasises the importance of mindfully living in accordance with one's values (Johns et al., 2020). It aims to increase psychological flexibility (PF), defined as the ability to be in contact with the present moment more fully and to be able to change or persist in behaviour when doing so serves personal values (Hayes et al., 2006). The core aim of ACT is to increase PF so that internal experiences, such as physical symptoms and unpleasant thoughts and feelings interfere less with engagement in meaningful activities (Hayes et al., 2006). There are six flexible processes which help to foster PF and six inflexible processes which are antagonistic concepts creating psychological inflexibility (Barnes-Holmes et al., n.d; See Hayes et al., (2012) for a detailed explanation). Psychological inflexibility is hypothesised to contribute to psychopathology and suffering (Hayes et al., 2013; Hayes et al., 2006). The processes are thought to be universal, appearing in different contexts, and ACT, as a process-driven model, is hypothesised to reduce suffering and improve wellbeing (Hayes et al., 2013; Hayes et al., 2019). Benefits of ACT on outcomes such as distress and functioning, are well recognised through various interventions (Ghorbani et al., 2021; Han et al., 2021; Johns et al., 2020; Li et al., 2021). However, despite consisting of universal processes, it is important to understand the experience of PF within specific contexts to inform the clinical application of theorised constructs. For example, in a recent systematic review and meta-analysis of ACT processes in cancer, several processes were under-researched and evidenced (Fawson et al., 2023), posing the question of the utility and experience of certain processes in the context of cancer. Understanding and evidencing ACT processes from the patient perspective will enable clinicians to tailor their support most appropriately and develop more suitable and effective interventions.

The current study will explore ACT processes in the context of hormone receptor positive (HR+) breast cancer survivors (BCS). Breast cancer is the most common cancer in the world (World Health Organisation, 2021) and 75% of diagnoses are HR+ (Cancer Research UK, 2020), representing a large proportion of BCS. It is recommended that BCS take hormone therapy (HT) for 5-10 years to reduce the rate of breast cancer recurrence and mortality (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al., 2011). However, this medication is associated with difficult side effects and women need to manage this as well as contending with general survivorship issues such as fear of cancer recurrence and reintegration into pre cancer lives (Davies et al., 2013; Dowsett et al., 2010; Lebel et al., 2016). Side effects and survivorship issues are associated with higher rates of depression and anxiety and lower quality of life (Koch et al., 2014; Simard & Savard, 2015; Thewes et al., 2016). Coping literature in this area finds that BCS use a variety of approaches including approach strategies, avoidant strategies, problem-focused coping and emotion-focused coping (Lashbrook et al., 2018). Some of these strategies are consistent with ACT processes suggesting BCS would be an ideal study population within whom theorised ACT processes can be examined.

One way to further understand ACT processes is to explore the ACT 'Hexaflex' model which contextualises how the flexible processes are interlinked to increase PF (see Hayes et al., 2012 for a detailed explanation). For example, 'mindfulness and acceptance processes' and 'commitment and behaviour change processes' explain how a person can both modify their thought patterns and behaviour respectively. Gaining a rich understanding of the ways in which processes are expressed and evidencing interconnectedness between processes could provide a deeper understanding of whether all universal processes are relevant in the context of BCS and how they interact. Flexible ACT processes such as acceptance, cognitive

defusion, being present, self-as-context, values and committed action increase psychological flexibility, so gaining a nuanced understanding of how these processes are interconnected in the context of BCS could inform intervention development.

ACT is an intervention which has been previously used in the context of BCS. Whilst results of evaluation trials have mostly been positive, suggesting a decrease in fear of cancer recurrence, depression and anxiety amongst patients supported using ACT principles, the studies are of mixed methodological quality (Ghorbani et al., 2021; Han et al., 2021; Johns et al., 2020; Li et al., 2021). Small sample sizes, use of self-report measures and under-powered trials limit the reliability of the results and make it difficult to ascertain ACT's true effect on distress in this population (Li et al., 2021). Understanding the processes in specific contexts may allow for more tailored and effective interventions to be developed, helping a large proportion of BCS who may continue to experience distress throughout survivorship. Interventions have the potential to improve outcomes (Li et al., 2021).

To the best of the researchers' knowledge, the way in which ACT processes are observed in lived experience of patients surviving breast cancer (without psychological intervention) has not been qualitatively studied. To address this gap in the literature, the current study aimed to understand and explore if and how BCS experiences map onto ACT processes and whether the expected outcomes that the model proposes are observed. This was achieved by conducting directed content analysis on participant interviews of HR+ BCS. Further, the study seeks to examine inter-relationships between processes proposed in the ACT 'Hexaflex' model. Gaining a rich understanding of how ACT processes are expressed by BCS could allow for more targeted and effective interventions to be developed for this group.

Method

Design

Secondary analysis of semi-structured interviews was undertaken to gain a rich understanding of how ACT processes are experienced by BCS. Deductive directed content analysis allowed exploration of the phenomenon of interest whilst using ACT theory to guide theme development (Hsieh & Shannon, 2005). The SRQR criteria for reporting qualitative research was adhered to (O'Brien et al., 2010). This study was approved by King's College London's research and ethics committee; reference HR-19/20-18770.

Participants and procedure

Convenience sampling was used to recruit participants via the study advert which was posted on Facebook, Instagram and Twitter pages between October 2020 and July 2021. Although the researchers aimed to increase sample diversity by targeting specific support groups and an effort was made to include a range of clinical experience and demographic factors, formal purposive sampling was not followed. Eligibility criteria included being female, over the age of 18, having stage I-III HR+ breast cancer, hormone therapy being prescribed within the last 2 years, speaking English fluently and living in the UK. Screening took place online via a clickable link on the study advert which directed respondents to a Qualtrics™ questionnaire. This included a participant information sheet and screening survey and if eligible, a consent form, as well as demographic and clinical questions. Informed consent was taken from all eligible respondents.

The sample size was determined using the 'information power tool' (Malterud et al., 2016). The aim of the study was broad, the sample was specific, an established theory was

used, and the interviews were of good quality, however, cross-case analysis was conducted. A total on the lower end of general standards for sample sizes for qualitative analysis was reached (Sim et al., 2018). Participants were contacted to schedule an interview via Microsoft Teams. An interview schedule (see Table 1), with an introduction, key questions, prompts and a debrief form were used to ensure the research question was answered whilst allowing for flexibility in conversation depending upon responses from interviewees. Respondents were asked about their experience and management of distress, physical symptoms and how they deal with their thoughts and feelings about breast cancer.

Table 1.

Interview schedule

Introductory questions: So first of all, please could you tell me a bit about your breast cancer diagnosis? Prompts if needed: How long have you been on hormone therapy? Which drug? **Core questions:** For the next few questions, I am going to ask you about your experiences since you've been prescribed hormone therapy. Have you experienced distress about your cancer or treatment? If so, can you tell me more about your experience of this? Use 'emotions' if unsure of term distress. And how did you or do you manage that distress? Have you experienced physical symptoms related to your cancer or treatment? If so, can you tell me about this? What do you do when you have these symptoms? And how did you or do you manage those symptoms? If participant indicates link between symptoms and distress, explore this: E.g., You mentioned your symptoms were distressing, can you explain what you mean by that? **ACT components:** I'm now going to ask you a bit more about how you deal with thoughts/feelings/physical sensations. How do you respond to negative or unhelpful thoughts? (this may have been covered by the first question) How do you manage these thoughts? How do you find this? What is your understanding of being in the present moment (if unsure: more commonly known as mindfulness)? Is this something you find yourself doing? How do you find this?

Do you ever notice that you are aware that you are having thoughts/feelings/sensations?
Prompt if needed: Or do you just feel it/think it, without being aware?
Do you feel that you are more than just your thoughts/feelings/sensations?
Can you tell me more about what this is like? How do you find this?
What do you feel is important to you in life, what do you value?
Do you feel you act in line with what is important to you?
And how do you do that? How do you find this?
Is there anything that gets in the way of you living the life that is important to you?

Do you have goals that are important to you?
What do you have in place to help you make progress on these goals?
What is your understanding of self-compassion?
Do you feel you act compassionately towards yourself?
How do you do this (self-compassion)? How do you find this?

Analysis and stages

Interviews were transcribed verbatim, pseudonymised and analysed using directed content analysis. NVivo (QSR International Pty Ltd. NVivo. 12 ed2018) was used to code transcripts and keep a record of themes. This method is suitable because the analysis is informed by prior research and aims to explore and extend ACT theory using predetermined categories (Hsieh & Shannon, 2005). A mixture of manifest and latent analysis was conducted to allow the researchers to stay close to the meaning in the text, but also extend to an interpretive level and seek underlying meanings in the text (Bengtsson, 2016). All transcripts were analysed by author FM.

Four stages of analysis were completed: decontextualising, recontextualising, categorisation and compilation (Bengtsson, 2016). Decontextualising required the researcher to familiarise themselves with the data and assign codes to meaning units. A sample coding manual (refer to e-component B) with definitions of codes was created *a priori* to minimise the effect of cognitive changes during the analysis process, increasing reliability (Bengtsson, 2016). FM, LH and SF were involved in the coding and theme development process.

Recontextualising involved checking whether all aspects of the content had been covered in relation to the aims. Categorisation required the data to be divided in relation to ACT processes and themes were developed. A paper trail (found in e-component C) showing the progression from initial codes to themes ensured that interpretations of data were transparent and consistent. The final step was compilation where the analysis and writing up process began. Although the researcher had knowledge and understanding of BCS experiences, having not experienced breast cancer themselves allowed them to disregard any preconceived ideas, distance themselves and allow full immersion into the data (Bengtsson, 2016).

Results

Thirty-two eligible women were recruited. Eight respondents did not respond to initial emails or reminders to arrange an interview. One respondent had not started HT yet and so was ineligible. The resulting respondents (n=23) were aged between 33 and 81; mean age 52.57 (SD=10.94). Most respondents were of White ethnicity (n=21). Respondents' demographic information is summarised in Table 2.

Table 2.

Respondents' demographic and clinical characteristics

	Aggregate n=23
Age (M, SD, range)	52.57 (10.94, 33-81)
Ethnicity (*n*)	
White British	18
Other White background	3
Black Caribbean	1
Indian	1
Stage of diagnosis (*n*)	
Stage I	10

Stage II	8
Stage III	5
Current HT (*n*)	
Tamoxifen	12
Aromatase inhibitors	11
Months on HT (M, SD, range)	9.34 (7.45; 1-27)
Previous therapy (*n*)	
Counselling	4
Art therapy	1
Cognitive Behavioural Therapy	1

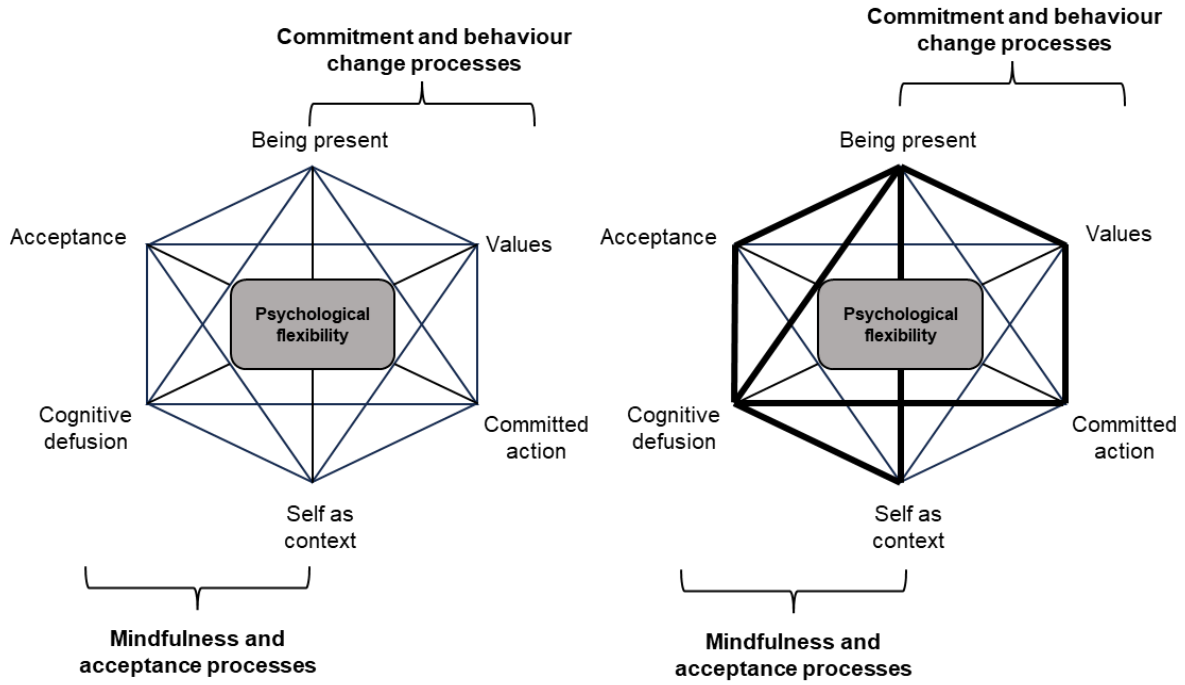
Note: M = mean, SD = standard deviation

Due to the deductive methodology, themes were created to reflect inflexible and flexible ACT processes. Notably, these themes are not distinct and there is overlap in areas due to the nature of ACT processes. As the processes of values, loss of contact with values, committed action and inaction are closely related to living in line with values, these were combined into one theme to allow for greater understanding of respondent's experiences. This resulted in nine themes.

Additionally, respondents sometimes communicated evidence of more than one process at the same time in line with the ACT 'Hexaflex' model (Figure 1). The second 'Hexaflex' in Figure 1 represents connections between processes found in the current study. Sub-themes were created to characterise the connection between processes. A summary of the themes and sub themes can be found in Table 3. Quotes providing additional support for themes can be found in (e-component D).

Figure 1

Comparison of theorised ACT 'Hexaflex' model with evidence for the 'Hexaflex' model found in the current study (adapted from Hayes et al., 2012)



'Hexaflex' model: ———

Evidence for 'Hexaflex' model found in the current study: ▬▬▬

Table 3

Summary of flexible and inflexible themes and sub-themes

Theme	Sub-theme	Flexible/inflexible
Acceptance	• Acceptance and cognitive defusion • Acceptance and being present	Flexible
Experiential avoidance		Inflexible
Cognitive defusion	• Cognitive defusion and being present • Cognitive defusion, being present and self as context • Cognitive defusion and committed action	Flexible
Cognitive fusion		Inflexible
Being present	• Being present and values	Flexible
Loss of contact with present moment		Inflexible
Self as context		Flexible
Self as content		Inflexible
Values		Flexible
Loss of contact with values		Inflexible
Stuck and unfulfilled vs moving forward		Mixed

Theme 1: Acceptance

Respondents clearly communicated the importance of acceptance by describing it as “a very big part of coming to terms with every single facet of breast cancer” (Ava). They describe the importance of experiencing “all the feelings” (Ava) as these emotions inevitably surface later and have a “much bigger impact” (Joy) psychologically on the person than they do if they are experienced when they initially arise.

Interestingly, respondents often posed limits on how long they would think about their emotions. They commented that it is “okay to have a little cry”, but this “can’t be all day,

every day" as there becomes a point where dwelling on negative emotions becomes unhelpful (Susan). In order to cope with their experiences, respondents talked about having to "move on" from these emotions (Elisabeth).

Others commented on the importance of being able to "release" (Ava) emotions whether its "screaming and crying" or they "end up laughing" (Alison); the important thing is that they have an "outlet for whatever emotions come up" (Alison).

Theme 1.1. Acceptance and cognitive defusion

Some respondents showed willingness to experience emotions such as anger and sadness and were able to observe these emotions without feeling attached to them, displaying evidence of both acceptance and cognitive defusion. Having this separation from the raw negative feelings helped respondents move forward.

> *"I can be angry…sometimes it feels really unfair, and I still cry because I'm like this is so fucking unfair…but it kind of doesn't still have that negative raw feeling attached to it."* – Charlotte

Theme 1.2. Acceptance and being present

Others talked about how their willingness to experience emotions and physical sensations whilst contacting the present moment has a beneficial impact. One respondent mentioned that if you "meditate on the pain" it can help with pain relief and fostering self-compassion (Ava).

> *"I give myself grace if something is going wrong or I've done something wrong and part of the grace is acceptance actually with what's happening with myself...I think the more time you give yourself and the more time you sit with yourself and the more*

you can be present with yourself, the more you can accept yourself and be compassionate." – Ava

Theme 2. Experiential avoidance

Many respondents communicated that they tend to "push down" (Meera) or "banish" (Gail) negative thoughts and feelings, displaying the inflexible process in action. Some do this for their own self-preservation whilst others do it for friends and family members as they feel "guilt" (Charlotte) about cancer-related distress.

Some respondents communicated behavioural avoidance through their inability to look at surgery scars, as they cause too much psychological distress. They also communicated avoiding thoughts and feelings in a more abstract sense whereby they cannot look in the mirror perhaps because this reminds them of their illness and potential recurrence.

"I must admit psychologically it took me a really long time to adjust to my new body...I had to get used to seeing scars...I've got an incision from hip to hip…that was very distressing. I must admit. For a long time I couldn't look in the mirror" – Chantale

When asked about how they deal with negative or unhelpful thoughts, respondents commonly expressed that they "distract" (Susan) themselves by listening to music, seeing friends and family, focusing on "house things" (Charlotte) or taking up a hobby. However, this regularly led to amplified negative thoughts at night-time, resulting in sleep issues for many respondents.

However, some respondents commented on how avoiding these negative thoughts was adaptive as they focused on activities which were beneficial for their health. Having structure distracted them from "obsessing about death" (Ava) and helped them to control thoughts

about death thereby stopping them from going “further down and down and down and down into that spiral” (Ava).

Theme 3. Cognitive defusion

However, other respondents talked about not feeling bound to thoughts and feelings as they recognise them as temporary states, highlighting an example of cognitive defusion.

> *“I recognize I don't really connect with my thoughts and feelings like that. Thoughts and feelings are fleeting then moving. They don't stay. So I see them as very transient.”*
>
> – Chantale

Some respondents do not attribute a label to thoughts as they recognise "thoughts are just thoughts” and that they as an individual “are something other than that [thought]” - showing an ability to observe their thoughts independently (Joy). Others explain that thoughts are “random things that can sometimes flick into your head” (Penny). However, some respondents must “work quite hard” (Susan) to separate themselves from thought processes and rationalise them because it is easy for thoughts to become “obsessive” (Charlotte).

One respondent communicated that they identify feelings as “transient states” that “will pass”, noting that they deserve to “cut themself some slack” after everything they have been through, although this is not “easy” (Joy). Some respondents expanded on why it is not easy, by identifying barriers such as tiredness which impacts the “severity of emotions and how controlled...the thoughts and emotions are” (Meredith).

Theme 3.1. Cognitive defusion and being present

For some, contacting the present moment aided their ability to separate themselves from thoughts. One respondent found that the ability to deal with thoughts and emotions more objectively "comes from meditation and mindfulness" (Joy).

> *"For me…the ability to go there definitely comes from the meditation and mindfulness. I think if you begin to have that recognition that we are not our thoughts and we are not our feelings, it's then much easier to be able to recognize frustration as a transient state."* – Joy

Theme 3.2. Cognitive defusion, being present and self-as-context

Some respondents take this concept a step further, whereby they communicated that being present, and mindful practice specifically, has not only aided their ability to separate themselves from thoughts, but also separate these thoughts from their self-concept whereby thoughts do not define who they are, highlighting an example of self-as-context.

> *"I feel like I'm more than my thoughts and I think that's been a big part of helping actually and having that observation ability which comes with mindfulness having that ability to observe your thoughts and let them also pass by and not take them on board as part of who you are. And you know the fibre of your personality I suppose"* – Ava

Theme 3.3. Cognitive defusion and committed action

One respondent reported that being able to step back and observe thoughts independently allows them to pursue valued living more clearly, as they can identify what is important in the "bigger picture" (Jackie).

"When I have a negative thought or something that's holding me back in the instant, I try to look at that bigger picture and think about, this is a set back at the moment, but what does it mean? And is it important in the bigger picture?" – Jackie

Theme 4. Cognitive fusion

In contrast to the previous theme, some respondents found it very difficult to separate themselves from thoughts and emotions whereby they end up "spiralling" (Ava) and this occurs more often when they are experiencing negative thoughts and feelings.

"I think there are times when I feel overwhelmed by that [negative] feeling and I don't feel separate to that feeling. I guess the unfortunate bit is that's probably those feeling when you're feeling negative" – Susan

Some respondents recognise that being fused with thoughts may not be helpful.

"I take them [negative or unhelp thought] deep within me and then keep thinking about them. Which isn't good" – Harriet

Respondents regularly voiced concerns about the cancer returning or spreading; not knowing how to "stop thinking that it might come back", hoping that maybe these thoughts "will subside with time" (Sharon).

Theme 5. Being present

Many respondents explain that they contact the present moment by "not dwelling on what's gone before, musing about what might come past and just enjoying" what they are doing (Susan). "Living for the now" (Megan) fosters a greater appreciation for life which is found to be helpful for BCS. The future is uncertain for many respondents, so being present can help to remind them that they are "still here" (Chantale).

Lots of respondents comment on ways in which they contact the present moment, for example “really enjoying taking a minute and having a look [around]” (Elizabeth) or commenting on how grateful they are to be “on this walk enjoying the countryside” (Charlotte). Many also note that this ability to contact the present moment has become much more important since they have had cancer.

Respondents mention that they sometimes feel “quite dissociated” (Ava) from their bodies, “especially after a cancer diagnosis” (Joy) which impacts their experience of pain. However, using mindfulness techniques can help to repair the mind-body connection and can “actually make it [pain] less painful” (Claire).

Theme 5.1. Being present and values

Some respondents connect their values with being in the present moment – whereby the present moment has become an important value. Others find that taking the time to be present and “enjoy the moment” (Gail) allows them to savour time spent connecting with their values.

> *“The present moment has become important, more important than worrying about what's going to happen”* – Meera

Theme 6. Loss of contact with present moment

Alternatively, some respondents found that they experienced a loss of contact with the present moment whereby they were caught up in thoughts about the past or future. For example, one respondent commented on how they “wanted to go backwards” to their old job and how they were pre-cancer (Sharon).

Another indication of loss of contact with the present moment is an inability to notice thoughts, feelings and physical sensations, as this suggests they have a lack of awareness of things happening internally and externally. Respondents regularly note this lack of awareness.

"Usually think it or feel it without being aware" – Joy

Theme 7. Self-as-context

Some respondents display evidence of knowing they are bigger than their experiences. For instance, they describe not identifying with the cancer patient label as an example of self-as-context:

"*I don't think of myself as the cancer patient"* – Meera

Others highlight another aspect of self-as-context where they can notice a distinction between inner and outer experiences. For example, one respondent talks about how there is a "gradual acceptance" of physical limitations which prevent them from doing some activities, but "you can adapt, you can adjust" (Joy).

Another aspect of self-as-context is flexible perspective taking. One respondent communicates this by taking a "step outside" themself and imagining what they would say to someone in their shoes (Gail). Others display flexible perspective taking by looking at their situation from different perspectives – instead of thinking "why me?" they think "why not me?" (Beth).

Theme 8. Self-as-content

In contrast to the previous theme, some respondents avoided going to the doctor when they found signs of cancer because they did not want to have the cancer patient identity. Beliefs and ideas about this label resulted in it being described as a "huge weight" whereby the

respondent did not know how to navigate life without “cancer becoming the only thing in [their] life now” (Meera).

Many respondents displayed evidence of being fused with previous ideologies that formed their self-identity. They discussed how having cancer and being on HT resulted in dramatic changes to their appearance and physical abilities resulting in difficulties accepting who they are now. For example, some found it difficult they are not the “strong” person they once were (Chantale) and others described how their “sense of self identity is just being chipped at” (Joy).

> *“You lose your identity because you’ve turned into someone that’s a couple of stones heavier, bloated with the steroids, bald, no eyelashes, no eyebrows, you kind of look like a freak and I think that’s when it’s really difficult accepting the diagnosis and accepting who you are”* – Joanne

Some respondents commented on how their physical appearance impacts the way others’ see them. Sometimes illness is very visible and other times it is not, but fusion with others’ judgements about their physical appearance can be very impactful on BCS.

> *“Someone else was asking why I wasn't in work 'cause I used to work with them, and I just said I was diagnosed [with cancer] ...she looked at me and she goes, well, you must be okay ‘cause you look okay... I’m not okay though, I don’t feel okay, I know I look okay, but I don't feel okay.”* – Sharon

Theme 9. Moving forward vs stuck and unfulfilled

The following theme discusses how the processes of values and committed action allow people to move forward and how loss of contact with values and inaction result in people

becoming stuck and unfulfilled. Only one respondent struggled to identify values and after thinking and talking about it they could identify what was important to them. Interestingly, having cancer prompted the respondent to think about their values which they presumably had not done before, suggesting that identifying things that matter to BCS is important when dealing with cancer-related distress.

> *"I hate that question because I've been trying to work it out for ages. Somebody says, you know, breast cancer is an opportunity for you to work out...what your values are…What's important to me? Meaningful connection. Depth…fun, laughter…Compassion is huge.... Hey, I do know what my values are!"* – Joy

In support of this finding, many respondents reported values becoming more salient after being diagnosed with cancer. Common values respondents identified as important were fairness, equality, integrity, kindness, loyalty, humour, dependability and compassion. Additionally, friends, family and happiness were described as "incredibly important" (Claire) and "paramount" (Joanne) after going through cancer diagnosis and treatment. Many respondents spoke about how they "re-evaluated" (Elisabeth) their priorities to act in line with the values they deemed most important. For example, some describe removing "unnecessary things" and how "people have become very close and precious" (Meera).

Some respondents went further than their explanation of how they have re-prioritised values by talking about how they pursue goals related to these values – an example of committed action. For example, one respondent talks about pursuing values around kindness and compassion by volunteering as a mentor. They believe "being in a helping relationship with other people" allows them to "exercise some compassion" (Aine).

Often, respondents displayed evidence of how committed they are to pursuing independence by recovering from physical limitations. They described setting short-term goals and adapting to be able to do things they enjoy like cooking.

> *"Short term goals are able to get into a jar without having to ask someone to open it for me or be able to chop up food properly. But I can start with softer foods like chopping up fruit and then work on to harder things like potatoes and turnips."* – Gail

Another important value that became salient to respondents after breast cancer diagnosis was health and fitness. Lots of respondents described setting small reachable goals to overcome challenges.

> *"Even during chemo and after surgery I was trying to get up to 5000 steps because the first time I got out of bed I couldn't even walk to reception"* – Josie

However, other respondents talked about the impact of diagnosis and treatment and how this affected their ability to live in line with values. Not having the physical or emotional capacity to pursue their values is an example of inaction:

> *"When I was diagnosed, actually, up until recently I didn't have much capacity. My capacity really reduced and what I could give to other people had reduced as well, naturally, because I was, kind of replete of energy. But I still hold those values, perhaps I've not been able to commit to them much over the last year since I've been diagnosed."* – Ava

Interestingly, one respondent mentioned only having vague goals because they spend more time focusing on the present moment than the future.

"I have vague goals they're...non-specific. The focus is on the present moment rather than what do I need to do...It's more about, how do I deal with now? What's important now?" – Jackie

Discussion

This study was the first to use directed content analysis to qualitatively examine ACT processes in the context of BCS. The in-depth interviews enabled a rich understanding of how BCS experiences relate to ACT processes and evidence all twelve of the processes. Support was found for the use of flexible processes in relation to managing cancer-related distress such as fear of cancer recurrence, side-effects of HT and body image issues in line with previous research (Ghorbani et al., 2021; Han et al., 2021; Johns et al., 2020; Saeedi-Seadi et al., 2015; Syrowatka et al., 2017). This is an important finding in terms of clinical application of ACT as it evidences ways in which flexible processes can be used by BCS to manage survivorship issues and provides a deeper understanding of the challenges they face.

Further, the communication of inflexible processes was often coupled with comments on poor distress management, as seen in previous research and theorised by the model (Dindo et al., 2019; Finger et al., 2020; Hayes et al., 2012; Sairanen et al., 2018). In some cases, inflexible processes such as experiential avoidance were described as being helpful for respondents whereby avoiding unhelpful thoughts and emotions resulted in a positive outcome. Similarly, some respondents reported that not pursuing valued goals i.e., inaction was beneficial because making plans was distressing due to the uncertainty of their future. Instead, they found fulfilment in focusing on the present moment.

In some ways these findings counter the model as inflexible processes were found to be beneficial, however, a benefit of ACT is that processes are deemed 'workable' and 'unworkable', so if the behaviour is 'working' in terms of effectively solving the problem and moving towards valued ends then it can be something the person builds on (Dindo, Van Liew & Arch, 2017). ACT processes are only seen as problematic if they are 'unworkable'. This nuance to ACT means that interventions can be tailored to the needs of individuals and inflexible processes can be incorporated into managing distress where they are 'workable'. This is in line with research finding that experiential avoidance can be adaptive during diagnosis and treatment, although research suggest it becomes maladaptive in the long term when difficult emotions are not addressed during survivorship (Fujimoto & Okamura, 2021; Johns et al., 2020). Therefore, it may be useful to explore this further at different stages of a diagnosis.

Whilst evidence was found for all ACT processes, some processes emerged more than others. For example, there was a lack of evidence for self-as-context and self-as-content. This is perhaps due to a combination of limitations both in the theory and interview schedule. The language used to describe ACT processes is complex, resulting in them often being described as confusing (Harris, 2019) and making them difficult to ask questions about. Whilst the researchers tried to mitigate this by providing examples, respondents regularly could not answer questions related to self-as-context. Additionally, the interview schedule did not include questions that were related to all aspects of self-as-context, further limiting the evidence for this process. This finding calls for research investigating lay people's understanding of the ACT processes because without this the acceptability and importance of different processes cannot be assessed, making it difficult to validate and extend ACT theory (Stockton et al., 2019).

Evidence for the ACT 'Hexaflex' model was found in the current study whereby respondents regularly communicated evidence of the use of more than one process at the same time, highlighting the overlapping nature of ACT processes (Hayes et al., 2012; Stockton et al., 2019). Unsurprisingly, 'mindfulness and acceptance processes' linked to each other more than they did with 'committed action and behaviour change processes', which also linked to each other more regularly. Additionally, respondents displayed more adaptive coping when using a combination of 'acceptance and mindfulness processes' and 'commitment and behaviour change processes' (Hayes et al., 2012). Some respondents found that allowing themselves to experience emotions (i.e. acceptance) became a maladaptive experience when they dwelled on these emotions for too long. However, those who communicated use of acceptance coupled with cognitive defusion or being present reported a greater ability to work through thoughts and emotions. This is in line with research finding that the use of multiple processes is related to better mental health outcomes across a wide range of contexts (Pakenham et al., 2020). Therefore, this research provides support for the use of a combination of processes to combat distress which is often seen in therapeutic interactions.

An interesting finding was that respondents often communicated use of both a flexible and corresponding inflexible process suggesting that they do not relate to processes in a binary manner. For example, in one instance a respondent may talk about being very cognitively fused to thoughts about recurrence, but in another display evidence of cognitive defusion whereby they could separate themselves from thoughts about why they got cancer. Without intervention, some women demonstrated PF for some aspects of survivorship whilst others did not, suggesting patients sit upon a continuum of PF, across different aspects of cancer survivorship. This highlights the importance of clinicians taking time to understand

various aspects of patients' experiences post cancer with a view to supporting specific aspects where patients have more difficulty employing PF (Prevedini et al., 2011).

Strengths and limitations

The current study has notable strengths. Firstly, to the best of the researchers' knowledge no paper has examined ACT processes qualitatively in the context of BCS; therefore, the current study is novel and addresses this gap in the literature by providing insight into how ACT processes are expressed. Second, this research provides empirical evidence for the ACT 'Hexaflex' model and the theorised relationships between flexible and inflexible processes and distress in the context of BCS. Third, this study was conducted with methodological rigour. Finally, the qualitative approach applied gains a richer understanding of BCS experiences allowing for greater understanding and insight into the challenges they face (Queirós et al., 2017).

There were also some limitations to the current study. The design was cross-sectional so experiences of BCS could not be examined over time. Many respondents noted that with time they may feel differently about thoughts and emotions, therefore longitudinal qualitative research is needed to establish whether BCS experiences change over time. Further, despite trying to recruit from ethnically diverse populations, the resulting sample included mostly White women and was therefore not representative of the wider population. However, HR+ breast cancers differ between ethnicities with a much higher prevalence in White women than Black, Hispanic and East Asian women (Hirko et al., 2022; O'Brien et al., 2010; Stringer-Reasor et al., 2021). There are also differences in the aetiology, treatment and prognosis of the cancer itself which suggest that it may be better to investigate these groups separately to understand their experiences (Hirko et al., 2022; Stringer-Reasor et al., 2021).

Implications and future directions

This study has relevant implications in terms of theory, research and clinical practice. This study provides rich examples of ACT processes in action and evidences ways in which these processes can be used to manage cancer-related distress and survivorship issues in BCS. Although, there was less frequent expression of evidence for self-as-context/self-as-content and committed action. Respondents regularly noted that values became more salient after their cancer diagnosis, however, there is clearly disconnect between value salience and pursuing valued goals, perhaps highlighting an opportunity for intervening.

In terms of clinical practice, the results of this study suggest that ACT may be a promising intervention for BCS as patients already display use of many flexible processes to combat distress. The study provides examples of the universal processes in the context of BCS with some inflexible processes linked to poorer outcomes. Some women have the ability to use flexible processes but not all, suggesting intervention might be needed for some. This coupled with evidence suggesting that ACT is effective when delivered in group format could make it a cost-effective and feasible intervention for BCS (Johns et al., 2020). Although, this needs to be rigorously tested in a well-designed randomised control trial.

Additionally, this study provides support for the importance of the interconnectedness between processes depicted in the ACT 'Hexaflex' model. However, not all processes overlapped suggesting that some processes may be more interlinked than others. This research calls for quantitative mediation studies examining whether all ACT processes equally influence PF as is theorised (Hayes et al., 2012).

Whilst not directly examined in the current research, issues surrounding lay people's understanding of some ACT processes, such as self-as-context/content, arose whereby the

language seemed too complex. Research investigating lay people's understanding of ACT processes would provide a clearer picture on this potential issue. The lack of validated measures for self-as-context, likely contribute to the sparse research examining patient views of ACT – an issue that requires attention to ensure that ACT interventions are feasible and acceptable (Stockton et al., 2019). If the constructs cannot be accurately understood or measured, this may contribute and lead to limitations within the field.

Conclusion

The current study is the first to qualitatively explore the expression of ACT processes, without intervention, in the context of BCS. Evidence of all twelve ACT processes and support for the use of flexible processes in relation to managing cancer-related distress was found. Support was also found for the ACT 'Hexaflex' model whereby interconnections between processes were observed. The use of multiple flexible processes in the same instance was coupled with more adaptive coping. These findings provide empirical evidence for the ACT 'Hexaflex' model. However, weak or non-existent connections between processes requires further investigation to discover if all flexible processes equally influence PF (Hayes et al., 2012). Nevertheless, this study hopes to inform the development of ACT interventions for BCS by providing a nuanced insight into the experiences of BCS and the ways in which they display use of ACT processes without intervention.

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Appendix C: Longitudinal study (Chapter 6)

C1) Study documents

C1.1) Participant Information Sheet

NIHR | Maudsley Biomedical Research Centre

KING'S College LONDON

INFORMATION SHEET FOR PARTICIPANTS

Ethical Clearance Reference Number: HR-19/20-18770

Title of project: Understanding acceptance and other psychological processes with symptoms and distress in women with breast cancer: PHASE 2 Observational Study

I would like to invite you to participate in this research study which forms part of my PhD research project. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve.

Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information by using the contact details at the end of this document.

What is the purpose of the project?

The purpose of the project is to understand women's experiences with breast cancer who have been prescribed hormone therapy. This is to help inform future research to support women with breast cancer.

Who is being invited to take part?

We are inviting participants into this project who have a diagnosis of stage I-III hormone receptor positive breast cancer and have been prescribed hormone therapy within the last 2 years. We are hoping to recruit 400 women into this part of the study, from all over the UK.

What will happen if I take part?

If you choose to take part in the project, it will involve completing 3 separate online questionnaires:

- One now
- One 6 months later
- One 12 months later

Therefore, participation will be able to take place at your own home. The questionnaires will take around 30-40 minutes to complete. After reading through this information sheet and answering a few questions to confirm eligibility, you will be asked to consent electronically. You will then go straight to the first questionnaire. There is no time limit to complete the questionnaire and the link will remain active for one week, so you can open it again using the same computer and internet browser to finish it. However, we do recommend completing it on the same day if you can. At the end of the questionnaire you will be shown a debriefing page and asked whether you would like to receive a summary of the research. You will automatically be sent the link to the follow up questionnaire, 6 and 12 months after.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in anyway. Once you have read the information sheet, please contact us if you have any questions that will help you make a decision about taking part. If you decide to take part we will ask you to complete some screening questions and then complete a consent form online. You will then be directed to the questionnaire. You will receive reminder emails 6 months and 12 months after you have completed the baseline questionnaire which will contain the questionnaire links.

What are the possible risks of taking part?

You may feel upset or a bit distressed when being asked questions about your breast cancer experience. At the end of the questionnaire you will be signposted to further support which you can access if you feel you need.

What are the possible benefits of taking part?

There are no clear personal benefits to taking part in the research, however you will be contributing to important research that could ultimately benefit other patients in similar positions. We aim to use the information we collect to inform future studies and develop an intervention to help manage distress and symptom burden in patients with breast cancer.

Data handling and confidentiality

Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). Your data will remain anonymous and confidential. Your data will be assigned a study ID number and the link file will only be accessed by members of the research team in order to contact you for the follow up questionnaires or to withdraw your data.
This will be stored on a password protected computer. The data will be checked for personally identifiable information and will be pseudo anonymised.
Your contact details and questionnaire data will be stored separately on the secure King's College London SharePoint server, password protected and shared only with the researchers on the project. Your research data will be kept for 7 years after the study has ended.
You will be not be identified in any publications or research outputs.
The data collected from the study may be deposited in an online journal repository. Many research journals now require authors of publications to upload their data. This allows for replication of the study findings, validity and reproducibility of the data, ensuring transparent science. This may happen with the data participants provide in this study. The data would not be personally identifiable (i.e. none of the following will be uploaded: i.e. no name, initials, IP addresses, dates, contact information or location).

Data Protection Statement

Your data will be processed in accordance with the General Data Protection Regulation 2016 (GDPR). If you would like more information about how your data will be processed in accordance with GDPR please visit the link below:

https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research

What if I change my mind about taking part?

You are free to withdraw at any point of the project, without having to give a reason. You can close the browser before you have completed the questionnaire and will have one week to finish it. You can access your questionnaire by clicking on the link on the same computer using the same internet browser. You will be sent a reminder email if you are 75% or more through. If you choose not to complete it during this time, we take this as withdrawing your data. Withdrawing from the project will not affect you in any way. You are also able to withdraw your data from the project up until 31st December 2022 by contacting the researcher, after which withdrawal of your data will no longer be possible due to your contact details being deleted and the data being fully anonymised. If you choose to withdraw from the project before this time, we will not retain the information you have given thus far.

How is the project being funded?

Sophie Fawson is in receipt of a PhD studentship funded by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London. The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

What will happen to the results of the project?

The results of the study may be published in a peer reviewed, scientific journal and disseminated at medical and psychological academic conferences in addition to being written up for the researchers PhD thesis. You will not be able to be identified in any publication, presentation or report. Upon request, a lay summary of results will be sent to participants.

Who should I contact for further information?

If you have any questions or require more information about this project, please contact me using the following contact details:
Sophie Fawson; sophie.fawson@kcl.ac.uk; Health Psychology Section, King's College London, 5th Floor Bermondsey Wing, Guy's Hospital, London Bridge, London, SE1 9RT

What if I have further questions, or if something goes wrong?

If this project has harmed you in any way or if you wish to make a complaint about the conduct of the project you can contact King's College London using the details below for further advice and information:
Dr Lyndsay Hughes; lyndsay.hughes@kcl.ac.uk; Health Psychology Section, King's College London, 5th Floor Bermondsey Wing, Guy's Hospital, London Bridge, London, SE1 9RT

Thank you for reading this information sheet and for considering taking part in this research.

C1.2) Participant Consent Form

CONSENT FORM ONLINE

Study Title:

Understanding acceptance and other psychological processes with symptoms and distress in women with breast cancer (Phase 2 Observational)

Ethical Review Reference Number: HR-19/20-18770

Please cross each box by clicking on the box

10. I confirm that I have read and understood the information sheet dated 25.05.2021 v4 for the above project. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

11. I consent voluntarily to be a participant in this project and understand that I can refuse to take part and can withdraw from the project at any time, without having to give a reason, up until 31/12/2022. ☐

12. I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled in accordance with the terms of the General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018. ☐

13. I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes. ☐

14. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs. ☐

15. I agree that the researcher/ research team may use my research data for future research and understand that no identifiable data would be included. ☐

16. I consent to my data being shared with third parties which are within the EU (cancer or health psychology journal) as outlined in the participant information sheet. The data uploaded to any repository will be anonymous. ☐

17. I agree to take part in the above study. ☐

C1.3) Sociodemographic and clinical characteristics questionnaire

1. What is your age?
2. What is your ethnic group? Choose one option that best describes your ethnic group or background.

White-English/Welsh/Scottish/Northern Irish/British
White Irish
White-Gypsy or Irish Traveller
Any other White background
White and Black Caribbean
White and Black African
White and Asian
Any other Mixed/Multiple ethnic background
Indian
Pakistani
Bangladeshi
Chinese
Any other Asian background
African
Caribbean
Any other Black/African/Caribbean background
Arab
Any other ethnic group

3. What is your relationship status?
   Single, Married/in a civil partnership, Widowed, Co-habiting, Separated/Divorced
4. How many children do you have?
   1. 0, 1, 2, 3, 4+
5. When were you first diagnosed with breast cancer? (MM/YY)
6. What stage was your breast cancer at diagnosis?
   Stage 1 (e.g. tumour was 2cm or smaller and had not spread to lymph nodes)
   Stage 2 (e.g. tumour was between 2-5cm and/or the lymph nodes in the armpit were affected)
   Stage 3 (tumour was over 5cm and may be attached to surrounding structures such as muscle or skin. The lymph nodes in the armpit were affected)
   Stage 4 (the cancer had spread to other parts of the body)
   Unsure
7. What type of cancer are you diagnosed with (continued)?
   1. Invasive **ductal** carcinoma (cancer that starts in the cells that line the milk duct in the breast/also referred to as invasive breast cancer no special type or not otherwise specified [NST/NOS])
   2. Invasive **lobular** carcinoma (cancer that starts in the cells in the milk producing glands/lobules)
   3. Other please specify
8. What treatment have your received for your breast cancer? Select all that apply.
   Lumpectomy (surgery to remove the cancerous lump)
   Single mastectomy (surgery to remove the whole breast)
   Double mastectomy (surgery to remove both breasts)
   Chemotherapy (the use of anti-cancer drugs to kill the cancer cells)
   Radiotherapy (the use of controlled radiation to kill cancer cells)
   Ovarian suppression or ablation (surgery or radiotherapy to stop the ovaries working
   Other (please specify)
9. When were you first prescribed hormone therapy? (MM/YY) (e.g. Tamoxifen, Letrozole, Anastrozole)
10. Which hormone therapy were you first prescribed: e.g. Tamoxifen, Letrozole etc

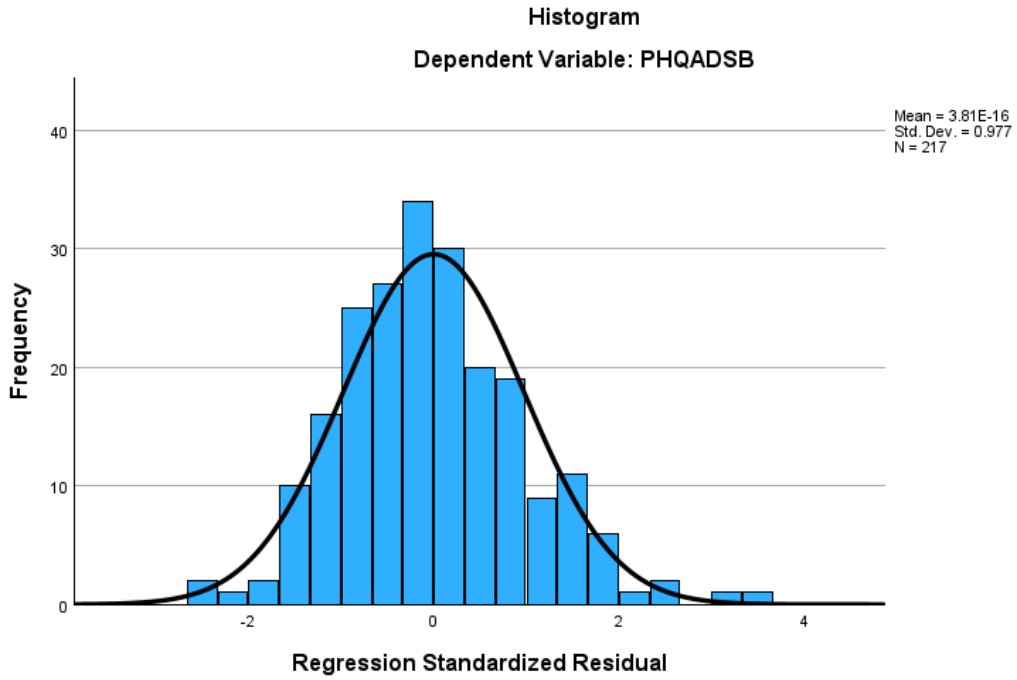
Table C2.

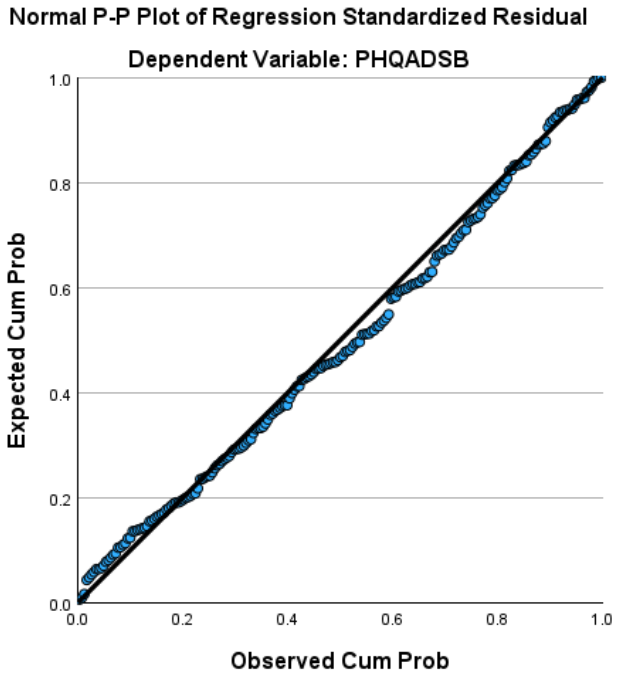
Full correlation matrix of psychological variables

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
1. Experiential avoidance	/																					
2. Cognitive fusion	.54**	/																				
3. Mindfulness	-.49**	-.62**	/																			
4. Self-as-context	-.45**	-.59**	.51**	/																		
5. Values progress	-.31**	-.35**	.28**	.53**	/																	
6. Values obstruction	.54**	.68**	-.60**	-.59**	-.41**	/																
7. Committed action	-.54**	-.54**	.53**	.64**	.61**	-.67**	/															
8. Self-compassion	-.49**	-.74**	.59**	.67**	.44**	-.65**	.60**	/														
9. Identity	0.11	.16**	-.22**	-.14*	-.02	.12	-.09	-.11	/													
10. Cure beliefs	-0.01	-.23**	.21**	.17**	.09	-.25**	.12	.21**	.00	/												
11. BC consequences	.33**	.50**	-.38**	-.40**	-.19**	.43**	-.32**	-.45**	.18**	-.34**	/											
12. HT consequences	.29**	.27**	-.31**	.27**	-.17**	.35**	-.30**	-.29**	.51**	-.10	.47**	/										
13. Recurrence	.21**	.39**	-.26**	-.25**	-.09	.29**	-.23**	-.29**	.10	-.39**	.37**	.19**	/									
14. Personal control	-.09	-.10	.06	.14*	.11	-.08	.16**	.09	-.01	.08	-.06	-.03	-.09	/								
15. Treatment control	-.15*	-.25**	.14*	.21**	.09	-.24**	.25**	.23**	-.00	.22**	-.13*	-.10	-.32**	.42**	/							
16. Coherence	-.23**	-.17**	.16**	.16**	.12	-.17**	.26**	.20**	.14*	.10	-.07	-.06	-.19**	.20**	.50**	/						
17. Emo reps	.45**	.62**	-.48**	-.45**	-.18**	.53**	-.40**	-.56**	.16**	-.30**	.58**	.34**	.50**	-.12	-.26**	-.16*	/					
18. Fear avoidance	.24**	.18**	-.15*	-.18**	-.13*	.20**	-.27**	-.22**	.20**	-.05	.18**	.26**	.17**	-.23**	-.26**	-.25**	.11	/				
19. Damage beliefs	.34**	.36**	-.29**	-.30**	-.17**	.29**	-.31**	-.32**	.14*	-.18**	.37**	.29**	.30**	-.06	-.27**	-.27**	.36**	.21**	/			
20. Embarrassment avoidance	.39**	.42**	-.44**	-.44**	-.27**	.44**	-.45**	-.51**	.31**	-.16**	.46**	.49**	.25**	-.10	-.15*	-.21	.40**	.35**	.47**	/		
21. Symptom focusing	.39**	.45**	-.44**	-.37**	-.21**	.41**	-.41**	-.41**	.29**	-.13*	.49**	.56**	.26**	-.01	-.08	-.13*	.45**	.30**	.45**	.65**	/	
22. All or nothing behaviour	.25**	.28**	-.32**	-.20**	-.12*	.25**	-.24**	-.29**	.29**	-.06	.30**	.29**	.14*	.04	.02	-.04	.24**	.19**	.20**	.43**	.45**	/
23. Resting behaviour	.19**	-.20**	-.20**	-.14*	-.15*	.18**	-.27**	-.14*	.10	-.09	.28**	.25**	.17**	-.03	-.08	-.17**	.22**	.17**	.19**	.31**	.34**	.39**

Figure C3.

Assumptions for cross-sectional hierarchical regressions (Model 1: ACT processes)





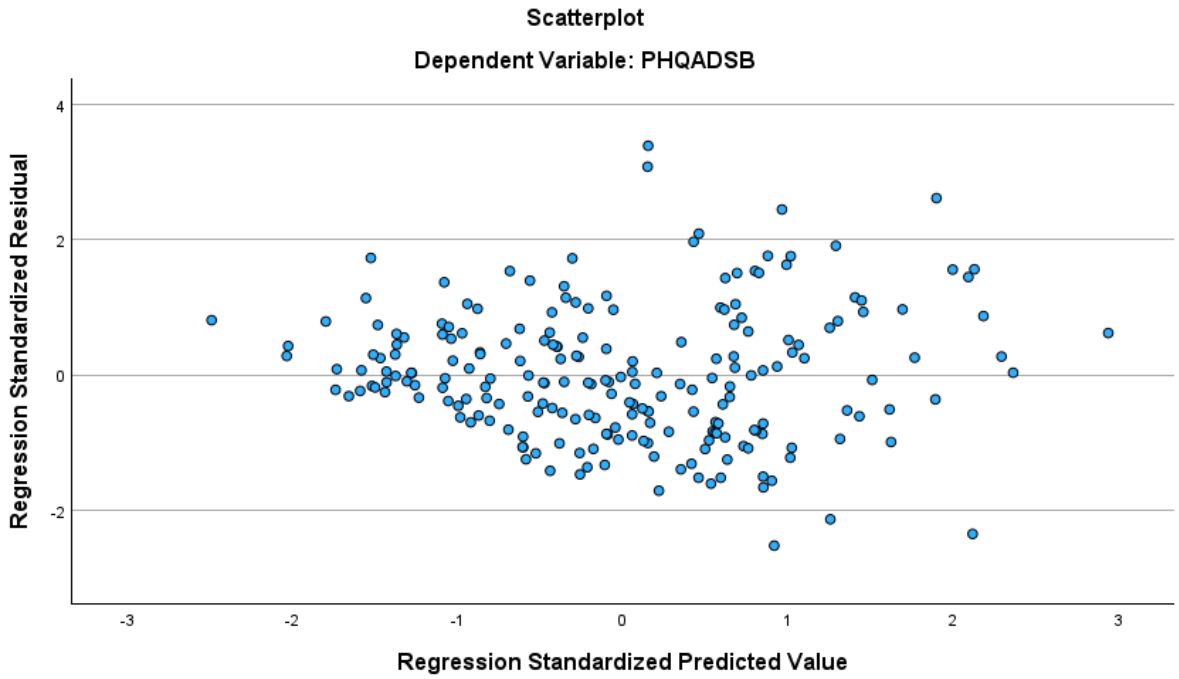
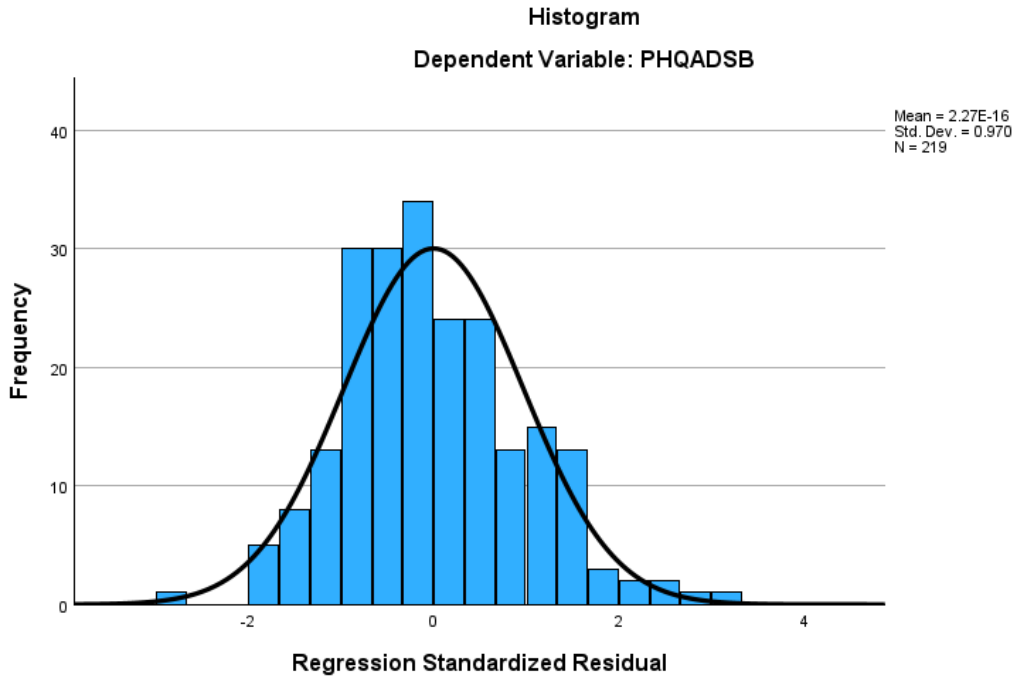
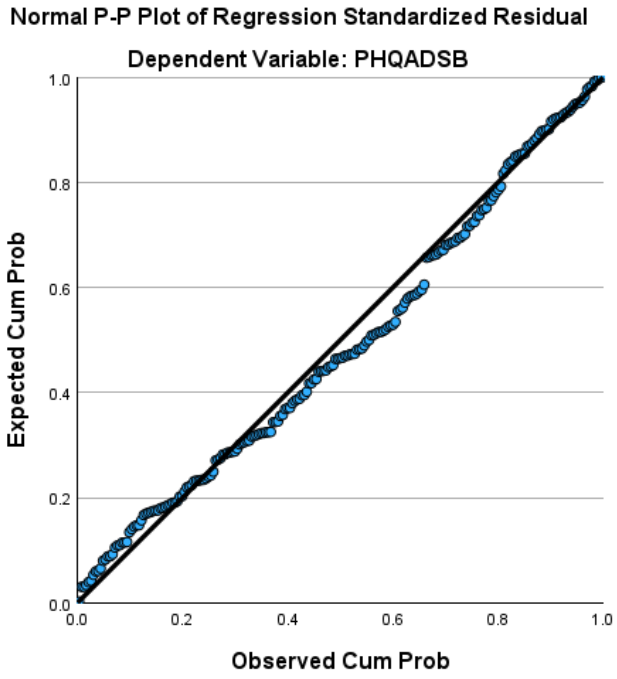


Figure C4.

Assumptions for cross-sectional hierarchical regressions (Model 2: CSM IP processes)




Normal P-P Plot of Regression Standardized Residual
Dependent Variable: PHQADSB
Expected Cum Prob
Observed Cum Prob
0.0
0.2
0.4
0.6
0.8
1.0

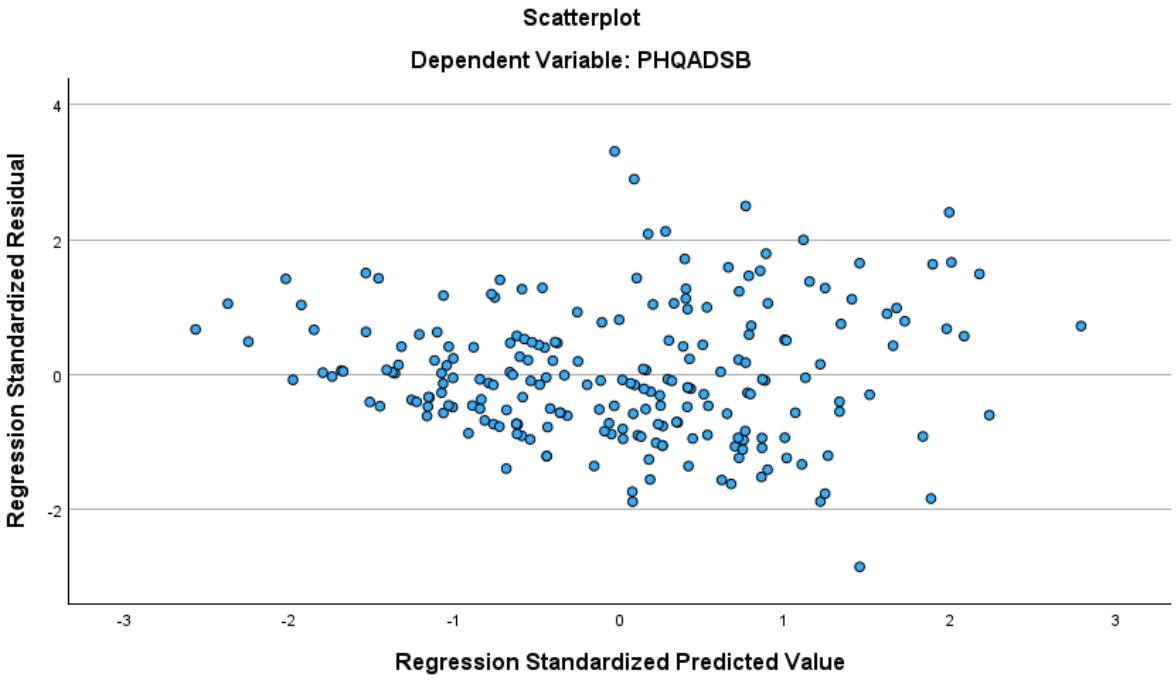
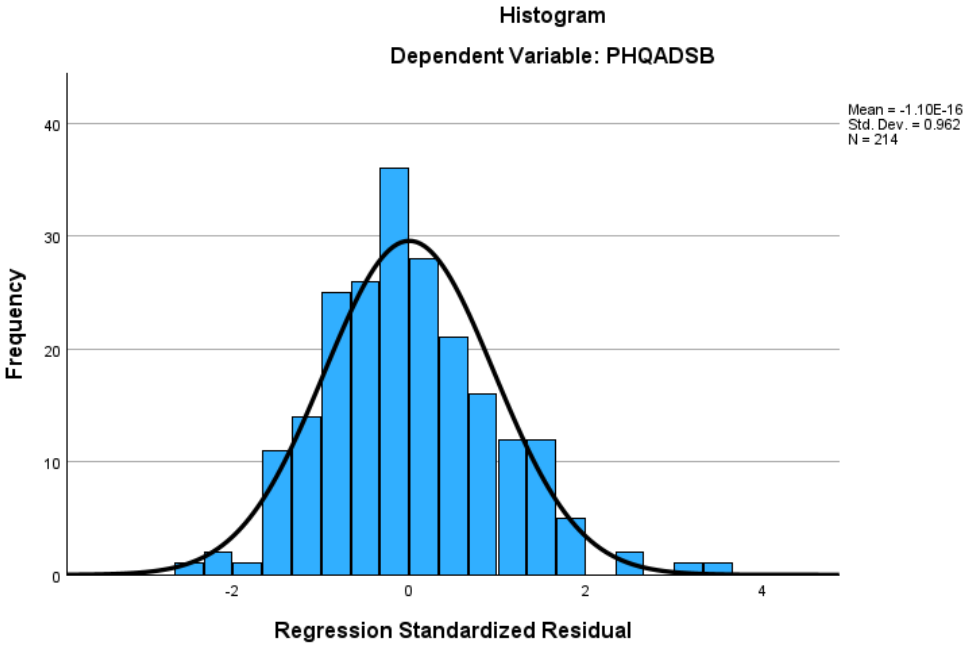
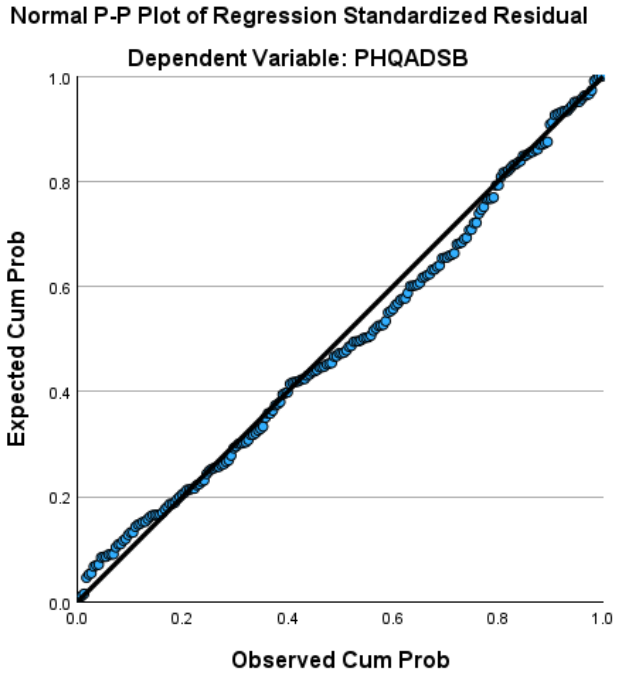

Scatterplot
Dependent Variable: PHQADSB
Regression Standardized Residual
Regression Standardized Predicted Value
4
2
0
-2
-3
-2
-1
0
1
2
3

Figure C5.

Assumptions for cross-sectional hierarchical regressions (Model 3: all significant CB processes)





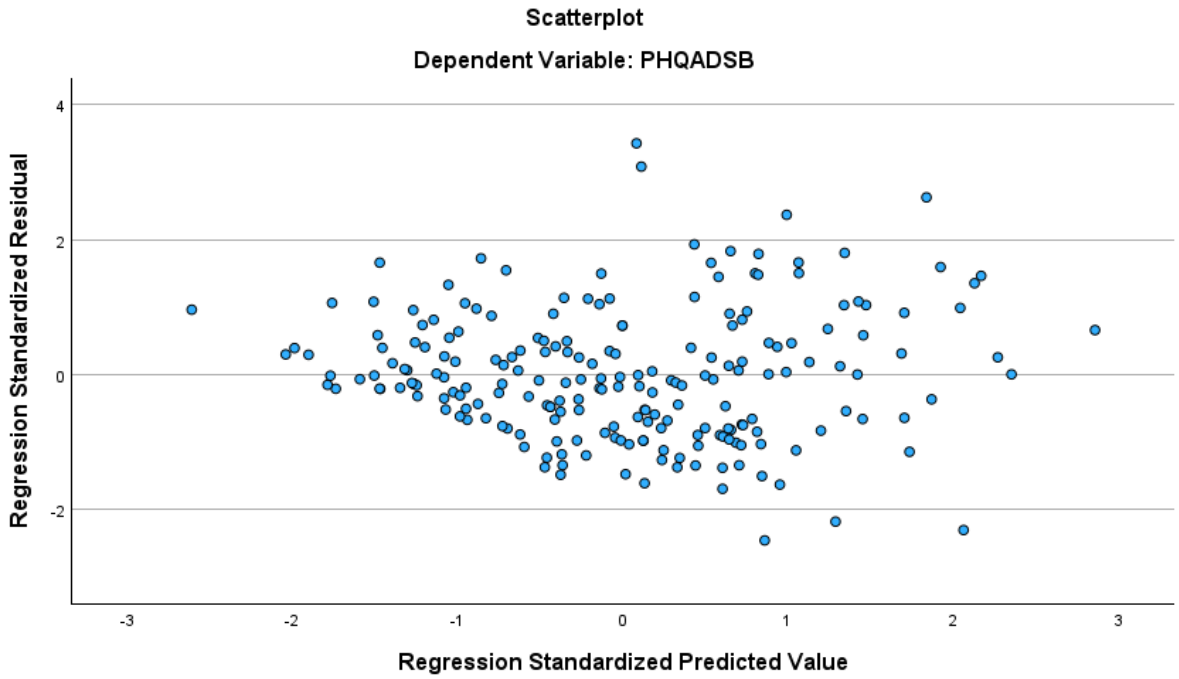


Table C6:

Correlations between psychosocial variables at baseline and distress and symptom burden at 12 months (using pooled estimates across 50 imputed datasets)

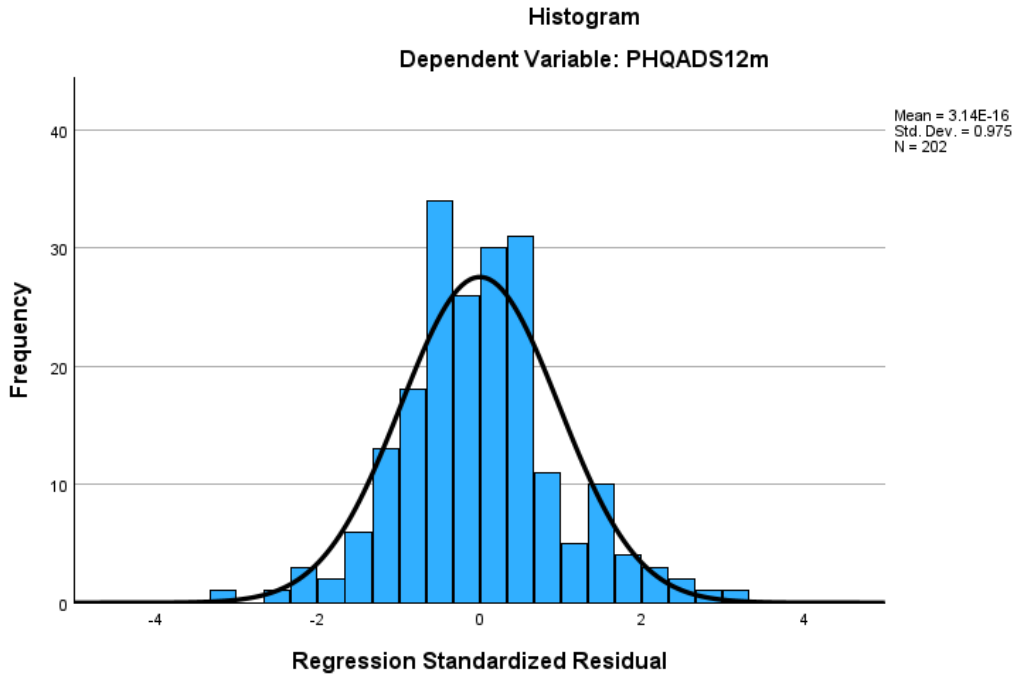
	Correlation with distress at 12 months (PHQ-ADS)
Demographics and clinical factors at baseline	
Age	-.23**
Partner (yes/no)	-.06
Number of children	.16*
Tumour type (lobular/ductal)	-.01
HT type (AIs/tamoxifen)	.06
Months on HT	.12
Chemo (yes/no)	-.01
Outcomes at baseline	
Distress (PHQ-ADS)	.65**
COVID distress	.34**
Quality of life overall	-.56**
Physical wellbeing	-.49**
Functional wellbeing	-.46**
Social wellbeing	-.25**
Emotional wellbeing	-.53**
Symptom burden	.47**
ACT processes at baseline	

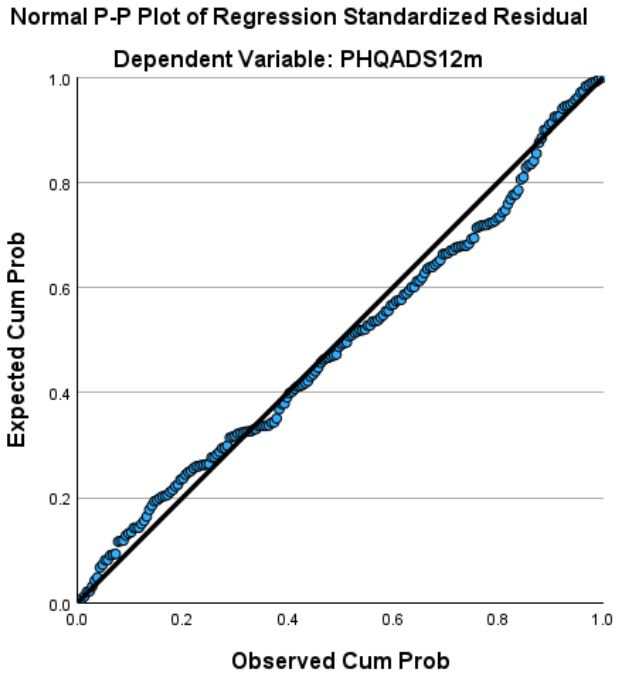
Experiential avoidance	.42**
Cognitive fusion	.53**
Mindfulness	-.46**
Self-as-context	-.45**
Values progress	-.21**
Values obstruction	.42**
Committed action	-.36**
Self-compassion	-.40**
Illness perceptions at baseline	
Identity (symptoms attributed to HT)	.23**
Cure beliefs	-.13*
Breast cancer consequences	.37**
Hormone therapy consequences	.24**
Recurrence	.29**
Personal control	-.17**
Treatment control	-.20**
Coherence	-.20**
Emotional representations	.41**
Cognitive behavioural responses at baseline	
CBRQ Total	.45**
Fear avoidance	.20**
Damage beliefs	.35**
Embarrassment avoidance	.42**
Symptom focusing	.37**
All or nothing behaviour	.23**
Resting behaviour	.24**

*Note: point biserial correlations are displayed for binary variables; HT: hormone therapy; AIs: aromatase inhibitors; SD: standard deviation; PHQ-ADS: patient health questionnaire anxiety and depression scale; BCPT: breast cancer prevention trial symptom list; ACT: acceptance and commitment therapy; CSM: common sense model; CBRQ: cognitive behavioural responses to symptoms questionnaire; significance levels: *** p < 0.001,** p < 0.01, * p < 0.05; ACT: acceptance and commitment therapy; CSM: common sense model*

Figure C7.

Assumptions for longitudinal hierarchical regressions (Model 4: ACT processes)





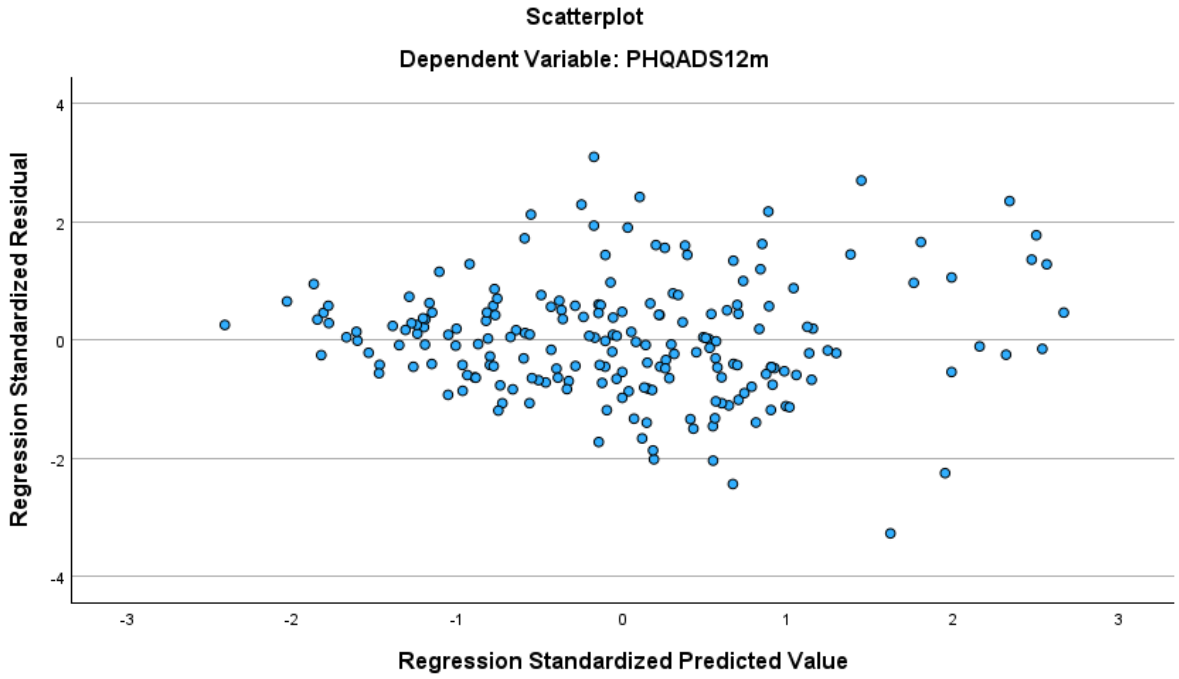
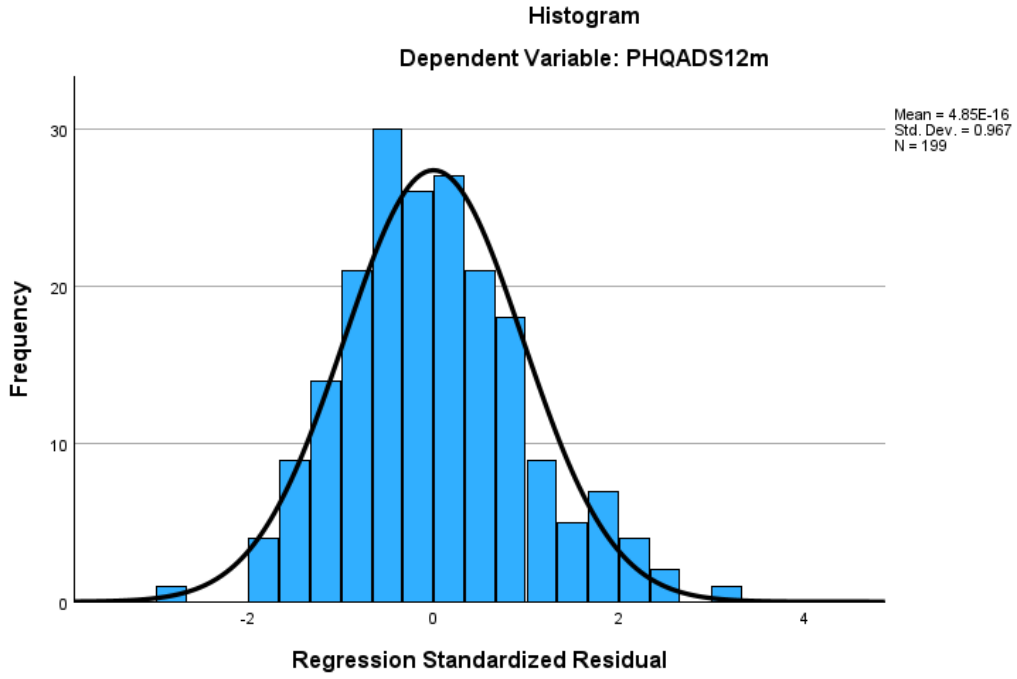
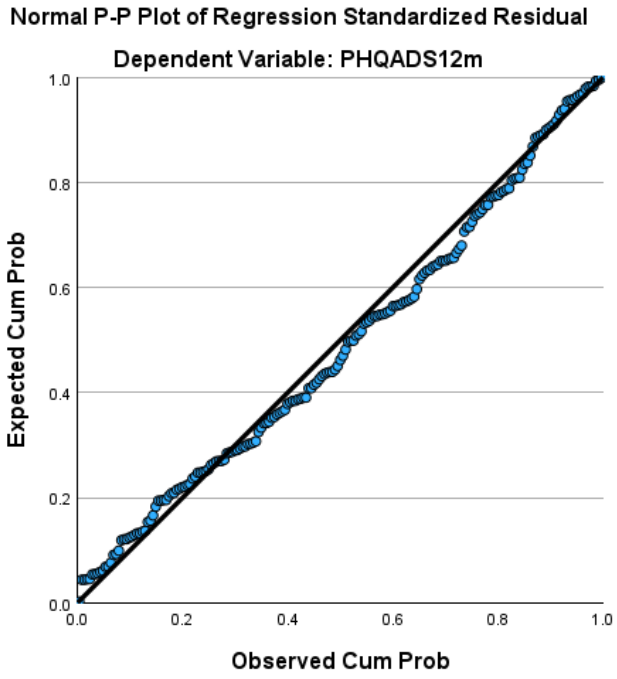


Figure C8.

Assumptions for longitudinal hierarchical regressions (Model 5: CSM processes)




Normal P-P Plot of Regression Standardized Residual
Dependent Variable: PHQADS12m
Expected Cum Prob
Observed Cum Prob
0.0
0.2
0.4
0.6
0.8
1.0

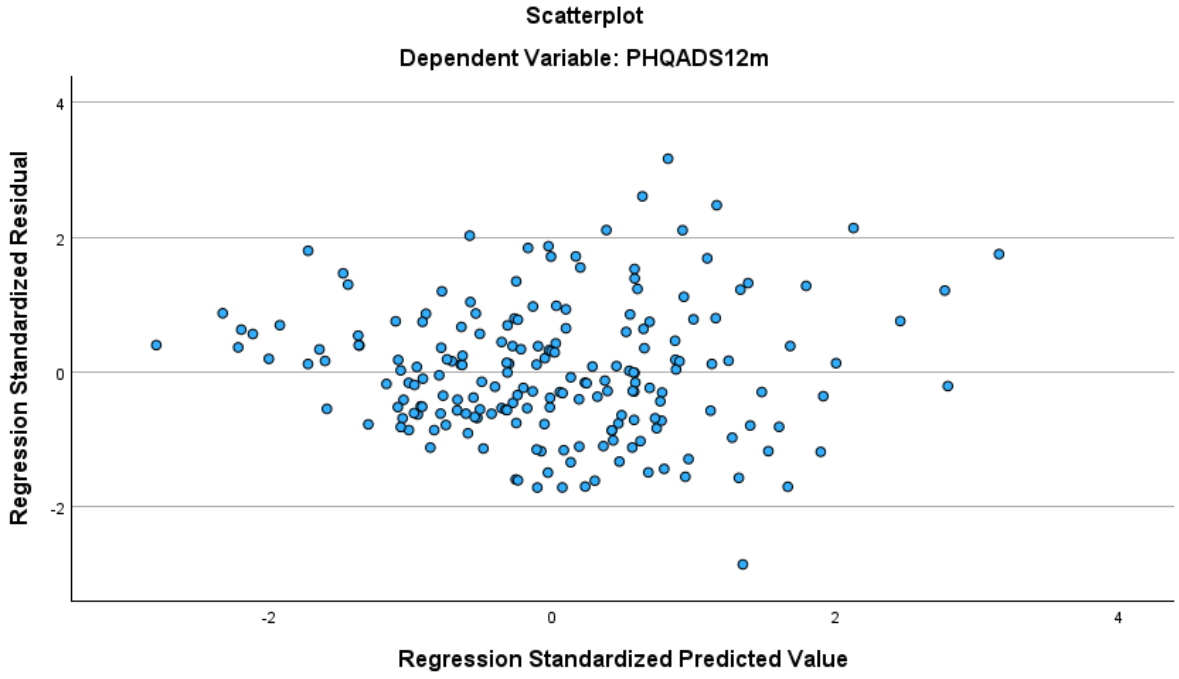
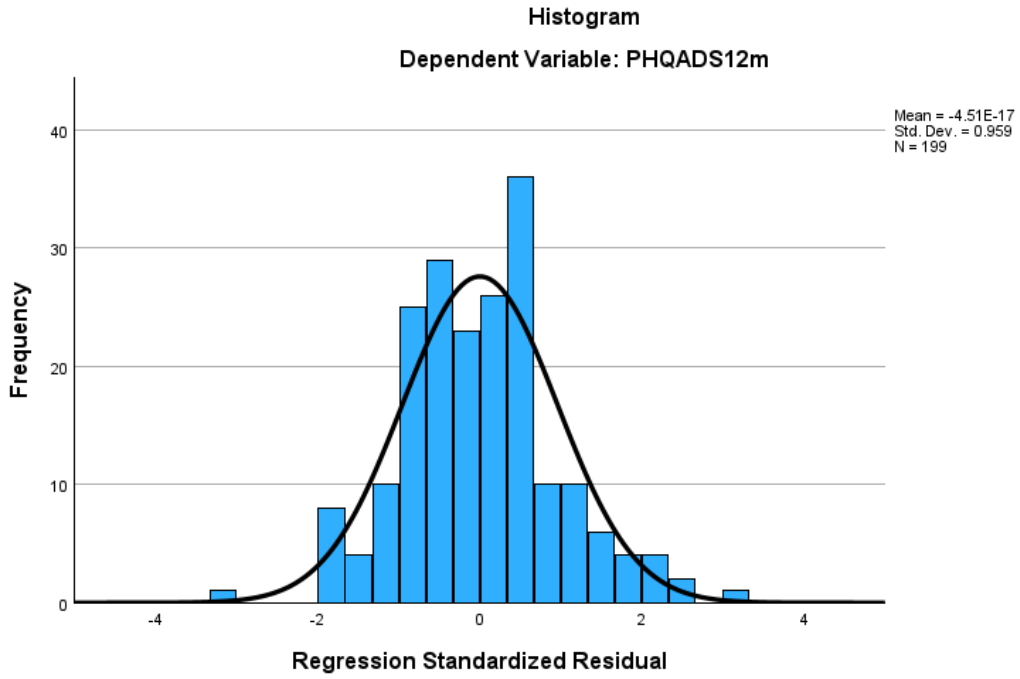
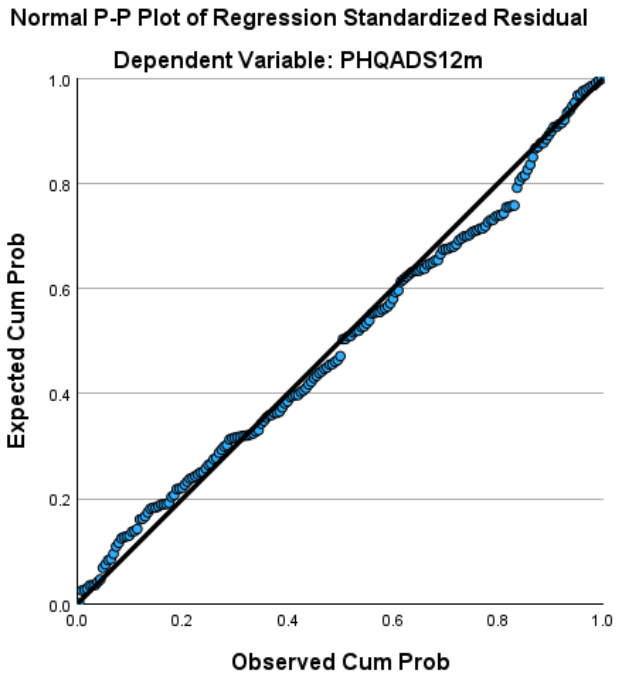

Scatterplot
Dependent Variable: PHQADS12m
Regression Standardized Residual
Regression Standardized Predicted Value
4
2
0
-2
-2
0
2
4

Figure C9.

Assumptions for longitudinal hierarchical regressions (Model 6: all cognitive-behavioural processes)





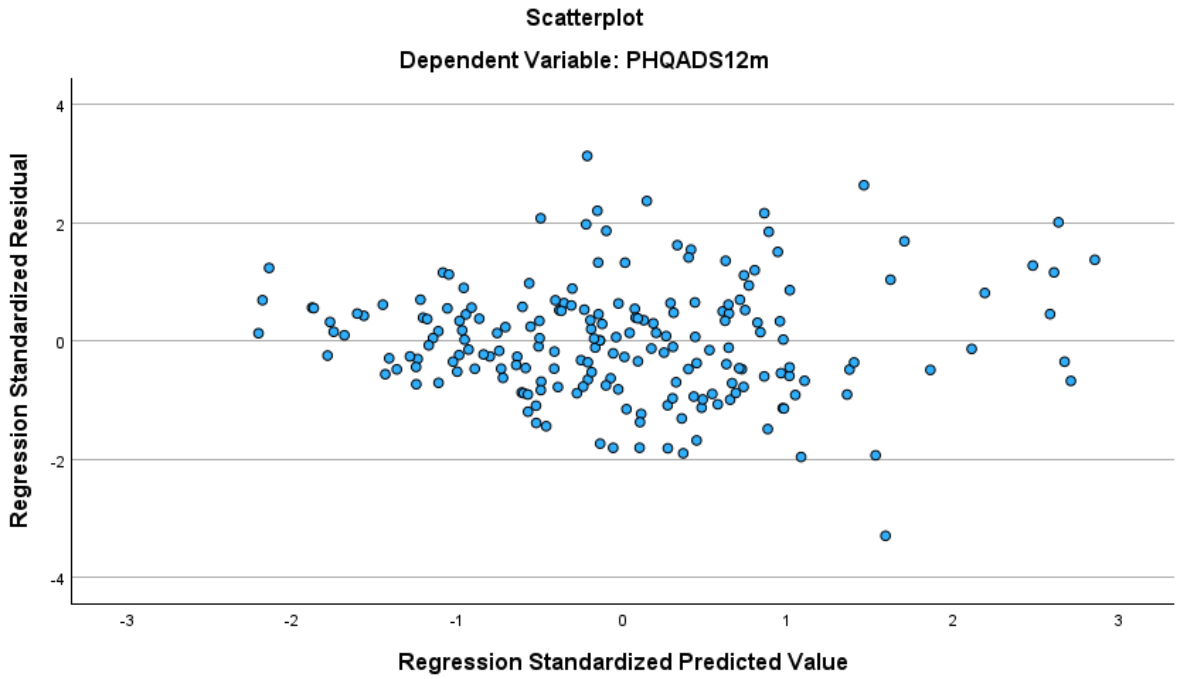


Table C10.

Multivariate hierarchical regression analyses for predicting distress at 12 months – beta coefficients reported for step 3 - sensitivity analysis table controlling for baseline distress

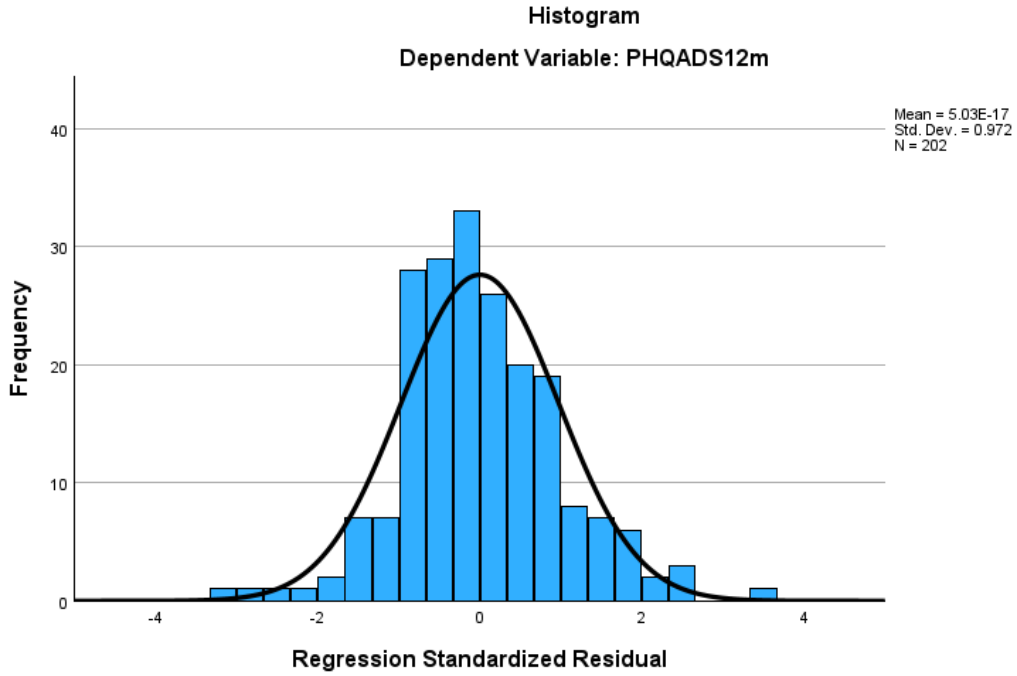
	Model 4a – ACT processes	Model 5a – CSM processes	Model 6a – process model
	β	β	β
Age	-0.07	-0.08	-0.08
Number of children	0.15**	0.15**	0.14**
COVID distress	-0.03	-0.01	-0.02
Baseline distress	0.43***	0.54***	0.42***
Symptom burden	0.11	0.15*	0.12
Experiential avoidance	0.02		0.00
Cognitive fusion	0.15		0.11
Mindfulness	-0.11		-0.13
Self-as-context	-0.06		-0.03
Values progress	-0.11		
Committed action	-0.00		0.06
Identity		0.09	
Cure beliefs		0.05	
Breast cancer consequences		0.08	-0.02
Hormone therapy consequences		-0.17*	
Recurrence		0.15*	0.10

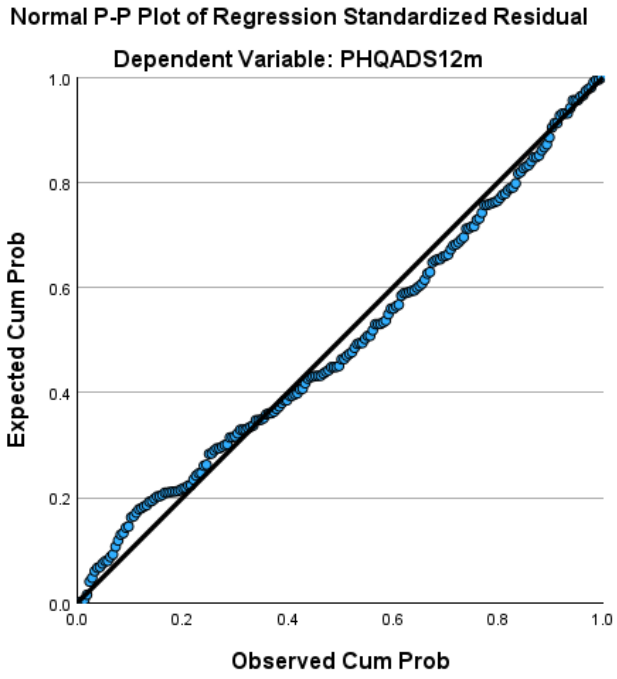
Personal control		-0.03	
Treatment control		0.01	
Coherence		-0.10	
Emotional representations		-0.02	-0.08
Damage beliefs			0.13*
Embarrassment avoidance			0.05
Symptom focusing			-0.04
Self-compassion			-0.03
Model statistics			
Step 1	*R^2 = 0.11, ΔR^2 = 0.10, F(2) = 12.60, p < .001*	*R^2 = 0.11, ΔR^2 = 0.10, F(2) = 12.33, p < .001*	*R^2 = 0.12, ΔR^2 = 0.11, F(2) = 12.98, p < .001*
Step 2	*R^2 = 0.49, ΔR^2 = 0.47, F(5) = 36.98, p < .001 R^2change = 0.37****	*R^2 = 0.50, ΔR^2 = 0.49, F(5) = 38.78, p < .001 R^2change = 0.39****	*R^2 = 0.48, ΔR^2 = 0.47, F(5) = 36.28, p < .001 R^2change = 0.37****
Step 3	*R^2 = 0.52, ΔR^2 = 0.50, F(11) = 19.01, p < .001 R^2change = 0.04**	*R^2 = 0.54, ΔR^2 = 0.51, F(14) = 15.60, p < .001 R^2change = 0.04*	*R^2 = 0.54, ΔR^2 = 0.50, F(17) = 12.66, p < .001 R^2change = 0.06**

*Note: Significance levels: *** p < .001,** p < .01, * p < .05; ACT: acceptance and commitment therapy; CSM: common sense model*

Figure C11.

Assumptions for longitudinal hierarchical regressions controlling for baseline (Model 4a: ACT processes)





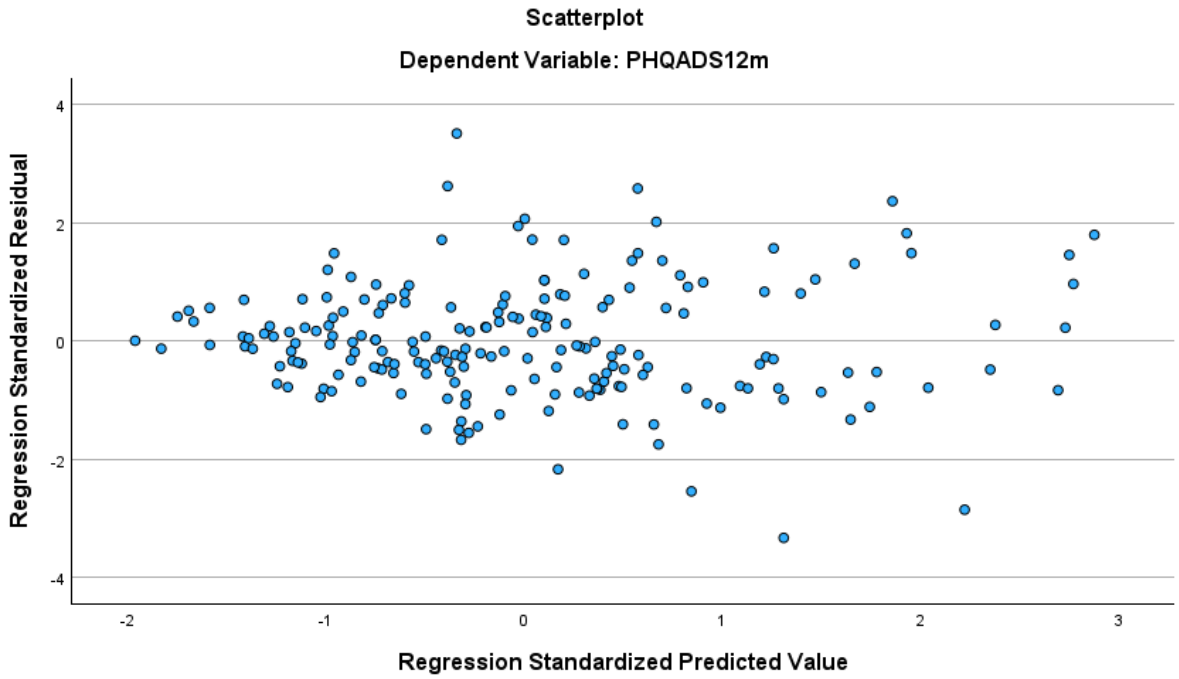
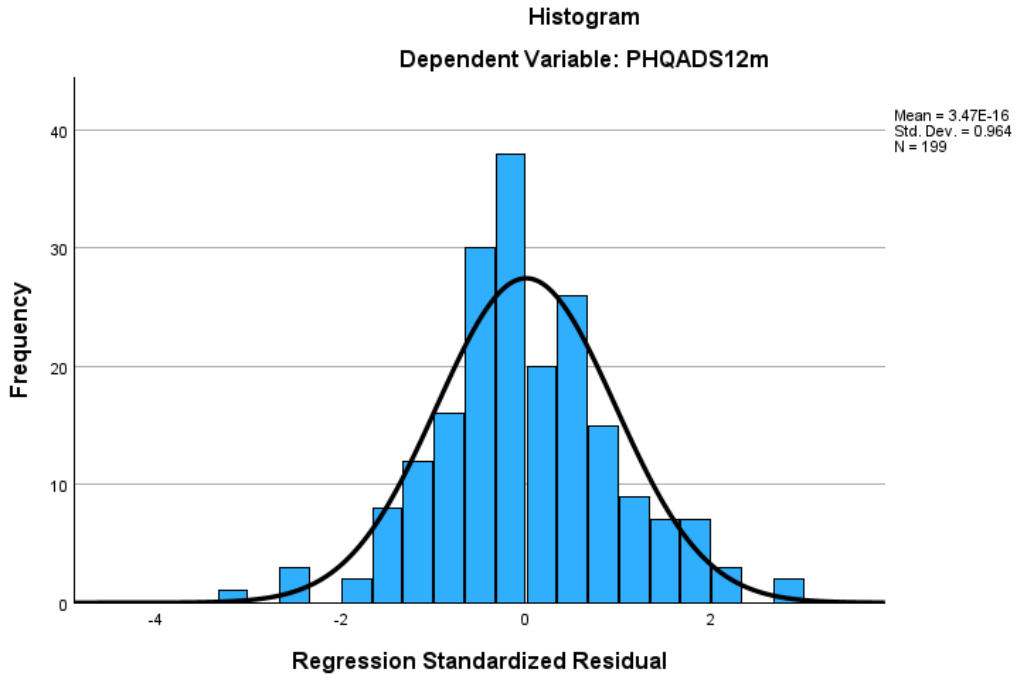
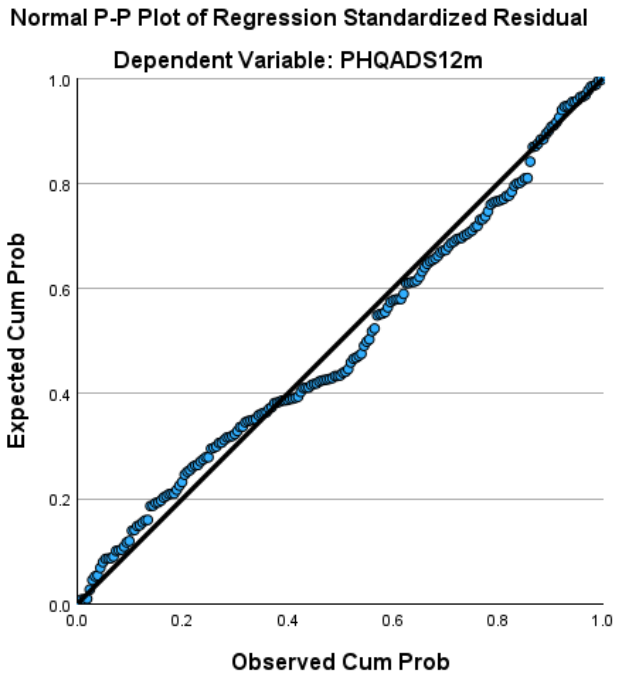


Figure C12.

Assumptions for longitudinal hierarchical regressions controlling for baseline (Model 5a: CSM processes)




Normal P-P Plot of Regression Standardized Residual
Dependent Variable: PHQADS12m
Expected Cum Prob
Observed Cum Prob
0.0
0.2
0.4
0.6
0.8
1.0

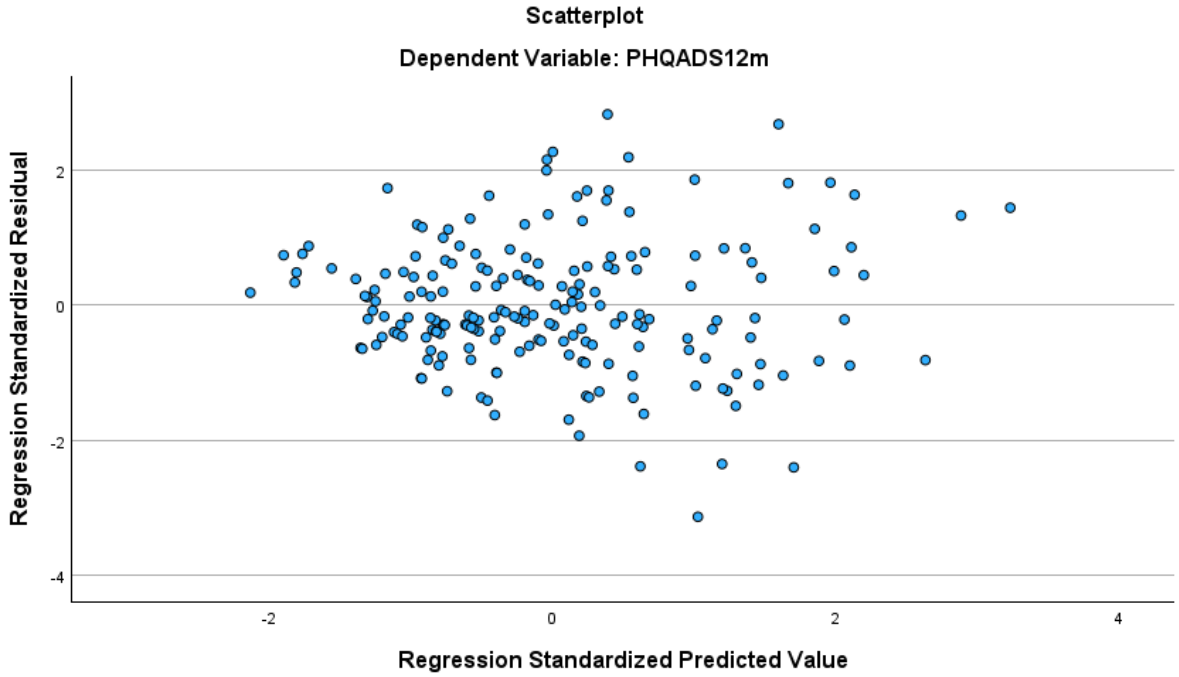
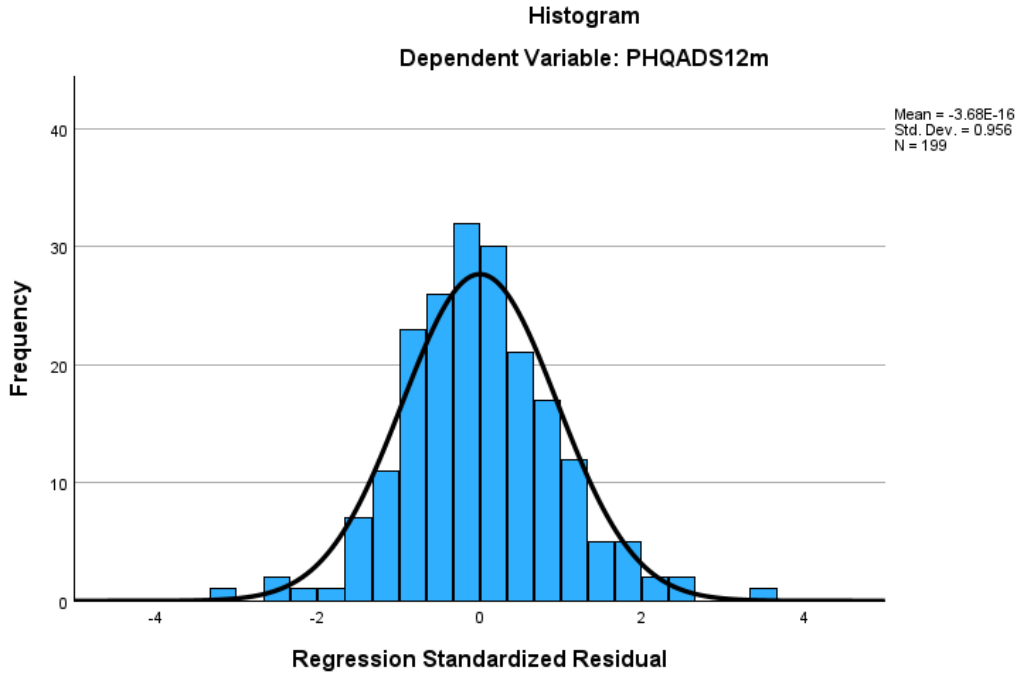
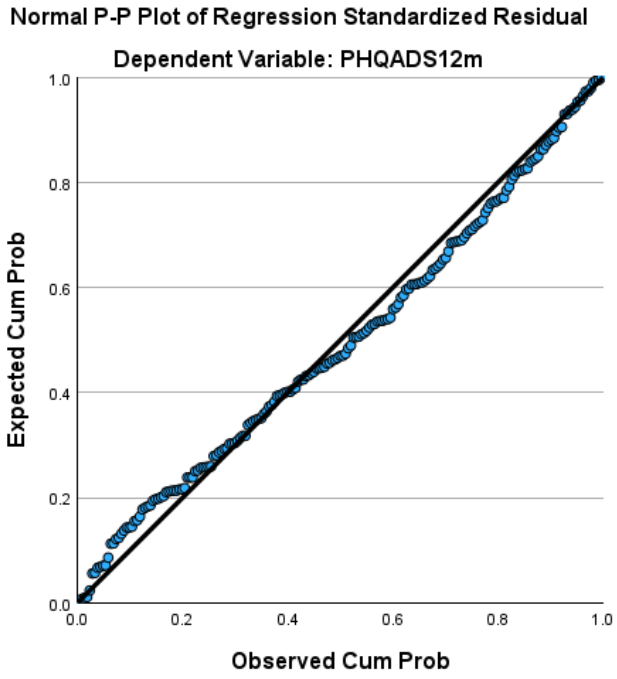

Scatterplot
Dependent Variable: PHQADS12m
Regression Standardized Residual
Regression Standardized Predicted Value
2
0
-2
-4
-2
0
2
4

Figure C13.

Assumptions for longitudinal hierarchical regressions controlling for baseline (Model 6a: all cognitive-behavioural processes)





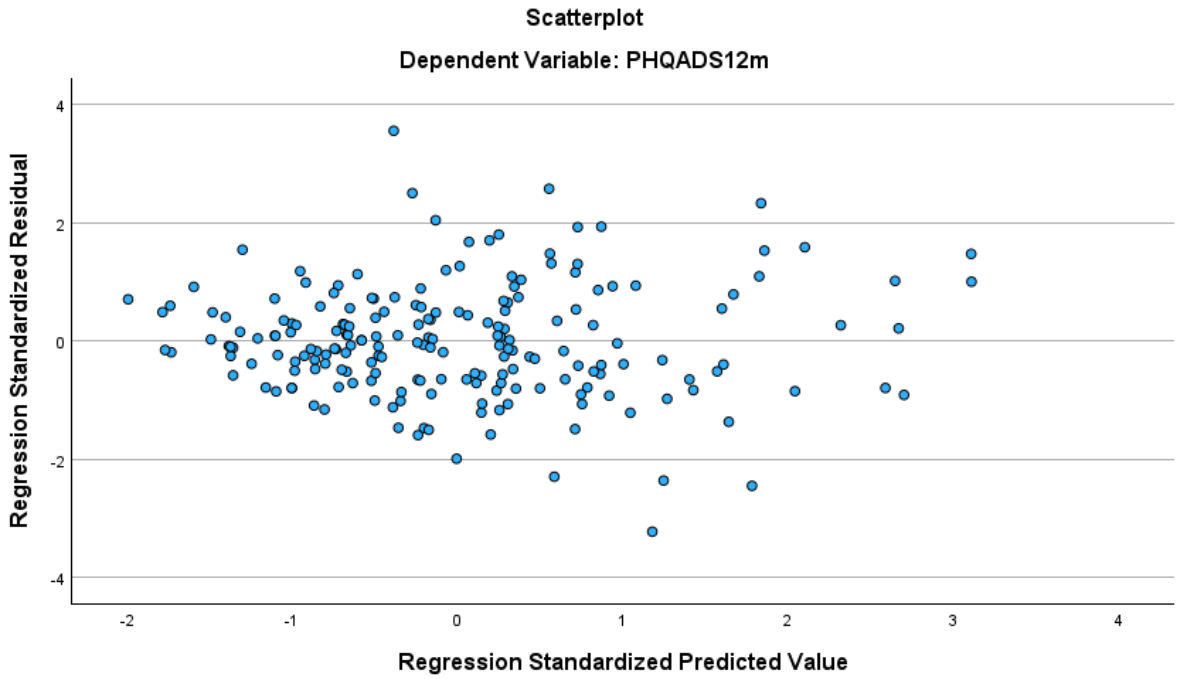


Table C14.

Multivariate hierarchical regression analyses for predicting distress at 12 months – standardised beta coefficients reported for step 3 – pooled estimates on 50 datasets

	Model 4MI – ACT processes	Model 5MI – CSM processes	Model 6MI – process model
	β	β	β
Age	-0.10	-0.11	-0.09
Number of children	0.15**	0.12*	0.14**
COVID distress	0.10	0.17**	0.10
Symptom burden	0.25***	0.36***	0.24***
Experiential avoidance	0.11		0.09
Cognitive fusion	0.25**		0.26**
Mindfulness	-0.11		-0.12
Self-as-context	-0.04		-0.02
Values progress	0.02		
Committed action	0.01		0.04
Identity		0.07	
Cure beliefs		0.02	
Breast cancer consequences		0.06	-0.04
Hormone therapy consequences		**-0.15**	
Recurrence		0.10	0.07
Personal control		-0.04	
Treatment control		0.02	
Coherence		**-0.13**	
Emotional representations		0.12	-0.03

Damage beliefs	0.09
Embarrassment avoidance	0.09
Symptom focusing	-0.03
Self-compassion	0.03

*Note: Significance levels: *** p < 0.001,** p < 0.01, * p < 0.05; ACT: acceptance and commitment therapy; CSM: common sense model*

Table C15.

Multivariate hierarchical regression analyses for predicting distress at 12 months controlling for baseline distress – standardised beta coefficients reported for step 3 – pooled estimates on 50 datasets

	Model 4MI – ACT processes	Model 5MI – CSM processes	Model 6MI – process model
	β	β	β
Age	-0.10	-0.10	-0.10
Number of children	0.12*	0.12*	0.12*
COVID distress	0.00	0.00	0.01
Baseline distress	0.47***	0.56***	0.47***
Symptom burden	**0.12**	**0.15**	**0.12**
Experiential avoidance	0.06		0.04
Cognitive fusion	0.12		0.11
Mindfulness	-0.07		-0.08
Self-as-context	-0.04		-0.02
Values progress	0.06		
Committed action	0.01		0.06
Identity		0.07	
Cure beliefs		0.03	
Breast cancer consequences		0.03	-0.06
Hormone therapy consequences		**-0.12**	
Recurrence		0.12*	0.09
Personal control		0.02	
Treatment control		0.01	
Coherence		-0.08	
Emotional representations		0.00	-0.05
Damage beliefs			**0.10**
Embarrassment avoidance			0.06
Symptom focusing			-0.02
Self-compassion			0.03

*Note: Significance levels: *** p < 0.001,** p < 0.01, * p < 0.05; ACT: acceptance and commitment therapy; CSM: common sense model*

Appendix D: Longitudinal study (Chapter 7)

Table D1.

Mediation analysis on imputed data for hypothesised mediators (50 datasets)

		β	SE	P value	95% CI
Cognitive fusion (CF)					
Direct effects	Symptoms to CF (a1)	0.24***	0.06	<.001	0.13, 0.35
	CF to distress (b2)	0.37***	0.06	<.001	0.26, 0.48
	Symptoms to distress (c')	0.31***	0.05	<.001	0.20, 0.41
Indirect effect	a1xb2	0.09***	0.02	<.001	0.04, 0.14
Total effect	(c)	0.40***	0.05	<.001	0.29, 0.50
Values obstruction (ValO)					
Direct effects	Symptoms to ValO (a1)	0.32***	0.06	<.001	0.21, 0.43
	ValO to distress (b2)	0.30***	0.06	<.001	0.19, 0.41
	Symptoms to distress (c')	0.30***	0.05	<.001	0.20, 0.41
Indirect effect	a1xb2	0.10***	0.03	<.001	0.05, 0.14
Total effect	(c)	0.40***	0.05	<.001	0.30, 0.50
Hormone therapy consequences (HT)					
Direct effects	Symptoms to HT (a1)	0.52***	0.05	<.001	0.43, 0.62
	HT to distress (b2)	0.06	0.07	.387	-0.07, 0.19
	Symptoms to distress (c')	0.36***	0.06	<.001	0.24, 0.49
Indirect effect	a1xb2	0.03	0.04	.389	-0.04, 0.10
Total effect	(c)	0.39***	0.05	<.001	0.29, 0.50
Symptom focusing (SF)					
Direct effects	Symptoms to SF (a1)	0.32***	0.06	<.001	0.20, 0.43
	SF to distress (b2)	0.18**	0.06	.002	0.07, 0.30
	Symptoms to distress (c')	0.34***	0.06	<.001	0.23, 0.44
Indirect effect	a1xb2	0.06**	0.02	.007	0.02, 0.10
Total effect	(c)	0.39***	0.05	<.001	0.29, 0.49

*Note: all path models controlling for age, COVID-19 distress and number of children; CF: cognitive fusion; ValO: values obstruction; HT: hormone therapy consequences; SF: symptom focusing; β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Table D2.

Mediation analysis on imputed data for exploratory mediators (50 datasets)

		β	SE	P value	95% CI
Embarrassment avoidance					
Direct effects	Symptoms to EA (a1)	0.29***	0.06	<.001	0.18, 0.40
	EA to distress (b2)	0.21**	0.06	.001	0.08, 0.33
	Symptoms to distress (c')	0.33***	0.06	<.001	0.22, 0.44
Indirect effect	a1xb2	0.06**	0.02	.006	0.02, 0.10
Total effect	(c)	0.39***	0.05	<.001	0.28, 0.49
Breast cancer consequences					
Direct effects	Symptoms to BC (a1)	0.33***	0.06	<.001	0.22, 0.44
	BC to distress (b2)	0.18**	0.06	.004	0.06, 0.31
	Symptoms to distress (c')	0.33***	0.06	<.001	0.22, 0.44
Indirect effect	a1xb2	0.06**	0.02	.009	0.02, 0.11
Total effect	(c)	0.39***	0.05	<.001	0.29, 0.49

*Note: all path models controlling for age, COVID distress and number of children; EA: embarrassment avoidance; BC: breast cancer consequences; β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Table D3.

Sensitivity analysis of moderators using imputed data; pooled estimates on 50 datasets

	β	SE	P value	95% CI
Coherence (hormone treatment)				
Age	-0.13**	0.05	.006	-0.23, -0.04
Covid distress	0.03	0.06	.581	-0.08, 0.14
Child	0.10*	0.05	.048	0.001, 0.20
Baseline distress	0.50***	0.06	<.001	0.39, 0.62
Symptom burden	0.16**	0.06	.005	0.05, 0.27
Coherence	0.13	0.13	.315	-0.12, 0.37
Symptom burden X coherence	-0.22	0.13	.085	-0.47, 0.03
Damage beliefs				
Age	-0.12	0.05	.010	-0.21, -0.03
Covid distress	0.01	0.05	.892	-0.10, 0.11
Child	0.12	0.05	.014	0.02, 0.21
Baseline distress	0.47	0.06	<.001	0.36, 0.59
Symptom burden	0.16	0.05	.002	0.06, 0.27
Damage beliefs	-0.01	0.11	.927	-0.22, 0.20
Symptom burden X damage beliefs	0.21	0.11	.058	-0.01, 0.42
Self-as-context				
Age	-0.11*	0.05	.021	-0.21, -0.02
Covid distress	0.02	0.06	.733	-0.09, 0.13
Child	0.11*	0.05	.026	0.01, 0.20
Baseline distress	0.48***	0.06	<.001	0.35, 0.60

Symptom burden	0.16**	0.06	.005	0.05, 0.27
Self-as-context	-0.07	0.12	.586	-0.31, 0.18
Symptom burden X self-as-context	-0.04	0.12	.740	-0.28, 0.20
Values progress				
Age	-0.13**	0.05	.006	-0.23, -0.04
Covid distress	0.03	0.06	.624	-0.09, 0.14
Child	0.11*	0.05	.024	0.02, 0.21
Baseline distress	0.52***	0.06	<.001	0.39, 0.64
Symptom burden	0.18**	0.06	.002	0.07, 0.29
Values progress	0.05	0.12	.686	-0.19, 0.29
Symptom burden X values progress	-0.03	0.13	.825	-0.28, 0.22
Committed action				
Age	-0.13**	0.05	.007	-0.23, -0.04
Covid distress	0.03	0.06	.654	-0.09, 0.14
Child	0.11*	0.05	.026	0.01, 0.21
Baseline distress	0.49***	0.07	<.001	0.37, 0.62
Symptom burden	0.17**	0.06	.003	0.06, 0.29
Committed action	-0.00	0.12	.975	-0.24, 0.23
Symptom burden X committed action	-0.04	0.12	.775	-0.27, 0.20
Recurrence beliefs				
Age	-0.12*	0.05	.016	-0.22, -0.02
Covid distress	0.02	0.06	.778	-0.10, 0.13
Child	0.11*	0.05	.029	0.01, 0.20
Baseline distress	0.50***	0.06	<.001	0.37, 0.62
Symptom burden	0.17**	0.06	.004	0.05, 0.28
Recurrence beliefs	0.07	0.13	.573	-0.17, 0.32
Symptom burden X recurrence beliefs	0.06	0.13	.639	-0.19, 0.31
Personal control				
Age	-0.13**	0.05	.007	-0.23, -0.04
Covid distress	0.03	0.06	.639	-0.09, 0.14
Child	0.10*	0.05	.047	0.00, 0.20
Baseline distress	0.52***	0.06	<.001	0.40, 0.64
Symptom burden	0.16**	0.06	.004	0.05, 0.28
Personal control	0.01	0.13	.970	-0.25, 0.26
Symptom burden X personal control	-0.04	0.13	.765	-0.30, 0.22
Treatment control				
Age	-0.13**	0.05	.008	-0.23, -0.03
Covid distress	0.02	0.06	.752	-0.10, 0.13
Child	0.10	0.05	.054	-0.00, 0.19
Baseline distress	0.52***	0.06	<.001	0.40, 0.64
Symptom burden	0.16**	0.06	.005	0.05, 0.28
Treatment control	-0.05	0.13	.708	-0.30, 0.20
Symptom burden X treatment control	-0.01	0.13	.922	-0.27, 0.25
All or nothing				
Age	-0.12*	0.05	.012	-0.22, -0.03
Covid distress	0.03	0.06	.610	-0.08, 0.14
Child	0.10*	0.05	.039	0.01, 0.20

Baseline distress	0.52***	0.06	<.001	0.40, 0.64
Symptom burden	0.16**	0.06	.010	0.04, 0.28
All or nothing	-0.03	0.11	.819	-0.24, 0.19
Symptom burden X all or nothing	0.11	0.11	.324	-0.11, 0.33
Resting				
Age	-0.13**	0.05	.008	-0.23, -0.04
Covid distress	0.03	0.06	.570	-0.08, 0.15
Child	0.11*	0.05	.029	0.01, 0.21
Baseline distress	0.51***	0.06	<.001	0.38, 0.63
Symptom burden	0.16**	0.06	.007	0.04, 0.27
Resting	0.01	0.11	.905	-0.21, 0.24
Symptom burden X resting	0.05	0.11	.633	-0.17, 0.28

*Note: β: standardised betas; SE: standard error; CI: confidence interval; * = p <.05, ** = p < .01, *** = p < .001*

Table D4.

Low, average and high values of moderators on the effect of symptom-distress

	β	SE	*p*	95% CI
Coherence				
Low	0.191***	0.053	< .001	0.077, 0.287
Average	0.102**	0.038	.007	0.028, 0.177
High	0.014	0.049	.776	-0.083, 0.112
Damage beliefs				
Low	0.035	0.041	.396	-0.049, 0.114
Average	0.099**	0.037	.008	0.025, 0.170
High	0.164***	0.051	.001	0.059, 0.261
Self-as-context				
Low	0.125	0.069	.071	-0.007, 0.264
Average	0.097*	0.043	.023	0.014, 0.179
High	0.069	0.044	.123	-0.023, 0.150
Values progress				
Low	0.12	0.07	.099	-0.02, 0.25
Average	0.11*	0.04	.015	0.02, 0.19
High	0.10*	0.05	.032	0.01, 0.19
Committed action				
Low	0.13*	0.06	.030	0.01, 0.24
Average	0.11*	0.04	.011	0.03, 0.19
High	0.08	0.05	.060	-0.01, 0.17
Recurrence beliefs				
Low	0.08	0.05	.072	-0.00, 0.17
Average	0.10**	0.04	.009	0.03, 0.18
High	0.13*	0.06	.025	0.01, 0.24
Personal control				

Low	0.11	0.06	.087	-0.02, 0.23
Average	0.11**	0.04	.009	0.03, 0.19
High	0.11*	0.05	.031	0.02, 0.21
Treatment control				
Low	0.11	0.06	.060	0.00, 0.24
Average	0.11**	0.04	.009	0.02, 0.17
High	0.10	0.05	.054	0.00, 0.21
All or nothing				
Low	0.06	0.04	.158	-0.02, 0.15
Average	0.09*	0.04	.022	0.01, 0.17
High	0.12*	0.06	.027	0.01, 0.24
Resting				
Low	0.08	0.05	.102	-0.01, 0.19
Average	0.10*	0.04	.014	0.02, 0.18
High	0.11*	0.06	.049	0.00, 0.23