Grant Agreement no. 777167

BOUNCE

Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back

Research and Innovation Action
SC1-PM-17-2017: Personalised computer models and in-silico systems for well-being

Deliverable: D2.4

Data-validated conceptual model of the role of resilience and resilience correlates in efficient adaptation to breast cancer

(*HUJ*, Report, M50)

Due date of deliverable: (12-31-2021)
Actual submission date: (1-02-2022)

Start date of Project: 01 November 2017 Duration: 48 months
Responsible WP: Hebrew University of Jerusalem (HUJI)

The research leading to these results has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 777167		
Dissemination level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission Service)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (excluding the Commission Services)	

0. Document Info

0.1. Author

Author	Company	E-mail
Ruth Pat-Horenczyk	HUJI	ruth.pat-horenczyk@mail.huji.ac.il
Ilan Roziner	TAU/ HUJI	ilanr@tauex.tau.ac.il

0.2. Documents history

Document version #	Date	Change
V0.1	1/11/2021	Starting version, template
V0.2	6/01/2022	First complete draft
V0.3	7/01/2022	Integrated version (send to WP members)
V0.4	8/01/2022	Updated version (send PCP)
V0.5	8/01/2022	Updated version (send to project internal reviewers)
V0.6	19/01/2022	Signed off version (for approval to PMT members)
Sign off	01/02/2022	Approved Version to be submitted to EU

0.3. Document data

Keywords	Resilience, Trajectories, Quality of Life, Somatic Symptoms
Editor Address data	Name: Partner: HUJI Address: Phone: +972-522-384216 Fax: +972-25701437 E-mail:
Delivery date	

1. Table of Contents

2. Introduction

2.1. Resilience in the context of coping with breast cancer

In the context of coping with breast cancer, resilience is conceptualized in a threefold manner: as a *personal potential*, as a *process*, and as an *outcome*. The working definition of resilience suggested by BOUNCE partners is:

"Resilience is a conglomerate of dynamic self-regulatory capacities that allow to mobilize and use internal and external resources over time in the face of adversity in order to maintain or promote wellbeing. The construct of resilience is used in three ways: (a) Resilience as a personal capacity or potential; (b) Resilience as an adaptive coping process or change trajectory; (c) Resilience as an outcome of maintaining healthy functioning and subjective well-being despite exposure to adversity. All these three aspects need to be measured."

The first aspect of resilience, *resilience as a personal potential*, relates to individual differences (traits) that allow a person to successfully cope with adversities of illness and its treatment. First of all, this is trait resilience itself, and also related constructs such as coping self-efficacy, coping flexibility or mindfulness. The last aspect, *resilience as outcome*, refers to the ultimate outcomes of coping with the adversities, such as the levels of quality of life, psychological symptoms like depression and anxiety, affective state, and experienced somatic symptoms. The second aspect, *resilience as process*, refers to the different reactions and behaviors that occur in the period between exposure to stressful events (breast cancer diagnosis and treatment), that include temporary changes in the levels of outcome variables, as well as specific perceptions and behaviors employed in coping with stress, such as those captured by questionnaires of illness representations and cancer-related reactions. The work presented in this document attempts to shed light on different ways in which these three aspects of resilience interact in the process of coping with breast cancer.

2.2. Task 2.4 in the context of WP2

The following Table places the current task in the context of other tasks within WP2 of BOUNCE project.

Table 1

WP2 – Resilience Definition, Assessment & Impact

Workpackage number:	WP2	**Start date:**	M1
Activity Type:	Implementation	**End Date:**	M40

Project Acronym	BOUNCE	PP1	PP2	PP3	PP4	PP5	PP6	PP7	PP8	PP9	TOTAL
Project Type	RIA	HUS	FORTH	IEO	ICCS	NHG	HUJI	SiLo	CHAMP	NOONA	PARTNERS
WP2	Implementation	6	10	9	4	2	**12**	0	5	2	**50**

Objectives

- To construct a measurement model of patient resilience to the physical and emotional challenges associated with breast cancer and with the burden incurred by associated treatments using data from the multi-centre clinical pilot
- To construct a conceptual model of multi-scale factors affecting individual resilience trajectories through diagnosis and treatments for breast cancer
- To identify expected personal, social and financial benefits of increased resilience in women recovering from breast cancer
- To address long-standing issues in the field of psycho-oncology regarding the dynamics of time-varying relationships between determinants of resilience and disease outcomes.

Description of work

Task 2.1 Definition and assessment of resilience in women with Breast Cancer *(HUJ, M1 – M6)*

State of the art in the definition and suitable measures of resilience as a dynamic process critically involved in effective illness adaptation and recovery.

Task 2.2 Definition and assessment of multi-level factors potentially affecting resilience *(HUJ, Duration: M1 – M6)*

Definition of multi-scale factors related to the evolution of resilience, in relation to both constant (i.e., sociodemographic, personal characteristics) and time-varying patient characteristics, changes in social context, and other significant life circumstances.

Task 2.3 Individual and societal benefits of high levels of resilience *(HUJ, M37 – M40)*

Systematic exploration of expected benefits of (a) increased resilience for effective adaptation and recovery from breast cancer, and (b) reliable assessment of resilience trajectories on health care services and costs (e.g., Lower burden on primary and specialist care services and associated costs, reduced duration of sick leave, etc). This task requires input from WP6.

Task 2.4 Structural and conceptual models of multi-scale factors related to efficient adaptation to breast cancer through patient resilience *(HUJ, M37 – M40)*

Structural models will be developed at both measured and latent variable levels in order to address specific mediation and/or moderation hypotheses linking sociodemographic, psychological, cancer-related, life-style habits, and biological indices of disease activity to individual resilience levels and eventually to distinct long-term disease outcomes (clinical, well-being, functionality). Data from the clinical pilots (WP6) will be used to complete this task.

Deliverables

D2.1 Conceptual model of resilience (*HUJ*, Report, M6, PU).

D2.2 Conceptual model of factors affecting resilience trajectory (*HUJ*, Report, M6, PU).

D2.3 Aggregated benefits of point-increases in patient resilience (*HUJ*, Report, M40, PU).

D2.4 Data-validated conceptual model of the role of resilience and resilience correlates in efficient adaptation to breast cancer (*HUJ*, Report, M40, PU)

2.3. Structure of the document

The main aims of this document are to provide preliminary results of testing models of resilience in effective adaptation to breast cancer. We will present some results that are currently under preparation for publications, based on the three perspectives of resilience as traits, processes and outcomes. It should be noted that the analyses reported here tap into only a small portion of data collected in the framework of BOUNCE: only a part of measures collected during only a part of data collection waves (two to three waves out of the total of seven). These analyses are only a beginning of a long journey towards extracting the numerous and important insights into the processes of coping with breast cancer from the rich dataset acquired in BOUNCE.

In what follows, we present the research methodology common to analyses reported in this document, and then (in Section 3) we present the rationales and the results of assessing seven conceptual models related to different aspects of resilience. These models test the role of *resilience as personal potential* (trait resilience in Sections 3.1 and 5.1; coping flexibility in Section 3.2; coping self-efficacy in Sections 3.1, 3.3, and 3.6) and *resilience as process* (illness perceptions and coping behaviors in Sections 3.3 and 3.6) in determining *resilience outcomes* (overall quality of life in Sections 3.1, 3.3 and 3.5; psychological symptoms and emotional distress in Sections 3.1, 3.3, 3.4 and 3.7; somatic symptoms in Sections 3.2 and 3.4). It should be noted that the models presented below demonstrate the dynamic nature of resilience measures. Thus, coping self-efficacy, conceptualized as a personal potential variable, also served as a mediator (a process variable) in Section 3.1. Emotional distress, conceptualized as an outcome, was conceptualized as having an additional role of a determinant (a process variable) of somatic symptoms in Section 3.4. The different trajectories of change in an outcome variable, quality of life, effectively depict different processes of coping with illness (Section 3.5). The results in Section 3.6 show how coping self-efficacy, a personal potential variable, and coping

reactions, a process variable, switch roles in course of time feeding each other. The same role-switching is demonstrated in Section 3.7, where two outcome variables, psychological symptoms and somatic symptoms, feed each other across time.

2.4. Methods

2.4.1 Participants and procedure

The data were collected in the research project entitled "BOUNCE: Predicting effective adaptation to breast cancer to help women to bounce back" funded by Horizon 2020 as part of the innovation program. The data were collected in four major oncology centers in Finland, Israel, Italy and Portugal during the years 2019-2021. The research project included repeated assessment, using a time adjusted version of a battery of self-reported questionnaires, every three months from the breast cancer diagnosis, for a period of 18 months (with a total of 7 waves of assessment). The analyses reported here focused on part of the measures collected in the first five measurement waves: at the time of diagnosis (M0 or baseline), three months post-diagnosis (M3), six months post-diagnosis (M6), nine months post-diagnosis (M9), and twelve months post-diagnosis (M12).

The inclusion criteria were: age 40 to 70 at the time of recruitment, a diagnosis of an invasive early or locally advanced operable breast cancer in stages I, II and III, after surgery and before any systemic treatment such as chemotherapy, radiotherapy, antiHER2 treatment or hormonal therapy.

The research project received the approval of all ethical committees of the participating medical centers (Helsinki approvals for research on human subjects; Approval No R868/18-IEO916), and the protocol was registered in ClinicalTrials.gov (Identifier number: NCT05095675). The participants were introduced to the research upon their first visit at the medical center by the treating oncologists followed by thorough explanations by the affiliated

research assistants. The participants who consented to participate in the longitudinal study fill in research questionnaires through an internet platform (Noona platform or Qualtrics platform) or their printed version when the online version was not accessible.

The total number of participants in the four-site study was 706 (Finland n = 225, Israel n = 151, Italy n = 190, Portugal n = 140). Additional data regarding 58 younger Pts were collected by BOUNCE, but these are not analysed in the models presented below. In the analyses reported here, different subsets of these data were used, according to the ways researchers decided to deal with missing data. The background socio-demographic and medical data of the participants are presented in Table 2. The *N* in this Table is 702, as used in the analyses in Section 3.2, which is representative of the whole sample.

2.4.2 Measures

There were close to 30 variables that were assessed over seven points of measurement in three months intervals (see Appendix 1 for the full list of research instruments). The analyses reported below used a subset of these variables and up to five measurement waves.

First, we will present four models regarding resilience as a personal potential (trait resilience, self-efficacy to cope with cancer, coping flexibility, and mindfulness). Following this, we will focus on resilience as a process and resilience as outcome – presenting the various trajectories of quality of life and the mutual relationship between psychological and somatic symptoms. Sociodemographic and medical background data were employed in the analyses as controls / covariates.

Background data included country of residence, age, education, marital status, employment status, income level, and body mass index (BMI). In addition, medical data were obtained regarding having previous chronic illnesses, breast cancer characteristics – stage (1-3), grade (1-4), and its treatment: mastectomy, Anti-Her2, chemotherapy, radiotherapy and endocrine therapy.

Table 2

Participants' socio-demographic and disease related characteristics (N=702)

Characteristic	Distribution
Origin Country, *N (%)*	
Israel	147 (20.94%)
Italy	190 (27.7%)
Finland	225 (32.05%)
Portugal	140 (19.94%)
Age, mean (SD)	54.96, (8.21)
Marital Status, *N (%)*	
Married / Living with a partner	509 (73.9%)
Single / widow / separated	183 (26.1%)
Educational status, *N (%)*	
Primary school	14 (1.99%)
Secondary school	44 (6.27%)
High school	163 (23.22%)
Vocational non-academic diploma	72 (10.26%)
Bachelor degree	240 (34.19%)
Postgraduate education	169 (24.07%)
Employment Status at baseline, *N (%)*	
Employed full time	376 (53.6%)
Employed part time	58 (8.3%)
Housewife	54 (7.7%)
Retired	114 (16.2%)
Self employed	76 (10.8%)
Unemployed	22 (3.1%)
Income, N (%)	
Very low income	153 (21.8%)
Average or high income	507 (72.2%)
BMI, mean (SD)	25.66 (4.70)
Chronic illnesses, N (%)	
Yes	229 (32.6%)
No	473 (67.4%)
Cancer stage at baseline, N (%)	
Stage 1	335 (47.72%)
Stage 2	289 (41.17%)
Stage 3	78 (11.11%)
Grade, N (%)	
Grade 1	130 (18.52%)
Grade 2	364(51.85%)
Grade 3	207 (29.49%)
Grade 4	1 (0.14%)
Type of treatment, N (%)	
Mastectomy	195 (27.8%)
Lumpectomy	499 (71.1%)
AntiHer2	109 (15.5%)
Chemotherapy	344 (49%)
Radiotherapy	526 (74.9%)
Endocrine therapy	571 (81.3%)

Trait resilience was assessed at M0 with the 10-item version of the Connor-Davidson Resilience Scale (CD-RISC; Connor & Davidson, 2003; Campbell-Sills & Stein, 2007). Each

item (e.g., I am able to adapt to change) is rated on a 5-point Likert-type scale, ranging from 0 = not true at all, to 4 = true nearly all the time. The answers to all items were combined into a single score (Cronbach *a* = .91). Higher scores reflect greater resilience.

Self-efficacy to cope with cancer was assessed at M0 and M6 with the brief version of the Cancer Behaviour Inventory (CBI-B; Heitzmann et al., 2011). It consists of 12 items (e.g., Maintaining a positive attitude; asking physicians questions). Respondents used a 9-point Likert type scale, ranging from 1=not at all confident, to 9=totally confident. A single overall score was produced (Cronbach *a*=.89). Higher scores indicate higher levels of coping self-efficacy.

Coping flexibility was assessed at M0 with PACT – Perceived ability to Cope with Trauma Scale Questionnaire (Bonanno et al., 2011), with its data collected at the study baseline. This is a 20- item questionnaire that assesses the individual's perceived ability to flexibly use two groups of coping strategies: Forward Focus assessed with 12 items (e.g. "the ability to focus on goals and plans") and Trauma Focus assessed with 8 items (e.g. "experiencing the emotional and cognitive of the traumatic event"), accompanied by a 7-point Likert scale ranging from 1 = "not at all able" to 7 "extremely able" the extent they were agreed with the statement. Higher scores reflect a higher flexible ability of coping. The internal consistency in the original sub scales was α =0.91 for the forward focus and α =0.79 for the trauma focus (Bonanno et al., 2011). The internal consistency in the current study was α = 0.91 for the forward focus and α = 0.76 for the trauma focus.

Mindfulness as a trait was assessed at M0 using the Mindful Attention Awareness Scale (MAAS, Brown & Ryan, 2003). Its 15 items (e.g., "I tend to walk quickly to get where I'm going without paying attention to what I experience along the way") are accompanied by a Likert scale ranging from 1 = "almost always" to 6 "almost never". The internal consistency in the present sample was α = 0.86.

Illness representations of control. Two items from the Brief Illness Perception Questionnaire (Broadbent et al., 2006) were used to assess patients' representations of control over their health condition at M3. They were asked to reply to the following questions using a Likert-type scale ranging from 0 (Not at all) to 10 (Very much/very well): "How much control do you feel you have over your illness", which assesses a sense of personal control; "How much do you think your treatment can help your illness", which assesses the personal evaluation of the efficiency of treatment.

Coping with cancer. To assess coping with cancer, the Mini – Mental Adjustment to Cancer Scale (Watson et al., 1994) was used at M3 and M6. It consists of five dimensions of behavior: helplessness-hopelessness (eight items, e.g., "I feel like giving up"; Cronbach *a* = .87), anxious preoccupation (eight items, e.g., "I am upset about having cancer; I have difficulty in believing that this happened to me"; Cronbach *a* = .85), cognitive avoidance (four items, e.g., "I make a positive effort not to think about my illness"; Cronbach *a* = .81), fighting spirit (four items, e.g., "I try to fight this illness"; Cronbach *a* = .62), and fatalism (five items, e.g., "I have put myself in the hands of God"; Cronbach *a* = .51). Due to the very low Cronbach *a* of fatalism, this subscale was not included in the analyses. Participants were asked to indicate how much each item applies to them on a four-point Likert scale ranging from 'Definitely does not apply to me' to 'Definitely applies to me'.

Quality of life: The Global Health Status scale from the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire (Aaronson et al., 1993) was used to assess overall quality of life at five measurement waves, M0 through M12. It consists of two items examining patients' overall evaluation of their condition during the past week (e.g., "How would you rate your overall quality of life"; Cronbach's *a*=.86). A seven-point Likert type scale (1 = very poor; 7 = excellent) was used to answer these questions. A linear

transformation was used to standardize the raw scores, so as to range from 0 to 100, with higher scores indicating higher quality of life.

***Psychological symptoms**:* The Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) was used to assess psychological symptoms at three time-points, M0, M3, and M6. The scale consists of 14 items (e.g**.,** I feel tense or 'wound up'; I still enjoy the things I used to enjoy). To answer, respondents used a 4-point frequency Likert type scale with higher scores indicating more intense symptoms. Given the typically high correlation between anxiety and depression symptoms, answers to all items were added up to create an overall symptoms score (Cronbach's *a* = .89).

Somatic symptoms were measured at three timepoints (M0, M3, and M6) using a new variable of somatic symptoms selected from two well-known QoL questionnaires: The Quality of Life- QoL-C30 (EORTC) questionnaire (Aaronson et al., 1993) (items 1-5, 8-19) and The Quality of life- QoL-BR23 (EORTC-BR23) questionnaire (Groenvold et al., 1996) (items 1-7, 17-23), summing up to 31 items (e.g., "Do you have any trouble taking a short walk outside of the house?"; "Have you had pain?"). All 31 items were scored on a 4-point Likert scale ranging from 1 "not at all' to 4 "very much". Higher level reflects more reported somatic symptoms. The internal consistency of these 31 items was α = 0.92 (at M0), α = 0.91 (M3), α = 0.92 (M6).

Positive and negative affect was assessed with the 20-item version of the Positive and Negative Affectivity Schedule (PANAS, Watson & Tellegen, 1988) at three timepoints, M0, M3, and M6. It consists of adjectives, ten for negative affect (e.g., distressed; Cronbach *a* = .75) and ten for positive affect (e.g., interested, active; Cronbach *a* = .84). Participants were asked to indicate the extent to which they felt each feeling/emotion during the past week on a 5-point Likert type scale ranging from "Very slightly or not at all" to "Extremely".

2.4.3 Data Analyses

Scale reliabilities, descriptive statistics, intercorrelations, and multiple linear regression models were computed using SAS software, Version 9.4 (SAS Institute Inc.) or IBM SPSS Statistics, Version 26 (IBM Corp.). Path models were assessed using Structural Equation Modeling (SEM) with Mplus Version 8.6 (Muthén & Muthén, 1998-2017). Multi-item scales were specified in such models as latent constructs, each measured, relying on the accepted approach of parcelling (Little et al., 2013), with three indicators calculated as random thirds of the scale items. Participants' sociodemographic and medical characteristics were modelled as observed variables. In models involving multiple measurements of the same construct, variance resulting from specific measurement occurrences was accounted for by correlating all the measurement errors of same indicators across time points (Marsh & Hau, 1996). To assure weak factorial invariance, factor loadings were constrained for equality across measurement waves. As there were missing values in the data, and the data deviated from normality, we used the Mplus MLR estimator that allows for maximum likelihood estimation with robust standard errors and chi-square calculation in presence of missing values (Little & Rubin, 2003). Following recommendations of Hu and Bentler (1999), we report two fit indexes: Tucker-Lewis Index (TLI) and Comparative Fit Index (CFI), and two indexes of misfit: Root Mean-Square Error of Approximation (RMSEA) and Standardised Root Mean-Square Residual (SRMR) are reported. TLI and CFI close to or above 0.95, combined with RMSEA below 0.06 and SRMR below 0.08, are considered indicative of acceptable fit.

3. Data-validated conceptual models

3.1. Resilience as a potential: Trait resilience and coping self-efficacy as determinants of quality of life and psychological symptoms

The analyses and the results in this section are based upon Karademas et al. (under review). Resilience, defined in this context as a trait individual characteristic, can be a significant predictor of quality of life and psychological distress (e.g., Harms et al., 2019; Min et al., 2013). Although not many relevant studies have been conducted in breast cancer patients, there is evidence that resilience may be also related to their well-being (Markovitz et al., 2015; Tu et al., 2020). This study tested the role that trait resilience, measured at baseline, soon after diagnosis with cancer, has in determining the quality of life and psychological symptoms measured three months later, at the time that is probably the peak of adverse effects of breast cancer treatment. Self-efficacy to cope with cancer refers to the perceived ability to perform behaviors that are important for dealing with relevant challenges and it has been found to be negatively related to symptoms of anxiety, depression, and fatigue, and positively to quality of life, across a variety of cancer diagnoses (e.g., Chirico et al., 2017; Heitzmann et al., 2011; Philip et al., 2013). The current analyses were designed to examine whether coping self-efficacy mediates the relation of resilience to the outcomes. It was hypothesized that trait resilience, as the general ability to adapt to a difficult situation and maintain good function (Johnston et al., 2015; Windle, 2011), would enhance a personal sense of efficacy to perform those behaviors that would lead to a successful adaptation to cancer. In turn, this would be related to better quality of life and less psychological symptoms (e.g., Albrecht et al., 2013). Trait resilience and coping self-efficacy were measured at M0, while the outcomes were measured at M3.

Results

The distributions and correlations between all variables are presented in Table 3. Trait resilience and self-efficacy to cope with cancer are highly correlated. Psychological symptoms at the 3-

month follow up were significantly associated with both of these variables, in a negative way. Also, overall quality of life at follow-up was positively, but more weakly, associated with both resilience and self-efficacy to cope with cancer. Mediation analyses (performed with the PROCESS macro of SPSS) revealed a statistically significant mediation effect of coping with cancer self-efficacy on the relation of resilience to quality of life (B=3.86, SE=1.20; 95% Confidence Intervals (CI)=1.65/6.41), after controlling for covariates. The mediation effect of self-efficacy on the relation of resilience to psychological symptoms was also significant (B=-.12, *SE*=.03; 95% CI=-.18/-.06). The associations between resilience, coping with cancer self-efficacy and outcomes did not vary significantly with country of origin (on either the pathway from the independent variable to the mediator or the pathway from the mediator to the dependent variable; Bs<3.90, *SE*s>.25, *t*s<1.56; 95% CI=-8.83/9.13, for quality of life, and Bs<.18, *SE*s>.06, *t*s<.69; 95% CI=-.45/.68, for psychological symptoms).

Table 3

Descriptive Statistics and Intercorrelations of Trait Resilience, Self-efficacy to Cope with Cancer, Overall Quality of Life (QoL), and Psychological Symptoms (N = 484)

	Mean	*SD*	Correlations (Pearson's *r*)			
			1	2	3	4
1. Trait resilience (M0)	2.79	.68	--			
2. Coping self-efficacy (M0)	7.11	1.29	.57*	--		
3. Overall QoL (M3)	68.46	20.88	.18*	.27*	--	
4. Psych. symptoms (M3)	.70	.49	-.36*	-.43*	-.58*	--

* $p < .001$

Implications

As hypothesized, trait resilience was related to less psychological symptoms and higher levels of overall quality of life, with self-efficacy to cope with cancer serving as a mediator of this

relationship. Our findings indicate that the general sense of personal efficiency may be translated into a more situation-specific perception of being able to cope with cancer and, through this, to enhanced well-being. This relationship provides us with further information about the potential pathways through which resilience can affect patients' well-being.

3.2 Resilience as a potential: The moderating role of coping flexibility in determining somatic symptoms

The analyses and the results in this section are based upon Dahabre et al (2022). The analyses presented here aimed at filling the gap of knowledge on the importance of coping flexibility as measured by PACT (Bonanno et al., 2011) in persistence of somatic symptoms that play a central role in determining the quality of life (QoL) of breast cancer patients. PACT, an individual-difference measure, is comprised of two scales assessing the extent of use of coping strategies in two directions: Forward focus and Trauma focus. The Forward focus subscale refers to the ability to look forward the trauma while focusing on the current goals and plans, using distractions, and caring for others. The Trauma focus subscale refers to the ability to temporarily focus on the trauma details and emotional reaction associated with the potential trauma event. In the context of BOUNCE project, coping flexibility is conceptualized as an individual-difference characteristic that can create greater resilience in coping with adverse consequences of the illness and its treatment. Several studies indicated that higher levels of coping flexibility may enhance the positive and effective adaption among patients facing medical illness (e.g., Hamama-Raz et al., 2018; Kato et al., 2021; Rudnik et al., 2019). The present model aimed to test the moderating role of both trauma- and forward-focused coping strategies measured at baseline on the relationship between the severity of somatic symptoms measured at two time points: three months and six months post breast cancer diagnosis. This

approach allowed for testing the effects of coping flexibility upon the change in reported somatic symptoms across time.

Results

The descriptive statistics and intercorrelations between the research variables appear in Table 4. The average of somatic symptoms at three months post diagnosis is the highest compared to somatic symptoms at baseline and at six months ($p < .001$, paired-samples *t*-tests). The PACT scores were very weekly correlated with the symptoms at all waves of data collection. The somatic symptoms at baseline were significantly correlated with somatic symptoms reported at three months and six months. In addition, the somatic symptoms at three months were significantly correlated with somatic symptoms at six months. In spite of the relative stability of the reported symptoms, the correlations magnitude left room for the possibility of their attenuation by third variables, i.e., the PACT measures.

Table 4

Descriptive statistics and intercorrelations of coping flexibility (Forward Focus and Trauma Focus), somatic symptoms at baseline, at 3 months, and at 6 months

Variable	Mean	SD	1	2	3	4
1. Forward focused coping	5.15	1.02	--			
2. Trauma focused coping	5.32	0.84	.66**	--		
3. Somatic symptoms M0	1.47	0.36	-.12**	-.11*	--	
4. Somatic symptoms M3	1.68	0.41	-.08**	-.04	-.57**	--
5. Somatic symptoms M6	1.59	0.38	-.10*	-.05	.053	.72**

* $p < .05$ ** $p < .01$

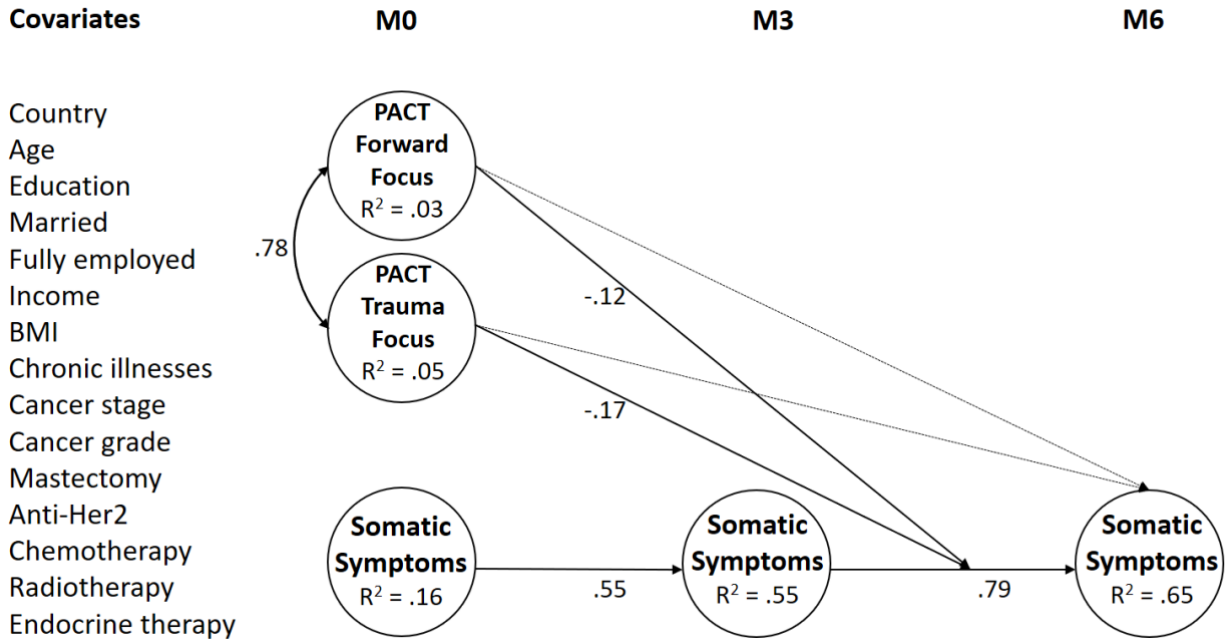
As a first step in the assessment of theoretical moderation model, we tested the hypothesized measurement model. The model fitted well to the data, with $\chi^2(75) = 140.90$, $p < 0.001$, TLI = 0.99, CFI = 0.99, RMSEA = 0.04 (90% CI = 0.03; 0.04), SRMR = .03. As the next step, we estimated the structural model. In addition to the theoretically meaningful paths depicted in Figure 1, this model included paths leading from each of the background variables to each of the main research variables. This model also fitted well to the data, $\chi^2(245) = 417.37$, $p < 0.001$, TLI = 0.98, CFI = 0.97, RMSEA = 0.03 (90% CI = 0.03; 0.04), SRMR = .04. At the final step, the interaction terms were added to the model one by one and both were found as statistically significant ($p < .01$) and negative (Figure 2). Interestingly, both main effects of PACT sub-scales were not statistically significant in this model. The negative sign of the interaction term coefficients implies offsetting (buffering) interaction effect: Higher levels of PACT are associated with weaker relationship between somatic symptoms related to physical QoL at M3 and its value at M6.

Implications

A possible interpretation of the moderation results is that women with higher coping flexibility may have more openness and perhaps more "degrees of freedom" for change in their somatic complaints during this critical period in treatment. It should be noted that the buffering of the strong association between somatic symptoms can manifest in change of symptoms or severity of the somatic symptoms. Any change may be perceived as a potential for further change and more response/ amenability for treatment. The results of this study contribute to the theory of the role the coping strategies have in coping with life threatening illness. In particular, how the focus on the nuances of coping and coping flexibility can contribute to breast cancer resilience and subsequently, to improved quality of their lives.

Figure 1

Moderating effects of PACT scales upon somatic symptoms temporal stability: *Standardized paths in the SEModel*



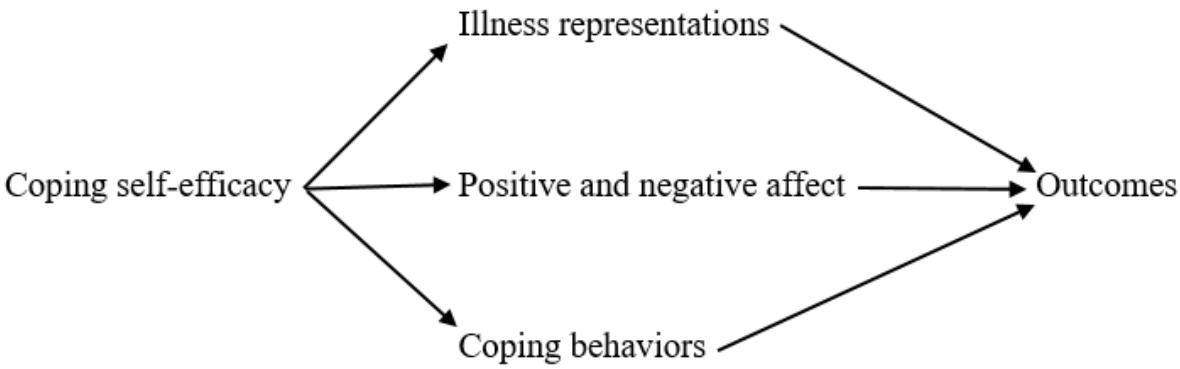
3.3 Resilience as a potential: Cognitive, emotional, and behavioural mediators

The analyses and the results in this section are based upon Karademas et al. (2021). It has been shown in Section 3.1 that self-efficacy to cope with cancer as measured at baseline was predictive of psychological symptoms and overall quality of life three months later, serving as the mediator of a closely related concept, trait resilience. While these, as well as other findings (e.g., Brandão et al., 2017; Henselmans et al., 2010; Raque-Bogdan, 2019), showcase the central role of coping self-efficacy in the process of adaptation to cancer, to the best of our knowledge, the exact pathways through which coping self-efficacy is linked to well-being have not been examined systematically. Thus, it is not yet clear how coping self-efficacy may impact adaptation to cancer. In light of the evidence that self-efficacy is strongly related to health-related behaviors, several cognitive processes such as illness representations, and emotion (e.g., Beckham et al., 1997; Lightsey et al, 2006; Schüz et al, 2012), we examined whether such

factors also mediate the relation of coping self-efficacy to breast cancer patients' well-being. Specifically, we examined whether illness representations of control (as a form of specific cognitive appraisals about breast cancer strongly related to adaptation and health-related outcomes), cancer-related coping behaviors, and positive and negative affect mediate the relation of self-efficacy to cope with cancer with psychological symptoms and global quality of life. The theoretical model is presented in Figure 2. Coping self-efficacy was measured at M0, the three mediators at M3, and the outcomes at M6.

Figure 2.

A schematic representation of the impact of coping self-efficacy on well-being outcomes (i.e., psychological symptoms, quality of life) through potential mediators.



Results

The correlations between coping self-efficacy, potential mediators, quality of life, and psychological symptoms are presented in Table 5. Coping self-efficacy was significantly correlated to all potential mediators. It was positively related to illness representations of control, positive affect, and fighting spirit (Pearson's *r*'s > .21, $p < .01$), and negatively to negative affect, helplessness, anxiety preoccupation, and avoidance (Pearson's *r*'s < -.22, *p*'s < .01). Coping self-efficacy was also negatively related to psychological symptoms, and positively to overall quality

of life (Pearson's r = -.43 and .23, respectively, $p < .01$). With the exception of fighting spirit, all other potential mediators were associated with the outcomes (Pearson's r's > |.20|, p's < .01).

Table 5

Descriptive Statistics and Intercorrelations of Coping Self-efficacy, Illness Representations, Affect, Coping Behaviors, Psychological Symptoms, and Overall Quality of Life (N=413)

	1	2	3	4	5	6	7	8	9	10	11	12
1. Coping self-efficacy	1.00											
2. Personal control	.24**	1.00										
3. Treatment control	.34**	.21**	1.00									
4. Negative affect	-.44**	-.28**	-.29**	1.00								
5. Positive affect	.22**	.14**	.08	-.11*	1.00							
6. Helplessness	-.39**	-.26**	-.30**	.46**	-.28**	1.00						
7. Anxiety preoccupation	-.36**	-.29**	-.21**	.53**	-.20**	.60**	1.00					
8. Fighting spirit	.23**	.18**	.18**	-.14**	.16**	-.25**	-.01	1.00				
9. Avoidance	-.22**	-.07	-.12*	.31**	.01	.32**	.45**	.18**	1.00			
10. Psychological symptoms	-.43**	-.21**	-.36**	.56**	-.23**	.44**	.46**	-.08	.24**	1.00		
11. Quality of life	.23**	.10	.24**	-.28**	.28**	-.32**	-.25**	.01	-.10	-.58**	1.00	
Mean	7.19	5.98	8.72	1.76	3.35	1.41	2.11	3.15	2.44	.63	75.44	
SD	1.16	2.79	1.58	.72	.77	.45	.57	.53	.70	.45	17.67	

* $p < .05$, ** $p < .01$

After controlling for covariates, coping self-efficacy was indirectly negatively related to psychological symptoms through the illness representation of treatment control, positive and negative affect, and anxiety preoccupation [R^2 = .22, $p < .001$; standardized effects (β), and confidence intervals (CI) of all significant effects are presented in Table 6]. Illness representations of personal control, and the other coping behaviors did not mediate the impact of coping self-efficacy on psychological symptoms (β's < |.02|, 95% CI = -.01/.04). Also, the illness representation of treatment control, positive affect, helplessness and fighting spirit mediated the positive relation of coping self-efficacy to overall quality of life (R^2 = .09, $p < .001$; see also Table 6). Illness representations of personal control, negative affect, anxiety preoccupation, and avoidance did not mediate this relationship (βs < |.03|, 95% CI = -.02/.08). Finally, coping self-

efficacy was also directly related to psychological symptoms (*B* = -.05, *SE* = .02, CI=-.08/-.01), but not to the overall quality of life (*B* = .29, *SE* = .84, CI = -1.36/1.93).

Table 6

*The Impact of Coping Self-efficacy on Psychological Symptoms and Overall Quality of Life Through Illness Representations, Affect, and Coping Behaviors**

Mediators	*b*	*SE*	Bootstrapping 95% Confidence Intervals†	
			Lower	Upper
	Dependent Variable: Psychological Symptoms			
Treatment control	-.05	.02	-.09	-.01
Positive affect	-.05	.02	-.08	-.01
Negative affect	-.10	.03	-.16	-.05
Anxiety preoccupation	-.04	.02	-.08	-.004
	Dependent Variable: Overall Quality of Life			
Treatment control	.05	.02	.01	.10
Positive affect	.08	.02	.03	.12
Helplessness	.08	.03	.01	.14
Fighting spirit	-.03	.01	-.06	-.001

Note. SE = standard error.

* Only the statistically significant effects are presented.

† Bootstrapping bias corrected and accelerated (5000 bootstrap samples); after controlling for covariates. Effects are significant at $p<.05$ for the 95% bootstrap confidence intervals, when the derived intervals do not include values of zero.

Implications

The findings of this model assessment provide partial support to our original hypotheses regarding the mechanisms through which self-efficacy to cope with cancer predicts two important outcomes, psychological symptoms and overall quality of life. These findings bear a significant practical implication. There is already evidence that self-efficacy is a modifiable characteristic that can be significantly enhanced in cancer patients (Merluzzi et al., 2019). Given the observed relationship of coping self-efficacy to several outcomes and its essential role in self-regulation, it might be sensible for all psychological interventions in breast cancer patients to target this factor toward achieving more effective self-regulation and improving diverse psychosocial outcomes.

3.4 Resilience as a potential: Mindfulness moderates the impact of emotional distress upon somatic symptoms

The analyses and the results in this section are based upon Roziner et al. (2022a). Psychological and physical health are inter-related (Naylor et al., 2016). The relationship is not only correlational: prospective studies showed that somatic symptoms influence psychological distress, and in turn, psychological distress can influence somatic symptoms (Ohrnberger et al., 2017a, 2017b). Specifically, it was found that depression among breast cancer survivors was related to a greater number and type of somatic complaints (McFarland et al., 2018) and that improving a patients' psychological well-being can improve their physical wellbeing and possibly their survival rate (Giese-Davis et al., 2011; Wang et al., 2020). In light of these findings, it is important to find psychological mechanisms that might moderate the causal links between psychological distress and somatic reactions to illness and treatment. Mindfulness is defined as an ability to accept emotional states in non-judgmental and non-reactive manner. According to Langer (1989), it denotes “a flexible state of mind, openness to novelty, a process

of actively drawing novel distinctions". In a recent meta-analysis (Leyland et al, 2019) it has been shown to plat a significant role in self-regulation processes. Mindfulness is thus one of the potential candidates for the role of mediator of the distress-soma link. In the present analysis, trait mindfulness measured at baseline was modelled as a moderator of the relation between psychological distress measured at three months afterwards and somatic symptoms measured three and six months after baseline. Psychological distress was defined as a combination of psychological symptoms measured by HADS scale and negative affect measured by PANAS scale.

Results

Descriptives and correlations between the research variables are presented in Table 7. Mindfulness is weakly related to emotional distress and somatic symptoms at all three measurements. Emotional distress is moderately related to somatic symptoms. These moderate correlations leave room for a third variable (such as mindfulness) to attenuate them. The symptoms measured at different times are rather strongly interrelated, showing temporal stability in this measure.

Table 7.

Descriptive statistics and intercorrelations of mindfulness, emotional distress, and somatic symptoms at baseline, at 3 months, and at 6 months*

	Mean	*SD*	1	2	3
1. Mindfulness M0	4.39	0.72	--		
2. Emotional distress M3	1.06	0.54	-0.26	--	
3. Somatic symptoms M3	1.66	0.42	-0.20	0.44	--
4. Somatic symptoms M6	1.58	0.38	-0.18	0.42	0.72

*$p < 0.001$

As a first step in the assessment of theoretical moderation model, we tested the hypothesized measurement model. The model fitted well to the data, with $\chi^2(66) = 5075.63$, $p < 0.001$, TLI = 0.97, CFI = 0.98, RMSEA = 0.057 (90% CI = 0.047; 0.068), SRMR = .05. As the next step, we estimated the structural model. In addition to the theoretically meaningful paths, this model included paths leading from each of the background variables to each of the main research variables. This model fitted fairly well to the data, $\chi^2(175) = 473.52$, $p < 0.001$, TLI = 0.92, CFI = 0.95, RMSEA = 0.050 (90% CI = 0.045; 0.056), SRMR = .04. In this model, mindfulness did not predict significantly somatic symptoms both at M3, but was significantly and negatively related to the symptoms at M6, of which M3 symptoms were partialled out, meaning that mindfulness predicted the change in somatic symptoms. At the final step, the paths of interaction terms were added to the model one by one and all of them were found as statistically significant ($p < .01$), albeit modest in magnitude, and negative (Figure 3). The negative sign of the interaction term coefficients implies offsetting (buffering) interaction effect: the higher is the level of mindfulness, the weaker is the relationship between emotional distress and somatic symptoms at M3 and M6, as illustrated in Figure 4.

Figure 3.

Mindfulness as a buffer of the prospective relation between emotional distress and reported somatic symptoms: a SEModel

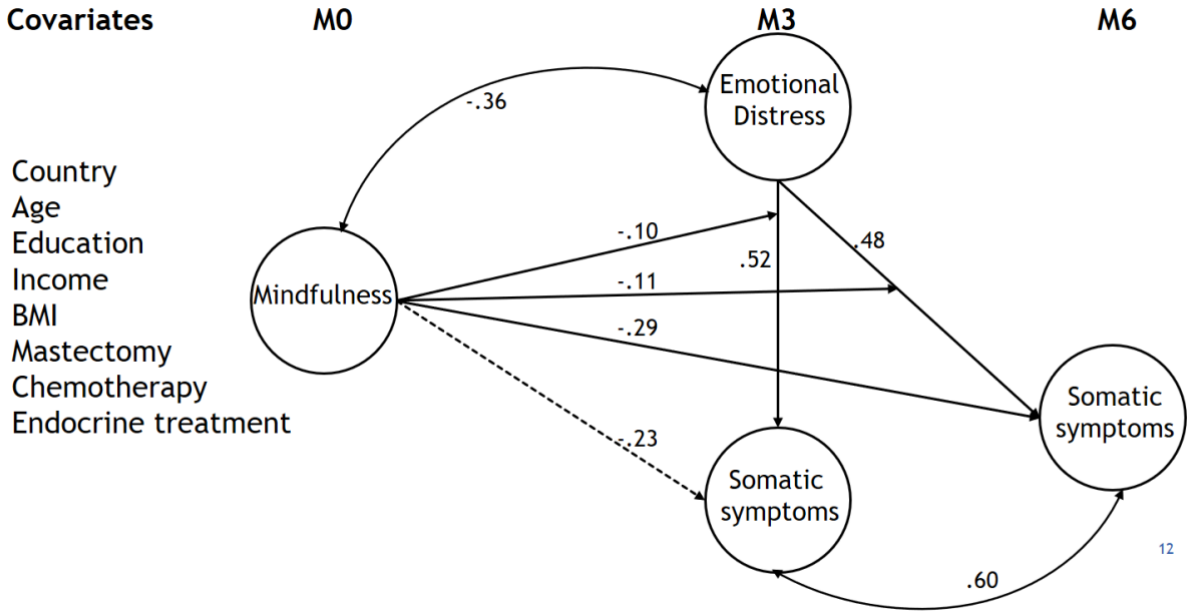
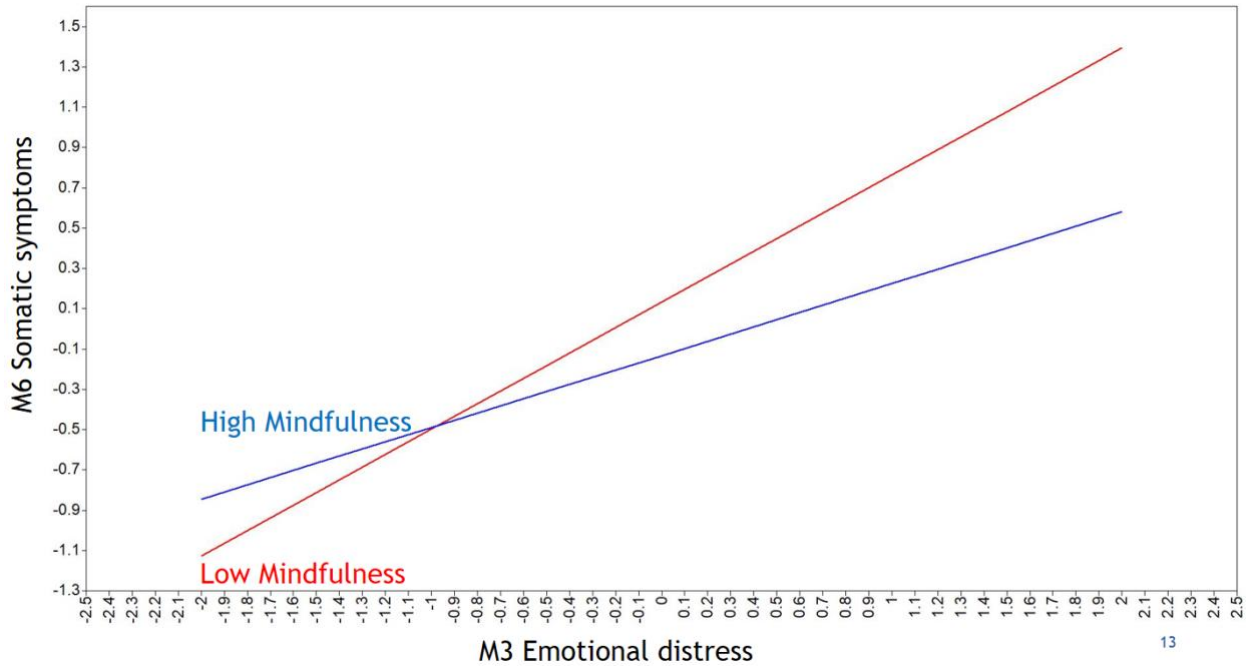


Figure 4.

Mindfulness as a buffer of relation between emotional distress and reported somatic symptoms: Illustration of the moderating effect



Implications

Two important findings emerged in the analyses. First, trait mindfulness predicts change in somatic symptoms over time: higher levels of mindfulness are associated will smaller increment of somatic complaints. Second, mindfulness mitigates the negative prospective relation between psychological distress and somatic complaints. These findings have important practical implication. Since mindfulness is known to be not only a personal trait, but also a malleable characteristic that can be enhanced in therapeutical interventions (Leyland et al., 2019), such interventions can serve as an important addition to the arsenal of treatment of breast cancer patients.

3.5 Resilience as a process: Trajectories of change in overall quality of life during the first year post diagnosis

The analyses and the results in this section are based upon Pat-Horenczyk et al. (2022). Analyses based on similar methodology are being performed by an additional BOUNCE partner (ICCS) and will be presented in another Deliverable. The main objective of the models presented here was to identify different trajectories of one outcome variable, the overall quality of life (QoL), as reflected in the single item of EORTC QLQ-C30: "How would you rate your overall quality of life during the past week?" (1 = very poor to 7 = excellent). QoL was measured at five time points during the first 12 months of coping with breast cancer. Additional objectives were to test the proportion of the participants exhibiting in each of these trajectories and to compare their background and characteristics as measured at baseline.

Results

A series of unconditional Latent Growth Curve Models were performed to determine possible classes of participants with similar trajectories of change in overall QoL over time, fitting models with one to six latent classes. Each model was specified with three parameters:

the intercept, the linear slope and the quadratic slope. We followed Nylund, Asparouhov, & Muthén's (2007) recommendations for choosing the number of classes, including interpretability considerations, a low value of log-likelihood, a high entropy index, the smallest value of Bayesian Information Criteria (BIC), and a significant bootstrapped likelihood ratio test (BLRT). We also preferred models with a substantial proportion of cases in the smallest class, based on estimated posterior probabilities. At the last stage of our analysis, we added covariates to the chosen model, leaving in the final model only those predictors that emerged as significant

The characteristics of each model appear in Table 8. The four-class solution was chosen basing on the criteria of significant p BLRT and an acceptable proportion of the smallest class (which was too small in five- or six-class solutions).

Table 8.

Comparison of Latent Growth Curve Models

# of classes	loglikelihood	BIC	*p* BLRT	entropy	Proportion of the smallest class
1	-4724.75	9501.89			
2	-4385.88	8850.36	<.001	.74	.30
3	-4278.25	8661.30	.009	.70	.12
4	-4248.41	8627.81	.021	.65	.09
5	-4211.61	8580.40	.005	.72	.02
6	-4195.24	8484.96	.449	.72	.02

In Table 9, the parameters of the Growth Curve Model for each of the four classes are presented. Class 1 is characterized by a relatively low baseline level (intercept) of reported QoL and insignificant rates of change across time (slopes) and therefore, this group can be labeled *low and stable*. Class 2 is characterized by a medium baseline level and a significant rate of linear change and therefore, this group can be labelled *medium and improving*. Class 3 is characterized by a relatively high baseline level and a significant rate of linear change and therefore, this

group can be labelled *high and improving*. Moreover, in this class the negative value of the quadratic slope is also significant, meaning that the improvement reaches an asymptote at some point. Finally, Class 4 is characterized by a relatively low baseline level of reported QoL and significant negative linear rate of change across time and therefore, this group can be labeled *low and declining*. The trajectories of change in the four classes are represented graphically in Figure 5.

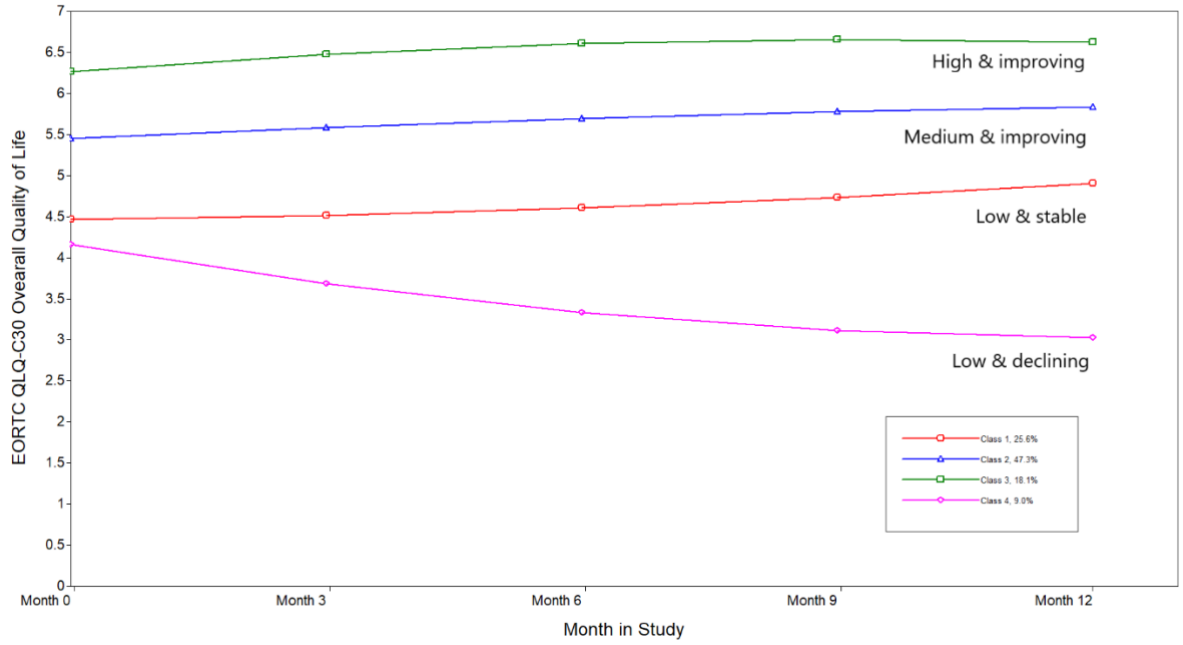
Table 9

Parameters of Growth Curve Models for the 4-class solution (means and SEs)

Class	Intercept	Linear Slope	Quadratic Slope	Proportion
Class 1	4.47*** (0.21)	0.01 (0.05)	0.002 (0.004)	.256
Class 2	5.45*** (0.09)	0.05* (0.03)	-0.002 (0.002)	.473
Class 3	6.26*** (0.08)	0.09*** (0.02)	-0.005** (0.002)	.181
Class 4	4.16*** (0.28)	-.02 (0.11)	0.007 (0.008)	.090

Figure 5

Trajectories of change in QoL in four classes



Finally, we attempted to predict the patients' latent class membership by regressing it on all the sociodemographic variables; medical background and illness characteristics; and psychological measures measured at baseline. First, a stepwise regression was tested for each of these three groups of variables. Of the sociodemographic variables, only age, number of children and marital status (married or in civil union vs others) contributed significantly ($p < .05$) to the regression. Of medical variables, only the number of pre-existing illnesses contributed significantly. Of the psychological variables, the resilience measure CD-RISK, the depression measure from HADS, and the positive affect measure from PANAS contributed significantly. At the second step of the analyses, all these variables were entered into a stepwise regression, with four of them surviving in the model ($p < .05$): number of children, resilience, depression, and positive affect. The distribution of these variables in the four groups is provided in Table 10.

Table 10

Distribution of predictors (means and SEs or percent) by latent class membership

Predictor	Low and declining	Low and stable	Medium and improving	High and improving
Number of children	1.96 (1.49)	1.71 (1.32)	2.00 (1.41)	2.35 (1.59)
Resilience	2.72 (0.71)	2.54 (0.73)	2.80 (0.65)	3.12 (0.61)
Depression	0.99 (0.66)	0.84 (0.53)	0.50 (0.41)	0.25 (0.30)
Positive affect	3.33 (0.82)	3.29 (0.75)	3.62 (0.70)	3.80 (0.60)

Implications

Early identification of probable class classification (based on initial data) and the prediction of potential trajectories of quality of life can guide clinicians in early screening and triage for psychosocial interventions. Our findings that the majority of patients tend to show adaptive coping is consistent with prior evidence and clinical experience. Early screening will enable

better allocation of resources and intervention efforts on the most vulnerable groups for impaired quality of life. Early implementations of personalized interventions can start soon after the stage of diagnosis and should focus on enhancement of quality of life throughout the treatment and recovery phase.

3.6 Resilience as a process: The mutual determination of self-efficacy to cope with cancer and cancer-related coping over time

This section is based upon Karademas et al. (in press). Two of the several factors that are important for psychological adaptation to a breast cancer diagnosis are self-efficacy to cope with cancer, and coping with cancer. Coping refers to the cognitive and behavioral efforts of a person to manage a stressful condition (such as an illness), by undertaking action to change the interaction with the environment (e.g., find possible solutions to the problem, ask for help, avoid the situation) or/and by regulating their emotions (e.g., deny the condition, manage negative emotions; Lazarus & Folkman, 1984). Although self-efficacy has been shown to relate strongly to coping (e.g., Beckham et al., 1997; Schwarzer, 1992), there is a controversy regarding the direction of this relationship (see, for example, Neal et al., 2017). The aim of this prospective study was to examine the relationships between self-efficacy to cope with cancer and the cancer-related coping of patients recently diagnosed with breast cancer over a period of nine months. Specifically, our aim was to examine the impact of coping self-efficacy on cancer-related coping and vice versa over time. Our basic hypothesis was that self-efficacy to cope with cancer predicts future cancer-related coping, which is turn predicts potential changes in subsequent coping self-efficacy and so on, in a chain of cognitive–behavioral feedback loops. Exploring this relationship is important as it may lead to an improved understanding of the psychological processes that impact patients' adjustment to breast cancer, which in turn may lead to the development of more effective psychological interventions for these patients.

Results

The descriptive statistics and correlations between coping self-efficacy and cancer-related coping reactions are presented in Table 2. Baseline coping self-efficacy was negatively related to helplessness/hopelessness, anxious preoccupation, and avoidance at M3 (Pearson *r*s = -.26 to -.43, $p < .01$) and at M9 (*r*s = -.21 to -.43, $p < .01$), and positively to fighting spirit at M3 and M9 (*r*s = .24 and .25, respectively, $p < .01$). Also, all coping reactions at M3 were significantly related to coping self-efficacy at M6, while the latter was associated with all coping reactions at M9 ($p < .01$).

Table 11

Descriptive statistics and intercorrelations of self-efficacy to cope with cancer and cancer-related coping reactions

	1	2	3	4	5	6	7	8	9	10
1. Coping SE–baseline	1.00									
2. Coping SE–M6	.53**	1.00								
3. Helplessness–M3	-.43**	-.41**	1.00							
4. Anxiety preoccupation–M3	-.42**	-.34**	.64**	1.00						
5. Fighting spirit–M3	.24**	.18**	-.29**	-.03	1.00					
6. Avoidance–M3	-.26**	-.24**	.32**	.42**	.11*	1.00				
7. Helplessness–M9	-.38**	-.48**	.57**	.44**	-.18**	.23**	1.00			
8. Anxiety preoccupation–M9	-.43**	-.45**	.52**	.71**	-.07	.31**	.69**	1.00		
9. Fighting spirit–M9	.25**	.29**	-.25**	-.09	.57**	.02	-.38**	-.18**	1.00	
10. Avoidance–M9	-.21**	-.24**	.22**	.36**	.03	.69**	.22**	.34**	.13**	1.00
Mean	7.24	7.39	1.41	2.12	3.14	2.40	1.45	2.05	3.05	2.46
SD	1.14	1.11	.44	.55	.51	.68	.44	.55	.49	.65

** $p < .01$

As a first step in the theoretical model assessment, we tested the hypothesized measurement model. The model fit fairly well to the data, with $\chi^2(404) = 794.23$, $p < 0.001$, TLI = 0.940, CFI = 0.951, RMSEA = 0.049 (90% CI = 0.044; 0.054), SRMR = .076.

Next, we estimated the structural model. In addition to theoretically meaningful paths, this model included paths leading from each of the control variables to each of the main research variables. In addition, cancer-related coping subscales were allowed to covary within each time point. This model fitted marginally well to the data, $\chi^2(755) = 1372.42$, $p < 0.001$, TLI = 0.909, CFI = 0.927, RMSEA = 0.045 (90% CI = 0.041; 0.049), SRMR = .069. Finally, we constrained to zero statistically nonsignificant ($p < .05$) paths emanating from the control variables. This improved somewhat the model fit, $\chi^2(645) = 1240.63$, $p < 0.001$, TLI = 0.921, CFI = 0.929, RMSEA = 0.048 (90% CI = 0.044; 0.052), SRMR = .079. The model paths appear in Figure 6.

As depicted in Figure 6, baseline coping self-efficacy significantly predicted all four coping reactions assessed three months later with absolute values of standardized coefficients (betas) ranging from .28 to .62. Also, baseline coping self-efficacy predicted the same variable at M6 ($\beta = .37$). Of the four coping reactions at M3, only helplessness-hopelessness was significantly related to M6 coping self-efficacy ($\beta = -.27$). Since baseline self-efficacy was partialled out of the corresponding M6 values, this finding shows that helplessness-hopelessness predicts the change in self-efficacy during this period. Stability paths from M3 to M9 coping reactions were moderate to high (betas ranging between .45 and .81). Three coping reactions at M9 partialled out of their M3 values (i.e., the change in coping reactions during half a year) were predicted by coping self-efficacy at M6: helplessness-hopelessness ($\beta = -.26$), anxious preoccupation ($\beta = -.22$), and fighting spirit ($\beta = .30$).

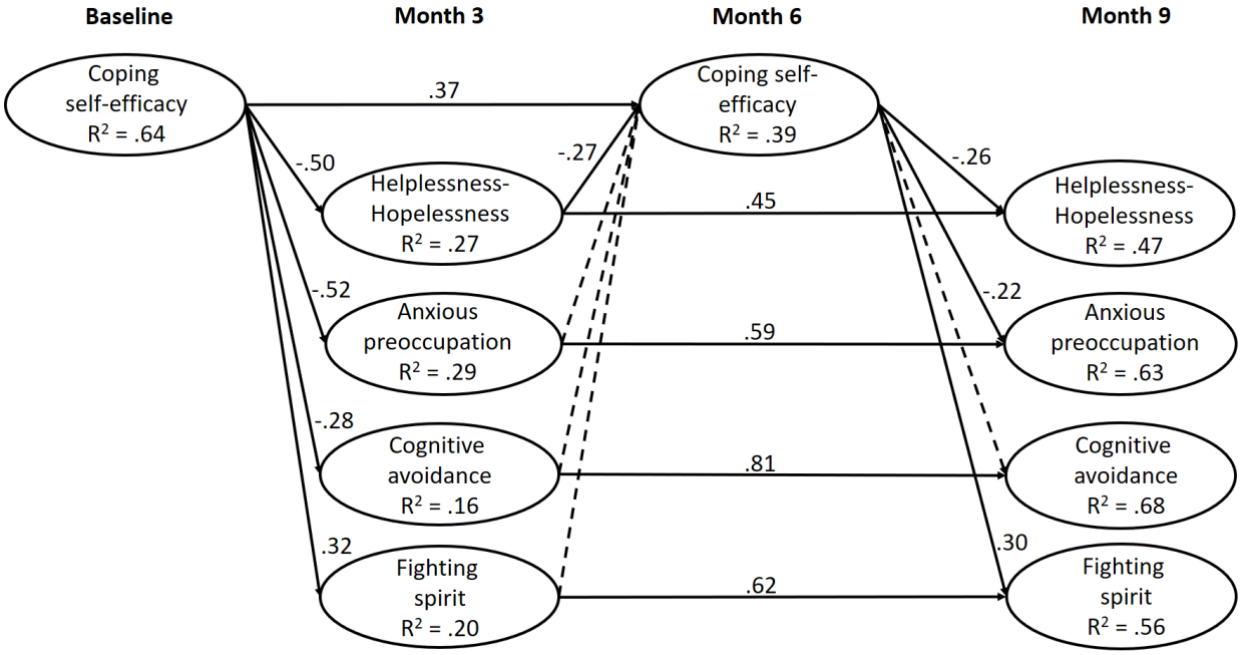
Implications

The findings provided partial support to our hypotheses regarding mutual determination of self-efficacy to cope with cancer and cancer-related coping as a chain of cognitive–behavioral

feedback loops evolving over time. Overall, our findings suggest that, as expected, a strong sense of self-efficacy to cope with cancer can predict less use of typically dysfunctional coping reactions, such as helplessness and anxious preoccupation, and more use of reactions that correspond to a problem-solving approach. This effect was significant even after controlling for several medical and socio-demographic variables, as well as baseline well-being. Also, as hypothesized, self-reported coping self-efficacy and cancer-related coping predicted the subsequent levels of both these factors over time. In other words, at least certain types of coping reactions (e.g., helplessness) and self-efficacy to cope with cancer were mutually determined in the long run. Our study was the first, to the best of our knowledge, to examine the relationship between self-efficacy to cope with cancer and cancer-related coping over time. In addition to a new theoretical perspective, this study has important practical implications. Self-efficacy is frequently addressed in psychological interventions for cancer patients as a way to facilitate their adaptation to illness and enhance well-being (Merluzzi et al., 2019). However, the present findings indicate that addressing only coping self-efficacy may not be sufficient to modify all dysfunctional coping reactions. It may be important to also include strategies to enhance adaptive coping so as (a) to achieve a mutual reinforcement between these two factors and, (b) address those coping reactions that are less strongly related to coping self-efficacy.

Figure 6

The paths with standardized coefficients between self-efficacy to cope with cancer and cancer-related coping: a SEModel



3.7 Resilience as a process: Mutual effects of psychological and somatic symptoms among breast cancer patients

This section is based upon Roziner et al. (2022b). Psychological and physical health are inter-related (Naylor et al., 2016). Research shows that somatic symptoms influence psychological distress, and in turn, psychological distress can influence somatic symptoms (Ohrnberger et al., 2017a, 2017b). Such relationships can be explained by the biopsychosocial model (Engel, 1981) which highlights the combined contributions of biological, psychological, and social factors in determining health. However, the biopsychosocial model has been criticized for being too broad, generic, and vague to provide any meaningful clinical utility (Benning, 2015; Farre & Rapley, 2017). Karunamuni and colleagues (2021) argued that the solution is to apply the

biopsychosocial model to one health condition at a time, and to measure the patients' subjective experiences, thus narrowing its scope and increasing its utility. Further, they posited that tracking the causal pathways within this model will enable health professionals to determine when and which interventions should be prioritized. In this study, we tracked the mutual inter-relationships between somatic symptoms and psychological symptoms (measured as depression and anxiety from HADS scale and negative affect from PANAS scale) among breast cancer patients during the first six months post diagnosis within the framework of cross-lagged panel model. Such models allow for interpreting correlational data collected in a longitudinal design in causal terms, that is, testing for the possibility that somatic symptoms determine psychological ones and vice versa.

Results

Distribution and first-order correlations between the research variables appear in Table 12. As can be seen, the psychological symptoms tended to improve between measurement waves, while somatic symptoms worsened after three months and then returned almost to their baseline level. At each time-point, the psychological and the somatic symptoms were moderately correlated, with *r*'s of .35 to .48. Psychological symptoms were relatively stable across time, with *r*'s of .71 and .68 between adjacent measurements. Somatic symptoms were slightly less stable during the first three months (r = .55) then between months three and six (r = .72).

Table 12

Distribution and intercorrelations of research variables at three times*

Variable	Mean	*SD*	1	2	3	4	5
1. Psychological symptoms T1	1.17	0.58					
2. Somatic symptoms T1	1.50	0.37	.35				
3. Psychological symptoms T2	1.06	0.55	.71	.41			
4. Somatic symptoms T2	1.65	0.41	.33	.55	.43		
5. Psychological symptoms T3	0.99	0.51	.60	.34	.68	.33	
6. Somatic symptoms T3	1.56	0.38	.30	.52	.41	.72	.48

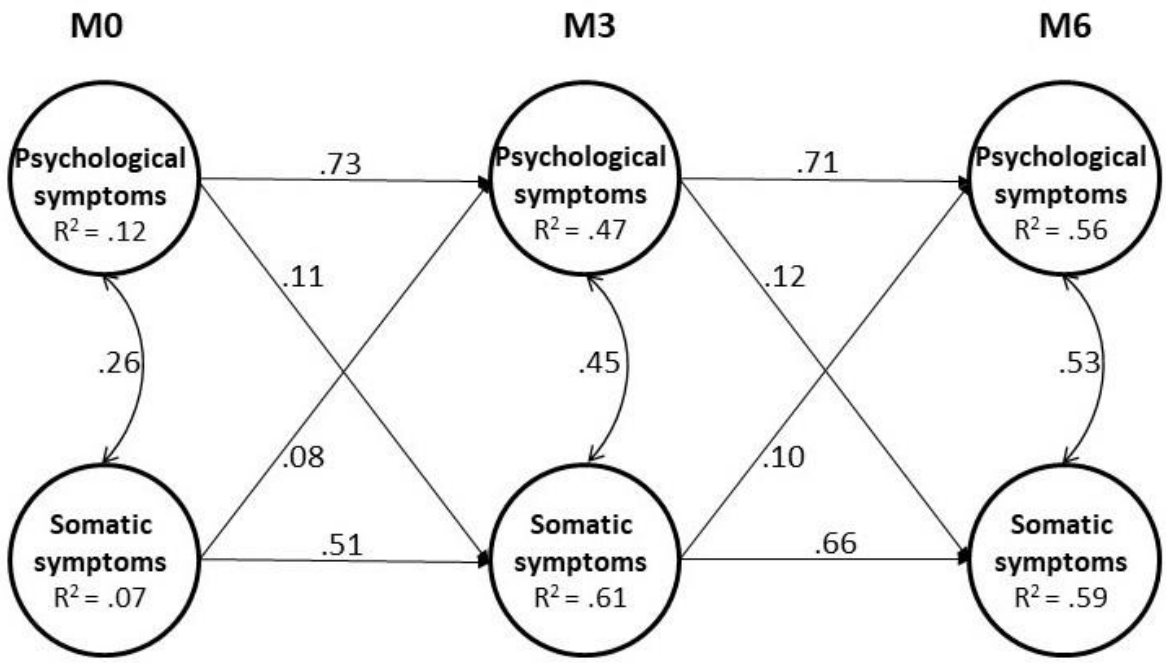
* All correlations significant at $p < .001$

As a preliminary step in the main analyses, we assessed the hypothesized measurement model. In this model, the measurement errors were set to be correlated, and factor loadings were constrained for equality across measurement waves. The model fit well to the data, with $\chi^2(110) = 338.73$, $p < 0.001$, TLI = 0.959, CFI = 0.970, RMSEA = 0.055 (90%CI = 0.048; 0.062); SRMR = .052. At the next step, we tested the autoregressive cross-lagged model with equality imposed upon path coefficients across waves. All sociodemographic and medical characteristics served as covariates of all variables in this model. The model fit fairly well to the data, $\chi^2(300) = 772.85$, $p < 0.001$, TLI = 0.927, CFI = 0.948, RMSEA = 0.048 (90%CI = 0.044; 0.052); SRMR = .058. Finally, for the sake of parsimony, we omitted from the model all non-significant (p >= .05) paths from covariates to the research model. The resulting model fit well to the data, $\chi^2(249) = 675.17$, $p < 0.001$, TLI = 0.942, CFI = 0.951, RMSEA = 0.050 (90%CI = 0.045; 0.054); SRMR = .075. The path coefficients in this model appear in Figure 7. As seen in the Figure, both psychological and somatic symptoms are rather stable across time (stability coefficients of .71 and .67, respectively) and are intercorrelated (r = .54). Nevertheless, the

cross-lagged paths leading from somatic to psychological symptoms and vice-versa are significant, albeit modest in magnitude, with standardized coefficients ranging between .08 and .11, suggesting that the change in each variable effects the change in the other variable.

Figure 6

Standardized paths in cross-lagged panel model of mutual effects of psychological and somatic symptoms



As an exploratory research question, we tested whether the model in Figure 6 varied among the four countries in which the BOUNCE data were collected. The multi-group model in which cross-lagged effects were constrained for equality yielded $\chi^2(1017) = 2655.44$, $p < 0.001$. The model in which these constrains were released yielded $\chi^2(1011) = 2645.62$, $p < 0.001$. The difference test between these models was nonsignificant ($p = .13$), supplying no evidence for cross-cultural differences in mutual effects of psychological and somatic symptoms.

Implications

Our results showed that quality of life, as reflected by the subjective report of somatic symptoms post diagnosis (or: at baseline) were associated with psychological symptoms (depressive and anxiety symptoms and negative affect), which in turn were associated with both somatic and psychological symptoms in later measurements and so forth. Our findings call for an innovative way to approach the somatic and psychological distress expressed by women after being diagnosed with breast cancer and to address their needs in an integrative manner acknowledging the interrelations and co-existence of the psycho-physiological distress including their mutual influence. The study bears clinical implication to early screening of distress and increase the awareness of health professionals to the close interaction between the psychological and somatic level of distress manifested by the patients. Psycho-social interventions in the context of the early phase of breast cancer treatment should include the identification and early interventions geared at the alleviation of distress on both psycho-soma levels. Comprehensive interventions that can address psycho-somatic aspects in synergy are likely to be beneficial for enhancement of quality of life.

4. Conclusions and future plans

Our preliminary analyses provided support to both prior evidence and clinician's impressions that the majority of breast cancer patients cope adaptively with the diagnosis of breast cancer and the related treatments. However, about a third of the patients do need help and support in order to reduce distress and maintain their quality of life. It is imperative to screen and identify these women in need, as early as possible in the process, and to tailor the interventions according to the risk and protective factors. In this report, we focused on several potential resilience-related factors that can mitigate the associations between the diagnosis of breast cancer and the perceived quality of life. We focused on psychological variables that play

a central role in coping and mental health of the patients. Moreover, we focused and examined factors that are amenable for change, and therefore, can be at the center of interventions geared for enhancing resilience. Our results point to the centrality of self-efficacy in coping with cancer, flexibility and mindfulness in the process of coping with breast cancer. In addition our results highlight the need that psycho-social interventions in the context of the early phase of breast cancer treatment should include the alleviation of distress on both psycho-soma levels. There findings can guide clinicians in developing effective interventions for enhancing resilience of women after breast cancer.

Our future plans are:

- To continue to analyse the data of all seven measurements from the perspective of resilience as a trait, a process, and an outcome.
- To examine resilience as an outcome after 18 months in terms of mental health, functioning abilities, subjective evaluations of bouncing back to the prior level of functioning, and the perceived quality of life.
- To compare findings across cultures.
- To identify additional moderating and mediating resilience factors and the precise timing of their potential influence.

5. References

Aaronson, N. K., Ahmedzai, S., Bergman, B., Bulliger, M., Cull, A., Duez, N., ... & de Haes, J. C. J. M. (1993). The European Organization for Research and Treatment of Cancer QLQC30: a quality of life instrument for use in international trials in oncology. *Journal of the National Cancer Institute*, *85*, 365-76. https://doi.org/10.1093/jnci/85.5.365

Albrecht, K., Droll, H., Giesler, J.M. Nashan, D., Meiss, F., & Reuter, K. (2013). Self-efficacy for coping with cancer in melanoma patients: its association with physical fatigue and depression. *Psycho-Oncology*, *22*, 1972–1978.

Beckham, J. C., Burker, E. J., Burker, E. J., Feldman, M. E., & Costakis, M. J. (1997). Self-Efficacy and adjustment in cancer patients: A preliminary report. *Behavioral Medicine, 23*, 138-142. doi:10.1080/08964289709596370

Benning, T. B. (2015). Limitations of the biopsychosocial model in psychiatry. *Advances in Medical Education and practice*, *6*, 347.

Bonanno, G. A., Pat-Horenczyk, R., & Noll, J. (2011). Coping flexibility and trauma: the perceived ability to cope with trauma (PACT) scale. *Psychological Trauma: Theory, Research, Practice, and Policy*, *3*, 117. https://doi.org/10.1037/a0020921

Brandão, T., Schulz, M. S., & Matos, P. M. (2017). Psychological adjustment after breast cancer: a systematic review of longitudinal studies. *Psycho-Oncology*, *26*, 917-926. doi:10.1002/pon.4230

Broadbent, E., Petrie, K. J., Main, J., & Weinman, J. (2006). The Brief Illness Perception Questionnaire. *Journal of Psychosomatic Research*, *60*, 631-637. doi:10.1016/j.jpsychores.2005.10.020

Brown, K. W., & Ryan, R. M. (2003). The benefits of being present: Mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology*, *84*, 822–848.

Campbell-Sills, L., & Stein, M. B. (2007). Psychometric analysis and refinement of the Connor–Davidson Resilience Scale (CD-RISC): validation of a 10-item measure of resilience. *Journal of Traumatic Stress, 20*, 1019–28.

Chirico, A., Lucidi, F., Merluzzi, T., Alivernini, F., De Laurentiis, M., Botti, G., & Giordano, A., (2017). A meta-analytic review of the relationship of cancer coping self-efficacy with distress and quality of life. *Oncotarget, 8,* 36800-36811.

Connor, K. M., & Davidson, J. R. T. (2003). Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). *Depression and Anxiety, 18,* 76–82.

Dahabre, R., Roziner, I., Perry, Sh., Bentley, G., Poikonen-Saksela, P., Mazzocco, K., Sousa, B., Karademas, E. C., & Pat-Horenczyk, R. (2022). Somatic symptoms of quality of life among early breast cancer patients: The moderating role of coping flexibility. Manuscript in preparation.

Engel, G. L. (1981). The clinical application of the biopsychosocial model. In *The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine* (Vol. 6, No. 2, pp. 101-124). Oxford University Press.

Farre, A., & Rapley, T. (2017, December). The new old (and old new) medical model: four decades navigating the biomedical and psychosocial understandings of health and illness. In *Healthcare* (Vol. 5, No. 4, p. 88). Multidisciplinary Digital Publishing Institute.

Giese-Davis, J., Collie, K., Rancourt, K. M., Neri, E., Kraemer, H. C., & Spiegel, D. (2011). Decrease in depression symptoms is associated with longer survival in patients with metastatic breast cancer: a secondary analysis. *Journal of clinical oncology*, *29*(4), 413.

Groenvold, M., Arraras, J. I., Franzini, L., & de Haes, H. (1996). *The European organization for research and treatment of cancer breast cancer-specific quality-of-life questionaire module: first results from a three-country field study [J Clin On... Impact of risk-reducing salpingo-oophorectomy View project Nausea and vomiting in patients with advanced*

cancer View project SEE PROFILE. https://www.researchgate.net/publication/254780292

Hamama-Raz, Y., Bergman, Y. S., Ben-Ezra, M., Tirosh, Y., Baruch, R., & Nakache, R. (2018). Attachment patterns moderate the relation between coping flexibility and illness acceptance among kidney transplant recipients. *Anxiety, Stress, & Coping*, *31*, 571-579. https://doi.org/10.1080/10615806.2018.1498667

Harms, G. A., Cohen, L., Pooley, J. A., Chambers, S. K., Galvão, D. A., & Newton, R. U. (2019). Quality of life and psychological distress in cancer survivors: The role of psycho-social resources for resilience. *Psycho-Oncology, 28*, 271–277.

Heitzmann, C. A., Merluzzi, T. V., Jean-Pierre, P., Roscoe, J. A., Kirsh, K. L., & Passik, S. D. (2011). Assessing self-efficacy for coping with cancer: Development and psychometric analysis of the brief version of the Cancer Behavior Inventory (CBI-B). *Psycho-Oncology, 20*, 302–312.

Henselmans, I., Fleer, J., de Vries, J., Baas, P. C., Sanderman, R., & Ranchor A. (2010). The adaptive effect of personal control when facing breast cancer: Cognitive and behavioral mediators. *Psychology & Health, 25*, 1023-1040. doi:10.1080/08870440902935921

Hu, L., & Bentler, P. (1999). Cutoff criteria for fit indices in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling, 6*, 1–55. https://doi.org/10.1080/10705519909540118

Johnston, M. C., Porteous, T., Crilly, M. A., Burton, C. D., Elliott, A., Iversen, L., McArdle, K., … & Black, C. (2015). Physical disease and resilient outcomes: A systematic review of resilience definitions and study methods. *Psychosomatics, 56*, 168–180.

Kato, T., Kadota, M., & Shimoda, S. (2021). Effects of coping flexibility in young women on depressive symptoms during chronic pain. *Behavioral Medicine*, 1-9. https://doi.org/10.1080/08964289.2019.1708250

Karunamuni, N., Imayama, I., & Goonetilleke, D. (2021). Pathways to well-being: Untangling the causal relationships among biopsychosocial variables. *Social Science & Medicine, 272*, 112846.

Karademas, E., Poikonen-Saksela, P., Mazzocco, K., Pat-Horenczyk, R., Sousa, B., Oliveira-Maia, A.J., Mattson, J., Roziner, I., Pettini, G., Kondylakis, H., Marias, K., & Simos, P. (under review). The Interplay Between Trait Resilience and Coping Self-efficacy in Patients with Breast Cancer: An International Study. Invited to revise and resubmit to *Journal of Clinical Psychology in Medical Settings*.

Karademas, E. C., Roziner, I., Mazzocco, K., Pat-Horenczyk, R., Sousa, B., Oliveira-Maia, A.J., Stamatakos, G., Cardoso, F., Frasquilho, D., Kolokotroni, E., Lemos, R., Marzorati, C., Mattson, J., Pettini, G., Spyropoulou, E., Poikonen-Saksela, P., & Simos, P. (in press). The Mutual Determination of Self-efficacy to Cope with Cancer and Cancer-Related Coping Over Time: A Prospective Study in Women with Breast Cancer. Accepted for publication in *Psychology and Health*.

Karademas, E. C., Simos, P., Pat-Horenczyk, R., Roziner, I., Mazzocco, K., Sousa, B., Oliveira-Maia, A.J., Stamatakos, G., Cardoso, F., Frasquilho, D., Kolokotroni, E., Marzorati, C., Mattson, J., Pettini, G., & Poikonen-Saksela, P. (2021). Cognitive, Emotional, and Behavioral Mediators of the Impact of Coping Self-efficacy on Adaptation to Breast Cancer: An International Prospective Study. *Journal of Psycho-Oncology*, 30, 1555-1562. doi.org/10.1002/pon.5730

Langer, E. (1989). *Mindfulness*. Reading, MA: Addison-Wesley.

Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer.

Leyland, A., Rowse, G., & Emerson, L. M. (2019). Experimental effects of mindfulness inductions on self-regulation: Systematic review and meta-analysis. *Emotion, 19*, 108-122.

Lightsey, O. R, Burke, M., Ervin, A., Henderson, D., Yee, C. (2006). Generalized self-efficacy, self-esteem, and negative affect. *Canadian Journal of Behavioural Science / Revue canadienne des sciences du comportement*, *38*, 72-80. doi:10.1037/h0087272

Little, T. D., Rhemtulla, M., Gibson, K., & Schoemann, A. M. (2013). Why the items versus parcels controversy needn't be one. *Psychological methods*, *18*, 285. https://doi.org/10.1037/a0033266

Little, R., & Rubin, D. (2003). *Statistical analysis with missing data*. Hoboken, NJ: Wiley.

Markovitz, S. E., Schrooten, W., Arntz, A., & Peters, M. L. (2015). Resilience as a predictor for emotional response to the diagnosis and surgery in breast cancer patients. *Psycho-Oncology, 24*, 1639–1645.

Marsh, H. W., & Hau, K. T. (1996). Assessing goodness of fit: Is parsimony always desirable? *The Journal of Experimental Education, 64*, 364-390. https://doi.org/10.1080/00220973.1996.10806604

McFarland, D. C., Shaffer, K. M., Tiersten, A., & Holland, J. (2018). Physical symptom burden and its association with distress, anxiety, and depression in breast cancer. *Psychosomatics*, *59*(5), 464-471.

Merluzzi, T., Pustejovsky, J. E., Philip, E. J., Sohl, S. J., Berendsen, M., & Salsman, J. M. (2019). Interventions to enhance self-efficacy in cancer patients: A meta-analysis of randomized controlled trials. *Psycho-Oncology*, *28,* 1781-1790. doi:10.1002/pon.5148

Min, Y., Yoon, S., Lee, C., Chae, J., Lee, C., Song, K., & Kim, T. (2013). Psychological resilience contributes to low emotional distress in cancer patients. *Supportive Care in Cancer, 21*, 2469–2476.

Muthén, L., & Muthén, B. (2017). *Mplus User's Guide*, 8th Ed., Los Angeles: Muthén & Muthén. https://doi.org/10.1201/9781315117430

Naylor, C., Das, P., Ross, S., Honeyman, M., Thompson, J., & Gilburt, H. (2016). Bringing together physical and mental health. *King's Fund*.

Neal, A., Ballard, T., & Vancouver, J. B. (2017). Dynamic self-regulation and multiple-goal pursuit. *Annual Review of Organizational Psychology and Organizational Behavior, 4*, 401-423. doi: 10.1146/annurev-orgpsych-032516-113156

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural equation modeling: A multidisciplinary Journal*, *14*, 535-569.

Ohrnberger, J., Fichera, E., & Sutton, M. (2017a). The dynamics of physical and mental health in the older population. *The Journal of the Economics of Ageing, 9*, 52-62.

Ohrnberger, J., Fichera, E., & Sutton, M. (2017b). The relationship between physical and mental health: A mediation analysis. *Social Science & Medicine, 195*, 42-49.

Pat-Horenczyk, R., …, & Roziner, I. (2022). Trajectories of change in quality of life of breast cancer patients during the first year after diagnosis. Manuscript in preparation.

Philip, E. J., Merluzzi, T. V., Zhang, Z., & Heitzmann, C. A. (2013). Depression and cancer survivorship: importance of coping self-efficacy in post-treatment survivors. *Psycho-Oncology, 22*, 987-94.

Raque-Bogdan, T. L., Lent, R. W., & Lamphere, B. (2019). Test of a social cognitive model of well-being among breast cancer survivors. *Journal of Health Psychology*, *24*, 661-670. doi:10.1177/1359105316681431

Roziner, I., …, & Pat-Horenczyk, R. (2022a). Mindfulness moderates the impact of emotional distress upon somatic symptoms in breast cancer patients. Manuscript in preparation.

Roziner, I., …, & Pat-Horenczyk, R. (2022b). Psychological and somatic symptoms among breast cancer patients in four European countries: A cross-lagged panel model. Manuscript in preparation.

Rudnik, A., Piotrowicz, G., Basińska, M. A., & Rashedi, V. (2019). The importance of cognitive flexibility and flexibility in coping with stress for the quality of life in inflammatory bowel

disease patients during biological therapy. A preliminary report. *Przeglad gastroenterologiczny, 14*, 121. https://doi.org/10.5114/pg.2018.81081

Schüz, B., Wurm S., Warner, L. M., Ziegelmann, J. P. (2012). Self-efficacy and multiple illness representations in older adults: A multilevel approach. *Psychology & Health*, *27*, 13-29. doi:10.1080/08870446.2010.541908

Schwarzer, R. (1992). Self-efficacy in the adoption and maintenance of health behaviors: Theoretical approaches and a new model. In R. Schwarzer (ed.), *Self-Efficacy: Thought control on action* (pp. 217-243). New York: Hemisphere.

Tu, P., Yeh, D., & Hsieh, H. (2020). Positive psychological changes after breast cancer diagnosis and treatment: The role of trait resilience and coping styles. *Journal of Psychosocial Oncology*, *38*, 156-170.

Zigmond, A.S., & Snaith, R.P. (1983). The Hospital Anxiety and Depression Scale (validity and reliability). *Acta Psychiatrica Scandinavica*, *67*, 361-370.

Appendix 1

Questionnaires collected in each wave (with number of items)

Domain	Abbreviatic	Measure name	M0	M3	M6	M9	M12	M15	M18
Personality	TIPI	Ten Item Personality Measure (brief "Big Five")	10						
	LOT-R	Optimism/Pessimism	10						
Meaning	SOC-13	Sense of Coherence	13						
Trauma and PTSD	PCL-5	PTSD Check-List			20		20		20
		Recent negative life events	1	1	1	1	1	1	1
		Recent illness-related events		1	1	1	1	1	1
Coping	PACT	The Perceived Ability to Cope With Trauma (Flexibility in coping)	20			20		20	
	CERQ short	Cognitive Emotion Regulation Questionnaire	18			18		18	
		MAAS - Mindfulness	15				15		
		Spirituality coping - a visual bar		1		1		1	
Social Support	mMOS-SS	modified Medical Outcomes Study Social Support Survey		8		8		8	
	F.A.R.E.	1. Communication and cohesion; 2. Perceived family coping subscales		12		12		12	
		Instrumental/emotional perceived social support	1	1	1	1	1	1	1
Resilience	CD-RISC	Connor-Davidson Resilience Scale	10			10		10	
		How much are you back to yourself?			1	1	1	1	1
Illness Perception & b	IPQ	Illness Perception Questionnaire			56		56		56
	B-IPQ	Items no 3 and 4 from B-IPQ		2	2	2	2	2	2
	mini-MAC	Mental Adjustment to Cancer		29		29		29	
		Single item: what has done to cope (open question)		1	1	1	1	1	1
	CBI-B	Cancer Behavior Inventory (self-efficacy in coping with cancer)	14		14		14		
		A general self-efficacy item	1	1	1	1	1	1	1
		Adherence to medical advice: item 5 from the MOS Adherence to medical		1	1	1	1		1
	PTGI	The Posttraumatic Growth Inventory - short form		10			10		10
Quality of life	QLQ-C30	EORTC quality of life questionnaire	30	30	30	30	30	30	30
	QLQ-BR23	EORTC quality of life questionnaire breast cancer module	23	23	23	23	23	23	23
Distress	FCRI-SF	Fear of Recurrence - short form (severity scale of original FCRI)	9		9		9		9
	HADS	Hospital Anxiety and Depression Scale	14	14	14	14	14	14	14
	DT	NCCN Distress Thermometer	1	1	1	1	1	1	1
	PANAS	Positive and Negative affectivity - short form	10	10	10	10	10	10	10