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# Psychological and somatic symptoms among breast cancer patients in four European countries: A cross-lagged panel model

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## Abstract

Psychological and physical health among women with breast cancer are linked. However, more research is needed to test the interrelations between psychological and somatic symptoms, over time and throughout the different phases of breast cancer treatment, to determine when and which interventions should be prioritized. Six hundred and eighty nine women from four countries (Finland, Israel, Italy and Portugal) completed questionnaires during their first clinical consultation following diagnosis with breast cancer, and again after 3 and 6 months. The questionnaires included self-reported measures of psychological symptoms (Hospital Anxiety and Depression Scale; the Positive and Negative Affect Schedule Short Form) and somatic symptoms [selected items from the International European Organization for Research and Treatment of Cancer (EORTC) questionnaires]. Psychological and somatic symptoms were relatively stable across the three time-points. Cross-lagged

<sup>#</sup>The BOUNCE Project, <https://www.bounce-project.eu/>

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paths leading from somatic to psychological symptoms (beta coefficients of 0.08–0.10), as well as vice-versa (beta 0.11–0.12), were found to be significant. No evidence was found for cross-cultural differences in mutual effects of psychological and somatic symptoms. The findings of this study call for tailoring personal interventions for breast cancer patients—either from a somatic perspective or a psychological perspective—and adjust them to the specific experiences of the individual patient.

#### KEYWORDS

breast cancer, psychological symptoms, somatic symptoms, theory of unpleasant symptoms

## 1 | INTRODUCTION

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 interpreted in accordance with 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 et al. (2021) argued that the solution is to apply the biopsychosocial model to one health condition at a time, and to measure patients' subjective experiences, thus narrowing its scope and increasing its utility. Subjective experiences, known as patient reported outcomes (PROs), pertain to the patient's perceived health, wellbeing and outcomes of their treatment (Korolija et al., 2007; Valderas & Alonso, 2008) and are important indicators of functioning and prognosis after cancer treatment (Basch et al., 2012; Gotay et al., 2008). Indeed, the Theory of Unpleasant Symptoms posits that an individual's perceptions of their symptoms are at the core of the patient experience (Lenz et al., 1997). The Theory of Unpleasant Symptoms includes three main elements: (1) the factors which influence an individual's symptoms; (2) the personal experiences of the symptoms; and (3) the consequences of those experiences (Lenz et al., 1997; Peterson & Bredow, 2009). Specifically, the influencing factors can be physiological (e.g., treatment, nutrition), psychological (e.g., mental state) and situational (e.g., socioeconomic status). Next, the Theory of Unpleasant Symptoms acknowledges that symptoms are multidimensional, including the timing, distress, intensity and quality of symptoms (Lenz et al., 1997; Peterson & Bredow, 2009). Finally, the individual's experiences of their symptoms can have consequences on their functioning and their cognitions. The pathways and relationships within the Theory of Unpleasant Symptoms are dynamic and reciprocal, including the relationships between different symptoms (Lenz et al., 1997). In other words, symptoms can overlap and influence each other (Lenz et al., 1997). Researchers have called for further research using the Theory of Unpleasant Symptoms with larger samples and complex statistical analysis to provide further understanding of symptom experiences (Blakeman, 2019;

Lenz, 2018). Moreover, given the broad nature of the Theory of Unpleasant Symptoms, researchers are encouraged to apply portions of the theory to distinct pathways in the symptoms experience (Lenz, 2018). For the current study, we will explain the interdependent experiences of somatic and psychological experiences among women with breast cancer.

In the specific case of breast cancer, it has been widely acknowledged that both somatic and psychological symptoms play an important role in determining quality of life among patients (Satin et al., 2009). Breast cancer, its treatments and related side effects can cause a range of negative somatic experiences in patients, such as pain, fatigue, insomnia, nausea and diarrhoea (Aziz, 2007), as well as negative psychological experiences, such as anxiety and depression (Alagizy et al., 2020; Ng et al., 2017). The somatic experiences have been found to be related to negative mood, anxiety symptoms and depression symptoms (Badr et al., 2006; McFarland et al., 2018). In turn, depression among breast cancer survivors is associated with a greater number and type of somatic complaints (McFarland et al., 2018). Indeed, in the context of breast cancer, research has shown that improving psychological wellbeing can improve physical wellbeing, and possibly also survival rate (Giese-Davis et al., 2011; McGregor & Antoni, 2009; Wang et al., 2020).

Despite these findings, research tracking the longitudinal interrelationships between somatic and psychological symptoms is scarce in the breast cancer literature. This information is important, as it can enable healthcare professionals to better screen for psychological and somatic symptoms, and to be informed when to provide tailored interventions to improve health outcomes and quality of life (Chiolero, 2018; Glass et al., 2013; Karunamuni et al., 2021). In other words, tracking the causal pathways of somatic and psychological symptoms will enable health professionals to determine when to prioritize which interventions (Karunamuni et al., 2021). Use of patient reported outcome measures (PROMs) can help with this goal, as they are essential to ensuring patient-centred service delivery (Fung & Hays, 2008; Lavalley et al., 2016). As such, researchers have called for ongoing research to determine the effect size and the timeline of the underlying causal pathways for specific health conditions (Bolton & Gillett, 2019; Karunamuni et al., 2021). In addition, this research is needed to assess the psychological and somatic experiences in the early period after a breast cancer diagnosis, so that interventions can be prioritized and integrated into routine care, and

thus potentially affect the success of treatment (Giese-Davis et al., 2011; Wang et al., 2020). Additionally, experiences of psychological and somatic symptoms after a cancer diagnosis have been found to vary across countries (Pilevarzadeh et al., 2019; Shim et al., 2006). Therefore, an exploration of the causal pathways for psychological and somatic symptoms after breast cancer diagnosis should also take possible cross-national differences into consideration. This is important to explore, as the results can help health professionals and researchers determine how physical and/or psychological interventions, and the timing of these interventions, should be adapted to each country.

This study is part of a larger prospective study on resilience in breast cancer in a multi sites consortium of four countries. Here we aimed to assess the inter-relations between somatic and psychological symptoms in breast cancer patients, during the initial acute phase of treatment in the first 6 months after diagnosis. In order to address our objectives, our main analytic tool was testing a cross-lagged panel model. Basing on the understanding of the role of temporality in coping with distress and resilience (Bonanno et al., 2015; Southwick et al., 2014), we hypothesized that psychological and somatic symptoms would be inter-related at each timepoint, and also that change in one variable would be associated with change in the other.

Previous research has found that breast cancer patients in different cultures may exhibit differential patterns of relations between their emotional quality of life and their symptom severity (e.g., Fischer et al., 2017) or the type of treatment they receive (e.g., Lu et al., 2016). We aimed therefore to compare the mutual relations of the psychological and somatic symptoms across the four participating countries in an explorative fashion. The four participating societies differ in several respects. For example, their Median income per capita ranges from €8439 in Portugal to €16,332 in Finland (World Population Review, 2022). Their 'tightness' (strength of social norms) ranges from 3.1 in Israel to 7.8 in Portugal (Gelfand et al., 2011). In terms of the World Values Survey, Israel, Italy, and Portugal are characterized by average values on the survival/self-expression continuum, while Finland is low on survival and high on self-expression (The Inglehart-Welzel World Cultural Map - World Values Survey 7, 2022). Although we did not have specific predictions, we asked whether such economic and cultural differences, as well as differences in health-care organization, could produce variation in values of our model parameters—or the model would be cross-culturally invariant. Using multi-group modelling, we tested whether the pattern of inter-relations between psychological and somatic symptoms would differ between countries.

## 2 | METHOD

The study is part of a multi-wave multicenter EU-financed research project entitled: "Predicting Effective Adaptation to Breast Cancer to Help Women to BOUNCE Back", carried out in Finland (Helsinki University Hospital), Israel (Shaare Zedek and Rabin Medical Centers, coordinated by the Hebrew University of Jerusalem), Italy (European

Institute of Oncology), and Portugal (Champalimaud Clinical Centre), and aimed at identifying psychosocial, biomedical, and functional factors that may predict patients' capacity to bounce back following a diagnosis of breast cancer (see <https://www.bounce-project.eu/> for project description).

### 2.1 | Participants

The participants were recruited to the study during the first clinical consultation following diagnosis with breast cancer. Inclusion criteria were age between 40 and 70; histologically confirmed invasive breast cancer, early or locally advanced, but operable; tumour stage I–III; receiving surgery as part of the local treatment; receiving systemic treatment for breast cancer; understanding and signing informed consent. Exclusion criteria were refusal to provide informed consent; presence of distant metastases; history of another malignancy or contralateral invasive breast cancer within the last 5 years, with exception of cured basal cell carcinoma of skin or carcinoma in situ of the uterine cervix; history of early-onset mental or severe neurologic disorder; other concomitant serious diseases, for example, active cardiac disease or myocardial infarction within the last 12 months; major surgery for severe disease or trauma within four previous weeks; treatment for any major illness in the last half-year; pregnancy or breastfeeding at the time of recruitment.

All women who met criteria were approached with regard to the study at all four research sites. The response rate ranged between 74% and 78%. The sample for the current study was comprised of 698 participants who provided full data at baseline, of whom 13% and 18% did not provide data at the 3 and 6 months follow-up assessments, respectively. Compared with participants retained in the study, patients lost to follow-up were significantly ( $p < 0.01$ ) less educated and with lower income, with lower proportions undergoing chemo-, radio- or endocrine therapy, and higher levels of depression and negative affectivity at baseline. Nevertheless the analyses presented here are based on all available data.

### 2.2 | Measures

*Psychological symptoms* were assessed through the Hospital Anxiety and Depression Scale (HADS, Zigmond & Snaith, 1983) and International Positive and Negative Affect Schedule Short Form (I-PANAS-SF, Thompson, 2007). The HADS was used to assess *anxiety* and *depression*. Each subscale consists of seven items (e.g., 'I feel tense or "wound up"'; 'I still enjoy the things I used to enjoy') accompanied by a 4-point Likert scale ranging from 'not at all' to 'most of the time'. *Negative affectivity* was assessed with the NA subscale of the I-PANAS-SF, with each of its five items (e.g., 'nervous') accompanied by a 5-point Likert scale ranging from 'not at all' to 'extremely'. For each of these psychological measures, the responses to all items were averaged after appropriate reverse coding so that the higher scores would indicate more intense symptoms. Cronbach's

$\alpha$ 's for the three psychological symptoms measures in each of the three timepoints ranged between 0.81 and 0.84.

Somatic symptoms perceptions were measured with items 1–19 from the European Organization for Research and Treatment of Cancer (EORTC) questionnaire (QLQ-C30, Aaronson et al., 1993) and items 31–37 and 47–53 from the EORTC Breast Cancer-Specific Quality of Life Questionnaire (QLQ-BR23, Sprangers et al., 1996). These items (e.g., 'Have you felt nauseated?', 'Was the area of your affected breast oversensitive?') were rated on a 4-point Likert scale ranging from 'not at all' to 'very much' and their values averaged to form overall scores. Cronbach's  $\alpha$ 's ranged from 0.91 to 0.92 across the three timepoints.

The items which specifically addressed physical symptoms were selected to be included in the somatic symptoms measure. A group of three clinician discussed and fully agreed on the inclusion of these 33 items.

## 2.3 | Procedure

The study was approved by the ethics committee of the European Institute of Oncology (Approval No R868/18 - IEO 916) and the ethics committees of each participating hospital. The study protocol was registered in [ClinicalTrials.gov](https://clinicaltrials.gov) (identifier number: NCT05095675). Eligible participants were identified using hospital medical files. The treating oncologist introduced the study to the patients and either the oncologist or a research assistant invited for participation in the study. Those who accepted and provided informed consent were guided by the research assistant to fill in the study questionnaires online or in printed form. The first wave of data collection took place several weeks after the diagnosis (after surgery for adjuvant therapy, but before systematic treatment—chemotherapy or hormonal therapy). The second and the third waves occurred three and 6 months thereafter, respectively. The participants were not remunerated in any tangible way.

## 2.4 | Statistical analyses

Drop-out and descriptive analyses were carried using SAS software, Version 9.4 (SAS Institute Inc.). The cross-lagged panel model was estimated using Structural Equation Modelling with Mplus Version 8.6 (Muthén & Muthén, 1998–2017). The main research variables were specified in the model as latent constructs. Psychological symptoms were measured with anxiety, depression, and negative affectivity. Somatic symptoms were measured, relying on the accepted approach of parcelling (Bandalos, 2002), with three indicators calculated as random thirds of the scale items. Participants' sociodemographic and medical characteristics were modelled as observed variables. 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 and deviations of data from normality (Little & Rubin, 2003). Following

recommendations of Hu and Bentler (1999), we report two fit indices: Tucker-Lewis Index (TLI) and Comparative Fit Index (CFI), and two indices of misfit: Root Mean-Square Error of Approximation (RMSEA) and Standardised Root Mean-Square Residual (SRMR). 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.

Variance resulting from specific measurement occurrences in the cross-lagged panel model was accounted for by correlating all the measurement errors of same indicators across time points (Marsh & Hau, 1996). To ensure weak factorial invariance across time points and stationarity of correlations across time (Finkel, 1995), we constrained factor loadings for equality across measurement waves and set all the coefficients of directional paths and correlations to be invariant across waves. To test for model (in)variance across the four participating countries, multi-group analysis was performed. In the multi-group model, the factor loadings were constrained to equality both across waves and across groups. Using chi-squared difference test, the multi-group SEM model in which the cross-lagged paths were constrained for equality was compared to the model where these paths were allowed to vary freely.

## 3 | RESULTS

### 3.1 | Descriptive statistics

Participant sociodemographic and medical characteristics are presented in Table 1. The participants' mean age was 54.94 (SD = 8.21); the majority (73.9%) were married, with postsecondary education (58.5%), and at least partially employed (69.5%). Distribution and first-order intercorrelations of the research variables appear in Table 2. As can be seen, the psychological symptoms became milder from T1 to T2 ( $p < 0.0001$ , paired-samples  $t$ -test, Cohen's  $d = 0.22$ ) and from T2 to T3 ( $p = 0.029$ ,  $d = 0.09$ ). The number of somatic symptoms at baseline wasn't negligible. Substantial numbers of participants reported symptoms such as hot flashes, headaches, need to rest, or being constipated. The somatic symptoms worsened after 3 months ( $p < 0.0001$ ,  $d = 0.29$ ) and then returned almost to their baseline level, although still remained significantly ( $p < 0.0001$ ,  $d = 0.27$ ) higher. At each time-point, the psychological and the somatic symptoms were moderately correlated, with  $r$ 's of 0.35 to 0.48. Psychological symptoms were relatively stable across time, with  $r$ 's of 0.71 and 0.68 between adjacent measurements. Somatic symptoms were slightly less stable during the first 3 months ( $r = 0.55$ ) than between months three and six ( $r = 0.72$ ).

### 3.2 | Cross-lagged panel model

As a preliminary step in the 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

**TABLE 1** Participant sociodemographic and medical characteristics ( $N = 689$ )

Country of data collection	
Finland	225 (32.2%)
Israel	138 (19.8%)
Italy	189 (27.1%)
Portugal	146 (20.9%)
Age (years)	
Mean = 54.94; SD = 8.21	
Family status	
Married/living with partner	516 (73.9%)
Single or widowed	182 (26.1%)
Education level	
Primary or secondary school	58 (8.3%)
High school or vocational diploma	232 (33.2%)
B.A.	240 (34.4%)
M.A. or higher	168 (24.1%)
Employment	
Fully or partially employed or self-employed	484 (69.5%)
Unemployed, housewife, retired	212 (30.5%)
Monthly income (Euro)	
1500 or lower	238 (36.3%)
1501-2500	286 (43.7%)
2501 or higher	131 (20.0%)
Background chronic disease	
Present	226 (32.4%)
Absent	472 (67.6%)
Body Mass Index (BMI)	
Mean = 25.68; SD = 4.72	
Cancer stage at baseline	
Stage I	333 (47.9%)
Stage II	284 (40.9%)
Stage III	78 (11.2%)
Cancer grade at baseline	
Grade I	130 (19.0%)
Grade II	347 (50.7%)
Grade III	207 (30.3%)
Type of treatment	
Lumpectomy	497 (71.2%)
Mastectomy	192 (27.5%)
Chemotherapy	343 (49.1%)
Radiotherapy	523 (74.9%)
Endocrine therapy	566 (81.1%)
Anti HER2 therapy	108 (15.7%)

$\chi^2(110) = 338.73$ ,  $p < 0.001$ ; TLI = 0.959; CFI = 0.970; RMSEA = 0.055 (90% CI = 0.048; 0.062); SRMR = 0.052. 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, with  $\chi^2(300) = 772.85$ ,  $p < 0.001$ ; TLI = 0.927; CFI = 0.948; RMSEA = 0.048 (90% CI = 0.044; 0.052); SRMR = 0.058. Finally, for the sake of parsimony, we omitted from the model all non-significant ( $p \geq 0.05$ ) paths from covariates to the research model. The resulting model fit well to the data, with  $\chi^2(249) = 675.17$ ,  $p < 0.001$ ; TLI = 0.942; CFI = 0.951; RMSEA = 0.050 (90% CI = 0.045; 0.054); SRMR = 0.075. The path coefficients in this model appear in Figure 1. As seen in the Figure, both psychological and somatic symptoms are rather stable across time (stability coefficients of 0.71 and 0.67, respectively) and are intercorrelated ( $r = 0.54$ ). 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 0.08 and 0.12, suggesting that the change in each variable is associated with change in the other variable.

In order to test whether the model parameters were sensitive to the chosen method of dealing with missing values, we repeated the analyses using only the data of the participants that provided data at T3 ( $N = 558$ ). The pattern of results was similar to those obtained for the full sample. Both cross-lagged paths leading from somatic to psychological symptoms were characterized by  $\beta = 0.09$ , and both paths leading from psychological to somatic symptoms by  $\beta = 0.13$ .

### 3.3 | Cross-cultural comparisons

A multi-group model in which the cross-lagged effects were constrained for equality yielded  $\chi^2(1033) = 2652.16$ ,  $p < 0.001$ . The same model in which these constraints were released yielded  $\chi^2(1027) = 2639.71$ ,  $p < 0.001$ . The difference between these models was not significant ( $p = 0.053$ ), which does not support existence of cross-cultural differences in the mutual effects of psychological and somatic symptoms.

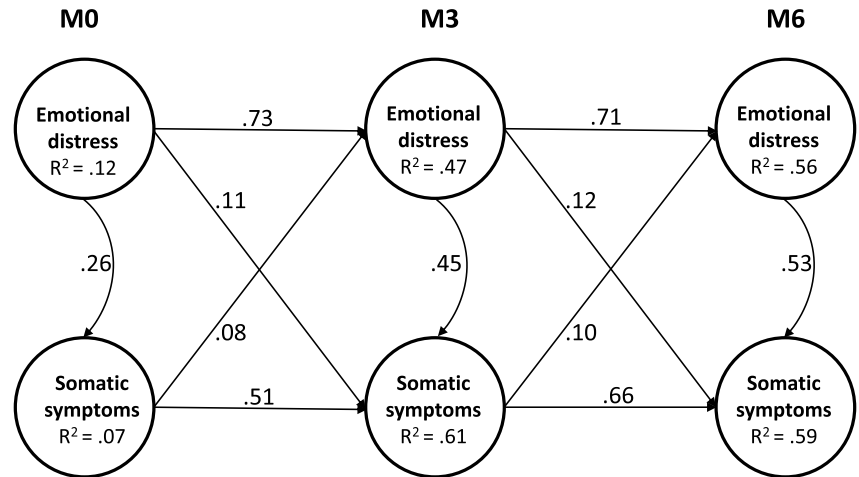
## 4 | DISCUSSION

The current research aimed to further clarify the nature of the inter-relations between somatic and psychological symptoms in breast cancer patients at diagnosis as well as three and 6 months later. We also aimed to explore differences in these inter-relations across four European countries. Our results showed support for Theory of Unpleasant Symptoms in relation to breast cancer in the early phase after diagnosis. Somatic symptoms are present soon after diagnosis, possibly as a result of diagnosis (cf. He et al., 2021). Using a cross-lagged model, we showed that these symptoms were predictive of change in psychological symptoms after 3 months, which in turn were

**TABLE 2** Distribution and intercorrelations of research variables at three times

Variable	N	Mean	SD	1	2	3	4	5
1. Psychological symptoms T1	689	1.17	0.58					
2. Somatic symptoms T1	683	1.50	0.37	0.35				
3. Psychological symptoms T2	615	1.06	0.55	0.71	0.41			
4. Somatic symptoms T2	610	1.65	0.41	0.33	0.55	0.43		
5. Psychological symptoms T3	555	0.99	0.51	0.60	0.34	0.68	0.33	
6. Somatic symptoms T3	552	1.56	0.38	0.30	0.52	0.41	0.72	0.48

**FIGURE 1** The cross-lagged model of psychological and somatic symptoms (standardized coefficients)



predictive of changes in somatic symptoms after 6 months. A similar pattern was found regarding the psychological symptoms. Taken together, these findings show the pattern of the mutual effects of somatic and psychological symptoms over time during the early and acute phase of coping with breast cancer and its related treatments. These findings are consistent with previous longitudinal research with breast cancer survivors post-treatment (Badr et al., 2006), and cross-sectional research with breast cancer patients during treatment (McFarland et al., 2018). These results reflect the Theory of Unpleasant Symptoms which emphasizes the complex and dynamic nature of symptoms (Lenz, 2018). Our results extend the previous literature to demonstrate the prospective associations between psychological and somatic symptoms in the acute phase after breast cancer diagnosis and during early treatment.

The differences in patterns of associations between psychological and somatic symptoms across the four countries were not statistically significant. In other words, the model was generalizable across countries. We were open to the possibility that there would cross-country differences given the previous research which has found that experiences of psychological and somatic symptoms after cancer diagnosis vary (Pilevarzadeh et al., 2019; Shim et al., 2006) and that the relations between may differ across countries (Fischer et al., 2017). However, contrary to the comparison between a Western (Holland) and an Eastern country (Japan) in Fischer et al. (2017), the four countries compared in the current study can be broadly characterized as possessing Western cultures, and thus their cultural differences may have been too small to reveal differences in

patterns of interrelations between experiences of psychological and somatic symptoms.

The study has clinical implications for early screening of symptoms of distress and to increase the awareness of health professionals to the close interaction between psychological and somatic symptoms. International clinical practice guidelines for management of breast cancer recommend that healthcare professionals screen for psychological distress and refer to psychosocial support where necessary (Gradishar et al., 2020). Despite this, research shows that many patients have needs for psychosocial support that are not met (Faller et al., 2017; Riedl et al., 2018). The current findings underline the importance of addressing psychological health—not only for psychological wellbeing proper, but also given the implications for physical wellbeing. In-line with the Theory of Unpleasant Symptoms, health professionals should monitor for changes in symptoms, and should measure the intensity, timing, distress and quality of symptoms to attain a rich understanding of the patient experience (Lenz, 2018). Early screening can ensure early interventions, which are important to the preventing the onset, or worsening, of symptoms (Vos et al., 2006). The temporality aspects of the model are especially relevant for timing the appropriate clinical interventions aimed at 'breaking the chain' of somatic and psychological symptoms. Understanding the mutual relationships between psychological and somatic symptoms over time has direct clinical implications. Clinicians can sensitively adapt their interventions to the specific preferences and needs of the patient either targeting the somatic or psychological symptoms.

Future studies may benefit from including objective biological measures of somatic symptoms, such as neuroendocrine processes and immune system functioning, alongside subjective measures. By using objective biological measures, future studies may be able to test the biopsychosocial model in the context of breast cancer. This is particularly important, as research suggests that psychological interventions may be able to influence neuroendocrine and immune functioning (McGregor & Antoni, 2009).

Psychosocial interventions in the context of early treatment for breast cancer should include screening and identification of distress and the adjustment of early interventions towards alleviation of distress on both the psychological and somatic levels. This is in line with the conclusion drawn from a meta-analysis by Cramer et al. (2017) that showed that complex yoga interventions (incorporating breath control and/or meditation beyond physical yoga postures) were effective supportive interventions for improving health-related quality of life, depression, anxiety, fatigue and sleep in women recently diagnosed with breast cancer. Other psychosocial interventions which may help to alleviate psychological and somatic symptoms include psychoeducation (Zimmermann et al., 2007), cognitive behavioural therapy (Fors et al., 2011), cognitive behavioural stress management (McGregor & Antoni, 2009), patient education and supportive group therapy (Johannsen et al., 2013), and mindfulness-based interventions (Li et al., 2020). Likewise, modular and comprehensive interventions that can address psychosomatic aspects synergically are likely to be beneficial for enhancement of quality of life (Faller et al., 2019). Further research is needed to determine whether these psychosocial interventions are equally successful across countries, or whether certain interventions are more suitable for different countries.

The current study has several limitations. First, the effect sizes shown in the statistical model are small, with beta coefficients ranging between 0.08 and 0.12. However, following Funder and Ozer (2019), we interpret the findings as non-negligible: they were obtained in a large sample and, if replicated in additional populations, they are highly consequential, as the symptoms to which they pertain are experienced by virtually every woman coping with breast cancer. Second, while self-reports of symptoms are a central tenant of the Theory of Unpleasant Symptoms, the use of self-reports alone may be a limitation of the study. Although self-reporting of purely somatic symptoms is less prone to reporting bias that can create artificial association with psychological symptoms, this possibility cannot be excluded. Third, the present study included 11% and 19% dropouts at Waves 2 and 3, respectively. As the dropouts were significantly less educated and with lower income, with lower proportions undergoing chemo-, radio- or endocrine therapy SH2, and higher levels of depression and negative affectivity at baseline, caution should be applied in generalization of the findings. Finally, the study was performed in four economically developed countries, and this might have been the reason for cross-country invariance in our empirical findings. Future studies are encouraged to replicate these findings in more culturally diverse populations and to test the generalizability in other types of cancer. Longer follow-ups may shed more light on the

complex ways that psychosomatic distress may interact, and also how they are dependent on the time elapsed from diagnosis and termination of treatments.

## 5 | CONCLUSION

Our study highlights the mutual and co-dependent trajectories of change in psychological and somatic symptoms among breast cancer patients during the first 6 months of active treatment, thus supporting the Theory of Unpleasant Symptoms. This synergy calls for greater awareness of the personalized style of expressing distress among breast cancer patients and for the need of adopting a sensitive and patient-centred approach, in order to implement interventions for patients according to individual patterns of manifestation of distress. The mutual relationship between psychological and somatic symptoms over time has direct clinical implications. Interventions can be tailored according to the preferences of the patient in targeting somatic and psychological symptoms. Any intervention geared at enhancing psychological wellbeing, or any intervention planned to improve physical wellbeing, can promote the quality of life of breast cancer patients during the early phase of treatment. The implementation of both somatic and psychosocial intervention, in synergy, may prove to be most beneficial.

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## CONFLICT OF INTEREST

Albino J. Oliveira-Maia was national coordinator for Portugal of a non-interventional study (EDMS-ERI-143085581, 4.0) to characterize a Treatment-Resistant Depression Cohort in Europe, sponsored by Janssen-Cilag, Ltd (2019–2020), is recipient of a grant from Schuhfried GmbH for norming and validation of cognitive tests, and is national coordinator for Portugal of trials of psilocybin therapy for treatment-resistant depression, sponsored by Compass Pathways, Ltd (EudraCT number 2017-003288-36 and 2020-001348-25), and of Esketamine for treatment-resistant depression, sponsored by Janssen-Cilag, Ltd (EudraCT NUMBER: 2019-002992-33). The remaining authors have no potential conflicts of interest to declare.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

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