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Persistent adverse effects of cancer treatments on mental health, fatigue, and sleep disturbances in breast cancer survivors

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Abstract

Background Breast cancer is the most diagnosed cancer worldwide, affecting one in four women diagnosed with cancer. Cancer treatments, particularly chemotherapy, can adversely impact mental health, contributing to increased stress, anxiety, depression, fatigue, and poor sleep quality. This study investigated the long-term psychological effects of cancer treatment among breast cancer survivors and explored interactions between these factors.

Methods We recruited Canadian women aged 30 to 65 with a history of breast cancer who were at least 6-months post-treatment ($n = 49$) and age-matched control participants ($n = 44$). Participants provided demographic and health information and completed online questionnaires assessing stress, depression, trait and state anxiety, fatigue, sleep quality, and physical activity.

Results Breast cancer survivors reported significantly higher levels of stress ($p = .004$), depression ($p < .001$), state anxiety ($p = .003$), trait anxiety ($p = .02$), fatigue ($p < .001$), as well as poorer sleep quality ($p < .001$) compared to non-cancer controls. Physical activity levels and leisure-time exercise did not differ between groups ($p = .13$ and $p = .17$, respectively). While physical activity was not significantly correlated with mental health factors in either group (p's > 0.05), most mental health factors were correlated with each other in both groups (p's < 0.05).

Conclusion Our findings enhance understanding of the long-term mental health effects of cancer treatment in breast cancer survivors, providing strong evidence that breast cancer survivors continue to experience significant psychological challenges – including stress, anxiety, depression, fatigue, and sleep disturbances. Given these persistent challenges, it is critical to incorporate comprehensive mental health assessments into cancer survivorship plans to identify psychological concerns and inform treatment strategies that address the interconnectedness of these issues.

Keywords Breast cancer, Depression, Anxiety, Fatigue, Sleep disturbances, Exercise, Stress, Post-treatment, Chemotherapy, Survivorship

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Introduction

Breast cancer is the most diagnosed cancer among women worldwide, affecting one in four women diagnosed with cancer [1]. Treatment decisions for breast cancer are determined by several factors, including the tumor size, location, stage, and estrogen and progesterone hormone receptor status [2]. Standard treatment options include surgery, radiation, chemotherapy, and hormonal therapy [2]. Although advancements in prevention strategies, screening, and treatment have significantly improved survival rates [2, 3], they have also increased awareness of treatment-related side effects.

Following diagnosis and surgery but prior to adjuvant therapy, 78.1% of breast cancer patients report experiencing high levels of stress [4]. Stress is highest before chemotherapy and immediately after surgery [5], but tends to decline in the year following treatment [5, 6]. In contrast, symptoms of depression are higher during treatment compared to pre-treatment [7, 8], peaking one year following treatment [8], particularly among those with pre-existing depressive symptoms [7], and can persist for up to a decade following diagnosis [8]. Younger patients (18–39 years) report more severe depression than older patients, likely due to differing psychosocial challenges across life stages [9]. Anxiety symptoms in breast cancer patients tend to peak at diagnosis [10] and during chemotherapy treatment [7], and while there is a progressive decrease, they can persist for up to six years post-diagnosis [10, 11]. Similarly to depression, patients with high pre-treatment trait anxiety experience higher state anxiety during treatment than those with lower baseline trait anxiety, indicating that individuals with a pre-existing anxious disposition are at higher risk for severe anxiety during treatment [10, 12]. Sleep disturbances affect 20%-70% of breast cancer patients [13] and can persist for up to a decade following treatment [14]. Commonly reported issues include difficulty falling asleep, staying asleep, and early morning awakenings [14, 15]. During treatment, 60%-90% of women also report experiencing fatigue [16], with higher rates among those undergoing chemotherapy compared to radiation therapy [17]. Cancer-related fatigue often emerges before treatment, worsens throughout the treatment period, and can persist for up to a decade following treatment [18]. Although fatigue severity tends to decrease over time, it often does not return to baseline levels [19].

Mental health difficulties frequently co-occur in this population. For instance, depressive symptoms are commonly linked to increased anxiety, fatigue, and reduced quality of life [8, 20, 21]. Similarly, anxiety is associated with heightened stress, sleep disturbances, fatigue, and lower quality of life [19, 22, 23]. Sleep disturbances and fatigue are closely related and often co-occur with depression and anxiety, further contributing to diminished well-being [19, 24]. In addition to these mental health concerns, survivors frequently report long-term issues with cognitive functioning, sexual health (including fertility), body image, self-esteem, social relationships, and financial stability [25–28]. These challenges are particularly pronounced among those who received chemotherapy as part of their cancer treatment [25, 27].

Strong evidence supports the benefits of physical activity interventions for breast cancer both during treatment [29] and throughout survivorship [30]. These interventions offer psychological advantages - including improved quality of life reductions in anxiety, depression, and fatigue [30–32] - as well as physiological benefits, such as enhanced cardiovascular health and reduced risk of cancer recurrence [31]. Consequently, integrating physical activity into survivorship plans is widely recommended [31]. However, there is evidence that while physical activity may reduce anxiety and improve quality of life, it does not consistently alleviate depressive symptoms in breast cancer survivors [33]. Adherence to exercise programs is critical for achieving these benefits, yet can be influenced by various factors, including motivation, fatigue, pain, and mental health challenges [34].

Extensive research has examined pre- and post-treatment psychosocial factors such as stress, anxiety, fatigue, depression, sleep quality, as well as exercise in breast cancer survivors [5, 8, 10, 14, 18, 33]. However, few studies have explored the long-term interplay among these factors from a synergistic perspective, or directly compared these outcomes to women without a history of breast cancer. This study addresses this gap by examining the long-term effects of cancer treatment on multiple, interrelated psychosocial domains and evaluating how these patterns differ from those observed in a non-cancer comparison group of women. We hypothesized that breast cancer survivors would report high levels of perceived stress, anxiety, depression, fatigue, and sleep disturbances compared to non-cancer controls. We also expected these psychosocial difficulties would be positively correlated, while greater engagement in physical activity would be associated with lower psychological distress. By examining these complex relationships, this study aims to inform the importance of comprehensive mental health assessments and the development of targeted interventions to enhance the long-term well-being and quality of life of breast cancer survivors.

Methods

Participants

We recruited female breast cancer survivors (BCS), aged 30 to 65, who were at least six-months post-chemotherapy treatment, and age-matched women without a history of breast cancer (healthy controls, HC). Participants were recruited through community outreach,

public advertisements on social media, the community Integrated System of Participation in Research at the University of Ottawa, and the Cancer Foundation Maplesoft-Jones Centre. Exclusion criteria included: [1] a mental health diagnosis within the past 12 months [2], a lifetime diagnosis of brain injury (e.g., concussion), neurodevelopmental (e.g., Attention-Deficit/Hyperactivity Disorder) or neurological disorder (e.g., stroke) [3], initiation of new mood-altering medications within the past 12 months [4], current substance dependence or consuming cannabis more than 7 times per month [5], lack of fluency in English, and [6] residence outside of Canada. Participants with these neurological disorders were excluded due to their potential impact on mental health outcomes. This study received full board review and approval from the University of Ottawa's Research Ethics Board (H-04-21-6706) and was conducted in accordance with the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans.

Procedure

Participants provided informed consent, then completed a comprehensive sociodemographic questionnaire assessing demographic (e.g., province of residence, education level, income) and health-related (e.g., mental health diagnoses, substance use, medications, and cancer treatment details) factors. Participants then completed self-reported measures evaluating psychological and physical health indicators, including stress, depression, trait and state anxiety, fatigue, sleep quality, leisure-time exercise, and physical activity. This session took up to 60 min to complete online via Qualtrics, an online questionnaire distribution tool (RRID: SCR_016728). Participants completed the online questionnaires while connected via Zoom, a videoconferencing platform, with a member of the research team present to provide support.

Measures

The Perceived Stress Scale (PSS) is a reliable instrument for assessing perceived stress levels experienced in the past month [35]. The self-reported questionnaire consists of 10 items rated on a 5-point Likert scale, with higher ratings indicating a higher level of perceived stress. The PSS demonstrates good reliability for perceived helplessness (McDonald's omega = 0.87) and acceptable reliability for self-efficacy (McDonald's omega = 0.73). Validity was assessed using confirmatory factor analysis and by assessing the relationship with another well validated measure assessing stress, anxiety, and depression (Depression Anxiety Stress Scale, DASS-21) which all demonstrated good validity in breast cancer patients [36]. The PSS has been used numerous times with this patient population [4–6].

The State-Trait Anxiety Inventory (STAI) is a widely used self-reported measure that differentiates between situational (state) and general (trait) anxiety [37]. It includes two 20-item scales: Form Y-1 or STAI-S (state anxiety), and Form Y-2 or STAI-T (trait anxiety), rated on a 4-point Likert scale, with scores above 39 indicating clinically significant levels of anxiety. Although no study has yet to formally assess the validity and reliability of this measure in breast cancer survivors, it has been widely used with this patient population [12, 19, 38, 39].

The Centre for Epidemiologic Studies Depression Scale-Revised (CESD-R) is a 20-item self-report measure assessing depressive symptoms experienced within the past week, rated on a 5-point Likert scale [40]. Higher scores indicate greater symptom severity. Scores below 16 indicate no clinical depression, whereas scores ≥ 16 indicate increasing levels of depressive severity, with thresholds for subclinical, possible, probable, and major depressive episodes based on the presence and frequency of anhedonia, dysphoria, and other symptoms. The psychometric properties of the CESD-R have only been measured in a sample of Chinese patients with cancer which revealed good internal consistency (Cronbach's alpha, $\alpha = 0.82 - 0.88$) and acceptable construct validity when the CESD-R was compared with the depression module of the Patient Health Questionnaire (*rho* = 0.73) [41]. The CESD-R has been previously used with this patient population [8, 18].

The Fatigue Severity Scale (FSS) is a 9-item self-report measure assessing fatigue over the past 30 days, rated on a 7-point Likert scale with higher scores indicating a greater level of fatigue [42]. While no specific clinical cut-off scores have been established for the FSS, the scale has excellent internal consistency in cancer patients ($\alpha = 0.96$) [43].

The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-report measure assessing sleep quality over the past month [44]. Items form seven subscales, or components, which are summed to produce a global score, with scores > 5 reflecting poor sleep. The PSQI has acceptable internal consistency ($\alpha = 0.79$) and convergent validity (r = .72 to 0.81) which was measured by assessing the relationship between the PSQI and four other sleep scales in cancer populations [45], and has been frequently used with breast cancer patients [14, 15, 24].

The Leisure Time Exercise Questionnaire (LTEQ) assesses weekly leisure-time physical activity [46]. It includes two items: the first items measure frequency of mild, moderate, and strenuous exercise (> 15 min per session), and the second assesses the frequency of heart rate elevation during these activities, using a 3-point Likert scale. Higher scores reflect greater activity, with < 14 units indicating sedentary behavior, 14–23 moderately active, and > 24 units active.

The International Physical Activity Questionnaire (IPAQ) short form is a 7-item self-report measure of physical activity and sedentary behavior over the past week [47]. It assesses time spent on vigorous and moderate activities, walking (> 10 min per session), and sitting. A composite Metabolic Equivalent Task (MET) score is calculated, with a higher score indicating greater physical activity. Activity levels are classified as: low (not meeting criteria for moderate or high activity), moderate (> 3 days/week of vigorous activity for > 30 min/day, > 5 days/week of moderate activity and/or walking for > 30 min/day, or > 5 days/week of any activity for > 600 MET-min/week), or high (> 3 days/week of vigorous activity for > 1500 MET-min/week, or 7 days/week of any activity for > 3000 MET-min/week).

Statistical analysis

Questionnaire data were collected using Qualtrics (RRID: SCR_016728) and scored using a script in R-Studio (RRID: SCR_001905). Statistical analyses were performed in SPSS 28 (RRID: SCR_002865). For this between-subjects design, independent sample t-tests evaluated group differences in stress, fatigue, anxiety, depression, sleep quality, and physical activity. To evaluate the interrelationships among key mental health constructs (stress, depression, anxiety, fatigue, sleep quality), Pearson correlation (r) analyses were conducted to assess the strength and direction of their associations. Statistical significance was set at $p < .05$, with Bonferroni corrections applied to adjust the alpha level for multiple comparisons. We conducted eight multiple regression analyses, one for each outcome variable—stress, trait anxiety, state anxiety, depression, sleep quality, fatigue, exercise, and physical activity. Each model included all demographic and health-related predictors: age, education, income, and menopausal status (for both groups), as well as time since treatment and current hormonal therapy (for breast cancer survivors only). Figures were created using GraphPad Prism (RRID: SCR_002798).

Results

Participant characteristics

A total of 109 participants completed the demographic, health, and mental health questionnaires. Of these, 16 were excluded ($n = 11$ BCS, $n = 5$ HC) based on the exclusion criteria. Among the 93 eligible participants ($n = 49$ BCS; $n = 44$ HC), the majority identified as White (BCS: 93.9%; HC: 81.8%), held a bachelor's degree (BCS: 46.9%; HC: 38.6%), and reported a family income between $100,000 and $200,000 (BCS: 46.9%; HC: 38.6%). Substance use was reported by 49.0% of breast cancer survivors and 61.4% of controls, with alcohol being the most used substance, and occasional cannabis use of no more than 7x per month. A lifetime history of mental health diagnoses (e.g., anxiety, depressive, eating, and post-traumatic stress disorders), was reported by 12.2% of breast cancer survivors and 18.2% of controls, with no participants reporting symptoms in the past 6 months. Long-term use of mood-altering medication (over one year) was reported by 14.3% of breast cancer survivors, compared to 11.4% of controls. Finally, 81.6% of breast cancer survivors and 54.5% of controls were post-menopausal (Table 1).

Among breast cancer survivors, most were diagnosed with stage 2 breast cancer (42.9%) between 2 and 5 years ago (51.0%). Survivors completed cancer treatment (excluding hormonal therapy) between 6 months to more than 10 years ago, with most completing treatment within the past 1 to 5 years (57.2%). Participants underwent a variety of treatments, including chemotherapy (100.0%), hormonal therapy (57.1%), radiation therapy (77.6%), surgery (100.0%), immunotherapy (4.1%), and targeted therapy (18.4%). Of those prescribed hormonal therapy, the majority (51.0%) were still taking these medications (e.g., Tamoxifen) while participating in this study (Table 2).

Group differences between stress, anxiety, depression, fatigue, sleep quality, and physical activity

Breast cancer survivors reported higher levels of perceived stress compared to non-cancer controls [$t(91) = 2.67$, $p = .004$, Cohen's $d = 0.55$] (Fig. 1A), where breast cancer survivors reported moderate levels of perceived stress whereas healthy controls reported low levels according to PSS cut-off scores. Despite breast cancer survivors reporting sub-clinical levels of anxiety (STAI > 39), they reported significantly more symptoms than controls [STAI-T: $t(91) = 2.08$, $p = .02$, $d = 0.43$; STAI-S: $t(91) = 2.76$, $p = .003$, $d = 0.57$] (Fig. 1B, C). Similarly, symptoms of depression were also higher among breast cancer survivors [$t(90.95) = 3.52$, $p < .001$, $d = 0.72$], although, these levels were within the non-clinical range (CESD-R < 16) (Fig. 1D). Sleep quality also significantly differed between groups [$t(86.01) = 5.23$, $p < .001$, $d = 1.06$] with breast cancer survivors categorized as poor sleepers (PSQI ≥ 5) and healthy controls classified as good sleepers (PSQI < 5) (Fig. 1E). Fatigue also differed among groups [$t(91) = 4.02$, $p < .001$, $d = 0.83$] with breast cancer survivors reporting heightened levels of fatigue compared to controls (Fig. 1F). After applying Bonferroni correction (adjusted $\alpha = 0.006$), group differences in perceived stress, state anxiety, depression, fatigue, and sleep disturbances remained statistically significant. While breast cancer survivors engaged in less leisure-time exercise, they reported a higher overall level of physical activity compared to controls; however, neither difference was statistically significant [leisure-time exercise:

Table 1 Participant demographics

	BCS (*n* = 49)	**HC (*n* = 44)**
	Mean (SD) or Percentage (sample size)	**Mean (SD) or Percentage (sample size)**
Age	50.71 (8.58)	50.16 (10.71)
Province of residence		
Alberta	0.00% (0)	4.50% (2)
British Columbia	4.10% (2)	9.10% (4)
Manitoba	8.20% (4)	0.00% (0)
New Brunswick	2.00% (1)	0.00% (0)
Nova Scotia	4.10% (2)	0.00% (0)
Northwest Territories	4.10% (2)	0.00% (0)
Ontario	59.20% (29)	68.20% (30)
Prince Edward Island	2.00% (1)	2.30% (1)
Quebec	12.20% (6)	11.40% (5)
Saskatchewan	4.10% (2)	2.30% (1)
Yukon	0.00% (0)	2.30% (1)
Race		
White	94.00% (46)	81.80% (36)
Black	0.00% (0)	2.30% (1)
Greek	2.00% (1)	0.00% (0)
East Asian	0.00% (0)	2.30% (1)
South Asian/East Indian	2.00% (1)	2.30% (1)
Indigenous	0.00% (0)	2.30% (1)
Latin American	0.00% (0)	2.30% (1)
Person of mixed origin	0.00% (0)	2.30% (1)
Turkish	2.00% (1)	0.00% (0)
West Asian, North African, Arab	0.00% (0)	2.30% (1)
I prefer not to answer	0.00% (0)	2.30% (1)
Completed Education Level		
High school diploma	6.10% (3)	2.30% (1)
College degree	24.50% (12)	20.50% (9)
Bachelor's degree	46.90% (23)	38.60% (17)
Master's degree	16.30% (8)	27.30% (12)
Doctorate degree	2.00% (1)	6.80% (3)
Other	4.00% (2)	4.60% (2)
Income		
< $30 000	0.00% (0)	6.80% (3)
$30 000 - $50 000	2.00% (1)	9.10% (4)
$50 000 - $100 000	24.50% (12)	22.70% (10)
$100 000 - $200 000	46.90% (23)	39.00% (17)
> $200 000	20.40% (10)	11.00% (5)
I prefer not to answer	6.10% (3)	11.40% (5)
Current Substance Use (Yes, %)	49.00% (24)	61.40% (27)
Drug-Frequency		
Daily	22.40% (11)	27.30% (12)
2–3 times per week	8.20% (4)	13.60% (6)
Once per week	2.00% (1)	9.10% (4)
Once per month	24.50% (12)	22.70% (10)
Not applicable	42.90% (21)	27.30% (12)
Mental Health Diagnosis (Yes, %)	12.20% (6)	18.20% (8)
Medications (Yes, %)	81.60% (40)	52.30% (23)
Mood Altering Medications (Yes, %)	14.30% (7)	11.40% (5)
Menopausal		
Pre-menopausal	18.40% (9)	45.50% (20)
Post-menopausal	81.60% (40)	54.50% (24)

Abbreviations: *BCS* Breast cancer survivors, *HC* Healthy controls, *SD* Standard deviation, % Percentage

Table 2 Breast cancer diagnosis ($n = 49$) and treatment details

	Percentage (sample size)
Time since Diagnosis	
1–2 years ago	16.00% (8)
2–5 years ago	51.00% (25)
5–10 years ago	20.40% (10)
> 10 years ago	12.20% (6)
Cancer Stage at Diagnosis	
Stage 0	2.00% (1)
Stage 1	18.00% (9)
Stage 2	42.90% (21)
Stage 3	32.70% (16)
Unknown	4.10% (2)
Treatment End	
6–12 months ago	14.30% (7)
1–2 years ago	28.60% (14)
2–5 years ago	28.60% (14)
5–10 years ago	20.40% (10)
> 10 years ago	8.20% (4)
Current Hormone Therapy	
Yes	51.00% (25)
No	6.10% (3)
Not applicable	42.90% (21)
Treatment	
Chemotherapy	100.00% (49)
Hormonal Therapy	57.10% (28)
Radiation Therapy	77.60% (38)
Surgery	100.00% (49)
Immunotherapy	4.10% (2)
Targeted Therapy	18.40% (9)

$t(91) = -0.93$, $p = .17$, $d = -0.19$ (Fig. 1G); MET activity: $t(91) = 1.12$, $p = .13$, $d = 0.23$] (Fig. 1H).

Based on Cohen's guidelines, the effect sizes indicated a negligible difference between breast cancer survivors and healthy controls in leisure time exercise [48]. Small effects were observed overall physical activity and moderate effect sizes were found for perceived stress, depression, and state anxiety. The largest differences emerged in fatigue and sleep quality, which showed large effect sizes.

Reliability analyses demonstrated excellent internal consistency for the PSS ($\alpha = 0.90$), STAI-S ($\alpha = 0.93$), STAI-T ($\alpha = 0.91$), and FSS ($\alpha = 0.90$). The CESD-R ($\alpha = 0.87$) demonstrated good internal consistency, while the PSQI ($\alpha = 0.78$) showed acceptable internal consistency among participants in this study. Given that the LTEQ and IPAQ are open-ended questions, and not a Likert scale, no reliability analyses were conducted for these measures.

Correlations between stress, anxiety, depression, fatigue, sleep disturbances, and physical activity

Pearson correlation analyses were conducted to examine relationships among the various constructs. In both groups, significant positive correlations were observed between stress and depression, state anxiety, trait anxiety, and fatigue (p's < 0.05). Similarly, state anxiety was positively correlated with stress, depression, trait anxiety, and fatigue (p's < 0.05), while trait anxiety showed significant correlations with depression and fatigue (p's < 0.05). Depression was also positively correlated with both fatigue and sleep quality (p's < 0.05), and physical activity was significantly correlated with leisure time exercise (p's < 0.05). Notably, sleep quality was significantly correlated with state and trait anxiety, and stress, but only in controls (p's < 0.05). Full correlation coefficients are presented in Table 3.

Exploratory multiple regression analyses

As a set, the variables age, education, income, menopausal status, time since treatment, and current hormonal therapy collectively predicted stress and physical activity in breast cancer survivors ($p = .004$ and $p = .03$, respectively), but not in healthy controls ($p = .06$ and $p = .07$, respectively). In contrast, these variables predicted depression in healthy controls ($p = .02$), but not in breast cancer survivors ($p = .45$). All variables predicted state anxiety in breast cancer survivors ($p = .02$) and healthy controls ($p = .01$). However, none of the variables collectively predicted trait anxiety, fatigue, sleep quality, or leisure exercise in either group (p's > 0.05). Examining individual predictors, multiple regression analyses in breast cancer survivors revealed that age significantly predicted stress, state anxiety, while income predicted both stress and physical activity (p's < 0.05). In the control group, education predicted depression and state anxiety, while both income and menopausal status were significant predictors of depression (p's < 0.05). Complete regression statistics can be found in Table 4.

Discussion

This study provides a comprehensive examination of the long-term psychological impacts of breast cancer treatment, identifying that survivors experience significantly elevated levels of stress, anxiety, depression, fatigue, and sleep disturbances compared to women without a history of cancer. These results are consistent with prior research identifying elevated levels of stress [6], anxiety [10, 11], depression [8], sleep disturbances [15], and fatigue [18, 19] in breast cancer survivors, some persisting up to a decade post-diagnosis [8, 10, 11, 14, 18]. Our findings contribute to the literature by directly comparing the psychological functioning of breast cancer survivors to that of non-cancer controls, offering a clearer understanding of the unique challenges associated with cancer survivorship.

Although breast cancer survivors reported greater symptoms of depression and anxiety compared to controls, both groups scored within the subclinical range

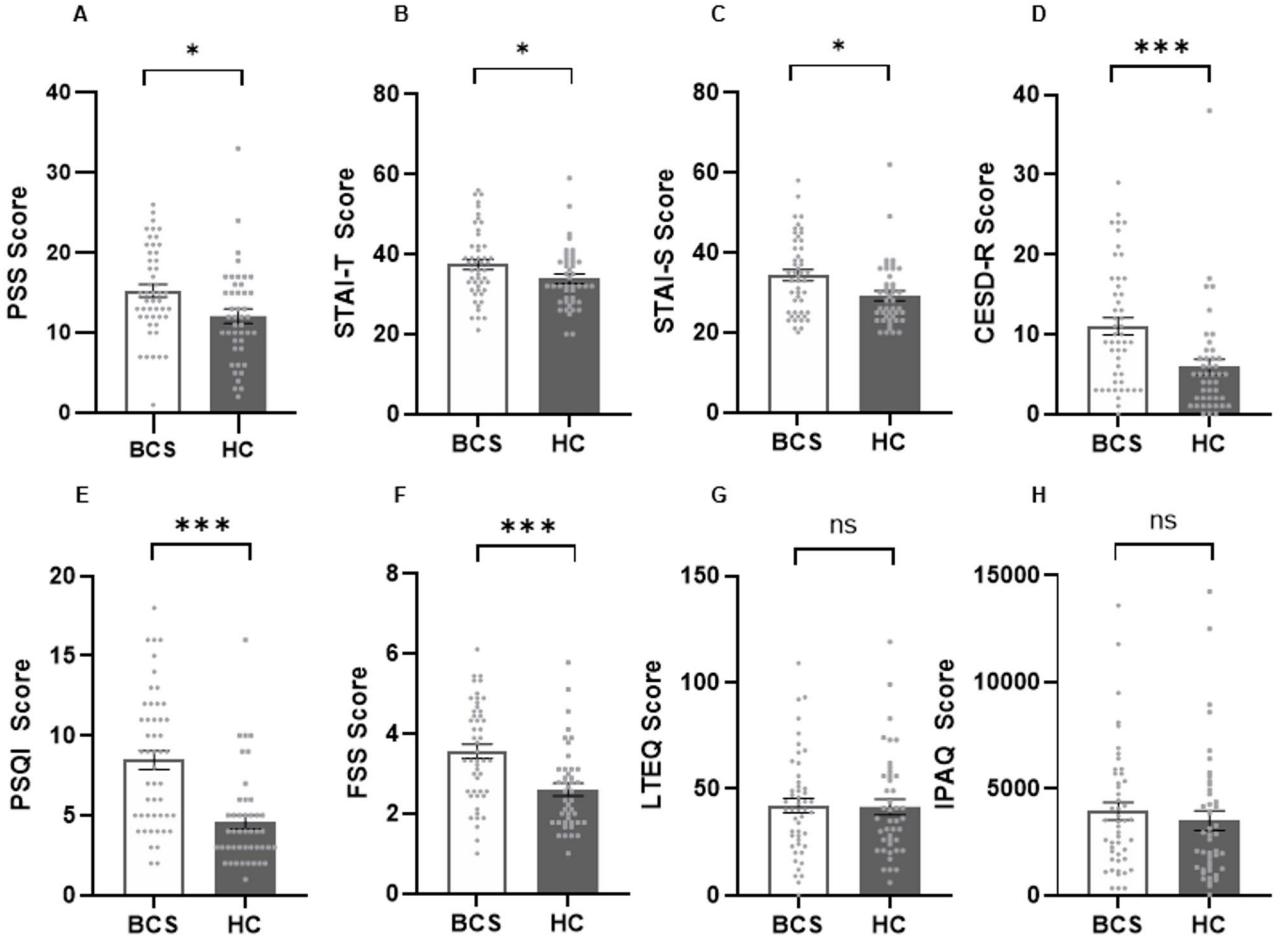

Fig. 1 Mean scores on the self-report questionnaires. **A** Perceived stress, (**B**) trait anxiety (did not survive correction for multiple comparisons), (**C**) state anxiety, (**D**) depression, (**E**) sleep quality, (**F**) fatigue, (**G**) leisure time exercise, and (**H**) physical activity among breast cancer survivors (white bars) and controls (grey bars). Individual data points for each group are presented in light grey. Error bars represent the standard error of the mean. *Abbreviations*: *BCS* Breast cancer survivor, *CESD-R* Center for epidemiologic studies depression scale-revised, *FSS* Fatigue severity scale, *HC* Healthy control, *IPAQ* International physical activity questionnaire, *LTEQ* Leisure time exercise questionnaire, *PSQI* Pittsburgh sleep quality inventory, *PSS* Perceived stress scale, *STAI-S* State-trait anxiety inventory – state scale, and STAI-T, state-trait anxiety inventory – trait scale. * denotes $p < .05$, *** denotes $p < .001$, ns denotes no significant difference ($p > .05$)

based on established cutoffs. Given that the measures used were intended for screening rather than diagnostic evaluation, a more comprehensive clinical assessment is necessary to determine whether survivors meet criteria for mood or anxiety disorders. Subclinical mental health symptoms, while often overlooked, can still impair quality of life, and may go untreated without proper screening and intervention. Overall, these findings point to an increased psychological vulnerability among breast cancer survivors, and emphasize the importance of proactive, ongoing monitoring. Preventive strategies and tailored support services may reduce the progression of subclinical symptoms into clinically significant mental health conditions.

Higher perceived stress was significantly correlated with increased depression, anxiety, and fatigue in both breast cancer survivors and non-cancer controls, consistent with prior reports [49]. Interestingly, while perceived stress was associated with greater sleep disturbances in controls, this relationship was not observed among breast cancer survivors. This finding contrasts with prior research in U.S. breast cancer survivors up to 5 years post-diagnosis, which reported a positive association between stress and sleep disturbances [50]. Similarly, higher anxiety levels were positively correlated with stress, depression, and fatigue in both groups, consistent with earlier reports [22, 49]. However, anxiety was linked to sleep disturbances only in the control group. This diverges from an earlier study that identified an association between anxiety and poor sleep quality in breast cancer survivors within 1–5 years post-treatment, although different measures were used [23]. Depression was associated with elevated stress, anxiety, fatigue, and sleep disturbances across both groups, consistent with

Table 3 Pearson correlation matrix between stress, depression, anxiety, fatigue, sleep quality, and physical activity for breast cancer survivors and healthy controls

Group		PSS	CESD	STAI-S	STAI-T	FSS	PSQI	LTEQ	IPAQ
BCS	PSS	1							
	CESD	0.67*	1						
	STAI-S	0.81*	0.65*	1					
	STAI-T	0.78*	0.59*	0.81*	1				
	FSS	0.53*	0.47*	0.36*	0.41*	1			
	PSQI	0.21	0.43*	0.14	0.07	0.08	1		
	LTEQ	0.04	0.026	0.01	0.07	−0.10	−0.09	1	
	IPAQ	−0.06	−0.03	−0.10	−0.05	−0.15	−0.13	0.65*	1
HC	PSS	1							
	CESD	0.69*	1						
	STAI-S	0.83*	0.77*	1					
	STAI-T	0.85*	0.69*	0.81*	1				
	FSS	0.52*	0.62*	0.52*	0.56*	1			
	PSQI	0.38*	0.53*	0.31*	0.27*	0.15	1		
	LTEQ	0.03	0.04	0.12	0.11	0.09	−0.14	1	
	IPAQ	−0.10	−0.02	0.01	−0.21	−0.06	−0.12	0.43*	1

Abbreviations: *BCS* Breast cancer survivor, *CESD-R* Center for epidemiologic studies depression scale-revised, *FSS* Fatigue severity scale, *HC* Healthy control, *IPAQ* International physical activity questionnaire, *LTEQ* Leisure time exercise questionnaire, *PSQI* Pittsburgh sleep quality inventory, *PSS* Perceived stress scale, *STAI-S* State-trait anxiety inventory – state scale, and STAI-T, state-trait anxiety inventory – trait scale

* denotes $p < .05$

Table 4 Regression between age, income, education, menopausal status, time since treatment and psychological and physical activity outcomes

Outcome	Group	Variables	B	Std. Error	t	β	*p*
Stress	BCS	Age	−0.35	0.11	-3.55	−0.54	0.001
		Income	3.72	1.65	2.25	0.29	0.03
Depression	HC	Income	0.95	0.45	2.09	0.32	0.03
		Education	4.41	2.01	2.18	0.31	0.04
		Menopausal status	-7.74	3.53	-2.19	−0.58	0.03
State Anxiety	BCS	Age	−0.55	0.18	-3.01	−0.48	0.004
	HC	Education	1.39	0.55	2.51	0.37	0.01
Physical Activity	BCS	Income	28.75	8.28	3.47	0.48	0.001

Abbreviations: *BCS* Breast cancer survivors, *HC* Healthy controls, *B* Unstandardized coefficients, *Std Error* Unstandardized standard error, β Standardized coefficient beta

prior reports [18, 22, 23]. These findings suggest a synergistic relationship, where difficulties in one domain may be associated with increased in others.

The role of physical activity in cancer survivorship is well-documented, with most studies focusing on intervention-based approaches [30, 31]. Observationally, we found no significant difference in self-reported physical activity levels among breast cancer survivors compared to non-cancer controls, which contrasts with prior reports of reduced physical activity among breast cancer survivors [51]. Further, physical activity did not significantly correlate with perceived stress, depression, anxiety, fatigue, or sleep quality in either group. Despite widespread recommendations for physical activity as part of cancer survivorship care, evidence for its psychological benefits is mixed. Our results align with studies reporting no significant impact of physical activity interventions on depression in breast cancer survivors (see review [33]). However, they contrast with research showing improvements in anxiety, fatigue, and depression, and sleep quality following physical activity interventions in survivors 2–10 years post-treatment [31, 32, 52]. These inconsistencies may reflect a range of factors, including time since diagnosis or treatment, age, treatment regime, types and intensities of physical activity, and assessment methods. Such variability suggests that the therapeutic benefits of physical activity may depend on specific contextual factors, and that a threshold of activity (e.g., duration, intensity, type) may be required to achieve robust benefits in cancer survivorship.

An exploratory analysis was conducted to examine the relationship between demographic and health-related variables (age, income, education, menopausal status, time since treatment, and current hormonal therapy) and mental health outcomes (stress, anxiety, depression, fatigue, and sleep disturbances) among breast cancer

survivors and healthy controls. Among breast cancer survivors, age significantly predicted perceived stress and state anxiety, while in non-cancer controls, age was a predictor only of depression. Income was associated with levels of stress and physical activity among breast cancer survivors, but predicted only depression in non-cancer controls. However, among non-cancer controls, education was a predictor of depression and state anxiety while menopausal status was associated with depression. These findings are consistent with previous research indicating that age is a predictor for mental health concerns, particularly in younger cancer survivors [53], and that younger survivors with a lower income are at a heightened risk for distress and diminished quality of life [54, 55]. Notably, time since diagnosis was not significantly associated with anxiety or depression in our sample, supporting earlier findings [22]. While some survivors experience improvements in mental health over time [56], our results suggest that many continue to struggle with psychological distress long after treatment completion. These enduring challenges can significantly impact survivors' quality of life, including their ability to return to work [8, 10, 11, 14]. However, our results contrast with prior studies that reported associations between menopausal status and income with sleep disturbances [14, 23], and between education level and psychological distress [55] in breast cancer survivors. Overall, mental health outcomes in breast cancer survivors are shaped by various demographic and health-related factors, with age emerging as the most significant predictor. However, some of these findings diverge from previous research, underscoring the complexity and variability of mental health experiences among cancer survivors.

This cross-sectional study was conducted online which allowed for the inclusion of a geographically diverse sample across Canada, reduced transportation burden, minimized risk for immunocompromised individuals, and was cost-effective. However, this recruitment method also has limitations. It relies heavily on access to social media, which tends to skew towards younger individuals and certain ethnic groups [57]. As a result, the participant sample was predominantly white and well-educated, limiting the generalizability of findings to the broader population of breast cancer survivors. Future studies should prioritize strategies to recruit more diverse and representative samples. Considering the limitations of self-report measures, future studies should incorporate clinical interviews alongside standardized questionnaires to gain a more comprehensive understanding of the mental health challenges, including symptom frequency, intensity, and duration. Additionally, objective measures (e.g., accelerometers or activity trackers) should be used to assess physical activity levels more accurately.

Given the heterogeneity of cancer treatments and their dose-dependent effects – particularly chemotherapy [58] – future research should collect detailed treatment data and adopt longitudinal designs to better understand the long-term impacts of cancer and its treatment. Finally, discrepancies across studies may be influenced by various factors, including menopausal status, age at diagnosis, cancer stage, time since treatment, treatment type and dosage, pre-existing psychological conditions, demographic variables, exercise regimes, and outcome measures. Sufficiently powered future studies should account for these covariates on mental health outcomes among cancer survivors.

Conclusion

This study contributes to the growing body of evidence highlighting the long-term psychological effects of cancer treatment in breast cancer survivors. Our findings demonstrate that many breast cancer survivors continue to experience substantial mental health challenges – including stress, anxiety, depression, fatigue, and sleep disturbances – long after completing primary cancer treatment. These issues are not isolated, but interconnected, collectively influencing survivors' overall well-being. Given these persistent challenges, it is essential to integrate continuous, comprehensive assessments into cancer survivorship plans, considering a wide range of demographic, clinical, and psychosocial factors that may affect mental health functioning. This approach will facilitate the identification of both emerging and ongoing psychological concerns. Such assessments can also inform the development of holistic interventions that address the interconnected nature of survivors' mental health needs. Future research should focus on identifying the underlying factors contributing to these persistent mental health challenges, and develop targeted, evidence-based strategies to minimize their impact and improve the quality of life for breast cancer survivors.

Abbreviations

*	$p < .05$
**	$p < .01$
***	$p < .001$
α	Cronbach's Alpha
β	Standardized Coefficient Beta
BCS	Breast Cancer Survivors
CESD-R	Centre For Epidemiologic Studies Depression Scale-Revised
d	Cohen's d
DASS-21	Depression Anxiety Stress Scale
HC	Healthy Controls
FSS	Fatigue Severity Scale
IPAQ	International Physical Activity Questionnaire
LTEQ	Leisure Time Exercise Questionnaire
MET	Metabolic Equivalent Task
n	Sample Size
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
r	Pearson's Correlation
R^2	Adjusted R Squared

SD	Standard Deviation
STAI	State-Trait Anxiety Inventory
STAI-S	State-Trait Anxiety Inventory (State Scale)
STAI-T	State-Trait Anxiety Inventory (Trait Scale)

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Authors' contributions
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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study received full board review and approval from the University of Ottawa's Research Ethics Board (H-04-21-6706). Informed consent was obtained by participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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