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SYMPTOMS OF ANXIETY AND DEPRESSION AMONG SLOVENIAN BREAST CANCER SURVIVORS POST-TREATMENT DURING THE COVID-19 PANDEMIC: A CROSS-SECTIONAL STUDY

SIMPTOMI ANKSIOZNOSTI IN DEPRESIJE PRI SLOVENSKIH BOLNICAH Z RAKOM DOJKE PO ZDRAVLJENJU V ČASU PANDEMIJE COVIDA-19: PRESEČNA ŠTUDIJA

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ABSTRACT

Background: Although anxiety and depression are important determinants of mental health, the literature in this area is sparse as most studies focus on the period during treatment. Mental health problems can affect cancer recovery as well as quality of life and survival. In this cross-sectional study, we investigated the prevalence of anxiety and depression in Slovenian cancer survivors after treatment and assessed the associated correlates during the COVID-19 pandemic.

Methods: From September 2021 to January 2022, we collected data from 430 breast cancer survivors one to five years after receiving post-local treatment and (neo)adjuvant chemotherapy. We used the Hospital Anxiety and Depression Scale (HADS) to measure anxiety and depression levels. Multivariate linear regression was used to identify factors associated with higher levels of anxiety and depression.

Results: Key findings from this study are increased levels of psychological distress and identification of relevant factors associated with those elevated levels. Approximately one-third of breast cancer survivors exhibited symptoms of elevated anxiety and depression, with one in eight meeting clinical thresholds. Multivariate linear regression revealed that age, lower quality of life, heightened fear of cancer recurrence (FCR), reduced resilience, limited social support, and unmet psychosocial and emotional needs correlated with increased anxiety symptoms. Additionally, lower quality of life, higher FCR, diminished resilience, and limited social support were associated with higher depression symptomatology.

Conclusions: Our study of Slovenian breast cancer survivors one to five years post-treatment observed a significant increase in anxiety and depression symptoms, possibly exacerbated by the COVID-19 pandemic. The demographic and psychosocial factors identified in this study offer valuable insights for future research. The study emphasises the importance of recognising and addressing the psychological needs of breast cancer survivors and the need to follow them throughout their cancer journey.

Keywords:
Anxiety
Depression
Psychological distress
Breast neoplasms
COVID-19

IZVLEČEK

Uvod: *Čeprav sta anksioznost in depresija pomembna dejavnika duševnega zdravja, ni veliko študij, ki bi se osredotočale na obdobje po koncu zdravljenja. Težave v duševnem zdravju lahko vplivajo na okrevanje po raku ter na kakovost življenja in preživetje. V tej presečni študiji smo preučevali prevalenco anksioznosti in depresije v času pandemije covida-19 pri slovenskih preživelih bolnicah z rakom dojke po koncu zdravljenja in ocenili z njima povezane korelacije.*

Metode: *Med septembrom 2021 in januarjem 2022 smo zbrali podatke 430 preživelih bolnic z rakom dojk, ki so bile 1-5 let po koncu zdravljenja in ki so prejele post-lokalno zdravljenje in (neo)adjuvantno kemoterapijo. Anksioznost in depresija sta bili merjeni z bolnišnično lestvico anksioznosti in depresije (HADS). Za ugotavljanje dejavnikov, povezanih z višjimi stopnjami anksioznosti in depresije, je bila uporabljena multivariatna linearna regresija.*

Rezultati: *Ključne ugotovitve te študije so visoka pojavnost simptomov psihološkega distresa in identifikacija spremenljivk povezanih z več simptomov psihološkega distresa. Približno tretjina preživelih bolnic z rakom dojke ima višje od normalnih ravni simptomov anksioznosti in depresije. Pri eni od osmih oseb ugotavljamo klinično pomembno anksioznost in depresijo. Z multivariatno linearno regresijo je bilo ugotovljeno, da so starost, slabša kakovost življenja, višja raven strahu pred ponovitvijo raka, manjša psihološka odpornost, manjša socialna podpora ter nezadovoljene potrebe po psihosocialni in čustveni podpori pomembni korelati simptomov anksioznosti. Poleg tega je bilo ugotovljeno, da so nižja kakovost življenja, višje ravni strahu pred ponovitvijo bolezni, nižja odpornost in nižja socialna podpora povezani z večjo simptomatiko depresije.*

Zaključek: *V našem vzorcu slovenskih preživelih bolnic z rakom dojk 1-5 let po zdravljenju je bila prevalenca simptomov anksioznosti in depresije visoka, kar bi lahko bilo povezano s pandemijo covida -19. Demografski in psihosocialni dejavniki, ugotovljeni v tej študiji, ponujajo obetavne usmeritve za prihodnje študije. Ključne ugotovitve študije so pomembnost prepoznavanja in obravnave psiholoških potreb preživelih bolnic z rakom dojke po končanem zdravljenju ter potreba po dolgoročnem spremljanju.*

Ključne besede:
anksioznost
depresija
psihološki distres
rak dojke
covid -19

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1 INTRODUCTION

Breast cancer (BC) is a common and significant cause of cancer-related deaths in women (1). The five-year survival rate has improved, exceeding the 90% threshold in high-income countries (2), resulting in a growing number of BC survivors. According to data extracted from GLOBOCAN, in the year 2020 there were approximately 2.3 million newly reported cases of breast cancer and 685.000 deaths. In Slovenia alone, around 1,500 women are diagnosed annually, and there are currently 20,000 women who have received a BC diagnosis at some point in their lives (3).

Breast cancer stands as the most frequently identified cancer, representing a quarter of all cancer cases and contributing to one-sixth of cancer-related fatalities. In most countries, it is one of the main causes of cancer-related deaths in women (3). Over the years there has been a significant enhancement in the five-year survival rate for breast cancer survivors, surpassing 90% in high-income nations. This has translated into a multitude of breast cancer survivors leading fulfilling lives well beyond their initial diagnosis.

A cancer diagnosis profoundly affects patients' physical and mental well-being (4). Depression and anxiety can complicate the recovery process (5), reduce quality of life (6), and impact cancer recurrence and survival (7). Unfortunately, mental health often receives inadequate attention during and after cancer treatment, as the main focus is on physical symptoms, treatments, and potential side effects. This challenge was compounded by the additional challenges faced by BC patients during the COVID-19 crisis, such as increased cancer-related deaths, disruptions in treatment services, and delayed diagnoses (8). Studies show that cancer patients are more likely to suffer from stress, anxiety and depression, especially during prolonged treatment (9). Therefore, it is important to understand the impact of the pandemic on patients' mental health.

Previous research has identified several factors linked to increased anxiety and depression in BC survivors. These include socio-demographic factors like younger age (10, 11), no partner (12), unemployment (12, 13), lower education (13) and living at home while being treated (14). Clinical characteristics such as undergoing chemotherapy (11) and experiencing physical symptoms (12, 14) are also significant contributors. Additionally, psychosocial factors, including quality of life (10, 11, 13, 15), social support (16), fear of cancer recurrence (FCR) (17) and resilience (18) have been identified as impacting symptoms of anxiety and depression.

Anxiety and depression rates are notably higher in cancer survivors than in the general population (19). However, these rates vary due to multiple factors such as time since treatment, the type of treatment, cancer stage, choice of measurement tools for anxiety/depression and their thresholds, study location, and overall design (20, 21). Most importantly, there is a lack of rigorous, methodologically sound research on psychological distress, especially in post-treatment cancer survivors.

In this study, we aimed to examine the prevalence of anxiety and depression symptoms among BC survivors in Slovenia and compare these rates with those in similar studies. Additionally, we sought to identify socio-demographic, psychological, and clinical factors associated with higher levels of depression and anxiety in this group. Through these objectives, we aim to gain a better understanding of the extent of this problem and uncover potential factors associated with higher levels of psychological distress. This information can then be used to develop more effective strategies for cancer care.

2 PATIENTS AND METHODS

2.1 Patients and procedure

Participants were recruited at the Institute of Oncology Ljubljana between September 2021 and January 2022. All eligible female BC survivors attending hospital follow-up appointments during this period were invited to participate. The detailed inclusion and exclusion criteria for this cross-sectional study have already been described in another publication (22). Prior to participation, all individuals were informed about the purpose of the study and gave informed consent.

2.2 Methods

In this study, we collected socio-demographic, clinical and patient-reported data. Comprehensive descriptions of these measures with validation reports can be found in the original study (22).

Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS), a validated tool with strong psychometric properties in its Slovenian version (23). HADS consists of two subscales, HADS-A for anxiety symptoms and HADS-D for depression symptoms, with scores ranging from 0 to 21, where higher scores indicate more severe symptoms (24). We categorized participants based on symptom severity, with scores of 11 or higher as clinically significant (probable cases), 8 to 10 as "possible cases", and below 8 as normal (25). To determine the overall prevalence of anxiety and depressive symptoms, we used a cutoff point of 8 and above, consistent with other similar studies (20, 21, 26).
Demographic and clinical characteristics were collected in self-reported questionnaires. This information included socio-demographic data, such as age, marital status, employment status, education, place of residence, and behavioural and clinical characteristics, such as smoking

status type of primary treatment, cancer stage, time since the diagnosis and presence of hormonal therapy.

The presence of comorbidities was measured using Comorbidity Questionnaire (SCQ-19) (27). For this study, the comorbidity status (SCQ-19 total score) and the number of comorbidities were analysed.

Quality of life was measured with the EuroQol Five-Dimension Questionnaire (EQ-5D), which includes five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and five different severity levels (no, mild, moderate, severe, extreme or unable to perform the activity) (28). The utility scores for this study were determined based on the norm set for the Slovenian population, using the EQ5DL crosswalk method SL (29).

Fear of cancer recurrence was assessed with the Fear of Cancer Recurrence Inventory (FCRI), a 42-item scale that measures the extent of patients' fear in this context. In this study, only the severity subscale was used, as this is the most commonly used report of the FCRI scale according to previous studies and best reflects FCR scores (30).

Social support was measured using the Multidimensional Scale of Perceived Social Support (MSPSS), a 12-item, self-administered scale that assesses perceived social support using three subscales: Significant Others, Family and Friends (31). For the purposes of this study, only the MSPSS total score was analysed.

Resilience was assessed with the 14-item Resilience Scale (RS-14), a widely used scale measuring adjustment and recovery from the effects of stressors (32). The RS-14 total score serves as a meaningful representation of the concept of resilience.

Unmet needs were measured with the Cancer Survivors' Unmet Needs (CaSUN) measure (33). The CaSUN is a 34-item instrument with five domains, including existential survivorship, comprehensive cancer care, psychological and emotional support, relationship and information. For the purpose of this study, only unmet needs (moderate or strong need) in all five domains were analysed.

2.3 Statistical analysis

The methodology for sample size calculation, responder/non-responder analysis, and handling missing data was detailed elsewhere (22). Here, we performed two stepwise multivariate linear regression analyses using IBM® SPSS® Statistics Version 27, focusing on anxiety and depression as primary outcomes.

All variables were first described with the mean and standard deviation (SD) or frequency and percentage. We then assessed the distribution of HADS-A and HADS-D scores and examined the normality of the residuals. Multicollinearity between potential factors associated with depression/anxiety was rigorously assessed using tolerance statistics, variance inflation factors and correlation values for each candidate variable. After confirming that the HADS-A and HADS-D scores were normally distributed and that there was no multicollinearity, we proceeded with univariate analysis to identify potential factors associated with symptoms of increased anxiety and depression symptoms.

A univariate analysis (t-test for independent samples or ANOVA) was used to compare the scores of anxiety and depression with theoretically or clinically relevant factors. Variables that had a significance level of less than 0.2 in the univariate analysis were included in a stepwise linear regression model divided into three different groups: sociodemographic, clinical and psychological factors. A significance level below 0.1 was required for variables to be included in the final model. For the final regression model, variables were considered statistically significant if their P-values were below 0.05.

3 RESULTS

3.1 Patients' characteristics

Sociodemographic and clinical variables are summarised in Table 1. On average, patients were 56 years old, with the majority being married or in a partnership (77.2%). Approximately half of the participants had a university degree or doctorate and 39.8% were employed full-time. In terms of clinical status, 58.6% were diagnosed at stage II and 37.9% had received chemotherapy and radiotherapy, with a mean duration since treatment of 30 months.

Table 1. Sociodemographic, disease and treatment-related variables (N=430).

Characteristic	Sample of BC survivors
Age (mean±SD), range: 18-90	55.7±12.4
Marital status, n (%)	
Married/partnered	332 (77.2)
Single, divorced	60 (14)
Widowed	38 (8.8)
Education (n, %)	
Primary Education	28 (6.5)
Secondary Education	194 (45.1)
University, PhD	208 (48.4)
Employment (n, %)	
Full-time employed	171 (39.8)
Half-time employed	86 (20.0)
Unemployed	13 (3.0)
Retired	146 (34.5)
Disabled retired	14 (3.3)
Place of residence (n, %)	
Urban	161 (37.4)
Suburban	155 (36.0)
Rural	114 (26.5)

Characteristic	Sample of BC survivors
Smoking status (n, %)	
Yes	41 (9.5)
No	313 (72.8)
No, but smoked in the past	76 (17.7)
Cancer stage (n, %)	
0-I	90 (20.9)
II	252 (58.6)
III	88 (20.5)
Primary treatment, besides surgery (n, %)	
Chemotherapy only (C)	48 (11.6)
Radiotherapy only (R)	169 (39.3)
C and R	163 (37.9)
None	50 (11.6)
Time since treatment (mean±SD), range: 8-66 months	29.9±18.2
Hormonal therapy (n, %)	
Yes	274 (63.7)
No	156 (36.3)

Legend: SD – standard deviation; n – number of participants; SCQ-19 – The Self Administered Comorbidity Questionnaire

3.2 Prevalence of anxiety and depression symptoms and its severity

The prevalence of anxiety and depression symptoms (HADS≥8) among BC survivors was 34.2% and 30.2%, respectively. Specifically, this included 22.8% possible cases and 11.4% probable cases of anxiety, while for depression the figures were 17.9% for possible cases and 12.3% for probable cases (Figure 1). The mean scores for HADS-A and HADS-D were 6.08 and 5.85, respectively.

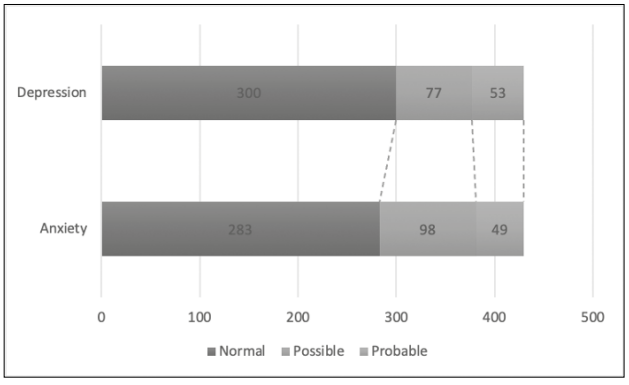
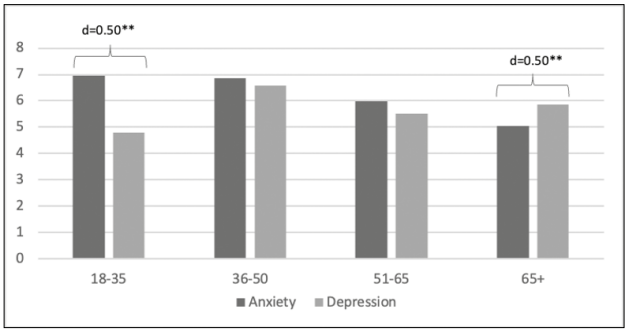


Figure 1. Distribution of depression and anxiety based on the HADS score (n=430).

We also conducted an analysis of the mean scores on the HADS-A and HADS-D in different age groups. While there were statistically significant differences in mean scores between all groups ($p<0.05$), the largest effect in the differences (Cohen's $d=0.5$) was observed in the youngest patient group (18-35 years), indicating a remarkable discrepancy in anxiety and depression scores in that age group (Figure 2).



The abbreviation 'd' represents Cohen's d effect size, while '**' denotes statistical significance with a p-value below 0.01.

Figure 2. Comparisons between the mean values of symptoms of anxiety and depression across age groups.

3.3 Factors associated with higher levels of anxiety and depression

The results of the final model are presented below. Higher levels of anxiety were significantly associated with younger age (β=0.13, $P<0.05$), lower quality of life (β=-0.27, $P<0.001$), higher levels of FCR (β=0.29, $P<0.001$), lower resilience (β=-0.15, $P<0.01$), and more unmet PES (β=0.16, $P<0.01$). The model demonstrated was found to be statistically significant ($F[22, 144]=23.82$, $P<0.01$) and explained 57% of the variance.

Higher levels of depression were significantly associated with lower quality of life (β=-0.27, $P<0.01$), higher levels of FCR (β=0.20, $P<0.001$), lower resilience (β=0.36, $P<0.01$) and lower perceived social support (β=-0.14, $P<0.01$). The model was statistically significant ($F[19, 202]=30.23$, $P<0.01$) and explained 59% of the variance.

4 DISCUSSION

The aim of this study was to determine the prevalence of anxiety and depression symptoms while identifying potential factors that may be associated with higher levels of these. This study shows that a significant proportion of BC survivors, about one third, have symptoms that indicate anxiety and depression above normal levels. One in eight people in this group suffers from clinically relevant anxiety or depression. Importantly, several factors have been identified that correlate with and contribute to increased levels of anxiety and depression.

Table 2. Final linear regression model predicting symptoms of anxiety and depression.

Variable	HADS-A	HADS-D
	Standardized beta	
Age	-0.13*	
Marital status (ref. married)		
Single, divorced[a]	0.04	0.06
Widowed[a]		0.03
Education (ref. Primary)		
Secondary[a]	-0.2	-0.05
University, PhD[a]	0.05	0.03
Employment status (ref. full-time)		
Half-time		0.04
Unemployed[a]	-0.05	
Disabled retired[a]	0.04	0.01
Place of residence (ref. urban)		
Rural[a]	0.06	0.02
Time since treatment	-0.01	
Treatment type (ref. None)		
Chemotherapy[a]	0.07	
Chemotherapy and radiotherapy[a]	0.00	0.05
No. of comorbidities	-0.01	0.06
Psychological support	0.03	
EQ-5D - index, quality of life	-0.27**	-0.27**
FCRI, fear of cancer recurrence	0.29**	0.20**
RS-14, resilience	-0.15**	-0.36**
MPSS-total, social support	-0.10*	-0.14**
CaSUN-PES, unmet needs	0.16**	

In our sample, we observed a significant prevalence of anxiety and depression (HADS≥8) with rates of 34.2% and 30.2%, respectively. Of these cases, 11.4% exhibited clinically relevant levels of anxiety (HADS≥11), while 12.3% met the same criteria for depression. Previous studies (11, 13, 34) conducted with BC survivors' post-treatment and before COVID-19 using the same measurement tools and cut-off point reported that prevalence for anxiety symptoms (HADS≥8) ranged from 12% to 29.1% and between 9% to 11.9% for clinically relevant cases (HADS≥11), placing our prevalence on the higher end of that range. For depression, on the other hand, the prevalence of depressive symptoms (HADS≥8) in previous studies ranged from 7% to 12.5% and for clinically relevant cases from 2.1% to 6.1% (11, 13, 34), which is notably lower compared to the prevalence found in our study. This discrepancy highlights the increased burden of depressive symptoms among our study's BC survivor population.

A recent systematic review reported that anxiety and depression prevalence (HADS≥8) among cancer patients post-COVID-19 was 36% for anxiety and 28% for depression (26), which closely matches the results of our study. However, it is essential to note that these rates were predominantly drawn from patients currently undergoing treatment, where higher prevalence rates are anticipated. The high prevalence observed in our study may be attributed to COVID-19-related factors, including reduced clinical consultations, increased home confinement, and limited interactions (8). These factors could potentially worsen anxiety and depression symptoms.

In Slovenia, studies have provided different insights into the prevalence of symptoms of depression. A study conducted by Klemenc-Ketiš et al. between 2010 and 2012 using Zung's self-rating depression scale found a prevalence of depression of 3.4% (35). The National Institute of Public Health reported a prevalence of depression of 5.5% in 2014, and 5.4% in the 25-34 age group. By 2019, the overall prevalence of depression had risen to 7.5%, while it remained relatively stable in the 25-34 age group at 5.7% (36). In the following year, a study by Jerala et al. used a two-question scale to assess depression and found a prevalence of 4.2% in the middle-aged people (37).

In the context of the COVID-19 pandemic, Mihevc et al. (38) conducted a study in which they used the PHQ-9 and GAD-7 questionnaires to assess symptoms of depression and anxiety in the general population. The prevalence of depression and anxiety was 24.4% and 12.9%, respectively (38). In 2021, Rus-Prelog et al. found that during the pandemic 25.5% of the population suffered from moderate-severe depressive symptoms and 21.6% from moderate-severe anxiety symptoms (39).

The prevalence of depressive symptoms observed in our study reflects the rates observed in the general population during the COVID-19 pandemic, as described in the two articles above. While these studies provide valuable insights, it is important to remember that they use different assessment tools and methods. On the other hand, the prevalence of anxiety appears to be more pronounced in BC survivors. The pandemic brought with it unique stressors, including social isolation and disrupted access to healthcare, which may have contributed to these changes. Understanding these dynamics is critical to developing effective interventions and support systems for BC survivors. Further research, including longitudinal studies, is needed to examine these trends in depth and develop strategies to improve the mental well-being of this population in times of crisis.

The results of our study also show a remarkable discrepancy in the prevalence rates of anxiety and depression (see Figure 2), especially in younger patient groups (18-35 years), consistent with previous research (40, 41). In the youngest group, 21.4% had clinically relevant cases, compared to 12% in the 36-50 and 51-65 age groups, and 5.8% in the 65+ group. This disparity may be due to the greater impact of a cancer diagnosis and treatment on younger patients, who often have a lot of professional and family responsibilities (6). Additionally, the financial strain of taking time off work

can heighten their concerns. Facing a life-threatening illness can be especially stressful for younger people, as older patients may have already developed coping strategies to deal with these challenges (42).

Our analysis identified age, quality of life, social support, FCR, resilience, and unmet psychosocial and emotional support needs as significant factors associated with increased anxiety levels, consistent with previous studies (11, 43, 44). Notably, increased anxiety correlated with a greater number of unmet psychological and emotional support needs, emphasising the importance of addressing these needs in psychosocial interventions. Our results show that, aside from age, no socio-demographic factors were associated with increased anxiety. Furthermore, marital status showed no significant relationship with the level of anxiety. However, a stronger perceived social support network was associated with lower anxiety scores, highlighting the central role of the quality of support in this context. It is important to recognise that having a partner is no guarantee that a patient's needs will be met. Our results show that sociodemographic factors are not linked to higher depression levels in post-treatment BC survivors. In our study, depression was significantly associated only with quality of life, resilience, FCR and social support. While this aligns with prior research linking depressive symptoms to these factors (43), our study yielded a surprising result: no statistical significance between the number of comorbidities, treatment type, and depression levels. This suggests that other factors like resilience, social support, or quality of life may be stronger factors associated with depressive symptoms, possibly masking the impact of comorbidities. Notably, both clinical variables showed significant associations with depressive symptoms in the univariate analysis. There could also be interaction effects involving some unaccounted for variables, such as personality traits like pessimism (45) or coping self-efficacy, which have been shown to explain a significant portion of depression variance in post-treatment cancer survivors (46).

The limitations and strengths of the design of our study are described in detail in the original work (22), and we mention them only briefly here. Due to the General Data Protection Regulation (GDPR), it was not possible to assess the differences between those who responded to the survey and those who did not. A significant drawback is that our study was not originally designed to identify correlates of anxiety and depression, which meant that some relevant variables (e.g., coping strategies, personality type) were not taken into account. This limited our ability to account for all relevant factors that could contribute to the model we propose here. As this study had a cross-sectional design, no information is available as to whether the symptoms of anxiety and depression remain stable or have a natural decrease. However, with a substantial sample of 430 BC survivors, this study does provide robust insights into anxiety and depression prevalence during the COVID-19 pandemic. Importantly, we have clearly distinguished between possible and probable cases of anxiety and depression, bringing attention to this issue for future research.

5 CONCLUSION

In conclusion, this study shows a high prevalence of anxiety and depression in BC survivors, highlighting the need for further research in Slovenia. Comparative data are crucial for a more accurate assessment of the severity of the problem. Importantly, this study highlights the mental health challenges faced by BC survivors following treatment during the COVID-19 pandemic. The study emphasises the importance of recognising and addressing the psychological needs of BC survivors. It also underlines the need for a multidisciplinary approach to cancer care, including mental health, and emphasises the importance of early intervention and of following-up BC survivors over a period of time to monitor and address ongoing mental health problems.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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ETHICAL APPROVAL

The research was conducted in accordance with the Declaration of Helsinki and its subsequent amendments and with the permission of the National Medical Ethics Committee (number: 0120-25/2019/6) and the Ethics Committee of the Institute of Oncology Ljubljana (number: EK-OI -16092021).

AVAILABILITY OF DATA AND MATERIALS

The data and materials used in this study are available upon request.

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