



Resilience as a Source of Easement to Health-Related Worries in Women at Increased Risk for Breast or Ovarian Cancer During the COVID-19 Pandemic

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Purpose: The COVID-19 pandemic has affected individuals' and society's physical and psychological well-being. The study was conducted in order to assess the predictors for health-related worries during the COVID-19 pandemic in vulnerable populations.

Patients and Methods: A cross-sectional web-based survey of women who had a higher risk of developing breast cancer (BC) or ovarian cancer (OC) was conducted, regardless of whether they had experienced an active malignant disease during the pandemic. A self-reported questionnaire was designed for this study to assess health-related worries. The PHQ-4 questionnaire was used to evaluate mental health, and the Brief Resilience Scale (BRS) questionnaire was employed to investigate resilience.

Results: History of BC or OC was recognized as an independent significant risk factor for worries regarding being more susceptible to a more severe course of COVID-19 disease (OR 3.593; 95% CI 1.030–12.536; $p = 0.045$). High scores in the BRS questionnaire were negatively correlated with health-related worries, such as an increased risk for occurrence of BC or OC (OR 0.332; 95% CI 0.118–0.933; $p = 0.37$) or worsening of oncological outcome as a result of an infection with the SARS-CoV-2 virus (OR 0.330; 95% CI 0.114–0.956; $p = 0.041$).

Conclusion: The obtained findings determined resilience as an independent and potent protective parameter in terms of health-related concerns in women at high risk for BC and OC. The results may assist in identifying women at risk for health-related concerns during adverse life events, allowing healthcare providers to respond fast and according to the patients' needs.

Keywords: health-related worries, resilience, mental health, COVID-19, BRCA 1 & 2

Introduction

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease-2019 (COVID-19) was first reported in China by the end of 2019 and spread rapidly to other countries by the beginning of 2020. On January 30, 2020, the World Health Organization (WHO) declared the outbreak a “public health emergency of international concern”, and subsequently announced a pandemic on March 11, 2020.¹ In order to prevent the spread of the disease, public health measures such as social distancing, quarantine, and economic lockdown were implemented.² Public health emergencies, like the COVID-19 pandemic, as well as measures to contain viral spread, can have a remarkable impact on various facets of life, such as the physical and psychological well-being of individuals and society. Additionally, they may cause health-related concerns in vulnerable populations, including anxiety and depression.^{2–4}

Due to a family history of cancer, some women may be at higher risk of developing breast cancer (BC) and ovarian cancer (OC) than the general population. Women with mutations in the breast cancer genes 1 and 2 (BRCA 1 and 2) are more likely to experience developing cancers. By the age of 80, they have a cumulative risk of up to 75 and 44%, respectively, for developing breast and ovarian cancers.⁵ Patients with active cancer appear to have a greater risk of acquiring community-onset and nosocomial SARS-CoV-2 infection, owing to their impaired health status and systemic immunosuppression.^{6,7} Moreover, they seem to be at a higher risk of experiencing a severe COVID-19 course of the

disease, necessitating admission to intensive care units and invasive ventilation.^{6–8} Based on research performed by Dai et al, 18.18% of breast cancer patients revealed critical symptoms after being infected by SARS-CoV-2.⁶ A recent analysis of a large cohort of US patients with recent cancer and COVID-19 infection revealed a higher risk for ICU stay (OR 1.69, 95% CI 1.54–1.87) and hospitalization (OR 1.19, 95% CI 1.11–1.27) than persons without cancer or without recent cancer treatment.⁹ People with pre-existing malignant disease have a significantly higher risk of fatal outcome after acquiring SARS-CoV-2 than people in the general population who do not have a pre-existing medical conditions or evidence of an active malignant disease.^{6,7,9} Moreover, the chances of developing a severe condition for admission to intensive care or death were even higher in patients with metastatic cancer.⁶

Health-related worries or concerns are widespread in the population, with a prevalence rate of up to 36%, and are more frequent in vulnerable groups, such as people with pre-existing mental disorders, patients with chronic health conditions, or cancers.^{10–14} Patients with breast cancer experienced increased health-related concerns related to recurrence due to the pandemic impact, which affected the access to medicine, the communication with health care providers and treatment plans.¹⁵ Women tend to experience a higher degree of mental health issues, eg anxiety, during the COVID-19 pandemic.¹⁶ Worries are defined as anticipations of possible but yet uncertain negative future events, as opposed to anxiety, which is often accompanied by somatic and behavioral aspects: thus, worries are considered as a component of anxiety.^{17,18} While non-chronic worry is observed as an acute adaptive response to a trigger or threat and may aid in problem-solving activities, chronic worry may increase anxiety, depression, or negative self-esteem, leading to impaired well-being.¹⁷ During the pandemic, vulnerable groups, such as patients with cancer or those at higher risk of cancer, faced a double-trigger: the threat of malignancy, as well as the possibility of acquiring COVID-19 infection.^{11,14,15,19,20} To date, several predictors of health-related worries have been identified, including younger age or physical impairment in cancer patients, as well as the level of control of the COVID-19 pandemic.^{11,19}

Resilience allows people to recover or bounce back from adversity or stressful events in their lives.^{21–26} Stressful events, such as cancer threats, cancer diagnosis, or other adversities in life, may impair mental well-being and reduce the quality of life. Numerous health-related outcomes have been reported to be positively influenced in highly resilient people, including less negative affect, more positive affect, fewer physical symptoms, and lower perceived stress.^{22,23,27} Moreover, resilience has been described as a predictor of threat coping and mental well-being in people affected by natural disasters and health crisis.^{28–32} Also, resilience is a potent cancer adaptation protective factor.³³ A high level of resilience helps patients to improve their psychological well-being and achieve psychological growth in survivors.^{33–35} Strategies such as cognitive reframing, meaning-making, and supporting positive affect can all assist in strengthening resilience.³⁶

This study aimed to identify patients at high risk of increased health-related worries in a vulnerable group of women at increased risk for BC or OC. As a result, regardless of whether women at risk had experienced an active malignant disease during the pandemic, we assessed potential risk and protective factors in women with an increased risk for hereditary BC and OC concerning health-related issues. It is crucial for health care professionals to identify and to be aware of potential risk factors and promising protectors of health-related concerns, as these can influence psychological and physical well-being.

Materials and Methods

Assessment of the Study Population

A direct link to the survey and an invitation to participate were distributed through the Facebook internet platforms of patients' support groups for hereditary breast cancer or ovarian cancer. All participants were aged at least 18 years old and agreed to take part in the study. Women with a family history of BC and OC were included, regardless of whether they had experienced an active malignant disease during or previous to the pandemic, and irrespective if they had a diagnosed mutation in the respective risk genes. The survey was active from January 29 to April 22, 2021. The data were collected anonymously using SoSciSurvey (a platform who stores all data in Germany and is subject to strict EU data protection laws) and included self-reported sociodemographic and clinical information from participants, including the BRS and PHQ-4 questionnaires. Furthermore, the following questions were used to assess the women's expectations and opinions on health-related issues:

1. Are you concerned that if you become infected with the SARS-CoV-2 virus on your own, you might infect someone in your family or social network? (no concerns/ moderate concerns/ severe concerns/ does not apply)
2. Are you concerned that you may be susceptible to a more severe course of COVID-19 disease due to your increased risk of breast or ovarian cancer? (no concerns/ moderate concerns/ severe concerns/ does not apply)
3. Are you concerned, that infection with the SARS-CoV-2 virus may increase the risk of developing breast or ovarian cancer? (no concerns/ moderate concerns/ severe concerns/ does not apply)
4. If you have or have had breast and/or ovarian cancer, are you concerned about worsening of the oncological outcome resulting from an infection with the SARS-CoV-2 virus? (no concerns/ moderate concerns/ severe concerns/ does not apply).

Patient Health Questionnaire for Depression and Anxiety (PHQ-4)

The Patient Health Questionnaire for Depression and Anxiety (PHQ-4) was employed to assess the psychological burden of the studied population. Two items of the Patient Health Questionnaire for Depression (PHQ-2) and the Generalized Anxiety Disorder Scale (GAD-2) were combined to form PHQ-4.³⁷ PHQ-4 is an overall screening tool for depression and anxiety.

Participants used a 4-point Likert-scale to respond; “not at all” = 0, “several days but less than a week” = 1, “more than half the days” = 2, and “nearly every day” = 3. PHQ-2, GAD-2, and PHQ-4 scores were computed by adding the scores of individual items.^{38–41}

The overall PHQ-4 score serves as a general marker of psychological distress, indicating symptom burden as well as impairment and disability.⁴¹ The reliability of the German version of the PHQ-4 was described with $\alpha=0.78$.³⁷

Brief Resilience Scale (BRS)

The BRS was used to assess how resilience affected mental health outcomes. Smith et al, were the first to describe the BRS, which was developed to identify one's ability to bounce back from stress.²¹ The BRS includes six items that are graded on a 5-point Likert scale: 1 = strong disagreement, 2 = disagreement, 3 = neutrality, 4 = agreement, and 5 = strong agreement. The first, third, and fifth items are positively worded, while the second, fourth, and sixth items are negatively phrased. The average of all six items is applied to calculate the score.⁴² The reliability for the German population was analyzed by Chmitorz et al with $\alpha = 0.85$, being in line with the results of the original validation study by Smith et al,²² The German version of the BRS questionnaire was positively correlated with well-being, social support, optimism, and the coping strategies active coping, positive reframing, acceptance, and humor. Moreover, it was negatively correlated with somatic symptoms, anxiety and insomnia, social dysfunction, depression, and the coping strategies religion, denial, venting, substance use, and self-blame, thus providing evidence for validity of the German adaptation of the BRS.⁴²

Statistical Analysis

For descriptive analyses, participants who did not respond to the survey's questions were considered missing data. SPSS 26.0 (SPSS Inc., Chicago, IL, USA) was applied to analyze the obtained data. Descriptive statistics were expressed as mean, standard deviation (SD), median, interquartile range (IQR), or proportions (%).

The examined health-related concerns were converted into binary variables: those who reported no concerns and those who revealed moderate to severe health-related concerns. Univariate analyses were used to identify variables with a proper discriminatory value for binary variables that define health-related worries. The predictability of selected independent variables on the odds of experiencing health-related concerns was evaluated by univariate logistic regression analyses. Missing data included all participants who did not respond to the relevant question or did not have a firm opinion on the subject (“does not know/does not apply”).

The significance of demographic factors (age, living alone, and educational level), pandemic-specific variables (having had COVID-19 disease, someone in the social network having had COVID-19 disease, and social network reduction level), cancer-related risk factor (having had BC or OC), and mental health parameters (PHQ-4 questionnaire assessing mental health burden and BRS questionnaire assessing resilience) were investigated.

Variables with p-values less than 0.25 in the univariate regression model were then entered into the final model multivariate logistic regression by backward stepwise selection to determine the independence of the variables mentioned

above for predicting health-related worries.^{43–45} The odds ratio (OR), variance (Nagelkerke R^2), p-value, and 95% confidence interval (95% CI) were utilized to express the data.

In order to assess the psychometric properties of the questionnaire regarding health-related worries, Cronbach's alpha coefficient was employed as an index of internal consistency reliability. Item internal validity was established by performing a Pearson (two-tailed) r correlation between scale items and respective full-scale scores.

All tests were two-tailed, with a significance level of $p < 0.05$. The analyses were carried out using SPSS[®] software Version 26.0 (Version 26.0 of IBM SPSS Statistics released in 2019 for Windows, Armonk, New York, USA).

Results

Psychometric Properties of the Employed Questionnaires

Reliability analyses for the PHQ-2, GAD-2, PHQ-4 and BRS questionnaires were assessed by Cronbach alpha. In this study population, the Cronbach alpha for the PHQ-2 scale and for the GAD-2 scale were 0.851 and 0.823, respectively. The PHQ-4 scale showed a Cronbach alpha of 0.899, and the BRS scale showed a Cronbach alpha of 0.820.

Next, we tested the psychometric properties for the questionnaire assessing health-related worries. The 4-item questionnaire was rationally constructed. The Cronbach alpha for the total scale (questionnaire regarding health-related worries) was 0.851 and showed a good reliability. Item-internal validity was computed by bivariate Pearson correlation with the full subscale total. All items showed good validity, and with a $df = 39$, the values obtained were $r > 0.724$, and $p < 0.001$ for all four items of the questionnaire regarding health-related worries.

Demographic Characteristics of the Study Population

The questionnaire was accessed by 89 individuals and 80 participants answered at least one question. 77 participants responded to at least one health-related question. Table 1 summarizes the demographic characteristics of the study population.

Moderate and severe concerns about spreading the infection to family members or the social network were expressed by 49.4% and 40.3%, respectively (Figure 1). A portion of 27.3% and 23.4% of the participants were moderately and severely concerned, that they might be susceptible to a more severe course of COVID-19 disease due to their predisposition for breast or ovarian cancer. In addition, 11.7% and 5.2% were moderately and severely worried about an increased risk of BC or OC (Figure 1). Furthermore, 24.3% and 14.9% were moderately and severely concerned regarding a potential unfavorable course of the pre-existing malignant disease if they were infected with SARS-CoV-2, respectively (Figure 1).

Predictors of Health-Related Worries

According to Table 2, being resilient was found to be a protective factor for fear of spreading the virus to family and friends (OR 0.044; 95% CI 0.044–0.525; $p = 0.013$).

Age (OR 1.098; 95% CI 1.039–1.161; $p = 0.001$) and a history of BC or OC (OR 6.531; 95% CI 2.250–18.954; $p = 0.001$) were risk factors for worries of being susceptible to a more severe course of COVID-19 disease due to the increased predisposition for BC or OC, as detailed in Table 3. The participants who expressed no concerns had an average age of 38.00 years (IQR: 31.50–46.00), while those who described moderate concern and severe worries had a median age of 47.00 (IQR: 38.50–54.00) and 51.00 (IQR: 43.00–54.50) years, respectively.

Age was also a risk factor for concerns regarding increased risk of BC or OC occurrence (OR 1.069; 95% CI 1.001–1.142; $p = 0.047$) (Table 4), and no, moderate, and severe concern levels were declared by the participants with the average age of 43.00 (IQR: 32.75–51.00), 48.00 (IQR: 35.50–56.00), and 56.00 (IQR: 51.00–58.75) years, respectively. Resilience was found to be protective against worries regarding an increased risk of occurrence of malignant disease after a SARS-CoV-2 infection (OR 0.314; 95% CI 0.111–0.886; $p = 0.029$) (Table 4).

Showing signs of higher mental distress elevated the probability of concerns about a worsening of the oncological outcome caused by the SARS-CoV-2 virus infection (OR 1.462; 95% CI 0.999–2.139; $p = 0.05$), but was not statistically

Table I Demographic Characteristics of the Study Population

Age		
	M(SD); N Mdn (IQR)	43.41 (10.37); 75 43.00 (34.00–52.00)
Having a stable partnership		
Yes	% (n/N)	92.2 (71/77)
No	% (n/N)	7.8 (6/77)
Living alone		
Yes	% (n/N)	7.8 (6/77)
No	% (n/N)	92.2 (71/77)
Education		
Up to secondary level	% (n/N)	55.3 (42/76)
Tertiary level education	% (n/N)	44.7 (34/76)
Did you have COVID-19 disease		
Yes	% (n/N)	3.9 (3/77)
No	% (n/N)	96.1 (74/77)
Someone in your social network having COVID-19		
Yes	% (n/N)	27.6 (21/76)
No	% (n/N)	72.4 (55/76)
Reduction of social network		
No to moderate reduction	% (n/N)	15.6 (12/77)
Strong to a very strong reduction	% (n/N)	84.4 (65/77)
Having a history of OC and BC		
Yes	% (n/N)	64.9 (50/77)
No	% (n/N)	35.1 (27/77)
Psychological variables		
PHQ-4 (cv)	M (SD); N Mdn (IQR)	6.05 (2.221); 64 6.00 (4.00–7.00)
BRS (cv)	M (SD); N Mdn (IQR)	3.37 (0.713); 64 3.33 (2.875–3.958)

Abbreviations: BRS, brief resilience score; PHQ-4, Patient Health Questionnaire for Depression and Anxiety; N, number of women for which data were available; n, sample size; M, mean; SD, standard deviation, Mdn, median; IQR, interquartile range; cv, continuous variable.

significant. In contrast, “being more resilient” was a protective factor (OR 0.330; 95% CI 1.114–0.953; $p = 0.041$) for the same subject (Table 5).

A multivariate logistic regression analysis was performed with the strongest predictors of health-related worries in univariate analyses ($p < 0.25$) to evaluate the independence of the aforementioned predicting variables.

Concerning the risk of infecting family or the social network, no other predictive factors other than resilience achieved the necessary p -value to enter the multivariate logistic model. As a result, we did not conduct multivariate analyses on this topic.

Age, living alone, knowing someone in the social network who had COVID-19 disease, having a history of BC or OC, the psychological burden, and resilience were identified as potential predictors of being concerned about gaining a more severe course of the COVID-19 disease due to the increased predisposition for BC or OC. In the multivariate

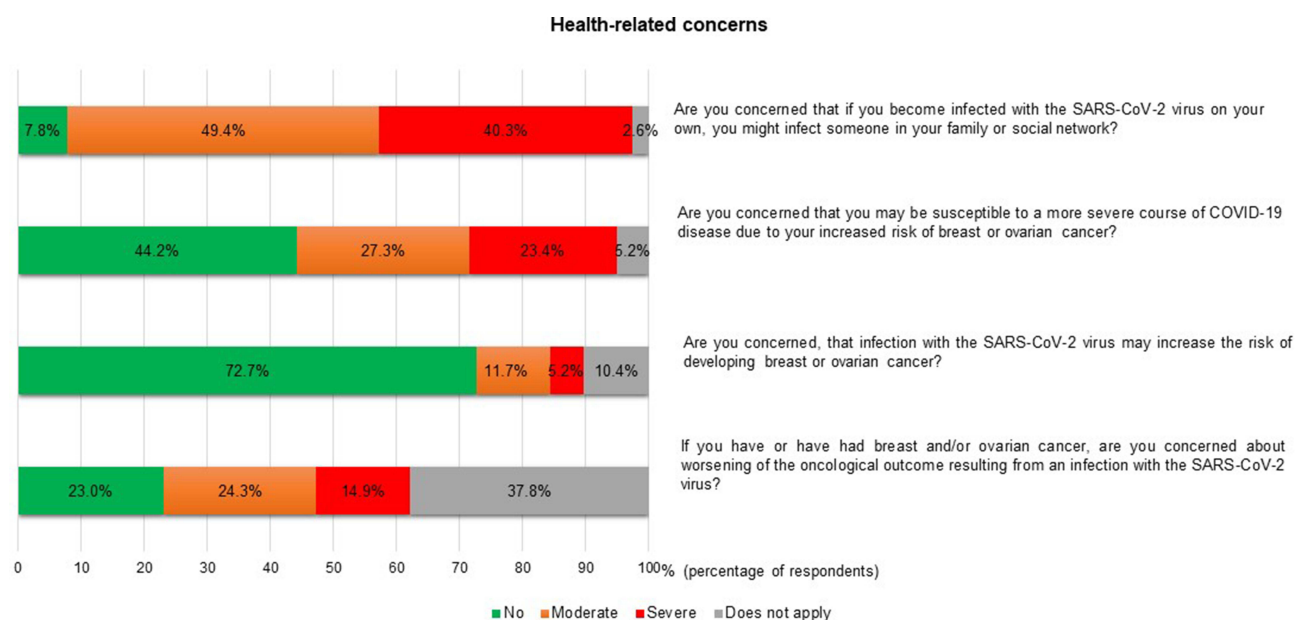


Figure 1 Participants' responses to health-related concerns. Patients' answers to each of the four questions regarding health-related worries during the COVID-19 pandemic are displayed as percentage of respondents.

logistic regression model, having a positive history for BC or OC was the only independently predicting factor, raising the odds of worries over three-fold when compared to participants without cancer diagnosis in their medical history (OR 3.593; 95% CI 1.030–12.536; $p = 0.045$). The final regression model ($n=59$) explained 26.8% of the variance and displayed 71.2% sensitivity for predicting the above-mentioned topic.

Table 2 Predictors of Health-Related Concern "Are You Concerned That if You Become Infected with the SARS-CoV-2 Virus on Your Own, You Might Infect Someone in Your Family or Social Network?" (Univariate Analysis)

	p-value	Nagelkerke R ²	OR	95% CI
Age (cv)	0.393	0.024	1.037	0.954–1.126
Stable partnership (co: no)	0.999	0.032	0.000	0.000–
Living alone (co: yes)	0.429	0.017	2.560	0.249–26.363
Tertiary educational level (co: yes)	0.259	0.042	2.759	0.473–16.089
Having had COVID-19 disease (co: yes)	0.999	0.016	0.000	0.000–
Someone in the social network having COVID-19 disease (co: yes)	0.779	0.002	1.289	0.218–7.632
Reduction of social contacts (co: serious and very serious)	0.963	0.000	0.948	0.101–8.923
Having a history of in situ or invasive BC or OC (co: no)	1.000	0.000	1.000	0.170–5.869
PHQ-4 (cv)	0.488	0.023	1.221	0.694–2.149
BRS (cv)	0.013	0.383	0.044	0.004–0.525

Note: Values in bold indicate statistical significance, as the level of statistical significance was set to $p < 0.05$.

Abbreviations: OR, odds ratio; CI, confidence interval; BC, breast cancer; OC, ovarian cancer; BRS, Brief Resilience Score; PHQ-4, Patient Health Questionnaire for Depression and Anxiety; cv, continuous variable; co, controls.

Table 3 Predictors of Health-Related Concern “Are You Concerned That You May Be Susceptible to a More Severe Course of COVID-19 Disease Due to Your Increased Risk of Breast or Ovarian Cancer?” (Univariate Analysis)

	p-value	Nagelkerke R ²	OR	95% CI
Age (cv)	0.001	0.231	1.098	1.039–1.161
Stable partnership (co: no)	0.502	0.009	0.547	0.094–3.191
Living alone (co: yes)	0.094	0.067	6.552	0.725–59.174
Tertiary educational level (co: yes)	0.359	0.016	1.547	0.609–3.928
Having had COVID-19 disease (co: yes)	0.643	0.004	0.561	0.049–6.470
Someone in the social network having COVID-19 disease (co: yes)	0.201	0.031	0.499	0.171–1.450
Reduction of social contacts (co: serious and very serious)	0.936	0.000	1.055	0.291–3.821
Having a history of in situ or invasive BC or OC (co: no)	0.001	0.224	6.531	2.250–18.954
PHQ-4 (cv)	0.082	0.069	1.246	0.972–1.598
BRS (cv)	0.142	0.048	0.578	0.278–1.202

Note: Values in bold indicate statistical significance, as the level of statistical significance was set to $p < 0.05$.

Abbreviations: OR, odds ratio; CI, confidence interval; BC, breast cancer; OC, ovarian cancer; BRS, Brief Resilience Score; PHQ-4, Patient Health Questionnaire for Depression and Anxiety; cv, continuous variable; co, controls.

Table 4 Predictors of Health-Related Concern “Are You Concerned, That Infection with the SARS-CoV-2 Virus May Increase the Risk of Developing Breast or Ovarian Cancer?” (Univariate Analysis)

	p-value	Nagelkerke R ²	OR	95% CI
Age (cv)	0.047	0.104	1.069	1.001–1.142
Stable partnership (co: no)	0.999	0.060	420,023,530.7	0.000 -
Living alone (co: yes)	0.999	0.060	420,023,440.6	0.000 -
Tertiary educational level (co: yes)	0.849	0.001	1.125	0.335–3.780
Having had COVID-19 disease (co: yes)	0.522	0.009	0.444	0.037–5.310
Someone in the social network having COVID-19 disease (co: yes)	0.220	0.034	0.447	0.123–1.618
Reduction of social contacts (co: serious and very serious)	0.440	0.013	1.800	0.405–7.999
Having a history of in situ or invasive BC or OC (co: no)	0.067	0.096	4.435	0.899–21.884
PHQ-4 (cv)	0.250	0.035	1.178	0.891–1.555
BRS (cv)	0.029	0.138	0.314	0.111–0.886

Note: Values in bold indicate statistical significance, as the level of statistical significance was set to $p < 0.05$.

Abbreviations: OR, odds ratio; CI, confidence interval; BC, breast cancer; OC, ovarian cancer; BRS, Brief Resilience Score; PHQ-4, Patient Health Questionnaire for Depression and Anxiety; cv, continuous variable; co, controls.

The multivariate logistic regression model for predicting worries with regard to an increased risk of BC or OC caused by SARS-CoV-2 infection included 57 women and took into account the following possible predictors: age, knowing someone in the social network who has faced COVID-19 disease, having a history of BC or OC, and resilience. Resilience was found to be an independent protective factor (OR 0.332; 95% CI 0.118–0.933; $p = 0.37$), while no

Table 5 Predictors of Health-Related Concern “If You Have or Have Had Breast and/or Ovarian Cancer, are You Concerned About Worsening of the Oncological Outcome Resulting from an Infection with the SARS-CoV-2 Virus?” (Univariate Analysis)

	p-value	Nagelkerke R ²	OR	95% CI
Age (cv)	0.178	0.058	1.046	0.979–1.118
Stable partnership (co: no)	0.999	0.083	0.000	0.000
Living alone (co: yes)	0.699	0.004	1.750	0.102–29.924
Tertiary educational level (co: yes)	0.146	0.062	2.500	0.727–8.598
Having had COVID-19 disease (co: yes)	0.298	0.034	3.733	0.312–44.626
Someone in the social network having COVID-19 disease (co: yes)	0.282	0.036	0.476	0.123–1.840
Reduction of social contacts (co: serious and very serious)	0.605	0.008	0.677	0.154–2.968
Having a history of in situ or invasive BC or OC (co: no)	n.a.	n.a.	n.a.	n.a.
PHQ-4 (cv)	0.050	0.158	1.462	0.999–2.139
BRS (cv)	0.041	0.168	0.330	0.114–0.953

Note: Values in bold indicate statistical significance, as the level of statistical significance was set to $p < 0.05$.

Abbreviations: OR, odds ratio; CI, confidence interval; BC, breast cancer; OC, ovarian cancer; BRS, Brief Resilience Score; PHQ-4, Patient Health Questionnaire for Depression and Anxiety; cv, continuous variable; co, controls; n.a., not applicable.

independent risk factors were identified. The proposed statistical model described 13.1% of the variance, and the model had an 80.7% sensitivity for predicting the topic.

Among participants, 37 women were involved in the multivariate logistic regression model to predict concerns about worsening oncological outcomes as a result of SARS-CoV-2 virus infection. Age, educational level, psychological burden, and resilience were the selected predictors. Resilience was the single identified independent predictor for above-mentioned health-related issue (OR 0.330; 95% CI 0.114–0.956; $p = 0.041$). The final regression model explained 17.5% of the variance and had a prediction sensitivity of 67.6%.

Discussion

The findings of this study revealed that health-related concerns were common in a population of women at increased risk for BC or OC, with more than 80% of respondents expressing at least one health-related worry. Several authors already described a high prevalence of anxiety during the COVID-19 pandemic, while worries are regarded as a component of anxiety without experiencing an adaptive difficulty or being pathological.^{4,17,18,46–51} In addition, the most frequent health-related concern was linked to the possibility of transmitting an infection to family or social network, with 40.3% experiencing severe levels of concern. Women at high risk for hereditary BC or OC usually have frequent contact with the healthcare system as a result of necessary cancer-prevention measures, anticancer therapy, supportive care, or survivorship programs. Cancer patients were 10-fold more susceptible than non-cancer patients to acquire nosocomial infections (either patient-to-patient and/or patient-to-healthcare-personnel) with the SARS-CoV-2 virus due to immunosuppression caused by active cancer therapy.⁶ The obtained results are in line with findings related to emotional distress in transmitting the virus to loved ones in another group that was more likely to catch the SARS-CoV-2 virus due to occupational exposure risks.^{51,52} We did not ask if the respondents worried about contracting the virus on their own. Nevertheless, a similar attempt conducted in India revealed 39% of cancer patients had minimal concerns, while 61% manifested moderate to severe worries to get infected by their own.⁵³ It is remarkable that almost 90% of respondents mentioned concerns about spreading the virus to their social network while fighting to maintain or regain their own health, thus putting additional strain and pressure on their mental health.

After COVID-19 disease, older age was related to higher mortality: the case-fatality rate was estimated 8% and 14.8% in people aged 70–79 and 80 years or older, respectively.^{8,54,55} Additional findings supported the notion that age was an important risk factor for increased mortality in COVID-19 patients in several European countries, with 0.1% in those <40 years, 13.0% in those 40–69 years, and 86.6% in those older than 70 years, among all COVID-19-related deaths.⁵⁶ A similar attempt by Cohen et al, revealed an age-dependent increase in intermediate care unit admission rates: 5.4%, 52.6%, and 41.8% for those aged <40–50, 40–69, and 60–70 years old, respectively.⁵⁶ The respondents of the current study were significantly younger, but it was obvious that even relatively young participants with a median age of 47 years had significantly more concerns (in univariate logistic regression analysis) about a more severe course of disease than the younger respondents with a median age of 38 years. Previously, older age was associated with reduced general health-related concerns in cancer patients.¹¹ In contrast, more advanced age was described as a vulnerability factor to SARS-CoV-2 health-related worries and other complications, in our evaluation and other publications during the COVID-19 pandemic.^{19,20} Nevertheless, when the variable age was adjusted for the medical history of having (had) a malignant disease, it lost significance. This could be linked to the fact that age is also strongly positively correlated with cancer occurring in people with a hereditary higher risk of BC and OC, making it more of a moderator than an independent factor.^{5,57}

Aside from age, education was found to be predictive of health worries (higher education led to less concerns) using univariate linear regression in a study conducted among the general population in Lebanon during the COVID-19 pandemic, while living status was not.⁵⁸ In our univariate or multivariate logistic regression analyses, the significance of educational level on health-related concerns was not confirmed, which is in contrast with the previous findings that linked lower education to increased anxiety.^{49,51} Nevertheless, it is possible, that age and educational level lost significance (with respect to health-related worries) after adjusting for other factors, as they may be an additional interrelationship eg between age and resilience or education and resilience, as reported previously.⁵⁹

Remarkably, none of the pandemic related variables, such as having had COVID-19 disease (3.9% of the study population), having a relative or someone in the social network infected (27.6% of the study population), or the level of social network reduction (84.4% severe reduction of social network), were negatively associated with health-related concerns. These results are consistent with those of another study of the general population in the United Kingdom, as no significant relation was reported between SARS-CoV-2 infection status (self or social network) and mental distress when they were adjusted for other influencing factors.⁶⁰ A currently published study assessing the distress of patients with breast cancer during the COVID-19 pandemic confirmed that neither resilience, nor psychological distress, nor positive personal resources were influenced by the level of exposure to COVID-19.¹⁴ This outcome could suggest that intrinsic, personal characteristics, such as optimism, self-efficacy, and positive acceptance, may be responsible for emerging health-related worries, rather than extrinsic factors.¹⁴ Nevertheless, the scientific findings are inconclusive, as some authors declared a higher level of psychological or emotional distress in study participants who had an infected relative.^{12,51,52,61} Fitzpatrick et al showed that COVID-related worries changed in the United States population as the pandemic progressed.⁶² Similar results were reported in several populations by a recent meta-analysis.¹² The emotional impact of having a close friend or relative who developed COVID-19 disease may be influenced by the stage of the pandemic itself, the available therapeutic options, such as the possibility of prevention of infection by vaccination, and the medical expertise at the time of data collection, as well as improved coping skills to deal with the situation later in the pandemic.¹²

In our investigation, a history of cancer diagnosis was a significant, independent risk factor for distress to be susceptible for a more severe course of COVID-19 disease, with the odds for health-related worries being 3.593 when other predictors were adjusted. Scientific findings support the concerns of 50.7% of study participants regarding above-mentioned health-related worry. Accordingly, 52% of cancer patients in India expressed similar concerns.⁵³ Interestingly, cancer patients and people with other pre-existing health conditions had an increased risk of COVID-19 related anxiety.^{49,60,61}

There is currently no evidence that infection with SARS-CoV-2 per se will worsen the oncological outcome. Nevertheless, since the duration of a COVID-19 disease is unpredictable, there is a risk of therapy or diagnostic delay due to SARS-CoV-2 infection, which may worsen the oncological outcome. Moreover, the incidence of primary malignant diseases may rise in the future due to a lack of healthcare facilities and the possibility of attending preventive measures during the pandemic. Also, postponed diagnosis due to delayed cancer screening may result in cancer upstaging

and, therefore, worsening prognosis.^{63,64} Sharpless et al proposed a mathematical model to assess the risk of excess BC deaths in the United States due to the pandemic and estimated a 1% increase in BC mortality.⁶³ Nevertheless, breast cancer survivors presenting higher levels of resilience showed less fear of recurrence, despite their failure to maintain medical appointments during the pandemic.⁶⁵

The observed findings could also result from the so-called “infodemic”, an overabundance of information that makes it challenging to distinguish trustworthy information from misinformation.^{66–68} In several populations, poor mental health outcomes were associated with low information quality during the pandemic, whereas the proper quality of information was inversely related to depression, anxiety, and posttraumatic stress disorder.^{49,61,69} Since the frequency and duration of medical consultations were reduced in many countries during the first waves of the pandemic, clinicians might have been unable to address adequately pandemic- or cancer-related health concerns.⁷⁰ Nevertheless, a comprehensive assessment in cancer patients or other vulnerable subgroups necessitates discussing the concerns related to health. It is crucial to understand the sometimes-unspoken fears and worries of the population and specific vulnerable groups.⁷¹ Hence, rapid online surveys, such as the one used in this study, were identified as an appropriate tool for evaluating underlying fears and perceptions, thereby reducing unnecessary anxiety.⁷¹ Proper and adequate risk communication is the responsibility of every single healthcare practitioner, and not just the obligation of state and sociality representatives.

The most important outcome of this study was that resilience is an independent and potent source of reassurance in the face of hardship associated with health-related concerns. During the COVID-19 pandemic or other natural or man-made disasters, the inverse relationship between mental health, such as anxiety or depression, and resilience was extensively studied and validated in various populations.^{28,30–32,68} With this study, resilience was confirmed to be a protective factor against health-related worries in German women with an increased risk for BC and OC during the COVID-19 pandemic. Taken together, the results of this study, as well as previous reports, confirmed the role of resilience in strengthening an individual’s ability to cope with adversities successfully. Subsequently, society and healthcare interventions should focus on resilience-promoting strategies to prevent the chronification of health-related concerns and maintain well-being in vulnerable groups. During this pandemic, specific personality traits, such as individuals with positive coping styles and secure and avoidant attachment styles, were identified as protective factors against mental disorders or health-related worries, but, with this study we recognized resilience as a protective parameter against health-related concerns during the COVID-19 pandemic.^{14,49,72–76}

Limitations

This study has faced several limitations due to the considered design (cross-sectional web-based survey). First, an overrepresentation of patients concerned about their health status due to recruitment from support groups and an underrepresentation of women without online access could be two possible sources of bias. Nevertheless, a recent systematic review displayed that samples recruited through Facebook were as representative as those recruited via traditional methods.⁷⁷ Second, since the patients responded to the questionnaire directly, social desirability bias was greatly limited. Next, the small sample size, the lack of a control group and the design of the study (non-randomized cross-sectional study) may have influenced representativeness. Finally, the obtained results reflected the health-related concerns of women who were at increased risk for BC and OC during the COVID-19 pandemic, and the results are not necessarily generalizable to other vulnerable groups or to other life adversities.

Conclusion

Adequate address of potential health-related concerns should be implemented even in the busy daily routine of the healthcare practitioner. While worrying in response to current stress or difficulties is an adaptive phenomenon that may help with problem-solving, chronic worrying can cause mental distress and deterioration of well-being. The clinician-patient connection and communication may be strengthened by identifying potential sources of health-related distress and offering advice, reassurance, and support. The government and society bear responsibility for properly addressing specific health-related concerns throughout the pandemic’s various stages in order to avoid possible chronification of mental health conditions, which could affect individuals and the entire society years after the pandemic or similar impacts. Because resilience can be a potent protective factor and source of reassurance for people dealing with health

issues during difficult times, regular resilience assessments can help identify people at risk for severe concerns and who may benefit from resilience-building strategies.

Institutional Review Board Statement

This study was conducted in accordance with the Declaration of Helsinki, and adhered to the principles of best clinical practices. Prior to participation in the study, all patients gave their informed consent. The participants' privacy and confidentiality were guaranteed following German and European laws and regulations. This survey was approved by the ethical review board of the medical association of Rhineland-Palatinate, an institution responsible for all physicians working in the area of Rhineland-Palatinate who perform any study involving patients (approval number 15612).

Data Sharing Statement

The data used to support the findings of this study are included within the article.

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Disclosure

Dr Roxana Schwab reports personal fees from Roche Pharma AG, personal fees from AstraZeneca, personal fees from Streamedup! GmbH, during the conduct of the study. Prof. Dr. Marcus Schmidt reports personal fees from AstraZeneca, personal fees from BioNTech, personal fees from Daiichi Sankyo, personal fees from Eisai, personal fees from Lilly, personal fees from MSD, personal fees from Novartis, personal fees from Pfizer, personal fees from Pierre Fabre, personal fees from Roche, personal fees from SeaGen, outside the submitted work. The authors report no other conflicts of interest in this work.

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