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ORIGINAL ARTICLE

Social relationships and their impact on health-related quality of life in a long-term breast cancer survivor cohort

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Abstract

Background: Health-related quality of life (HRQOL) has become increasingly important for breast cancer survivors, but clinically relevant declines often persist for many years after treatment. This study aimed to investigate whether social relationships can mitigate or prevent this decline in HRQOL.

Methods: Data were used from the German population-based Mamma Carcinoma Risk Factor Investigation (MARIE) cohort of 2022 breast cancer cases with follow-up information for more than 15 years after diagnosis. Correlations between social integration, social support, and global health status (GHS) as an overall measure of HRQOL were analyzed, and linear regression analysis was performed with structural equation modeling.

Results: The majority of participants reported high levels of social integration and social support and moderate levels of GHS. Social integration 5 years after diagnosis was associated with GHS 5 years after diagnosis (β = 1.12; 95% CI, 0.25–1.99), but no longitudinal effects were found. Social support 5 years after diagnosis was associated with better GHS 5 years (β = 0.42; 95% CI, 0.36–0.48) and 10 years after diagnosis (β = 0.12; 95% CI, 0.02–0.22), whereas social support 10 years after diagnosis was associated with GHS 10 years (β = 0.29; 95% CI, 0.20–0.39) and 15 years after diagnosis (β = 0.10; 95% CI, 0.01–0.21).

Conclusions: These results confirm that social relationships positively influence HRQOL in long-term breast cancer survivors and that their association should receive more attention clinically and beyond routine care.

KEYWORDS
breast cancer, quality of life, social networking, social support, survivorship

INTRODUCTION

Breast cancer remains the most commonly diagnosed cancer in women worldwide, and is expected to increase as a result of population growth and aging.[1] In Western countries, breast cancer is by far the most common cancer,[2] with approximately 72,000 new cases each year in Germany.[3] Advances in diagnosis and treatment have significantly improved the survival of people diagnosed with breast cancer, which has led to a decrease in mortality rates.[2] As a result, the number of long-term cancer survivors will continue to grow. However, many breast cancer survivors continue to suffer from the adverse effects of cancer diagnosis and treatment, including physical and mental health problems, even decades later.[4] Therefore, general resilience resources,[5] including social relationships,[6] are necessary to cope with these health-related challenges.

Social relationships include several different features of social connectedness: quantity of social relationships, such as social integration and social isolation; and quality of social relationships, including positive aspects of relationships, such as emotional support from significant others, and strained aspects of relationships, such as conflict and stress.[7]

Research on the concept of social relationships and breast cancer is scarce.[8] A meta-analysis has shown that longevity in patients with cancer is associated with higher perceived social support, larger social networks, and being married.[9] However, most research has focused on social relationships and health-related quality of life (HRQOL) during and shortly after breast cancer treatment.[8,10,11] A study examining the mechanisms by which social networks influence HRQOL in patients with breast cancer within 1 year of diagnosis found that socially isolated women had significantly lower HRQOL scores and more breast cancer symptoms than socially integrated women.[12] In addition, larger social networks and greater social support were associated with better HRQOL.[12] A prospective study of breast cancer survivors who were on average 4 years postdiagnosis found clinically relevant differences in HRQOL between socially integrated and socially isolated women.[13] Another study showed that social support at diagnosis appeared to be an important predictor of HRQOL at 3-year follow-up in women diagnosed with breast cancer.[14] However, the impact of social relationships, including social networks and social support, on HRQOL in long-term survivors (≥5 years postdiagnosis) remains unclear.

There is evidence that HRQOL is lowest during treatment but improves during the first 5 years after diagnosis.[15–18] On the other hand, two studies[15,19] found a steady decline in HRQOL from 5 to 10 years after diagnosis. We aimed to investigate whether social relationships can mitigate or prevent this decline in HRQOL by assessing the potential effect of indicators of social relationships, including social integration and perceived social support, on HRQOL in a cohort of long-term breast cancer survivors.

MATERIALS AND METHODS

Study population and procedure

We used data from breast cancer cases originally enrolled in the Mamma Carcinoma Risk Factor Investigation (MARIE), a population-based case-control study,[20] with follow-up approximately every 5 years for more than 15 years. A total of 3813 women aged 50–74 years with a histologically confirmed diagnosis of primary invasive (stage I–IV) or in situ breast cancer between January 1, 2001, and September 30, 2005, were recruited from two study regions in Germany: Hamburg and Rhine-Neckar-Karlsruhe. At enrollment, participants completed an in-person interview that included questions about socioeconomic status, prediagnostic lifestyle factors, medical history, and specific medications, regimens, and duration of use. Three follow-ups were conducted in 2009 (follow-up 1 [FU1]) and 2014 (FU2) via telephone interviews and in 2019 (FU3) via self-administered questionnaires. Information on HRQOL was collected at FU1, FU2, and FU3, whereas information on social relationships was collected only at FU1 and FU2.

At FU1, FU2, and FU3, 510 (13.4%), 392 (11.9%), and 448 (15.4%) participants had died, respectively, 15 participants were lost to follow-up, and 10 participants had emigrated. Women who did not attend FU1 (n = 1271) or did not provide information on exposure (n = 177) or outcome (n = 343) at FU1 were excluded from the analysis. The final analytic sample was 2022 patients with breast cancer for the social relationship and HRQOL analyses (see Figure S1). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all study participants. The study was approved by the Ethics Committee of the University of Heidelberg, the Hamburg Medical Council, and the Medical Board of the State of Rhineland-Palatinate.

Measures

Social integration was measured with the Social Network Index (SNI) by Berkman and colleagues.[21,22] The SNI includes three domains, each scored from 0 to 2: (1) cohabitation with a spouse or partner, (2) contacts with close friends and family, and (3) membership in voluntary associations. Cohabitation was scored as 2 if the participant reported living with a spouse or partner and 0 if not. Frequency of contact with close friends and family (in person or by phone, at least once a month) was scored as 2 for ≥12 contacts, 1 for 3–11 contacts, and 0 for <3 contacts. Membership was assigned a score of 2 if a participant participated regularly, a score of 1 if she participated irregularly, and a score of 0 if a participant did not belong to any voluntary associations. The SNI ranges from 0 to 6, with a score of 0 or 1 indicating strong social isolation (low degree), a score of 2 or 3 indicating a moderate degree of social integration, and 4–6 indicating a high degree of social integration. The SNI was calculated for each individual at the time of FU1 and FU2.

Perceived social support was measured with the Multidimensional Scale of Perceived Social Support, which was designed to measure perceptions of support from family, friends, and significant others.[23,24] The scale consists of a total of 12 items, with a seven-point Likert scale ranging from very strongly disagree to very strongly agree, with a total score ranging from 12 to 84. Higher scores indicate higher levels of perceived social support. Scores of 12–48, 49–68, and 69–84 indicate low, moderate, and high perceived social support, respectively.

The European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) has been used to assess HRQOL in patients with breast cancer. Reference values in the general population are available for several European countries, including Germany.[25] The questionnaire consists of 30 items and assesses the HRQOL of patients with cancer multidimensionally, with two items for the global health status (GHS), the primary outcome of this study. Participants were asked to rate their overall health and quality of life over the past week on a seven-point Likert scale ranging from very poor to excellent. Via the EORTC QLQ-C30 scoring manual,[26] the GHS scale was linearly transformed into a range from 0 (minimum) to 100 (maximum), with higher values indicating better overall HRQOL. The clinical relevance of the mean difference within and between different time points is interpreted qualitatively according to Cocks et al.[27]

Statistical analysis

Descriptive statistics were used to identify participant characteristics. Spearman correlation and linear structural equation modeling (SEM) were used to test our hypotheses regarding the influence of social integration and perceived social support on HRQOL in separate models. SEM was considered most appropriate for this analysis because it is a powerful multivariate technique for testing and evaluating multivariate causal relationships. We used full information maximum likelihood estimation to handle missingness in exposure and outcome variables at FU2 and FU3. Adjustments were made for age, education (high, medium, or low), and migration background (no or yes), which were considered potential confounders. In addition, we included breast cancer staging as a precision covariate for GHS at FU1 to isolate the "unconfounded" effect of social relationships on HRQOL. We used causal directed acyclic graphs and the backdoor criterion to select the minimal sufficient adjustment set of variables for SEM analyses. The adequacy of the structural models was assessed with the following model fit criteria: χ^2 statistic/degrees of freedom < 3.0, root mean square error of approximation (RMSEA) ≤ 0.06, comparative fit index (CFI) ≥ 0.90, and Tucker–Lewis index ≥ 0.90.[28] All tests were two sided, and a p value of less than .05 was considered statistically significant. We computed 95% confidence intervals (CIs) from 1000 bootstrap samples. All analyses were performed with STATA/MP 18.

RESULTS

Table 1 summarizes the characteristics of the study population (N = 2022) by time of measurement. The majority of participants reported a high level of social integration (FU1, 66.6%; FU2, 56.3%). Low levels were reported by 1.6% (FU1) and 4.5% (FU2), which indicates social isolation. In addition, a minority of participants perceived a low level of social support (FU1, 11.7%; FU2, 15.3%) but the majority perceived a high level (FU1, 68.2%; FU2, 61.4%). The mean (SD) GHS approximately 5 years after diagnosis (FU1), 10 years after diagnosis (FU2), and 15 years after diagnosis (FU3) was 67.2 (23.0), 63.8 (24.5), and 64.4 (21.4), respectively.

Table 2 displays means (95% CI) for the GHS stratified by social integration and perceived social support groups (low vs. medium to high) by time of measurement. Socially isolated participants and those with low social support reported a lower GHS than socially integrated participants and those with medium to high social support. The differences within each measurement time point are all clinically relevant, most of which have a mean difference of more than seven points. For socially isolated participants and those with low social support at FU1, GHS scores increased slightly from FU1 to FU2 but decreased from FU2 to FU3. In contrast, for socially integrated participants and those with medium to high social support at FU1, GHS scores decreased slightly from FU1 to FU2 but increased from FU2 to FU3. The largest group difference in the GHS score, in terms of nonoverlapping 95% CIs, of more than 14 points, measured at FU3 was found between socially isolated and socially integrated participants at FU2. In addition, there was a small but clinically relevant deterioration in the GHS score from FU2 to FU3 of seven points in socially isolated participants at FU2. The largest group difference in the GHS score between participants with low and moderate to high social support was also more than 14 points and measured at FU1.

Table 3 shows Spearman's correlation coefficients between social integration, perceived social support, and GHS. The results show that social integration was not related to the GHS score. Social support at FU1 was weakly correlated with the GHS score at FU1, FU2, and FU3. Weak correlations were also found between social support at FU2 and the GHS score at FU2 and FU3.

Figure 1 illustrates the SEM of social integration on the GHS score, adjusted for age and education at baseline, which shows an acceptable fit. No longitudinal associations were found between social integration and GHS. However, there was a positive association between social integration at FU1 and GHS at FU1 (β = 1.12; 95% CI, 0.25–1.99). In addition, higher social integration at FU1 is associated with higher social integration at FU2. Higher GHS at FU1 was associated with higher GHS at FU2 and FU3, and higher GHS at FU2 was associated with higher GHS at FU3.

Figure 2 shows the SEM of perceived social support on the GHS score, adjusted for age and education at baseline, which also shows an acceptable fit. Cross-sectional and longitudinal associations were found between social support and GHS. Social support at FU1 was associated with GHS at FU1 (β = 0.42; 95% CI, 0.36–0.48) and FU2 (β = 0.12; 95% CI, 0.02–0.22), whereas social support at FU2 was

TABLE 1 Characteristics of the MARIE study patient population by time of measurement.

		FU1 (*N* = 2022)	FU2 (*N* = 1517)	FU3 (*N* = 1154)
Follow-up time, mean ± SD, years		5.0 ± 0.9	10.5 ± 0.9	15.5 ± 0.9
Age at baseline, mean ± SD, years		61.9 ± 5.9	61.3 ± 5.7	60.8 ± 5.5
Education at baseline, No. (%)	High	333 (16.5)	271 (17.9)	220 (19.1)
	Medium	588 (29.0)	451 (29.7)	365 (31.6)
	Low	1101 (54.5)	795 (52.4)	569 (49.3)
Migration background, No. (%)	No	1929 (95.4)	1443 (95.1)	1096 (94.9)
	Yes	87 (4.3)	69 (4.6)	54 (4.7)
	Missing values	6 (0.3)	5 (0.3)	4 (0.4)
Social integration	Mean ± SD	3.7 ± 1.1	3.4 ± 1.2	–
	Missing values, No. (%)	0 (0.0)	24 (1.5)	–
Perceived social support	Mean ± SD	70.3 ± 16.1	67.4 ± 18.3	–
	Missing values, No. (%)	0 (0.0)	198 (13.0)	–
Global health status	Mean ± SD	67.2 ± 23.0	63.8 ± 24.5	64.4 ± 21.4
	Missing values, No. (%)	0 (0.0)	137 (9.0)	15 (1.3)
Tumor status at baseline, No. (%)	T1, <2 cm	1156 (57.1)	888 (58.5)	715 (61.9)
	T2, 2–5 cm	602 (29.8)	436 (28.7)	309 (26.8)
	T3, >5 cm	48 (2.4)	35 (2.3)	17 (1.5)
	T4[a]	24 (1.2)	14 (0.9)	9 (0.8)
	Neoadjuvant CT	62 (3.1)	45 (3.0)	29 (2.5)
	In situ	128 (6.3)	98 (6.5)	74 (6.4)
	Missing values	2 (0.1)	1 (0.1)	1 (0.1)
Nodal status at baseline, No. (%)	N0	1307 (64.7)	1005 (66.2)	791 (68.6)
	N1 (1–3)	401 (19.8)	288 (19.0)	213 (18.5)
	N2 (4–9)	84 (4.1)	56 (3.7)	35 (3.0)
	N3 (≥10)	40 (2.0)	25 (1.7)	12 (1.0)
	Neoadjuvant CT	62 (3.1)	45 (3.0)	29 (2.5)
	In situ	128 (6.3)	98 (6.4)	74 (6.4)
Metastasis at baseline, No. (%)	No	1876 (92.8)	1414 (93.2)	1076 (93.2)
	Yes	18 (0.9)	5 (0.3)	4 (0.4)
	In situ	128 (6.3)	98 (6.5)	74 (6.4)
Grading at baseline, No. (%)	G1	391 (19.3)	296 (19.5)	245 (21.2)
	G2	1002 (49.6)	751 (49.5)	577 (50.0)
	G3	432 (21.4)	321 (21.1)	223 (19.4)
	Neoadjuvant CT	62 (3.1)	45 (3.0)	29 (2.5)
	In situ	128 (6.3)	98 (6.5)	74 (6.4)
	Missing values	7 (0.3)	6 (0.4)	6 (0.5)
Staging at baseline, No. (%)	0	128 (6.3)	98 (6.4)	74 (6.4)
	IA/IB	935 (46.2)	722 (47.5)	582 (50.4)
	IIA/IIB	726 (35.9)	543 (35.7)	405 (35.1)
	IIIA/IIIB/IIIC	154 (7.6)	103 (6.8)	59 (5.1)

(Continues)

TABLE 1 (Continued)

		FU1 (*N* = 2022)	FU2 (*N* = 1517)	FU3 (*N* = 1154)
	IV	16 (0.8)	5 (0.3)	4 (0.3)
	Neoadjuvant CT	63 (3.1)	46 (3.0)	30 (2.6)

Abbreviations: CT, chemotherapy; FU, follow-up; MARIE, Mamma Carcinoma Risk Factor Investigation; SD, standard deviation.
[a]Infiltration of skin or chest wall.

TABLE 2 Global health status stratified by social integration and perceived social support groups by time of measurement.

	Social integration											
	FU1						FU2					
	Low[a]			Medium to high[b]			Low[a]			Medium to high[b]		
		95% CI			95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Global health status												
FU1	58.3	49.5	67.1	67.4	66.3	68.4	–			–		
FU2	59.2	47.0	71.4	63.9	62.6	65.2	57.7	52.0	63.5	64.2	62.8	65.5
FU3	55.5	43.8	67.2	64.6	63.3	65.8	50.6	43.5	57.7	65.2	63.9	66.5
	Perceived social support											
	FU1						FU2					
	Low[c]			Medium to high[d]			Low[c]			Medium to high[d]		
		95% CI			95% CI			95% CI			95% CI	
	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper	Mean	Lower	Upper
Global health status												
FU1	54.6	51.6	57.6	68.9	67.8	69.9	–			–		
FU2	56.5	52.5	60.6	64.7	63.4	66.1	52.1	48.8	55.4	65.8	64.4	67.2
FU3	55.5	51.7	59.3	65.6	64.3	66.9	54.7	51.1	58.4	66.1	64.7	67.5

Abbreviations: CI, confidence interval; FU, follow-up.
[a]Social Network Index (SNI) score of 0–1.
[b]SNI score of 2–6.
[c]Multidimensional Scale of Perceived Social Support (MSPSS) score of 12–48.
[d]MSPSS score of 49–84.

associated with GHS at FU2 (β = 0.29; 95% CI, 0.20–0.39) and FU3 (β = 0.10; 95% CI, 0.01–0.21). Higher social support at FU1 was positively associated with social support at FU2. GHS at FU1 was also positively associated with GHS at FU2 and FU3, and GHS at FU2 with GHS at FU3.

DISCUSSION

This study examined the impact of social integration and perceived social support as indicators of social relationships on GHS as an overall measure of HRQOL in a cohort of long-term breast cancer survivors. Our findings on GHS over time are largely consistent with the few longitudinal studies of HRQOL in long-term breast cancer survivors, which suggests improvement or stability.[16,29] In our study, the majority of participants reported high levels of social integration and perceived social support and scores on GHS comparable to those of the general German population.[25] However, our findings suggest that there are clinically relevant differences in GHS between socially isolated and socially integrated long-term breast cancer survivors. Another prospective study of breast cancer survivors who were on average 4 years postdiagnosis showed similar mean differences in HRQOL between socially integrated and socially isolated women,[13] but HRQOL was measured by the 36-Item Short Form Health Survey and different subscales were examined. However, after adjusting for age and education in the longitudinal SEM, no direct long-term associations between social integration and GHS were found in our study. Solely better social integration at 5 years postdiagnosis was

TABLE 3 Spearman correlation between social integration, perceived social support, and global health status.

	Social integration FU1	Social integration FU2	Perceived social support FU1	Perceived social support FU2	Global health status FU1	Global health status FU2	Global health status FU3
Social integration							
FU1	1.000						
FU2	0.572***	1.000					
Perceived social support							
FU1	0.250***	0.242***	1.000				
FU2	0.201***	0.226***	0.596***	1.000			
Global health status							
FU1	0.053	—	0.296***	—	1.000		
FU2	0.044	0.082**	0.152***	0.263***	0.441***	1.000	
FU3	0.042	0.093**	0.186***	0.243***	0.432***	0.423***	1.000

Abbreviation: FU, follow-up.

*$p < .05$.

**$p < .01$.

***$p < .001$.

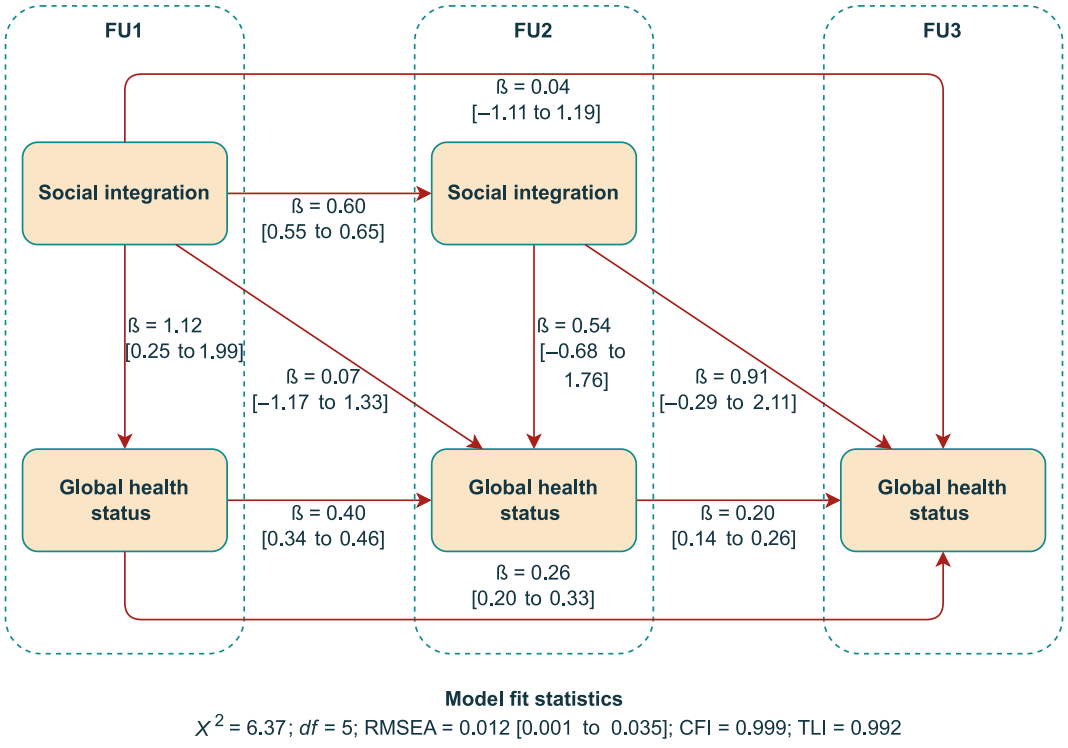

FIGURE 1 Structural equation modeling of social integration on the global health status score, adjusted for age, education, and migration background at baseline. ß indicates the regression coefficient with a 95% confidence interval from 1000 bootstrap samples; CFI, comparative fit index; *df*, degrees of freedom; FU, follow-up; RMSEA, root mean square error of approximation; TLI, Tucker–Lewis index.

associated with higher GHS at 5 years postdiagnosis, and via this pathway, GHS at 5 years postdiagnosis was positively associated with GHS at 10 and 15 years postdiagnosis.

For perceived social support, we found both cross-sectional and longitudinal associations with GHS among long-term breast cancer survivors. Social support at 5 years postdiagnosis had a weak positive association with GHS at 5 and 10 years postdiagnosis, and social support at 10 years postdiagnosis had a weak positive association with GHS at 10 and 15 years postdiagnosis. In contrast, no adjusted direct association of social support at 5 years postdiagnosis with GHS at 15 years postdiagnosis was found, whereas GHS at 5 years postdiagnosis was directly associated with GHS at 15 years postdiagnosis.

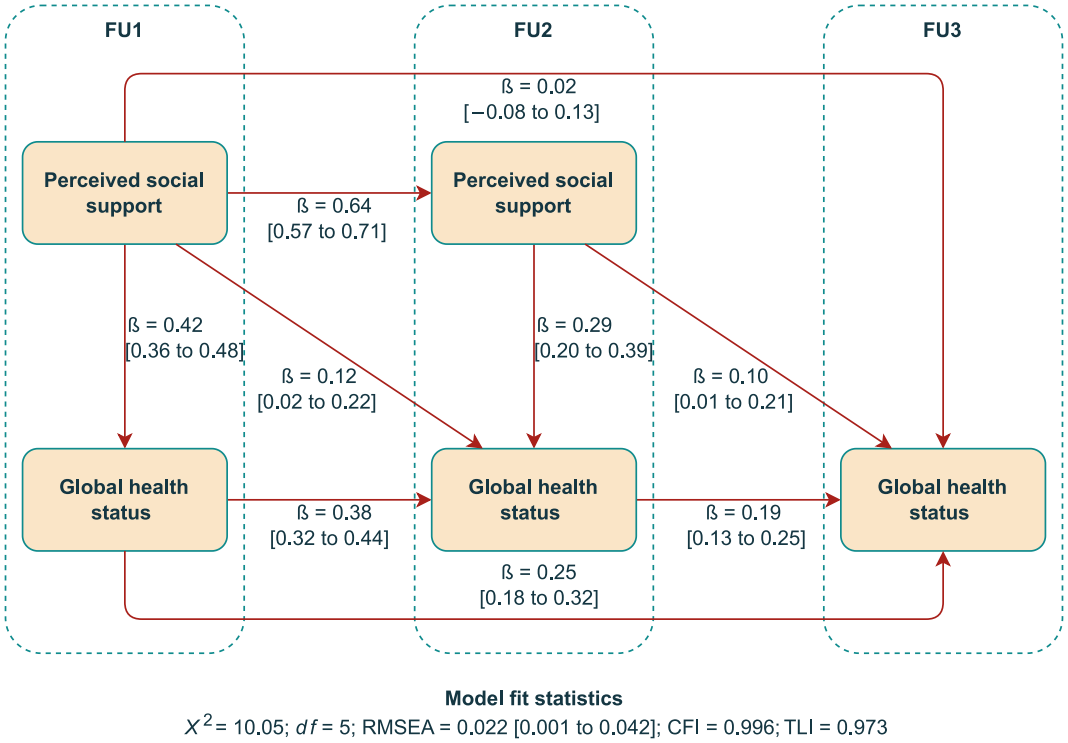

FIGURE 2 Structural equation modeling of perceived social support on the global health status score, adjusted for age, education, and migration background at baseline. *ß* indicates the regression coefficient with a 95% confidence interval from 1000 bootstrap samples; CFI, comparative fit index; *df*, degrees of freedom; FU, follow-up; RMSEA, root mean square error of approximation; TLI, Tucker–Lewis index.

The majority of previous studies found positive associations between social support and HRQOL via different validated measures of social support and HRQOL in short-term survivors.[11] A small study (N = 163) that focused on long-term survivors (5–13 years post-diagnosis) found no associations.[30] However, a larger study (N = 1280), which followed breast cancer survivors annually for up to 7 years (median, 4.5 years) after diagnosis, found that low social support was associated with low HRQOL over time,[31] which is consistent with our findings.

The findings of this study should be considered in the context of the following limitations. First, this is a secondary data analysis, and data on social relationships at baseline and FU3 are lacking, pathways in SEM that should be explored in a future study. Second, there may be a selection bias by including only survivors with complete exposure and outcome data at FU1. This reduced the study population by 14% for the association of social integration with GHS and by 19% for the association of social support with GHS. Excluded women were older, but they did not differ in education or disease stage (data not shown). Third, we cannot exclude the possibility of response shift bias, defined as an adaptation process after a life-threatening serious illness that involves changes in internal norms, values, and conceptualizations of HRQOL.[32] If internal norms, values, or conceptualizations of HRQOL change over time, then responses to the same items from the same individuals may not be comparable over time. Finally, we might not have accounted for all factors that could confound the relationship between social relationships and HRQOL. Potential confounders that we were unable to adjust for include living conditions,[33] ethnicity,[34] and mental health[35] over time. Our study sample predominantly included women of European ancestry, and therefore generalizing our findings to women of other ethnicities should be done with prudence.

Despite these limitations, this study contributes to a better understanding of the relationship between social relationships and HRQOL in long-term breast cancer survivors. Health care providers can assess a survivor's social network during aftercare to determine whether the network is providing the necessary resources and whether additional support from professionals such as social workers or psychologists is needed to improve social conditions and ensure better HRQOL. Because the most relevant time according to the results is (up to) 5 years postdiagnosis, interventions aimed at improving social networks during this time may be valuable for HRQOL in long-term breast cancer survivors. Future research should continue to examine this relationship by simultaneously including psychosocial confounders or mediators, such as depressive symptoms.

In conclusion, first, our results confirm that social relationships influence HRQOL in long-term breast cancer survivors. Second, our results suggest that there are clinically relevant differences in HRQOL between socially isolated and socially integrated breast cancer survivors and between those with low and moderate to high perceived social support. Third, the strength and direction of the effects of social integration and perceived social support on HRQOL

are nearly identical, but the results suggest that perceived social support is more important than social integration. Fourth, our results indicate that social relationships and HRQOL and their association should receive more attention clinically and beyond routine care to ensure that HRQOL remains high in the years after diagnosis and treatment.

AUTHOR CONTRIBUTIONS

Matthias Hans Belau: Conceptualization, methodology, formal analysis, writing–original draft, writing–review and editing, and visualization. **Lisa Jung**: Writing–review and editing and formal analysis. **Tabea Maurer**: Writing–review and editing. **Nadia Obi**: Writing–review and editing, conceptualization, and investigation. **Sabine Behrens**: Conceptualization, investigation, and writing–review and editing. **Petra Seibold**: Writing–review and editing. **Heiko Becher**: Conceptualization, investigation, and writing–review and editing. **Jenny Chang-Claude**: Conceptualization, investigation, funding acquisition, writing–review and editing, and project administration.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data sets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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