



Employment trajectories of young women with breast cancer: an ongoing prospective cohort study in Italy and Switzerland

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Abstract

Purpose Despite extensive research on cancer and work-related outcomes, evidence from longitudinal cohort studies is limited, especially in young women with breast cancer (BC). We aimed to investigate employment trajectories in young BC survivors and to identify potential factors associated with changes in work activity.

Methods The HOHO European prospective multicenter cohort study enrolled 300 young women (≤ 40 years) with newly diagnosed BC. Women completed surveys at baseline and every 6 months for 3 years, then yearly for up to 10 years to assess, among other variables, employment status, sociodemographic, medical, and treatment data. Symptoms were assessed by the Breast Cancer Prevention Trial symptom scales and single items from the Cancer Rehabilitation Evaluation System. Univariable and multivariable multinomial logistic regression analyses identified factors associated with changes in employment status.

Results Among the 245 women included in this analysis, 85% were employed at the last individual post-baseline assessment (1 to 10 years). At 5 years, women had a 29.4% probability (95% CI: 23.6–35.5) of experiencing any reduction and a 14.9% probability (95% CI: 10.6–19.9) of experiencing any increase in work activities. Being enrolled in Switzerland (vs. Italy) and reporting more trouble in performing daily activities were significantly associated with work reduction.

Conclusion Our results suggest that most young BC survivors remain employed in the long-term.

Implications for Cancer Survivors Regular evaluation of symptoms which may interfere with daily life and identification of financial discomfort is critical in providing timely and individually tailored interventions and in limiting unwanted reductions in work activities.

Introduction

The number of women with breast cancer (BC) living beyond 5 years after their diagnosis has been steadily increasing over the most recent decades [1], leading to a growing research interest in survivorship issues. Work-related outcomes are a relevant topic for cancer survivors because cancer not only can interfere with employment during active treatment but also beyond [2, 3]. The most

common work-related outcomes of BC survivors addressed in the literature include (un)employment [4–6], return to work (RTW) [7–9], non-return to work [10], work ability [2, 11, 12], and work performance [2, 13]. Based on systematic reviews, the prevalence rates of RTW 1 year after diagnosis ranged from 43 to 93% [8], whereas the prevalence of unemployment after BC surgery varies between 6 and 53% [5].

A range of factors have been identified that may impact work-related outcomes, including individual, disease and treatment characteristics, symptoms, level of physical, cognitive, emotional and interpersonal functioning, work demands, environment, and economic factors [14]. For BC survivors, individual characteristics associated with negative work-related outcomes include lower education [2, 5, 8, 9, 15, 16], lower income level [5], African-American

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ethnicity [5], and not having children [5]. Disease and treatment-related variables associated with negative work-related outcomes include higher cancer stages (II, III, or IV) [5], mastectomy (vs. conservative surgery) [5], axillary surgery [15], chemotherapy [4, 5, 8], targeted therapies [15], or a combination of chemotherapy and targeted therapies [10]. Among physical and psychological factors, arm morbidity [2, 9, 13], lymphedema [13], fatigue [2, 8, 9, 13], sleep disturbances [16], depression [2, 8–10, 15], emotional distress [8], and anxiety [2, 10] have been reported to negatively affect work-related outcomes. Some studies also suggest that concerns about body image may influence return to work [17]. In women with BC, uncertainties about physical appearance affected their decisions concerning working during the treatment phase [18]. On the other hand, women who returned to work [19] and those who were satisfied with their occupational performance [20] reported higher body image-related quality of life (QoL).

Despite the extensive literature on BC survivors and work, most studies report on a relatively short time frame (during the first 2 years) after diagnosis [21]. Prospective studies investigating changes in employment status several years after diagnosis [15, 22] remain the exception, although longitudinal studies focusing on risk factors for employment disruption are considered a research priority in cancer survivorship [23]. In addition, most studies included women at any legal working-age. Young BC survivors are underrepresented in the existing literature addressing cancer and work. Approximately 5% of BC diagnoses occur in women < 40 years in the USA in 2019 [24] and in the EU in 2020 [25]. BC in young women often requires more aggressive systemic therapies [26] resulting in potentially significant acute side effects and long-term sequelae that may interfere with work.

The Helping Ourselves, Helping Others (HOHO), Young Women's Breast Cancer Study (YWS; NCT01468246), a North American multicenter prospective cohort study found most women to be employed 1-year post-diagnosis [27]. Only 7% of women employed before diagnosis reported unemployment at year 1 with about half being unemployed for health reasons. In this report, we describe employment trajectories over several years post-diagnosis and factors associated with changes in employment status based on data from the European ancillary HOHO/YWS study (IBCSG 43–09 HOHO) [28].

Participants and methods

IBCSG 43–09 HOHO is a longitudinal cohort study that enrolled women ≤ 40 years diagnosed with stages I–IV BC < 6 months before enrollment in Italy and Switzerland. After obtaining informed consent, participating women

completed a comprehensive survey at baseline and every 6 months for the first 3 years, then yearly for additional 7 years. The treating physicians collected medical data on disease outcome, treatment, and comorbidities yearly during follow-up visits. Due to limited resources, the present study was not designed as a comparative multiethnic/country survey. The European survey was shortened compared with the US questionnaire with the assistance of the Europa Donna advocacy group of Southern Switzerland to increase the likelihood of women's long-term engagement in survey completion.

Measures

Baseline assessment of employment status consisted of one question adapted from the National Statistics Classification — Standard Occupational Classification [27, 29] asking participants to describe their work life in the 3 months before the BC diagnosis. Response options included employed full-time, employed part-time, self-employed, unemployed for health reasons, unemployed for other reasons, and full-time homemaker. At the following yearly assessments, participants were asked about their work life “right now,” with the same response options. We categorized women who reported any type of employment (full-time, part-time, or self-employed) as “employed,” and those who reported unemployment or being a homemaker as “not employed” to be consistent with the US cohort [27]. Furthermore, any change from full-time or self-employment to part-time or not employed, as well as any transition from part-time to not employed, was classified as a “reduction in work activity.” Similarly, any transition from part-time to full-time (or self-) employment, as well as any transition from not employed to employed, was classified as an “increase in work activity.” Four additional employment-related variables were assessed by single questions: (1) satisfaction with work; (2) degree to which cancer or cancer treatment limited one's ability to perform work responsibilities; (3) employer's accommodations to make it easier to work; and (4) likelihood that the respondent would be working at all in 1 year (Table S1) [27, 30].

We selected factors potentially associated with employment changes based on data from published studies [2, 8, 13] and on the availability of these variables in the HOHO European cohort (Table S1). Socio-demographic characteristics included education, marital status, parity, and self-perceived financial situation at baseline and during follow-up (based on the availability of data) [27, 31]. Information on surgery, chemotherapy, endocrine therapy, and the presence of psychological problems (depression, anxiety, irritability, nervousness, and anger affecting “somewhat” or “a great deal” the day-to-day activities) were extracted from the self-report survey and medical records collected longitudinally.

Selected symptoms most likely to impact work abilities were assessed longitudinally by the Breast Cancer Prevention Trial (BCPT) [32, 33] symptom scales and by single-items from the Cancer Rehabilitation Evaluation System (CARES) [34, 35] and its short form (CARES-SF) [36]. The BCPT evaluates commonly reported physical and psychological symptoms after BC. We selected three symptom scales including musculoskeletal pain (3 items), cognitive problems (3 items), and arm problems (2 items). Women indicated how much they were bothered by each symptom during the past 4 weeks on a 5-point severity scale (0–4). Scores for each scale were calculated by averaging the items. Higher scores indicate greater bothering by symptoms. Single-item symptoms from the CARES included sleep problems, lack of energy, and general pain. Difficulty with daily activities caused by disease or treatment were assessed by the CARES-SF physical domain. Body image was measured by the subscale of the CARES psycho-social summary scale [35], which includes three questions: (1) I am uncomfortable with the changes in my body; (2) I am embarrassed to show my body to others because of my illness; (3) I am uncomfortable showing my scars to others. For all CARES and CARES-SF items, respondents were asked how much each statement applied to them on a 0–4 scale. Higher scores indicate more difficulty and a poorer QoL (Table S1).

Statistical analyses

Socio-demographic and clinical characteristics were analyzed using descriptive statistics for the overall cohort and according to employment status at baseline. Categorical variables were reported with absolute and relative frequencies, continuous variables with median and interquartile range (IQR).

Changes in employment status were evaluated applying two different strategies:

1. Analyses of the employment change between baseline and last follow-up assessment (including all available assessments up to 10 years).
2. Analyses of the employment change between consecutive follow-up time points, for which all assessments and all changes in employment status (trajectories) were considered. If a woman missed a follow-up assessment, we considered the assessments before and after the missing assessment (e.g., if the 5-year assessment was not completed, the 4- and 6-year assessments were considered consecutive).

Employment status was assessed until any recurrence (loco-regional, distant metastases, contralateral, or second primary events) or until completion of the last follow-up questionnaire, whichever occurred first.

To visualize the onset of changes in employment status, we estimated the cumulative probability of the first change in employment status (reduction or increase in work activity) at follow-up, according to methods described by Kalbfleisch and Prentice [37]. To estimate the cumulative probability of any reduction in work activity, we considered competing events any increase in work activity. Likewise, to estimate the cumulative probability of an increase in work activities, we considered competing events any reduction in work activity. Recurrences among patients with stable status (full- or part-time employed, self-employed, not employed) were considered competing events in both cases. For women who changed the employment status at least once during follow-up (event of interest), we considered the time from enrollment to the first change as observation time. Those who maintained a stable work status throughout the observation period were censored at the last follow-up assessment.

Univariable and multivariable multinomial logistic regression was applied to identify factors (fixed at baseline or time-dependent) associated with changes in employment status. Reduction and increase in work activities were considered two distinct outcome levels in the multinomial model. Standard errors of parameter estimates were adjusted using generalized estimating equation (GEE) methods to account for multiple trajectories within the same woman. For the multivariable analysis, we first considered variables with p values < 0.10 , or an odds ratio (OR) > 1.25 or < 0.80 from the univariable analyses. From this multivariable model, only variables with p values < 0.10 , or an OR > 1.25 or < 0.80 , were retained in the final multivariable model. Analyses were conducted using the SAS software v. 9.4 (SAS Institute, Cary, NC).

Results

Sample characteristics

The IBCSG 43–09 HOHO cohort enrolled 300 women from 18 institutions in Italy and Switzerland between July 2009 and January 2016. The cohort analyzed for this report includes 245 women with a median time between diagnosis and baseline survey of 2.3 months (IQR 1.6–3.6 months). Reasons for exclusion are listed in Fig. S1 in the supplement. The median follow-up time was 6.0 years (IQR 4.1–7.1).

Table 1 summarizes characteristics of the study population overall and according to employment status at baseline. Median age at baseline was 37 years (IQR 34–39), 38% of the women had a university education, 65% were married or in a stable relationship, and 50% had children before cancer diagnosis. Almost

Table 1 Women's socio-demographic and clinical characteristics at baseline, overall, and according to employment status

	Unemployed at baseline (N=40)		Employed at baseline (N=205)		Overall (N=245)	
	N	%	N	%	N	%
Country of enrollment						
Italy	33	82.5	138	67.3	171	69.8
Switzerland	7	17.5	67	32.7	74	30.2
Age at baseline < 35 years	14	35.0	61	29.8	75	30.6
Age at baseline, median (IQR)	36.8 (32.9–39.1)		37.0 (34.1–39.2)		37.0 (33.9–39.2)	
University education	9	22.5	84	41.0	93	38.0
Married or in a significant relationship at baseline	30	75.0	128	62.4	158	64.5
Financial comfort						
Enough money for special things	8	20.0	103	50.2	111	45.3
Enough money to pay bills but little spare money for extras	12	30.0	59	28.8	71	29.0
Money to pay bills but only after cutting back/difficulty paying bills	16	40.0	34	16.6	50	20.4
Missing/unknown	4	10.0	9	4.4	13	5.3
First-degree relative with breast or ovarian cancer at baseline	13	32.5	94	45.9	107	43.7
Psychological problems at baseline ^a	2	5.0	4	2.0	6	2.4
Received/receiving chemotherapy at baseline	27	67.5	149	72.7	176	71.8
Already receiving endocrine therapy at baseline	14	35.0	89	43.4	103	42.0
Underwent mastectomy at baseline/after neo-adjuvant treatment	20	50.0	90	43.9	110	44.9
Had children before cancer diagnosis	28	70.0	95	46.3	123	50.2
Pathological tumor size						
1	22	55.0	106	51.7	128	52.2
2	13	32.5	66	32.2	79	32.2
3/4	2	5.0	9	4.4	11	4.5
X ^b	3	7.5	24	11.7	27	11.0
Pathological regional lymph nodes						
0	21	52.5	97	47.3	118	48.2
1	12	30.0	59	28.8	71	29.0
2/3	5	12.5	26	12.7	31	12.7
X ^b	2	5.0	23	11.2	25	10.2
Distant metastasis ^c						
0	40	100.0	205	100.0	245	100.0
Grade						
1	1	2.5	9	4.4	10	4.1
2	15	37.5	81	39.5	96	39.2
3	23	57.5	104	50.7	127	51.8
Unknown	1	2.5	11	5.4	12	4.9
ER/PgR positive	30	75.0	164	80.0	194	79.2
HER2 positive	12	30.0	47	22.9	59	24.1

^aThe following psychological problems affecting “somewhat” or “a great deal” the day-to-day activities were taken into consideration: depression, anxiety, irritability, nervousness, and anger. ^bReceived neoadjuvant treatment. ^cWomen with advanced disease were not included in this analysis

half of the women (45%) indicated that they felt financially comfortable at baseline. Forty-five percent of women had a mastectomy, 72% received or were receiving chemotherapy, and 42% were receiving endocrine therapy.

Employment change between baseline and last follow-up

At baseline, 205 (83.7%) women were employed, and 40 (16.3%) were not employed. Among the employed women, 124 were employed full-time, 53 part-time, and 28 were

self-employed. Among the not employed women, two were not employed for health reasons, 15 for other reasons, and 23 were homemakers. At the last follow-up, 209 (85.3%) women were employed (96 full-time, 82 part-time, 31 self-employed) while 36 (14.7%) were not employed (9 for health reasons, 8 for other reasons, 19 were homemakers). Figure S1 reports the time-points considered for the last follow-up and the number of women with available information on employment status. Employment trajectories between baseline and last follow-up are displayed in Fig. 1.

Among the 205 employed women at baseline, 170 (83%) continued to be employed over time (Table S2). The proportion of participants who reported to be somewhat or completely satisfied with their job was 87% at baseline and over 80% at each of the later time points up to 5 years t. While at year 1, almost 20% of employed women indicated that cancer or cancer treatment limited their ability to perform their job quite a bit or very much, and the proportion dropped to less than 10% for the following 4 years. Up to year 5, around 90% said they were somewhat or very likely to be working 1 year later. Approximately 40% of women reported willingness by their employer to make accommodations following the BC diagnosis at year 1, with a decreasing proportion of women saying that this was the case from years 2 to 5.

Employment trajectories

During the follow-up period, 88 women (36%) were consistently employed full-time or self-employed, 30 (12%) continued to work part-time, and 16 (6%) were always not

employed. For those women who changed their employment status at least once during follow-up, 75 (31%) first reduced their work activities by transitioning from full-time or self-employed to part-time (49 women) or to being not employed ($N=15$). The remaining 11 women transitioned from a part-time job to being not employed. Conversely, 36 (15%) women first increased their work activities by transitioning from part-time to full-time or self-employment ($N=12$) or by changing from being not employed to being employed (full/part-time) or self-employed ($N=24$). Among women with a stable trajectory, 17 recurrences were reported. The cumulative probability to have any reduction in work activities at 5 years was 29.4% (95% confidence interval (CI) 23.6–35.5) while the cumulative probability to have any increase in work activities at 5 years was 14.9% (95% CI 10.6–19.9; Fig. 2).

Considering the employment status from two consecutive follow-up time points, we observed 1237 trajectories, 209 (16.9%) of which indicated a change in employment status (Table S3). Work activities were reduced in 114 trajectories (71 from employed full-time/self-employed to part-time, 26 from employed full-time/self-employed to not employed, and 17 from employed part-time to not employed) while they increased in 95 trajectories (48 from part-time to full-time employment/self-employment, 24 from not employed to full-time/self-employed, and 23 from not employed to a part-time job; Table S3).

Of the 111 women who reduced or increased their work activities at least once during follow-up, 51 women changed only once, and 60 women changed more than once.

Fig. 1 Employment status at baseline and at last follow-up, and transitions between the two time points

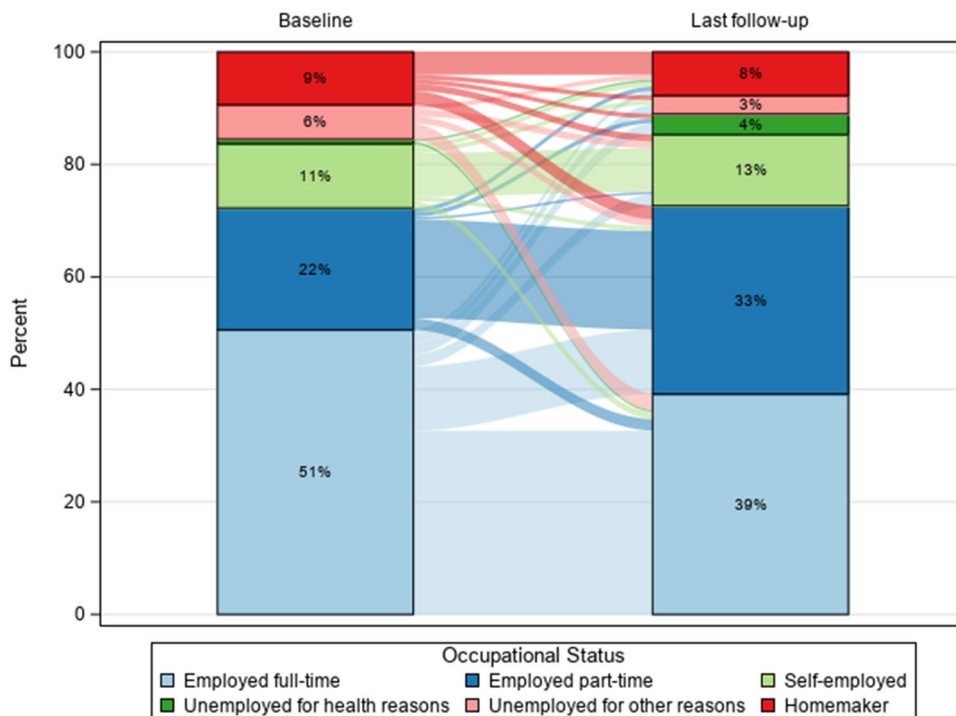


Fig. 2 Cumulative incidence of first change in employment status

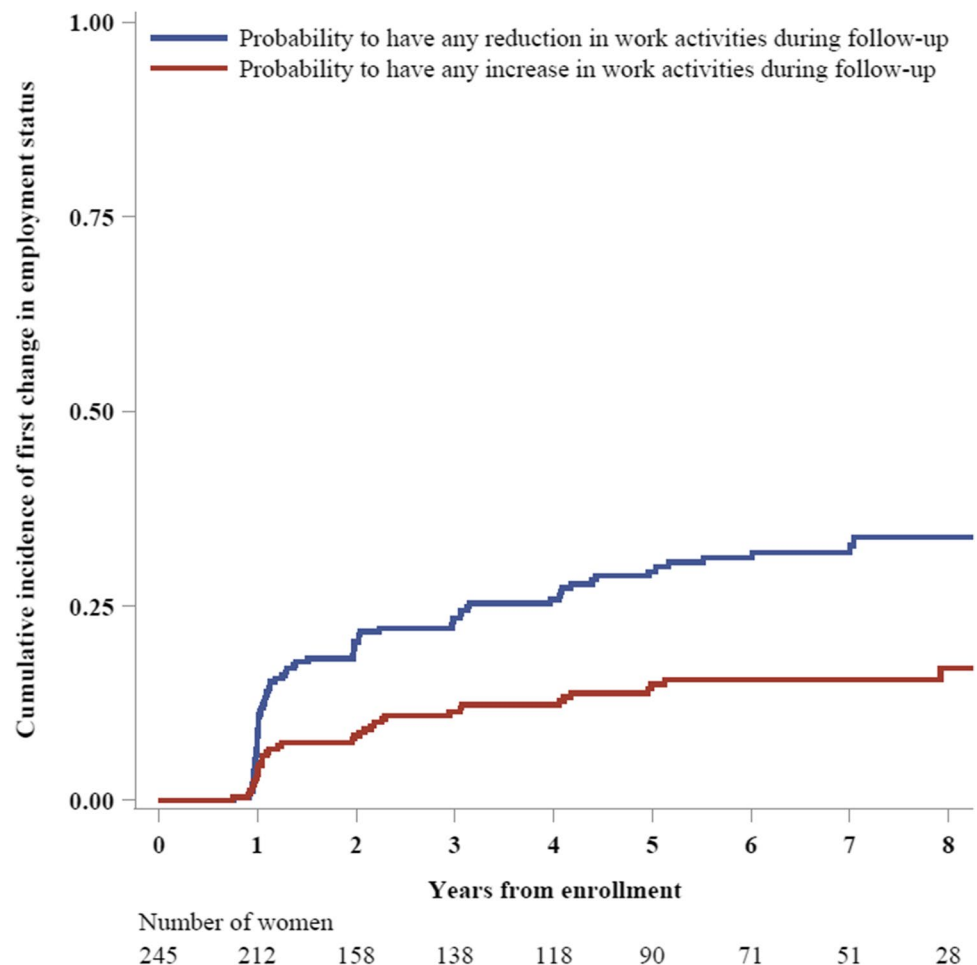


Table 2 presents factors (fixed at baseline or time-dependent) associated with a reduction in work activities, compared to a stable employment status, between two consecutive assessments. In univariable analysis, women enrolled in Switzerland (vs. enrolled in Italy) having higher levels of fatigue, cognitive and arm problems, general and musculoskeletal pain, more difficulty with daily activities (CARES-SF physical domain), and worse body image were significantly associated with reduced work activities over time. In multivariable analyses, being enrolled in Switzerland (vs. Italy), and reporting more difficulty with daily activities remained significantly associated with work reduction. Age, university education, relationship status, reporting financial difficulties, having psychological problems, receiving chemo- or endocrine therapy, type of surgery (mastectomy vs. breast conserving surgery), and parity were not associated with reducing work in either univariable or multivariable analyses (Table 2). Univariable sensitivity analysis of the factors associated with changes in employment status in women with at least 5 years of follow-up ($N=164$ women) revealed similar results: women enrolled in Switzerland, having a university education, with children, more bothered

by symptoms, who reported more difficulty with daily activities or had worse body image were more likely to reduce their work activities over time (Tables S4). Being enrolled in Switzerland (vs. Italy), having a university education and reporting financial difficulties were also associated in multivariable analysis with an increase in work activities (Table S5).

Discussion

While numerous qualitative, cohort, and register-based studies have investigated work retention or work resumption of cancer survivors [38], data about the temporal trajectory of employment over multiple time points and after several years beyond cancer treatment is still limited [39]. In our study, the vast majority (85%) of young women with BC was employed at the last individual follow-up time point 1–10 years post-diagnosis. Considering individual trajectories, at 5 years after the initial assessment, about half of the women changed at least once their employment status during follow-up. Previous US studies

Table 2 Univariable and multivariable analysis of factors associated with a reduction in work activities compared with stable employment status ($N=1142$ trajectories) between two consecutive assessments

	Univariable analysis						Multivariable analysis		
	N. (%c) of trajectories	N. (%r) of trajectories with stable employment status	N. (%r) of trajectories with a reduction in work activities	OR	95% CI	p-value	OR	95% CI	p-value
<i>Socio-demographics and clinical variables</i>									
Country of enrollment									
Italy	854 (69.0)	734 (85.9)	63 (7.4)	1.00			1.00		
Switzerland	383 (31.0)	294 (76.8)	51 (13.3)	2.02	1.30–3.13	<0.01	2.15	1.37–3.38	<0.01
Age at baseline < 35 years									
No	859 (69.4)	731 (85.1)	73 (8.5)	1.00					
Yes	378 (30.6)	297 (78.6)	41 (10.8)	1.38	0.88–2.18	0.16			
University education									
No	748 (60.5)	634 (84.8)	63 (8.4)	1.00			1.00		
Yes	489 (39.5)	394 (80.6)	51 (10.4)	1.30	0.84–2.01	0.23	1.54	0.96–2.47	0.08
Married or in a significant relationship (time-dependent)									
No	383 (31.0)	317 (82.8)	33 (8.6)	1.00					
Yes	854 (69.0)	711 (83.3)	81 (9.5)	1.09	0.69–1.75	0.71			
Financial comfort at baseline									
Enough money for special things	606 (51.2)	517 (85.3)	51 (8.4)	1.00			1.00		
Enough money to pay bills but little spare money for extras	367 (31.0)	302 (82.3)	34 (9.3)	1.14	0.67–1.94	0.63	1.18	0.68–2.03	0.56
Money to pay bills but only after cutting back/difficulty paying bills	210 (17.8)	166 (79.0)	23 (11.0)	1.40	0.80–2.46	0.23	1.33	0.72–2.47	0.37
Having psychological problems (time-dependent) ^a									
No	1188 (96.0)	988 (83.2)	106 (8.9)	1.00					
Yes	49 (4.0)	40 (81.6)	8 (16.3)	1.86	0.80–4.34	0.15			
Received/receiving chemotherapy									
No	347 (28.1)	282 (81.3)	36 (10.4)	1.00					
Yes	890 (71.9)	746 (83.8)	78 (8.8)	0.82	0.51–1.33	0.42			
Receiving endocrine therapy (time-dependent) ^b									
No	461 (37.3)	390 (84.6)	36 (7.8)	1.00					
Yes	776 (62.7)	638 (82.2)	78 (10.1)	1.32	0.86–2.03	0.20			
Underwent mastectomy at baseline/after neo-adjuvant treatment									

Table 2 (continued)

	Univariable analysis			Multivariable analysis					
	N. (%c) of trajectories	N. (%r) of trajectories with stable employment status	N. (%r) of trajectories with a reduction in work activities	OR	95% CI	p-value	OR	95% CI	p-value
No	674 (54.5)	556 (82.5)	66 (9.8)	1.00					
Yes	563 (45.5)	472 (83.8)	48 (8.5)	0.86	0.56–1.32	0.48			
Parity (time-dependent) ^c									
No	614 (49.6)	497 (80.9)	63 (10.3)	1.00					
Yes	623 (50.4)	531 (85.2)	51 (8.2)	0.76	0.50–1.15	0.20			
Health-related quality of life variables (continuous time-dependent)	1237	1028	114						
Sleep problems ^d				1.17	0.99–1.39	0.06			
Fatigue/tiredness ^e				1.29	1.09–1.53	<0.01			^j
Pain ^e				1.48	1.18–1.86	<0.01			^j
Musculoskeletal pain ^f				1.30	1.05–1.61	0.01			
Cognitive problems ^f				1.27	1.04–1.54	0.02			
Arm problems ^g				1.35	1.02–1.78	0.03			
Body image ^h				1.27	1.06–1.53	<0.01			
CARES-SF physical scale ⁱ				1.97	1.40–2.77	<0.01	1.98	1.38–2.84	<0.01

Abbreviations: %c, column percentage; %r, row percentage. ^aForty-four women who indicated to have psychological problems (depression, anxiety, irritability, nervousness, anger) affecting “somewhat” or “a great deal” the day-to-day activities at baseline or during follow-up. ^bOne hundred and five women started endocrine therapy during follow-up. ^cEleven women had children during follow-up. ^dSingle item from CARES-SF psychosocial subscale. ^eSingle item from CARES-SF physical subscale. ^fAverage score from BCPT 3-items scale. ^gAverage score from BCPT 2-items scale. ^hGlobal score from 3-items subscale of CARES long version. ⁱGlobal score. ^jSingle items not included in the multivariable model. The global CARES-SF physical scale was included instead

in younger women with BC reported slightly lower proportions of employment but referred to shorter follow-up periods. In the HOHO/YWS cohort, the proportion of employed women was 80% at 1 year [27]. Naughton et al. reported 72% of women ≤ 45 years to work full- or part-time 18-months after diagnosis [40]. This is somewhat surprising as earlier findings found BC survivors residing in the USA to be more likely to return to work compared to other countries. There is no universal healthcare coverage in the USA, rather health insurance is provided through the employer for the majority of the working population [5]. Although the health insurance systems differ between Switzerland and Italy, in both countries, the access to health insurance is unrelated to employment status. Pooled estimates of prevalence of work retention beyond 2 years in survivors across cancer types and age groups based on a systematic review were 75% between 4 and 6 years, and 65% at 6 years from diagnosis, respectively [39]. However, most of the included studies were cross-sectional, covering just one specific time point in the survivorship phase.

Our results indicate that job satisfaction and confidence in work ability remain high several years after the BC diagnosis for women who continue working. Nevertheless, about 10% of women constantly employed reported some limitations in performing their job due to their disease. With a 29% probability of having any reduction in work activities in our sample, such limitations may have led women to cut down their working hours. However, our survey did not query whether the reduction was voluntary or not. Prior research reported that among long-term BC survivors, 20% had to reduce their working time, which was involuntarily in 12% and negatively affected their satisfaction with occupational development [41]. According to the women in our study, the willingness of employers to accommodate work conditions to their needs decreased over time, possibly because women who said that their employer accommodated work conditions at year 1 indicated no need for special accommodations at later years.

Women from Switzerland were more likely to reduce their work activities than women from Italy. In 2021, 87%

of women between 25 and 39 years were employed in Switzerland, about half full-time and half part-time [42]. Corresponding statistics from Italy in 2021 report 36% of young women (15–34 years) and 63% (34–49 years) were employed [43]. In 2020, the number of women forced into involuntary part-time work (i.e., all those who settled for a part-time job even though looking for a full-time one) was 61.2% in Italy [44] compared with 30% in Europe in 2019 [45]. Besides having higher employment rates, Switzerland is a wealthier country, and the likelihood of being financially dependent on paid work may be greater in Italy. Swiss women may therefore feel more confident to change their work activities depending on their health situation. Financial independency has been reported to be correlated with negative work-related outcomes in BC survivors [2]. Our study also indicated that financial discomfort was associated with an increase in work activity suggesting that women, who encounter financial difficulties, may be forced to re-join the workforce or intensify their work activities, regardless of their health status. Similar to the results reported from the US HOHO/YWS cohort [27], having children was not associated with a reduction in work activity in our cohort of young women.

In the univariable analysis, individual symptoms were associated with a reduction in work activities confirming previously reported negative effects of a range of symptoms on work-related outcomes [2, 9, 13, 16, 17, 21]. Data from a systematic review article supports the association of higher symptom burden with trends of poorer work-related outcomes among cancer survivors [17]. In our final multivariable model, we only included the CARES-SF physical domain as it covered a mix of symptoms (pain and lack of energy) and difficulties with daily activities (e.g., doing household chores), and one question on the interference of cancer and treatment on work ability. The association we found between the CARES-SF physical domain and reduction of work activity is consistent with results from prior studies indicating that impairments in physical functioning negatively affected RTW in BC survivors [46]. Although psychological symptoms such as depression [2, 8, 10] or anxiety [2, 11] can negatively affect work-related outcomes, patient-reported psychological problems were not associated with reduction of work in our study. As we used a crude indicator consisting of a single question concerning any additional illness and no validated measures were used to assess depression or anxiety specifically, interpretation of this result requires caution.

Interestingly, none of the treatment-related variables (mastectomy, chemotherapy, endocrine therapy) were significantly associated with reduction of work activities. In contrast, a meta-analysis in BC at any age reported that mastectomy was associated with unemployment [5]. Consistent with our results, chemotherapy was not associated

with employment in young BC survivors in the US HOHO/YWS cohort [27]. The negative impact of chemotherapy on work may be less relevant in the long-term, as most women complete chemotherapy within the first year of diagnosis. Overall, our results indicated that BC treatment is unlikely to be a major contributor to changes in employment status in young women.

Lacking an age-matched comparison group, we were unable to compare our results with employment trajectories of healthy young women. BC survivors aged 35–45 at diagnosis may experience increased risk of losing their job compared with general population norms [4]. For those who were self-employed, we did not assess the impact of BC on productivity or earnings. We did not investigate several factors that have been associated with employment including disease-related variables, such as stage [5, 27], comorbidities [10], high psychological and physical job demand [5], or adjustments of work conditions [6, 39]. Attrition and missing data are further limitations, as some women did not complete questionnaires at each follow-up or stopped completing them after less than 5 years. Sensitivity analysis for predictors of changes in employment status in women with at least 5 years of follow-up revealed similar results. Finally, we cannot exclude a recall bias as time between diagnosis and first assessment varied between participants. However, we consider the 2 months of median time elapsed as negligible, because job situation may not change very rapidly and usually requires thorough considerations from the affected individual.

Overall, our results provide some ground for optimism regarding the long-term employment of young BC survivors, as the proportion of women being (self-)employed remains high several years after the diagnosis. However, our results also suggest that about one third of the changes in work activities are represented by a reduction during follow-up care and we identified troubles performing daily activities as a potential risk factor. Clinicians should therefore discuss with their patients their work ability considering their individual situation by regularly evaluating symptoms that could interfere with daily life. In addition, other professionals including social workers or vocational psychologist may support clinicians in identifying financial discomfort and other work-related concerns to support sustainable work participation [47]. Interventions involving physical, psycho-educational, social work support, and/or vocational components such as supportive work places have been recommended to enhance RTW for cancer patients in general [48]. Future research should address whether and how available interventions can be tailored to the specific needs of young BC survivors.

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Author contribution Karin Ribi PhD: manuscript writing — original draft; manuscript review, editing, and approval. Eleonora Pagan PhD: statistical analysis, manuscript writing — original draft; manuscript review, editing, and approval. Isabella Sala MSc: statistical analysis, manuscript writing — original draft; manuscript review, editing, and approval. Monica Ruggeri: conceptualization and study design; data management; manuscript writing — original draft; manuscript review, editing, and approval. Nadia Bianco MD: data acquisition; manuscript review, editing, and approval. Eraldo Oreste Bucci MD: data acquisition; manuscript review, editing, and approval. Rossella Graffeo MD: data acquisition; manuscript review, editing, and approval. Markus Borner MD: data acquisition; manuscript review, editing, and approval. Monica Giordano MD: data acquisition; manuscript review, editing, and approval. Lorenzo Gianni MD: data acquisition; manuscript review, editing, and approval. Manuela Rabaglio MD: data acquisition; manuscript review, editing, and approval. Andrea Freschi MD: data acquisition; manuscript review, editing, and approval. Elisabetta Cretella MD: data acquisition; manuscript review, editing, and approval. Elena Seles MD: data acquisition; manuscript review, editing, and approval. Alberto Farolfi MD: data acquisition; manuscript review, editing, and approval. Edda Simoncini MD: data acquisition; manuscript review, editing, and approval. Mariangela Ciccarese MD: data acquisition; manuscript review, editing, and approval. Daniel Rauch MD: data acquisition; manuscript review, editing, and approval. Adolfo Favaretto MD: data acquisition; manuscript review, editing, and approval. Agnes Glaus PhD, MSc: data acquisition; manuscript review, editing, and approval. Rossana Berardi MD: data acquisition; manuscript review, editing, and approval. Alessandra Franzetti-Pellanda MD: data acquisition; manuscript review, editing, and approval. Vincenzo Bagnardi PhD: conceptualization and study design, statistical analysis, manuscript writing — original draft; manuscript review, editing, and approval. Shari Gelber PhD, MSc: conceptualization and study design; statistical analysis; manuscript review, editing, and approval. Ann H. Partridge MD, MPH: conceptualization and study design; manuscript review, editing, and approval. Aron Goldhirsch MD: conceptualization and study design. Olivia Pagani MD: conceptualization and study design; data acquisition; manuscript writing — original draft; manuscript review, editing, and approval.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication The manuscript does not contain any individual person's data in any form, and consent for publication was therefore not obtained from the patients included in this study.

Competing interests Karin Ribi reports no conflicts related to this study, Eleonora Pagan reports no conflicts related to this study, Isabella Sala reports no conflicts related to this study, Monica Ruggeri reports no conflicts related to this study, Nadia Bianco reports no conflicts related to this study, Eraldo Oreste Bucci receives consulting or advisory fees from Astra Zeneca and travels/accommodations from Astellas, BMS, Lilly, Merck Serono, Roche, Takeda, Rossella Graffeo reports no conflicts related to this study, Markus Borner reports no conflicts related to this study, Monica Giordano reports no conflicts related to this study, Lorenzo Gianni receives consulting or advisory fees from Astra Zeneca and travels/accommodations from Novartis, Manuela Rabaglio reports no conflicts related to this study, Andrea Freschi reports no conflicts related to this study, Elisabetta Cretella reports no conflicts related to this study, Elena Seles reports no conflicts related to this study, Alberto Farolfi receives honoraria from Janssen Oncology, GSK-Tesaro, Astrazeneca, Clovis, Edda Simoncini reports no conflicts related to this study, Mariangela Ciccarese reports no conflicts related to this study, Daniel Rauch (*pending*), Adolfo Favaretto reports no conflicts related to this study, Agnes Glaus reports no conflicts related to this study, Rossana Berardi receives donations to her institution and/or fees for advisory board participations from AZ, BI, Novartis, MSD, Otsuka, Lilly, Roche, Amgen, GSK, EISAI (none related to this study), Alessandra Franzetti-Pellanda reports no conflicts related to this study, Vincenzo Bagnardi reports no conflicts related to this study, Shari Gelber reports no conflicts related to this study, Ann H. Partridge (*pending*), and Olivia Pagani reports no conflicts related to this study.


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