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ORIGINAL ARTICLE

## Breast cancer and early retirement: Associations with disease characteristics, treatment, comorbidity, social position and participation in a six-day rehabilitation course in a register-based study in Denmark

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### Abstract

**Introduction.** The purpose of this register-based study was to identify factors related to disease, treatment, sociodemographics and comorbidity associated with taking early retirement among women treated for breast cancer, and to evaluate the risk for taking early retirement among breast cancer survivors who attended a six-day rehabilitation course. **Material and methods.** The study population consisted of 856 women who attended the rehabilitation course and a comparison group of 1 805 women who did not attend the course identified through the Danish Breast Cancer Cooperative Group. We obtained information on receipt of unemployment benefits, sickness benefits and early retirement pension for each of the years 1996–2007. Multivariate cox-regression models were used to analyze disease-specific, treatment-related, comorbidity and sociodemographics factors associated with early retirement after breast cancer and to evaluate the effect of attending a rehabilitation course on taking early retirement. **Results.** The rate of retirement was higher for women with somatic comorbidity (hazard ratio [HR], 1.91; 95% CI, 1.3; 2.9 for score 1, and HR 1.42; 95% CI, 0.7; 2.7 for score  $\geq 2$ ), previous depression (HR, 2.29; 95% CI, 1.7; 3.2) or having received sickness benefits in the year before their breast cancer diagnosis (HR, 3.75; 95% CI, 1.8; 7.8). Living with a partner was associated with a reduced hazard ratio for taking early retirement (HR, 0.70; 95% CI, 0.5–0.9). Having received chemotherapy, alone or in combination with anti-hormone treatment, reduced the hazard ratio (HR, 0.49; 95% CI, 0.3; 0.8 and HR, 0.5; 95% CI, 0.3; 0.8, respectively). The rate of retirement was higher for women the year after attending the rehabilitation course but returned to unity by three years. **Discussion.** The results of this study contribute to the identification of at-risk women and point to the need for tailored rehabilitation to avoid unnecessary marginalization of breast cancer survivors due to permanent labor market withdrawal.

For most people, work is the primary source of income and provides a social tie, meaning and independence. The World Health Organization has stated that many of the essential ingredients of life satisfaction, health and well-being are inherently interwoven with work and occupation [1]. As diagnostics improve, leading to earlier diagnosis of breast cancer, more women are part of the work force at the time of a breast cancer diagnosis. Many cancer patients face not only physical and psychosocial difficulties but also concern about their occupation, including having to take sick leave for treatment, potential job loss

and, as a consequence, decreased income. International studies have shown that a substantial proportion of women (13–33%) with breast cancer reduce their working hours or stop working altogether 4–6 years after a cancer diagnosis [2–4]. Relapse, comorbidity, older age, manual work, medium income, vocational education and sick leave in the year before diagnosis have all been found to increase the risk for taking early retirement and for unemployment [5–7]. In a social security system such as that of Denmark, where social benefits are provided by the State irrespective of socioeconomic position, leaving the labor

market on an early retirement pension (ERP) might be a good alternative for some cancer survivors, when deciding between the beneficial effects of not being confronted with work-related problems and the potential negative effects on self-esteem and social connections. Although most women might welcome a temporary reduction in working hours, a permanent reduction might lead to loss of income, social connections and self-esteem. The resulting psychological distress can reduce the quality of life [8].

Little research has been conducted on the effect of rehabilitation programmes on returning to work. A systematic review of interventions targeted at returning to work after breast cancer identified only four studies, one with controls ( $n=150$ ) and three without ( $n=50-800$ ), three of which were published before 1990 [9], indicating that studies are needed of the effect of rehabilitation on labor market affiliations in the context of modern breast cancer treatment.

The aim of this registry-based, retrospective cohort study was to identify cancer-specific, treatment and socioeconomic factors associated with taking early retirement among women treated for breast cancer, and also to evaluate the risk for early retirement among breast cancer survivors who attended a six-day rehabilitation course and in a matched control group of survivors who did not attend the course.

## Material and methods

Since 1 January 2001, people with cancer who have completed primary treatment and in need for rehabilitation have been offered a residential course at the Dallund Rehabilitation Centre, run by the Danish Cancer Society. The aim of the course is to strengthen individual physical, mental and social functioning after a cancer diagnosis. All participants are referred by a medical doctor. They have to have completed primary treatment, to need rehabilitation as evaluated by a physician, and be physically able to participate in the activities offered.

People with cancer at any site can be enrolled, but about 65% of the female participants are breast cancer survivors. The intervention has been described in detail by Høybye and colleagues [10]. Briefly, during the six-day course, the participants attend a combination of lectures and patient group work on themes such as treatment of cancer, psychological reactions, spirituality, effects on working life, sexuality, health behavior and participate in physical activities. We included only survivors of female breast cancer in the present study.

### *Study population and information on breast cancer*

All residents of Denmark have a unique personal identification number, which is assigned by the

Central Population Register and is used in most medical and administrative records. This number enables accurate linkage of individual information between the many registers existing in Denmark. We identified our cohort from the Danish Breast Cancer Cooperative Group registry, which has registered breast cancer patients and conducted protocol-based randomized trials of surgery, radiation, chemotherapy and endocrine therapy in patients with primary invasive breast cancer since 1977. The registry contains information on approximately 95% of all Danish women below 75 years of age in whom breast cancer has been diagnosed [11]. We identified all women with breast cancer diagnosed between March 1996 and 2007 which included 95% of all women with breast cancer attending the rehabilitation course through 2007.

The study population consisted of all 1 377 women with a diagnosis of breast cancer who attended the six-day rehabilitation course at Dallund Rehabilitation Centre between 1 January 2002 and 31 December 2007 and a comparison group of women with breast cancer who had not attended the course. The comparison group was individually-matched on age, date of surgery and treatment protocol on a 2:1 basis ( $n=3\,434$  women). Date of breast cancer surgery, tumor characteristics, adjuvant treatment and date of relapse were obtained from the Danish Breast Cancer Cooperative Group. Information on death, emigration and disappearance was obtained by linkage to the Central Population Registry.

In Denmark, unemployment benefits are available only for people actively seeking a job and only for a limited period. During the study period this period has changed from four years in 1996 to  $2 \times 52$  weeks within a three year period, which is the current limit. If a person is unable to work due to disability or illness, he or she cannot receive unemployment benefits. A person can receive sickness benefits for a maximum of 52 weeks within a period of 18 months or retire permanently from the labor market. People on sickness benefits are assumed to be able to resume work after a recovery period, but, if the disability is so severe that it permanently reduces the ability to work by more than 50%, they may be granted an early retirement pension (Figure 1).

We excluded women who were not part of the workforce one year before their breast cancer diagnosis ( $n=931$ ), women who underwent primary surgery in 2004 or later ( $n=1\,121$ ) in order allow at least one year of follow-up for labor market affiliation after breast cancer surgery and women with unknown tumor size ( $n=98$ ). We based our main analyses on 2 661 women diagnosed from 1996 through 2003, comprising 856 women who attended the rehabilitation course and 1 805 women in the comparison

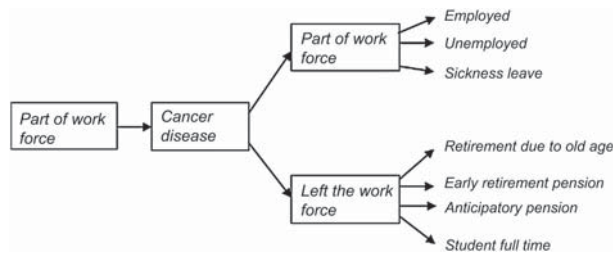


Figure 1. Pathway into or out of the workforce after a cancer disease under Danish legislation.

group. The women were followed up till 2007 with respect to early retirement.

#### *Socioeconomic variables*

Information on socioeconomic characteristics was obtained by data linkage to the population-based Integrated Database for Labor Market Research, administered by Statistics Denmark since 1980 and updated at the end of each year [12]. The core variables were derived by linkage to the Central Population Registry, to all companies with more than one employee, to the tax authorities, to the Registry for Education Statistics and to the Registry Relating to Unemployment. We obtained information at the individual level on attained education, affiliation to the labor market and civil status for each of the years 1996–2007. We also obtained information on receipt of unemployment benefits, sickness benefits and early retirement pension (ERP: no affiliation to a work place, not self-employed or assisting a spouse for people under 60 years of age and receipt of a public pension) for each of the years 1996–2007.

#### *Comorbidity and vital status*

From the Hospital Discharge Register, which holds information on all hospitalizations in Denmark since 1977, we obtained a full history of illnesses leading to hospitalization or an outpatient visit for each woman in the study. The Register is close to complete for all somatic hospital events [13] and includes the hospital and department number, dates of admission and discharge and diagnoses coded according to the International Classification of Disease (ICD), revision 8 or 10. Comorbidity was defined according to a modified version of the Charlson comorbidity index [14] for 19 selected diseases scored for severity on a scale from 1 to 6. Cancer diagnoses were extracted from the index and analyzed separately [15]. On the basis of the accumulated sum of scores, the comorbidity index was grouped into scores of 0, 1 and  $\geq 2$ .

#### *Use of antidepressant medication*

The National Prescription Drug Database is a research database coordinated by Statistics Denmark,

which holds information on prescription-based drugs dispensed from all pharmacies in Denmark between 1995 and 2007. The information includes the customers' personal identification number, type of drug prescribed according to the Anatomic Therapeutic Chemical (ATC) classification system and date of delivery from the pharmacy [16]. We obtained information on all prescriptions for antidepressants, classified as ATC group N06A [17], for 1995–2007. We defined previous depression as two or more prescriptions for antidepressants redeemed at least one year before the diagnosis of breast cancer.

#### *Statistical analysis*

Possible differences in baseline characteristics between the two groups were evaluated by  $\chi^2$ , Student t or log-rank tests. We used multivariate Cox regression models to analyze factors associated with early retirement after breast cancer surgery, using time since breast cancer diagnosis as the underlying time scale. All women were followed from the date of breast cancer surgery until early retirement, date of death, date of emigration or 1 January 2007, whichever came first. All models were stratified on age group ( $< 40$ , 40–50,  $> 50$  years), allowing for separate underlying intensities in the three age groups. The power of this study did not allow stratification into finer intervals.

The proportional hazards assumption was evaluated graphically on Kaplan Meier plots for each categorical covariate. For continuous variables, the assumption was tested with time-dependent variables. No variables were considered to violate the proportional hazards assumption. All continuous variables were entered linearly into the model. The linearity of associations was evaluated graphically with linear splines, the nine boundaries being placed at the percentiles. We found no departures from linearity [18]. All analyses were performed with SAS 9.1. As information on the outcome, early retirement was available only once a year, the Cox model was fitted with the 'exact' option.

The risk factors included in the model were disease-specific variables: size of tumor (linear), having tumor-positive axillary lymph nodes (yes/no), number of tumor-positive lymph nodes (linear), grade of malignancy (I–III and non-ductal), oestrogen receptor status (positive/negative) and menopausal status (pre/post); treatment-specific variables: type of surgery (mastectomy, lumpectomy, lumpectomy changed to mastectomy during surgery), radiation (yes/no), chemotherapy (yes/no) and anti-hormone therapy (yes/no); and socio-demographic factors: level of attained education (basic, vocational, higher), cohabitation status (living alone, cohabiting), number of children living at home (0/1,



2/3 or more), household income per person adjusted for number of persons in the household (linear), receipt of sickness benefit in the year prior to diagnosis (yes/no), previous depression (yes/no), and Charlson comorbidity index (score 0, 1,  $\geq 2$ ). Relapse and other malignancies were entered into the model as time-dependent covariates.

In the evaluation of the effect of the rehabilitation stay on taking early retirement, we restricted the analysis to women who attended Dallund Rehabilitation Centre between 1 January 2002 and 31 December 2005 to ensure at least two years of follow-up after rehabilitation, resulting in the exclusion of a further 21 women. We evaluated the association by entering the rehabilitation stay as a time-dependent variable in the fully adjusted model and stratified the analysis by time since breast cancer.

## Results

The 2 661 breast cancer survivors in this study were followed for a mean of 2.8 years (range, 0–7 years); overall, 231 (8.7%) women took early retirement during the follow-up period. The women attending the Rehabilitation Centre were more likely to have had positive axillary lymph nodes, a longer education but a lower income, and more lived alone. Mean time from diagnosis to attendance was 1.5 years (range 0–11 yrs). During the overall follow-up period, more women who attended rehabilitation had a diagnosis of another cancer and more took early retirement (Table I).

In the fully adjusted analyses somatic comorbidity (HR, 1.91; 95% CI, 1.3; 2.9 for score 1, and HR 1.42; 95% CI, 0.7; 2.7 for score  $\geq 2$ ) and previous depression (HR, 2.29; 95% CI, 1.7; 3.2) were associated with taking early retirement, as was receipt of sickness benefits in the year before breast cancer surgery (HR, 3.75; 95% CI, 1.8; 7.8) (Table II). Likewise, relapse or diagnosis of another cancer increased the hazard ratio for taking early retirement, although these effects were based on few events. The size of the tumor (HR, 1.04; 95% CI, 1.0; 1.1) and the number of positive lymph nodes (HR, 1.03; 95% CI, 1.0; 1.1) were also associated with increased hazard ratios, whereas higher level of education (HR, 0.56; 95% CI, 0.4; 1.0) and higher income (HR, 0.93; 95% CI, 0.9; 1.0) were associated with a decreased hazard ratio for taking early retirement, although these associations were all of borderline significance. Living with a partner was associated with a reduced hazard ratio of 0.7 (95% CI, 0.5; 0.9). Having received chemotherapy, either alone or in combination with anti-hormone treatment or radiotherapy also reduced the hazard ratio although not reaching significance for the latter combination (Table II).

In the model that included the effect of rehabilitation, the women who had attended the Dallund Rehabilitation Centre had an increased adjusted hazard ratio of 1.6 (95% CI, 1.1; 2.4) for taking early retirement in the year after the rehabilitation stay, but the ratio had returned to unity 1–2 years later (HR, 1.57; 95% CI, 1.0; 2.5) and  $\geq 2$  years later (HR, 1.31; 95% CI, 0.7; 2.5). The estimates changed very little for the other factors included in the model (data not shown).

## Discussion

In this study of breast cancer survivors, depression, somatic comorbidity and sick leave in the year before a diagnosis of breast cancer were associated with taking early retirement, as were indicators of disease severity and progression and the advent of another cancer. Further, there were indications that low social position increased the risk. Our findings support the results of previous studies in the Nordic countries [5,19–22], but ours is the first to evaluate the characteristics of cancers and labor market affiliation. By utilizing sociodemographics, general health and breast cancer-specific clinical information, we had a comprehensive picture of the factors of importance for permanent withdrawal from the labor market after a breast cancer.

While we found a protective effect of chemotherapy on early retirement, other studies of predictors of returning to work [23,24] or the duration of absence from work after breast cancer [25] found a negative effect; a study of unemployment after breast cancer found no significant effect of chemotherapy [7]. These disparities might be due in part to methodological differences, in the outcome or in control of confounding factors; alternatively, chemotherapy might be a marker of prolonged active treatment. Women receiving chemotherapy might not be evaluated for their ability to return to work before their treatment has ended, and they may be at another point in their disease trajectory. Although measures of the disease and its treatment to some extent reflect the same aspect, we saw an increased hazard ratio with increased disease severity (as represented by tumor size and positive lymph nodes) and a reduced hazard ratio for adjuvant treatment. Previous studies of the return of cancer survivors to the labor market are inconclusive with regard to the effect of chemotherapy, and our finding must thus be interpreted with caution.

Our study has a number of advantages, including access to virtually complete sociodemographic factors and extensive cancer and treatment characteristics and having a matched comparison group of women with breast cancer. Information on all the variables included in the analyses was obtained from nationwide

Table I. Descriptive characteristics at time of breast cancer diagnosis of 856 women who later attended rehabilitation and 1 805 frequency-matched comparison women, Denmark, 2002–2007.

Characteristic	Attended rehabilitation		Comparison group		p-value
	N	%	N	%	
Age at breast cancer diagnosis (years)					
< 40	108	13	211	12	
40–50	322	38	653	36	
> 50	426	50	941	52	
Age when attending rehabilitation (years)					
< 40	74	9	–		
40–50	295	34	–		
> 50	487	57	–		
Mean follow-up (years)	2.8	1.0–6.0	2.8	1.0–6.0	
(5–95% percentile)					
Tumor size (mm)					0.8
0–20	490	57	1 038	58	
21–50	331	39	685	38	
≥ 51	35	4	82	5	
Positive lymph nodes					0.02
0	345	40	846	47	
1–3	310	36	617	34	
4–9	124	14	201	11	
≥ 10	77	9	141	8	
Grade					0.5
I	157	18	361	20	
II	336	39	669	37	
III	219	26	458	25	
Non-ductal carcinoma	124	14	290	16	
Missing	20	2	27	1	
Receptor status					0.4
Negative	196	23	433	24	
Positive	647	76	1 355	75	
Missing	13	2	17	1	
Menopause status					0.4
Post	329	38	722	40	
Surgical method					0.04
Mastectomy	448	52	926	51	
Lumpectomy	376	44	840	47	
Lumpectomy changed to mastectomy during surgery	32	4	39	2	
Adjuvant treatment					0.5
Only surgery	61	7	144	8	
Only anti-hormone treatment	135	16	333	18	
Only chemotherapy	116	14	245	14	
Only radiotherapy	31	4	74	4	
Chemotherapy and anti-hormone	199	23	354	20	
Chemotherapy and radiotherapy	39	5	88	5	
Anti-hormone treatment and radiotherapy	33	4	67	4	
Chemotherapy, anti-hormone treatment and radiotherapy	38	4	85	5	
Unknown	204	24	415	23	
Education					< 0.0001
Basic	193	23	550	30	
Vocational	322	38	658	36	
Higher	339	40	580	32	
Missing	2	0	17	1	
Labor market affiliation at breast cancer diagnosis					
Employed	781	91	1 627	90	
Unemployed	72	8	164	9	
On sick leave <sup>c</sup>	3	0	14	1	

(Continued)

Table I. (Continued).

Characteristic	Attended rehabilitation		Comparison group		p-value
	N	%	N	%	
Income (Euros)					0.008
First quartile	18 134	18 467			
Median	22 841	23 694			
Third quartile	28 931	30 212			
Cohabitation status					0.001
Cohabiting	600	70	1 370	76	
Living alone	256	30	434	24	
Missing	0	0	1	0	
Number of children < 18 years living at home					0.06
0	541	63	1 195	66	
1–2	285	33	527	29	
≥ 3	30	4	82	5	
Charlson co-morbidity index <sup>b</sup> (score)					0.2
0	763	89	1 638	91	
1	61	7	111	6	
≥ 2	32	4	56	3	
Previous depression <sup>a</sup>					0.08
Yes	107	13	184	10	
Relapse during follow-up					Log rank p = 0.4
Yes	101	12	168	9	
Other malignancy					Log rank p = 0.001
Yes	16	2	10	1	
Alive on the 1 January 2007					Log rank p = 0.4
Yes	795	93	1 644	91	
Early retirement during follow-up					Log rank p = 0.003
Yes	96	11	135	7	

<sup>a</sup>Two or more issues of drugs with an Anatomic Therapeutic Chemical (ATC) code starting with N06A.

<sup>b</sup>This index provides an overall score for co-morbidity on the basis of a composite of values weighted by level of severity assigned to 19 selected conditions, scored from 1 to 6 [14]. We used a modified version containing no cancers [26]. Scores are summarized on the basis of information on hospitalization from 1978 onwards. Score 1: myocardial infarct, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes type 1 and diabetes type 2. Score 2: hemiplegia, moderate-to-severe renal disease, diabetes with end-organ damage type 1 or type 2. Score 3: moderate-to-severe liver disease. Score 6: AIDS.

<sup>c</sup>The variable “Sick leave year before breast cancer diagnosis” used in analyses as described in text and Table II.

population-based registers, thus reducing the risk for recall and information bias. The limitations of the study include the fact that the association between early retirement and other factors of interest, such as quality of life, could not be addressed in the dataset. As the study addressed a selected population of breast cancer survivors, the external validity may be limited, although the internal validity remains unaffected. Another limitation to the study is the lack of information on occupation and work related factors such as “physical workload”, which has been found associated with increased risk of retirement on disability pension [5].

The finding that rehabilitation increased the hazard ratio for early retirement may be due to what could be considered a “beneficial effect”. Thus, women attending the Rehabilitation Centre are in close contact with social workers during their stay, which could make them more aware of the possibility of being assessed for an early retirement pension

but at the same time also ensure relevant guidance to women still interested in and able to be a part of the labor market. Furthermore, interaction with other women at the Centre may influence their self-perception, and they might be encouraged to seek professional assistance for their problems, hence increasing the rate of early retirement. In evaluating these hypotheses, it is important to remember that the women attending the Dallund Rehabilitation Centre are a selected group who have been referred by their physician. Thus, the two groups of women might not have had the same view of taking early retirement when they entered the study, and the groups may have differed in characteristics that we did not measure. It could be hypothesized that the women attending the rehabilitation center are more often having difficulties in staying at work or finding a new job than those not attending, and this would result in the increased risk for early retirement. These hypotheses, in

Table II. Adjusted hazard ratios for early retirement for 2 661 women with breast cancer, Denmark, 2002–2007.

	Adjusted HR	95% CI
Tumor size: 10-mm increase	1.04	1.0–1.1
Lymph nodes		
Any positive	1	–
None positive	0.80	0.5–1.3
Per additional positive node	1.03	1.0–1.1
Grade		
I	1	–
II	1.43	0.7–2.3
III	1.67	0.8–2.7
Non-ductal carcinoma	1.01	0.5–1.7
Receptor status		
Negative	1	–
Positive	0.98	0.6–1.7
Menopause		
Pre	1	–
Post	0.96	0.6–2.0
Surgery		
Mastectomy	1	–
Lumpectomy	0.89	0.6–1.3
Lumpectomy changed to mastectomy during surgery	1.12	0.6–2.5
Adjuvant treatment		
Only surgery	1	–
Only anti-hormone treatment	0.76	0.5–1.3
Only chemotherapy	0.49	0.3–0.8
Only radiotherapy	1.02	0.5–1.9
Chemotherapy and anti-hormone	0.50	0.3–0.8
Chemotherapy and radiotherapy	0.62	0.3–2.0
Anti-hormone treatment and radiotherapy	0.70	0.4–3.0
Chemotherapy, anti-hormone treatment and radiotherapy	1.04	0.5–3.0
Education		
Basic	1	–
Vocational	0.70	0.5–1.1
Higher	0.56	0.4–1.0
Income (DKr) increased by 20 000	0.93	0.9–1.0
Cohabitation status		
Cohabiting	0.70	0.5–0.9
Number of children < 18 years living at home		
0	1	–
1–2	0.81	0.5–1.2
≥ 3	0.54	0.2–1.2
Charlson co-morbidity index score		
0	1	–
1	1.91	1.3–2.9
≥ 2	1.42	0.7–2.7
Depression before breast cancer diagnosis		
Yes	2.29	1.7–3.2
Sick leave year before breast cancer diagnosis <sup>a</sup>		
Yes	3.75	1.8–7.8
Relapse		
None	1	–
1 year after relapse	2.93	1.3–11.8
2 years after relapse	4.82	1.2–12.9
≥ 3 years after relapse	3.52	0.9–11.7
Other malignancy <sup>b</sup>		
No	1	–
Yes	8.68	3.3–22.4

All HRs mutually adjusted. Model includes: Tumor size, lymph nodes, grade, receptor status, menopause, surgery, adjuvant treatment, education, income, cohabiting status, number of children, Charlson comorbidity index, previous depression, sick leave year before breast cancer diagnosis, relapse and other malignancy.

<sup>a</sup>Based on few events in the year before breast cancer.

<sup>b</sup>Based on 26 events diagnosed after the breast cancer.



combination with the larger percentage of attendees who lived alone, could explain the apparent paradox that a stay at a rehabilitation center focused at helping people to overcome their cancer increased the rate of early retirement among attendees. If these hypotheses hold to be true it would seem plausible that the effect levels out after two years.

In conclusion, we found that comorbidity, both somatic and psychiatric, taking sick leave, relapse of breast cancer and having another primary cancer during follow-up were associated with an increased rate of early retirement whereas living with a partner and a higher educational level were associated with a decreased rate. The rate of early retirement was higher among the women who attended the Dallund Rehabilitation Centre but only in the years immediately after their stay. Our study indicates that both sociodemographic and general health factors are related to permanent withdrawal from the labor market after a breast cancer. The results presented here might help identify women at-risk and help focus future rehabilitation programs to their specific needs. This could in turn help both avoiding unnecessary marginalization of breast cancer survivors still able and willing to be part of the labor market, but also ensure relevant guidance for women who might not be able to uphold a job.

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