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Original article

Causes of sick leave, disability pension, and death following a breast cancer diagnosis in women of working age

Anna Plym [a, *], Anna L.V. Johansson [a, b], Hannah Bower [a], Margaretha Voss [c], Lars Holmberg [d, e], Irma Fredriksson [f, g], Mats Lambe [a, h]

[a] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
[b] Cancer Registry of Norway, Oslo, Norway
[c] Division of Insurance Medicine, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
[d] Translational Urology and Oncology Research, Division of Cancer Studies, King's College London, London, UK
[e] Department of Surgical Sciences, Uppsala University, Uppsala, Sweden
[f] Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden
[g] Department of Breast and Endocrine Surgery, Karolinska University Hospital, Stockholm, Sweden
[h] Regional Cancer Center, Uppsala University Hospital, Uppsala, Sweden

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ABSTRACT

Objectives: Women diagnosed with breast cancer during working age are at increased risk of permanent absence from work, but the underlying medical causes have rarely been studied. We examined the risk of cause-specific sick leave, disability pension, and the competing event death after a breast cancer diagnosis in a population-based cohort study.

Materials and methods: From the Breast Cancer Data Base Sweden, we identified 16,603 women diagnosed with stage I-III breast cancer between 2000 and 2012, and 63,773 control women. Using multistate modelling, we calculated probabilities and durations of sick leave, disability pension, and death by registered cause, together with cause-specific hazard ratios.

Results: Five years after diagnosis, causes other than cancer accounted for around half of all sick leave (3.5% out of 6.8% of women) and disability pension (1.4% out of 2.6%) in women with breast cancer. Compared with control women, women with breast cancer were at increased risk of sick leave and disability pension due to mental disorders (HR 1.24, 95% CI 1.15–1.33 and HR 1.54, 95% CI 1.29–1.85, respectively) and disability pension due to inflammatory diseases (HR 1.46, 95% CI 1.05–2.03). The risk of sick leave and disability pension due to cardiovascular disease was also elevated, although only statistically significant for disability pension in women diagnosed after 2005 (HR 2.24, 95% CI 1.22–4.13).

Conclusion: Follow-up, support, and rehabilitation programs for women diagnosed with breast cancer must address a wide range of psychological and physical conditions to limit the consequences on working life.

1. Introduction

A prolonged period of sick leave is common after a breast cancer diagnosis. During the first year after diagnosis, women with breast cancer spend on average 180 days on sick leave or disability pension, mainly because of intense treatments followed by a period of convalescence [1]. While around 70–80% of women with breast cancer are able to return to work within one year [2–4], they remain at an increased risk of both sick leave and disability pension for several years [1,5–7]. In a recent study, over 30% of all women with breast cancer had received disability pension within a ten-year period after diagnosis, compared with 14% in the background population [7]. The risk appears not only to be elevated in women with advanced stage disease, another study found that women with stage I breast cancer were at nearly doubled risk of disability pension compared with population controls [8].

Despite the increased risk of leaving the labor market prematurely after a breast cancer diagnosis, the underlying causes have rarely been studied. A few previous studies have reported that fatigue, lymphedema, and impaired arm/shoulder function negatively influence return to work, sick leave, and work ability

* Corresponding author. Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, PO Box 281, SE-171 77, Stockholm, Sweden.
E-mail address: anna.plym@ki.se (A. Plym).

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[6,9–13], but for other conditions data are sparse or results have been conflicting [14]. Only one earlier study has examined cause-specific sick leave and disability pension [1]. In that Swedish study, 42% of days on sick leave and 12% of days on disability pension in year five after diagnosis were attributed to breast cancer, without specification of the other causes.

In the present study, we assessed the risk of cause-specific sick leave, disability pension, and the competing event death following a breast cancer diagnosis in a population-based cohort of Swedish women, both in comparison with breast cancer-free control women and by tumor characteristics and treatment. We also examined the contribution of post-diagnostic intermediate events on the risk of cancer-specific disability pension. We hypothesized that elevated risks of prolonged sick leave and disability pension not only reflect disease progression, but also psychological and physical morbidity secondary to breast cancer diagnosis and treatment.

2. Material and methods

2.1. Study design and population

We performed a population-based register study using data available in the Breast Cancer Data Base Sweden (BCBaSe), a research database based on the Breast Cancer Quality Registers in Stockholm-Gotland, Uppsala-Örebro, and the Northern regions of Sweden. The quality registers include data on tumor characteristics and treatment for 99% of all women diagnosed with breast cancer and residing in the capture areas [15], which together include approximately 60% of the Swedish population. By means of individual-level record-linkage, the quality registers have been enriched with data on sick leave and disability pension from the MiDAS database held by the Swedish Social Insurance Agency, education and labor market participation from the Longitudinal Integration Database for Health Insurance and Labour Market Studies held by Statistics Sweden, cause of death from the Cause of Death Register and hospital visits from the Patient Register, both held by the National Board of Health and Welfare. BCBaSe also includes a randomly selected cohort of breast cancer-free control women, matched on year of birth and county of residence (1:5 ratio) as described previously [16].

We identified all women aged 30–64 years diagnosed with stage I-III breast cancer (UICC TNM classification, 7th edition) [17] between January 1, 2000 and December 31, 2012 and their controls, excluding women with receipt of disability benefits prior to diagnosis and women on sick leave one month prior to diagnosis. This resulted in a final study population of 16,603 women with breast cancer and 63,773 control women (Table 1). Follow-up started from the date of diagnosis and ended on death, emigration, reaching age 65, or end of follow-up (December 31, 2013), whichever came first.

2.2. Cause-specific sick leave and disability pension

The Swedish Social Insurance Agency grants sick leave compensation to individuals with an income from work or unemployment benefits if work capacity is reduced because of disease or injury, and disability pension to residents aged 30–64 years in case of permanently reduced work capacity. Since the employer usually reimburses day 2–14 of a sick leave spell, only sick leave >14 days were included. Based on the main diagnosis reported by the certifying physician according to the International Classifications of Diseases (ICD-9/ICD-10), we defined the outcomes of primary interest as sick leave and disability pension attributed to cancer, mental disorders (i.e. depression, anxiety and stress-related disorders), musculoskeletal disease, cardiovascular disease, inflammatory disease, fatigue, pain, or insomnia, and lymphedema-related diagnoses (Supplementary Table 1). The completeness of medical diagnoses was high; less than three percent of all records of granted disability pension lacked information on the main underlying diagnosis. The analysis of cause-specific sick leave was restricted to women diagnosed 2005 or later from when information on the diagnosis was available.

Table 1
Baseline characteristics of women with stage I-III breast cancer and breast cancer-free control women aged 64 years and below at diagnosis in the Breast Cancer Data Base Sweden.

Characteristic	Women with breast cancer	Breast cancer-free women
	N (%)	N (%)
Total	16,603 (100)	63,773 (100)
Age at diagnosis (years)		
Median (IQR)	53 (46–59)	52 (46–58)
Year of diagnosis[a]		
2000–2004	5860 (35)	22,028 (35)
2005–2009	6511 (39)	24,748 (39)
2010–2012	4232 (25)	16,997 (27)
Education		
Low (0–9 yr)	2148 (13)	8551 (13)
Middle (10–12 yr)	7156 (43)	28,656 (45)
High (>12 yr)	7185 (43)	25,693 (40)
Missing	114 (1)	873 (1)
Prior sick leave		
No	14,532 (88)	56,071 (88)
Yes	2071 (12)	7702 (12)
Prior hospitalization for one of the studied causes		
No	15,542 (94)	60,106 (94)
Yes	1061 (6)	3667 (6)
Pathologic TNM stage		
I	7932 (48)	
II	6525 (39)	
III	2146 (13)	
Tumor size (mm)		
<10	2586 (16)	
10–20	8473 (51)	
>20	5295 (32)	
Missing	249 (1)	
ER status		
Negative	2743 (17)	
Positive	13,016 (78)	
Missing	844 (5)	
Lymph node involvement		
N0	10,386 (63)	
N1	4501 (27)	
N2	1233 (7)	
N3	462 (3)	
Missing	21 (0)	
Surgery		
Breast-conserving	10,273 (62)	
Mastectomy	6085 (37)	
None/Missing	243 (1)	
Axillary surgery		
SNB only	4474 (27)	
ALND	11,178 (67)	
None/Missing	951 (6)	
Radiotherapy		
No	2825 (17)	
Yes	13,778 (83)	
Chemotherapy		
No	7900 (48)	
Yes	8703 (52)	
Endocrine treatment		
No	4478 (27)	
Yes	12,125 (73)	

Abbreviations: ALND, axillary lymph node dissection; ER, estrogen receptor; IQR, interquartile range; SNB, sentinel node biopsy.
[a] Index year for breast cancer-free women.

2.3. Cause-specific death

Information on cause of death was obtained from the Cause of

Death Register and was categorized into death from cancer, cardiovascular disease, inflammatory disease, or other causes.

2.4. Tumor and treatment characteristics

From the quality registers, we extracted information on tumor size, estrogen-receptor (ER) status, lymph node involvement, type of surgery, type of axillary surgery, radiotherapy, chemotherapy, and endocrine treatment.

2.5. Post-diagnostic intermediate events

Information on hospital care was obtained from the Patient Register, which has nationwide coverage of inpatient hospitalizations from 1987 and outpatient specialized care from 2001. We retrieved information on the first inpatient or outpatient hospital visit following the breast cancer diagnosis for the same set of conditions used for sick leave and disability pension, with the addition of metastatic disease and infectious diseases (Supplementary Table 1). Inpatient hospital visits before diagnosis were also recorded to enable adjustment for previous medical history.

2.6. Statistical analysis

We performed two separate analyses. In the first analysis, which was based on data from women diagnosed between 2005 and 2012 (Supplementary Table 2), we estimated probabilities, duration, and hazard ratios (HR) of sick leave using a multi-state Markov model including disability pension and death. The multi-state model had one working state, eight sick leave states (one state for each cause), eight disability pension states, and four death states (Supplemental Fig. 1). All women started in the working state. Using the non-parametric Aalen-Johansen estimator [18], cause-specific plots of the transition probabilities were generated. Due to few events, the multistate model was simplified by combining causes of sick leave, disability pension, and death, reducing the number of transitions (Supplemental Fig. 2). By fitting flexible parametric survival models to each transition [19], we predicted model-based probabilities of being in a state, as well as length of stay in the sick leave states for women with and without breast cancer.

In the second analysis, based on data on women diagnosed between 2000 and 2012 (Supplementary Table 3), we estimated cause-specific HR of disability pension associated with breast cancer, breast cancer treatment, and tumor characteristics using standard flexible parametric survival analysis, while censoring for death and the other causes of disability pension. We further examined the contribution of post-diagnostic intermediate events on disability pension attributed to cancer in women with breast cancer by including the first time point of the intermediate event as a time-varying covariate.

In both analyses, the baseline hazard was modelled with restricted cubic splines with 3 or 5 degrees of freedom (df) using time since diagnosis as the underlying time scale. Both proportional and non-proportional models were fitted, with 1 or 3 df for the time-varying effect of exposures. The estimated HR express the rate of sick leave or disability pension receipt in women with breast cancer compared with breast cancer-free women, or by treatment or tumor characteristics. The following covariates were adjusted for: age at diagnosis (categorized in five-year intervals or continuous time using splines), calendar year of diagnosis (2000–2003, 2004–2007, 2008–2012), highest level of education, region of residence, sick leave in the period 366–730 days prior to diagnosis and hospitalization for the medical condition of interest in the five years prior to diagnosis. In models estimating HR by treatment and tumor characteristics, tumor size, ER status, lymph node involvement, and treatment modality were also adjusted for. Models included either only tumor characteristics or both tumor characteristic and treatment modality.

Analyses were performed using R (version 3.4.1) and STATA (version 15.0/IC; Stata Corporation, College Station, TX). We considered p values of 0.05 or less to be statistically significant; all tests were two-sided.

3. Results

The proportion of women on sick leave, disability pension, and death by reported cause and time since diagnosis is presented in Fig. 1. At year five post-diagnosis, 15% of women with breast cancer were on all-cause sick leave, disability pension, or were deceased, compared with 5% among control women. Causes other than cancer accounted for around half of all sick leave (3.5% out of 6.8% of women) and disability pension (1.4% out of 2.6%) but only a few deaths (0.5% out of 5.6%) in women with breast cancer. In control women, diseases other than cancer was the recorded cause for nearly all sick leave (3.2% out of 3.5%) and disability pension (1.1% out of 1.1%), and around half of all deaths (0.3% out of 0.7%). During the five-year period following diagnosis, women with breast cancer spent on average 341 days on sick leave, of which the majority (281 days) were attributed to cancer, compared with a total sick-leave period of 56 days in control women (Table 2). In addition to sick leave due to cancer, women with breast cancer had an increased risk of sick leave due to mental disorders (HR 1.24, 95% CI 1.15–1.33) and other diseases (HR 1.63, 95% CI 1.56–1.70).

Women with breast cancer were also at increased risk of disability pension due to mental disorders (HR 1.54, 95% CI 1.29–1.85) and inflammatory diseases (HR 1.46, 95% CI 1.05–2.03) (Table 3). The risk of disability pension due to cardiovascular disease was also elevated, although only statistically significant in women diagnosed after 2005 (HR 2.24, 95% CI 1.22–4.13). In analyses stratified by stage of disease, women with stage III breast cancer had the highest risk of disability pension due to cancer, mental disorders, and cardiovascular disease. Several clinical factors were independently associated with a higher risk of disability pension attributed to cancer, including axillary lymph node dissection, chemotherapy, and mastectomy. Few factors were associated with disability pension attributed to the other causes under study, among them mastectomy which was associated with a higher risk of disability pension due to mental disorders.

When allowing for non-proportional hazards, we found that women with breast cancer eight years after diagnosis remained at a ten-fold increased risk of disability pension attributed to cancer (Fig. 2). While the risk of disability pension due to mental disorders was highest two years after diagnosis (HR 1.96, 95% CI 1.41–2.74), and declined to equal that of control women after eight years; the risk due to cardiovascular disease increased steadily over the whole follow-up period (HR 2.22, 95% CI 0.94–5.23 at year eight).

Since cancer was the most commonly recorded cause of disability pension, we further investigated the possible contribution of post-diagnostic intermediate events (Table 4). Metastatic disease was the strongest contributing factor, but mental disorders, fatigue, pain or insomnia, and infections were also significant contributors in models both excluding (Model 1) and including treatment and tumor characteristics (Models 2 and 3).

4. Discussion

In this large population-based cohort study, women with breast cancer were at increased risk of sick leave and disability pension because of a wide range of medical conditions. Disease progression

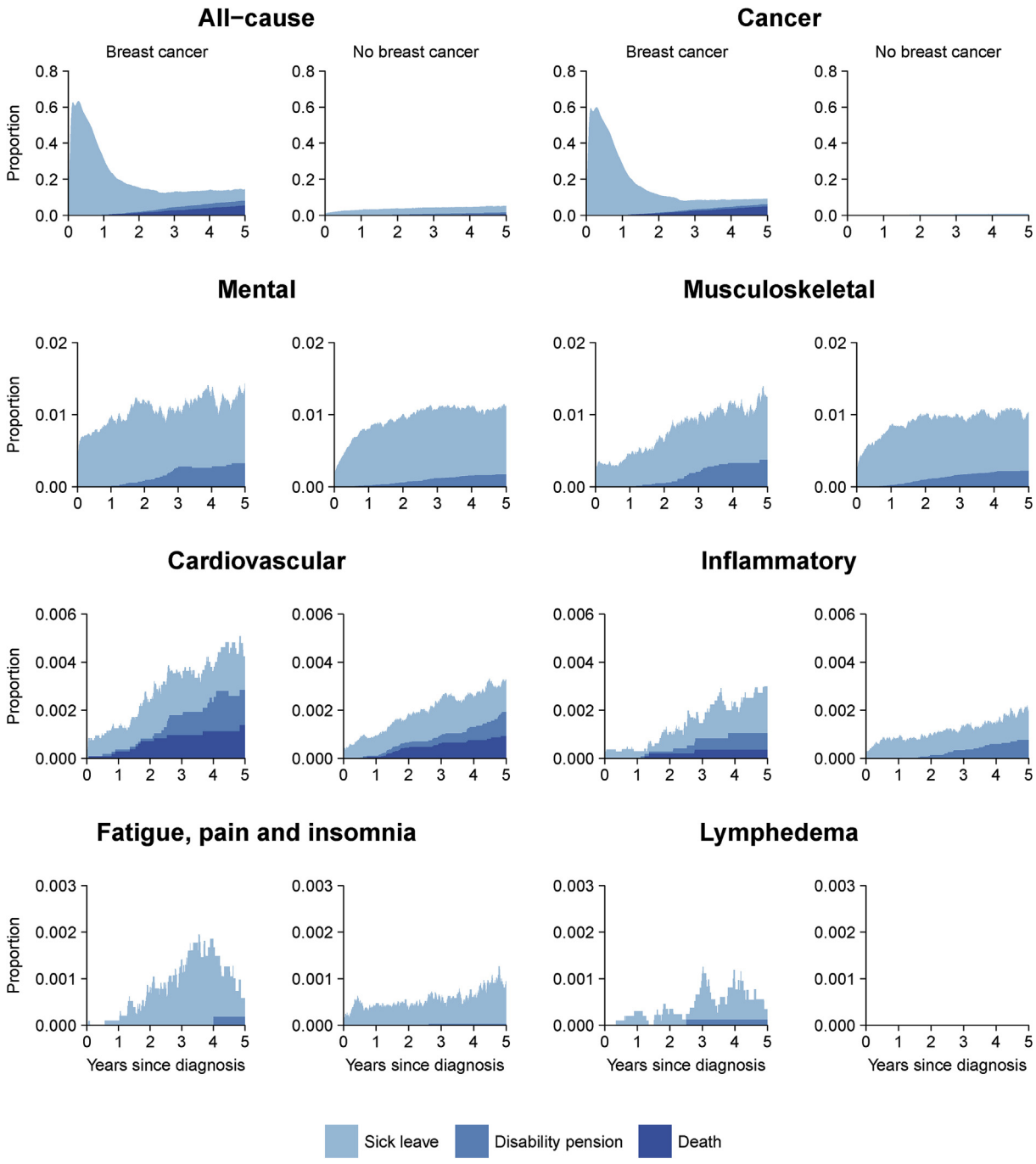

Fig. 1. Proportion of women on sick leave, disability pension, or death by reported cause and years since diagnosis. The figure includes women of working age diagnosed with breast cancer 2005–2012.

was a strong contributing factor, but also mental disorders, cardiovascular and inflammatory diseases, lymphedema, and fatigue and pain-related conditions were more commonly reported causes of sick leave and disability pension in women with breast cancer compared with control women. Women with stage III breast cancer generally had the highest risk of the studied causes of disability pension, but the risk of disability pension due to mental disorders and inflammatory disease was also increased in women with stage I disease. Although the absolute risk increase of sick leave and disability pension was small for causes other than cancer, the relative risk estimates indicate that breast cancer represents an important risk factor also for these less common causes.

Corroborating results of a previous study [1], we found that nearly half of all women on sick leave or disability pension at year five post-diagnosis were reported as absent from work because of cancer. Metastatic disease was the strongest, but not the only, contributing factor for cancer-specific disability pension, indicating that when cancer was assigned as a cause, a number of conditions directly or indirectly related to the cancer diagnosis could be involved. Whether or not coded as cancer, side effects of treatment have been suggested to increase the risk of absence from work in previous studies [5–8,20,21]. For example, Paalman et al. found that receipt of chemotherapy increased the risk of disability pension, also after controlling for new cancer events [7]. Axillary

Table 2
Length of stay with 95% confidence intervals in the sick leave states during the first five years after diagnosis and cause-specific hazard ratio of sick leave with 95% confidence intervals in women of working age diagnosed with breast cancer 2005–2012.

Cause	Women with breast cancer	Breast cancer-free women	
	Length of stay[a], days (95% CI)	Length of stay[a], days (95% CI)	HR (95% CI)[b]
All	341 (331–348)	56 (53–58)	
Cancer	281 (273–288)	4 (3–5)	97.3 (90.6–104.5)
Mental disorders	16 (14–18)	15 (14–17)	1.24 (1.15–1.33)
Musculoskeletal diseases	11 (10–13)	14 (13–15)	0.86 (0.80–0.93)
Cardiovascular diseases	3 (2–4)	2 (1–3)	1.21 (0.97–1.49)
Inflammatory diseases	2 (1–2)	2 (1–2)	0.80 (0.63–1.02)
Other diseases	26 (24–28)	18 (17–19)	1.63 (1.56–1.70)

[a] Estimates are controlled for matching factors (age and region) but otherwise unadjusted.
[b] Hazard ratio comparing women with breast cancer with breast cancer-free women (reference group), adjusted for age at diagnosis, calendar year of diagnosis, highest level of education, region, prior sick leave and prior hospitalization for the medical condition of interest.

Table 3
Cause-specific hazard ratios of disability pension with 95% confidence intervals in women of working age diagnosed with breast cancer 2000–2012.

Characteristic		Cancer	Mental disorders	Musculoskeletal diseases	Cardiovascular diseases	Inflammatory diseases
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Breast cancer	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	53.6 (40.6–70.7)	1.54 (1.29–1.85)	1.13 (0.95–1.34)	1.45 (0.98–2.15)	1.46 (1.05–2.03)
Breast cancer	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes, diagnosed 2000–2004	63.0 (45.6–87.2)	1.52 (1.25–1.85)	1.11 (0.92–1.34)	1.11 (0.66–1.86)	1.49 (1.04–2.14)
	Yes, diagnosed 2005–2012	29.8 (17.4–51.0)	1.74 (1.12–2.71)	1.30 (0.84–2.00)	2.24 (1.22–4.13)	1.29 (0.55–3.01)
Breast cancer	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes, stage I	27.1 (20.0–36.8)	1.58 (1.24–2.00)	1.07 (0.85–1.35)	1.09 (0.61–1.94)	1.83 (1.23–2.73)
	Yes, stage II	67.7 (50.8–90.3)	1.45 (1.10–1.90)	1.15 (0.89–1.48)	1.45 (0.82–2.59)	1.22 (0.72–2.08)
	Yes, stage III	117.6 (86.7–159.6)	1.72 (1.10–2.69)	1.32 (0.86–2.04)	3.17 (1.54–6.52)	0.55 (0.14–2.24)
Lymph node involvement	N0	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	N1	1.75 (1.38–2.20)	1.28 (0.76–2.13)	1.13 (0.70–1.82)	0.82 (0.31–2.19)	1.13 (0.45–2.87)
	N2+	2.05 (1.55–2.72)	1.71 (0.89–3.29)	1.40 (0.72–2.73)	1.30 (0.42–4.07)	0.51 (0.060–4.27)
Tumor size (mm)	<10	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	10–20	1.18 (0.87–1.61)	1.42 (0.80–2.54)	1.11 (0.66–1.88)	2.35 (0.52–10.6)	1.40 (0.53–3.73)
	>20	1.37 (0.99–1.90)	0.80 (0.41–1.55)	0.93 (0.51–1.70)	2.96 (0.61–14.3)	0.76 (0.22–2.57)
ER status	Positive	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Negative	1.09 (0.82–1.44)	1.28 (0.71–2.32)	1.54 (0.89–2.67)	0.84 (0.27–2.62)	1.21 (0.38–3.86)
Surgery	Breast-conserving	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Mastectomy	1.33 (1.09–1.61)	1.74 (1.11–2.72)	0.83 (0.52–1.32)	2.08 (0.89–4.86)	1.14 (0.46–2.84)
Axillary surgery	SNB only	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	ALND	1.79 (1.15–2.79)	0.81 (0.44–1.49)	3.15 (1.14–8.72)	1.81 (0.40–8.30)	1.24 (0.41–3.71)
Radiotherapy	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.38 (1.06–1.81)	1.24 (0.72–2.13)	1.01 (0.57–1.79)	1.16 (0.43–3.15)	0.45 (0.18–1.13)
Chemotherapy	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.33 (1.04–1.69)	0.80 (0.49–1.31)	0.79 (0.49–1.27)	1.29 (0.49–3.46)	0.48 (0.19–1.23)
Endocrine therapy	No	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	0.85 (0.66–1.11)	1.17 (0.69–1.99)	1.30 (0.82–2.08)	0.53 (0.20–1.38)	1.64 (0.64–4.22)

Abbreviations: ALND, axillary lymph node dissection; ER, estrogen receptor; SNB, sentinel node biopsy.
Hazard ratios were adjusted for age at diagnosis, calendar year of diagnosis, highest level of education, region, prior sick leave, and prior hospitalization for the medical condition of interest. Hazard ratios for tumor and treatment characteristics were also adjusted for each other. A model adjusted for only tumor characteristics is presented in Supplementary Table 4. The distribution of events over the various categories is presented in Supplementary Table 5.

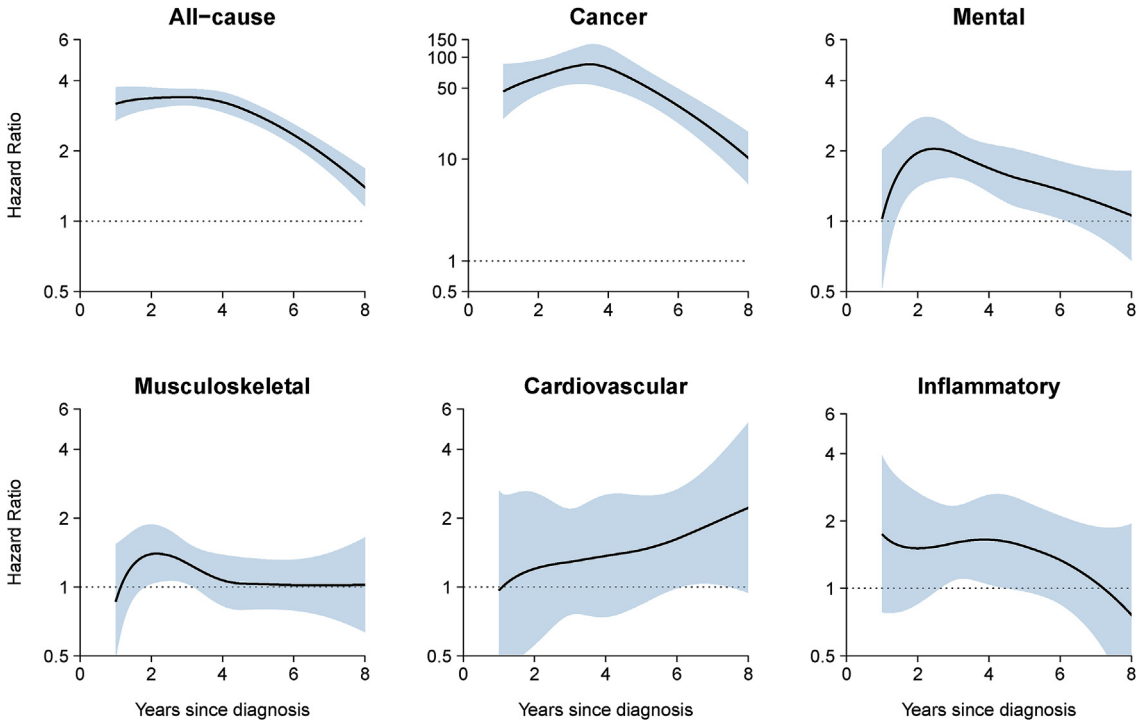

Fig. 2. Hazard ratio with 95% confidence intervals of being granted disability pension by time since diagnosis, comparing women with breast cancer (diagnosed 2000–2012) to breast cancer-free women (reference group). Hazard ratios were adjusted for age at diagnosis, calendar year of diagnosis, highest level of education, region, prior sick leave, and prior hospitalization for the medical condition of interest. Due to few events in the first year, hazard ratios are plotted from year one onward.

lymph node dissection, which increases the risk of lymphedema and pain, has also been associated with a higher risk of disability pension [7,21]. Other studies have reported that fatigue, a well-known side effect of cancer treatment, strongly affects ability to work [10,11,13,22]. In addition to side effects, our study provides further support to the notion that factors not directly related to cancer treatment, such as education and previous sick leave, also increases the risk of work-related outcomes after a breast cancer diagnosis [23].

To our knowledge, our study is the first to find evidence of an increased risk of sick leave and disability pension because of mental disorders in women with breast cancer. This is not surprising, given that earlier studies have reported increased rates of depression, anxiety, and stress-related disorders following a breast cancer diagnosis [24–28]. The risk of psychological problems has been reported to be highest in the first two years [26], which is likely to reflect immediate reactions to the cancer diagnosis. Our study provides evidence that women with breast cancer of all disease stages are at an increased risk of mental health problems affecting working life for several years after diagnosis.

Previous studies have found an increased risk of cardiovascular events in women with breast cancer [24,29–32]. We found that it was more common for women with breast cancer than for control women to leave the labor market because of cardiovascular disease. The cardiotoxic effects of certain breast cancer treatments are well-known; anthracycline-based chemotherapy, trastuzumab, and radiotherapy are associated with an increased risk of cardiovascular events [33]. Breast cancer and cardiovascular disease also share common risk factors such as tobacco use, physical inactivity, and diabetes, which may also explain the coincidence of the diseases [33].

We also observed an increased risk of disability pension due to inflammatory diseases. It has been suggested that treatment for breast cancer can induce autoimmune or inflammatory diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and psoriasis [34,35]. Rheumatoid symptoms of joint pain and joint swelling are common following breast cancer treatment, but do not necessarily involve systemic inflammation [36]. It cannot be excluded that the association may be the opposite; many chronic inflammatory diseases (and their treatments) are associated with increased cancer risks [37], although current literature point towards no increased risk of breast cancer in some of the most common inflammatory diseases [38,39].

The major strength of this study was the use of data from Swedish population-based registers with high completeness, minimizing selection and information bias. Through linkage between different registers we were able to study the underlying causes of absence from work, taking several important factors such as for example disease progression into account. Another important strength included the use of multi-state models, which captures the complexity of the data with multiple, closely related and possibly also recurrent outcomes. Our finding that treatment-related adverse events can cause permanent work loss in women with breast cancer is generalizable also to other countries with high female labor force participation rates, although the observed impact on working life might differ according to legislation and generosity of sickness benefits.

One limitation of the study was uncertainty of the precision of registered diagnoses. Sickness benefits are granted based on the assigned diagnoses, but coding practices may have varied by local routines, between certifying physicians, and calendar periods. Social insurance legislation has changed during the study period, which led to a more strict assessment of the entitlement for long-term sick leave and disability pension. It cannot be excluded that these changes also influenced which diagnoses were recorded and accepted on the medical certificate. Additionally, information on the diagnosis was only available for the start of a period with sick leave or disability pension; changes of the original diagnosis were

Table 4
Hazard ratio with 95% confidence intervals of being granted disability pension attributed to cancer in women of working age diagnosed with breast cancer 2000–2012.

		Model 1[a]	Model 2[b]	Model 3[c]
		HR (95% CI)	HR (95% CI)	HR (95% CI)
Post-diagnostic cancer metastasis	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	5.82 (4.50–7.51)	4.62 (3.48–6.13)	4.57 (3.43–6.08)
Post-diagnostic mental disorder	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.69 (1.21–2.36)	1.59 (1.10–2.30)	1.58 (1.09–2.28)
Post-diagnostic musculoskeletal disease	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.04 (0.84–1.28)	0.99 (0.79–1.25)	1.01 (0.81–1.27)
Post-diagnostic cardiovascular disease	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.39 (1.04–1.85)	1.28 (0.95–1.73)	1.23 (0.91–1.68)
Post-diagnostic inflammatory disease	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.09 (0.78–1.54)	1.03 (0.71–1.49)	1.01 (0.69–1.48)
Post-diagnostic fatigue, pain, or insomnia	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.67 (1.23–2.28)	1.57 (1.12–2.21)	1.57 (1.11–2.21)
Post-diagnostic lymphedema	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.11 (0.53–2.35)	1.16 (0.55–2.47)	1.11 (0.52–2.35)
Post-diagnostic infection	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.39 (1.13–1.71)	1.38 (1.11–1.72)	1.37 (1.10–1.70)
Age at diagnosis	<45	1 (Ref.)	1 (Ref.)	1 (Ref.)
	45–49	1.29 (1.00–1.67)	1.38 (1.04–1.82)	1.43 (1.08–1.89)
	50–54	1.23 (0.96–1.58)	1.37 (1.05–1.79)	1.42 (1.08–1.87)
	55–59	1.64 (1.29–2.07)	1.86 (1.44–2.40)	2.01 (1.55–2.61)
	60–64	1.84 (1.36–2.49)	2.10 (1.51–2.91)	2.11 (1.51–2.96)
Education	Low (0–9 yr)	1.38 (1.09–1.74)	1.53 (1.20–1.95)	1.53 (1.19–1.96)
	Middle (10–12 yr)	1.32 (1.11–1.57)	1.35 (1.12–1.63)	1.37 (1.14–1.66)
	High (>12 yr)	1 (Ref.)	1 (Ref.)	1 (Ref.)
Prior sick leave	No	1 (Ref.)	1 (Ref.)	1 (Ref.)
	Yes	1.55 (1.28–1.88)	1.60 (1.30–1.96)	1.60 (1.30–1.97)
Lymph node involvement	N0		1 (Ref.)	1 (Ref.)
	N1		2.29 (1.90–2.76)	1.63 (1.29–2.07)
	N2+		2.57 (2.02–3.27)	1.73 (1.30–2.31)
Tumor size	<10		1 (Ref.)	1 (Ref.)
	10–20		1.20 (0.88–1.62)	1.17 (0.85–1.61)
	>20		1.48 (1.08–2.03)	1.30 (0.93–1.82)
ER status	Positive		1 (Ref.)	1 (Ref.)
	Negative		1.28 (1.05–1.56)	1.10 (0.82–1.46)
Surgery	Breast-conserving			1 (Ref.)
	Mastectomy			1.28 (1.05–1.56)
Axillary surgery	SNB only			1 (Ref.)
	ALND			1.72 (1.08–2.74)
Radiotherapy	No			1 (Ref.)
	Yes			1.33 (1.01–1.75)
Chemotherapy	No			1 (Ref.)
	Yes			1.31 (1.03–1.67)
Endocrine therapy	No			1 (Ref.)
	Yes			0.90 (0.69–1.17)

Abbreviations: ALND, axillary lymph node dissection; ER, estrogen receptor; SNB, sentinel node biopsy.
[a] Model 1: Adjusted for age at diagnosis, calendar year of diagnosis, highest level of education, region, prior sick leave, prior hospitalization for cancer, and all of the post-diagnostic intermediate events (treated as time-varying covariates).
[b] Model 2: Adjusted for the same variables as in Model 1 and tumor characteristics.
[c] Model 3: Adjusted for the same variables as in Model 1 and tumor and treatment characteristics.

not recorded. It is likely that the influence on absence from work due to causes other than breast cancer has been underestimated since conditions secondary to breast cancer treatment could have been coded as "breast cancer" by the treating physician. We were able to partly address these limitations by using medical diagnoses from other registers. Furthermore, calendar time trends were accounted for by design, and estimates of relative risk are presumable not affected by policy changes over time. Another limitation is that we lacked information on work-related risk factors for sick leave and disability pension such as workplace demand and work environment.

5. Conclusion

In conclusion, we found that breast cancer has a significant impact on working life that is not only attributed to disease progression. Women with breast cancer were at increased risk of leaving the labor market because of mental health problems, fatigue and pain-related symptoms, lymphedema, cardiovascular, and inflammatory diseases. To limit the consequences of breast

cancer in women of working age, follow-up, support, and rehabilitation programs must therefore address a wide range of psychological and physical conditions.

Ethical approval

The study was approved by the Ethical Review Board in Stockholm, Sweden (Approval Number: 2013/1272-31/4).

Conflicts of interest

Mats Lambe owns Pfizer and AstraZeneca shares. All other authors declare no competing interests.

Previous presentation

Preliminary results were presented at the Association of Nordic Cancer Registries (ANCR) Symposium 2018 in Hella, Iceland June 12–14, 2018.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2019.02.012.

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Role of the funding source

The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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