

ORIGINAL ARTICLE

Sickness absence and disability pension among swedish women prior to breast cancer relapse with a special focus on the roles of treatment and comorbidity

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ABSTRACT

Objective: We aimed to determine the longitudinal prevalence and the predictors of sickness absence (SA) and disability pension (DP) in breast cancer (BC) women who eventually developed relapse.

Methods: A total of 1293 BC women, who were ages 20–63 years, diagnosed between 1996 and 2011 and by 2016 had all developed relapse, were identified in Swedish registers and were followed from two years before to five years after their primary diagnosis, while they were relapse-free. Annual prevalence of SA and DP was calculated. Logistic regression was used to estimate adjusted odds ratios (AOR) for long-term SA (>30 days) at one (y1) and three (y3) years post-diagnosis.

Results: Prevalence of long-term SA was 68.1% in y1 and 16.3% in y5. Prevalence of DP progressively increased from 16.3% in y1 to 29.0% in y5. Predictors of long-term SA included age <50 years (y1:AOR = 1.79 [1.39–2.29]), TNM stage III (y1:AOR = 1.54 [1.03–2.31]; y3:AOR = 2.21 [1.32–3.72]), metastasis (y1:AOR = 1.64 [1.26–2.12]; y3:AOR = 1.51 [1.05–2.18]), comorbidity (y1:AOR = 2.41 [1.55–3.76]; y3 AOR = 4.62 [2.49–8.57]) and any combination of radiotherapy, chemotherapy and hormonal therapy (y1:AOR = 2.05–5.71).

Conclusion: Among BC women who later developed relapse, those who had higher stages of BC, had comorbidity and received neoadjuvant and/or adjuvant therapy were at significantly higher risk of needing long-term SA after their diagnosis.

KEYWORDS

breast cancer, comorbidity, disability pension, sickness absence, treatment factors

1 | INTRODUCTION

Breast cancer (BC) is the most common form of cancer in females, with an annual global incidence of 2.1 million; of those affected, 1.4

million (68%) are of working age (<65 years) (Ferlay et al., 2019). In Sweden, the annual new case average between 2008 and 2019 was 8,500, of which 4,500 (53%) involved working-age women (Swedish Association of Local Authorities & Regions, 2020). The refinement

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of older treatments and introduction of new therapies have resulted in improved outcomes (Clarke et al., 2005; The Early Breast Cancer Trialists' Collaborative Group, 2018; Weitz et al., 2005). Despite this, between 20% and 30% of patients will develop loco-regional recurrence or distant metastases in the years following primary treatment (Cardoso et al., 2018; Patrick & Khan, 2015; Voinea et al., 2017).

During primary BC treatment, most patients in Sweden take advantage of sickness absence (SA) benefits. The reported rates of women with BC in Sweden returning to work within two years post-diagnosis have ranged from 60% to 80% (Bouknight et al., 2006; Hedayati et al., 2013; Johnsson et al., 2007, 2009; Kvillemo et al., 2017). However, compared to those without BC, women with BC have SA rates that remain higher for up to five years after their primary diagnosis, and they also have higher rates of receiving disability pension (DP) benefits during that time (Eaker et al., 2011; Hauglann et al., 2012; Torp et al., 2012).

It is not surprising that women with BC have higher post-diagnosis SA and DP rates than their healthy counterparts. Oncological treatments for BC may cause both acute and long-term side effects. Along with the morbidity of the disease itself, these side effects can impair the physiological and psychological wellness of patients, leading to limitations in their abilities to execute daily activities and participate in social events (Campbell et al., 2012; Shapiro, 2018; Zaidi et al., 2017). In addition, long-term sequelae associated with BC and its treatment, such as anxiety and depression, fatigue, chronic pain, cognitive impairment and peripheral neuropathy, are known to reduce physical, mental and emotional capacity (Bjerkeset et al., 2020; Colombino et al., 2020; De Iulius et al., 2015; Dumas et al., 2020; Hedayati et al., 2012; Landeiro et al., 2018; Lundh et al., 2014; Rivera et al., 2018; Wefel et al., 2014; Zomkowski et al., 2018). Deterioration in the sense of physical and emotional well-being, and limitations in the functional capacity of patients with BC, negatively affects their quality of life and ability to work (Zaidi et al., 2017).

Several studies looking at post-diagnosis SA and DP in large cohorts of patients in Sweden with various stages of primary BC have been published (Chen & Alexanderson, 2020; Kvillemo et al. 2017; Lundh et al., 2014). However, we are not aware of any studies that have evaluated patients with BC who at some point in the future experienced a relapse (i.e. loco-regional recurrence or metastasis), focusing specifically on their patterns of use of SP and DP during the interval between their BC diagnosis and their relapse. Because about one in four patients with primary BC do in fact experience a relapse, and these patients are more likely to suffer additional disease-related symptoms and treatment morbidity, a better understanding of the pattern of use of SA and DP in this population would be valuable.

In this study, we aimed to study the patterns over time of the prevalence of SA and DP in women in Sweden with primary BC who at some time later had a relapse, focusing on the period of time before they had their relapse. We restricted the study of each patient to the period of time that started two years before their primary diagnosis and ended no more than either five years after their primary diagnosis, or when they relapsed, whichever came first. We also aimed to estimate the impact of various demographic and clinical

risk factors on the likelihood that patients in this population would need long-term SA or any DP benefits.

2 | METHODS

This study complied with the Declaration of Helsinki and was approved by the regional ethics review board at Karolinska Institute (Dnr 2012/745-31). According to Swedish legislation, patients registered in national quality registers do not need to provide written informed consent; however, they are informed that their data will be included in registers and that they can opt-out at any time.

2.1 | Study population

This was a population-based prospective cohort study using data initially obtained from two Swedish registers: (i) the BC registry (RBC) for the Stockholm-Gotland healthcare region, which included data on patients who were diagnosed with primary BC from 1 January 1996 to 31 December 2007; and (ii) the National Quality Register for Breast Cancer (NKBC), which included data on patients from the Stockholm-Gotland region who were diagnosed with primary BC from 1 January 2008 to 31 December 2011. For the cohort obtained from these two registers, we then used the National Social Insurance Agency's Microdata for Analyses of Social Insurance (MiDAS) database to access SA and DP benefits data for the interval between 1 January 1994 (two years before any of the patients were diagnosed with BC) and 31 December 2016 (five years after any of the patients were diagnosed with BC).

Data linkage for patients was made possible by the unique national identification number assigned to each resident in Sweden at birth or when establishing permanent residency. We used the RBC and NKBC to obtain information about patient age, BC diagnosis date and tumour characteristics, type of treatment, follow-up (alive or deceased; relapsed or not) and date and type of relapse (loco-regional recurrence or metastasis). When compared to the Swedish Cancer Registry, to which it is obligatory to report all new cancer cases, the two registers that we used have been reported to capture 98% of women with BC in Sweden (Emilsson et al., 2015; Löfgren et al., 2019). We then used the MiDAS database to obtain information about whether SA and/or DP benefits were received, any time between 1994 and 2016, along with the dates those benefits were received and whether the benefits were full or partial.

2.2 | Study design

We included in the study all women in the RBC and NKBC databases from the Stockholm-Gotland healthcare region who were diagnosed with primary BC between 1 January 1996 and 31 December 2011 had TNM stages 0 to III, were between the ages of 20 years and 63 years at the time of their diagnosis and had complete SA and/or

DP benefit data available in the MiDAS database extending from two years before to five years after their primary BC diagnosis. Based on these criteria, 1,293 patients qualified for inclusion in the study.

The study patients were then followed for at least five years after their diagnosis or until 31 December 2016. All patients were included in the SP and DP calculations during the interval from two years before to the date of their primary BC diagnosis. Then, patients remained part of the SP and DP prevalence calculations and risk factor regression analyses as during the period that they were relapse-free, had not turned 65 years old and had not died.

2.3 | Demographic and clinical characteristics

For each patient, we recorded data about age at primary BC diagnosis, calendar year of diagnosis, type of neoadjuvant and/or adjuvant oncological treatment (e.g. radiotherapy, chemotherapy, hormonal therapy, unspecified treatment, no treatment and/or missing treatment data) and date and type of relapse (loco-regional or metastasis). We used any SA more than 30 days during the 12 months before primary BC diagnosis as a surrogate for patients having a comorbidity. The TNM classification system was used for tumour staging (Sobin et al., 2011), but if any T, N or M data were unavailable, tumour stage was designated as missing.

2.4 | Sickness absence (SA) and disability pension (DP) benefits

The Swedish Social Insurance Agency (SSIA) grants SA benefits to those 16 years or older who belong to the workforce and have reduced work capacity due to a disease or injury that is specified in a medical certificate (Swedish Ministry of Health & Social Affairs, 2010). The employer usually provides reimbursement for the first 14 days of SA; then, the SSIA provides reimbursement after that (Swedish Ministry of Health & Social Affairs, 2010). If an employee is unable to work after 14 days, the SSIA will grant an SA benefit consisting of full (100%) or partial (75%, 50%, or 25%) reimbursement of lost earnings. Those whose work capacity is considered permanently reduced by at least one-quarter are entitled to receive full (100%) or partial (75%, 50% or 25%) DP benefits.

2.5 | Outcomes

The two outcomes investigated were SA benefits and DP benefits. For each patient, we identified the benefits received at any point between two years before and five years after the primary BC diagnosis, up until 31 December 2016 or until they turned 65 years old, relapsed or died, if one of those occurred earlier. We calculated SA and DP net days by multiplying the level of benefit received (i.e. 25%, 50% or 100%) by the total number of SA or DP days. SA net days were then grouped into the following categories: 0, 1 to 30, 31 to 90,

91 to 180 and more than 180 net days. We defined post-diagnosis long-term SA as SA longer than 30 net days. DP net days were dichotomised as either 0 or more than 0, with the latter indicating a part-time or full-time disability.

2.6 | Statistical methods

Results for variables with skewed distributions are presented as medians with interquartile ranges (IQR). Annual SA and DP net day results from two years before diagnosis to five years after diagnosis were calculated and are presented as means with standard deviations. Annual prevalence of patients in each SA and DP net day category was calculated and is presented as frequencies and proportions.

During each of the five years of follow-up after the diagnosis of BC, patients were censored (i.e. removed from prevalence and risk calculations) if they: (i) turned 65 years old (because they transitioned into the old-age pension system), (ii) died or (iii) or were diagnosed with a relapse (because the aim of the study was to assess the prevalence of and risk factors for SA and/or DP during the period of time when patients were relapse-free). As a result, the population denominators used for these calculations steadily declined over the post-diagnosis years.

Univariable and multivariable logistic regression analyses were performed to estimate the crude odds ratio (OR), adjusted odds ratio (AOR) and 95% confidence interval (CI) of the primary outcome variable, for each demographic and clinical characteristic group. To perform these analyses, we dichotomised the SA net days as either up to 30 days or longer than 30 days, and we used SA longer than 30 net days, indicative of long-term SA, as the primary outcome variable. We did separate regression analyses for the first and third years post-diagnosis. For the adjusted models, age at BC diagnosis and SA net days during the year prior to BC diagnosis was included as continuous variables.

In the regression analysis for the outcome of long-term SA (longer than 30 net days) during the first year after the diagnosis of BC, age, TNM stage and SA net days during the year prior to diagnosis were adjusted for all other variables, except for type of relapse (which is already captured within TNM stage). Also, type of oncological treatment was only adjusted for age, because of power limitations. Finally, type of relapse was adjusted for all other variables, except for TNM stage (because of its similarity to type of relapse). All 1293 patients were available for the first-year regression analysis.

In the regression analysis for the outcome of long-term SA (longer than 30 net days) during the third year after the diagnosis of BC, patients were excluded if during the previous two years they turned 65 years old, died, experienced a relapse or received any DP benefits. This resulted in 618 patients being available for the third-year regression analysis. In this analysis, age was adjusted for all other variables, except for type of relapse. TNM stage was adjusted for age and SA net days during the year prior to diagnosis. Type of relapse was adjusted for all other variables, except for TNM stage. SA net days during the year prior to diagnosis were adjusted for age.

Finally, only crude ORs were presented for type of oncological treatment, because of power limitations.

Statistical significance was defined at the 5% ($p \leq 0.05$) level. The statistical analysis was performed using SPSS, version 25.

3 | RESULTS

The median age of all patients was 51 (IQR 43 to 57) years. By the end of the study (31 December 2011), of the original 1293 patients, 314 (24.3%) remained alive, under the age of 65 and relapse-free. By the end of follow-up (31 December 2016), all patients had relapsed: 577 (44.6%) with loco-regional recurrence and 716 (55.4%) with metastases. Median time between BC diagnosis and loco-regional recurrence was 2.5 (IQR 1.3 to 4.3) years, and between BC diagnosis and metastasis was 2.4 (IQR 1.3 to 4.1) years. Among all patients, 684 (52.9%) received chemotherapy, 797 (61.6%) received radiotherapy, and 556 (43.0%) received hormonal therapy as part of their treatments. In addition, 5 (0.4%) patients received an unspecified treatment by itself, 103 (8.0%) received no treatment, and 192 (14.8%) had missing treatment data. A summary of other demographic and clinical characteristics of the study population may be found in Table 1.

The annual prevalence rates of the patients in each SA and DP net day category are listed in Table 2. During the year before primary BC diagnosis, of all 1293 patients, 150 (11.6%) had over 30 days of SA, 61 (4.7%) had over 180 days of SA, and 198 (15.3%) had at least one day on DP.

During the first year after diagnosis, all 1293 patients remained in the analysis, 880 (68.1%) patients had SA over 30 days, and 640 (9.5%) patients had over 180 days of SA (Table 2 and Figure 1). Three years post-diagnosis, 618 patients remained in the analysis, and 214 (29.1%) had experienced SA over 30 days. Five years post-diagnosis, a total of 979 (75.8%) patients had been censored, because of either loco-regional recurrence ($n = 373$), metastasis ($n = 359$), turning 65 years old ($n = 71$) or death ($n = 176$).

Through the course of the five years post-diagnosis, the proportion of patients with more than 30 days of SA and more than 180 days of SA steadily decreased each year, eventually reaching 19.4% (61 of 314 patients) and 8.6% (27 of 314) patients, respectively, by the fifth year (Table 2). Conversely, from two years pre-diagnosis to five years post-diagnosis, the proportion of patients on DP for at least a day steadily increased each year, from 13.8% (179 of 1293) to 29.0% (91 of 314), respectively.

3.1 | Risk factors for long-term sickness absence (SA)

For the first year post-diagnosis, the risk of having long-term (more than 30 net days) SA was significantly higher for those patients 50 years old or younger compared to those over 50 years old (AOR = 1.79; 95% CI, 1.39–2.29); who were diagnosed with stage III

TABLE 1 Demographic and clinical characteristics of 1293 female patients with primary breast cancer (BC) who received sickness absence and/or disability pension benefits, 1 January 1996 to 31 December 2011, Stockholm-Gotland Region, Sweden

Characteristics	Patients n (%)
Total population ^a	1293 (100.0)
Age at primary BC diagnosis, years	
<50	602 (46.6)
≥50	691 (53.4)
Calendar year of primary BC diagnosis	
1996–2000	731 (56.6)
2001–2005	392 (30.3)
2006–2011	170 (13.1)
TNM BC stage	
Stage I	254 (19.7)
Stage II	373 (28.8)
Stage III	303 (23.4)
Missing TNM data	363 (28.1)
Type of neoadjuvant or adjuvant oncological treatment	
Radiotherapy only	90 (7.0)
Radiotherapy and chemotherapy	277 (21.4)
Radiotherapy and hormonal therapy	157 (12.1)
Radiotherapy, chemotherapy, and hormonal therapy	273 (21.1)
Chemotherapy only	70 (5.4)
Chemotherapy and hormonal therapy	64 (4.9)
Hormonal therapy only	62 (4.8)
Unspecified treatment	5 (0.4)
No treatment	103 (8.0)
Missing treatment data	192 (14.9)
Type of BC relapse	
Loco-regional recurrence	577 (44.6)
Metastasis	716 (55.4)
Sickness absence (SA) during year before BC diagnosis, net days ^b	
0	1016 (78.6)
1–30	127 (9.8)
>30	150 (11.6)
Disability pension (DP) during year before BC diagnosis, net days ^b	
0	1095 (84.7)
>0	198 (15.3)

^aPatients in population were all between ages of 20 years and 63 years at time of primary breast cancer diagnosis, and all eventually developed relapse by the end of follow-up, 31 December 2016.

^bNet days calculated by multiplying the level of benefit received (i.e. 25%, 50%, 75% or 100%) by the total number of SA or DP days the benefit was received.

BC compared to stage I (AOR = 1.54; 95% CI, 1.03–2.31); who eventually developed metastasis compared to loco-regional recurrence (AOR = 1.64; 95% CI, 1.26–2.12); and who had more than 30 days

TABLE 2 Net sickness absence (SA) and disability pension (DP) days received by female patients before and after diagnosis of primary breast cancer, 1 January 1996 to 31 December 2011, Stockholm-Gotland Region, Sweden.

	Net Days ^a n	Before Breast Cancer Diagnosis		After Breast Cancer Diagnosis				
		Year -2 n (%)	Year -1 n (%)	Year +1 n (%)	Year +2 ^b n (%)	Year +3 ^c n (%)	Year +4 ^d n (%)	Year +5 ^e n (%)
Population analysed ^f	-	1293 (100.0)	1293 (100.0)	1293 (100.0)	1098 (100.0)	735 (100.0)	491 (100.0)	314 (100.0)
Sickness absence (SA)	0	1035 (80.0)	1016 (78.6)	289 (22.4)	543 (49.5)	455 (61.9)	336 (68.4)	223 (71.0)
	1-30	110 (8.5)	127 (9.8)	124 (9.6)	114 (10.4)	66 (9.0)	38 (7.7)	30 (9.6)
	31-90	65 (5.0)	59 (4.6)	119 (9.2)	119 (10.8)	55 (7.5)	26 (5.3)	22 (7.0)
	91-180	34 (2.7)	30 (2.3)	121 (9.3)	107 (9.7)	54 (7.3)	28 (5.7)	12 (3.8)
	>180	49 (3.8)	61 (4.7)	640 (49.5)	215 (19.6)	105 (14.3)	63 (12.8)	27 (8.6)
Disability pension (DP)	0	1114 (86.2)	1095 (84.7)	1082 (83.7)	906 (82.5)	590 (80.3)	368 (74.9)	223 (71.0)
	> 0	179 (13.8)	198 (15.3)	211 (16.3)	192 (17.5)	145 (19.7)	123 (25.1)	91 (29.0)
Population censored ^f	-	0	0	0	195	363	244	177

^aNet days calculated by multiplying level of benefit received (i.e. 25%, 50%, 75% or 100%) by total number of SA or DP days benefit received.

^bTotal 195 patients censored from population, because 91 had loco-regional recurrence, 83 had metastases, 21 died in previous year.

^cTotal 363 patients censored from population, because 115 had loco-regional recurrence, 123 had metastases, 34 turned 65 years old, 91 died in previous year.

^dTotal 244 patients censored from population, because 93 had loco-regional recurrence, 93 had metastases, 16 turned 65 years old, 42 died in previous year.

^eTotal 177 patients censored from population, because 74 had loco-regional recurrence, 60 had metastases, 21 turned 65 years old, 22 died in previous year.

^fPopulation analysed net after excluding those censored; patients in population were between ages of 20 years and 63 years at time of primary breast cancer diagnosis, and all eventually developed relapse by the end of follow-up, 31 December 2016.

of SA compared to 30 days or less during the year prior to diagnosis (AOR = 2.41; 95% CI, 1.55–3.76) (Table 3). Also, the risk of having long-term SA was significantly higher for those treated with radiotherapy or hormonal therapy (AOR = 2.05; 95% CI, 1.23–3.41), radiotherapy combined with chemotherapy and/or hormonal therapy (AOR = 3.88; 95% CI, 2.53–5.94) and chemotherapy with/without hormonal therapy (AOR = 5.71; 95% CI, 3.19–10.23), all when compared to those having no additional adjuvant or neoadjuvant oncological treatment.

For the third year, the risk of having long-term SA was significantly higher for those patients who were diagnosed with stage II (AOR = 1.93; 95% CI, 1.20–3.11) or stage III BC (AOR = 2.21; 95% CI, 1.32–3.72) compared to stage I; whose relapse type was metastasis compared to loco-regional recurrence (AOR = 1.51; 95% CI, 1.05–2.18); and who had more than 30 days of SA compared to 30 days or less during the year prior to diagnosis (AOR = 4.62; 95% CI, 2.49–8.57) (Table 4).

4 | DISCUSSION

In a cohort of patients with primary BC stages I to III, who were evaluated when they were relapse-free, the prevalence of long-term SA (longer than 30 days) was 68.1% during the first year after

diagnosis, and then, it progressively declined until it reached 19.4% during the fifth year, never returning to the pre-diagnosis level of 11.6%. Throughout each of the first four years after diagnosis, the majority of patients with long-term SA actually received it for more than 180 days. In contrast to SA, the prevalence of DP increased over the duration of the study, so that by end of the study period 29% of the analysed patients were receiving a DP.

One year after the diagnosis of BC, the factors that were predictive of long-term SA were age younger than 50 years, high TNM stage (III), any neoadjuvant or adjuvant therapy, future metastasis and comorbidity (when defined as SA more than 30 days during the year prior to BC diagnosis). Three years after the diagnosis, the predictive factors of long-term SA were higher TNM stages (II and III), future metastasis and comorbidity. Because of power limitations, AOR could not be calculated for the impact of the various oncological treatments on long-term SA at three years post-diagnosis.

Some of our risk factor results were similar to those found in a recent Swedish register study of 3536 women, ages 19 to 64 years, who had primary BC diagnosed in 2010 (Chen & Alexanderson, 2020). The authors reported that BC stages II through IV and SA for more than 90 days during the two years before a BC diagnosis were the strongest predictors for SA and DP at one and three years post-diagnosis. However, their study differed from ours in that 39.3%

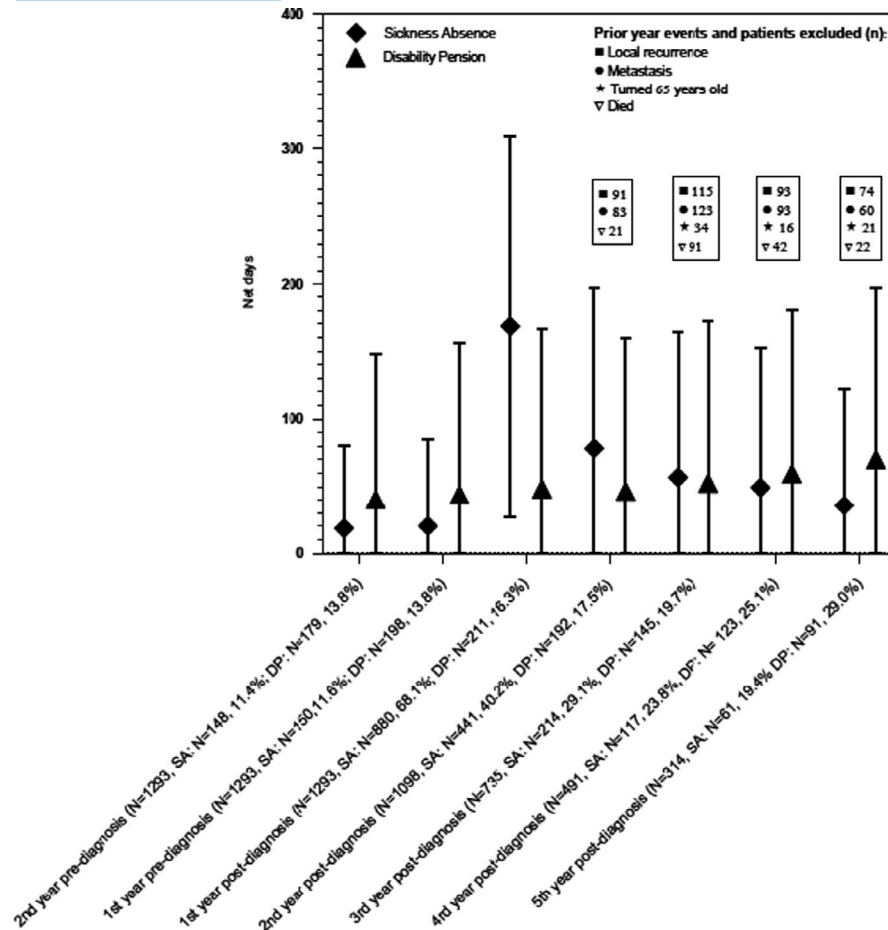


FIGURE 1 Sickness absence (SA) and disability pension (DP) net days among female patients with loco-regional recurrence or metastasis after diagnosis of primary breast cancer (BC), 1 January 1996 to 31 December 2011, Stockholm-Gotland Region, Sweden. Net days calculated by multiplying level of benefit received (i.e. 0%, 25%, 50% or 100%) by total number of SA or DP days benefit received. Annual net days of SA (diamond) and DP (triangle) from two years before diagnosis to five years after diagnosis presented in the line graph as means with standard deviations. Number of patients excluded from analysis per year (because of local recurrence or metastasis, death or turning 65 years old during previous year) shown in boxes. For each year, total number of patients analysed and proportion of patients with over 30 net days of SA and over one net day of DP in that year are shown in descriptions along x-axis.

of their patients had high-stage (II through IV) BC, whereas 52.3% of our patients had a high-stage (II and III) BC, not surprising given that all of our patients eventually developed a relapse. Also similar to our study, other studies have shown that women with comorbidities at the time of a primary BC diagnosis have a higher risk for needing long-term SA after their diagnosis, compared to those without comorbidities (Chen & Alexanderson, 2020; Lundh et al., 2014). We agree that when counselling patients with primary BC in Sweden, clinicians can use these findings to help those with comorbidities and higher stages of BC be aware that they are more likely to need long-term SA during and after treatment (Chen & Alexanderson, 2020).

Another recent Swedish registry study determined SA prevalence rates in 3547 women, ages 20 to 65 years, who had stages 0 through IV primary BC diagnosed in 2005 (Kvillemo et al., 2017). In their study cohort, the prevalence of long-term SA (longer than 30 days) was 61.2% during the first year post-diagnosis and 20.6% during the third year post-diagnosis, and it eventually returned five years post-diagnosis to 10.8%, which was the level seen before the

women were diagnosed with BC. However, once again, only 37.7% of the women in their study had a high disease stage (II through IV), compared to 52.3% of our patients who had a high stage (II and III). Given that our study consisted of a selected cohort with a higher proportion of patients with high-stage BC, it is not surprising that we found a higher prevalence of long-term SA (e.g. 68.1% at one year, 29.1% at three years and 19.4% at five years post-diagnosis) than they did. This might relate to the fact that patients with higher stages of BC are more likely to receive intensive oncological treatments, have treatment-related sequelae and experience psychological distress, when compared to patients with lower stages (Eaker et al., 2011; Kvillemo et al., 2017; Lundh et al., 2014). And, the differences between our study and theirs would probably have been even greater had not over half the women in our study been diagnosed with BC prior to 2001 and received less toxic polychemotherapy (cyclophosphamide, methotrexate and fluorouracil [CMF]) than the anthracycline- and taxane-based regimens that were used in later years (Anampa et al., 2015).

TABLE 3 Crude and adjusted odd ratios of long-term (more than 30 net days^a) sickness absence (SA), among 1293 total female patients during first year after primary breast cancer (BC) diagnosis, 1 January 1996 to 31 December 2011, Stockholm-Gotland Region, Sweden

Characteristics	On Sickness Absence/Total n/N (%)	Crude Odds Ratio ^b (95% CI)	p value	Adjusted Odds Ratio ^{b,c} (95% CI)	p value
Age at primary BC diagnosis, years					
<50	448/602 (74.4)	1.74 (1.37–2.22)	<0.01	1.79 (1.39–2.29)	<0.01
≥50	432/691 (62.5)	1		1	
TNM BC stage					
Stage I	175/254 (68.9)	1		1	
Stage II	263/373 (70.5)	1.08 (0.76–1.53)	0.67	0.96 (0.67–1.38)	0.82
Stage III	240/303 (79.2)	1.72 (1.17–2.53)	<0.01	1.54 (1.03–2.31)	0.04
Missing TNM data	202/363 (55.6)	0.57 (0.40–0.79)	<0.01	0.67 (0.43–1.04)	0.07
Type of neoadjuvant or adjuvant oncological treatment					
Radiotherapy or hormonal therapy	89/152 (58.6)	1.99 (1.20–3.29)	<0.01	2.05 (1.23–3.41)	<0.01
Radiotherapy with chemotherapy and/or hormonal therapy ^d	518/708 (73.2)	3.84 (2.52–5.85)	<0.01	3.88 (2.53–5.94)	<0.01
Chemotherapy with/without hormonal therapy ^e	109/135 (80.7)	5.91 (3.32–10.51)	<0.01	5.71 (3.19–10.23)	<0.01
No treatment ^f	44/106 (41.5)	1		1	
Missing treatment data	120/192 (62.5)	2.35 (1.45–3.81)	<0.01	2.23 (1.23–3.64)	<0.01
Type of BC relapse					
Loco-regional recurrence	348/577 (60.3)	1		1	
Metastasis	532/716 (74.3)	1.90 (1.50–2.41)	<0.01	1.64 (1.26–2.12)	<0.01
Sickness absence (SA) during year before BC diagnosis, net days ^a					
0–30	758/1143 (66.3)	1		1	
>30	122/150 (81.3)	2.21 (1.44–3.40)	<0.01	2.41 (1.55–3.76)	<0.01

Abbreviations: CI, Confidence Interval; TNM, tumour, nodes, metastasis.

Bold results statistically significant, with statistical significance defined at 5% ($p \leq 0.05$) level.

^aNet days calculated by multiplying level of benefit received (i.e. 25%, 50%, 75% or 100%) by total number of SA days benefit received.

^bIn regression analysis, SA net days during year before diagnosis and age treated as continuous variables.

^cAge, TNM stage, and SA net days during year before diagnosis adjusted for all other variables, except for type of relapse; type of oncological treatment adjusted for age; type of relapse adjusted for all other variables, except for TNM stage.

^dA single patient in this group received radiotherapy with an unspecified treatment.

^eA single patient in this group received chemotherapy with an unspecified treatment.

^fA total of 3 patients in this group had an unspecified treatment, and the other 103 patients had no treatment.

At least two previous studies have also confirmed our finding that the proportion of patients with long-term SA escalated dramatically during the first year after the BC diagnosis and that this proportion then steadily declined annually during the five years post-diagnosis (Bjerkeset et al., 2020; Kvillemo et al., 2017). However, unlike others, we found that the prevalence of long-term SA never did return to the pre-diagnosis level (Johnsson et al., 2007, 2009; Kvillemo et al., 2017). Once again, this is most likely the result of the intensive oncological treatments, treatment-related sequelae and psychological distress experienced by the large proportion of patients with high-stage BC in our cohort (Eaker et al., 2011; Kvillemo et al., 2017; Lundh et al., 2014).

We used a pre-diagnosis SA of more than 30 days in the year prior to the diagnosis of BC as a surrogate for comorbidity, and we

found that comorbidity was a significant predictor of long-term SA at both one and three years post-diagnosis. In Sweden, to certify that a patient is qualified to receive full or partial SA benefits, a clinician is required to complete a medical certificate that identifies one or more diagnoses (with ICD code) that may reduce the capacity for work (The Swedish Ministry of Health & Social Affairs, 2010). Consequently, SA is considered a reliable indicator of the presence of one or more significant comorbidities (Kivimaki et al., 2003; Marmot et al., 1995). Our findings fit with the current understanding of the role played by comorbidity in both the use of post-diagnosis SA and the delayed ability of patients to return to work after the diagnosis and treatment of BC. Indeed, multiple studies have shown that comorbidity, manifested as long-term pre-diagnosis SA, is predictive of long-term SA, reduced functional capacity and inability to return

TABLE 4 Crude and adjusted odd ratios of long-term (more than 30 net days^a) sickness absence (SA), among 618 total female patients^b during third year after primary breast cancer (BC) diagnosis, 1 January 1996 to 31 December 2011, Stockholm-Gotland, Sweden.

Characteristics	On Sickness Absence/Total n/N (%)	Crude Odds Ratio ^c (95% CI)	p value	Adjusted Odds Ratio ^{c,d} (95% CI)	p value
Age at primary BC diagnosis, years					
<50	105/311 (33.8)	1.16 (0.82–1.62)	0.40	1.13 (0.79–1.60)	0.50
≥50	94/307 (30.6)	1		1	
TNM BC stage					
Stage I	39/160 (24.4)	1		1	
Stage II	70/188 (37.2)	1.84 (1.15–2.94)	0.01	1.93 (1.20–3.11)	<0.01
Stage III	49/125 (39.2)	2.00 (1.20–3.33)	<0.01	2.21 (1.32–3.72)	<0.01
Missing TNM data	41/145 (28.3)	1.22 (0.73–2.04)	0.44	1.31 (0.78–2.20)	0.31
Type of neoadjuvant or adjuvant oncological treatment ^e					
Radiotherapy or hormonal therapy	21/83 (25.3)	1.16 (0.51–2.61)	0.72	-	
Radiotherapy with chemotherapy and/or hormonal therapy	121/360 (33.6)	1.73 (0.88–3.41)	0.11	-	
Chemotherapy with/without hormonal therapy	29/70 (41.4)	2.42 (1.09–5.38)	0.03	-	
No treatment	12/53 (22.6)	1		-	
Missing treatment data	16/52 (30.8)	1.52 (0.64–3.63)	0.35	-	
Type of BC relapse					
Loco-regional recurrence	77/299 (26.6)	1		1	
Metastasis	122/328 (37.2)	1.64 (1.16–2.31)	<0.01	1.51 (1.05–2.18)	0.03
Sickness absence (SA) during year before BC diagnosis, net days ^a					
0–30	167/569 (29.3)	1		1	
>30	32/49 (65.3)	4.53 (2.45–8.38)	<0.01	4.62 (2.49–8.57)	<0.01

Abbreviations: CI, Confidence Interval; TNM, tumour, nodes, metastasis.

Bold results statistically significant, with statistical significance defined at 5% ($p \leq 0.05$) level.

^aNet days calculated by multiplying level of benefit received (i.e. 25%, 50%, 75% or 100%) by total number of SA days benefit received.

^bPatients excluded from initial population of 1293 if during the previous two years they turned 65 years old (because they may have transitioned into old-age pension system); received disability pension (DP) benefits; experienced loco-regional recurrence or metastasis; or died. This resulted in 618 patients available for regression analysis.

^cIn regression analysis, SA net days during year before diagnosis and age treated as continuous variables.

^dAge adjusted for all other variables, except for type of relapse; TNM stage adjusted for age and SA net days during the year before diagnosis; type of relapse adjusted for all other variables, except for TNM stage. SA net days during year before diagnosis adjusted for age.

^eOnly crude odds ratios presented for type of oncological treatment, adjusted odds ratios could not be calculated because of power limitations.

to work after a primary BC diagnosis (Chen & Alexanderson, 2020; Kvillemo et al., 2017; Lundh et al., 2014). Furthermore, others have reported a strong association between comorbidity and long-term SA among patients in general (Kivimaki et al., 2003; Marmot et al., 1995). It has even been documented that clinician certification of a health condition severe enough to miss work can be a powerful predictor of mortality (Kivimaki et al., 2003; Marmot et al., 1995). Based on our findings and those of others, comorbidity certainly appears to be a barrier to a timely resumption of functional capacity and return to work after BC treatment has been completed.

Nevertheless, there are a number of other factors that may also be involved in determining the amount of SA taken by patients in Sweden, including low levels of education, not being born in Sweden, perception of work situation, level of motivation to return to work,

supportiveness of the workplace, BC tumour stage and types of BC treatment (Bouknight et al., 2006; Kvillemo et al., 2017; Johnsson et al., 2007; Johnsson et al., 2010; Nilsson et al., 2013; Torp et al., 2012). Interestingly, women's attitudes about returning to work and other work-related factors were reported in one study to explain up to half of all SA taken (Johnsson et al., 2007). These findings suggest that SA is a complex phenomenon and that it is influenced by a variety of factors, some of which were not included in the registers that we had access to.

In our study, we observed a small steady post-diagnosis increase in DP prevalence in our cohort. In the first post-diagnosis year, 16.3% of patients were on DP, and by the fifth year, 29.0% were on DP. Others have noted the same phenomena, though reporting that DP increased over the first four years post-diagnosis, and then

showed a slight decline down to 23.4% in year five (Kvillemo et al., 2017). We had also hoped to report on the impact of demographic and clinical risk factors on DP. However, the prevalence of DP in our cohort was too low to adequately power the statistical analysis of which factors were significant predictors of DP.

4.1 | Strengths and limitations

Our study results contribute to the existing body of knowledge about SA and DP for patients with primary BC in Sweden. Our findings add depth to the understanding of factors that influence SA after a diagnosis of primary BC. High female employment rates and complete coverage of SA and DP by insurance in Sweden, and the use of data from high-quality Swedish registers with minimal drop-outs make the internal validity of the study strong (Lundh et al., 2014; Sjövall et al., 2012). In addition, although the accuracy of the diagnoses used for SA and DP in Swedish registers has not been extensively investigated, one study has reported that the diagnoses used for SA were highly accurate when compared with the diagnoses listed in medical records (Ludvigsson et al., 2016). Another strength of this study is that when doing annual prevalence calculations, we censored patients who were no longer at risk for SA or DP as a result of death, turning 65 years of age or developing loco-regional recurrence or metastasis during follow-up. These strengths suggest that our findings can be generalised to women who have been diagnosed with loco-regional recurrence or metastasis after primary BC and who live in countries with comparable employment frequencies and SA and DP benefits.

Our study has some limitations. Despite the rigorous routines used by the SCR and NKBC to obtain data about patients in Sweden with BC, we found that almost 30% of the patients in our study lacked complete information about their BC TNM stages, confirming findings reported in a separate validation study (Löfgren et al., 2019). However, we found that those with missing TNM stage information in our study did not have increased odds of long-term SA during the first and third years post-diagnosis, so the absence of this information did not likely bias our results in that direction. Finally, although the use of pre-diagnosis SA of more than 30 days as a surrogate for comorbidity allowed us to identify this as a potential predictive factor for long-term SA in patients with BC and relapse, a study using specific comorbidity diagnoses will be necessary to confirm our findings and determine whether certain comorbidities are more predictive than others.

4.2 | Implications for research and practice

According to the Social Insurance Code in Sweden, patients must have an active disease, specified in a medical sickness certificate, in order to qualify for SA benefits (The Swedish Ministry of Health & Social Affairs, 2010). Although consultations for sickness certification are part of everyday clinical practice for oncologists,

well-established policies regarding collaboration with and referrals to other healthcare professionals involved in the sickness absence certification process are lacking (Bränström et al., 2014). Given our findings that comorbidity and high-stage BC increased the risk that women would need long-term SA after their diagnosis, a cohort of women who have both high-stage BC and comorbidities should be studied prospectively to validate our findings. In addition, an effort should be made to implement a structured process to improve the collaboration between general practitioners and oncologists during the follow-up of women with high-stage BC who have comorbidities and are of working age. These women should receive more intensive medical care and rehabilitation during and after completion of their cancer treatment. Furthermore, depending on local expertise and facilities, these patients should be referred to a social worker, nurse practitioner or other qualified healthcare professional to assist them with a smooth return to work after treatment for primary BC.

4.3 | Conclusions

Women with BC who later develop relapse appear to be a unique group. In particular, those with higher stages of BC, who had comorbidity or who received neoadjuvant and/or adjuvant therapy were at significantly higher risk of needing post-diagnosis long-term SA. In this group, the prevalence of long-term SA was highest during the first year post-diagnosis and steadily decreased over the next five years, but never returned to pre-diagnosis levels. These women should receive more intensive medical care during and after completion of their cancer treatment, to help address the adverse effects of treatment and to assist with a smooth return to work. Future studies using Swedish national registers to evaluate specific comorbidity diagnoses and criteria used to grant SA and DP would be beneficial.

5 | DATA AVAILABLE ON REQUEST DUE TO PRIVACY/ETHICAL RESTRICTIONS

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONFLICTS OF INTEREST

None.

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