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Title: Return to work and psychosocial trajectories after breast cancer: a longitudinal and sequential approach

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Abstract

Purpose

We aimed to describe the psychosocial adjustments according to return-to-work (RTW) trajectories in breast cancer survivors (BCS) using a sequential and temporal approach.

Methods

We used BCS data included from February 2015 to April 2016 in the Longitudinal Study on Behavioural, Economic and Sociological Changes after Cancer (ELCCA) cohort. RTW trajectories were identified using the sequence analysis method followed by a clustering. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale and the EORTC quality of life questionnaire was used at inclusion and all follow-up visits to assess Health-Related Quality of Life (HRQoL).

Results

Fifty-two BCS were included in the study among whom four clusters of RTW trajectories were identified and labelled: slow RTW (N=10), quick RTW (N=27), partial RTW (N=8) and part-time work (N=7). Quick and slow RTW clusters showed slightly lower baseline mean levels of anxiety and higher levels of HRQoL. In the 4 years following diagnosis, BCS in the quick RTW cluster tended to report higher HRQoL in terms of functioning and less symptoms of pain and fatigue while those in the partial RTW cluster showed a lower HRQoL on almost all dimensions. All clusters showed an increase in pain and fatigue symptoms until 6 months followed by a tendency to recover baseline levels.

Conclusions

The results of this study suggest that BCS who return to full-time work (slow and quick RTW patterns) recover better than patients who return to part-time work (partial and part-time RTW patterns).

Keywords : return-to-work, trajectories, Health-Related Quality of Life, breast cancer

Introduction

Breast cancer (BC) is the most commonly diagnosed cancer in women worldwide. In 2020, ~2.3 million women were newly diagnosed, representing 11.7% of all new cancer cases [1]. Advances in BC prevention, diagnosis and treatment [1], [2] have supported long-term cancer survival rates [3]. Approximately two-thirds of diagnosed women were of working age (1.5 million women between 20-64 years old). With an estimated 3 million new cases by 2040, mainly due to population growth and aging [4], the number of Breast Cancer Survivors (BCSs) in the working population is expected to increase in the coming years. A systematic review from 2014 [5] highlighted that the prevalence of Return-To-Work (RTW) in BCSs varies widely according to time since diagnosis and country (i.e., from 43% in the Netherlands to 93% in the USA within one year of diagnosis). Previous French studies showed that 79% and 82% of BCSs of working age were back at work between 2 to 5 years after their diagnosis, respectively [6], [7], [8].

Determinants to predict RTW after BC have been extensively studied in international literature and are currently well known [9], driving recommendations for clinical practice [10]. However, to date, it is mainly disease-related, work-related or sociodemographic variables [6], [7], [11]-[13] that have been studied in relation to the RTW, rather than psychological variables such as Health-Related Quality of Life (HRQoL; [11], depression or anxiety [15]) and RTW after BC. Results from the French CANTO cohort suggest that the probability of unemployment is higher in patients who report severe physical and psychological symptoms [6]. In this study, as in many others, the resumption of professional activities after a period of sick leave due to cancer is assessed as returning or not to work. It would be interesting to study the relationship between HRQoL over time by using a method that would take into consideration the complexity of RTW.

RTW has been described as a complex dynamic process having several phases [12], [13], [14], [15], [16]. First, a distinction is made between the three following main phases for cancer survivors [16]: «before RTW» (including cancer disclosure and the period of sick leave), «during RTW» (the actual RTW) and «after RTW» (maintenance at work). Moreover within these phases, RTW trajectories are not always linear. For instance, within the “during RTW” phase, BCSs may return part-time or full-time, or transition from part-time into full-time. To further describe the complexity of returning to work, some employees may decide after full-time that part-time suits their situation better. Differences in trajectories are well identified in the literature [17], and using a sequential method would be relevant to describe RTW as it would take into consideration its complexity. Second, BCSs can

experience ambivalent emotions regarding RTW [16], [18]. While RTW can be considered as a positive experience of returning to a “normal life” [5], individuals can simultaneously experience unpleasant emotions regarding their working capacities altered by the long-term side effects of treatment [19]. Some people might not want to RTW but find themselves in financial situations requiring them to work, as suggested by significant lower unemployment rates after cancer in countries which do not benefit from universal healthcare compared to countries which do [20]. Finally, it was reported that many BCSs reorder their priorities after a cancer diagnosis, thereby making work lower on their priority list [15], [21], [22]. Thus, changes in anxiety, depression and HRQoL may be different according to the RTW trajectory.

Therefore, the present study aims to 1) identify patterns of RTW trajectories after breast cancer diagnosis and 2) to describe changes in anxiety, depression and HRQoL according to the identified RTW trajectory patterns.

Methods

Study population

We used data from the Longitudinal Study on Behavioural, Economic and Sociological Changes after Cancer (ELCCA), a prospective cohort that aimed to explore non-medical consequences of cancer, including psychosocial and occupational aspects (ClinicalTrials.gov Identifier: NCT02893774) [23]. Patients were recruited by the clinical services of Department of Onco-Dermatology at Nantes University Hospital (for melanoma patients) and the Integrative Center for Oncology (ICO) in Nantes (France) for breast cancer patients. Patients were included in the ELCCA cohort if they had been diagnosed with breast cancer or melanoma with a tumor at stages I and II (early stage, non-metastatic), were 18 years or older and were residing in the Pays de la Loire region (France).

Our study focused on the 128 BCS included from February 2015 to April 2016 who received the occupational questionnaire at the follow-up conducted in 2019. Patients with BC recurrence, with other severe chronic or mental diseases, pregnant or breastfeeding women were excluded from the study.

The study was approved by an ethical research committee (Comité de Protection des Personnes), hosted by Nantes University hospital, and participants were informed about the study and invited to sign an informed consent agreement. Informed consent was obtained from all individual participants included in the study.

Measures

Sociodemographic and medical variables

Patients completed self-administered questionnaires (either distributed during patient visits to the hospital or sent out by post) within the month of their BC diagnosis, 6, 12, 24 and 48 months later.

The socio-demographic and medical information were collected at every visit. It included information on age, gender, marital status, education, occupation, income, treatment characteristics, type and stage of cancer.

Anxiety and depression measures

Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) Questionnaire at inclusion and all follow-up visits [24], [25]. Both anxiety and depression scores are the sum of the responses of the seven corresponding items coded from 0 to 3 and ranges from 0 to 21. A higher score represents a higher level of symptomatology.

QoL measures

The EORTC quality of life questionnaire (QLQ-C30 version 3.0 [26]) was used at inclusion and all follow-up visits to assess Health-Related Quality of Life (HRQoL). The QLQ-C30 is composed of five functional scales: physical, role, emotional, cognitive, and social functioning, and nine symptom scales: fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties using items with four-point Likert response scales (from 1: Not at all to 4: Very much). The global health status was assessed from two questions with seven-point Likert response scales (from 1: Very poor to 7: Excellent). All scale scores were computed following the EORTC QLQ-C30 scoring procedures [26]. They ranged from 0 to 100, so a higher score for a functional scale represents a higher level of functioning, whereas a higher score for a symptom scale represents a higher level of symptomatology or problems.

Identification and classification of RTW trajectories

RTW trajectories were assessed using a 6-month time scale self-administered occupational calendar from diagnosis up to 3 years later (T_0 : date of diagnosis, T_1 : 6 months after diagnosis, ..., T_6 : 36 months after diagnosis) delivered in February 2019 only in patients with BC included from 2015 to 2016. Patients had to notify whether they were either in one of the following five occupational situations or states: “full-time”, “part-time”, “sickness absence”, “unemployment”, “other reason for inactivity” every six months from their diagnosis

up to 3 years later. The sequence analysis method was then used to identify and then classify RTW trajectories within homogeneous groups (i.e. clusters) using three sequential steps. First, a sequence was generated for every BCS based on her individual occupational situation at each 6-month interval from her diagnosis (T_0) up to 3 years later (T_6). Then, each pair of BCS sequences (i.e. RTW trajectories) was compared for similarity using the optimal matching (OM) distance algorithm [27]. This algorithm generates a distance matrix that measures dissimilarity between each pair of BCS' sequences to determine whether they are close or far away from each other by attributing a cost of inserting/deleting or substituting elements in one sequence in order to transform it into another [28]. Lastly, an agglomerative hierarchical clustering employing Ward's linkage method and Euclidian distance was used to identify patterns of RTW trajectories (i.e., clusters) based on the distance matrix previously elaborated (Supplementary file Figure S1). The number of clusters was selected based on the highest relative loss of inertia and the average silhouette width (ASW) criterion [29]. The sequence analysis method was performed using the TraMineR package [28] for R (version 4.1.2).

Results

Characteristics of study population

Based on our inclusion criteria, the study population consisted of 52 BCS who participated at the follow-up in 2019 (response rate: 62.5%), who were working at the time of their diagnosis and that completed their occupational calendar post-diagnosis (Figure 1). Table 1 presents the characteristics of the study population. BCS mean age at diagnosis was 47.9 (SD = 6.7). Most were in a couple relationship (76.9 %) and had children. Fifty-two percent felt discomfort in their career development. Most of our study population was diagnosed with a stage II grade of BC (69.2 %). Seventy-five percent got a tumorectomy and 34.6% got a lymph node dissection. Half of them underwent chemotherapy, 78.8% radiotherapy and 90.4 % had followed a hormonal therapy.

[Insert Figure 1]

Figure 1: Flow-chart of study population's selection
BCS: Breast Cancer Survivors, RTW Return To Work

Table 1 Description of the study population (N=52)

	n	%	Mean (SD)
Age at diagnosis (SD)	49		47.9 (6.7)
<i>Missing</i>	3		
Marital status			
Married/couple relationship	40	76.9	
Single	10	19.2	
<i>Missing</i>	2	3.9	
Children in the household			
Yes	45	86.5	
No	5	9.6	
<i>Missing</i>	2	3.9	
Household income per month			
< 2 290 €	10	19.2	
≥ 2 290 € and < 3 090 €	13	25.0	
≥ 3 090 €	26	50.0	
<i>Missing</i>	3	5.8	
Discomfort in career's development after RTW			
No	22	42.3	
Yes	27	51.9	
<i>Missing</i>	3	5.8	
Presence of comorbidities at inclusion			
No comorbidity	27	51.9	
At least one comorbidity	29	55.8	
SBR grade			
1	11	21.2	
2	36	69.2	
3	5	9.6	
Surgery			

Mastectomy	8	15.4
Tumorectomy	39	75.0
No surgery performed	5	9.6
Lymph node dissection		
Yes	18	34.6
No	34	65.4
Chemotherapy (received or in progress)		
Yes	28	53.9
No	24	46.1
Radiotherapy (received or in progress)		
Yes	41	78.8
No	11	21.2
Hormone therapy (received or in progress)		
Yes	47	90.4
No	5	9.6

SD : standard deviance

Description of RTW trajectories

Four patterns (clusters) of RTW trajectories were identified (Figure 2 and Figure S1). The first cluster grouped mainly BCS with a long (minimum of 1 year) period of sick leaves (SL) that first returned to work part-time and then full-time (n=10, 19.2%). The second cluster included BCS with a short period of sick leaves followed by a full-time RTW (n=27, 51.9%). The third pattern included BCS that returned to work part-time after a long period of SL and were still working part-time three years after their diagnosis (n=8, 15.4%). Finally, the fourth pattern included BCS that were working part-time at their diagnosis and kept working part-time after without SL after their BC diagnosis or short period of SL (n=7, 13.5%). For the sake of brevity, clusters will be labelled as slow RTW (cluster 1, N=10), quick RTW (cluster 2, N=27), partial RTW (cluster 3, N=8) and part-time work (cluster 4, N=7).

[Insert Figure 2]

Figure 2: Index plots of RTW trajectories patterns (n=52);

T0 : diagnosis, T1: 6 months ,T2: 12 months, T3:18 months, T4: 24 months, T5: 30 months, T6: 36 months after diagnosis); RTW, Return To Work

Mental health scores (anxiety, depression, emotional functioning) according to RTW trajectories' patterns

The anxiety and depression observed mean scores from the HADS and the emotional functioning observed mean scores from the QLQ-C30 for the four clusters at the different follow-ups are presented in Figures 3a, 3b and 3c, respectively. Quick and slow RTW clusters showed a slightly lower baseline mean levels of anxiety and a decrease of anxiety mean scores up to 12 months after their diagnosis. Anxiety scores remained stable afterwards on average in these clusters. Similarly, emotional functioning mean scores showed an increase over the first year post-diagnosis and remained stable afterwards for the quick and slow RTW clusters. However, for the part-time work cluster, means scores of anxiety seemed to decrease until 6 months, then increase until 12 months, and to decrease again.

In the partial RTW cluster, anxiety and emotional functioning mean scores varied over time, quite markedly at the start of follow-up, then more slightly. As for the part-time work cluster, emotional functioning seemed to increase slowly over the 5-year period. Anxiety also tends to decrease slowly on the long-term after a decrease until 6 months and an increase until 12 months.

Depression scores were low on average and stable over time. Trajectories of depression scores were similar across clusters.

[Insert Figure 3]

Figure 3: a- Observed mean scores by RTW trajectory patterns and by time point: Anxiety dimension assessed from the HADS questionnaire (scale varies from 0 to 21); **b-** Observed mean scores by RTW trajectory patterns and by time point: Depression dimension assessed from the HADS questionnaire (scale varies from 0 to 21); **c-** Observed mean scores by RTW trajectory patterns and by time point: Emotional Functioning dimension assessed from the EORTC QLQ-C30 questionnaire (scale varies from 0 to 100); Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; HADS, Hospital Anxiety and Depression Scale; RTW, Return To Work

HRQoL scores according to RTW trajectories' patterns

The observed mean scores from the QLQ-C30 for the four clusters at the different follow-ups are presented in figure 4 for global health (GH), and physical (PF), social (SF) and role (RF) functioning and figure 5 for cognitive functioning, pain and fatigue. In the quick RTW cluster, BCS tended to show higher mean scores of functioning and lower mean scores of pain and fatigue indicating a higher HRQoL on all these dimensions. On the opposite, in the partial RTW cluster, BCS showed a lower HRQoL on almost all dimensions (Figure 4).

[Insert Figure 4]

Figure 4 Observed mean scores from the EORTC QLQ-C30 (scale varies from 0 to 100); by RTW trajectory patterns and by time point. Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. Global Health (a), Physical (b), social (c) and Role functioning (d) assessed using the EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; RTW, Return To Work

For the quick RTW cluster, GH, PF, SF and RF mean scores decreased between 1 and 6 months post-diagnosis, increased between 6 and 12 months and showed a recovery to baseline level later on. For the slow RTW cluster, the trajectories of HRQoL seemed to be similar and to display a higher deterioration at 6 months for SF and RF. Of note, the time for recovery to baseline seems to be longer for RF. BCS in the part-time and the slow RTW cluster seem to have similar trajectories of GH, PF and SF. On the other hand, for the part-time work cluster, the trajectory of RF observed mean score seems to differ from the others, it slowly decreased until 12 months and then tended to increase to the baseline level. In the long-term, in the partial RTW cluster, observed mean scores also show a decrease until 6 months followed by an increase until 12 months and a tendency to recover baseline levels for PF, RF and SF. Of note, the recovery seems to take more time for SF in this pattern compared with the others. Finally, in the partial RTW cluster, the GH scores were stable in the first year and tended to slightly increase afterwards.

The trajectories of the CF observed mean scores were different for the quick RTW and slow RTW clusters until 12 months, then were similar. A small increase was observed at 6 months followed by a small decrease for the quick RTW cluster whereas a higher increase was observed first followed by a decrease for the slow RTW

cluster. There was an overall tendency to recover baseline level for these clusters. BCS in the partial and the quick RTW cluster showed trajectories of CF with a higher improvement of HRQoL in the first 6 months (Figure 5). All clusters, except partial RTW, showed an increase in pain and fatigue symptoms until 6 months followed by a tendency to the recovery to baseline levels on the long term. The recovery tended to be faster for quick RTW, slow RTW and part-time work than for the partial RTW cluster (Figure 5).

[Insert Figure 5]

Figure 5 Observed mean scores for the cognitive functioning (a), pain (b) and fatigue (c) dimensions from the EORTC QLQ-C30 questionnaire (scale varies from 0 to 100); by RTW trajectory patterns and by time point.

Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. EORTC QLQ-C30, European Organisation for Research and Treatment of

Cancer Quality of Life Questionnaire C30; RTW, Return To Work

Discussion

The present descriptive study aimed to 1) describe patterns of RTW trajectories after breast cancer diagnosis and 2) depict changes in anxiety, depression and HRQoL over time according to the identified patterns of RTW. Four patterns of RTW trajectories were identified after BC from our sample, that we entitled “slow RTW”, “quick RTW”, “partial RTW” and “part-time RTW”. Finding several patterns is consistent with patients’ reported experience of RTW [30]. Some patients mentioned that they had stopped working temporarily (to recover from surgery or during treatment), while others worked throughout the treatment period. Some patients also indicated that they had not returned to work, either due long SL or unemployment. In addition, the RTW could be associated with changes in working hours or job type. There is a wide variety of patterns for returning to work, and the time between initial sick leave and sustainable RTW can vary from a few months to several years [31]

Whatever the cluster, BCS usually returned to work between 6 and 12 months after diagnosis, similar with data reported in French and European studies [32], [33], [34]. They seem to be returning to work when symptoms of pain and fatigue started to decrease and HRQoL –with the exception of cognitive functioning- started to increase. Cancer-related cognitive impairment is common among cancer patients, even among those who returned to work, and may persist many years after the completion of treatment [35], [36]. The majority of patients returned to work sustainably between 18 and 24 months after diagnosis. This may be because BCS patients in our study were diagnosed at stage I and II, which implies long-term cancer survival rates, so that RTW is possible [3]. For all the patients, depression scores were stable over time.

Returning to full-time work (quick and slow RTW)

Approximately half of the BCS included into the study experienced a full-time return-to-work, either after short or long period of sick leave (i.e., quick and slow RTW, respectively). At time of diagnosis, their anxiety seemed to be higher than four years later. A diagnosis of cancer can be perceived as traumatic, triggering a range of unpleasant emotions, such as fear, which can lead to anxiety [37] and associated intrusive thoughts. With time, patients can adjust to the situation and gain more control over their ruminations, so that intrusive thoughts are transformed into more deliberate ones [38].

Our results suggest an improvement in mental health. Consistent with studies suggesting that work has a positive influence on quality of life and is a “normalizing” factor for cancer patients [34], [42], anxiety of these patients continuously decreased over the first 12 months after BC diagnosis, differentiating them from the partial and

part-time RTW patterns. By returning to work, cancer patients try to restore the every-day life they had in their pre-cancer life, that is perceived as a healthy and normal existence [39]. Work gives structure to individuals and provides them with an identity and social relationships (Rasmussen & Elverdam, 2008). In the same vein, a commentary of [40] describes how the loss of the occupational identity can generate anxiety in cancer patients. Nevertheless, BCS still experienced physical symptoms four years after the diagnosis. Pain and fatigue, which are symptoms frequently reported by BCS after treatment [43] seemed to remain a bit higher at 48 months than at the time of diagnosis, suggesting long-term side effects of the cancer treatment. While distinct, it seems that patients who returned to full-time work, whatever their specific trajectory, i.e. slow or quick, reported a little less anxiety at time of diagnosis than patients from partial and part-time RTW patterns.

Partial RTW

BCS of the partial RTW pattern reported higher scores of depression at the time of diagnosis and higher anxiety at 48 months than the other three patterns. While the time of sick leave could vary widely among patients in this pattern, it is the one for which the cumulative duration of sick leave was the highest compared with the other three patterns. A study comparing mental health of non-working cancer patients and working cancer patients found that non-working patients reported higher levels of anxiety and depression than working patients over time [41]. It has also been suggested that cessation of work after breast cancer may be associated with worse HRQoL [17]. Moreover, it was the only pattern for which some patients reported being on sick leave four years after diagnosis. Consistent with these observations, their scores of role and social functioning, that are both dealing with the involvement in social life, were lower at all the study time-points than those reported by the patients of the three other patterns. In addition, patients of this pattern sometimes alternated work times and sick leave. Results from a qualitative study conducted with workers who partially returned to work while being on long-term sick leave due to common mental disorders suggest that a gap between solutions and their implementation in the workplace may explain the stagnation of the return-to-work process [42]. Some difficulties to perceive the work capacities might be also an explanation of alternation between work and sick leave, especially because these patients reported lower global health and higher symptoms (fatigue and pain) at time of diagnosis than patients from other patterns.

Part-time RTW

In this pattern, the majority of patients were working part-time at the time of diagnosis and maintained their part-time activity during cancer treatments. It is possible that these BCS found themselves in financial situations requiring them to work. But work could also have been experienced as a way of distracting themselves from illness or treatment and regaining a sense of normality. These arguments were underlined by breast cancer survivors in focus groups in which they talked about their experience of returning to work [43]. BCS could also have enjoyed their social environment at work [34]. The cumulative duration of sick leave in this pattern was lower than in the other three patterns. Four years after the diagnosis of BC, their global health score remained lower than those of BCS who returned to full-time work (quick and slow RTW) while their scores on the other dimensions of HRQoL (physical, social, fatigue and pain functioning) reached the same levels of those of BCS who returned to full-time work.

Strengths and weaknesses

This study has the strength of relying on a rarely investigated method to describe RTW trajectories and the longitudinal aspects of psychosocial factors using a temporal and sequential approach. Nevertheless, the sample size of this study is relatively small, which limits interpretation and allows only descriptive results to be drawn. The results must therefore be interpreted with caution. A study with a higher sample size would benefit from modelling changes of psychological variables with linear mixed models and would have facilitated the disentanglement of a greater variety of patterns in return-to-work trajectories.

There is also a possible bias of selection. We could not make any assumption regarding the relationship between the patterns and the position, as the time until RTW can change according to age, education, support from colleagues, treatments or the constraints of the job [33]. The absence of any information regarding the patients and their occupational position is also an important weakness of this study, since working cancer patients can experience more or less work specific cognitive symptoms according to their job [44] and it limits data interpretation. It is also important to note that the results are specific to French BC patients at stage I or II. Different patterns would probably have been observed whether the study would have been conducted in another country, since sick leave laws vary between countries.

Conclusion and perspectives

Half of the BCS who took part in this descriptive study reported a rapid return to full-time work. The results of this study suggest that BCS who returned to full-time work (slow and quick RTW patterns) recovered better than patients who returned to part-time work (partial and part-time RTW patterns). Further studies with a bigger sample using additional data, such as occupational ones, are needed to interpret work trajectories. Finally, combining quantitative and qualitative data collections would be beneficial to further describe the experience of BCS according to the patterns and especially focus on the emotions BCS experienced during RTW.

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Competing interests

The authors have no relevant financial or non-financial interests to disclose

Authors contributions

Elise Rubion contributed to the statistical analysis and was responsible for writing the draft for methods and results. Myriam Blanchin contributed to methodology (psychosocial indicators and their relative figures). Marianne Bourdon was responsible for writing introduction and discussion sections. Véronique Sébille contributed to the discussions and revised substantially the final draft. Mélanie Bertin contributed to conceptualization, methodology, investigation, and was responsible for supervision. All authors contributed to discussions on methodological aspects, reviewed and edited the final draft.

Ethics approval

The ELCCA cohort received ethical approval from the French national Data Protection authority. All participants gave informed consent to participate. The authors certify that the study was performed in accordance

with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

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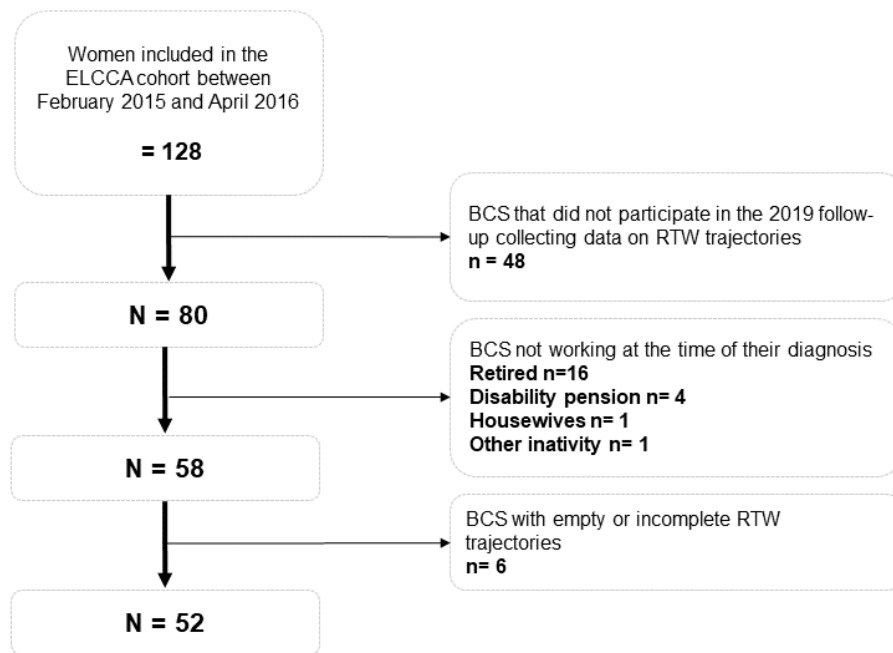


Figure 1: Flow-chart of study population’s selection
BCS: Breast Cancer Survivors, RTW Return To Work

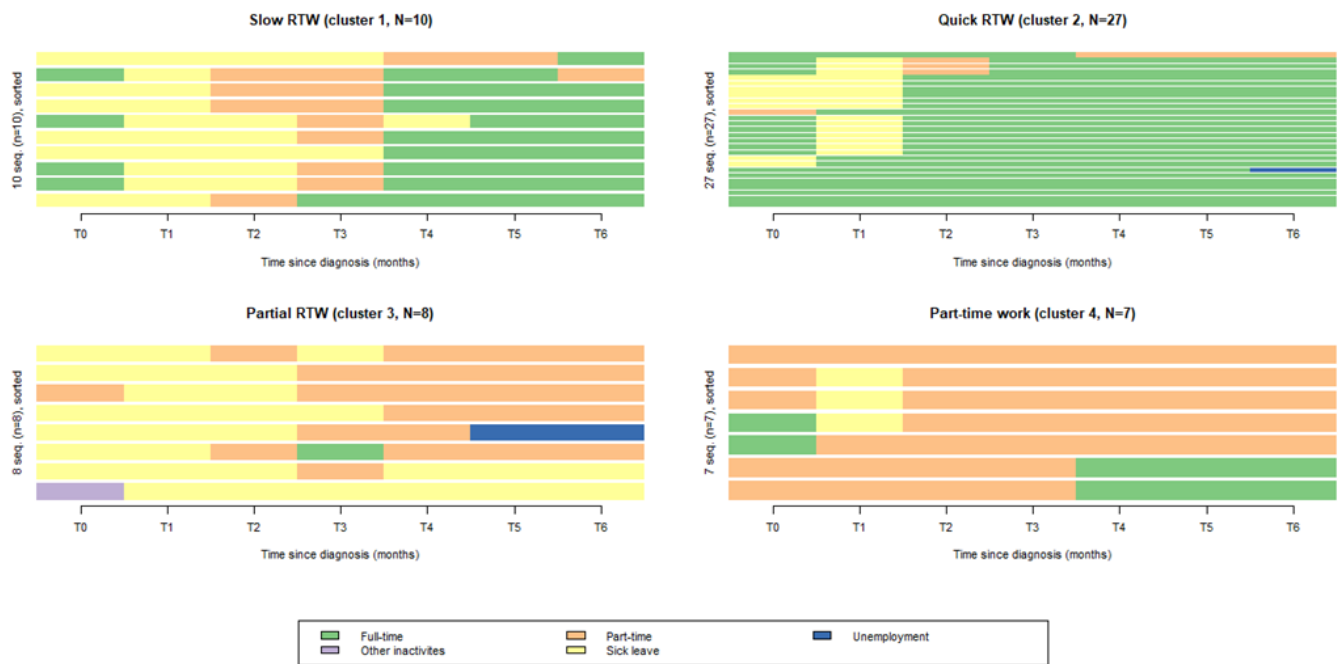


Figure 2: Index plots of RTW trajectories patterns (n=52);
T0 : diagnosis, T1: 6 months ,T2: 12 months, T3:18 months, T4: 24 months, T5: 30 months, T6: 36 months after diagnosis); RTW, Return To Work

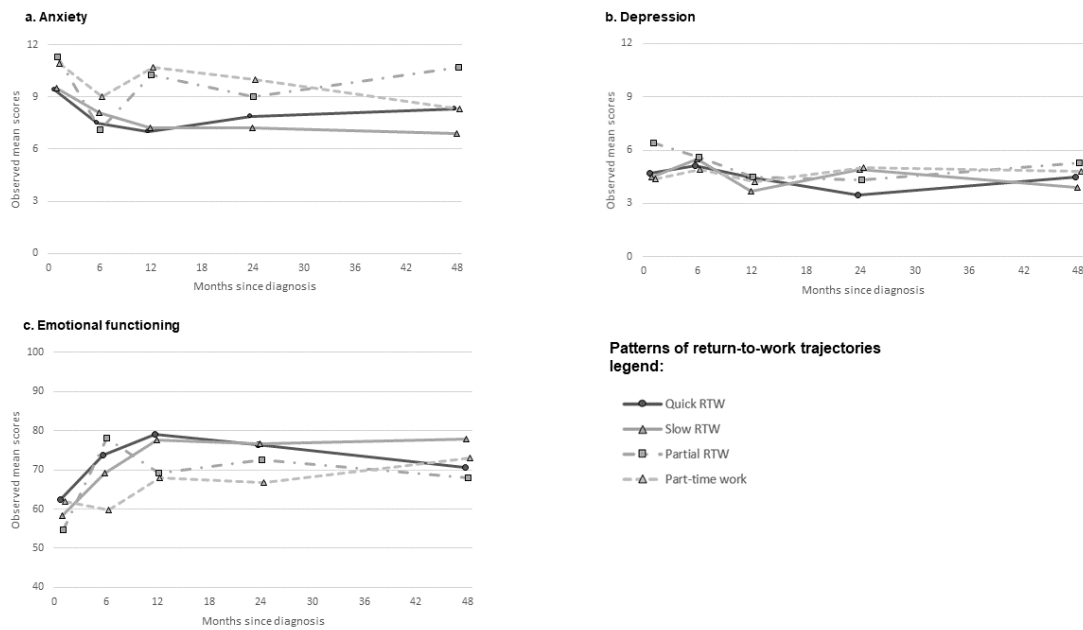


Figure 3: a- Observed mean scores by RTW trajectory patterns and by time point: Anxiety dimension assessed from the HADS questionnaire (scale varies from 0 to 21); b- Observed mean scores by RTW trajectory patterns and by time point: Depression dimension assessed from the HADS questionnaire (scale varies from 0 to 21); c- Observed mean scores by RTW trajectory patterns and by time point: Emotional Functioning dimension assessed from the EORTC QLQ-C30 questionnaire (scale varies from 0 to 100); Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; HADS, Hospital Anxiety and Depression Scale; RTW, Return To Work

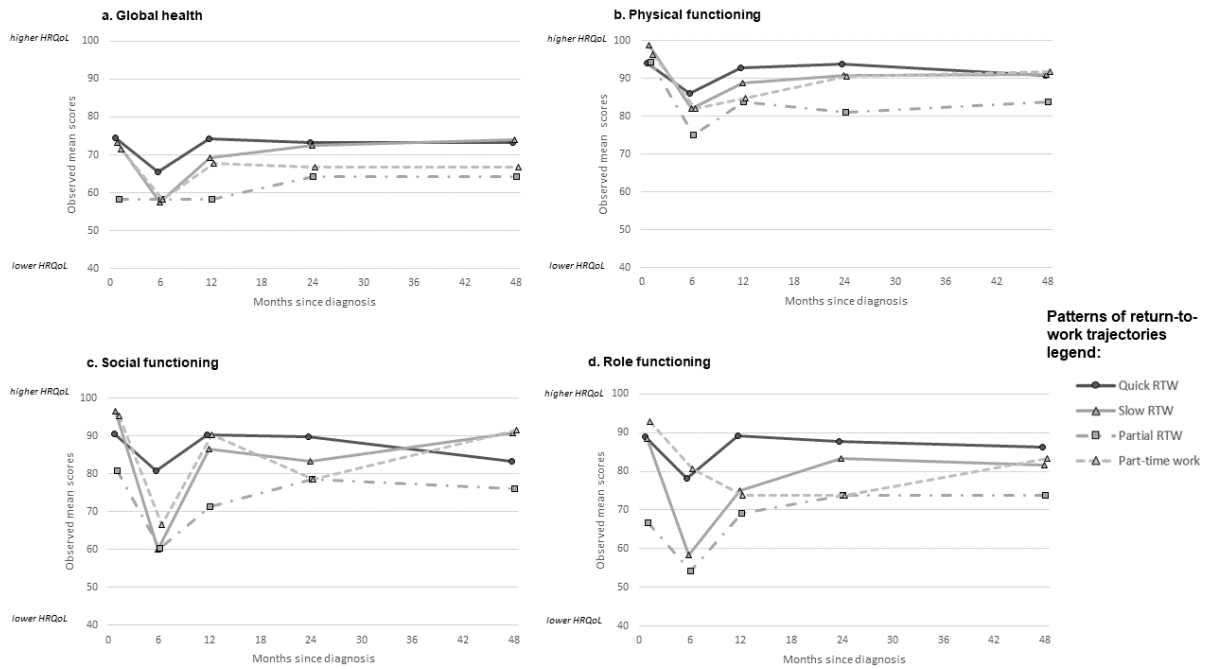


Figure 4 Observed mean scores from the EORTC QLQ-C30 (scale varies from 0 to 100); by RTW trajectory patterns and by time point. Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. Global Health (a), Physical (b), social (c) and Role functioning (d) assessed using the EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; RTW, Return To Work

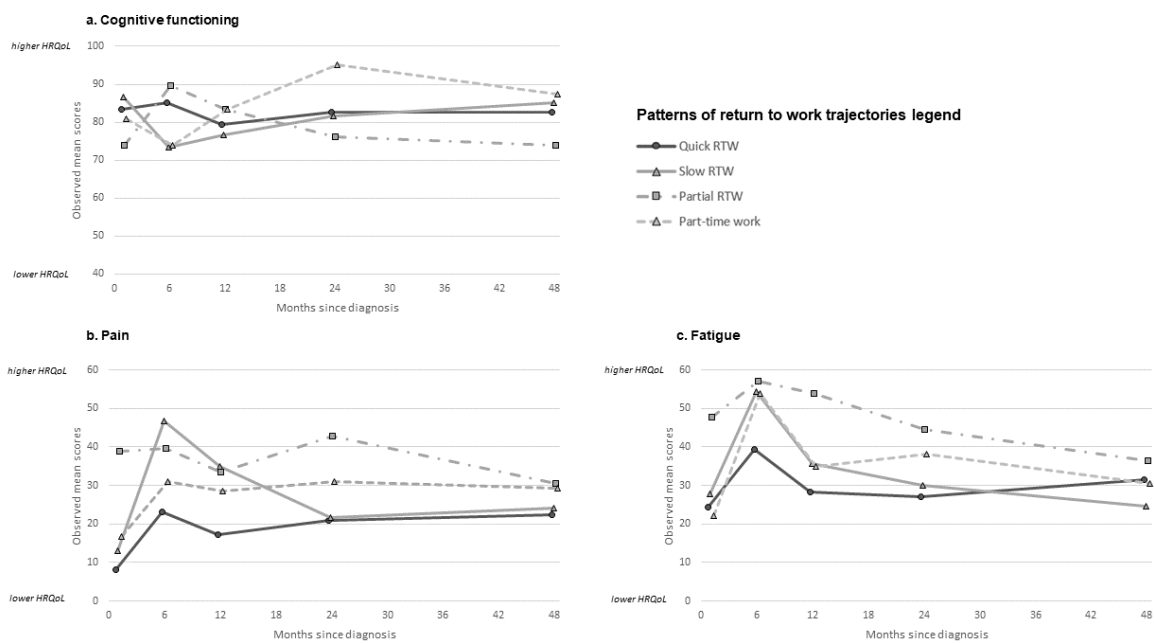


Figure 5 Observed mean scores for the cognitive functioning (a), pain (b) and fatigue (c) dimensions from the

EORTC QLQ-C30 questionnaire (scale varies from 0 to 100); by RTW trajectory patterns and by time point.

Higher scores indicate greater functionality and symptomatology. Respective 95% CIs for the means are available in the Supplementary file. EORTC QLQ-C30, European Organisation for Research and Treatment of

Cancer Quality of Life Questionnaire C30; RTW, Return To Work