BMJ Open

Determinants of maintenance at work of breast cancer patients: results from the OPTISOINS01 prospective study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020276
Article Type:	Research
Date Submitted by the Author:	29-Oct-2017
Complete List of Authors:	Arfi, Alexandra; Institut Curie, Surgery Baffert, Sandrine; CEMKA-EVAL, Health Economist Soilly, A-L; Universite de Bourgogne IUT Dijon-Auxerre, Health Economist huchon, cyrille; Hôpital Poissy, Gynecology Reyal, Fabien; Institut Curie, Surgery Asselain, Bernard; Institut Curie, Biostatistics Neffati, Souhir; Institut Curie, Clinical Research and Innovation Department Rouzier, Roman; Institut Curie, Surgery Hequet, Delphine; Institut Curie-Centre René Huguenin, Surgical oncology
Keywords:	Breast tumours < ONCOLOGY, OCCUPATIONAL & INDUSTRIAL MEDICINE, PUBLIC HEALTH

Determinants of maintenance at work of breast cancer patients: results from the OPTISOINS01 prospective study.

Authors:

Alexandra Arfi[1], Sandrine Baffert[2], Anne-Laure Soilly[3], Cyrille Huchon[4,5], Fabien Reyal[1,6], Bernard Asselain[7], Souhir Neffati[8], Roman Rouzier[1,9], Delphine Héquet[1,9]

Affiliations :

1: Department of Surgical Oncology, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

2: Health Economics, CEMKA-EVAL, Bourg-la-Reine, 43 boulevard du Maréchal-Joffre, 92340 Bourg-la-Reine, France

3: Health Economics, Bourgogne Franche-Comté University, EA 7467, 2 boulevard Gabriel, 21000 Dijon, France

4: Department of Obstetrics and Gynecology, Hôpital de Poissy-St Germain, 10 Rue du Champ Gaillard, 78300 Poissy, France

5: Equipe d'Accueil 7285, Risk and Safety in Clinical Medicine for Women and Perinatal Health, University Versailles-Saint-Quentin, 2 av de la source de la Bièvre, 78180 Montigny-le-Bretonneux, France

6: Residual Tumor and Response to Treatment Lab, Translational Research Department, Institut Curie, 75005, Paris, France

7: Department of Biostatistics, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

8: Clinical Research and Innovation Department, Sponsorship division, Institut Curie, 92210 Saint-Cloud, France

9: René-Huguenin hospital, Institut Curie, Inserm U900 – Bioinformatics, biostatistics, epidemiology and computational systems. Cancer biology, 35, rue Dailly, 92210 Saint-Cloud, France

Corresponding author:

Delphine HEQUET

Postal address: 35 rue Dailly, 92210 St Cloud, France

e-mai l: delphine.hequet@gmail.com

Phone number: 0033147111515

Word count: 2431

Contributorship statement:

Delphine Hequet, Roman Rouzier and Sandrine Baffert designed the study.

Bernard Asselain and Souhr Neffati contributed to the design and implementation of the research.

Sandrine Baffert and Anne-Laure Soilly performed the health economic analysis.

Alexandra Arfi and Delphine Hequet performed all the remaining statistical analysis and wrote the manuscript.

Cyrille Huchon and Fabien Reyal contributed to the clinical study, patients' inclusion and analysis of the results.

All the authors reviewed and approved the final version of the manuscript.

ABSTRACT

Introduction: Return to work (RTW) after breast cancer (BC) is still a new field of research. The factors determining maintenance at work of BC patients have not been clearly identified. The aim of this study was to describe work during BC management and to identify factors associated with maintenance at work.

Materials and methods: An observational, prospective, multicenter study was conducted among women with operable BC. A logbook was given to all working patients to record sociodemographic and work-related data over a one-year period.

Results: Work-related data after BC were available for 178 patients (60%). Sick leave was prescribed for 165 patients (92.7%) for a median of 155 days. On univariate analysis, invasive BC (p=0.025), lymph node involvement (p=0.005), radical surgery (p=0.025), axillary dissection (p=0.004), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the patient information booklet on RTW (p=0.047) were associated with a longer duration of sick leave. On multivariate analysis, chemotherapy was associated with longer sick leave (OR: 3.5; [95%CI: 1.6-7.9]; p=0.002). The cost of sick leave to French National Health Insurance was fourfold higher in the case of chemotherapy (p<0.001).

Conclusion: Advanced disease and chemotherapy are major factors that influence maintenance at work during the management of BC. Systematic screening can help to diagnose earlier disease and reduce the need for aggressive therapy.

Keywords: breast cancer, return to work, maintenance at work, absence duration, chemotherapy.

Article summary

- This study explored prospectively maintenance and return to work during 1 year follow-up after diagnosis of breast cancer.
- The analysis is multimodal, exploring the impact of cancer on professional activity, determinants of longer sick leaves and cost of sick leaves.
- The results highlight the need to develop patients' support to improve return to work and decrease sick leaves.
- The main factor of longer sick leaves is adjuvant chemotherapy.
- section consisting of the heading: 'Strengths and limitations of this study', and containing up to five bullet points that relate specifically to the study reported

Data sharing statement: No additional data available

Ethics: This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

Funding: This study was supported by a grant from the French National Cancer Institute, dedicated to economic studies of innovative techniques. Delphine Hequet benefitted from a "Fondation pour la Recherche Medicale" (FDM20140630453) grant to conduct this study.

What is already known on this subject?

Return to work after breast cancer is a delicate step in the real-life reintegration. Breast cancer patients have difficulties at work even 5 years after the end of the treatments. The factors that maintain patients at work during breast cancer are rarely described.

What this study adds?

This prospective study describes work maintenance and sick leaves during the first year following the diagnosis of early breast cancer. After one year, 20% of the patients did not return to work. Chemotherapy dramatically increased the duration of sick leaves, whereas an early information on support can reduce sick leaves. Costs of sick leaves are major

INTRODUCTION

Improvements in early detection and treatment have resulted in an increasing number of breast cancer (BC) survivors.[1] Treatments mostly focus on curing the disease and preventing metastatic relapse. About one-third of women diagnosed with BC are under the age of 55 with a 10-year survival close to 80%.[2] Many patients therefore recover and resume their activities of daily living during or after treatment, including return to work (RTW). RTW after BC is still a new, but important aspect of survivorship research, not only from a societal point of view, as it provides financial resources for rehabilitation of cancer survivors,[3,4] and contributes to psychosocial well-being, including physical and mental health.[5] Some BC cancer survivors experience reduced work ability.[6-11] Difficulties at work or unemployment differ according to the type of BC treatment. Cancer treatment varies according to the stage of the disease and can include surgery, chemotherapy, radiotherapy and hormone therapy. For many cancer patients, return to work helps them to recover from treatment and also constitutes a positive step towards the future. However, factors that maintain patients at work during treatment of their BC have not been clearly identified. The identification of these factors could help healthcare professionals to more accurately identify patients at risk of RTW difficulties in order to provide them with adapted support during BC management designed to maintain them at work. The aim of this prospective study was to describe work during BC management and identify factors associated with either cessation or maintenance at work.

MATERIALS AND METHODS

OPTISOINS01 was an observational, prospective, multicenter study conducted from December 2014 to March 2016 among BC patients from a regional health territory. The primary objective of the Optisoins01 study was to identify the main care pathway after 1 year of early BC and to evaluate costs from various perspectives. Maintenance and return to work evaluation was one of the secondary objectives of the study. The Optisoins01 study design has been previously described.[12] Eight nonprofit hospitals participated in the study: 3 teaching hospitals, 4 general hospitals and 1 comprehensive cancer center. Inclusion criteria were: women aged ≥18 years with previously untreated, first, histologically confirmed, operable BC. Exclusion criteria were: metastatic, locally advanced, or inflammatory BC, previous history of BC.

After BC diagnosis, a work and cancer information booklet had to be given to all working patients. Our Institute has designed an information booklet in collaboration with occupational physicians and the Paris Regional Health Insurance (Caisse Régionale d'Assurance Maladie d'Île-de-France). This document includes the testimonies from employees, advice and practical information to help patients anticipate difficulties and find support: possibility of part-time work, career development plan, roles of occupational physicians and general practitioners. The booklet is freely available online with the support of the "ARC" Foundation.[13]

After inclusion, all patients were given a logbook in which to record, throughout the year, sociodemographic data, out-of-pocket health expenses and an occupational questionnaire for employed women including dates of work and absence from work during treatments, job adjustments, on-shift status and the perceived quality of reintegration. During the second half of the year, clinical research assistants made 2 phone calls to remind patients to fill in

the logbook. Types of occupations were classified according to the French *Institut National de la Statistique et des Etudes Economiques (INSEE)* classification.

Two groups of patients were compared in order to determine the factors associated with maintenance at work: longer sick leave (longer than the median duration) and shorter sick leave (shorter than the median duration). Fisher's exact test or Student's t-test were used to analyze these factors. Multivariate analysis was performed using a logistic regression model. Sick leave over a 1-year period was described according to whether or not the patients were treated by chemotherapy. Differences in the areas under the curves of the 2 populations were compared to 1,000 permutations of random allocation of chemotherapy. The same analysis was performed according to whether or not the patients had received the work information booklet. Differences were considered significant for $p<0.05$. All statistical analyses were performed with R software.[14]

The cost of sick leave for National Health Insurance was calculated on the basis of the monthly income declared by the patients, the duration of sick leave and the national sick leave allowance scale.

This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

RESULTS

Six hundred and four patients with a median age of 58 years (range: 24-98) were included in the Optisoins01 study, including 297 patients (48.2%) who were working at the time of BC diagnosis. The present study focused on these 297 patients.

Detailed patient characteristics and cancer characteristics are presented in Table 1. The median age of the women was 50 (range: 37-77) years, 54 women (18.2%) were single, 153 (51.5%) were married, 39 (13.1%) were divorced and 3 (1.0%) were widows. Two hundred and sixty-one patients (87.9%) had invasive BC and 35 (11.8%) had *in situ* BC. Seventy-five women (25.3%) presented axillary lymph node involvement.

Table 1: Patient and cancer characteristics and breast cancer treatments (n=297)

	n or median	% or range
Patient characteristics		
Age (years)	50	(27-77)
Marital status		
Single	54	18.2%
Married	153	51.5%
Divorced	39	13.1%
Widow	3	1%
NA	48	16.2%
Breast cancer characteristics		
Modes of diagnosis		
Organized screening	60	20.2%
Individual screening	114	38.4%
Clinical signs	123	41.4%
Type of cancer		
Invasive	261	87.9%
In situ	35	11.8%
NA	1	0.3%
Lymph node involvement		
Yes	75	25.3%
No	222	74.7%
Surgery		
Breast surgery		
Conservative	220	74.1%
Radical	77	25.9%
Lymph node surgery		
Sentinel lymph node procedure	203	68.4%
Axillary dissection	72	24.2%

	NA	22	7.4%
Surgical revision			
	no	227	76.4%
	1	60	20.2%
	>1	10	3.4%
Type of hospitalization			
	Outpatient surgery	107	36%
	Conventional surgery	190	64%
Adjuvant therapies			
Radiotherapy			
	No	27	9.1%
	Yes	270	90.9%
Chemotherapy			
	Yes	143	48.1%
	No	154	51.9%
Trastuzumab			
	Yes	36	12.1%
	No	100	33.7%
	NA	161	54.2%
Hormone therapy			
	Yes	220	74.1%
	No	77	25.9%

Two hundred and twenty women (74.1%) underwent breast-conserving surgery and 77 (25.9%) underwent radical mastectomy (Table 1). A sentinel lymph node procedure was performed for 203 patients (68.4%). Seventy patients required at least 1 reoperation for the following reasons: positive surgical margins and secondary mastectomy, sentinel lymph node procedure following discovery of an invasive tumor, axillary dissection following positive sentinel lymph node biopsy and surgical complications (abscess, hematoma, etc.). After surgery, 90.9% of patients received radiotherapy 48.1% of patients received adjuvant chemotherapy and 74.1% of patients received hormone therapy.

Most patients were executives (31.4%) or employees (33.3%). Most patients (47.1%) had a monthly income > €1,900. Work data after BC were available for 178 patients (60%,

supplemental Figure 1). Patients who did not complete the 1-year work questionnaire were globally less compliant with the study and less medicalized (supplemental table 1). Sick leave was prescribed for 165 patients (92.7%). Patients had only one sick leave in 52.2% of cases, 2 sick leaves in 21.9% of cases and 3 or more sick leaves in 18.5% of cases. Median duration of sick leave was 155 days (range: 5-365). After treatment, 7 patients (3.9%) lost their jobs and 46.1% had reduced income. Patients encountered difficulties with their co-workers in 3.4% of cases, with their superiors in 3.9% of cases and for undocumented reasons in 12.9% of cases. Work-related factors are summarized in Table 2.

Table 2: Work characteristics before and after BC

	n or median	% or range
Work characteristics before breast cancer, n=297		
Type of occupation		
Farmer	1	0.3%
Self-employed	8	2.5%
Executive	99	31.4%
Employee	105	33.3%
Intermediate profession	29	9.2%
Blue-collar worker	2	0.6%
NA	53	22.9%
Personal income per month (€)		
no income	6	2%
< 1900	104	35%
>1900	140	47.1%
NA	47	15.8%
Work characteristics after breast cancer, n=178		
Dismissal	7	3.9%
Income change		
decreased	82	46.1%
increased	3	1.7%
stable	73	41%
NA	20	11.2%
Decreased income (%), n=82		
<10%	37	45.1%
10-30%	13	15.8%

	30-60%	5	6.1%
	>60%	3	3.7%
	NA	24	29.3%
Sick leave			
	Yes	165	92.7%
	No	13	7.3%
Number of sick leaves			
	1	93	52.2%
	2	39	21.9%
	>2	33	18.5%
Duration of sick leave (days)		155	(5-365)
Difficulties at work			
	with coworkers	6	3.4%
	with superiors	7	3.9%
	other	23	12.9%

On univariate analysis, the presence of clinical signs leading to a diagnosis of BC (p<0.001), an invasive form of BC (p=0.02), lymph node involvement (p=0.005), radical surgery (p=0.02), axillary dissection (p<0.001), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the work and cancer information booklet (p=0.047) were associated with a longer total duration of sick leave (Table 3). Moreover, patients with longer sick leave were more likely to have reduced income after treatment of their disease (p=0.0012).

Table 3: Determinants and consequences of long sick leave

		Sick leave <155 days, n=79		Sick leave >155, days n=77		
		n or median	% or range	n or median	% or range	p
Patient characteristics						
Age (years)		50.6	(27-59)	50	(29-77)	0.52
Type of occupation						0.09
	Farmer	0	0%	0	0%	

Self-employed	3	3.8%	1	1.3%	
Executive	36	45.6%	29	37.7%	
Employee	25	31.6%	38	49.4%	
Intermediate profession	13	16.5%	7	9.1%	
Blue-collar worker	1	1.3%	0	0%	
NA	1	1.3%	2		
Personal income per month (€)					**0.03**
< 1900	25	31.6%	37	48.1%	
> 1900	54	68.4%	38	49.4%	
NA	0	0%	2	2.6%	
Marital status					0.76
Single	18	22.8%	12	15.6%	
Married	47	59.5%	49	63.6%	
Divorced	12	15.2%	14	18.2%	
Widow	1	1.3%	1	1.3%	
NA	1	1.3%	1	1.3%	
Breast cancer characteristics					
Type of cancer					**<0.001**
Invasive	63	79.7%	74	96.1%	
In situ	16	20.3%	3	3.9%	
Lymph node involvement					**0.005**
Yes	11	13.9%	26	33.8%	
No	68	86.1%	52	67.5%	
Surgery					
Breast surgery					**0.02**
Conservative	66	83.5%	50	64.9%	
Radical	13	16.5%	27	35.1%	
Lymph node surgery					**<0.001**
Sentinel lymph node procedure	62	78.5%	48	62.3%	
Axillary dissection	9	11.4%	26	33.8%	
NA	8	10.1%	3	3.9%	
Surgical revision					0.06
Yes	13	16.5%	23	29.9%	
No	66	83.5%	54	70.1%	
Radiotherapy					0.53
Yes	72	91.1%	74	96.1%	
No	7	8.9%	3	3.9%	
Chemotherapy					**<0.001**
Yes	25	31.6%	56	72.7%	
No	54	68.4%	21	27.3%	

Trastuzumab						0.54
	Yes	9	11.4%	12	15.6%	
	No	16	20.3%	40	51.9%	
	NA	54	68.4%	25	32.5%	
Hormone therapy						0.05
	Yes	50	63.3%	61	79.2%	
	No	29	36.7%	16	20.8%	
Patient management						
Modes of diagnosis						**<0.001**
	Organized screening	15	19%	21	27.3%	
	Individual screening	43	54.4%	20	26%	
	Clinical signs	21	26.6%	36	46.8%	
Type of hospitalization						**<0.001**
	Outpatient surgery	58	73.4%	34	44,.2%	
	Inpatient surgery	21	26.6%	43	55.8%	
Work and cancer information booklet						
	Yes	64	81%	52	67.5%	**0.047**
	No	15	19%	25	32.5%	
Return to work						
Dismissal		1	1.3%	3	3.9%	0.62
Income change						
	decreased	23	29.1%	48	62.3%	**<0.001**
	increased	0	0%	2	2.6%	
	stable	37	46.8%	24	31.2%	
	NA	19	24.1%	3	3.9%	
Decreased income (%)						0.61
	<10%	11	13.9%	21	27.3%	
	10-30%	4	5.1%	7	9.1%	
	30-60%	0	0%	4	5,2%	
	>60%	0	0%	3	3.9%	
	NA	64	81%	42	54.5%	
Difficulties at work						
	with coworkers	2	2.5%	3	3.9%	0.67
	with superiors	0	0%	6	7.8%	0.17
	other	7	8.9%	14	18.2%	0.93

On multivariate analysis, chemotherapy was the only independent factor associated with longer sick leave (OR: 3.5, [95%CI: 1.6-7.9], p=0.002). Patients treated by chemotherapy had

longer sick leave than those not treated by chemotherapy (Figure 1). The difference in terms of the 1-year distribution of sick leave was not statistically significant between patients according to whether or not they had received the work information booklet (Figure 2). The cost of sick leave for National Health Insurance was fourfold higher in patients treated by chemotherapy with a median allowance of €8,841.

DISCUSSION

This study confirms that RTW after BC is a difficult process. Sick leave is frequently prescribed and is often long, with a median sick leave of 155 days in this study.

Factors associated with long sick leave (>155 days) were severe or advanced forms of BC. The duration of sick leave was also associated with the mode of diagnosis, as patients diagnosed by breast screening presented shorter sick leaves. Public health authorities should therefore promote breast screening in order to decrease the proportion of advanced forms of BC and aggressive therapies with severe consequences on work and personal activities. Consequently, longer sick leave was also associated with more aggressive therapy, such as radical surgery, axillary dissection, and chemotherapy. These results are similar to those published in the literature.[6,10,11, 15-17] Chemotherapy is an aggressive treatment that is necessary in order to ensure survival, but which has long-lasting consequences in terms of self-esteem (alopecia…), chronic pain (neuropathy…), and chronic fatigue, that play an important role in return to work and maintenance at work.[9] BC survivors may have to deal with the side effects specific to this type of treatment. Although many side effects of chemotherapy are only temporary,[18] some studies have shown that chemotherapy may impact on cognitive functioning [19] and fatigue [20] up to 10 years after diagnosis.

Cognitive functioning and fatigue have both been associated with impaired work functioning.[21] Munir et al [22] reported that up to 62–84% of women resumed work either during treatment with chemotherapy or following completion of treatment. As a result of their cognitive limitations, women reported that they experienced difficulties with their work ability, particularly difficulties doing multiple tasks, reduced clarity of decisions, deficits in clear thinking and feelings of being inept due to short-term memory.[15] Rapid progress is being made in the field of chemotherapy with the routine use of new genomic signature tests that allow more accurate targeting of patient likely to benefit from chemotherapy. According to Nesvold et al [23] and Eaker et al,[18] mastectomy and axillary lymph node dissection may influence working life long after treatment due to an increased risk of chronic pain. BC survivors are more likely to suffer from upper extremity impairments or lymphedema than are other cancer survivors,[24-28] which are responsible for difficulties returning to work or maintenance at work.[27,29-31]

The work and cancer information booklet appeared to help patients return to work with significantly shorter sick leave. The first key to successful return to work is anticipation. The information booklet advises women to attend the occupational medicine service. In France, occupational medicine plays an essential role, but the patient is not obliged to consult the occupational physician when sick leave is < 3 months. However, at 3 months, the occupational physician and the employee must determine the modalities of return to work, based on the employee's state of health and the characteristics of the workplace. These arrangements concern the employee himself and the work collective with, if necessary, actions so that the reception is assured to the return. Setting up of a schedule, reduction of working hours, modification of physical, mental or workplace loads can also be instituted at

the time of return to work. The occupational physician can provide recommendations to the employer, unless the employer refuses. The results obtained with this handbook are particularly encouraging and suggest that more individual supports should be developed. Patient support appears to be one of the keys to successful RTW. Health coaching by telephone and/or face-to-face interview have already been tested,[30,32,33] showing positive significant outcomes on physical activity, body mass index, pain management, acceptance of disease and self-confidence among cancer survivors. Coaching methods have never been tested in the management of work maintenance. Our Institute is therefore setting up a prospective randomized study (OPTICOACH) with tailored support intervention to enhance RTW after BC in collaboration with a professional coach, consisting of individual interviews or small group workshops over a period of 3 years.

Difficulties returning to work appear to extend over a period of many years. Sevellec et al [34] showed that, six years after returning to work, one employee out of two was still working in the same company. Rather than disappearing, the difficulties identified many years after BC persist for a long time after stopping treatment. It is therefore essential to identify the factors associated with longer sick leave and RTW difficulties in order to help working patients and prevent these long-term problems. The VICAN 2 study focused on the factors associated to difficulties at RTW.[33] This large study was carried out in 2014 by the French National Cancer Institute, on the living conditions of people with cancer (not only BC), two years after the diagnosis. The people most vulnerable to job loss two years after the cancer diagnosis are mainly those working in the so-called socio-professional execution categories, the youngest and oldest, married people with a level of education below the baccalaureate level, and those with precarious contracts.

One of the potential biases of this study concerns the characteristics of the study population, as almost the majority of women belonged to the wealthiest social classes, as 45.6% of patients were executives and only 1.3% were blue collar workers. More than sixty-eight percent of patients had a personal monthly income > €1,900 and 36.7% had a personal monthly income > €2,600. This distribution does not exactly reflect French society; in France, according to the INSEE statistics of 2014, the median monthly income was €1,772. Similarly to our results, a Canadian team [34] has shown that women with an annual income less than C$20,000 were less likely to return to work than those whose income exceeded C$50,000. The French social protection system also plays a role, as it provides cancer survivors with the possibility of replacement income, allowing women to decide whether or not they wish to return to work immediately. Moreover, BC almost exclusively concerns women, affecting them in their roles as mother, wife and working woman; after treatment, some women sometimes prefer to devote themselves more to their personal life and therefore decide to stop working. This notion of changing priorities has already been reported. [35,36] After reassessing their priorities, some women choose to lower their career ambitions and devote more time to their family and themselves. However, this attitude would particularly concern patients with other sources of income. Providing assistance and support to all working patients should therefore be a priority.

CONCLUSION

Advanced disease and chemotherapy are major factors that influence maintenance at work. Systematic screening or use of innovative tools, such as genomic signatures, can facilitate earlier diagnosis and reduce aggressive therapies. One of the keys to success of RTW is anticipation; a cancer and work information booklet given to the patient during treatment,

together with strong support by the occupational medicine service appear promote return to work and maintenance at work. Personalized coaching methods have been successfully used to promote acceptance of disease and self-confidence and should be tested in the management of maintenance at work.

Supplemental Table 1: Differences between patients who returned the 1-year questionnaire and patients who did not return the questionnaire

	Data on sick leave, n=178		No data on sick leave, n=70		
	n or median	% or range	n or median	% or range	p
Patient characteristics					
Age (years)	50	(29-67)	49	(27-77)	0.36
Type of occupation					**<0.05**
Farmer	1	1%	0	0%	
Self-employed	5	3%	0	0%	
Executive	72	40%	3	4%	
Employee	72	40%	27	39%	
Intermediate profession	22	12%	33	47%	
Blue-collar worker	2	1%	7	10%	
NA	4	2%	0	0%	
Personal income per month (€)					**<0.05**
<1900	71	40%	20	29%	
>1900	103	58%	37	53%	
NA	4	2%	13	19%	
Marital status					**<0.05**
Single	34	19%	18	26%	
Married	110	62%	39	56%	
Divorced	29	16%	10	14%	
Widow	2	1%	1	1%	
NA	3	2%	2	3%	
Breast cancer characteristics					
Type of cancer					0.32
Invasive	156	87,6%	61	87%	
In situ	21	11,8%	9	13%	
Lymph node involvement					0.12
Yes	43	24%	23	33%	
No	135	76%	47	67%	
Surgical patient care					
Breast surgery					**<0.05**
Conservative	133	75%	46	66%	
Radical	45	25%	24	34%	
Lymph node surgery					0.48

Sentinel lymph node procedure	122	69%	40	57%	
Axillary dissection	42	24%	24	34%	
NA	14	8%	6	9%	
Surgical revision					0.24
Yes	43	24%	16	23%	
No	135	76%	54	77%	
Radiotherapy					**<0.05**
Yes	167	94%	61	87%	
No	11	6%	9	13%	
Chemotherapy					**<0.05**
Yes	92	52%	33	47%	
No	86	48%	37	53%	
Trastuzumab					0.42
Yes	24	13%	9	13%	
No	63	35%	22	31%	
NA	91	51%	39	56%	
Hormone therapy					0.69
Yes	129	72%	49	70%	
No	49	28%	21	30%	
Patient management					
Modes of diagnosis					0.45
Organized screening	37	21%	12	17%	
Individual screening	74	42%	26	37%	
Clinical signs	67	38%	32	46%	
Type of hospitalization					0.78
Outpatient surgery	108	61%	43	61%	
Inpatient surgery	70	39%	27	39%	

Figures:

Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

Supplemental Figure 1: Flow Chart

Competing Interests: The authors declare that they have no competing interests.

Funding: This study was supported by a grant from the French National Cancer Institute dedicated to economic studies of innovative techniques. Delphine Héquet benefit from a grant of "Fondation pour la Recherche Médicale" to conduct this study.

Reference

1. Spelten ER, Sprangers MAG, Verbeek JHAM. Factors reported to influence the return to work of cancer survivors: a literature review. *Psychooncology* 2002;11(2):124‐31.

2. Verdecchia A, Francisci S, Brenner H, et al. Recent cancer survival in Europe: a 2000-02 period analysis of EUROCARE-4 data. *Lancet Oncol* 2007;8(9):784‐96.

3. Clark JC, Landis LL. Reintegration and maintenance of employees with breast cancer in the workplace. *AAOHN J Off J Am Assoc Occup Health Nurses* 1989;37(5):186‐93.

4. Mellette SJ. The cancer patient at work. *CA Cancer J Clin* 1985;35(6):360‐73.

5. Anderson NB, Armstead CA. Toward understanding the association of socioeconomic status and health: a new challenge for the biopsychosocial approach. *Psychosom Med* 1995;57(3):213‐25.

6. Balak F, Roelen CAM, Koopmans PC, et al. Return to work after early-stage breast cancer: a cohort study into the effects of treatment and cancer-related symptoms. *J Occup Rehabil* 2008;18(3):267–72.

7. Bouknight RR, Bradley CJ, Luo Z. Correlates of return to work for breast cancer survivors. *J Clin Oncol Off J Am Soc Clin Oncol* 2006;24(3):345–53.

8. de Boer AGEM, Taskila TK, Tamminga SJ, et al. Interventions to enhance return-to-work for cancer patients. *Cochrane Database Syst Rev* 2015;(9):CD007569.

9. Fantoni SQ, Peugniez C, Duhamel A, et al. Factors related to return to work by women with breast cancer in northern France. *J Occup Rehabil* 2010;20(1):49–58.

10. Hedayati E, Johnsson A, Alinaghizadeh H, et al. Cognitive, psychosocial, somatic and treatment factors predicting return to work after breast cancer treatment. *Scand J Caring Sci* 2013;27(2):380–7.

11. Lavigne JE, Griggs JJ, Tu XM, et al. Hot flashes, fatigue, treatment exposures and work productivity in breast cancer survivors. *J Cancer Surviv Res Pract* 2008;2(4):296–302.

12. Baffert S, Hoang HL, Brédart A, et al. The patient-breast cancer care pathway: how could it be optimized? *BMC Cancer* 2015;15:394.

13. https://www.fondation-arc.org/support-information/brochure-retour-au-travail-apres-cancer.

14. R Core Team (2012) R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0. Available at: http://www.R-project.org/ [http://lib.stat.cmu.edu/r/CRAN. (last accessed 20 November 2016).

15. Drolet M, Maunsell E, Mondor M, et al. Work absence after breast cancer diagnosis: a population-based study. *CMAJ Can Med Assoc J J Assoc Medicale Can* 2005;173(7):765–71.

16. Johnsson A, Fornander T, Rutqvist L-E, et al. Predictors of return to work ten months after primary breast cancer surgery. *Acta Oncol Stockh Swed* 2009;48(1):93–8.

17. Jagsi R, Hawley ST, Abrahamse P, et al. Impact of adjuvant chemotherapy on long-term employment of survivors of early-stage breast cancer. *Cancer* 2014;120(12):1854–62.

18. Eaker S, Wigertz A, Lambert PC, et al. Breast cancer, sickness absence, income and marital status. A study on life situation 1 year prior diagnosis compared to 3 and 5 years after diagnosis. *PloS One* 2011;6(3):e18040.

19. de Ruiter MB, Reneman L, Boogerd W, et al. Cerebral hyporesponsiveness and cognitive impairment 10 years after chemotherapy for breast cancer. *Hum Brain Mapp* 2011;32(8):1206–19.

20. Reinertsen KV, Cvancarova M, Loge JH, et al. Predictors and course of chronic fatigue in long-term breast cancer survivors. *J Cancer Surviv Res Pract* 2010;4(4):405–14.

21. Islam T, Dahlui M, Majid HA, et al. Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health* 2014;14 Suppl 3:S8.

22. Munir F, Burrows J, Yarker Jet al. Women's perceptions of chemotherapy-induced cognitive side affects on work ability: a focus group study. *J Clin Nurs* 2010;19(9–10):1362–70.

23. Nesvold I-L, Fosså SD, Holm I, et al. Arm/shoulder problems in breast cancer survivors are associated with reduced health and poorer physical quality of life. *Acta Oncol Stockh Swed* 2010;49(3):347–53.

24. Assis MR, Marx AG, Magna LA, et al. Late morbidity in upper limb function and quality of life in women after breast cancer surgery. *Braz J Phys Ther* 2013;17(3):236–43.

25. Devoogdt N, Van Kampen M, Christiaens et al. Short- and long-term recovery of upper limb function after axillary lymph node dissection. *Eur J Cancer Care* 2011;20(1):77‑86.

26. Hayes SC, Rye S, Battistutta D, et al. Upper-body morbidity following breast cancer treatment is common, may persist longer-term and adversely influences quality of life. *Health Qual Life Outcomes* 2010;8:92.

27. Quinlan E, Thomas-MacLean R, Hack T, et al. The impact of breast cancer among Canadian women: disability and productivity. *Work Read Mass* 2009;34(3):285‑96.

28. Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. *PM R* 2014;6(2):170‑83.

29. Boyages J, Kalfa S, Xu Y, et al. Worse and worse off: the impact of lymphedema on work and career after breast cancer. *SpringerPlus* 2016;5:657.

30. Hawkes AL, Gollschewski S, Lynch BM, et al. A telephone-delivered lifestyle intervention for colorectal cancer survivors « CanChange »: a pilot study. *Psychooncology* 2009;18(4):449‑55.

31. Peugniez C, Fantoni S, Leroyer A, et al. Return to work after treatment for breast cancer: single-center experience in a cohort of 273 patients. *Ann Oncol Off J Eur Soc Med Oncol* 2010;21(10):2124‑5.

32. Sevellec M, Belin L, Bourrillon M-F, et al. Work ability in cancer patients: Six years assessment after diagnosis in a cohort of 153 workers. *Bull Cancer* 2015;102(6 Suppl 1):S5-13.

33. VICAN2- https://www.inserm.fr/.../rapport_complet_la-vie-2-ans-apres-un-diagnostic-de-cancer-2014.

34. Drolet M, Maunsell E, Brisson J, et al. Not working 3 years after breast cancer: predictors in a population-based study. *J Clin Oncol Off J Am Soc Clin Oncol* 2005;23(33):8305‑12.

35. Maunsell E, Drolet M, Brisson J, et al. Work situation after breast cancer: results from a population-based study. *J Natl Cancer Inst* 2004;96(24):1813‑22.

36. Kennedy F, Haslam C, Munir F, et al. Returning to work following cancer: a qualitative exploratory study into the experience of returning to work following cancer. *Eur J Cancer Care* 2007;16(1):17‑25.

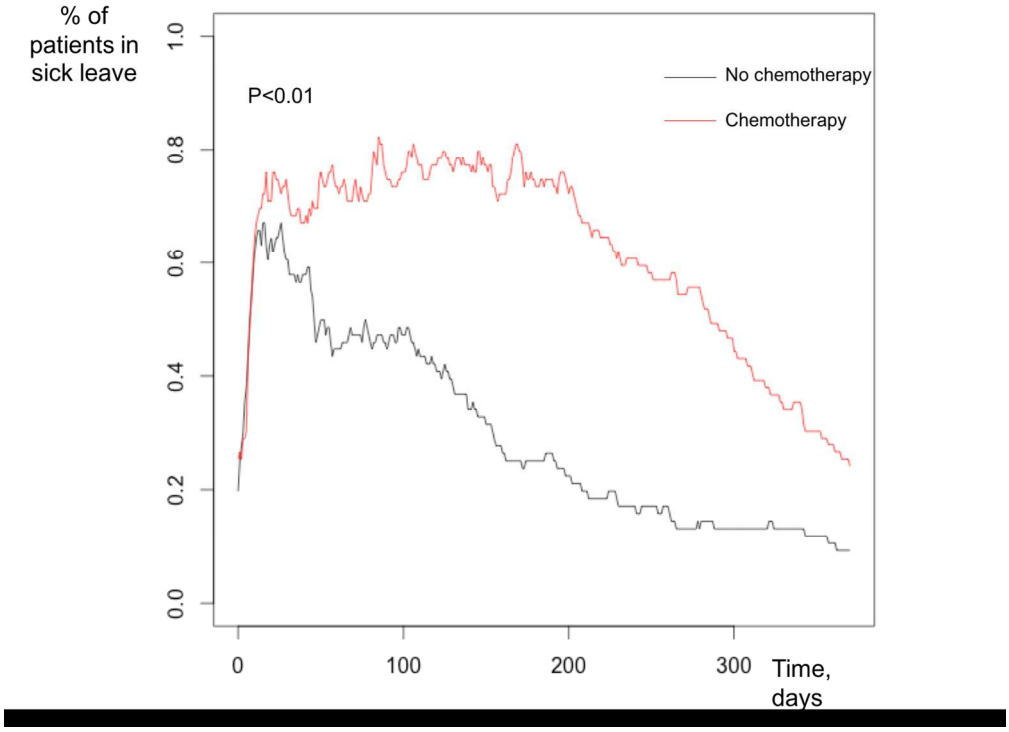


Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

264x200mm (150 x 150 DPI)

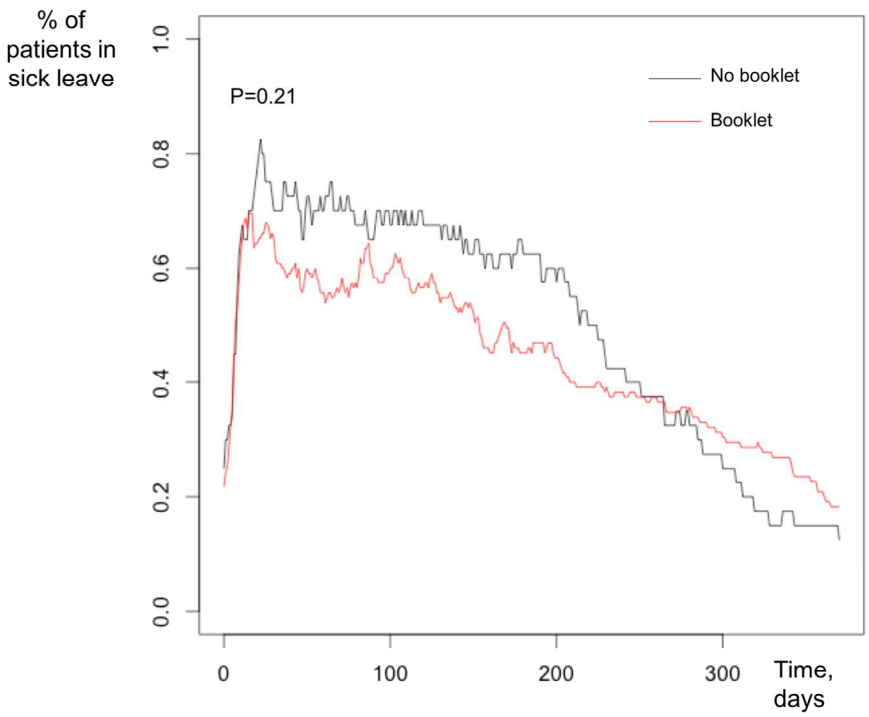
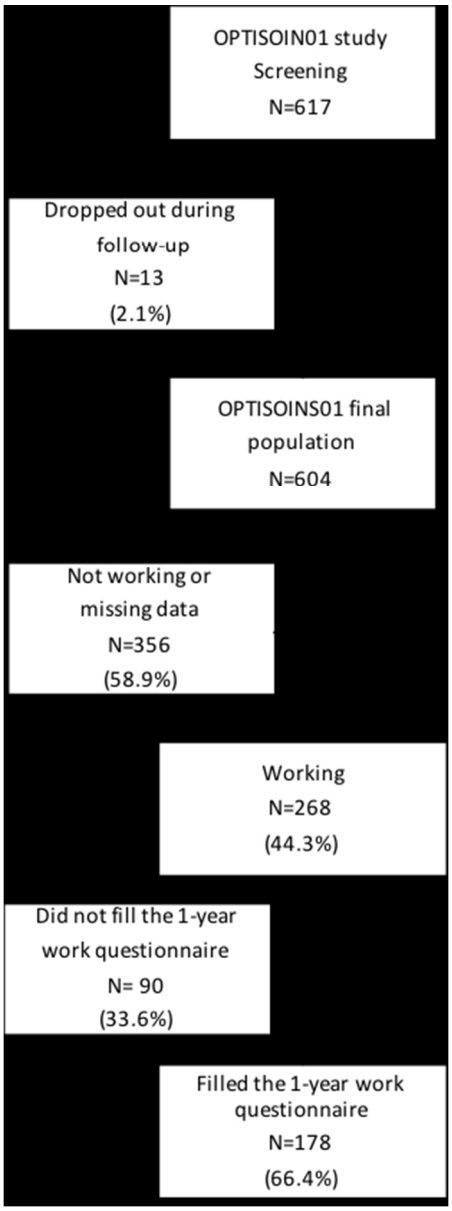


Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

262x205mm (150 x 150 DPI)



52x141mm (150 x 150 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4 and 5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	9
		(*e*) Describe any sensitivity analyses	9
Results			9

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Supplemental figre 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 and 11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
		(*b*) Report category boundaries when continuous variables were categorized	12-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12-14
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13, 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Determinants of maintenance at work of breast cancer patients: results from the OPTISOINS01 prospective study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020276.R1
Article Type:	Research
Date Submitted by the Author:	07-Feb-2018
Complete List of Authors:	Arfi, Alexandra; Institut Curie, Surgery Baffert, Sandrine; CEMKA-EVAL, Health Economist Soilly, A-L; Universite de Bourgogne IUT Dijon-Auxerre, Health Economist huchon, cyrille; Hôpital Poissy, Gynecology Reyal, Fabien; Institut Curie, Surgery Asselain, Bernard; Institut Curie, Biostatistics Neffati, Souhir; Institut Curie, Clinical Research and Innovation Department Rouzier, Roman; Institut Curie, Surgery Hequet, Delphine; Institut Curie-Centre René Huguenin, Surgical oncology
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Breast tumours < ONCOLOGY, OCCUPATIONAL & INDUSTRIAL MEDICINE, PUBLIC HEALTH

Determinants of maintenance at work of breast cancer patients: results from the OPTISOINS01 prospective study.

Authors:

Alexandra Arfi[1], Sandrine Baffert[2], Anne-Laure Soilly[3], Cyrille Huchon[4,5], Fabien Reyal[1,6], Bernard Asselain[7], Souhir Neffati[8], Roman Rouzier[1,9], Delphine Héquet[1,9]

Affiliations :

1: Department of Surgical Oncology, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

2: Health Economics, CEMKA-EVAL, Bourg-la-Reine, 43 boulevard du Maréchal-Joffre, 92340 Bourg-la-Reine, France

3: Health Economics, Bourgogne Franche-Comté University, EA 7467, 2 boulevard Gabriel, 21000 Dijon, France

4: Department of Obstetrics and Gynecology, Hôpital de Poissy-St Germain, 10 Rue du Champ Gaillard, 78300 Poissy, France

5: Equipe d'Accueil 7285, Risk and Safety in Clinical Medicine for Women and Perinatal Health, University Versailles-Saint-Quentin, 2 av de la source de la Bièvre, 78180 Montigny-le-Bretonneux, France

6: Residual Tumor and Response to Treatment Lab, Translational Research Department, Institut Curie, 75005, Paris, France

7: Department of Biostatistics, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

8: Clinical Research and Innovation Department, Sponsorship division, Institut Curie, 92210 Saint-Cloud, France

9: René-Huguenin hospital, Institut Curie, Inserm U900 – Bioinformatics, biostatistics, epidemiology and computational systems. Cancer biology, 35, rue Dailly, 92210 Saint-Cloud, France

Corresponding author:

Delphine HEQUET

Postal address: 35 rue Dailly, 92210 St Cloud, France

e-mai l: delphine.hequet@gmail.com

Phone number: 0033147111515

Word count: 2431

Contributorship statement:

Delphine Hequet, Roman Rouzier and Sandrine Baffert designed the study.

Bernard Asselain and Souhr Neffati contributed to the design and implementation of the research.

Sandrine Baffert and Anne-Laure Soilly performed the health economic analysis.

Alexandra Arfi and Delphine Hequet performed all the remaining statistical analysis and wrote the manuscript.

Cyrille Huchon and Fabien Reyal contributed to the clinical study, patients' inclusion and analysis of the results.

All the authors reviewed and approved the final version of the manuscript.

ABSTRACT

Introduction: Return to work (RTW) after breast cancer (BC) is still a new field of research. The factors determining maintenance at work of BC patients have not been clearly identified. The aim of this study was to describe work during BC treatment and to identify factors associated with maintenance at work.

Materials and methods: An observational, prospective, multicenter study was conducted among women with operable BC. A logbook was given to all working patients to record sociodemographic and work-related data over a one-year period.

Results: Work-related data after BC were available for 178 patients (60%). Median age at diagnosis was 50 years (27-77), 87.9% of patients had an invasive form of BC and 25.3% a lymph node involvement. 25.9% had a radical surgery and 24.2% had an axillary dissection. Radiotherapy was performed in 90.9% of patients and chemotherapy in 48.1%. Sick leave was prescribed for 165 patients (92.7%) for a median of 155 days. On univariate analysis, invasive BC (p=0.025), lymph node involvement (p=0.005), radical surgery (p=0.025), axillary dissection (p=0.004), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the patient information booklet on RTW (p=0.047) were associated with a longer duration of sick leave. On multivariate analysis, chemotherapy was associated with longer sick leave (OR: 3.5; [95%CI: 1.6-7.9]; p=0.002). The cost of sick leave to French National Health Insurance was fourfold higher in the case of chemotherapy (p<0.001).

Conclusion: Advanced disease and chemotherapy are major factors that influence maintenance at work during the management of BC. Systematic screening can help to diagnose earlier disease and reduce the need for aggressive therapy.

Strengths and limitations of this study:

- Prospective multicentric study
- Description of factors associated to long sick leave
- Multimodal analysis including evaluation of costs of sick leave
- Few qualitative information

Keywords: breast cancer, return to work, maintenance at work, absence duration, chemotherapy.

Data sharing statement: No additional data available

Ethics: This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

Funding: Delphine Hequet benefitted from a "Fondation pour la Recherche Medicale" (FDM20140630453) grant to conduct this study. This study was supported by a grant from the French National Cancer Institute (Institut National du Cancer, PRME-K2013), dedicated to economic studies of innovative techniques.

What is already known on this subject?

Return to work after breast cancer is a delicate step in the real-life reintegration. Breast cancer patients have difficulties at work even 5 years after the end of the treatments. The factors that maintain patients at work during breast cancer are rarely described.

What this study adds?

This prospective study describes work maintenance and sick leaves during the first year following the diagnosis of early breast cancer. After one year, 20% of the patients did not return to work. Chemotherapy dramatically increased the duration of sick leaves, whereas an early information on support can reduce sick leaves. Costs of sick leaves are major.

INTRODUCTION

Improvements in early detection and treatment have resulted in an increasing number of breast cancer (BC) survivors [1] .Treatments mostly focus on curing the disease and preventing metastatic relapse. About one-third of women diagnosed with BC are under the age of 55 with a 10-year survival close to 80% [2].Many patients therefore recover and resume their activities of daily living during or after treatment, including return to work (RTW). RTW after BC is still a new, but important aspect of survivorship research, not only from a societal point of view, as it provides financial resources for rehabilitation of cancer survivors and contributes to psychosocial well-being, including physical and mental health [3]. Some BC cancer survivors experience reduced work ability [4–8]. Difficulties at work or unemployment differ according to the type of BC treatment. Cancer treatment varies according to the stage of the disease and can include surgery, chemotherapy, radiotherapy and hormone therapy. For many cancer patients, return to work helps them to recover from treatment and also constitutes a positive step towards the future. The identification of factors that maintain patients at work during and after BC treatment could help healthcare professionals to more accurately identify patients at risk of RTW difficulties in order to provide them with adapted support during BC management. The aim of this prospective study was to describe work during and after BC management and identify factors associated with either cessation or maintenance at work.

MATERIALS AND METHODS

OPTISOINS01 was an observational, prospective, multicenter study conducted from December 2014 to March 2016 among BC patients from a regional health territory. The

primary objective of the Optisoins01 study was to identify the main care pathway after 1 year of early BC and to evaluate costs from various perspectives. Maintenance and return to work evaluation was one of the secondary objectives of the study. The Optisoins01 study design has been previously described [9]. Eight non-profit hospitals participated in the study: 3 teaching hospitals, 4 general hospitals and 1 comprehensive cancer center. Inclusion criteria were: women aged ≥18 years with previously untreated, first, histologically confirmed, operable BC. Exclusion criteria were: metastatic, locally advanced, or inflammatory BC, previous history of BC.

After BC diagnosis, a work and cancer information booklet had to be given to all working patients. Our Institute has designed an information booklet in collaboration with occupational physicians and the Paris Regional Health Insurance (Caisse Régionale d'Assurance Maladie d'Île-de-France). This document includes the testimonies from employees, advice and practical information to help patients anticipate difficulties and find support: possibility of part-time work, career development plan, roles of occupational physicians and general practitioners. The booklet is freely available online with the support of the "ARC" Foundation [10].

After inclusion, all patients were given a logbook in which to record, throughout the year, sociodemographic data (age, marital status, type of occupation, personal income…), out-of-pocket health expenses and an 1-year-occupational questionnaire for employed women including dates of work and absence from work during treatments, job adjustments, on-shift status and the perceived quality of reintegration with standardized self-questionnaire (income change, difficulties at work with co-workers and/or with superiors…). Patients were asked to fill the questionnaire prospectively during the all study period. During the second half of the year, clinical research assistants made 2 phone calls to remind patients to fill in

the logbook. Questionnaires were collected at the end of the study. Types of occupations were classified according to the French *Institut National de la Statistique et des Etudes Economiques (INSEE)* classification.

Two groups of patients were compared in order to determine the factors associated with maintenance at work: longer sick leave (longer or equal to the median duration) and shorter sick leave (shorter than the median duration). Fisher's exact test or Student's t-test were used to analyze these factors. These tests were two sided with a 0.05 level of significance. Multivariate analysis was performed using a logistic regression model. We considered adjusted p-value for multiple comparisons. Sick leave over a 1-year period was described according to whether or not the patients were treated by chemotherapy. Differences in the areas under the curves of the 2 populations were compared to 1,000 permutations of random allocation of chemotherapy. The same analysis was performed according to whether or not the patients had received the work information booklet. Differences were considered significant for $p<0.05$. All statistical analyses were performed with R software [11].

The cost of sick leave for National Health Insurance was calculated on the basis of the monthly income declared by the patients, the duration of sick leave and the national sick leave allowance scale.

This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

RESULTS

Six hundred and four patients with a median age of 58 years (range: 24-98) were included in the Optisoins01 study, including 297 patients (48.2%) who were working at the time of BC diagnosis. The present study focused on these 297 patients.

Detailed patient characteristics and cancer characteristics are presented in Table 1. The median age of the women was 50 (range: 27-77) years, 54 women (18.2%) were single, 153 (51.5%) were married, 39 (13.1%) were divorced and 3 (1.0%) were widows. Two hundred and sixty-one patients (87.9%) had invasive BC and 35 (11.8%) had *in situ* BC. Seventy-five women (25.3%) presented axillary lymph node involvement.

Table 1: Patient and cancer characteristics and breast cancer treatments (n=297)

	n or median	% or range
Patient characteristics		
Age (years)	50	(27-77)
Marital status		
Single	54	18.2%
Married	153	51.5%
Divorced	39	13.1%
Widow	3	1%
NA	48	16.2%
Breast cancer characteristics		
Modes of diagnosis		
Organized screening	60	20.2%
Individual screening	114	38.4%
Clinical signs	123	41.4%
Type of cancer		
Invasive	261	87.9%
In situ	35	11.8%
NA	1	0.3%
Lymph node involvement		
Yes	75	25.3%
No	222	74.7%
Surgery		
Breast surgery		

Conservative	220	74.1%
Radical	77	25.9%
Lymph node surgery		
Sentinel lymph node procedure	203	68.4%
Axillary dissection	72	24.2%
NA	22	7.4%
Surgical revision		
no	227	76.4%
1	60	20.2%
>1	10	3.4%
Type of hospitalization		
Outpatient surgery	107	36%
Conventional surgery	190	64%
Adjuvant therapies		
Radiotherapy		
No	27	9.1%
Yes	270	90.9%
Chemotherapy		
Yes	143	48.1%
No	154	51.9%
Trastuzumab		
Yes	36	12.1%
No	100	33.7%
NA	161	54.2%
Hormone therapy		
Yes	220	74.1%
No	77	25.9%

Two hundred and twenty women (74.1%) underwent breast-conserving surgery and 77 (25.9%) underwent radical mastectomy (Table 1). A sentinel lymph node procedure was performed for 203 patients (68.4%). Seventy patients required at least 1 reoperation for the following reasons: positive surgical margins and secondary mastectomy, sentinel lymph node procedure following discovery of an invasive tumor, axillary dissection following positive sentinel lymph node biopsy and surgical complications (abscess, hematoma, etc.).

After surgery, 90.9% of patients received radiotherapy 48.1% of patients received adjuvant chemotherapy and 74.1% of patients received hormone therapy.

Most patients were executives (31.4%) or employees (33.3%). Most patients (47.1%) had a monthly income > €1,900. Work data after BC were available for 178 patients (60%, supplemental Figure 1). Patients who did not complete ~~the 1-year~~ work questionnaire in the logbook during one year were globally less compliant with the study and less medicalized (supplemental table 1). Sick leave was prescribed for 165 patients (92.7%). Patients had only one sick leave in 52.2% of cases, 2 sick leaves in 21.9% of cases and 3 or more sick leaves in 18.5% of cases. Median duration of sick leave was 155 days (range: 5-365). After treatment, 7 patients (3.9%) lost their jobs and 46.1% had reduced income. Patients encountered difficulties with their co-workers in 3.4% of cases, with their superiors in 3.9% of cases and for undocumented reasons in 12.9% of cases. Work-related factors are summarized in Table 2.

Table 2: Work characteristics before and after BC

	n or median	% or range
Work characteristics before breast cancer, n=297		
Type of occupation		
Farmer	1	0.3%
Self-employed	8	2.5%
Executive	99	31.4%
Employee	105	33.3%
Intermediate profession	29	9.2%
Blue-collar worker	2	0.6%
NA	53	22.9%
Personal income per month (€)		
no income	6	2%
< 1900	104	35%
>1900	140	47.1%
NA	47	15.8%
Work characteristics after breast cancer, n=178		

Dismissal		7	3.9%
Income change			
	decreased	82	46.1%
	increased	3	1.7%
	stable	73	41%
	NA	20	11.2%
Decreased income (%), n=82			
	<10%	37	45.1%
	10-30%	13	15.8%
	30-60%	5	6.1%
	>60%	3	3.7%
	NA	24	29.3%
Sick leave			
	Yes	165	92.7%
	No	13	7.3%
Number of sick leaves			
	1	93	52.2%
	2	39	21.9%
	>2	33	18.5%
Duration of sick leave (days)		155	(5-365)
Difficulties at work			
	with coworkers	6	3.4%
	with superiors	7	3.9%
	other	23	12.9%

On univariate analysis, the presence of clinical signs leading to a diagnosis of BC (p<0.001), an invasive form of BC (p=0.02), lymph node involvement (p=0.005), radical surgery (p=0.02), axillary dissection (p<0.001), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the work and cancer information booklet (p=0.047) were associated with a longer total duration of sick leave (Table 3). Moreover, patients with longer sick leave were more likely to have reduced income after treatment of their disease (p=0.0012).

Table 3: Determinants and consequences of long sick leave

	Sick leave <155 days, n=79		Sick leave ≥155, days n=77		
	n or median	% or range	n or median	% or range	p
Patient characteristics					
Age (years)	50.6	(27-59)	50	(29-77)	0.52
Type of occupation					0.09
Farmer	0	0%	0	0%	
Self-employed	3	3.8%	1	1.3%	
Executive	36	45.6%	29	37.7%	
Employee	25	31.6%	38	49.4%	
Intermediate profession	13	16.5%	7	9.1%	
Blue-collar worker	1	1.3%	0	0%	
NA	1	1.3%	2		
Personal income per month (€)					**0.03**
< 1900	25	31.6%	37	48.1%	
> 1900	54	68.4%	38	49.4%	
NA	0	0%	2	2.6%	
Marital status					0.76
Single	18	22.8%	12	15.6%	
Married	47	59.5%	49	63.6%	
Divorced	12	15.2%	14	18.2%	
Widow	1	1.3%	1	1.3%	
NA	1	1.3%	1	1.3%	
Breast cancer characteristics					
Type of cancer					**<0.001**
Invasive	63	79.7%	74	96.1%	
In situ	16	20.3%	3	3.9%	
Lymph node involvement					**0.005**
Yes	11	13.9%	**26**	**33.8%**	
No	68	86.1%	**52**	**67.5%**	
Surgery					
Breast surgery					**0.02**
Conservative	66	83.5%	50	64.9%	
Radical	13	16.5%	27	35.1%	
Lymph node surgery					**<0.001**
Sentinel lymph node procedure	62	78.5%	48	62.3%	
Axillary dissection	9	11.4%	26	33.8%	
NA	8	10.1%	3	3.9%	
Surgical revision					0.06

	Yes	13	16.5%	23	29.9%	
	No	66	83.5%	54	70.1%	
Radiotherapy						0.53
	Yes	72	91.1%	74	96.1%	
	No	7	8.9%	3	3.9%	
Chemotherapy						**<0.001**
	Yes	25	31.6%	56	72.7%	
	No	54	68.4%	21	27.3%	
Trastuzumab						0.54
	Yes	9	11.4%	12	15.6%	
	No	16	20.3%	40	51.9%	
	NA	54	68.4%	25	32.5%	
Hormone therapy						0.05
	Yes	50	63.3%	61	79.2%	
	No	29	36.7%	16	20.8%	
Patient management						
Modes of diagnosis						**<0.001**
	Organized screening	15	19%	21	27.3%	
	Individual screening	43	54.4%	20	26%	
	Clinical signs	21	26.6%	36	46.8%	
Type of hospitalization						**<0.001**
	Outpatient surgery	58	73.4%	34	44,.2%	
	Inpatient surgery	21	26.6%	43	55.8%	
Work and cancer information booklet						
	Yes	64	81%	52	67.5%	**0.047**
	No	15	19%	25	32.5%	
Return to work						
Dismissal		1	1.3%	3	3.9%	0.62
Income change						
	decreased	23	29.1%	48	62.3%	**<0.001**
	increased	0	0%	2	2.6%	
	stable	37	46.8%	24	31.2%	
	NA	19	24.1%	3	3.9%	
Decreased income (%)						0.61
	<10%	11	13.9%	21	27.3%	
	10-30%	4	5.1%	7	9.1%	
	30-60%	0	0%	4	5,2%	
	>60%	0	0%	3	3.9%	
	NA	64	81%	42	54.5%	
Difficulties at work						
	with coworkers	2	2.5%	3	3.9%	0.67
	with superiors	0	0%	6	7.8%	0.17

	other	7	8.9%	14	18.2%	0.93

On multivariate analysis, chemotherapy was the only independent factor associated with longer sick leave (OR: 3.5, [95%CI: 1.6-7.9], p=0.002). Patients treated by chemotherapy had longer sick leave than those not treated by chemotherapy (Figure 1). The difference in terms of the 1-year distribution of sick leave was not statistically significant between patients according to whether or not they had received the work information booklet (Figure 2).

Considering the working population of OPTISOINS01 study with complete data on sick leave and salary, the median cost of sick leave for National Health Insurance was €8,841 per patient per year from diagnosis. In univariate and multivariate analysis, the only determinant of sick leave costs found in this study was the administration of chemotherapy, with a fourfold higher median allowance for patients treated with adjuvant chemotherapy.

DISCUSSION

Although many BC cancer survivors are able to return to a normal work life after treatment, our study confirms that many women of working ages do not. Sick leave is frequently prescribed and is often long, with a median sick leave of 155 days in this study.

Factors associated with long sick leave (>155 days) were severe or advanced forms of BC. The duration of sick leave was also associated with the mode of diagnosis, as patients diagnosed by breast screening presented shorter sick leaves. Public health authorities should therefore promote breast screening in order to decrease the proportion of advanced forms of BC and aggressive therapies with severe consequences on work and personal activities.

Consequently, longer sick leave was also associated with more aggressive therapy, such as radical surgery, axillary dissection, and chemotherapy. These results are similar to those published in the literature [4,7,8,12,13]. Chemotherapy is an aggressive treatment that is necessary in order to ensure survival, but which has long-lasting consequences in terms of self-esteem (alopecia…), chronic pain (neuropathy…), and chronic fatigue, that play an important role in return to work and maintenance at work [6]. BC survivors may have to deal with the side effects specific to this type of treatment. Although many side effects of chemotherapy are only temporary [14], some studies have shown that chemotherapy may impact on cognitive functioning [15] and fatigue [16] up to 10 years after diagnosis. Cognitive functioning and fatigue have both been associated with impaired work functioning [17]. Munir et al [18]reported that up to 62–84% of women resumed work either during treatment with chemotherapy or following completion of treatment. As a result of their cognitive limitations, women reported that they experienced difficulties with their work ability, particularly difficulties doing multiple tasks, reduced clarity of decisions, deficits in clear thinking and feelings of being inept due to short-term memory [19] . Rapid progress is being made in the field of chemotherapy with the routine use of new genomic signature tests that allow more accurate targeting of patient likely to benefit from chemotherapy. According to Nesvold et al [20] and Eaker et al [14] mastectomy and axillary lymph node dissection may influence working life long after treatment due to an increased risk of chronic pain. BC survivors are more likely to suffer from upper extremity impairments or lymphedema than are other cancer survivors [21–24], which are responsible for difficulties returning to work or maintenance at work [25,26].

The work and cancer information booklet appeared to help patients return to work with significantly shorter sick leave in univariate analysis. The strong impact of chemotherapy on sick leave duration eliminated the influence of booklet in the multivariate analysis. However, this suggests that an action, such as an active support, could help to reduce sick leave duration. The information booklet advises women to attend the occupational medicine service. In France, occupational medicine plays an essential role, but the patient is not obliged to consult the occupational physician when sick leave is < 3 months. However, at 3 months, the occupational physician and the employee must determine the modalities of return to work, based on the employee's state of health and the characteristics of the workplace. These arrangements concern the employee himself and the work collective with, if necessary, actions so that the reception is assured to the return. Setting up of a schedule, reduction of working hours, modification of physical, mental or workplace loads can also be instituted at the time of return to work. The occupational physician can provide recommendations to the employer, unless the employer refuses. The results obtained with this handbook are particularly encouraging and suggest that more individual supports should be developed. Health coaching by telephone and/or face-to-face interview have already been tested [27–29], showing positive significant outcomes on physical activity, body mass index, pain management, acceptance of disease and self-confidence among cancer survivors. Coaching methods have never been tested in the management of work maintenance. Our Institute is therefore setting up a prospective randomized study (OPTICOACH) with tailored support intervention to enhance RTW after BC in collaboration with a professional coach, consisting of individual interviews or small group workshops over a period of 3 years.

Difficulties returning to work appear to extend over a period of many years. Sevellec et al [28] showed that, six years after returning to work, one employee out of two was still

working in the same company. Rather than disappearing, the difficulties identified many years after BC persist for a long time after stopping treatment. It is therefore essential to identify the factors associated with longer sick leave and RTW difficulties in order to help working patients and prevent these long-term problems. The VICAN 2 study [29] focused on the factors associated to difficulties at RTW. This large study was carried out in 2014 by the French National Cancer Institute, on the living conditions of people with cancer (not only BC), two years after the diagnosis. The people most vulnerable to job loss two years after the cancer diagnosis are mainly those working in the so-called socio-professional execution categories, the youngest and oldest, married people with a level of education below the baccalaureate level, and those with precarious contracts.

One of the potential biases of this study concerns the characteristics of the study population, as almost the majority of women belonged to the wealthiest social classes, as 45.6% of patients were executives and only 1.3% were blue collar workers. More than sixty-eight percent of patients had a personal monthly income > €1,900 and 36.7% had a personal monthly income > €2,600. This distribution does not exactly reflect French society; in France, according to the INSEE statistics of 2014, the median monthly income was €1,772. Similarly to our results, a Canadian team [30] has shown that women with an annual income less than C$20,000 were less likely to return to work than those whose income exceeded C$50,000. The French social protection system also plays a role, as it provides cancer survivors with the possibility of replacement income, allowing women to decide whether or not they wish to return to work immediately. Providing assistance and support to all working patients should therefore be a priority.

CONCLUSION

Advanced disease and chemotherapy are major factors that influence return to work with longer sick-leave. Systematic screening or use of innovative tools, such as genomic signatures, can facilitate earlier diagnosis and reduce aggressive therapies.

Depending on the type of treatment, on the stage of the disease and on the type of occupation, information and coaching methods with the occupational medicine service should systematically be given to working women, helping them to anticipate job adjustments with flexibility of work schedule for example.

Personalized coaching methods have been successfully used to promote acceptance of disease and self-confidence and should be tested in the management of return to work and maintenance at work.

Figures:

Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

Supplemental Figure 1: Flow Chart

Competing Interests: The authors declare that they have no competing interests.

Funding: This study was supported by a grant from the French National Cancer Institute dedicated to economic studies of innovative techniques. Delphine Héquet benefit from a grant of "Fondation pour la Recherche Médicale" to conduct this study.

REFERENCES

1 Breast Cancer Facts & figures 2013-2014 (2013) Atlanta: American Cancer Society, Inc. http://cancer. org/acs/groups/content/@research/documents/document/acspc-042725.pdf. Accessed 9/20/2014.

2 Verdecchia A, Francisci S, Brenner H, *et al.* Recent cancer survival in Europe: a 2000-02 period analysis of EUROCARE-4 data. *Lancet Oncol* 2007;**8**:784–96. doi:10.1016/S1470-2045(07)70246-2

3 Mehnert A, de Boer A, Feuerstein M. Employment challenges for cancer survivors: Employment Challenges. *Cancer* 2013;**119**:2151–9. doi:10.1002/cncr.28067

4 Balak F, Roelen CAM, Koopmans PC, *et al.* Return to work after early-stage breast cancer: a cohort study into the effects of treatment and cancer-related symptoms. *J Occup Rehabil* 2008;**18**:267–72. doi:10.1007/s10926-008-9146-z

5 de Boer AGEM, Taskila TK, Tamminga SJ, *et al.* Interventions to enhance return-to-work for cancer patients. *Cochrane Database Syst Rev* 2015;:CD007569. doi:10.1002/14651858.CD007569.pub3

6 Fantoni SQ, Peugniez C, Duhamel A, *et al.* Factors related to return to work by women with breast cancer in northern France. *J Occup Rehabil* 2010;**20**:49–58. doi:10.1007/s10926-009-9215-y

7 Hedayati E, Johnsson A, Alinaghizadeh H, *et al.* Cognitive, psychosocial, somatic and treatment factors predicting return to work after breast cancer treatment. *Scand J Caring Sci* 2013;**27**:380–7. doi:10.1111/j.1471-6712.2012.01046.x

8 Lavigne JE, Griggs JJ, Tu XM, *et al.* Hot flashes, fatigue, treatment exposures and work productivity in breast cancer survivors. *J Cancer Surviv Res Pract* 2008;**2**:296–302. doi:10.1007/s11764-008-0072-z

9 Baffert S, Hoang HL, Brédart A, *et al.* The patient-breast cancer care pathway: how could it be optimized? *BMC Cancer* 2015;**15**:394. doi:10.1186/s12885-015-1417-4

10 https://www.fondation-arc.org/support-information/brochure-retour-au-travail-apres-cancer.

11 R Core Team (2012) R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0. Available at: http://www.R-project.org/ [http://lib.stat.cmu.edu/r/CRAN. (last accessed 20 November 2016).

12 Jagsi R, Hawley ST, Abrahamse P, *et al.* Impact of adjuvant chemotherapy on long-term employment of survivors of early-stage breast cancer. *Cancer* 2014;**120**:1854–62. doi:10.1002/cncr.28607

13 Johnsson A, Fornander T, Rutqvist L-E, *et al.* Predictors of return to work ten months after primary breast cancer surgery. *Acta Oncol Stockh Swed* 2009;**48**:93–8. doi:10.1080/02841860802477899

14 Eaker S, Wigertz A, Lambert PC, *et al.* Breast cancer, sickness absence, income and marital status. A study on life situation 1 year prior diagnosis compared to 3 and 5 years after diagnosis. *PloS One* 2011;**6**:e18040. doi:10.1371/journal.pone.0018040

15 de Ruiter MB, Reneman L, Boogerd W, *et al.* Cerebral hyporesponsiveness and cognitive impairment 10 years after chemotherapy for breast cancer. *Hum Brain Mapp* 2011;**32**:1206–19. doi:10.1002/hbm.21102

16 Reinertsen KV, Cvancarova M, Loge JH, *et al.* Predictors and course of chronic fatigue in long-term breast cancer survivors. *J Cancer Surviv Res Pract* 2010;**4**:405–14. doi:10.1007/s11764-010-0145-7

17 Islam T, Dahlui M, Majid HA, *et al.* Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health* 2014;**14 Suppl 3**:S8. doi:10.1186/1471-2458-14-S3-S8

18 Munir F, Burrows J, Yarker J, *et al.* Women's perceptions of chemotherapy-induced cognitive side affects on work ability: a focus group study. *J Clin Nurs* 2010;**19**:1362–70. doi:10.1111/j.1365-2702.2009.03006.x

19 Hoving J, Broekhuizen M, Frings-Dresen M. Return to work of breast cancer survivors: a systematic review of intervention studies. *BMC Cancer* 2009;**9**. doi:10.1186/1471-2407-9-117

20 Nesvold I-L, Fosså SD, Holm I, *et al.* Arm/shoulder problems in breast cancer survivors are associated with reduced health and poorer physical quality of life. *Acta Oncol Stockh Swed* 2010;**49**:347–53. doi:10.3109/02841860903302905

21 Assis MR, Marx AG, Magna LA, *et al.* Late morbidity in upper limb function and quality of life in women after breast cancer surgery. *Braz J Phys Ther* 2013;**17**:236–43.

22 Devoogdt N, Van Kampen M, Christiaens MR, *et al.* Short- and long-term recovery of upper limb function after axillary lymph node dissection. *Eur J Cancer Care (Engl)* 2011;**20**:77–86. doi:10.1111/j.1365-2354.2009.01141.x

23 Hayes SC, Rye S, Battistutta D, *et al.* Upper-body morbidity following breast cancer treatment is common, may persist longer-term and adversely influences quality of life. *Health Qual Life Outcomes* 2010;**8**:92. doi:10.1186/1477-7525-8-92

24 Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. *PM R* 2014;**6**:170–83. doi:10.1016/j.pmrj.2013.08.605

25 Boyages J, Kalfa S, Xu Y, *et al.* Worse and worse off: the impact of lymphedema on work and career after breast cancer. *SpringerPlus* 2016;**5**:657. doi:10.1186/s40064-016-2300-8

26 Peugniez C, Fantoni S, Leroyer A, *et al.* Return to work after treatment for breast cancer: single-center experience in a cohort of 273 patients. *Ann Oncol Off J Eur Soc Med Oncol* 2010;**21**:2124–5. doi:10.1093/annonc/mdq556

27 Hawkes AL, Gollschewski S, Lynch BM, *et al.* A telephone-delivered lifestyle intervention for colorectal cancer survivors "CanChange": a pilot study. *Psychooncology* 2009;**18**:449–55. doi:10.1002/pon.1527

28 Sevellec M, Belin L, Bourrillon M-F, *et al.* [Work ability in cancer patients: Six years assessment after diagnosis in a cohort of 153 workers]. *Bull Cancer (Paris)* 2015;**102**:S5-13. doi:10.1016/S0007-4551(15)31212-1

29 VICAN2- https://www.inserm.fr/.../rapport_complet_la-vie-2-ans-apres-un-diagnostic-de-cancer-2014.

30 Drolet M, Maunsell E, Brisson J, *et al.* Not working 3 years after breast cancer: predictors in a population-based study. *J Clin Oncol Off J Am Soc Clin Oncol* 2005;**23**:8305–12. doi:10.1200/JCO.2005.09.500

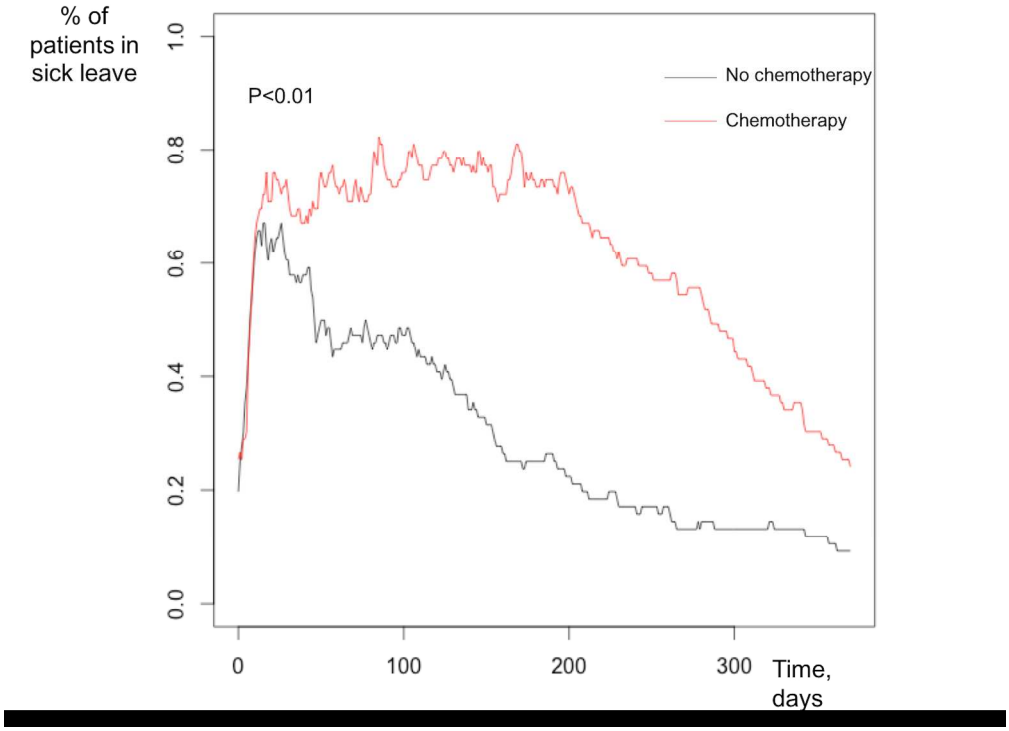


Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

264x200mm (300 x 300 DPI)

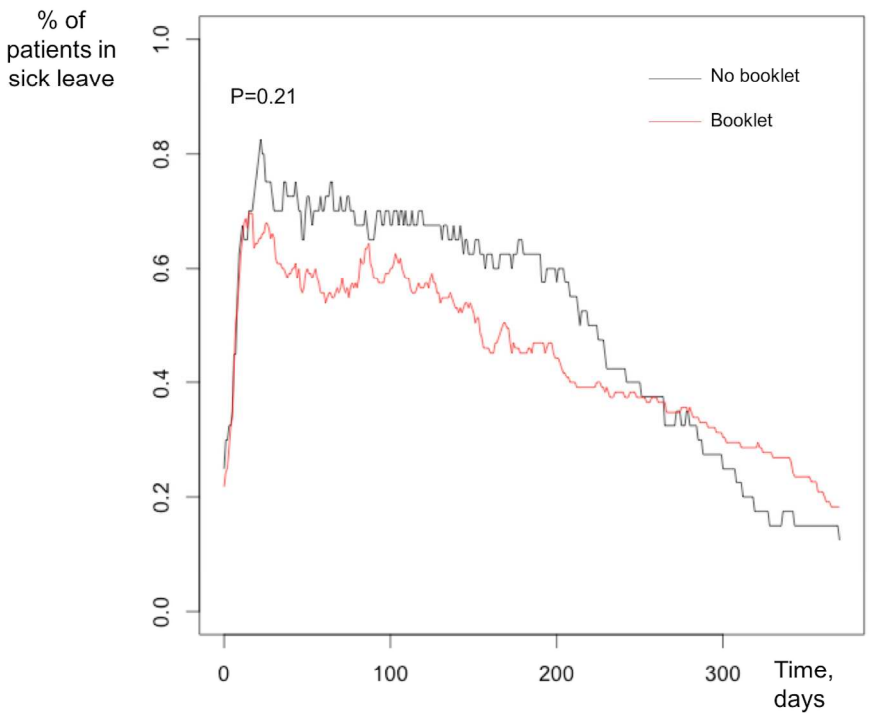
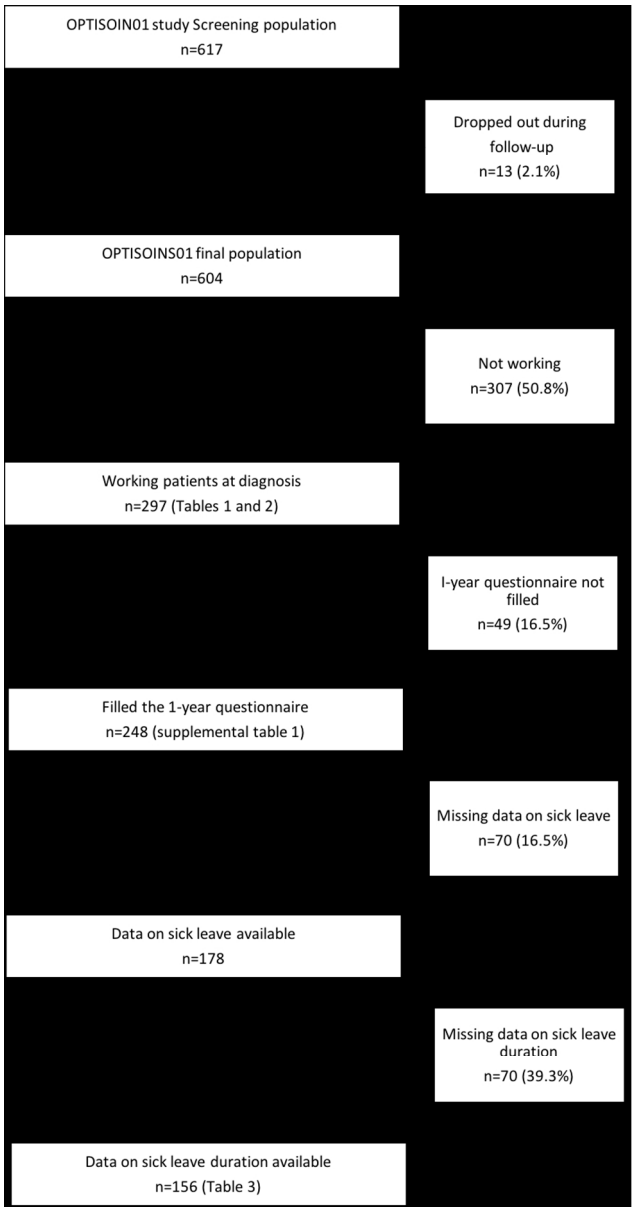


Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

262x205mm (300 x 300 DPI)



146x279mm (150 x 150 DPI)

Supplemental Table 1: Differences between patients who returned the 1-year questionnaire with data on sick leave (n=178) and no data on sick leave (n=70)

	Data on sick leave, n=178		No data on sick leave, n=70		
	n or median	% or range	n or median	% or range	p
Patient characteristics					
Age (years)	50	(29-67)	49	(27-77)	0.36
Type of occupation					**<0.05**
Farmer	1	1%	0	0%	
Self-employed	5	3%	0	0%	
Executive	72	40%	3	4%	
Employee	72	40%	27	39%	
Intermediate profession	22	12%	33	47%	
Blue-collar worker	2	1%	7	10%	
NA	4	2%	0	0%	
Personal income per month (€)					**<0.05**
<1900	71	40%	20	29%	
>1900	103	58%	37	53%	
NA	4	2%	13	19%	
Marital status					**<0.05**
Single	34	19%	18	26%	
Married	110	62%	39	56%	
Divorced	29	16%	10	14%	
Widow	2	1%	1	1%	
NA	3	2%	2	3%	
Breast cancer characteristics					
Type of cancer					0.32
Invasive	156	87,6%	61	87%	
In situ	21	11,8%	9	13%	
Lymph node involvement					0.12
Yes	43	24%	23	33%	
No	135	76%	47	67%	
Surgical patient care					
Breast surgery					**<0.05**
Conservative	133	75%	46	66%	
Radical	45	25%	24	34%	
Lymph node surgery					0.48
Sentinel lymph node procedure	122	69%	40	57%	
Axillary dissection	42	24%	24	34%	

	NA	14	8%	6	9%	
Surgical revision						0.24
	Yes	43	24%	16	23%	
	No	135	76%	54	77%	
Radiotherapy						**<0.05**
	Yes	167	94%	61	87%	
	No	11	6%	9	13%	
Chemotherapy						**<0.05**
	Yes	92	52%	33	47%	
	No	86	48%	37	53%	
Trastuzumab						0.42
	Yes	24	13%	9	13%	
	No	63	35%	22	31%	
	NA	91	51%	39	56%	
Hormone therapy						0.69
	Yes	129	72%	49	70%	
	No	49	28%	21	30%	
Patient management						
Modes of diagnosis						0.45
	Organized screening	37	21%	12	17%	
	Individual screening	74	42%	26	37%	
	Clinical signs	67	38%	32	46%	
Type of hospitalization						0.78
	Outpatient surgery	108	61%	43	61%	
	Inpatient surgery	70	39%	27	39%	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4 and 5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	9
		(*e*) Describe any sensitivity analyses	9
Results			9

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Supplemental figre 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 and 11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
		(*b*) Report category boundaries when continuous variables were categorized	12-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12-14
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13, 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Determinants of return at work of breast cancer patients: results from the OPTISOINS01 French prospective study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020276.R2
Article Type:	Research
Date Submitted by the Author:	01-Mar-2018
Complete List of Authors:	Arfi, Alexandra; Institut Curie, Surgery Baffert, Sandrine; CEMKA-EVAL, Health Economist Soilly, A-L; Universite de Bourgogne IUT Dijon-Auxerre, Health Economist huchon, cyrille; Hôpital Poissy, Gynecology Reyal, Fabien; Institut Curie, Surgery Asselain, Bernard; Institut Curie, Biostatistics Neffati, Souhir; Institut Curie, Clinical Research and Innovation Department Rouzier, Roman; Institut Curie, Surgery Hequet, Delphine; Institut Curie-Centre René Huguenin, Surgical oncology
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Occupational and environmental medicine
Keywords:	Breast tumours < ONCOLOGY, OCCUPATIONAL & INDUSTRIAL MEDICINE, PUBLIC HEALTH

Determinants of return at work of breast cancer patients: results from the OPTISOINS01 French prospective study.

Authors:

Alexandra Arfi[1], Sandrine Baffert[2], Anne-Laure Soilly[3], Cyrille Huchon[4,5], Fabien Reyal[1,6], Bernard Asselain[7], Souhir Neffati[8], Roman Rouzier[1,9], Delphine Héquet[1,9]

Affiliations :

1: Department of Surgical Oncology, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

2: Health Economics, CEMKA-EVAL, Bourg-la-Reine, 43 boulevard du Maréchal-Joffre, 92340 Bourg-la-Reine, France

3: Health Economics, Bourgogne Franche-Comté University, EA 7467, 2 boulevard Gabriel, 21000 Dijon, France

4: Department of Obstetrics and Gynecology, Hôpital de Poissy-St Germain, 10 Rue du Champ Gaillard, 78300 Poissy, France

5: Equipe d'Accueil 7285, Risk and Safety in Clinical Medicine for Women and Perinatal Health, University Versailles-Saint-Quentin, 2 av de la source de la Bièvre, 78180 Montigny-le-Bretonneux, France

6: Residual Tumor and Response to Treatment Lab, Translational Research Department, Institut Curie, 75005, Paris, France

7: Department of Biostatistics, Institut Curie-Centre René Huguenin, 35 Rue Dailly, 92210 Saint-Cloud, France

8: Clinical Research and Innovation Department, Sponsorship division, Institut Curie, 92210 Saint-Cloud, France

9: René-Huguenin hospital, Institut Curie, Inserm U900 – Bioinformatics, biostatistics, epidemiology and computational systems. Cancer biology, 35, rue Dailly, 92210 Saint-Cloud, France

Corresponding author:

Delphine HEQUET

Postal address: 35 rue Dailly, 92210 St Cloud, France

e-mai l: delphine.hequet@gmail.com

Phone number: 0033147111515

Word count: 2431

Contributorship statement:

Delphine Hequet, Roman Rouzier and Sandrine Baffert designed the study.

Bernard Asselain and Souhr Neffati contributed to the design and implementation of the research.

Sandrine Baffert and Anne-Laure Soilly performed the health economic analysis.

Alexandra Arfi and Delphine Hequet performed all the remaining statistical analysis and wrote the manuscript.

Cyrille Huchon and Fabien Reyal contributed to the clinical study, patients' inclusion and analysis of the results.

All the authors reviewed and approved the final version of the manuscript.

ABSTRACT

Introduction: Return to work (RTW) after breast cancer (BC) is still a new field of research. The factors determining shorter sick leave duration of BC patients have not been clearly identified. The aim of this study was to describe work during BC treatment and to identify factors associated with sick leave duration.

Materials and methods: An observational, prospective, multicenter study was conducted among women with operable BC. A logbook was given to all working patients to record sociodemographic and work-related data over a one-year period.

Results: Work-related data after BC were available for 178 patients (60%). Median age at diagnosis was 50 years (27-77), 87.9% of patients had an invasive form of BC and 25.3% a lymph node involvement. 25.9% had a radical surgery and 24.2% had an axillary dissection. Radiotherapy was performed in 90.9% of patients and chemotherapy in 48.1%. Sick leave was prescribed for 165 patients (92.7%) for a median of 155 days. On univariate analysis, invasive BC (p=0.025), lymph node involvement (p=0.005), radical surgery (p=0.025), axillary dissection (p=0.004), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the patient information booklet on RTW (p=0.047) were associated with a longer duration of sick leave. On multivariate analysis, chemotherapy was associated with longer sick leave (OR: 3.5; [95%CI: 1.6-7.9]; p=0.002). The cost of sick leave to French National Health Insurance was fourfold higher in the case of chemotherapy (p<0.001).

Conclusion: Advanced disease and chemotherapy are major factors that influence sick leave duration during the management of BC.

Strengths and limitations of this study:

- Prospective multicentric study
- Description of factors associated to long sick leave
- Multimodal analysis including evaluation of costs of sick leave
- Few qualitative information

Keywords: breast cancer, return to work, absence duration, chemotherapy.

Data sharing statement: No additional data available

Ethics: This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

Funding: Delphine Hequet benefitted from a “Fondation pour la Recherche Medicale” (FDM20140630453) grant to conduct this study. This study was supported by a grant from the French National Cancer Institute (Institut National du Cancer, PRME-K2013), dedicated to economic studies of innovative techniques.

What is already known on this subject?

Return to work after breast cancer is a delicate step in the real-life reintegration. Breast cancer patients have difficulties at work even 5 years after the end of the treatments. The factors that maintain patients at work during breast cancer are rarely described.

What this study adds?

This prospective study describes sick leaves during the first year following the diagnosis of early breast cancer. After one year, 20% of the patients did not return to work. Chemotherapy dramatically increased the duration of sick leaves, whereas an early information on support can reduce sick leaves. Costs of sick leaves are major.

INTRODUCTION

Improvements in early detection and treatment have resulted in an increasing number of breast cancer (BC) survivors [1] .Treatments mostly focus on curing the disease and preventing metastatic relapse. About one-third of women diagnosed with BC are under the age of 55 with a 10-year survival close to 80% [2].Many patients therefore recover and resume their activities of daily living during or after treatment. Return to work (RTW) is an event at the end of sick leave, consisting in resuming professional activity. RTW after BC is still a new, but important aspect of survivorship research, not only from a societal point of view, as it provides financial resources for rehabilitation of cancer survivors and contributes to psychosocial well-being, including physical and mental health [3]. Some BC cancer survivors experience reduced work ability [4–8]. Difficulties at work or unemployment differ according to the type of BC treatment. Cancer treatment varies according to the stage of the disease and can include surgery, chemotherapy, radiotherapy and hormone therapy. For many cancer patients, return to work helps them to recover from treatment and also constitutes a positive step towards the future. The identification of factors that maintain patients at work during ~~and after~~ BC treatment could help healthcare professionals to more accurately identify patients at risk of ~~RTW~~ work-related difficulties in order to provide them with adapted support during BC management. The aim of this prospective study was to describe work during and after BC management and identify factors associated with either cessation or maintenance at work.

MATERIALS AND METHODS

OPTISOINS01 was an observational, prospective, multicenter study conducted from December 2014 to March 2016 among BC patients from a regional health territory. The primary objective of the Optisoins01 study was to identify the main care pathway after 1 year of early BC and to evaluate costs from various perspectives. Return to work evaluation was one of the secondary objectives of the study. The Optisoins01 study design has been previously described [9]. Eight non-profit hospitals participated in the study: 3 teaching hospitals, 4 general hospitals and 1 comprehensive cancer center. Inclusion criteria were: women aged ≥18 years with previously untreated, first, histologically confirmed, operable BC. Exclusion criteria were: metastatic, locally advanced, or inflammatory BC, previous history of BC.

After BC diagnosis, a work and cancer information booklet had to be given to all working patients. Our Institute has designed an information booklet in collaboration with occupational physicians and the Paris Regional Health Insurance (Caisse Régionale d'Assurance Maladie d'Île-de-France). This document includes the testimonies from employees, advice and practical information to help patients anticipate difficulties and find support: possibility of part-time work, career development plan, roles of occupational physicians and general practitioners. The booklet is freely available online with the support of the "ARC" Foundation [10].

After inclusion, all patients were given a logbook in which to record, throughout the year, sociodemographic data (age, marital status, type of occupation, personal income…), out-of-pocket health expenses and an 1-year-occupational questionnaire for employed women including dates of work and absence from work during treatments, job adjustments, on-shift status and the perceived quality of reintegration with standardized self-questionnaire (income change, difficulties at work with co-workers and/or with superiors…). Patients were

asked to fill in the questionnaire prospectively during the all study period. During the second half of the year, clinical research assistants made 2 phone calls to remind patients to fill in the logbook. Questionnaires were collected at the end of the study. Types of occupations were classified according to the French *Institut National de la Statistique et des Etudes Economiques (INSEE)* classification.

Two groups of patients were compared in order to determine the factors associated with sick leave duration: longer sick leave (longer or equal to the median duration) and shorter sick leave (shorter than the median duration). Fisher's exact test or Student's t-test were used to analyze these factors. These tests were two sided with a 0.05 level of significance. Multivariate analysis was performed using a logistic regression model. We considered adjusted p-value for multiple comparisons. Sick leave over a 1-year period was described according to whether or not the patients were treated by chemotherapy. Differences in the areas under the curves of the 2 populations were compared to 1,000 permutations of random allocation of chemotherapy. The same analysis was performed according to whether or not the patients had received the work information booklet. Differences were considered significant for $p<0.05$. All statistical analyses were performed with R software [11].

The cost of sick leave for National Health Insurance was calculated on the basis of the monthly income declared by the patients, the duration of sick leave and the national sick leave allowance scale.

This study was registered with ClinicalTrials.gov (Identifier: NCT02813317) and was approved by the French National ethics committee (CCTIRS Authorization No. 14.602 and CNIL DR-2014-167) covering research at all participating hospitals.

Patient and public Involvement: A sample of patients participated to the questionnaire development concerning work activity before implementation of the study. Patients were

involved in the study by actively completing the questionnaires during 1 year. A results report will be sent to the study participants.

RESULTS

Six hundred and four patients with a median age of 58 years (range: 24-98) were included in the Optisoins01 study, including 297 patients (48.2%) who were working at the time of BC diagnosis. The present study focused on these 297 patients.

Detailed patient characteristics and cancer characteristics are presented in Table 1. The median age of the women was 50 (range: 27-77) years, 54 women (18.2%) were single, 153 (51.5%) were married, 39 (13.1%) were divorced and 3 (1.0%) were widows. Two hundred and sixty-one patients (87.9%) had invasive BC and 35 (11.8%) had *in situ* BC. Seventy-five women (25.3%) presented axillary lymph node involvement.

Table 1: Patient and cancer characteristics and breast cancer treatments (n=297)

	n or median	% or range
Patient characteristics		
Age (years)	50	(27-77)
Marital status		
Single	54	18.2%
Married	153	51.5%
Divorced	39	13.1%
Widow	3	1%
NA	48	16.2%
Breast cancer characteristics		
Modes of diagnosis		
Organized screening	60	20.2%
Individual screening	114	38.4%
Clinical signs	123	41.4%
Type of cancer		
Invasive	261	87.9%
In situ	35	11.8%
NA	1	0.3%

Lymph node involvement			
	Yes	75	25.3%
	No	222	74.7%
Surgery			
Breast surgery			
	Conservative	220	74.1%
	Radical	77	25.9%
Lymph node surgery			
	Sentinel lymph node procedure	203	68.4%
	Axillary dissection	72	24.2%
	NA	22	7.4%
Surgical revision			
	no	227	76.4%
	1	60	20.2%
	>1	10	3.4%
Type of hospitalization			
	Outpatient surgery	107	36%
	Conventional surgery	190	64%
Adjuvant therapies			
Radiotherapy			
	No	27	9.1%
	Yes	270	90.9%
Chemotherapy			
	Yes	143	48.1%
	No	154	51.9%
Trastuzumab			
	Yes	36	12.1%
	No	100	33.7%
	NA	161	54.2%
Hormone therapy			
	Yes	220	74.1%
	No	77	25.9%

Two hundred and twenty women (74.1%) underwent breast-conserving surgery and 77 (25.9%) underwent radical mastectomy (Table 1). A sentinel lymph node procedure was performed for 203 patients (68.4%). Seventy patients required at least 1 reoperation for the following reasons: positive surgical margins and secondary mastectomy, sentinel lymph

node procedure following discovery of an invasive tumor, axillary dissection following positive sentinel lymph node biopsy and surgical complications (abscess, hematoma, etc.). After surgery, 90.9% of patients received radiotherapy 48.1% of patients received adjuvant chemotherapy and 74.1% of patients received hormone therapy.

Most patients were executives (31.4%) or employees (33.3%). Most patients (47.1%) had a monthly income > €1,900. Work data after BC were available for 178 patients (60%, supplemental Figure 1). Patients who did not complete ~~the 1-year~~ work questionnaire in the logbook during one year were globally less compliant with the study and less medicalized (supplemental table 1). Sick leave was prescribed for 165 patients (92.7%). Patients had only one sick leave in 52.2% of cases, 2 sick leaves in 21.9% of cases and 3 or more sick leaves in 18.5% of cases. Median duration of sick leave was 155 days (range: 5-365). After treatment, 7 patients (3.9%) lost their jobs and 46.1% had reduced income. Patients encountered difficulties with their co-workers in 3.4% of cases, with their superiors in 3.9% of cases and for undocumented reasons in 12.9% of cases. Work-related factors are summarized in Table 2.

Table 2: Work characteristics before and after BC

	n or median	% or range
Work characteristics before breast cancer, n=297		
Type of occupation		
Farmer	1	0.3%
Self-employed	8	2.5%
Executive	99	31.4%
Employee	105	33.3%
Intermediate profession	29	9.2%
Blue-collar worker	2	0.6%
NA	53	22.9%
Personal income per month (€)		
no income	6	2%

	< 1900	104	35%
	>1900	140	47.1%
	NA	47	15.8%
Work characteristics after breast cancer, n=178			
Dismissal		7	3.9%
Income change			
	decreased	82	46.1%
	increased	3	1.7%
	stable	73	41%
	NA	20	11.2%
Decreased income (%), n=82			
	<10%	37	45.1%
	10-30%	13	15.8%
	30-60%	5	6.1%
	>60%	3	3.7%
	NA	24	29.3%
Sick leave			
	Yes	165	92.7%
	No	13	7.3%
Number of sick leaves (n=165)			
	1	93	52.2%
	2	39	21.9%
	>2	33	18.5%
Duration of sick leave (days)		155	(5-365)
Difficulties at work (n=36)			
	with coworkers	6	3.4%
	with superiors	7	3.9%
	other	23	12.9%

On univariate analysis, the presence of clinical signs leading to a diagnosis of BC (p<0.001), an invasive form of BC (p=0.02), lymph node involvement (p=0.005), radical surgery (p=0.02), axillary dissection (p<0.001), chemotherapy (p<0.001), personal income < €1,900/month (p=0.03) and not having received the work and cancer information booklet (p=0.047) were associated with a longer total duration of sick leave (Table 3). Moreover, patients with

longer sick leave were more likely to have reduced income after treatment of their disease (p=0.0012).

Table 3: Determinants and consequences of long sick leave

	Sick leave <155 days, n=79		Sick leave ≥155, days n=77		
	n or median	% or range	n or median	% or range	p
Patient characteristics					
Age (years)	50.6	(27-59)	50	(29-77)	0.52
Type of occupation					0.09
Farmer	0	0%	0	0%	
Self-employed	3	3.8%	1	1.3%	
Executive	36	45.6%	29	37.7%	
Employee	25	31.6%	38	49.4%	
Intermediate profession	13	16.5%	7	9.1%	
Blue-collar worker	1	1.3%	0	0%	
NA	1	1.3%	2		
Personal income per month (€)					**0.03**
< 1900	25	31.6%	37	48.1%	
> 1900	54	68.4%	38	49.4%	
NA	0	0%	2	2.6%	
Marital status					0.76
Single	18	22.8%	12	15.6%	
Married	47	59.5%	49	63.6%	
Divorced	12	15.2%	14	18.2%	
Widow	1	1.3%	1	1.3%	
NA	1	1.3%	1	1.3%	
Breast cancer characteristics					
Type of cancer					**<0.001**
Invasive	63	79.7%	74	96.1%	
In situ	16	20.3%	3	3.9%	
Lymph node involvement					**0.005**
Yes	11	13.9%	**26**	**33.8%**	
No	68	86.1%	**52**	**67.5%**	
Surgery					
Breast surgery					**0.02**
Conservative	66	83.5%	50	64.9%	
Radical	13	16.5%	27	35.1%	
Lymph node surgery					**<0.001**

Sentinel lymph node procedure	62	78.5%	48	62.3%	
Axillary dissection	9	11.4%	26	33.8%	
NA	8	10.1%	3	3.9%	
Surgical revision					0.06
Yes	13	16.5%	23	29.9%	
No	66	83.5%	54	70.1%	
Radiotherapy					0.53
Yes	72	91.1%	74	96.1%	
No	7	8.9%	3	3.9%	
Chemotherapy					**<0.001**
Yes	25	31.6%	56	72.7%	
No	54	68.4%	21	27.3%	
Trastuzumab					0.54
Yes	9	11.4%	12	15.6%	
No	16	20.3%	40	51.9%	
NA	54	68.4%	25	32.5%	
Hormone therapy					0.05
Yes	50	63.3%	61	79.2%	
No	29	36.7%	16	20.8%	
Patient management					
Modes of diagnosis					**<0.001**
Organized screening	15	19%	21	27.3%	
Individual screening	43	54.4%	20	26%	
Clinical signs	21	26.6%	36	46.8%	
Type of hospitalization					**<0.001**
Outpatient surgery	58	73.4%	34	44,.2%	
Inpatient surgery	21	26.6%	43	55.8%	
Work and cancer information booklet					
Yes	64	81%	52	67.5%	**0.047**
No	15	19%	25	32.5%	
Return to work					
Dismissal	1	1.3%	3	3.9%	0.62
Income change					
decreased	23	29.1%	48	62.3%	**<0.001**
increased	0	0%	2	2.6%	
stable	37	46.8%	24	31.2%	
NA	19	24.1%	3	3.9%	
Decreased income (%)					0.61
<10%	11	13.9%	21	27.3%	
10-30%	4	5.1%	7	9.1%	
30-60%	0	0%	4	5,2%	

	>60%	0	0%	3	3.9%	
	NA	64	81%	42	54.5%	
Difficulties at work						
	with coworkers	2	2.5%	3	3.9%	0.67
	with superiors	0	0%	6	7.8%	0.17
	other	7	8.9%	14	18.2%	0.93

On multivariate analysis, chemotherapy was the only independent factor associated with longer sick leave (OR: 3.5, [95%CI: 1.6-7.9], p=0.002). Patients treated by chemotherapy had longer sick leave than those not treated by chemotherapy (Figure 1). The difference in terms of the 1-year distribution of sick leave was not statistically significant between patients according to whether or not they had received the work information booklet (Figure 2).

Considering the working population of OPTISOINS01 study with complete data on sick leave and salary, the median cost of sick leave for National Health Insurance was €8,841 per patient per year from diagnosis. In univariate and multivariate analysis, the only determinant of sick leave costs found in this study was the administration of chemotherapy, with a fourfold higher median allowance for patients treated with adjuvant chemotherapy.

DISCUSSION

Although many BC cancer survivors are able to return to a normal work life after treatment, our study confirms that many women of working ages do not. Sick leave is frequently prescribed and is often long, with a median sick leave of 155 days in this study.

Factors associated with long sick leave (>155 days) were severe or advanced forms of BC. The duration of sick leave was also associated with the mode of diagnosis, as patients diagnosed by breast screening presented shorter sick leaves. Public health authorities should

therefore promote breast screening in order to decrease the proportion of advanced forms of BC and aggressive therapies with severe consequences on work and personal activities. Consequently, longer sick leave was also associated with more aggressive therapy, such as radical surgery, axillary dissection, and chemotherapy. These results are similar to those published in the literature [4,7,8,12,13]. Chemotherapy is an aggressive treatment that can be necessary in order to improve survival, but which has long-lasting consequences in terms of self-esteem (alopecia…), chronic pain (neuropathy…), and chronic fatigue, that play an important role in return to work and maintenance at work [6]. BC survivors may have to deal with the side effects specific to this type of treatment. Although many side effects of chemotherapy are only temporary [14], some studies have shown that chemotherapy may impact on cognitive functioning [15] and fatigue [16] up to 10 years after diagnosis. Cognitive functioning and fatigue have both been associated with impaired work functioning [17]. Munir et al [18]reported that up to 62–84% of women resumed work either during treatment with chemotherapy or following completion of treatment. As a result of their cognitive limitations, women reported that they experienced difficulties with their work ability, particularly difficulties doing multiple tasks, reduced clarity of decisions, deficits in clear thinking and feelings of being inept due to short-term memory [19] . Rapid progress is being made in the field of chemotherapy with the routine use of new genomic signature tests that allow more accurate targeting of patient likely to benefit from chemotherapy. According to Nesvold et al [20] and Eaker et al [14] mastectomy and axillary lymph node dissection may influence working life long after treatment due to an increased risk of chronic pain. BC survivors are more likely to suffer from upper extremity impairments or lymphedema than are other cancer survivors [21–24], which are responsible for difficulties returning to work [25,26].

The work and cancer information booklet appeared to help patients return to work with significantly shorter sick leave in univariate analysis, but not in the multivariate analysis. However, this suggests that an action, such as an active support, could help to reduce sick leave duration. The information booklet advises women to attend the occupational medicine service. In France, occupational medicine plays an essential role, but the patient is not obliged to consult the occupational physician when sick leave is < 3 months. However, at 3 months, the occupational physician and the employee must determine the modalities of return to work, based on the employee's state of health and the characteristics of the workplace. These arrangements concern the employee himself and the work collective with, if necessary, actions so that the reception is assured to the return. Setting up of a schedule, reduction of working hours, modification of physical, mental or workplace loads can also be instituted at the time of return to work. The occupational physician can provide recommendations to the employer, unless the employer refuses. The results obtained with this handbook are particularly encouraging and suggest that more individual supports should be developed. Health coaching by telephone and/or face-to-face interview have already been tested [27–29], showing positive significant outcomes on physical activity, body mass index, pain management, acceptance of disease and self-confidence among cancer survivors. Coaching methods have never been tested in the management of working patients during cancer treatment ~~maintenance~~. Our Institute is therefore setting up a prospective randomized study (OPTICOACH) with tailored support intervention to enhance RTW after BC in collaboration with a professional coach, consisting of individual interviews or small group workshops over a period of 3 years.

Difficulties returning to work appear to extend over a period of many years. Sevellec et al [28] showed that, six years after returning to work, one employee out of two was still

working in the same company. Rather than disappearing, the difficulties identified many years after BC persist for a long time after stopping treatment. It is therefore essential to identify the factors associated with longer sick leave and RTW difficulties in order to help working patients and prevent these long-term problems. The VICAN 2 study [29] focused on the factors associated to difficulties at RTW. This large study was carried out in 2014 by the French National Cancer Institute, on the living conditions of people with cancer (not only BC), two years after the diagnosis. The people most vulnerable to job loss two years after the cancer diagnosis are mainly those working in the so-called socio-professional execution categories, the youngest and oldest, married people with a level of education below the baccalaureate level, and those with precarious contracts.

One of the potential biases of this study concerns the characteristics of the study population, as almost the majority of women belonged to the wealthiest social classes, as 45.6% of patients were executives and only 1.3% were blue collar workers. More than sixty-eight percent of patients had a personal monthly income > €1,900 and 36.7% had a personal monthly income > €2,600. This distribution does not exactly reflect French society; in France, according to the INSEE statistics of 2014, the median monthly income was €1,772. Similarly to our results, a Canadian team [30] has shown that women with an annual income less than C$20,000 were less likely to return to work than those whose income exceeded C$50,000. The French social protection system also plays a role, as it provides cancer survivors with the possibility of replacement income, allowing women to decide whether or not they wish to return to work immediately. Providing assistance and support to all working patients should therefore be a priority.

CONCLUSION

Advanced disease and chemotherapy are major factors that influence return to work with longer sick-leave. Systematic screening or use of innovative tools, such as genomic signatures, can facilitate earlier diagnosis and reduce aggressive therapies.

Depending on the type of treatment, on the stage of the disease and on the type of occupation, information and coaching methods with the occupational medicine service should systematically be given to working women, helping them to anticipate job adjustments with flexibility of work schedule for example.

Personalized coaching methods have been successfully used to promote acceptance of disease and self-confidence and should be tested in the management of return to work.

Figures:

Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

Supplemental Figure 1: Flow Chart

Competing Interests: The authors declare that they have no competing interests.

Funding: This study was supported by a grant from the French National Cancer Institute dedicated to economic studies of innovative techniques. Delphine Héquet benefit from a grant of "Fondation pour la Recherche Médicale" to conduct this study.

REFERENCES

1 Breast Cancer Facts & figures 2013-2014 (2013) Atlanta: American Cancer Society, Inc. http://cancer. org/acs/groups/content/@research/documents/document/acspc-042725.pdf. Accessed 9/20/2014.

2 Verdecchia A, Francisci S, Brenner H, *et al.* Recent cancer survival in Europe: a 2000-02 period analysis of EUROCARE-4 data. *Lancet Oncol* 2007;**8**:784–96. doi:10.1016/S1470-2045(07)70246-2

3 Mehnert A, de Boer A, Feuerstein M. Employment challenges for cancer survivors: Employment Challenges. *Cancer* 2013;**119**:2151–9. doi:10.1002/cncr.28067

4 Balak F, Roelen CAM, Koopmans PC, *et al.* Return to work after early-stage breast cancer: a cohort study into the effects of treatment and cancer-related symptoms. *J Occup Rehabil* 2008;**18**:267–72. doi:10.1007/s10926-008-9146-z

5 de Boer AGEM, Taskila TK, Tamminga SJ, *et al.* Interventions to enhance return-to-work for cancer patients. *Cochrane Database Syst Rev* 2015;:CD007569. doi:10.1002/14651858.CD007569.pub3

6 Fantoni SQ, Peugniez C, Duhamel A, *et al.* Factors related to return to work by women with breast cancer in northern France. *J Occup Rehabil* 2010;**20**:49–58. doi:10.1007/s10926-009-9215-y

7 Hedayati E, Johnsson A, Alinaghizadeh H, *et al.* Cognitive, psychosocial, somatic and treatment factors predicting return to work after breast cancer treatment. *Scand J Caring Sci* 2013;**27**:380–7. doi:10.1111/j.1471-6712.2012.01046.x

8 Lavigne JE, Griggs JJ, Tu XM, *et al.* Hot flashes, fatigue, treatment exposures and work productivity in breast cancer survivors. *J Cancer Surviv Res Pract* 2008;**2**:296–302. doi:10.1007/s11764-008-0072-z

9 Baffert S, Hoang HL, Brédart A, *et al.* The patient-breast cancer care pathway: how could it be optimized? *BMC Cancer* 2015;**15**:394. doi:10.1186/s12885-015-1417-4

10 https://www.fondation-arc.org/support-information/brochure-retour-au-travail-apres-cancer.

11 R Core Team (2012) R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; ISBN 3-900051-07-0. Available at: http://www.R-project.org/ [http://lib.stat.cmu.edu/r/CRAN. (last accessed 20 November 2016).

12 Jagsi R, Hawley ST, Abrahamse P, *et al.* Impact of adjuvant chemotherapy on long-term employment of survivors of early-stage breast cancer. *Cancer* 2014;**120**:1854–62. doi:10.1002/cncr.28607

13 Johnsson A, Fornander T, Rutqvist L-E, *et al.* Predictors of return to work ten months after primary breast cancer surgery. *Acta Oncol Stockh Swed* 2009;**48**:93–8. doi:10.1080/02841860802477899

14 Eaker S, Wigertz A, Lambert PC, *et al.* Breast cancer, sickness absence, income and marital status. A study on life situation 1 year prior diagnosis compared to 3 and 5 years after diagnosis. *PloS One* 2011;**6**:e18040. doi:10.1371/journal.pone.0018040

15 de Ruiter MB, Reneman L, Boogerd W, *et al.* Cerebral hyporesponsiveness and cognitive impairment 10 years after chemotherapy for breast cancer. *Hum Brain Mapp* 2011;**32**:1206–19. doi:10.1002/hbm.21102

16 Reinertsen KV, Cvancarova M, Loge JH, *et al.* Predictors and course of chronic fatigue in long-term breast cancer survivors. *J Cancer Surviv Res Pract* 2010;**4**:405–14. doi:10.1007/s11764-010-0145-7

17 Islam T, Dahlui M, Majid HA, *et al.* Factors associated with return to work of breast cancer survivors: a systematic review. *BMC Public Health* 2014;**14 Suppl 3**:S8. doi:10.1186/1471-2458-14-S3-S8

18 Munir F, Burrows J, Yarker J, *et al.* Women's perceptions of chemotherapy-induced cognitive side affects on work ability: a focus group study. *J Clin Nurs* 2010;**19**:1362–70. doi:10.1111/j.1365-2702.2009.03006.x

19 Hoving J, Broekhuizen M, Frings-Dresen M. Return to work of breast cancer survivors: a systematic review of intervention studies. *BMC Cancer* 2009;**9**. doi:10.1186/1471-2407-9-117

20 Nesvold I-L, Fosså SD, Holm I, *et al.* Arm/shoulder problems in breast cancer survivors are associated with reduced health and poorer physical quality of life. *Acta Oncol Stockh Swed* 2010;**49**:347–53. doi:10.3109/02841860903302905

21 Assis MR, Marx AG, Magna LA, *et al.* Late morbidity in upper limb function and quality of life in women after breast cancer surgery. *Braz J Phys Ther* 2013;**17**:236–43.

22 Devoogdt N, Van Kampen M, Christiaens MR, *et al.* Short- and long-term recovery of upper limb function after axillary lymph node dissection. *Eur J Cancer Care (Engl)* 2011;**20**:77–86. doi:10.1111/j.1365-2354.2009.01141.x

23 Hayes SC, Rye S, Battistutta D, *et al.* Upper-body morbidity following breast cancer treatment is common, may persist longer-term and adversely influences quality of life. *Health Qual Life Outcomes* 2010;**8**:92. doi:10.1186/1477-7525-8-92

24 Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. *PM R* 2014;**6**:170–83. doi:10.1016/j.pmrj.2013.08.605

25 Boyages J, Kalfa S, Xu Y, *et al.* Worse and worse off: the impact of lymphedema on work and career after breast cancer. *SpringerPlus* 2016;**5**:657. doi:10.1186/s40064-016-2300-8

26 Peugniez C, Fantoni S, Leroyer A, *et al.* Return to work after treatment for breast cancer: single-center experience in a cohort of 273 patients. *Ann Oncol Off J Eur Soc Med Oncol* 2010;**21**:2124–5. doi:10.1093/annonc/mdq556

27 Hawkes AL, Gollschewski S, Lynch BM, *et al.* A telephone-delivered lifestyle intervention for colorectal cancer survivors "CanChange": a pilot study. *Psychooncology* 2009;**18**:449–55. doi:10.1002/pon.1527

28 Sevellec M, Belin L, Bourrillon M-F, *et al.* [Work ability in cancer patients: Six years assessment after diagnosis in a cohort of 153 workers]. *Bull Cancer (Paris)* 2015;**102**:S5-13. doi:10.1016/S0007-4551(15)31212-1

29 VICAN2- https://www.inserm.fr/.../rapport_complet_la-vie-2-ans-apres-un-diagnostic-de-cancer-2014.

30 Drolet M, Maunsell E, Brisson J, *et al.* Not working 3 years after breast cancer: predictors in a population-based study. *J Clin Oncol Off J Am Soc Clin Oncol* 2005;**23**:8305–12. doi:10.1200/JCO.2005.09.500

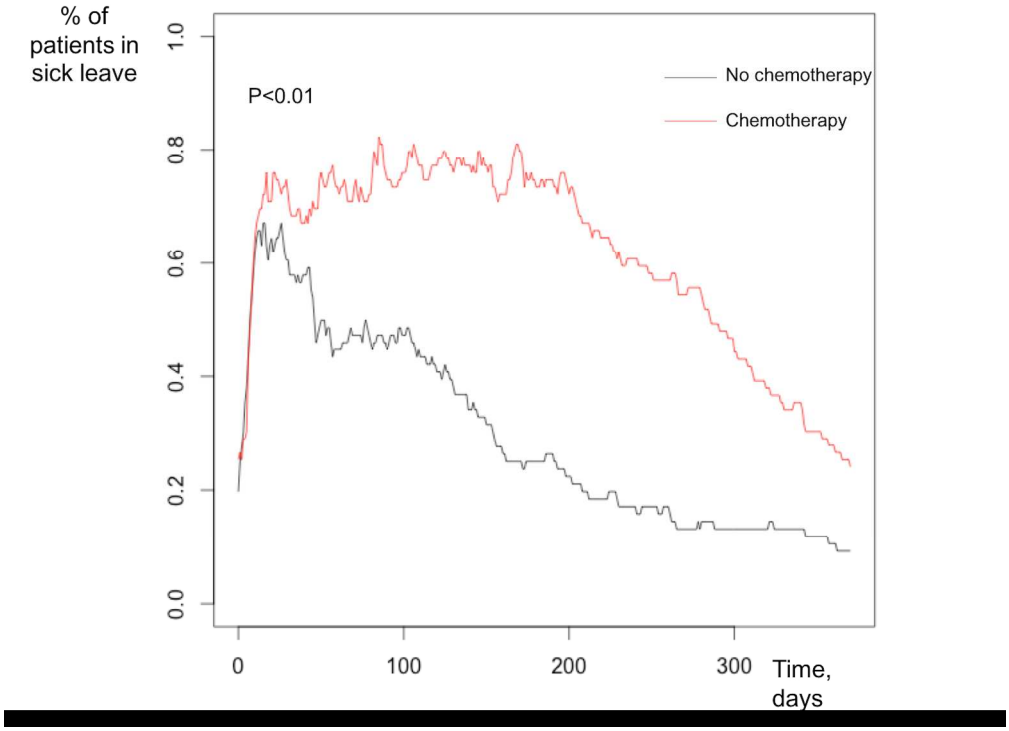


Figure 1: Percentage of patients on sick leave at 1-year follow-up depending on the presence or absence of chemotherapy

264x200mm (300 x 300 DPI)

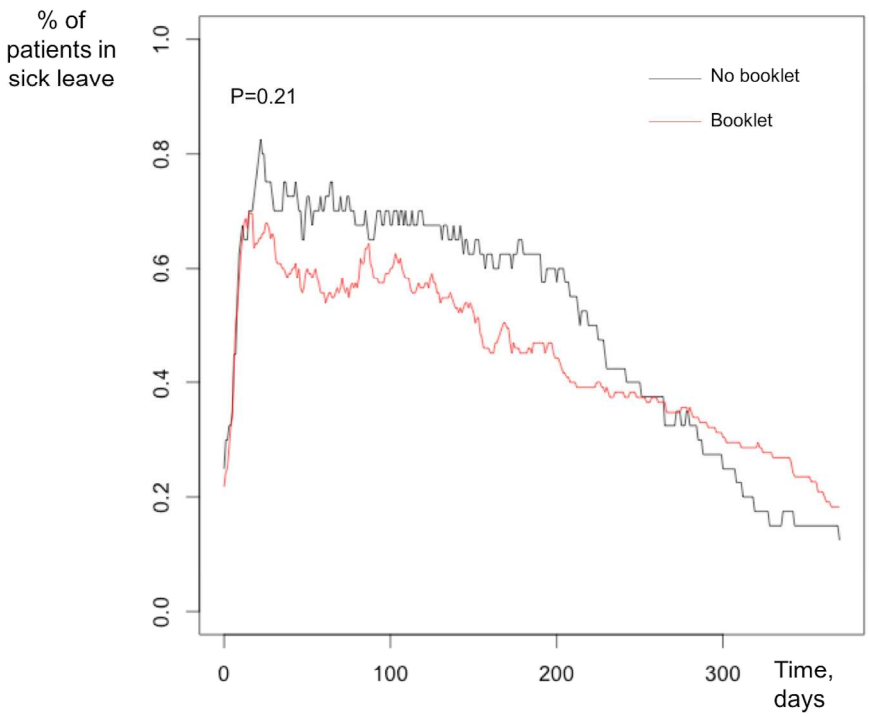
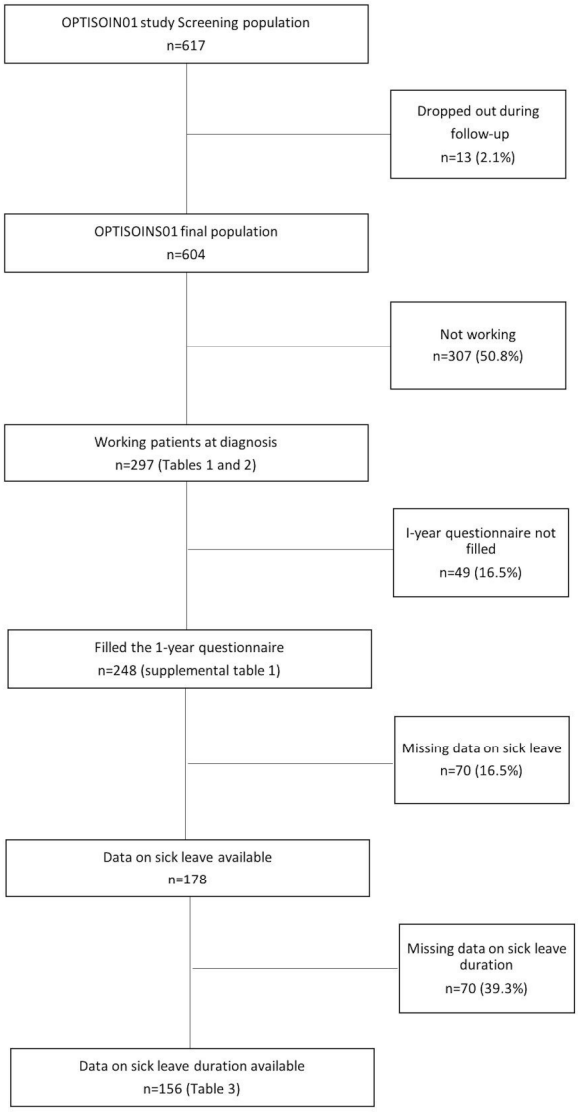


Figure 2: Percentage of patients on sick leave at 1-year follow-up depending on whether or not they had been given the work information booklet

262x205mm (300 x 300 DPI)



191x304mm (300 x 300 DPI)

Supplemental Table 1: Differences between patients who returned the 1-year questionnaire with data on sick leave (n=178) and no data on sick leave (n=70)

	Data on sick leave, n=178		No data on sick leave, n=70		
	n or median	% or range	n or median	% or range	p
Patient characteristics					
Age (years)	50	(29-67)	49	(27-77)	0.36
Type of occupation					**<0.05**
Farmer	1	1%	0	0%	
Self-employed	5	3%	0	0%	
Executive	72	40%	3	4%	
Employee	72	40%	27	39%	
Intermediate profession	22	12%	33	47%	
Blue-collar worker	2	1%	7	10%	
NA	4	2%	0	0%	
Personal income per month (€)					**<0.05**
<1900	71	40%	20	29%	
>1900	103	58%	37	53%	
NA	4	2%	13	19%	
Marital status					**<0.05**
Single	34	19%	18	26%	
Married	110	62%	39	56%	
Divorced	29	16%	10	14%	
Widow	2	1%	1	1%	
NA	3	2%	2	3%	
Breast cancer characteristics					
Type of cancer					0.32
Invasive	156	87,6%	61	87%	
In situ	21	11,8%	9	13%	
Lymph node involvement					0.12
Yes	43	24%	23	33%	
No	135	76%	47	67%	
Surgical patient care					
Breast surgery					**<0.05**
Conservative	133	75%	46	66%	
Radical	45	25%	24	34%	
Lymph node surgery					0.48
Sentinel lymph node procedure	122	69%	40	57%	
Axillary dissection	42	24%	24	34%	

	NA	14	8%	6	9%	
Surgical revision						0.24
	Yes	43	24%	16	23%	
	No	135	76%	54	77%	
Radiotherapy						**<0.05**
	Yes	167	94%	61	87%	
	No	11	6%	9	13%	
Chemotherapy						**<0.05**
	Yes	92	52%	33	47%	
	No	86	48%	37	53%	
Trastuzumab						0.42
	Yes	24	13%	9	13%	
	No	63	35%	22	31%	
	NA	91	51%	39	56%	
Hormone therapy						0.69
	Yes	129	72%	49	70%	
	No	49	28%	21	30%	
Patient management						
Modes of diagnosis						0.45
	Organized screening	37	21%	12	17%	
	Individual screening	74	42%	26	37%	
	Clinical signs	67	38%	32	46%	
Type of hospitalization						0.78
	Outpatient surgery	108	61%	43	61%	
	Inpatient surgery	70	39%	27	39%	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4 and 5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*9*
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	9
		(*e*) Describe any sensitivity analyses	9
Results			9

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	Supplemental figre 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 and 11
		(b) Indicate number of participants with missing data for each variable of interest	11
		(c) Summarise follow-up time (eg, average and total amount)	11
Outcome data	15*	Report numbers of outcome events or summary measures over time	11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
		(*b*) Report category boundaries when continuous variables were categorized	12-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12-14
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13, 14
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.