

## Original article

## Self-reported work ability in breast cancer survivors; a prospective cohort study in the Netherlands



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## ABSTRACT

**Purpose:** To evaluate patient-reported work ability of breast cancer patients, to compare scores with the Dutch general population, and to identify determinants of reduced work ability in breast cancer patients.

**Methods:** In a prospective cohort study, we identified 939 patients <67 years. Employed patients filled out the Work Ability Index (WAI) questionnaire before the start of radiotherapy treatment (baseline) and at 6, 18, and 30 months. Work ability was compared with a matched Dutch cancer-free population (n=3,641). The association between (clinical) characteristics and work ability over time was assessed using mixed-effects models.

**Results:** At baseline, 68% (n=641) of the respondents were employed and 64% (n=203) were employed at 30 months. Moderate or poor work ability was reported by 71% of patients at baseline, by 24% of the patients at 30 months and by 14% of the general population. Axillary lymph node dissection, (neo) adjuvant chemotherapy and locoregional radiotherapy were associated with reduced work ability. After 30 months, 18% of employed patients reported to have reduced their working hours, made substantial modifications to their work or were unable to work.

**Conclusion:** Patient-reported work ability is strongly reduced during breast cancer treatment. Thirty months after treatment the proportion of women reporting poor or moderate work ability remains higher compared to the general population. Even though the proportion of women with paid employment is rather stable over time, substantial amendments in work are needed in 18% of patients. These findings emphasize the importance of informing patients on potential changes in work ability to allow shared decision making.

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## 1. Introduction

In the Netherlands, the ten-year overall survival rate has improved from 61% to 79% since 1981 [1]. Due to the increasing breast cancer incidence and improved survival, the number of women surviving and living with consequences of breast cancer is rising [2–4]. Approximately, 60% of the Dutch women diagnosed

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with breast cancer are of working age (<67 years) and seek to continue working after cancer treatment [5]. As many breast cancer patients will transit from patient to cancer survivor, evaluation of patients' work ability during and after treatment is of high importance.

Return to work after cancer treatment is an important sign of recovery for patients and is often experienced as a transition from considering oneself a patient to functioning normally again [6]. Still, nearly half of the Dutch patients reported difficulties returning to work or report not to return to work after a cancer diagnosis [5,7]. For breast cancer patients who do return to work after their disease, long-term side effects of breast cancer treatment may impair their ability to meet the physical and mental demands of a job (work ability) [5].

There is evidence that the risk for unemployment and early retirement among cancer patients is increased after treatment [8,9]. Also, compared to cancer-free controls, women who have undergone breast cancer treatment show more impaired work ability [10].

Knowledge on factors that affect work ability is important, since suboptimal work ability is associated with reduced productivity and lower quality of life [11,12]. Insight into work ability during and after breast cancer treatment and the identification of (clinical) factors affecting work ability may help physicians to inform patients adequately on potential challenges after treatment. This may facilitate shared-decision making on breast cancer treatment between patients and physicians.

The aim of the present study was to evaluate patient-reported work ability in a prospective cohort of breast cancer patients, to compare scores with the Dutch general population, and to identify determinants of reduced work ability.

## 2. Methods

This study was conducted within the prospective 'Utrecht cohort for Multiple BREast cancer intervention studies and Long-term evaluation' (UMBRELLA) [13]. UMBRELLA invites all adult patients (>18 years) diagnosed with breast cancer, referred to the Department of Radiation Oncology at the University Medical Center Utrecht (UMCU, the Netherlands, indicated to receive adjuvant (local or locoregional) radiotherapy. Informed consent for the longitudinal collection of clinical data and patient-reported outcomes (PROs) during and after treatment was obtained from all individuals before cohort entry (i.e. before the start of radiotherapy treatment). The UMBRELLA study was reviewed by the institutional review board of the UMCU and ethical approval was obtained. The UMBRELLA study adheres to the Declaration of Helsinki and is registered on [clinicaltrials.gov](http://clinicaltrials.gov) [14].

Within UMBRELLA we identified all participants <67 years of age, enrolled between October 2014 and August 2017. Patients with a minimum follow-up of six months after enrollment and those who completed at least two questionnaires including the baseline and at least one follow-up questionnaire (i.e. responders), were included. Following the Dutch guidelines for breast cancer treatment, all patients had undergone breast cancer surgery (breast-conserving or mastectomy) and combined axillary staging and/or surgery, were scheduled for local breast/chest wall irradiation ± regional radiotherapy of the lymph nodes, and -if indicated- they were treated with (neo)adjuvant systemic treatment.

### 2.1. Data collection

Patient-, disease- and treatment characteristics were provided by the Netherlands Comprehensive Cancer Organization (IKNL) [15]. Patient-reported work ability was assessed at baseline, 6, 18,

and 30 months, and collected within the Patient-Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES) registry [16]. Work ability was assessed using the Work Ability Index (WAI) questionnaire [17,18]. The WAI questionnaire was developed and validated by the Finnish Institute of Occupational Health (FIOH, Helsinki 1998) to measure an individual's ability to work in the general population. The WAI is widely applied for conceptualizing the work ability by obtaining information related to diseases, functional limitations, sick leave, and mental resources. The first part of the questionnaire contains demographic information such as gender, age, the region of the employer's main location, type of predominant work activity, and the branch of industry. The second part includes questions about workers' health status and their capability to work and comprises seven dimensions with a different scoring range; (1) current work ability compared to best (previous) work ability (scoring range; 0–10), (2) work ability in relation to the work demands (physical, mental or both) (scoring range; 2–10), (3) number physician-diagnosed diseases (scoring range; 1–7), (4) estimated work impairment due to diseases (scoring range; 1–6), (5) days of absenteeism in the previous year (scoring range; 1–5), (6) perceived future work ability (scoring range; 1–7), (7) mental resources, referring to psychological attitudes, and resources to do the job (scoring range; 1–4) [19]. The WAI score encompasses the sum score of all dimensions, ranging from 7 to 49 and is categorized into four levels of work ability; poor (7–27), moderate (28–36), good (37–43) and excellent (44–49).

The Dutch foundation 'Stichting Blik op Werk' collects the WAI questionnaire cross-sectionally via employers from a large amount of Dutch employees, including women without a history of cancer [20]. To compare the WAI scores of our study population to the working population, we matched UMBRELLA patients to a cancer free reference group of Dutch women on age, level of education and job demands (i.e. physically or psychologically demanding job or both) on a 1:5 ratio (one breast cancer patient on 5 controls). This resulted in a cancer-free population (i.e. reference population) of 3,641 women.

In the set of questionnaires sent to all patients within the UMBRELLA cohort, including the EORTC QLQ-C30 questionnaire, only patients with paid employment were asked to complete the WAI questionnaire. For this study, patients were considered employed when; 1) they completed the WAI questionnaire and 2) indicated to be involved in permanent employment, temporary employment, independent contractor or other (paid) employment status at baseline. Patients were considered unemployed when they had completed and returned the set of questionnaires including the EORTC QLQ-C30, without completing the WAI questionnaire (as indicated in the instructions). Patients who did not return the WAI questionnaire nor the EORTC QLQ-C30 at baseline were considered non-responders.

### 2.2. Statistical analysis

Frequencies, proportions, and medians with interquartile ranges, were used to describe baseline characteristics stratified by patients in employment, patients without employment, and non-responders to questionnaires.

The Work Ability score was calculated according to the Work Ability Index algorithm including different weights per work ability dimension. Mann-Whitney *U* test for non-Gaussian distributed continuous measures was used to test for the difference in total work ability score and Chi-square test for categorical variables were used to compare the different work ability domains at baseline between employed patients and the general population.

The association between (clinical) determinants and work

ability was evaluated using linear mixed-effect models [21]. Clinical factors were chosen based on literature and clinical expertise. The model included a random intercept per patient and factors, i.e. time-point, age, educational level (low/medium/high), neoadjuvant chemotherapy, axillary lymph node dissection (ALND), endocrine therapy, adjuvant chemotherapy  $\pm$  immunotherapy, and irradiated volumes (local (whole breast or chest wall radiotherapy)/locoregional (local and radiotherapy of the lymph nodes)). The interaction of each factor with time was included in the model and based on the maximum likelihood function, non-significant interactions were eliminated. A model including only significant time-variant effects and all main effects was developed. A significant main effect indicates that there are similar significant differences in work ability between factor levels irrespective of the moment in time, whereas a time-variant effect indicates that the effect of a factor changes with time. In other words, the effect of a time-variant (clinical) factor on work ability score is different at each time point. An autoregressive covariance structure of the first order was used to define the correlations among observations, assuming correlations would be greater between measurements that were closer together in time compared with those further apart [21]. Changes in work ability were presented as mean differences (MD) accompanied with 95% confidence intervals (CI), reflecting the difference in work ability affected by each factor.

The standardized effect size (ES) was calculated by dividing the mean difference by the pooled standard deviation. ES of 0.2–0.4 were considered small, 0.5–0.7 moderate and  $>0.8$  large [22]. Statistical Package for Social Sciences (SPSS) version 23 was used and 'MatchIt' and 'optmatch' packages in R version 3.5.1.

### 3. Results

Between October 2013 and August 2017, 1,751 patients were enrolled in UMBRELLA (Fig. 1). In total, 1,325 were  $<67$  years, of whom 939 (71%) responded to the baseline and at least one follow-up questionnaire (Fig. 1). Of the responders, 641 (68%) indicated to

be employed at baseline. This percentage was 64% at 30 months, after accounting for patients reaching the retirement age. The response rates per time point accounted for follow-up time and patients who reached 67 years during follow-up, ranged between 86% ( $n = 806$ ) and 67% ( $n = 319$ ).

Employed patients ( $n = 640$ ) had a median age of 52 years, unemployed patients ( $n = 298$ ) 59 years, and non-responders ( $n = 386$ ) 52 years (Table 1). Employed and unemployed patients were comparable in terms of adjuvant systemic treatment, axillary treatment, and irradiated volumes. Employed patients were more frequently treated with neoadjuvant chemotherapy (30%,  $n = 188$  versus 19%,  $n = 58$ ) and received a mastectomy more frequently (17%,  $n = 107$  versus 10%,  $n = 31$ ) compared to unemployed patients. Compared with responders (unemployed and employed patients), non-responders ( $n = 386$ ) more often received extensive treatment.

#### 3.1. Work ability in patients versus the general population

At baseline, work ability of breast cancer patients was significantly lower than the work ability score of the general population, 30 vs. 43, respectively,  $p < 0.001$ . Work ability improved significantly over time with a median WAI of 33, 39, and 41 at respectively 6, 18, and 30 months (Fig. 2). At 30 months, 8% ( $n = 16$ ) of survivors reported poor (score: 7–27) work ability and 16% ( $n = 34$ ) moderate (score: 28–36) work ability, compared with 2% ( $n = 69$ ) poor and 12% ( $n = 435$ ) moderate work ability in the general population.

At baseline, breast cancer patients reported significant lower (i.e. worse) scores on all work ability dimensions compared with the general population (Table 2). From 18 months onwards, patients' current work ability score compared to their (previous) best work ability, and perceived work ability concerning the demands of the job were similar to scores of the general population (Fig. 3A). At baseline, 64% ( $n = 394$ ) of the patients needed substantial adaptations in work, worked reduced hours or were unable

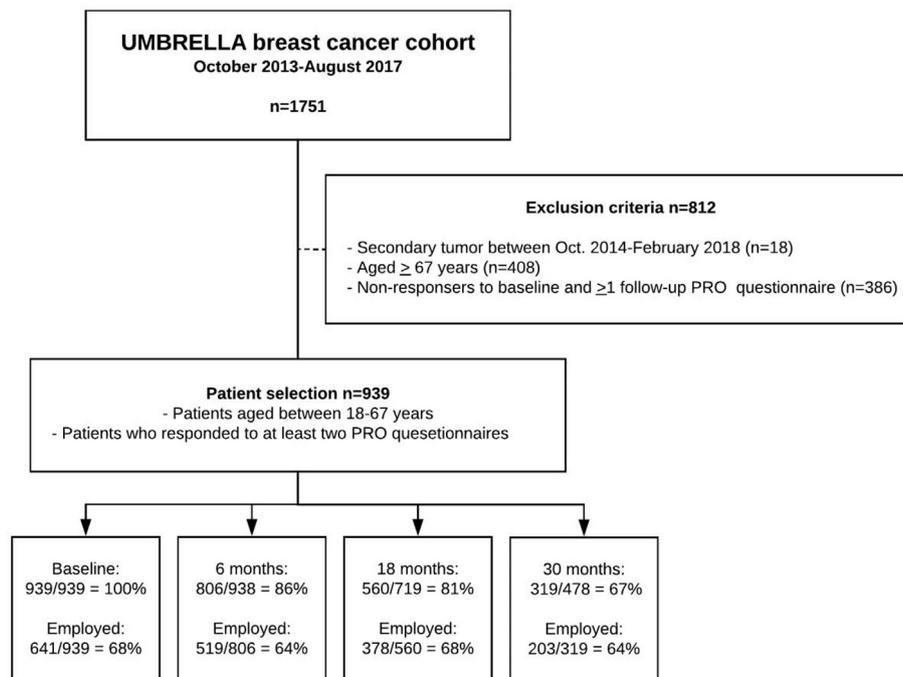


Fig. 1. Flowchart of patient selection and work ability index (WAI) questionnaire response rates within the prospective breast cancer cohort (UMBRELLA).

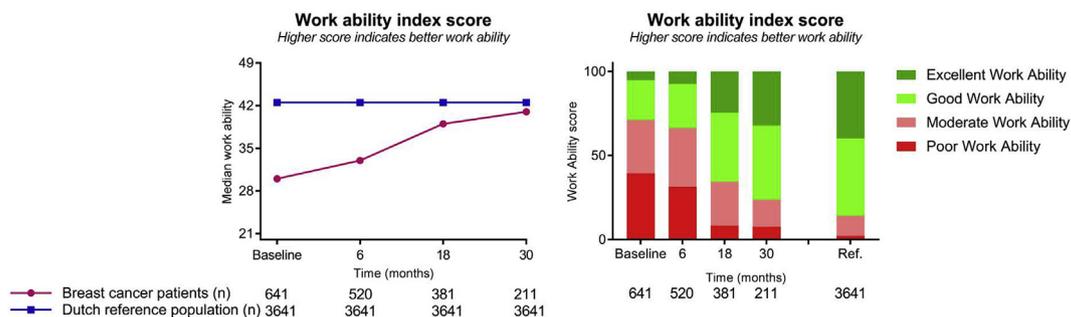
**Table 1**

Baseline characteristics of breast cancer patients participating in the UMBRELLA cohort aged &lt;67 years at the time of enrollment in October 2013 to August 2017.

Total no. of patients	Employed	Unemployed	Non-responders
	641 (%)	298 (%)	386 (%)
<b>Age in years at inclusion, median (IQR)</b>	52 (48-57)	59 (51-64)	52 (45-60)
<b>Neo-adjuvant systemic treatment</b>			
None	453 (71)	240 (81)	239 (62)
Chemotherapy	146 (23)	39 (13)	120 (31)
Chemotherapy and immunotherapy	42 (7)	19 (6)	27 (7)
<b>Surgical treatment</b>			
Breast conserving	533 (83)	266 (89)	298 (77)
Mastectomy	107 (17)	31 (10)	85 (22)
Other	1 (0)	1 (0)	3 (1)
<b>Pathological tumor stage (pT)</b>			
Ductal carcinoma in situ	67 (11)	33 (11)	31 (8)
T0	70 (11)	21 (7)	45 (12)
T1	353 (55)	186 (62)	210 (54)
T2	128 (20)	52 (17)	87 (23)
≥ T3	23 (4)	6 (2)	13 (3)
<b>Most invasive axillary procedure</b>			
Sentinel lymph node biopsy	514 (80)	237 (80)	274 (71)
Axillary lymph node dissection	76 (12)	38 (13)	62 (16)
Unknown <sup>a</sup>	51 (8)	23 (8)	50 (13)
<b>Estrogen receptor status</b>			
Negative	91 (14)	39 (13)	74 (19)
Positive <sup>b</sup>	472 (74)	222 (74)	279 (72)
Unknown	78 (12)	37 (12)	33 (9)
<b>HER2 receptor status</b>			
Negative	471 (74)	223 (75)	285 (74)
Positive	88 (14)	36 (12)	68 (18)
Unknown	82 (13)	39 (13)	33 (9)
<b>Adjuvant chemotherapy treatment</b>			
No	447 (70)	200 (67)	255 (66)
Yes	194 (30)	98 (33)	131 (34)
<b>Adjuvant endocrine therapy</b>			
No	315 (49)	155 (52)	179 (46)
Yes	326 (51)	143 (48)	207 (54)
<b>Radiotherapy treatment<sup>c</sup></b>			
Local radiotherapy	477 (74)	234 (78)	251 (65)
Locoregional radiotherapy <sup>d</sup>	164 (26)	64 (22)	135 (35)

NOTE. Categories may not sum to total 100% because of missing values or rounding.

Abbreviations: IQR; inter quartile range, HER2; human epidermal growth factor receptor 2.

<sup>a</sup> Sentinel lymph node biopsy and/or axillary lymph node dissection is not indicated in patients with ductal carcinoma in situ.<sup>b</sup> Estrogen receptor positive >10%.<sup>c</sup> Radiotherapy on the breast or chest wall with or without boost on the tumor bed.<sup>d</sup> Includes radiotherapy on axillary and/or periclavicular lymph nodes.**Fig. 2.** Work ability index (WAI) score in employed breast cancer patients during the first thirty months after the start of radiotherapy treatment and the scores of the matched Dutch general working population as reference group. Outcomes are presented in median scores for all patients who responded to baseline and at least one follow-up questionnaire.

to work due to their disease. At 30 months after treatment, 18% ( $n = 37$ ) of the employed patients reported an inability to work, worked reduced hours or required substantial adapted work versus 6% ( $n = 225$ ) of the general population (Fig. 3B). No limitations in work due to disease were reported by 17% ( $n = 111$ ) of the survivors at 30 months and by 66% ( $n = 2392$ ) of the general

population. Absenteeism of 100–365 days in the previous year, was highest at 6 months (52%,  $n = 270$ ) and decreased to 4% ( $n = 8$ ) at 30 months. At 30 months, 42% ( $n = 88$ ) of the patients reported zero absenteeism, which was comparable to the general population (42%, Fig. 3C).

**Table 2**

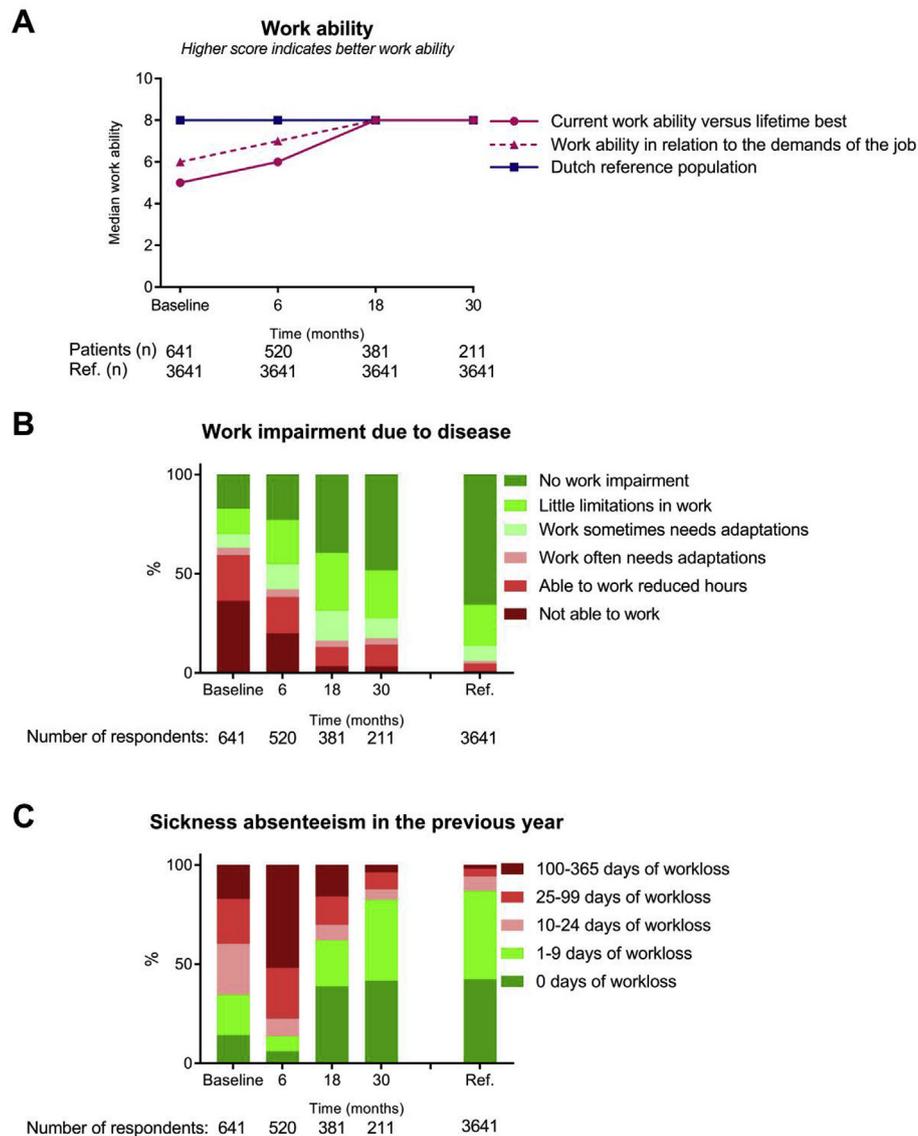
Work related characteristics at baseline of employed patients at the time of cohort enrollment (before start radiotherapy), compared with outcomes of the matched (age, educational level and job content) Dutch, cancer-free, general working population.

Total no. of patients	Employed breast cancer patients	Dutch general female population	p-value
	641 (%)	3641 (%)	
<b>Age, median (IQR)</b>	52 (48-57)	52 (48-57)	ND
<b>Educational level<sup>a</sup></b>			ND
Low	93 (14)	476 (13)	
Medium	198 (31)	1197 (33)	
High	350 (55)	1963 (54)	
Missing	0 (0)	5 (0)	
<b>Type of employment</b>			ND
Permanent employment	440 (69)	2574 (71)	
Temporary employment	58 (9)	220 (6)	
Independent contractor	79 (13)	29 (1)	
Other	58 (9)	16 (0)	
Unknown	6 (1)	802 (22)	
<b>Working hours, median (IQR)</b>	28 (21.0–34.0)	30 (24.0–36.0)	0.065
<b>Irregular working hours</b>			<0.001
Yes	182 (28)	1283 (35)	
No	438 (68)	1911 (52)	
Missing	21 (3)	447 (12)	
<b>Job content</b>			ND
Physically demanding	80 (13)	512 (14)	
Psychologically demanding	346 (54)	1919 (53)	
Both	215 (34)	1210 (33)	
<b>D1. Current vs. best (previous) work ability, median (IQR)</b>	6 (3.0–8.0)	8 (7.0–9.0)	<0.001
<b>D2. Work ability in relation with physical demands</b>			<0.001
(very) Poor	185 (29)	54 (2)	
Moderate	186 (29)	324 (9)	
Good	193 (30)	2181 (60)	
Excellent	77 (12)	1082 (30)	
<b>D2. Work ability in relation to mental demands</b>			<0.001
(very) Poor	170 (27)	72 (2)	
Moderate	211 (33)	399 (11)	
Good	202 (32)	2385 (66)	
Excellent	58 (9)	785 (22)	
<b>D3. Number of current diseases</b>			<0.001
0 diagnoses	47 (7)	1763 (48)	
1 diagnosis	278 (43)	929 (26)	
2-3 diagnoses	236 (37)	766 (21)	
≥4 diagnoses	80 (13)	183 (5)	
<b>D4. Work ability limited by disease</b>			<0.001
Not able to work	233 (36)	38 (1)	
Able to do part-time work	148 (23)	138 (4)	
I often have to make adaptations	23 (4)	49 (1)	
I sometimes have to make adaptations	44 (7)	275 (8)	
I have little limitations in work	82 (13)	749 (21)	
No limitations in work due to disease	111 (17)	2392 (66)	
<b>D5. Sickness absenteeism in the previous year</b>			<0.001
100–365 days	110 (17)	74 (2)	
25–99 days	145 (23)	143 (4)	
10–24 days	165 (26)	264 (7)	
1–9 days	130 (20)	1621 (45)	
0 days	91 (14)	1539 (42)	
<b>D6. Self-prognosis of work ability in two years from now</b>			<0.001
Unlikely to maintain current job	12 (2)	49 (1)	
Likely to maintain current job	80 (13)	249 (7)	
Very likely to maintain current job	549 (86)	3343 (92)	
<b>D7. Enjoyment in regular daily activities</b>			<0.001
Never/rarely	9 (1)	56 (2)	
Sometimes	88 (14)	288 (8)	
Frequently	339 (53)	1700 (47)	
Always	205 (32)	1597 (44)	
<b>D7. Feeling of being active and fit</b>			<0.001
Never/rarely	69 (11)	121 (3)	
Sometimes	180 (28)	512 (14)	
Frequently	269 (42)	1827 (50)	
Always	123 (19)	1181 (32)	
<b>Confidence in the future</b>			<0.001
Never/rarely	19 (3)	79 (2)	
Sometimes	122 (19)	458 (13)	
Frequently	313 (49)	1467 (40)	
Always	187 (29)	1637 (45)	
<b>Work ability score, median (IQR)</b>	30 (23.5–37.5)	43 (39.0–45.0)	<0.001

Abbreviations: IQR; interquartile range, ND: Not determined.

NOTE. Categories may not sum to total 100% because of missing values or rounding.

<sup>a</sup> High: Higher professional or university education. Medium: higher secondary or pre-university education or vocational education. Low: pre-vocational education or lower.



**Fig. 3.** Selected dimensions of the work ability index (WAI) questionnaire in employed breast cancer patients during the first thirty months after the start of radiotherapy and the matched Dutch general working population as reference group. Current work ability versus lifetime best work ability and work ability in relation to the demands of the job (A). Work impairment due to disease (B) and sickness and absenteeism in the previous year (C).

### 3.2. Association between clinical factors and work ability

Results from linear mixed effect models showed a significant main effect of time, neoadjuvant chemotherapy, and irradiated volumes (Table 3). In other words, work ability significantly improved with time and at all time-points. Patients treated with neoadjuvant chemotherapy and patients receiving locoregional radiotherapy had significantly lower work ability score compared to patients treated with adjuvant or no chemotherapy, and/or local radiotherapy, respectively. The effect of ALND and adjuvant chemotherapy on work ability changed with time (Table 3). At baseline (shortly after surgery), patients treated with ALND reported significantly lower (i.e. worse) work ability (MD;  $-3.08$ ) compared to those treated without ALND. This effect was no longer observed at 6, 18, and 30 months (MD;  $0.34$ ,  $-0.52$ , and  $0.49$  respectively). Adjuvant chemotherapy was associated with lower work ability at baseline, 6, and 18 months (MD;  $-4.27$ ,  $-7.35$ , and  $-2.25$ ), whereas at 30 months, patients receiving adjuvant chemotherapy had similar work ability as non-chemotherapy

patients (MD;  $0.04$ ). All effect sizes accompanying these significant differences were small/moderate, ranging from 0.1 to 0.5 (Table 3).

## 4. Discussion

This study showed that patient-reported work ability in employed breast cancer patients is substantially reduced during treatment and gradually improves over time. However, at 30 months after treatment, work ability of breast cancer patients remains lower than that of the general population. Furthermore, thirty months after treatment, the employment rate was only slightly lower than that of the general population, but a quarter of the survivors still report poor (8%) or moderate (16%) work ability which is worse compared to the general population [23,24]. Moreover, 30 months after treatment, 18% of the survivors were unable to work, worked reduced hours or needed substantial adaptations in work, and only 17% of the survivors did not have any limitations at work due to their disease. This compares unfavorably to the general population, where 67% of female employees report to

**Table 3**

Effect of patient and treatment characteristics on patient-reported work ability assessed with the Work Ability Index (WAI) score in the first thirty months after start of radiotherapy in breast cancer patients.

		Main effects			Time-variant effects											
				ES <sup>a</sup>	Baseline			6 months			18 months			30 months		
		MD <sup>c</sup>	95% CI		MD <sup>c</sup>	95% CI	ES <sup>a</sup>	MD <sup>c</sup>	95% CI	ES <sup>a</sup>	MD <sup>c</sup>	95% CI	ES <sup>a</sup>	MD <sup>c</sup>	95% CI	ES <sup>a</sup>
Axillary treatment	No ALND	Ref.			Ref.			Ref.			Ref.			Ref.		
	ALND	-0.74	-3.46; 0.98	NS	<b>-3.08</b>	-5.00; -1.06	0.3	0.34	-1.79; 2.45	NS	-0.52	-2.34; 3.50	NS	0.49	-3.03; 4.01	NS
Adjuvant chemotherapy	No	Ref.			Ref.			Ref.			Ref.			Ref.		
	Yes	-0.31	-1.63; 1.01	NS	<b>-4.27</b>	-7.06; 1.47	0.3	<b>-7.35</b>	-8.59; -6.11	0.5	<b>-2.25</b>	-3.75; -0.75	0.1	0.04	-1.94; 2.02	NS
Time	Baseline	Ref.														
	6 months	<b>2.97</b>	1.07; 4.97	0.2		NA			NA			NA			NA	
	18 months	<b>9.29</b>	8.18; 12.44	0.5		NA			NA			NA			NA	
	30 months	<b>11.82</b>	9.01; 13.66	0.6		NA			NA			NA			NA	
Age		-0.01 <sup>b</sup>	-0.09; 0.07	NS		NA			NA			NA			NA	
Education <sup>c</sup>	Low	Ref.														
	Medium	0.67	-1.36; 2.70	NS		NA			NA			NA			NA	
	High	0.44	-1.48; 2.36	NS		NA			NA			NA			NA	
Neoadjuvant chemotherapy	No	Ref.														
	Yes	<b>-2.66</b>	-3.98; -1.33	0.2		NA			NA			NA			NA	
Endocrine therapy	No	Ref.														
	Yes	-0.81	-1.98; 0.36	NS		NA			NA			NA			NA	
Radiotherapy	Local	Ref.														
	Locoregional	<b>-1.73</b>	-3.37; -0.09	0.2		NA			NA			NA			NA	

Abbreviations: MD; mean difference, CI; confidence interval, ES; effect size, SNB; sentinel node biopsy, ALND; axillary lymph node dissection, Ref; reference category, NA; not applicable.

Main effects and significant time variant effects based on a linear-mixed effects model with backward stepwise selection of non-significant time interactions (i.e. interaction of time with age, level of education, neoadjuvant chemotherapy, endocrine therapy and radiotherapy were not significant and removed from the model). Results from the final mixed model are adjusted for multiple testing.

<sup>a</sup> Effect size for significant effects as a measure for minimal clinically important change ( $p < 0.050$  based on linear mixed-effects model and the restricted maximum likelihood). Defined as the group mean difference divided by the pooled standard deviation and interpreted. Small effect if  $ES \geq 0.2-0.4$ , moderate effect if  $ES \geq 0.5-0.7$ , large effect if  $ES \geq 0.8$ .

<sup>b</sup> Regression coefficient, increase in WAI score per year of age.

<sup>c</sup> High: Higher professional or university education. Medium: higher secondary or pre-university education or vocational education. Low: pre-vocational education or lower.

have no limitations at work. ALND, impaired work ability substantially in the early months after diagnosis, whereas chemotherapy and locoregional radiotherapy were associated with long-term reduced work ability.

In the present cohort, the percentage of women reporting to be employed was 68% at baseline and 64% at 30 months. This is slightly lower than the 67% employment rate of Dutch women aged 45–65 years reported in 2018 by the electronic databank of Statistics Netherlands (CBS) [23,24].

The relatively high employment rate in the first 18 months can be explained by the fact that Dutch employees are protected by the Dutch law from being laid off within the first 24 months of sickness. The employee is entitled to a minimum of 70% of the wages in the first two years, meaning that patients are financially well supported for 2 years after diagnosis. Still, also 30 months after treatment, when this provision does no longer hold, 64% of breast cancer survivors reported being employed, which is relatively high [5].

Previous cross-sectional studies have shown that return to work is hampered following a breast cancer diagnosis [25,26]. In a smaller American study including 68 employed breast cancer survivors, work ability measured using the WAI, was reduced five years post-treatment. Ten percent of the women ( $n = 7$ ) reported poor work ability, which is comparable to our findings at 30 months (8%) [26]. Cognitive impairment was significantly related to work performance and work productivity [26]. Our findings showed that exposure to (neo)adjuvant chemotherapy was associated with reduced work ability. Chemotherapy is known to be associated with cognitive impairment in cancer survivors [27,28]. Women receiving chemotherapy, more often report difficulties with memory and attention, which may hamper the return to work and could affect patients with (partly) psychologically demanding jobs [29].

A recent review on return to work in European cancer survivors

showed that higher socioeconomic status and educational level facilitated maintaining one's job [30]. Although, it is known that education and income levels are strongly linked to different social outcomes, including work, we did not observe an association between educational level and work ability like other studies [12,31,32]. Differences in outcome, follow-up time, and/or study population (relatively small group of low-educated women in our study ( $n = 94$ , 14%) may explain why educational level was not associated with work ability in our study.

Our results indicate that patients' work ability substantially improves over time but remains lower than that of the general population. These results are in line with findings from a Danish study [34]. Carlsen et al. indicated that the work ability, measured with the WAI, of breast cancer survivors ( $n = 170$ ) who survived 5 years after diagnosis was significantly poorer than cancer-free controls [34]. Survivors with a low income, who experienced fatigue, and who lacked support from their closest supervisor appeared to be at higher risk for impaired work ability.

Findings from our study should be considered in the context of its limitations. Response rates declined during follow-up. We acknowledge that reduced response rates have induced bias since we cannot rule out selective non-response. Selective non-response may have over or underestimated the proportion of employed survivors, and also selective response among employed patients could have under- or overestimated WAI scores (lower or higher), especially since responders and non-responders differed in terms of treatment characteristics (i.e. non-responders were more often treated with neoadjuvant systemic treatment, mastectomy, and locoregional radiotherapy). Although the reason for non-response is unclear, it could be that we missed patients who experience more morbidity which could potentially impact the work ability (i.e. overestimated the work ability of breast cancer patients). Also,

we might have missed the effects of some potential (clinical) factors (i.e. educational level) impacting the work ability might since the number of patients was too small in some groups to detect any effect on work ability. We found that 18% of the patients still worked reduced hours 30 months after treatment, however, it is unknown what the reason for the reduced working hours was, whether this was a personal preference of patient's due reprioritisation for example or whether patients were unable to work more hours.

In this study patients referred to the UMCU indicated to receive adjuvant radiotherapy are invited. Although we only invite women indicated to receive radiotherapy, the generalisability of the outcomes derived from the cohort to other patients with breast cancer indicated to receive radiotherapy treatment is high. The majority of all breast cancer patients (approximately 70%) are indicated to receive radiotherapy in the Netherlands [35]. Especially, when patients are treated with breast-conserving surgery the indication for radiotherapy is high (i.e. 97%). The results of this study may be less generalisable to patients treated with mastectomy only.

The results of this study can offer support to breast cancer patients in clinical care. Especially to patients treated with breast-conserving therapy who are expected, based on treatment decisions (e.g. patients receiving neoadjuvant systemic treatment and/or locoregional radiotherapy), to face challenges in their working environment. Furthermore, these results may be used to adequately inform patients with breast cancer prior to starting treatment about the expected effect of treatment on their work ability. This enables patients to carefully outweigh the clinical benefits of for example neoadjuvant chemotherapy or extensive radiotherapy treatment, against the expected side effects. Also, when an impaired work ability after treatment is expected, interventions (e.g. provide professional employee assistance services, tailor work to accommodate individual needs or refer for mental health counselling) to improve employment outcomes following cancer, can be offered enabling women to stay in the work force [36–38]. This is important since research has revealed that women who continue working throughout treatment and recovery, or who resume work after treatment demonstrate lower levels of psychological distress, higher levels of physical, mental and social functioning [37,38].

In conclusion, this study showed that patient-reported work ability is reduced in patients under treatment for breast cancer. At 30 months after treatment, the proportion of women reporting poor or moderate work ability remained higher compared to the general population. The proportion of women with paid employment remains rather stable over time, but a substantial proportion of patients, 18%, reported to have reduced their working hours, made substantial modifications to their work or were unable to work. More extensive (neo)adjuvant treatment modalities were associated with long-term reduced work ability. These findings emphasize the importance of informing patients on potential changes in work ability during breast cancer treatment to allow shared-decision making.

### Conflicts of interest

The authors declare that they have no conflict of interest.

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This research did not receive any specific grant from funding agencies in the public, commercial or not-for profit sectors.

### Ethical approval

“All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.”

### Informed consent

“Informed consent was obtained from all individual participants included in the study.”

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