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ABSTRACT

Background Many breast cancer (BC) survivors are employed at diagnosis and are expected to return to work after treatment. Among them, around 50% are overweight or obese. There are limited data about the impact of body weight on their ability to return to work.

Methods We used data from CANcer TOxicity (NCT01993498), a prospective, multicentre cohort of women with stage I–III BC. Professionally active women who were ≥5 years younger than retirement age were identified. Multivariable logistic regression models examined associations of body mass index (BMI) at diagnosis and subsequent weight changes with non-return to work 2 years after diagnosis, adjusting for psychosocial, treatment and behavioural characteristics.

Results Among 1869 women, 689 were overweight or obese. Overall, 398 patients (21.3%) had not returned to work 2 years after diagnosis. Non-return to work was more likely for overweight or obese than underweight or normal weight patients (adjusted OR (aOR) 1.32; 95% CI, 1.01 to 1.75; p=0.045). Weight loss (≥5%) was observed in 15.7% overweight or obese and 8.7% underweight or normal weight patients and was associated with significant increases in physical activity only among overweight or obese patients (mean change, +4.7 metabolic-equivalent-of-task-hour/week; 95% CI +1.9 to +7.5). Overweight or obese patients who lost weight were more likely to return to work compared with those who did not lose weight (aOR of non-return-to-work, 0.48; 95% CI 0.24 to 0.97, p=0.0418), whereas weight loss was associated with increased odds of non-return to work among underweight or normal weight women (aOR 2.07; 95% CI 1.20 to 3.56, p=0.0086) ($p_{interaction}$BMI×weight changes=0.0002). The continuous trend of weight gain on non-return to work was significant for overweight or obese patients (aOR for one-percent-unit difference, 1.03; 95% CI 1.01 to 1.06, p=0.030).

Conclusions Excess weight may be a barrier to return to work. Among overweight or obese BC survivors, weight loss was associated with higher rates of return to work, whereas further weight gain was associated with lower likelihood of return to work. Employment outcomes should be evaluated in randomised studies of weight management.

Key questions

What is already known about this subject?

► A large portion of breast cancer survivors are employed at the moment of diagnosis and are expected to return to work after treatment. Employment concerns and inability to rejoin the workforce can lead to financial difficulties, depression, anxiety and relationship changes, and can negatively affect breast cancer survivors' quality of life. Around 50% of women with breast cancer are overweight or obese at diagnosis and represent a significant part of the workforce. Previous studies have largely only included unemployment rates after cancer as a secondary outcome and there are few data concerning how body weight and weight changes, which are common after breast cancer treatment, relate to post-treatment job reintegration.

What does this study add?

► This manuscript addresses the important topic of a cancer survivor returning to work post-treatment, using one of the largest contemporary cohorts of breast cancer survivors available, the CANcer TOxicity cohort. This paper highlights the relationship between body weight at diagnosis, post-diagnosis weight changes and return to work 2 years afterwards. Over 20% of women in this study did not return to work overall and over 27% were still unemployed 2 years after breast cancer diagnosis among overweight and obese survivors. Our data show that excess weight may represent a significant barrier to rejoin the workplace and that, among overweight and obese patients, there is an association between weight loss and return-to-work. These findings suggest that addressing return to work adequately is still an unmet need in the survivorship arena, particularly among overweight and obese survivors.

INTRODUCTION

Due to early diagnosis and advances in multimodal treatments, survival rates of patients with breast cancer (BC) have markedly improved in the last decades, with a 5-year relative survival estimated at 80%–90% in women diagnosed with BC in developed Countries.[1 2] However, cancer survivors may face long-term and late physical and psychosocial effects of BC treatment that

Key questions

How might this impact on clinical practice?

- Overweight and obese women with breast cancer are at risk of poorer outcomes, impaired quality of life and re-employment concerns. In addition to many physical and psychological benefits, weight management strategies may also facilitate job reintegration and help avoid premature exit from the workforce for a continuously growing number of overweight and obese survivors. This study suggests (1) that re-employment issues after cancer should be better and more systematically addressed in clinical practice and (2) that employment outcomes should be evaluated in randomised studies of weight management, to help mitigate the societal and economic impact of surviving breast cancer.

could affect their ability to recover precancer social relations and work capacity or productivity.[3] Unemployment has been shown to be higher in cancer survivors in general and particularly in BC survivors.[4] Employment concerns can in turn lead to financial difficulties, depression, anxiety and relationship changes, and can negatively affect BC survivors' quality of life (QoL). Conversely, return to work has been shown to be associated with better QoL and feelings of full recovery from cancer.[5 6] Considering the growing number of BC survivors, of whom 25% are under the age of 60,[7 8] and the importance of return to work for both survivors and society, strategies to facilitate their return to work should be further explored.

Overweight and obesity are a substantial public health problem in developed countries and higher body mass index (BMI) has been shown to be consistently associated with lower overall and BC survival.[9] Randomised controlled trials have been conducted or are underway to evaluate the impact of weight loss interventions on BC recurrence and patients' QoL.[10 11] Although several factors have been previously identified that may negatively affect return to work after BC, including sociodemographic features, such as lower education level and income,[12 13] presence of concomitant medical problems,[14] psychological factors such as anxiety and depression,[15–17] higher disease burden,[13] more aggressive BC treatment modalities,[18 19] treatment-related side effects that lead to loss of functionality and reduced work capacity[15–17] as well as disadvantageous working conditions,[20] limited data are currently available on whether BMI at BC diagnosis and subsequent weight changes correlate with return to work among BC survivors.

We aimed to answer this question using the CANcer TOxicity (CANTO) cohort, a prospective, longitudinal dataset of survivors of early stage BC that includes extensive clinical, social and work-related information, purposefully designed to characterise long-term BC toxicities.

PATIENTS AND METHODS

Data source

We used data from a prospective multicentre cohort of women with stage I–III BC enrolled in 26 French cancer centres since 2012; CANTO, NCT01993498).

Patients exit CANTO at any BC recurrence (other than local) or second cancers. Extensive sociodemographic, clinical, tumour and treatment information were assessed. [21]

Study cohort

Information from 5801 patients enrolled between March 2012 and January 2015 was accessed. We included women who were professionally active, age 57 years or younger at the time of BC diagnosis (at least 5 years younger than legal retirement age in France) and who had updated work status 2 years after BC diagnosis (figure 1).

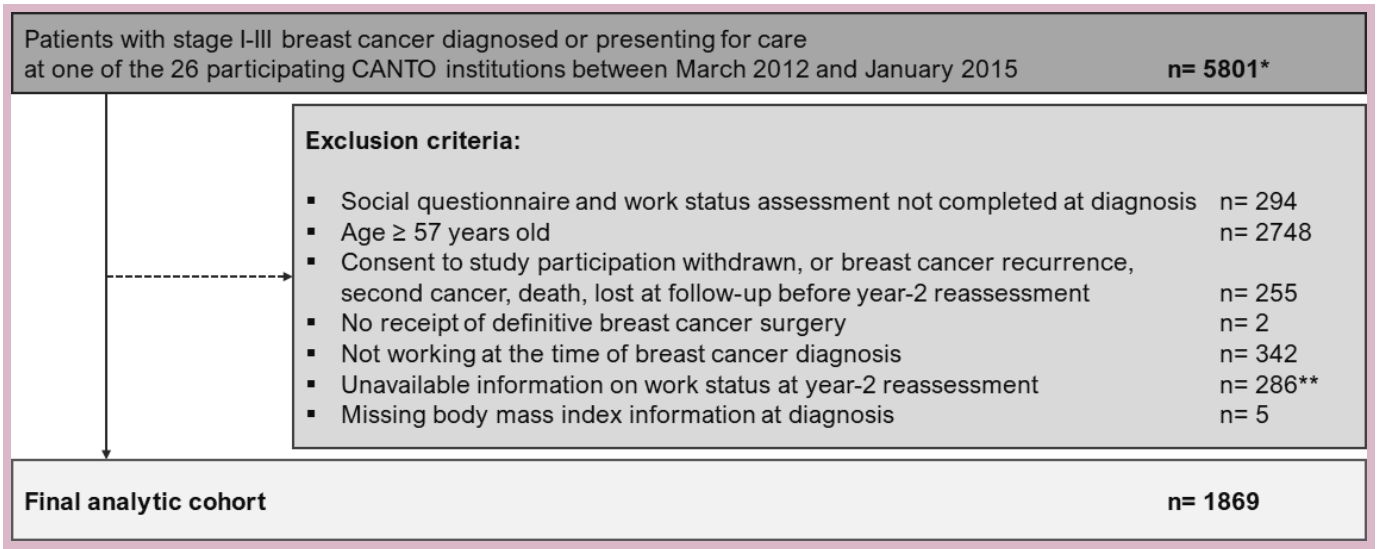

Figure 1 CONSORT diagram. *Total accural in CANTO = 12 012 patients. We accessed information from 5801 women who were enrolled from March 2012 to January 2015. **Response rate to work status reassessment questions was associated with age and receipt of endocrine therapy, without major differences in terms of tumour stage, comorbidities, type of breast or axillary surgery, receipt of chemotherapy and radiation therapy. CONSORT, Consolidated Standards of Reporting Trials; CANTO, CANcer TOxicity.

Variables

Our outcome of interest was non-return to work 2 years after BC diagnosis. Exposure variables were objectively assessed BMI at diagnosis (baseline) and weight changes between diagnosis and 2 years afterwards. Covariates previously identified as associated with the outcome of interest were explored and these included baseline socioeconomic and clinical variables, treatment-related covariates, behavioural characteristics, including physical activity (we considered physical activity as a mean of transportation (travel to/from places) and leisure-related domains (eg, sports and fitness), assessed using the Global Physical Activity Questionnaire-16 and measured as metabolic-equivalent-of-task (MET)-hours/week[22]; work-related domains were not included), psychosocial factors, including anxiety and depression (Hospital Anxiety and Depression Scale[23]) and baseline working conditions. Patient-reported measures of QoL were obtained using the European Organisation for Research and Treatment of Cancer (EORTC) QoL questionnaires (EORTC QLQ-C30 and QLQ-BR23).[24 25] Objectively documented toxicities (Common Terminology Criteria for Adverse Events (CTCAE) V4.0) were obtained by trained clinical research nurses during health examinations. Variables were categorised as per table 1 and online supplemental table 1.

Statistical analyses

Patient characteristics were tabulated for the overall cohort. Then, distribution of variables by baseline BMI was described using χ^2 tests for categorical variables and Wilcoxon rank sum tests for continuous variables, as appropriate. BMI was categorised according to the WHO international classification, as follows: <25.0 kg/m^2=under or normal weight; ≥25.0 kg/m^2=overweight or obese. Multivariable logistic regression models were used to examine associations between baseline BMI with non-return to work 2 years afterwards and returned adjusted Odds Ratios (aORs) with respective 95% Confidence Intervals (CIs). Using multivariable logistic regression, we also assessed the association between weight changes occurring after BC diagnosis with non-return to work. Weight change was modelled both as categorical variable (weight loss (at least 5% of baseline weight), no weight loss (stable weight, within 5%, or weight gain, of at least 5%)) and as continuous (percent-unit weight difference compared with baseline weight). Covariates were selected for inclusion in the models in order to account for significant differences between BMI groups at baseline (with a univariate p value <0.05) and for variables that had been previously identified to affect employment after BC.

Analyses that assessed the association between weight changes occurring after BC diagnosis with non-return to work were further stratified by baseline BMI (<25 vs ≥25.0 kg/m^2), after testing for significant interactions between baseline BMI and weight changes.

As sensitivity analyses, we entered in the models also patient-reported outcomes (fatigue (EORTC QLQ-C30) and arm symptoms (QLQ-BR23)) and late toxicities (arthralgia and myalgia (CTCAE V.4.0)) evaluated at return to work assessment.[26]

All tests were two sided. P values <0.05 were considered significant. Analyses were conducted using SAS software (V.9.4; SAS Institute).

RESULTS

Cohort characteristics

A total of 1869 patients were included. Baseline characteristics for the overall cohort population and according to BMI at diagnosis are shown in table 1. Mean age at diagnosis for the overall cohort was 46.8 years (Standard Deviation (SD) 6.4), with a mean weight of 66.4 kg (SD 13.3) and a mean BMI of 24.7 kg/m^2 (SD 4.9). At BC diagnosis, 1180 (63.1%) were under or normal weight and 689 (36.9%) were overweight or obese. Overweight or obese women tended to be slightly older, postmenopausal, non-smokers, less physically active and to have lower education, lower income and higher tumour stage. Finally, 16.9% overweight or obese versus 12.3% under or normal weight women had at least one comorbidity (p=0.0073) (table 1). Working conditions were similar between under or normal weight and overweight or obese patients respective to work sector (private/public), type of contract (permanent/fixed-term position), workload (full/part time) and length of daily home-work commuting (more/less than 1 hour) (all p>0.05). However, compared with under or normal weight patients, overweight or obese patients were more likely to have lower rank job positions (43.6% vs 36.8% were employees and 18.1% vs 28.4% were professionals or managers; p<0.0001) (online supplemental table 1).

Work status at 2 years after BC diagnosis

At 2 years after BC diagnosis (median time from diagnosis to work status reassessment=23.3 months (Interquartile Range (IQR), 21.2–25.3), no differences between under or normal weight patients and overweight or obese patients (p=0.5276)), 398 patients (21.3%) had not returned to work. The rate of non-return to work was 17.7% among under or normal weight patients versus 27.4% among overweight or obese patients (p<0.0001). The distribution of women who had not returned to work among those who were overweight or obese was as follows: 121/434 (27.9%) in patients with BMI of 25.0–29.9 kg/m^2; 49/169 (29.0%) in patients with BMI of 30.0–34.9 kg/m^2 and 19/86 (22.1%) in patients with BMI ≥35.0 kg/m^2. Overall, among women who had not returned to work, the majority (n=294, 73.9%) was still on sick leave 2 years after BC diagnosis. However, compared with under or normal weight women, overweight or obese survivors were less likely to declare that they were on sick leave (69.8% vs 77.5%) or actively looking for a job (7.9% vs 9.1%) and more likely to have received a long-term disability benefit (7.9% vs 3.4%) or to have permanently retired (9.5% vs 3.8%) (p=0.0398). In addition, compared with under or normal weight women, overweight or obese

Table 1 Cohort characteristics

N (%)	Whole cohort	By body mass index at breast cancer diagnosis		P value*
		Under/normal weight <25 kg/m^2	Overweight/Obese ≥25 kg/m^2	
Total	1869 (100)	1180 (63.1)	689 (36.9)	
Age at diagnosis, years				<0.0001
Mean (SD)	46.8 (6.4)	46.3 (6.3)	47.8 (6.3)	
Missing	–	–	–	
Weight, kg				NA
Mean (SD)	66.4 (13.3)	59.0 (6.5)	79.1 (12.3)	
Missing	–	–	–	
BMI, kg/m^2				NA
Mean (SD)	24.7 (4.9)	21.8 (1.9)	29.7 (4.4)	
Missing	–	–	–	
BMI, categorical				NA
Underweight	54 (2.9)			
Normal weight	1126 (60.2)	NA	NA	
Overweight	434 (23.2)			
Obese	255 (13.6)			
Missing	–			
Marital status				
In a relationship	1560 (84.2)	983 (83.8)	577 (84.9)	0.5035
Not in a relationship	292 (15.8)	190 (16.2)	102 (15.0)	
Missing	17	7	10	
Highest education level				<0.0001
Primary or lower	76 (4.1)	29 (2.5)	47 (6.9)	
High school	852 (46.2)	475 (40.7)	377 (55.8)	
College graduate or higher	914 (49.6)	662 (56.8)	252 (37.3)	
Missing	27	14	13	
Household Income				<.0001
<3000 Euro/month	800 (44.2)	461 (40.2)	339 (51.3)	
≥3000 Euro/month	1008 (55.7)	686 (59.8)	322 (48.7)	
Missing	61	33	28	
Menopausal status				0.0003
Premenopausal	1369 (76.0)	906 (78.8)	463 (71.1)	
Postmenopausal	432 (24.0)	244 (21.2)	188 (28.9)	
Missing	68	30	38	
Charlson comorbidity index				0.0073
0	1502 (86.0)	977 (87.7)	525 (83.1)	
1+	244 (14.0)	137 (12.3)	107 (16.9)	
Missing	123	66	57	
Anxiety, categorical				0.953
Non-case	667 (36.1)	419 (36.0)	248 (36.3)	
Doubtful	474 (25.7)	297 (25.5)	177 (25.9)	
Case	706 (38.2)	448 (38.5)	258 (37.8)	
Missing	22	16	6	

Continued

Table 1 Continued

N (%)	Whole cohort	By body mass index at breast cancer diagnosis: Under/normal weight <25 kg/m^2	By body mass index at breast cancer diagnosis: Overweight/Obese ≥25 kg/m^2	P value*
Depression, categorical				0.0684
Non-case	1514 (82.0)	954 (82.0)	560 (82.0)	
Doubtful	206 (11.1)	120 (10.3)	86 (12.6)	
Case	127 (6.9)	90 (7.7)	37 (5.4)	
Missing	22	16	6	
Smoking behaviour				0.0055
Current smoker	396 (21.5)	274 (23.5)	122 (18.0)	
Former/never smoker	1448 (78.5)	892 (76.5)	556 (82.0)	
Missing	25	14	11	
Alcohol consumption				0.1434
≥1 drink/daily	178 (9.8)	122 (10.6)	56 (8.5)	
<1 drink/daily	1637 (90.2)	1031 (89.4)	606 (91.5)	
Missing	54	27	27	
Physical activity, MET-hours/week, median (IQR)				
Work, travel, leisure	16.0 (1.0–43.7)	16.0 (3.3–42.0)	12.0 (0.0–45.0)	0.0706
Travel, leisure	8.0 (0.0–22.0)	10.0 (0.0–26.0)	5.3 (0.0–17.3)	<.0001
Leisure only	0.0 (0.0–12.0)	2.0 (0.0–14.0)	0.0 (0.0–8.0)	<.0001
Missing max	11	5	6	
Tumour stage				0.0005
I	837 (44.8)	567 (48.0)	270 (39.2)	
II	823 (44.0)	496 (42.0)	327 (47.5)	
III	209 (11.2)	117 (9.9)	92 (13.3)	
Missing	–	–	–	
Tumour subtype				0.1401
HR+/HER–	1366 (73.5)	866 (73.9)	500 (72.8)	
HR+/HER2+	254 (13.7)	169 (14.4)	85 (12.4)	
HR–/HER2+	82 (4.4)	50 (4.3)	32 (4.7)	
HR–/HER2–	157 (8.4)	87 (7.4)	70 (10.2)	
Missing	10	8	2	
Breast surgery				0.3924
Partial surgery	1307 (69.9)	817 (69.2)	490 (71.1)	
Mastectomy	562 (30.1)	363 (30.8)	199 (28.9)	
Missing	–	–	–	
Axillary surgery				0.0378
Sentinel lymph node	1008 (53.9)	658 (55.8)	350 (50.8)	
Axillary dissection	861 (46.1)	522 (44.2)	339 (49.2)	
Missing	–	–	–	
Adjuvant radiation therapy				0.2817
No	158 (8.4)	106 (9.0)	52 (7.5)	
Yes	1711 (91.5)	1074 (91.0)	637 (92.4)	
Missing	–	–	–	

Continued

Table 1 Continued

N (%)	Whole cohort	By body mass index at breast cancer diagnosis: Under/normal weight <25 kg/m^2	Overweight/Obese ≥25 kg/m^2	P value*
(Neo)adjuvant chemotherapy				0.3813
No	642 (34.3)	414 (35.1)	228 (33.1)	
Yes	1227 (65.6)	766 (64.9)	461 (66.9)	
Missing	–	–	–	
Adjuvant endocrine therapy				0.2522
No	328 (17.5)	198 (16.8)	130 (18.9)	
Yes	1541 (82.4)	982 (83.2)	559 (81.1)	
Missing	–	–		
Adjuvant anti-HER2 therapy				0.5628
No	1586 (84.9)	997 (84.5)	589 (85.5)	
Yes	283 (15.1)	183 (15.5)	100 (14.5)	
Missing	–	–	–	

*Chi square for categorical variables, Wilcoxon rank sum test for continuous variables.
BMI, body mass index; HER2, human-epidermal-growth-factor-receptor-2; HR, hormone-receptor; MET, metabolic-equivalent-of-task; NA, non-applicable.

survivors scored worse on fatigue (mean (SD) 38.8 (24.7) vs 37.1 (25.4)) and arm symptoms (26.9 (26.1) vs 23.3 (16.2)) scales and reported more frequently late symptoms including arthralgia (56.5% vs 46.4%) and myalgia (33.9% vs 28.8%) at return to work assessment.

After multivariable adjustment, the OR of non-return-to-work for overweight or obese versus under or normal weight was 1.32 (95% CI 1.01 to 1.75), p=0.045. In addition, aORs of non-return-to-work were also significantly increased in patients who had lower household income (<3000 vs ≥3000 Euro/month, OR 1.37 (95% CI 1.03 to 1.80)), lower education level (primary school vs college graduate or higher, 2.96 (1.56 to 5.60)), more comorbidities (Charlson score 1+ vs 0, 1.55 (1.08 to 2.18), higher anxiety (case vs non-case, 1.42 (1.01 to 2.00)), those who were current smokers (vs former/never, 1.56 (1.14 to 2.12)), those who had higher tumour stage (III vs I, 2.03 (1.23 to 3.36)), those who had undergone mastectomy (vs partial surgery, 1.46 (1.07 to 1.99)), and those receiving anti-human epidermal growth factor receptor-2 therapy (vs no, 1.71 (1.21 to 2.42)) (table 2). Being overweight or obese remained independently associated with non-return to work also after adjustment for imbalances in working conditions at baseline (aOR of non-return-to-work vs under or normal weight, 1.33 (95% CI 1.01 to 1.76), p=0.043; no significant associations were found between prior job position and return to work status). Consistent results were obtained from sensitivity analyses that accounted for late toxicity symptoms. Odds of non-return to work remained elevated among overweight or obese compared with under or normal weight patients (aOR 1.40 (95% CI 1.05 to 1.88)). There were also significant associations of fatigue (continuous, aOR 1.011 (95% CI 1.005 to 1.017)), arm symptoms (continuous, 1.013 (1.008 to 1.019)) and myalgia (any grade vs no, 1.36 (95% CI 1.02 to 1.83)) with non-return to work (online supplemental table 2).

Post-treatment weight changes

In the overall cohort, 1010 patients (55.7%) reported stable weight, whereas 599 (33.0%) reported ≥5% weight gain and 205 (11.3%) reported ≥5% weight loss. Respectively, among under or normal weight patients and overweight or obese patients, 677 (59.1%) and 333 (49.8%) reported stable weight, 369 (32.2%) and 230 (34.4%) reported ≥5% weight gain, whereas 100 (8.7%) and 105 (15.7%) reported ≥5% weight loss.

There seemed to be no significant association between weight change and change in physical activity among under or normal weight patients (mean change: −6.3 vs +1.4 MET-hour/week among whose weight decreased vs was stable or increased, respectively, p=0.539). Conversely, changes in physical activity were significantly associated with weight change in patients who were overweight or obese, with those who lost weight being also more likely to have reported an increase in physical activity compared with those whose weight was stable or increased (mean change: +4.7vs +1.0 MET-hour/week, respectively, p=0.010) (table 3). Compared with those whose weight remained stable or increased, patients who were under or normal weight at baseline and lost weight also reported worse QoL 2-year postdiagnosis, including scoring significantly worse for emotional, social, cognitive and role function as well as reporting more severe fatigue and arm symptoms. On the contrary, overweight or obese patients who lost weight reported significantly better physical function and body image as well as reduced pain, dyspnoea

Table 2 Multivariable logistic regression of factors associated with non-return-to-work (N=1869)

	Adjusted OR	95% CI	P
BMI at diagnosis (vs underweight/normal)			
Overweight/obese	1.32	1.01 to 1.75	0.045
Age (continuous, 1 year increase)	1.01	0.98 to 1.04	0.391
Highest education level (vs college graduate or higher)			
Primary or lower	2.96	1.56 to 5.60	0.0008
High school	1.58	1.18 to 2.10	0.002
Household Income (vs. ≥3000 Euro/month)			
<3000 Euro/month	1.37	1.03 to 1.80	0.0271
Menopausal status (vs premenopausal)			
Postmenopausal	1.38	0.96 to 1.98	0.083
Comorbidities (vs Charlson 0)			
Charlson 1+	1.55	1.08 to 2.18	0.016
Anxiety (vs non-case)			
Doubtful	1.41	1.01 to 1.99	0.0481
Case	1.42	1.01 to 2.00	0.0438
Depression (vs non-case)			
Doubtful	1.31	0.88 to 1.95	0.1888
Case	1.32	0.79 to 2.20	0.2905
Smoking behaviour (vs former/never smoker)			
Current smoker	1.56	1.14 to 2.12	0.0049
23 Physical activity (travel, leisure) (continuous, 1-MET-hour/week increase)	0.99	0.99 to 1.00	0.296
Tumour stage (vs I)			
II	1.20	0.85 to 1.70	0.290
III	2.03	1.23 to 3.36	0.00581
Breast surgery (vs partial surgery)			
Mastectomy	1.46	1.07 to 1.99	0.0179
Axillary surgery (vs sentinel lymph node)			
Axillary dissection	1.27	0.89 to 1.80	0.1845
(Neo)adjuvant chemotherapy (vs no)			
Yes	1.01	0.69 to 1.45	0.9847
Adjuvant endocrine therapy (vs no)			
Yes	0.77	0.55 to 1.09	0.1398
Adjuvant anti-HER2 therapy (vs no)			
Yes	1.71	1.21 to 2.42	0.0024

*For all factors in the table.
BMI, body mass index; HER2, human-epidermal-growth-factor-receptor-2; MET, metabolic-equivalent-of-task.

and breast symptoms compared with those whose weight was stable or increased (online supplemental table 3).

Post-treatment weight changes and return-to-work

Rates of non-return to work in the overall cohort were 18.2% for those with stable weight, 26.0% for those who gained ≥5% weight and 23.4% for those who lost ≥5% weight (p=0.0008). When considering non-return to work according to BMI at BC diagnosis, among patients who were under or normal weight, rates of non-return to work were 15.2% for those who remained stable, 20.6% for those who gained ≥5% wt and 26.0% for those who lost ≥5% wt (p=0.0082). Among those who were overweight or obese, rates of non-return to work were 24.3% for those who remained stable, 34.8% for those who gained ≥5% wt and 20.9% for those who lost ≥5% wt (p=0.0065).

Non-return to work was associated with weight changes when modelled as categorical variable in a multivariable setting, with the effect of weight changes on return to work status being dependent on BMI at diagnosis ($p_{interaction}$=0.0002). For under or normal weight women who lost ≥5% weight, the odds of non-return to work were twofold (aOR, 2.07; 95% CI 1.20 to 3.56, vs no weight loss, p=0.0086), whereas for overweight or obese women who lost ≥5% wt, odds of non-return to work were halved (aOR 0.48; 95% CI 0.24 to 0.97, vs no weight loss, p=0.0418) (table 4). Similar results were obtained after adjustment for imbalances in work conditions at baseline (data not shown).

Additionally, the continuous trend of weight gain on non-return-to-work was significant among overweight or obese patients (aOR for each one-percent-unit increasing weight difference from baseline, 1.03; 95% CI 1.01 to 1.06, p=0.030) but not among under or normal weight women (aOR 0.99; 95% CI 0.97 to 1.02, p=0.823) ($p_{interaction}$=0.036) (online supplemental table 4).

DISCUSSION

The CANTO cohort allowed us to explore how body weight and employment trends are related in early stage BC survivors, who make up a relevant portion of the modern workforce.[13] In this large, prospective, contemporary cohort, we have shown that excess body weight at BC diagnosis is independently associated with increased rates of non-return-to-work 2 years afterwards, among young, previously employed BC survivors.

From a societal perspective, overweight and obesity have multiple implications in the job market and excess weight correlates with worse occupational characteristics regardless of having a cancer history. Excess weight is a visible status and can predispose individuals to stigma and bias.[27] Data indicate that there is substantial appearance-based discrimination in employment,[28] and that employers favour hiring workers whose BMI is in the normal range.[29] As a result, people with higher BMI, particularly individuals with obesity, tend to be less likely to be hired and more frequently remain long-term unemployed.[30] Excess weight is also associated with lower education and income,[31] and with having lower job profiles, with worse monetary compensation as well as with less appealing non-pecuniary characteristics, including work content, job security or work-related social prestige.[32] From a patient perspective, prior research suggests that

Table 3 Associations between changes in physical activity and weight

	Weight stability/gain	Weight loss	P*
Physical activity (travel, leisure), mean change (95% CI)			
Whole cohort	+1.3 (+0.2 to +2.3)	−0.7 (−9.3 to +7.9)	0.046
Under/normal weight	+1.4 (−0.1 to +2.9)	−6.3 (−23.7 to +11.1)	0.539
Overweight/obese	+1.0 (−0.2 to +2.2)	+4.7 (+1.9 to +7.5)	0.010

*Wilcoxon rank-sum test.

reasons for unemployment among cancer survivors most frequently include physical limitations, cancer-related symptoms and impairments in social and role functioning resulting from cancer treatment.[4 33] In a large meta-analysis, de Boer *et al*[34] reported that cancer survivors are 1.37 times more likely to be unemployed than healthy controls, with a pooled rate of unemployment of 33.8% overall and 35.6% specifically among BC survivors, and authors concluded that the mechanism that most likely explains these higher figures among cancer survivors is a higher disability rate. Analogously, among women in the Young Women's Breast Cancer Study who were employed before BC diagnosis and reported subsequent unemployment, half declared that they were unemployed for health reasons,[13] while work productivity and job performance were shown to be substantially and negatively impacted by symptom burden after BC, with increased probability of work-related distress.[12 13] Moreover, supporting the notion that transitioning out of the workforce is more often due to health-related issues than to other reasons, previous studies showed that voluntary unemployment that is not linked to health conditions is infrequent unless patients benefit from sufficiently high alternative resources for income, other than their job compensation.[4] Overweight and obese patients are generally particularly susceptible to experience negative and long-lasting effects after cancer treatment and are exposed to worse physical and psychological struggles. Patients with higher BMI more often develop fatigue, pain and cognitive troubles that are prone to become chronic and can also affect return to work.[35]

Table 4 Association of weight changes (weight loss vs non-weight loss (stability/gain)) with non-return-to-work in multivariable logistic regression models (N=1814)

	Adjusted OR*	95% CI	P
Whole cohort			
Weight stability/gain	Ref.	–	–
Weight loss	1.11	0.73 to 1.68	0.632
p for interaction weight change-by-BMI=0.0002			
Under/normal weight			
Weight stability/gain	Ref.	–	–
Weight loss	2.07	1.20 to 3.56	0.0086
Overweight/obese			
Weight stability/gain	Ref.	–	0.0418
Weight loss	0.48	0.24 to 0.97	

*For factors in Table 2 + change in physical activity.
BMI, body mass index.

Putting our results into the context of the existing literature, overweight and obese patients in our cohort were more likely to have lower education and to have low-ranking jobs, and more than half had also reported a low household income at diagnosis. These characteristics make it unlikely for these survivors to have remained voluntarily unemployed. Further, concomitant medical conditions also seemed to impair return to work ability of patients in this cohort, and indeed one in six overweight or obese women had at least one comorbidity at the time of BC diagnosis. Presence of concomitant morbid conditions may have had also an implication in the higher observed proportion of overweight and obese patients that received a disability pension compared with under or normal weight patients, leading in turn to a reduced number of overweight and obese women who were actively seeking a job 2-year postdiagnosis. Finally, rates of patients who permanently retired after BC were higher among overweight or obese compared with under or normal weight patients, despite a mean age of approximately 48 years at the time of diagnosis for the former group. This is a relatively premature age for retirement in a country like France, where legal retirement age for women is 62 years, and specifically among women who were included in this cohort, all professionally active and mostly employed on long-term, permanent work contracts at the time of BC diagnosis.

We also reported significant associations between weight changes, which are known to be common after BC,[36] and return to work. In CANTO, patients who were overweight or obese at diagnosis and who experienced a weight loss of at least 5% of initial body weight (corresponding to approximately 4 kg in this cohort) were less likely to be unemployed 2 years from diagnosis compared with those who did not lose weight. Several controlled trials have assessed the impact of weight loss interventions on a number of outcomes among overweight and obese BC survivors. These interventions have been shown to be feasible, safe and effective in improving physical fitness, cardiorespiratory parameters and other health-related QoL outcomes.[10 37 38] Ongoing studies will confirm whether weight loss improves BC-specific outcomes, including recurrence and survival.[11] Our results add to

the existing literature showing an association of weight loss with return to work in overweight and obese women, for which there are several possible mediators. These include improved QoL, reduced psychophysical distress, attenuated downstream effects of cancer treatment and healthier overall physical status that can facilitate rejoining the workplace. Our findings also suggest that weight loss in patients who present with excess weight at diagnosis should be further explored as a way to facilitate re-employment, thus mitigating the societal and economic impact of surviving BC. In this context, this study advocates for the urgent need of evaluating employment outcomes in large trials of weight management in cancer survivors, including the assessment of the aetiology and duration of sick leave and absence from work, rates of re-employment and longitudinal patterns of work ability, work capacity and wage losses. Particularly, future trials should look beyond whether an overweight or obese patient has returned to work or not after cancer. For many cancer survivors, returning to work is indicative of a complete recovery and regained life routine.[33] However, although a survivor's well-being may be higher within the group of those who return to work compared with those that do not,[5 6] perceived health-related QoL may also range widely among those who do actually go back to work. Patients may be forced to change career tracks or not be able to perform at the same level as before their cancer or experience particular physical, psychological and financial challenges while trying to balance treatment side effects with several other employment concerns in daily life.[13] This may translate into worse QoL and increase distress and job dissatisfaction even after a patient has managed to successfully rejoin the workplace. All these aspects are relevant to overweight and obese individuals, who were shown to be particularly vulnerable to long-lasting and more severe physical and psychosocial stressors during the survivorship period compared with patients within a normal BMI range.[39 40]

The current study has a number of strengths. Previous studies have largely only included unemployment rates after cancer as a secondary outcome and there are few data concerning the relationship between body weight and job reintegration in cancer survivorship. Our findings are based on a prospective clinical study of patients recruited across France, strengthened by a large sample size. To be able to evaluate patients who would be available for labour market and seeking re-employment, we only identified those who were too young to be retired 2 years after BC diagnosis, attempting to avoid including patients who would directly transition from cancer leave into permanent retirement. Additionally, body weight was objectively and longitudinally assessed by dedicated study nurses. Also, CANTO had availability of data regarding other behavioural characteristics, including physical activity, with low rates of missing data. As such, in this study, we were able to better describe behavioural traits of BC survivors over time and to conclude that overweight or obese patients who lost weight were also more likely to report significant increases in physical activity, which is an important component of weight management. In contrast, weight loss was not accompanied by a concomitant increase in physical activity for under or normal weight patients, who reported reduced or at most similar activity levels, possibly reflecting unintentional weight changes due to more severe symptom burden and treatment toxicity. These behavioural differences are also mirrored by differential patterns of QoL observed 2 years after BC diagnosis when analysing patients by baseline BMI and weight change category. Women who were overweight or obese at diagnosis and who lost weight scored indeed significantly better on a number of functional and symptom domains compared with those whose weight was stable or increased, with no apparent detriments in QoL associated with their weight loss (consistently with a previous CANTO publication[41]), whereas women who were under or normal weight at diagnosis and had lost weight seemed to fare worse than those who reported a stable or increased weight, being more likely to report of impaired functionality and more severe symptomatology.

Some limitations must also be acknowledged. First, we used an arbitrary cut-off of 5% to define weight change categories. However, this was based on previously observed clinically meaningful benefits of such a weight loss in the overweight patient population,[42] and the association between non-return to work and weight changes remained consistent when weight change was modelled as continuous. Second, we used self-reported instruments for physical activity, with possible recall and reporting biases. Third, we acknowledge that our data do not allow to assess intentionality of weight changes. However, we provided additional descriptive information to better characterise patients whose weight decreased, particularly focusing on other closely related health behaviours such as changes in physical activity, and we were able to access an extensive list of patient-reported outcomes that helped us better define several parameters of health-related QoL and correlate them with weight variations. Moreover, to rule out unintentional weight changes that could be due to disease progression, we upfront included only patients who were disease-free 2 years after diagnosis, without evidence of BC recurrence or diagnosis of second cancers. Fourth, French law does not allow to collect race/ethnicity information, which we acknowledge as a potential confounder when assessing determinants of return to work. Fifth, we could not evaluate patients who had not provided information on work status at year 2 reassessment and this may have introduced some selection bias. However, respondents to work status questions were very similar to non-respondents in term of baseline characteristics. Finally, differences in insurance programmes and social security systems may limit generalisability of our findings to work and healthcare systems that are different from France.

CONCLUSION

In conclusion, our data suggest that excess body weight at BC diagnosis may be a significant barrier to return to work and that overweight and obese patients represent a vulnerable group for unemployment after BC. However, while among overweight or obese women in this cohort there was an association between weight loss and higher rates of return to work, further weight gain was associated with reduced likelihood of returning to work. Future research, including ongoing randomised studies testing interventions of weight management and weight loss among BC survivors, should consider including measures of social rehabilitation and employment outcomes.

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Body weight and return to work among survivors of early-stage breast cancer.

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Supplementary data

Supplementary Table 1. Working conditions at breast cancer diagnosis.

Supplementary Table 2. Multivariable logistic regression of factors associated with non-return-to-work, sensitivity analysis including late toxicity symptoms.

Supplementary Table 3. Associations between patient-reported quality of life at return to work assessment and weight changes. Data are presented by baseline body mass index.

Supplementary Table4. Association of weight changes (continuous, difference from baseline) in multivariable logistic regression models.

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Supplementary Table 1. Working conditions at breast cancer diagnosis.

N (%)	Whole cohort	By body mass index at breast cancer diagnosis		
		Under/Normal weight (<25 Kg/m^2)	Overweight/Obese (≥25 Kg/m^2)	*p**
Total	1869 (100)	1180 (63.1)	689 (36.9)	
Job position				
Professionals and managers	455 (24.6)	331 (28.4)	124 (18.1)	<.0001
Technicians and associate professionals	445 (24.0)	287 (24.6)	158 (23.1)	
Clerks	728 (39.3)	430 (36.8)	298 (43.6)	
Manual workers	125 (6.7)	62 (5.3)	63 (9.2)	
Self-employed[a]	98 (5.3)	57 (4.9)	41 (6.0)	
Missing	18	13	5	
Work sector				0.324
Private	685 (39.4)	415 (37.7)	270 (42.2)	
Public	861 (49.5)	559 (50.8)	302 (47.3)	
Self-employed	138 (7.9)	90 (8.2)	48 (7.5)	
Other	55 (3.2)	36 (3.3)	19 (3.0)	
Missing	130	80	50	
Type of job contract				0.089
Permanent position	1386 (82.9)	861 (81.7)	525 (84.9)	
Fixed-term position	102 (6.1)	71 (6.7)	31 (5.0)	
Self-employed	69 (4.1)	40 (3.8)	29 (4.7)	
Other	115 (6.9)	82 (7.8)	33 (5.3)	
Missing	197	126	71	
Workload				0.337
Full-time	425 (24.6)	272 (24.8)	153 (24.3)	
Part-time (<40 hours/week)	983 (56.9)	612 (55.8)	371 (58.9)	
Part-time (≥40 hours/week)	319 (18.5)	213 (19.4)	106 (16.8)	
Missing	142	83	59	
Length of daily commuting				0.967
< one hour	1173 (65.3)	743 (65.3)	430 (65.2)	
≥ one hour	623 (34.7)	394 (34.6)	229 (34.7)	
Missing	73	43	30	

[a]Includes farmers, craftsmen, and shopkeepers. *Chi square test.

Supplementary Table 2. Multivariable logistic regression of factors associated with non-return-to-work, sensitivity analysis including late toxicity symptoms (N=1869).

	Adjusted* Odds Ratio	95% Confidence Interval	*p*
BMI at diagnosis (vs. Underweight/Normal)			
Overweight/Obese	1.40	1.05 - 1.88	0.022
Age (continuous, 1-year increase)	1.01	0.98 - 1.04	0.496
Highest education level (vs. College graduate or higher)			
Primary or lower	2.13	1.06 - 4.27	0.033
High school	1.44	1.06 – 1.96	0.018
Household Income (vs. ≥3000 Euro/month)			
<3000 Euro/month	1.26	0.94 - 1.68	0.123
Menopausal status (vs. premenopausal)			
Postmenopausal	1.37	0.93 - 2.01	0.106
Comorbidities (vs. Charlson 0)			
Charlson 1+	1.39	0.95 - 2.02	0.085
Anxiety (vs. Non-case)			
Doubtful	1.30	0.90 - 1.87	0.153
Case	1.22	0.85 - 1.75	0.274
Depression (vs. Non-case)			
Doubtful	1.04	0.67 - 1.60	0.860
Case	1.16	0.67 - 1.99	0.597
Smoking behavior (vs. Former/Never smoker)			
Active smoker	1.44	1.04 – 1.99	0.029
Physical activity (Travel, leisure) (continuous, 1-MET-hour/week increase)	0.99	0.99 - 1.00	0.275
Tumor stage (vs. I)			
II	1.26	0.87 - 1.81	0.222
III	1.98	1.16 - 3.38	0.012
Breast surgery (vs. Partial surgery)			
Mastectomy	1.40	1.01 - 0.95	0.049
Axillary surgery (vs. Sentinel lymph node)			
Axillary dissection	1.09	0.75 - 1.59	0.647
(Neo)adjuvant chemotherapy (vs. No)			
Yes	1.03	0.69 - 1.53	0.874
Adjuvant endocrine therapy (vs. No)			
Yes	0.77	0.54 - 1.10	0.153
Adjuvant anti-HER2 therapy (vs. No)			
Yes	1.80	1.24 - 2.61	0.002
Fatigue (continuous)	1.011	1.005 - 1.017	0.0005
Arm symptoms (continuous)	1.013	1.008 - 1.019	<.0001
Arthralgia (vs. No)			
Any grade	1.079	0.80 - 1.46	0.621
Myalgia (vs. No)			
Any grade	1.36	1.02 - 1.83	0.039

BMI= Body Mass Index; MET= metabolic-equivalent-of-task; HER2= human-epidermal-growth-factor-receptor-2. *for all factors in the Table.

Supplementary Table 3. Associations between patient-reported quality of life at return to work assessment and weight changes. Data are presented by baseline body mass index.

Domain	Under/Normal weight			Overweight/Obese		
	Weight stability/gain	Weight loss	*p**	Weight stability/gain	Weight loss	*p**
Global Health	67.59	63.78	0.065	64.42	65.46	0.693
Physical Function	88.45	86.87	0.066	83.73	87.55	0.015
Emotional Function	68.94	63.69	0.048	70.40	68.92	0.924
Social Function	85.12	80.76	0.020	82.99	87.00	0.146
Cognitive Function	74.27	69.05	0.038	75.39	74.50	0.762
Role Function	84.40	81.12	0.048	78.34	82.33	0.110
Fatigue	36.72	41.27	0.033	38.75	37.78	0.668
Pain	25.68	29.59	0.113	33.61	28.00	0.048
Insomnia	42.37	48.45	0.098	44.47	44.00	0.955
Nausea/Vomit	4.60	8.16	0.015	5.42	6.33	0.533
Dyspnea	15.93	14.29	0.515	22.76	14.00	0.001
Appetite Loss	8.13	14.29	0.006	5.24	10.33	0.007
Constipation	17.32	19.39	0.484	14.10	18.18	0.260
Diarrhea	6.56	9.52	0.262	9.58	9.33	0.295
Financial difficulties	9.31	14.63	0.076	9.93	6.80	0.416
Body Image	75.29	77.89	0.221	69.93	80.25	0.0002
Sexual Function	36.71	34.40	0.395	31.22	34.88	0.175
Sexual Enjoyment	61.84	60.32	0.879	57.54	59.68	0.407
Future Perspective	58.39	54.98	0.310	57.17	52.67	0.232
Side Effects	17.56	18.12	0.528	19.88	18.18	0.352
Breast Symptoms	19.75	20.49	0.919	23.88	19.19	0.032
Arm Symptoms	22.63	29.34	0.018	27.03	25.83	0.934
Upset by Hair Loss	40.55	47.06	0.451	41.95	41.27	0.960

Quality of life scores are summarized using mean scores. Standard scoring algorithms were applied, with higher scores reflecting better quality of life for global health or functional scales and greater severity for symptoms.
*Wilcoxon rank-sum test

Supplementary Table 4. Association of weight changes (continuous, difference from baseline) in multivariable logistic regression models.

	Odds Ratio	95% Confidence Interval	*p*
Whole cohort			
Weight change, continuous (1 percent unit increase)	1.01	0.99-1.03	0.1597
	P for interaction weight change-by-BMI=0.036		
Under/Normal weight			
Weight change, continuous (1 percent unit increase)	0.99	0.97-1.02	0.808
Overweight/Obese			
Weight change, continuous (1 percent unit increase)	1.03	1.01-1.06	0.030

Adjusted for age, menopausal status, comorbidities, education, income, smoking, stage, breast and axillary surgery, chemotherapy, endocrine therapy, anti-HER2 therapy, anxiety/depression, change in physical activity (travel, leisure). Weight changes modeled as continuous, odds ratios to be interpreted for one increasing percent-unit in weight from diagnosis.