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The frequency, magnitude and timing of post-diagnosis body weight gain in Dutch breast cancer survivors

W.H. Heideman[a], N.S. Russell[b], C. Gundy[a], M.A. Rookus[a,*], D.W. Voskuil[a]

[a]The Netherlands Cancer Institute, Division of Psychosocial Research and Epidemiology, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
[b]The Netherlands Cancer Institute, Department of Radiotherapy, Amsterdam, The Netherlands

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ABSTRACT

To evaluate the association between systemic treatments and post-diagnosis weight gain in breast cancer patients during longer follow-up periods, we conducted a retrospective cohort study ($n = 271$). Information on adjuvant systemic treatments and repeated body weight measurements was obtained from medical records, and analysed using multi-level regressions.

During the first year, a mean weight change of +2.0 kg (SD 4.9) was observed. Overall, 29% of all breast cancer patients had gained 5 kg or more in body weight during total follow-up (median: 3 years). In multi-level analyses, women who received combined systemic treatment gained significantly more weight as compared with women who received no systemic treatment (4.5 kg versus 2.0 kg at 5 years post-diagnosis, $p < 0.05$).

Significant weight gain occurs in breast cancer patients in the Netherlands during the first year post-diagnosis. After the first year, further weight gain mainly occurs in women who receive chemotherapy in combination with endocrine therapy.

1. Introduction

The prevalence of overweight and obesity in Europe has increased over the last decades.[1] Overweight and obesity are associated with an increased risk of chronic diseases including post-menopausal breast cancer.[2] Moreover, adverse prognostic effects of obesity at diagnosis have been observed in both pre- and post-menopausal women.[3,4]

In addition to a high prevalence of overweight and obesity in breast cancer patients at diagnosis, unintentional body weight gain during and after adjuvant treatment is frequently observed. A review of the literature shows that the mean gain in body weight ranges from 2.5 to 6.2 kg in studies of weight gain in breast cancer patients during the first year after diagnosis.[3] Suggested causes of post-diagnosis body weight gain in breast cancer patients are often related to the effects of systemic treatments, i.e. especially women who receive chemotherapy are likely to gain body weight.[5–7] Earlier onset of menopause experienced with chemotherapy is a plausible cause of body weight gain in breast cancer patients who are pre-menopausal at diagnosis.[5,6,8] Reduced physical activity-related energy expenditure is possibly a major determinant of weight gain after diagnosis, as marked reductions in the level of physical activity after breast cancer diagnosis were observed.[9–12] Resting energy expenditure was shown not to change markedly during and after chemotherapy.[9,13–16] In addition, most studies did not find an increased dietary intake in breast cancer patients.[9,15] Besides adjuvant chemotherapy, adjuvant endocrine therapy (e.g. Tamoxifen) is often suggested as a predictor for body weight gain.[17,18] However, a study on the effects of Tamoxifen on the health-related quality of life within the National Surgical Adjuvant Breast and

* *Corresponding author:* Tel.: +31 20 512 2491; fax: +31 20 512 2322.
E-mail address: m.rookus@nki.nl (M.A. Rookus).
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Bowel Project P-1 Trial did not show differences in body weight gain between women randomised to Tamoxifen compared to a placebo treatment.[19]

Post-diagnosis body weight gain is associated with increased risk of recurrence and reduced survival in some observational studies, but not all.[10,18,20] Body weight gain and subsequently obesity could not only increase the risk of contralateral breast cancer, but also contribute to the development of other diseases, such as diabetes and hypertension, and other cardiovascular problems.[21–23] In addition, body weight gain after breast cancer diagnosis could have a serious negative impact on self-image and quality of life of the breast cancer patients.[10] Most studies on body weight after breast cancer were conducted in the United States (US), where prevalence of obesity is much higher than in some European countries. The role of endocrine treatments for breast cancer in the development of weight gain remains to be elucidated, as do the long-term effects of adjuvant systemic treatments on body weight.

Considering the potential adverse consequences of body weight gain, the objective of this study was to investigate the frequency and magnitude of post-diagnosis body weight gain in relation to breast cancer treatment in Dutch breast cancer survivors. We explored the associations between post-diagnosis body weight gain and treatment regimens, i.e. chemotherapy and/or endocrine therapy, during the first year after diagnosis as well as during longer periods of follow-up.

2. Patients and methods

2.1. Study population

This study was based on a hospital-based retrospective cohort. Data were collected from medical records of breast cancer patients who had been diagnosed and/or treated at The Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital (NKI–AVL) in Amsterdam, The Netherlands. The cohort consisted of all breast cancer patients from the files of one radiation-oncologist (NSR), who measured and recorded body weights of patients at follow-up consults on a regular basis. The file contained 315 breast cancer patients. Twenty two medical records were irretrievable or missing, usually because the patient had been discharged, and another 22 patients were excluded because only one recorded body weight was available. This resulted in the medical records of 271 individuals, which were available for analyses in our study. Thirty women developed a second primary mammary tumour. We used information on body weight after diagnosis of the first primary tumour in 250 women and of the second tumour in 21 women, as these were the tumours for which information on post-diagnosis body weight was available. In cases of breast cancer recurrence ($n = 15$) or contralateral breast cancer ($n = 9$), the data on body weight were only included up to 6 months before diagnosis of the metastasis or contralateral tumour.

2.2. Data collection

Information on body weight (in kg, no decimals), including date of measurement, was extracted from the medical records using a standardised protocol. We obtained information from reports of clinical examination, follow-up history, anaesthesiology reports, chemotherapy medication reports and from medical correspondence.

Additional information on date of diagnosis, type of systemic treatment and recurrence of breast cancer was obtained from the NKI–AVL tumour registry. Age at diagnosis, menopausal status at diagnosis and date of start with chemotherapy or endocrine therapy were collected from the medical records. For each treatment including radiotherapy, chemotherapy and endocrine therapy, the exact starting date was collected. Data on menopausal status at diagnosis were only included if recorded within 3 months before or after diagnosis (pre-menopausal or post-menopausal, respectively). If menopausal status was missing patients were categorised based on age ($n = 103$), i.e. pre-menopausal if age at diagnosis was 50 years or younger, post-menopausal if age at diagnosis was 51 years or older.

2.3. Data analyses

Post-diagnosis weight gain in relation to treatment was evaluated in two phases. Firstly, we assessed frequency and magnitude of body weight change in subgroups based on treatment and menopausal status. Secondly, to fully utilise all information on repeated measurements of body weight, several multi-level regression analyses were conducted.

For the descriptive analyses, three different body weight variables were created, i.e. body weight at diagnosis, body weight 1 year after diagnosis and body weight 5 years after diagnosis. When body weight at diagnosis was not available, we used the first body weight measured between 1 month before diagnosis and 3 months after diagnosis, but before start of systemic treatments. Body weight 1 year after diagnosis was defined as the last body weight measured in the period from 3 to 15 months after diagnosis (median 0.9 years; range 0.3–1.7 years). Body weight 5 years after diagnosis was defined as the last body weight measured between 15 months and 6 years after diagnosis (median 3.1 years; range 1.3–6.0 years). One-sample *t*-tests were used to determine whether the changes in body weight between diagnosis, 1 year after diagnosis, and 5 years after diagnosis were significantly different from zero. Differences between groups based on treatment or menopausal status were compared using independent samples *t*-tests. A two-sided *p*-value of 0.05 was considered statistically significant. Descriptive analyses were conducted using SPSS version 12.0.1.

To analyse the repeated body weight measurements for each individual using exact time of measurement, we conducted a multi-level analysis. Follow-up time (in years) represents the period between date of diagnosis and the dates of measurement of each body weight, with maximum follow-up time in the model set at 10 years post-diagnosis. For modelling body weight development over time we fitted two slopes in our basic model; the first slope estimated linear change in body weight over time, the second slope described a second order polynomial with time, to allow for departures from linearity. Age at diagnosis was added to the model as a time-independent variable. Therefore, the intercept was body weight at diagnosis, which will differ by age at diagnosis. To

evaluate the effects of treatment, all individual body weights were categorised into one of 10 treatment categories, i.e. (0) no chemo- or endocrine therapy, (1) during chemotherapy (0–6 months since start of chemotherapy), no endocrine therapy, (2) shortly after chemotherapy (6–12 months after start of chemotherapy), no endocrine therapy, (3) during longer follow-up after chemotherapy (12–24 months), no endocrine therapy, (4) more than 2 years after chemotherapy, no endocrine therapy, (5) during endocrine therapy, no chemotherapy, (6) 0–6 months after start of chemotherapy, during endocrine therapy, (7) 6–12 months, (8) 12–24 months and (9) more than 2 years after start of chemotherapy during endocrine therapy. In this way, we were able to distinguish changes in body weight with different treatment combinations. Likelihood ratio tests were used to assess the levels of significance for the fixed and random effects. The multi-level analyses were performed with MLWin software, version 2.02.

3. Results

All women included in this study ($n = 271$) were diagnosed with breast cancer between 1974 and 2006, and were treated with surgery and radiotherapy. Median follow-up time was 3.1 years with a range of 0.1–32.1 years. Clinical and tumour characteristics of the study population are shown in Table 1. Mean age was 54 years (SD 12). Fourteen percent received only chemotherapy as systemic treatment, 25% received only endocrine therapy, 32% received combined systemic treatment (i.e. chemotherapy and endocrine therapy) and 29% received no adjuvant systemic treatment (Table 1). Mean body weight at diagnosis was 70.3 kg (SD 12.9) and mean BMI was 25.4 kg/m^2 (SD 4.3). Table 2 shows age, menopausal status and anthropometric measurements stratified by treatment group. Women who received only chemotherapy were significantly younger (mean ± SD: 48.4 ± 9.6 years) than women who received only endocrine therapy (61.6 ± 11.1 years, $p < 0.001$). Women who received only chemotherapy were most often pre-menopausal (66%), whereas most women who received endocrine therapy only were post-menopausal (84%). Body weight at diagnosis did not differ significantly between the four treatment groups.

In our study population, a significant mean change in body weight of +2.4 ± 5.6 kg was observed during approximately 3.4 years of follow-up (Table 3). Most of the weight gain occurred in the first year after diagnosis (mean ± SD: +2.0 ± 4.9 kg). Twenty six percent of all patients gained 5 kg or more during the first year. In the period after the first year, 43% of the women had a stable body weight. On comparing the treatment groups, marked differences in body weight change were observed (Table 3). Women who did not receive any systemic treatment gained some weight during the first year after diagnosis (mean ± SD: 1.5 ± 3.9 kg; $p < 0.05$). However, during total follow-up no significant weight gain was observed in this group, as some weight was lost after the first year. Women who were treated with chemotherapy, either with or without endocrine therapy, gained on average more than 2 kg in body weight during the first year after diagnosis (mean ± SD: only chemotherapy: 2.2 ± 4.3; combined therapy: 2.6 ± 6.0; $p < 0.05$). Interestingly, women who received only chemotherapy lost some weight during follow-up after the first year, whereas women who received combined systemic treatment experienced further weight gain. The highest overall body weight gain in the 5 years after diagnosis was found in women who received combined systemic treatment

Table 1 – Baseline characteristics at diagnosis and therapy received by the study population

Age, years (mean ± SD)	54 ± 12	
Stage, n (%)		
0 (TisN0)	13	(4.8)
I (T1N0)	86	(31.7)
II (T1N1; T2N[a], T3N0)	104	(38.4)
III (T3N1)	42	(15.5)
Chemotherapy regimen, *n* (%)		
No chemotherapy	146	(53.9)
AC or EC	71	(26.2)
CMF	12	(4.4)
FAC or FEC	22	(8.1)
Other (incl Herceptin)	18	(6.6)
Endocrine therapy, *n* (%)		
No endocrine therapy	117	(43.2)
Tamoxifen	120	(44.3)
Other	34	(12.5)
Body weight, kg (mean ± SD)	70.4 ± 12.9	
Height, cm (mean ± SD)	1.67 ± 0.07	
Body mass index, kg/m^2 (mean ± SD)	25.5 ± 4.4	
Menopausal status[a], *n* (%)		
Pre-menopausal	127	(46.9)
Post-menopausal	144	(53.1)
Follow-up (years), median (range)	3.1	(0.1–32.1)

a Menopausal status at diagnosis; if menopausal status was missing, patients were categorised based on age ($n = 103$; i.e. post-menopausal if age at diagnosis $\geqslant 51$).

Table 2 – Characteristics of the study population, by treatment group

	No systemic treatment	Chemotherapy only	Endocrine therapy only	Combined systemic treatment
	n = 79	*n* = 38	*n* = 67	*n* = 87
Age, years (mean ± SD)	56.5 ± 11.7[a–c]	48.4 ± 9.6[a]	61.6 ± 11.1[a,b,d]	46.9 ± 8.8[d,c]
Body weight, kg (mean ± SD)	71.6 ± 13.9	70.5 ± 11.5	70.1 ± 11.4	69.5 ± 13.8
Height, m (mean ± SD)	1.66 ± 0.07	1.68 ± 0.07	1.65 ± 0.06	1.68 ± 0.08
Menopausal status				
Pre-menopausal, *n* (%)	31 (39.2)	25 (65.8)	11 (16.4)	60 (69)
Post-menopausal, *n* (%)	48 (60.8)	13 (34.2)	56 (83.6)	27 (31)
Body mass index				
BMI, kg/m^2 (mean ± SD)	26.1 ± 4.5	25.2 ± 3.8	25.9 ± 4.4	24.7 ± 4.4
<25, *n* (%)	32 (49.2)	19 (54.3)	26 (46.4)	43 (60.6)
25–30, *n* (%)	20 (30.8)	11 (31.4)	20 (35.7)	20 (28.2)
>30, *n* (%)	13 (20.0)	5 (14.3)	10 (17.9)	8 (11.3)

[a–d]Figures with same letter are significantly different ($p < 0.01$).
At diagnosis, data were missing on body weight in *n* = 27, height *n* = 22 and BMI *n* = 42.

Table 3 – Change in body weight according to adjuvant systemic treatment

	n	Follow-up	Change (kg)	Body weight change (% of *n*)			
		Median (range)	Mean ± SD	Loss ⩾ 2 kg	Stable ± 1 kg	Gain 2–4 kg	Gain ⩾ 5 kg
All women							
$W_{5\ years}$ versus dx	173	3.4 (1.3–6.0)	2.4 ± 5.6*	15.6	29.5	25.4	29.5
$W_{1\ year}$ versus dx	179	0.9 (0.3–1.3)	2.0 ± 4.9*	18.4	29.1	26.8	25.7
$W_{5\ years}$ versus $1\ year$	136	3.1 (1.3–6.0)	0.5 ± 4.8	22.8	43.4	18.4	15.4
No systemic treatment							
$W_{5\ years}$ versus dx	45	3.0 (1.3–5.8)	0.9 ± 4.0	22.2	40.0	22.2	15.6
$W_{1\ year}$ versus dx	49	0.9 (0.3–1.2)	1.5 ± 3.9*	16.3	38.8	22.4	22.4
$W_{5\ years}$ versus $1\ year$	32	2.8 (1.4–5.5)	–1.2 ± 5.2	34.4	46.9	12.5	6.3
Chemotherapy only							
$W_{5\ years}$ versus dx	23	2.9 (1.3–6)	1.7 ± 5.1	13.0	39.1	17.4	30.4
$W_{1\ year}$ versus dx	31	1.0 (0.3–1.2)	2.2 ± 4.3*	16.1	19.4	38.7	25.8
$W_{5\ years}$ versus $1\ year$	19	2.7 (1.3–5.5)	–1.4 ± 2.6*	31.6	57.9	10.5	0.0
Endocrine therapy only							
$W_{5\ years}$ versus dx	41	4.0 (1.4–6.0)	0.9 ± 5.0	17.1	29.3	36.6	17.1
$W_{1\ year}$ versus dx	33	0.9 (0.3–1.2)	1.4 ± 4.2	18.2	36.4	21.2	24.2
$W_{5\ years}$ versus $1\ year$	27	3.6 (1.7–5.6)	0.0 ± 2.7	29.6	37.0	29.6	3.7
Combined systemic treatment							
$W_{5\ years}$ versus dx	64	3.3 (1.3–6.0)	4.7 ± 6.3[a,*]	10.9	18.8	23.4	46.9
$W_{1\ year}$ versus dx	67	1.0 (0.3–1.3)	2.6 ± 6.0*	21.2	22.7	27.3	28.8
$W_{5\ years}$ versus $1\ year$	58	3.3 (1.3–6.0)	2.2 ± 5.3[b,*]	10.3	39.7	19.0	31.0

W_{dx} = body weight at diagnosis, $W_{1\ year}$ = approximation of weight one year after diagnosis, last measured weight between 3 and 15 months after diagnosis, and $W_{5\ years}$ = approximation of weight at 5 years after diagnosis, last measured weight between 15 months and 6 years after diagnosis.
Individuals were only included if body weights were available in both periods.
[a,b]Body weight change significantly different compared to all other treatment groups.
* Significantly different from zero (one-sample *t*-test).

(4.7 ± 6.3 kg; $p < 0.05$; median follow-up: 3.3 years). No significant body weight changes were observed in women who received endocrine therapy only. Stratified analysis by menopausal status showed that body weight gain was mostly limited to pre-menopausal women in our study population (Table 4). Changes in body weight did not markedly differ between normal weight and overweight/obese women and between smokers and non-smokers at diagnosis (data not shown).

We conducted multi-level analyses to optimally use the data on repeated body weight measurements and duration of systemic treatment. The coefficients of the model including age at diagnosis and the dummy variables for the 10-category treatment variable are shown in Table 5. The (fixed)

Table 4 – Body weight change in pre- and post-menopausal women

	n	Follow-up	Change (kg)	Body weight change (% of *n*)			
		Median (range)	Mean ± SD	Loss ⩾ 2 kg	Stable ± 1 kg	Gain 2–4 kg	Gain ⩾ 5 kg
Pre-menopausal women							
$W_{5\ years\ versus\ dx}$	82	3.5 (1.3–6.0)	3.9 ± 5.8[a,*]	13.4	25.6	18.3	42.7
$W_{1\ year\ versus\ dx}$	89	1.0 (0.3–1.2)	2.3 ± 5.3[*]	16.9	32.6	21.3	29.2
$W_{5\ years\ versus\ 1\ year}$	68	3.1 (1.3–6.0)	1.3 ± 4.6[b,*]	17.6	38.2	20.6	23.5
Post-menopausal women							
$W_{5\ years\ versus\ dx}$	91	3.3 (1.3–6.0)	1.1 ± 5.0[a,*]	17.6	32.9	31.9	17.6
$W_{1\ year\ versus\ dx}$	90	0.9 (0.3–1.3)	1.7 ± 4.4[*]	20.0	25.6	32.2	22.2
$W_{5\ years\ versus\ 1\ year}$	68	3.0 (1.3–5.5)	–0.4 ± 4.8[b]	27.9	48.6	16.1	7.4

W_1 = body weight at diagnosis, W_2 = approximation of weight one year after diagnosis, last measured weight between 3 and 15 months after diagnosis, and W_3 = approximation of weight at 5 years after diagnosis, last measured weight between 15 months and 6 years after diagnosis. Individuals were only included if body weights were available in both periods.Menopausal status at diagnosis; if menopausal status was missing, patients were categorised based on age (n = 103; i.e. post-menopausal if age at diagnosis ⩾ 51).[a,b]Body weight change significantly different between pre and post-menopausal women.

[*] Significantly different from zero (one-sample *t*-test).

Table 5 – Multi-level model

Diagnostic variable	Body weight	
	Coefficient	95% Confidence interval
Intercept (at age 0 years)	64.10	
Age at diagnosis (years)	0.12	0.00, 0.25
Body weight change per year of follow-up		
Per year	1.05	0.50, 1.60
Per year^2	–0.13	–0.21, –0.05
Chemotherapy only		
During 0–6 months since starting chemotherapy	–0.50	–1.15, 0.16
During 6–12 months since starting chemotherapy	0.75	–0.47, 1.96
During 12–24 months since starting chemotherapy	1.06	–0.46, 2.59
During >24 months since starting chemotherapy	0.30	–1.55, 2.15
Endocrine therapy only	0.01	–0.95, 0.96
Combined systemic treatment		
During 0–6 months since starting chemotherapy	0.83	–0.46, 2.12
During 6–12 months since starting chemotherapy	1.17	0.13, 2.12
During 12–24 months since starting chemotherapy	1.26	0.12, 2.40
During >24 months since starting chemotherapy	2.53	0.99, 4.07

time-dependent coefficients were estimated at 1.05 kg per year (95% confidence interval (95% CI): 0.50–1.60) and –0.13 kg per year squared (95% CI: –0.21 to –0.05). This reflects a mean increase of 0.92 kg one year post-diagnosis (i.e. 1.05 * 1 minus 0.13 * 1^2), 1.58 kg after 2 years (i.e. 1.05 * 2 minus 0.13 * 2^2), 1.98 kg after 3 years (i.e. 1.05 * 3 minus 0.13 * 3^2) and so on, in women who received no systemic therapy (see top bar in Fig. 1). Weight gain was statistically significantly higher in women who received combined systemic treatment from 6 months since starting chemotherapy onwards, as compared with women who received no systemic therapy (coefficients; at 6–12 months since starting chemotherapy: 1.17 kg, 95% CI: 0.13–2.12; at 12–24 months since starting chemotherapy: 1.26 kg, 95% CI: 0.12–2.40 and at more than 24 months since starting chemotherapy: 2.53 kg, 95% CI: 0.99–4.07). Fig. 1 illustrates the estimated body weight change for each treatment group, based on the parameters presented in Table 5. After 5 years since diagnosis a 4.5 kg increase in body weight was observed in women who received combined systemic therapy. In concordance with the results of our descriptive analysis, we did not find a significant body weight change in women who received only endocrine therapy (Table 5). Including tumour stage in the multi-level regression model did not result in relevant changes to the other coefficients. The magnitude of weight gain may differ by menopausal status, as suggested by the results of our descriptive analyses. However, due to multi-collinearity it was not possible to fit a model including both age and menopausal status at diagnosis, as menopausal status was directly derived from age in a substantial proportion of the population. Exchanging age for menopausal status in the model did not result in markedly different coefficients or interpretation based on likelihood ratio tests.

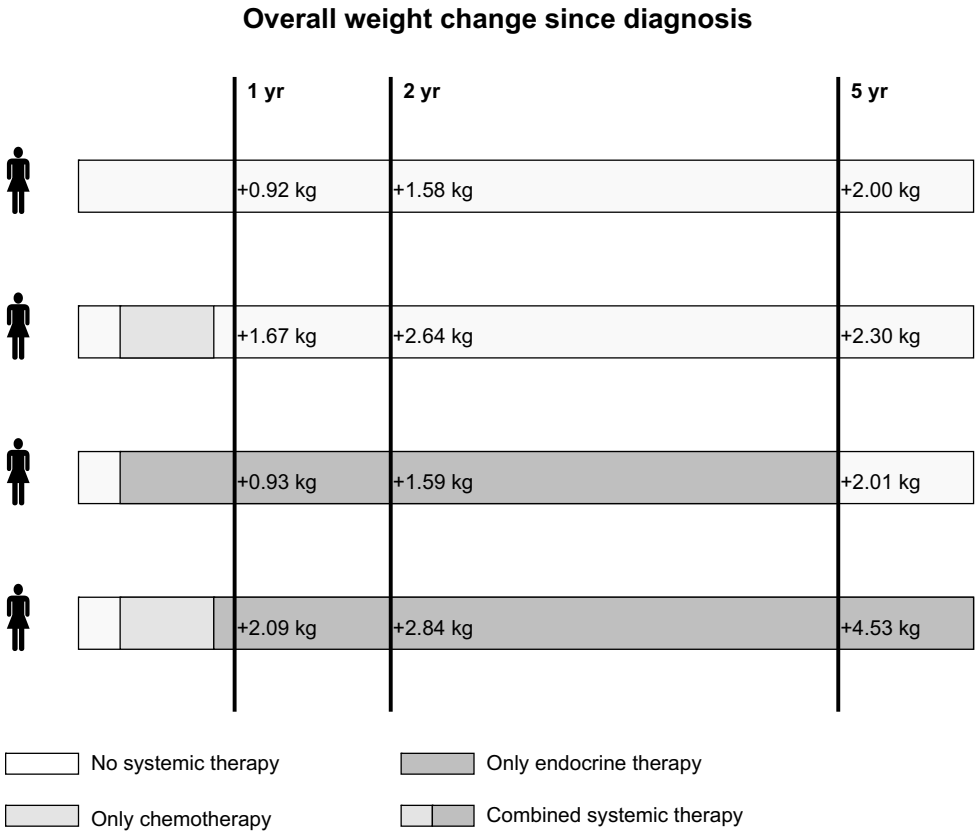

Fig. 1 – Schematic overview of overall weight change since breast cancer diagnosis for treatment-specific groups, based on multi-level regression analysis.

4. Discussion

In our study population, a mean post-diagnosis body weight change of +2.4 kg was observed during a median follow-up time of 3.5 years. The majority of women (55%) gained more than 2 kg, 29% gained 5 kg or more. Body weight gain during the first year after diagnosis was most prominent in women who received chemotherapy, either with or without endocrine therapy. Interestingly, we found that receiving combined systemic treatment was strongly related to body weight gain during longer follow-up.

Our study has several strengths and limitations with regard to design and analysis. We used retrospective data from medical records, and therefore could not control timing and method of body weight measurements. Minor, random measurement errors may have occurred due to the use of different weighing scales, the lack of adequate calibration and to differences in time of the day at which patients were weighed and type of clothing patients were wearing. All patients were regularly seen by the same radiation-oncologist, who measured and recorded body weights at follow-up visits.

Another limitation of the current analysis is that we only examined the changes in body weight based on the general treatment categories without taking into account the type of chemotherapy or endocrine therapy that was used. Considering the small numbers of patients in such treatment subgroups, we would have limited power to detect significant differences. The mean duration of follow-up was 3.4 years overall, and differed slightly among treatment groups, which may have influenced our results. The shortest durations of follow-up were observed in the chemotherapy only group, and therefore the power to detect long-term effects of chemotherapy only on body weight in our population is limited. Our multi-level regression model suggests that in the overall population some weight loss occurs beyond 5 years post-diagnosis. However, due to limited long-term follow-up measurements (i.e. >5 years), power is strongly decreased and the data are, therefore, not suitable to provide estimates of weight change beyond 5 years. We selected our study population from the file of one radiation-oncologist, whereby we only included patients who received radiotherapy. Hence, the independent effects of radiation on body weight gain could not be estimated.

Most previous studies examined body weight change in breast cancer patients only during the first year after diagnosis.[5,9,24,25] In addition, most studies were restricted to data on body weight measurements at two time points.[5,11,20,25,26] Goodwin et al. were among the first to report on weight gain in relation to therapy in breast cancer patients (n = 535).[5] During the first year after diagnosis, mean body weight change in women who received chemotherapy, Tamoxifen only and no systemic treatment was 2.5 kg (95% CI: 1.8–3.2), 1.3 kg (0.7–1.8) and 0.6 kg (0.0–1.3), respectively. These body weight changes are similar to our data during the first year after diagnosis. Goodwin et al. did not observe significant differences between women who received only chemotherapy and those

who received combined systemic treatment. Endocrine therapy was also not statistically significantly associated with weight gain at 1, 2 and 3 years post-diagnosis in a study of 185 breast cancer patients.[27] In the large Women's Healthy Eating and Living (WHEL) study ($n = 3088$), body weight was measured at baseline and years one through six.[28] Chemotherapy was significantly associated with weight gain of $\geqslant$5% body weight (OR = 1.65, 95% CI: 1.12–2.43), whereas Tamoxifen was not (OR = 1.03, 95% CI: 0.71–1.51). Tamoxifen also did not modify the effect of chemotherapy on weight gain, which is in contrast to what our data suggest. We found that body weight gain in the combined systemic treatment group significantly increased with increasing follow-up time, whereas this was not the case in the chemotherapy only group. The currently available data suggest that post-diagnosis weight gain in breast cancer patients is a long-term effect. This is confirmed by the findings in the WHEL study in which only 10% of participants returned to their pre-cancer body weight over the course of the study.[28]

The onset of menopause is often mentioned as a predictor for post-diagnosis weight gain, especially in women receiving chemotherapeutic agents.[5,6] Our data indeed suggest that the treatment groups in which most women were pre-menopausal at diagnosis, i.e. those who received chemotherapy, gained most body weight. Information on the timing of menopausal transition was not available, therefore, we were unable to examine the effect on body weight change during the transition. Estradiol is known to reduce appetite, decrease food intake, increase energy expenditure and reduce adiposity,[29–31] which may explain the increase in body weight and fat mass observed with menopause. However, we would argue that it is unlikely that the association between chemotherapy and weight gain is entirely due to the endocrine effects of menopausal transition. Based on the review of several observational studies, Simkin-Silverman and Wing conclude that weight gain during menopausal transition is more strongly associated with ageing than with menopause per se.[32] In the SWAN-study, an observational study of the menopausal transition, change in the menopausal status was not associated independently with weight gain, whereas the decreased physical activity was.[33]

The Netherlands is a country with a relatively low prevalence of obesity (i.e. 10% in adult women; BMI > 30) as compared to many other western countries (e.g. England and the US: 25% and 33% in women).[34] Moreover, in a healthy population of midlife women from the Netherlands only about 10% of women gained $\geqslant$5% body weight in 1 year.[35] Seen in this light, the weight gain of more than 5 kg observed in 25% of breast cancer patients, and 40% of pre-menopausal breast cancer patients, in our study is probably due to a combination of factors. Besides (therapy-induced) menopausal transition, this may include other metabolic effects of chemotherapy and endocrine therapy, and reductions in physical activity. The decrease in physical activity after a cancer diagnosis may be due to the negative side-effects of chemotherapy, including pain, fatigue and nausea, as well as due to psychosocial factors. Indeed, in the HEAL cohort of 1.185 breast cancer survivors, levels of recreational physical activity significantly decreased between diagnosis and 1 year after diagnosis regardless of age at diagnosis.[11]

In conclusion, women diagnosed with primary breast cancer frequently gain body weight after diagnosis. Those who received chemotherapeutic agents gained more body weight during the first year after diagnosis than women who received only endocrine therapy or no systemic treatment. Body weight gain during longer follow-up was mainly observed in women who received combined systemic treatment, although we cannot be certain about long-term effects of only chemotherapy, due to shorter follow-up in this group. This study shows that body weight gain after breast cancer diagnosis also occurs in a relatively 'non-obesogenic' environment like the Netherlands. We suggest rapid development of weight management interventions for breast cancer patients and survivors, and further studies to elucidate the effects of combined systemic therapy on body weight and composition.

Conflict of interest statement

None declared.

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