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Symptoms, weight loss and physical function in a lifestyle intervention study of older cancer survivors

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Abstract

Objectives—Many older cancer survivors are overweight or obese, with additional illness burden increasing functional decline, which may affect their ability to engage in lifestyle interventions. This study examined how overweight long-term survivors' symptom severity associated with comorbidity prior to a diet and exercise intervention was associated with post-intervention function and examined symptoms' effects on function through change in physical activity, diet quality, and weight status.

Materials and Methods—This is a secondary data analysis of 514 breast, prostate, and colorectal cancer survivors who participated in the one-year home-based diet and exercise intervention Reach-Out to Enhance Wellness trial. Measures included symptoms, weight, physical activity, diet quality, overall physical function (PF), and basic and advanced lower extremity function (BLEF and ALEF). Simple and serial mediation analyses were conducted to examine direct effects of symptom severity on PF, BLEF and ALEF and indirect effects of symptom severity through changes in diet quality, physical activity, and weight.

Results—Symptom severity was directly associated with lower functioning scores for PF ($b=-0.63$ $p<0.001$), BLEF ($b=-0.33$, $p<0.001$) and ALEF ($b=-0.22$, $p<0.001$). Indirect effects of symptom severity through weight loss, physical activity and diet were not significant. Weight loss and physical activity were associated with higher PF and ALEF and diet quality was associated with higher BLEF.

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Conclusion—Symptom severity of older, overweight cancer survivors negatively affects physical function. However, greater weight loss and more physical activity were associated with higher functioning scores, regardless of symptom severity.

Keywords

survivors; prostate; breast; symptoms; physical activity; weight loss; functioning

Introduction

Older cancer survivors (≥65 years) experience more rapid functional decline compared to younger cancer survivors, as well as age-matched counterparts in the general population.[1,2] Declines in physical function are concerning because of the consistent associations with inability to perform activities of daily living,[3] therefore threatening the propensity for independent living among older adults.[4] Functional decline may be compounded by obesity – an increasingly prevalent problem among cancer survivors and the elderly.[5,6] Physical activity and dietary interventions have had positive effects on preventing or slowing functional decline in obese and overweight cancer survivors.[7,8] One mechanism through which interventions may prevent functional decline is through physical activity's positive effects on muscular strength and balance.[9] Alternatively, physical activity and diet may influence function through weight loss in those who are overweight and obese.[9,10]

Similar to their non-cancer counterparts, aging and overweight cancer survivors are also more likely to be "sicker" than normal weight survivors (e.g., comorbidities and associated symptoms, such as muscle weakness, chest pain or balance issues [11]) which may influence behavior change, such as improving physical activity[12] or dietary habits. The relationship between symptom severity, physical activity and diet quality, weight loss, and the impact on function is not straightforward. Among overweight survivors, symptoms may have independent effects on functional limitations as well as through their relationship with physical activity,[12,13] diet, and weight loss. Physical activity and diet quality may improve symptoms,[14–17] but changes in these behaviors, whether positive or negative, may also be indicative of the baseline health state of survivors who had activity-limiting symptom severity at the time activity and diet was measured.

Understanding the influence of older overweight cancer survivors' health states on their ability to successfully change health behaviors, lose weight, and ultimately retain function is critical for intervention development and evaluation. Examining this issue is timely given the American Society of Clinical Oncology's recent position on weight management and recognition that comorbidity is exceptionally prevalent in this population.[18] The Reach-Out to Enhance Wellness (RENEW) trial provides a unique data source to examine the relationship between symptom severity, behavioral intervention (exercise and diet quality), weight loss and lower extremity function in overweight long-term cancer survivors.[7] The trial used a multicomponent approach of both diet and exercise to purposefully initiate gradual weight loss among older obese and overweight breast, prostate, and colorectal cancer survivors to positively impact physical functioning.

Our objective was to examine how pre-intervention symptom severity was associated with post-intervention overall physical functioning and lower extremity functioning through its effects on survivors' weight loss via physical activity and diet quality changes. To accomplish this objective, we examined the mediating effects of physical activity and diet quality changes and weight loss on the relationship between survivors' pre-intervention symptom severity and post-intervention function (Appendix A). We hypothesized that baseline symptom severity would have negative direct effects on post-intervention function. We also hypothesized that symptom severity would have negative effects weight loss through lower changes in physical activity and diet quality, and subsequently lead to lower function.

Materials and Methods

Study Design and population

This is a secondary data analysis of the RENEW trial which has been described in detail elsewhere.[9,19] Briefly, RENEW was a 12-month home-based diet-exercise intervention delivered to overweight or obese (body mass index (BMI) ≥25 kg/m^2) and inactive (<150 minutes of exercise/week) survivors of breast, prostate, and colorectal cancer. Survivors were at least 5 years from diagnosis with no evidence of progressive disease. Survivors with health conditions that precluded them from unsupervised exercise were excluded. Tailored mailed-print materials and telephone counseling were delivered to 641 survivors in a cross-over design with the primary goals of increasing physical functioning and quality-of-life by improving diet quality and physical activity. The mailed material included personalized workbooks as well as exercise and diet "tools" (i.e., resistance bands, tableware to enhance portion control) designed to assist survivors in meeting national guidelines. Telephone counseling was provided to help survivors overcome barriers to change and monitor change. Intervention details are described in Snyder et al, 2009.[19] All surveys were delivered each of the three measurement periods. The current study focuses on survivors with complete pre- and post-intervention data (n=514; Appendix B). The study was approved by the Duke University Health System and the North Carolina Cancer Registry Institutional Review Boards.

Measures

Overall physical function—The physical functioning (PF) subscale of the Medical Outcomes Study Short Form-36 (MOS SF-36)[20] served as the primary outcome of the RENEW trial and the present analysis. This 10-item subscale assesses a range of function, from basic activities (i.e., self-care) to participation in vigorous activities and is scored on a 0 to 100 scale. The RENEW intervention prevented the significant decline in PF.[9] Therefore, our primary outcome of interest was the post-intervention PF subscale score.

Lower extremity function—We also used the Basic and Advanced Lower Extremity Function subscales of the Late-Life Function and Disability Index to create two other primary outcome measures.[21] These included: basic lower extremity function (BLEF) and advanced lower extremity function (ALEF). Questions ask how much difficulty the respondent has doing a particular activity without the help of others or assistive devices.

Responses range from “none” to “cannot do.” Responses are summed and scored as 0–100 with higher scores indicating higher functioning. The BLEF assesses the ability to perform activities such as stooping and walking without assistance while the ALEF assesses the ability to perform physical activities that require a significant degree of ability and endurance. Similar to PF, we used post-intervention BLEF and ALEF scores.

Symptom severity—Symptom severity was measured using items from a modified version of the Duke Older American Resources and Services (OARS) physical health items.[22] Survivors were asked to what degree 22 different symptoms limited normal activities (e.g., chest pain, shortness of breath; Appendix C) on a scale of 1–4 with 1=not all and 4=quite a bit. The OARS symptom items are designed to measure common symptoms associated with general aging, not specifically for cancer treatment side-effects, given that these are long-term survivors. Total scores of baseline measures were calculated where higher scores indicate worse symptoms.

Change in physical activity—The Community Healthy Activities Model Program for Seniors (CHAMPS) physical activity (PA) scale[23] is a 41-item measure to assess PA in adults 50 years and older. We used the change in total minutes of PA and energy expended weekly in all physical activities of moderate or higher intensity from pre- to post-intervention. Higher values indicated an increase in PA.

Change in diet quality—The Healthy Eating Index (HEI) measured diet quality (DQ). The HEI uses dietary intake data averaged from two unannounced 24-hour recalls using the Nutrition Data System for Research software.[24] The Healthy Eating Index 2005 criterion, in practice during the time of the RENEW trial, was used to create scores pre- and post-intervention.[25,26] Change in DQ was calculated by subtracting the baseline HEI score from the follow-up HEI score. Higher values indicated DQ improvement.

Weight loss—Self-reported height and weight were used to calculate BMI pre- and post-intervention. We examined the change in BMI [$BMI_{change}=BMI_{baseline}–BMI_{follow\text{-}up}$]. Higher values (positive) indicated a greater weight loss.

Demographic and clinical characteristics—Age, race, gender, income, stage at diagnosis, treatment received, years since diagnosis, and comorbidities were all self-reported at baseline. Comorbidities were measured using the Duke OARS comorbidity scale. The OARS is a “yes or no” checklist of 32 comorbid conditions.[22] To reduce survey administration burden, the RENEW study assessed six of the most common comorbid conditions (arthritis or rheumatism, high blood pressure, heart trouble, circulation trouble in arms or legs, osteoporosis, cataracts). Scores were summed to create a total number of comorbidities with a range of 0 to 6 conditions.

Statistical approach

Data were analyzed using SAS statistical software Version 9.3 (Cary, NC).[27] Frequencies were calculated for categorical variables, and means and standard deviations were calculated for continuous variables. We first tested bivariate relationships between the hypothesized

mediating variables, covariates, and functioning outcomes (PF, BLEF, ALEF). We used the PROCESS macro developed by Hayes[28] to examine a series of multiple regression models examine the relationship between pre-intervention symptom severity and post-intervention function, both directly and through the intervention[29,30].

We used linear regression to evaluate the bivariate relationships between the three dependent variables and pre-intervention symptoms, PA change, DQ change, weight loss, age, race, gender, income, stage at diagnosis, time since diagnosis, number of comorbidities, and treatment received. We did not require statistically significant relationships between all hypothesized mediators, dependent variables, and primary independent variable, but required a significant relationship between the primary independent variable (symptom severity) and each dependent variable (function) for the mediation model. This approach is tested and supported by MacKinnon and colleagues and is valid with bootstrapping and resampling techniques in the Hayes' PROCESS macro.[28–30]

Multiple regression analyses were used to test for mediation. We conducted both simple (Appendix A, Model A) and serial mediation (Appendix A, Model B) adjusting each model for pre-intervention values of function, DQ, and PA as well as age, race, gender, income, stage at diagnosis, time since diagnosis, treatment received, comorbidity, and randomization level.

We examined the direct effect (e.g., associations between two variables) of pre-intervention symptoms on post-intervention function outcomes (PF, BLEF, ALEF) and the effect of symptoms on function through weight loss (indirect effects). Indirect effects refer to the amount of mediation introduced by including additional relationships between the primary independent variable and the dependent variable (Y) in to the model (e.g., the association of symptoms with post-intervention function score through weight loss). Using PROCESS, weight loss (M) is estimated from symptom severity (X) controlling for covariates (Appendix A). Then, the indirect effect of X on Y through M is estimated as the product of coefficients linking X to M and X to Y.[30,31]

We then examined the associations of symptom severity on post-intervention function through weight loss via the effect of change in DQ and PA on weight loss. For serial mediation, estimation of direct and indirect effects requires coefficients from up to 4 equations: one for each mediator and one for function (Appendix C). Indirect effects are the product of coefficients for variables linking symptom severity to function through one or more mediators.

The significance of indirect effects of symptom severity through mediators was determined using a bootstrap procedure[32] which uses non-parametric resampling that provides empirical approximation of the sampling distributions of indirect effects.[31] The procedure does not require distributional assumptions of the shape of variables nor sampling distribution of the statistic.[33] We report bias-corrected and accelerated 95% CIs for the significance of the mean indirect effects from the 5,000 bootstrap resampling results.[34]

Results

Study characteristics

The sample was mostly white (89%) and female (55%) (Table 1). The mean age of participants was 79 years and almost half were breast cancer survivors (44%). At baseline, participants were on average 8.6 years post-diagnosis and had two comorbid conditions. Table 2 shows the mean PF, BLEF and ALEF post-intervention scores were 74, 78 and 52, respectively.

Bivariate regression

Table 3 shows that higher symptom severity was significantly associated with lower post-intervention PF, BLEF, and ALEF scores (B=−1.49, p<0.001; B=−0.89, p<0.001; B=−0.96, p<0.001, respectively). Symptom severity explained about one-quarter of the variance in all three function outcomes. Increased PA was significantly associated with PF, BLEF, and ALEF, but explained <1% of the variance. Increased DQ was significantly associated with BLEF and ALEF. Older age was associated with lower BLEF and ALEF. Female gender, lower income, more comorbidities, and hormonal therapy were significantly negatively associated with all three outcomes.

Simple mediation (Figure 1)

Symptom severity was directly associated with lower PF, BLEF, and ALEF (Figure 1A–C). Conversely, weight loss was directly associated with higher PF and ALEF scores. The specific indirect effect of symptom severity on function through weight loss was not significant (Table 4).

Serial mediation (Figure 2)

In Figure 2, symptom severity remained directly associated with lower PF, BLEF and ALEF scores, with a similar magnitude of effect within each function outcome. Greater weight loss remained significantly and directly associated with higher PF and ALEF scores. Similar to Figure 1A–C, the indirect effects of symptom severity were not significant. A greater increase in PA was also directly associated with higher PF, BLEF, and ALEF scores. Symptom severity and weight loss remained directly associated with PF and ALEF while change in DQ was significantly associated with BLEF, and marginally significantly associated with ALEF (B=0.07, p=0.05).

Discussion

While physical functioning has been an important target for improvement among older cancer survivors, obesity is a new concern, and oncologists may be reluctant to advise weight loss, especially among older, sicker survivors. However, findings from this secondary analysis suggest that despite the symptom burden experienced by older survivors, purposeful weight loss may indeed be a key factor for overall physical functioning and advanced lower extremity function. Our sample of “at-risk” cancer survivors, i.e., overweight and obese with an average of two comorbid conditions, provides additional evidence to the few previous studies,[35] that overweight long-term cancer survivors stand

to improve their functioning through purposeful weight loss. We were also able to examine whether common symptoms influenced diet and exercise changes aimed at improving function. While some of our findings were anticipated, we also uncovered some that were unexpected.

We had hypothesized that the relationship between symptom severity, weight loss, and function would be partially due to the effects of symptoms on the ability to change behaviors. However, our findings indicate that symptom severity did not deter survivors' behavior change. This is in contrast to other studies where symptoms, including fatigue, psychological distress, or lymphedema, were associated with less physical activity,[36] and better diet quality was associated with decreased fatigue.[37] It is likely that factors in the fully adjusted model, particularly comorbidities, explained some of the variance in the relationship between symptoms and weight loss in our models. We considered whether cancer type may have an effect on the relationship between symptoms, weight loss, and function, but cancer type did not affect the results and was not significant. The type of treatment received was more strongly associated with both symptoms and function.

Thus, this study provides unique findings regarding the effect of symptom severity on function via impact on lifestyle intervention "engagement" and associated weight loss; moreover, it does so in an understudied patient population, i.e., long-term cancer survivors age 65 and older.[11] These older survivors are in need of lifestyle intervention studies as much, if not more than, their younger counterparts. Targeting this group of older survivors, as opposed to excluding, for functional improvement and purposeful weight loss when needed will require innovative intervention approaches to deal with complex illness burden associated with aging. Future studies should determine whether symptom alleviation actually result in improvement in physical function, as is suggested in our preliminary study, and identify which symptoms are critical barriers to function.

Despite these strengths and implications, limitations should be considered. First, the sample was largely homogenous based on sample characteristics and there was 23% loss-to-follow-up thus limiting generalizability to other populations. Second, we relied on self-reported measures of diet, weight and physical activity and function. Finally, the primary RENEW intervention trial was not designed to achieve adequate power to detect indirect effects from this secondary analysis, therefore results are preliminary.

To conclude, while symptom severity among older, overweight cancer survivors negatively affected all aspects of physical functioning, it did not significantly influence diet or physical activity changes, or weight loss. Findings are especially relevant given the increasing number of aging cancer survivors and the health care burden associated with functional problems that limit independence.[38] Furthermore, our findings build from the recent emphasis on the negative effects of obesity on survivor outcomes to highlight weight loss as an important factor in maintaining function in older cancer survivors.[39] Weight loss and physical activity change interventions can successfully influence functioning despite the underlying symptom severity of overweight survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

PF	physical functioning (SF-36 domain)
BLEF	basic lower extremity functioning
ALEF	advanced lower extremity functioning
PA	physical activity
DQ	diet quality
BMI	body mass index
CI	confidence interval

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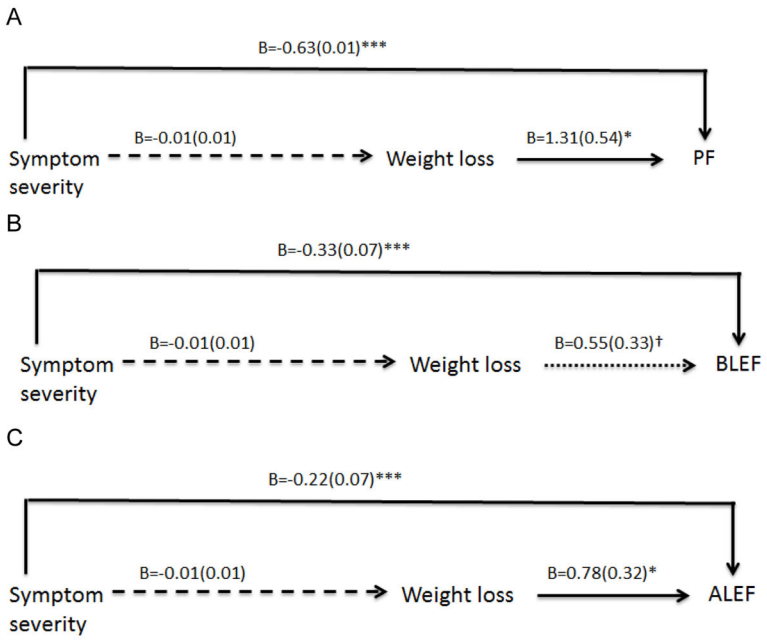

Figure 1.

Simple mediation models: physical functioning (PF), basic (BLEF) and advanced (ALEF) lower extremity functioning. Unstandardized coefficients and standard deviations are presented. All Models adjusted for pre-intervention values, comorbidities, age, gender, race, income, and diagnosis stage, treatment, and years since diagnosis. PA and DQ change remain as covariates. Solid lines indicate statistically significant relationships. *p<0.001; **p<0.01; ***p<0.05; †p<0.10.

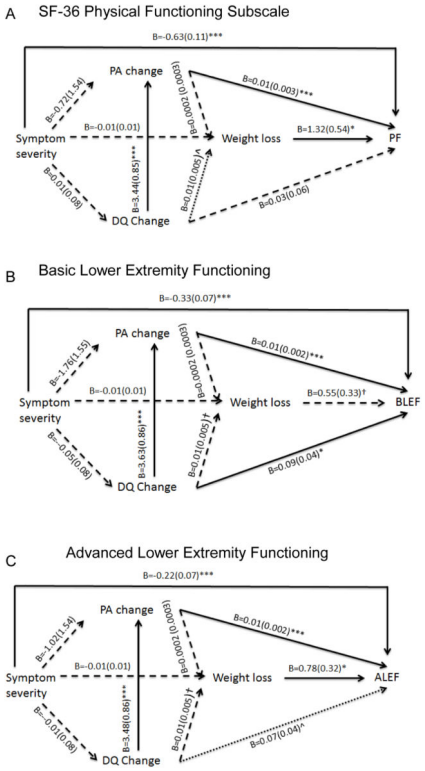

Figure 2.

Serial mediation models. Unstandardized coefficients and standard deviations are presented. All models adjusted for pre-intervention values for change scores and function, comorbidities, age, gender, race, income, and stage at diagnosis, and treatment. → statistically significant relationships; *p<0.001; **p<0.01; ***p<0.05. ⇢ marginal significance at ^p=0.05. †p<0.10

Table 1

Sample characteristics (n=514)

	N	%[a]
Age		
Mean (SD)	72.97 (5.1)	
Range	(65–87)	
Race		
White	459	89.3
Gender		
Male	233	45.3
Income		
<$50,000	180	35.0
>$50,000	334	65.0
Education		
Less than high school	29	5.6
High school	160	31.2
Some college	125	24.4
College graduate or higher	198	38.6
Missing	2	0.39
Cancer type		
Colon/rectal cancer	80	15.6
Breast cancer	229	44.6
Prostate	205	39.9
Stage at diagnosis		
In situ	4	0.8
Localized	350	68.1
Regional	141	27.4
Unknown/unstaged	10	2.0
Missing	8	1.56
Number of conditions[b]		
Mean (SD)	1.99 (1.28)	
(range)	(0–6)	
Time from diagnosis to baseline (years)		
Mean (SD)	8.61 (2.6)	
(Range)	(5–26)	
Received surgery		
Yes	460	89.5
Received chemotherapy		
Yes	131	25.5
Received radiation		
Yes	229	44.6
Received hormone therapy		

	N	%[a]
Yes	216	42.0
BMI		
Pre-intervention	28.9 (3.5) (22–46)	
Post-intervention	28.2 (3.5) (21–44)	

[a] Variables with no missing category had no missing data.

[b] Arthritis or rheumatism, high blood pressure, heart trouble, circulation trouble in the arms or legs, osteoporosis, cataracts.

Table 2

Mean scores and standard deviations for function scores, symptom severity, change in PA, change in DQ, and weight loss.

	Mean (SD)	Range
Physical functioning		
Pre-intervention	71.7 (23.1)	5–100
Post-intervention[a]	73.5 (20.4)	5–100
Basic lower extremity function		
Pre-intervention	77.7 (14.8)	34.5–100
Post-intervention[a]	78.1 (15.5)	0–100
Advanced lower extremity function		
Pre-intervention	52.4 (15.7)	0–100
Post-intervention[a]	52.3 (17.1)	0–100
Symptom severity[b]	8.1 (7.9)	0–52
Change in PA score (minutes per week exercise)[c,d]	45.8 (288.77)	−2265–1720
Change in DQ (HEI) [c,d]	6.2 (14.3)	−37.7–54.7
Weight lost by BMI (kg/m^2) [d]	0.69 (1.39)	−4–11

[a] Post-intervention score was used as the outcome for mediation models.

[b] Pre-intervention score.

[c] Significant change from pre- to post-

[d] Higher (positive) values indicate more PA, better DQ, and more weight lost

Table 3

Bivariate relationship between physical functioning, mediators, and demographic and clinical characteristics

	SF-36 physical functioning[a]			Basic lower extremity function[a]			Advanced lower extremity function[a]		
	B (SD)	p-value	Adj R^2	B (SD)	p-value	Adj R^2	B (SD)	p-value	Adj R^2
Symptom severity[b]	−1.49 (0.11)	<0.001	0.26	−0.89 (0.11)	<0.001	0.28	−0.96 (0.07)	<0.001	0.26
Change in physical activity[c]	0.01 (0.004)	0.001	0.01	0.01 (0.002)	0.01	0.01	0.01 (0.003)	0.011	0.01
Change in diet quality[c]	0.10 (0.07)	0.144	<0.01	0.12 (0.05)	0.024	0.01	0.15 (0.06)	0.011	0.01
Change in BMI (kg/m^2)[c]	1.37 (0.73)	0.061	<0.01	0.95 (0.49)	0.050	0.01	0.83 (0.54)	0.123	<0.01
Age (years)	−0.39 (0.20)	0.056	0.01	−0.38 (0.13)	0.005	0.01	−0.63 (0.15)	<0.001	0.03
Gender (ref*=female)									
Male	7.03 (2.02)	<0.001	0.02	5.66 (1.35)	<0.001	0.03	9.54 (1.46)	<0.001	0.08
Race (ref=Non-minority)									
Minority	4.36 (3.29)	0.186	0.002	3.88 (2.20)	0.078	<0.01	2.56 (2.44)	0.295	<0.01
Income (ref=>$50,000)									
<$50,000	−7.62 (2.11)	<0.001	0.02	−4.89 (1.42)	0.001	0.02	−6.92 (1.56)	<0.0001	0.04
Stage at diagnosis (ref=Stage 0/I)									
Stage II–III	−0.54 (2.23)	0.808	<0.01	−0.84 (1.50)	0.576	0	−0.12 (1.65)	0.943	0
Number of comorbidities[b]	−5.23 (0.75)	<0.001	0.08	−4.09 (0.51)	<0.001	0.11	−5.48 (0.55)	<0.001	0.16
Surgery (ref=no)									
Yes	−1.29 (3.32)	0.697	<0.01	−4.23 (2.22)	0.057	0.01	−3.00 (2.46)	0.224	<0.01
Chemotherapy (ref=no)									
Yes	−3.12 (2.33)	0.182	<0.01	−2.35 (1.56)	0.133	<0.01	−3.78 (1.73)	0.029	0.01
Radiation (ref=no)									
Yes	−5.88 (2.03)	0.004	0.01	−2.63 (1.37)	0.055	0.01	−4.12 (1.51)	0.007	0.01
Hormone therapy (ref=no)									
Yes	−5.99 (2.05)	0.004	0.01	−4.69 (1.37)	0.001	0.02	−5.59 (1.51)	<0.001	0.02

B=unstandardized coefficients; SD=standard deviation. Ref=reference group.

[a] Post-intervention.

[b] Pre-intervention.

[c] Change scores; higher (positive) values indicate improvement, i.e., more physical activity.

Table 4

Total and Indirect effects and 95% confidence intervals

Mediation model	**SF-36 PF[a]**	**BLEF[a]**	**ALEF[a]**
Figure 1	**B 95% CI**	**B 95% CI**	**B 95% CI**
Symptom[b]–weight loss[c]–function	−0.018(−0.061, 0.004)	−0.005(−0.026, 0.003)	−0.010(−0.036, 0.002)
Total effects	−0.649(−0.869, −0.428)	−0.330(−0.463, −0.198)	−0.232(−0.361, −0.102)
Adjusted R^2	0.53	0.62	0.69
Figure 2			
Symptom–weight loss–function	−0.018(−0.061, 0.004)	−0.005(−0.026, 0.003)	−0.0102(−0.036, 0.002)
Symptom–DQ change[c]–function	0.0003(−0.011, 0.018)	−0.004(−0.029, 0.011)	0.0004(−0.013, 0.018)
Symptom–PA change[c]–function	−0.010(−0.055, 0.027)	−0.015(−0.039, 0.005)	−0.01(−0.039, 0.0134)
Symptom–PA change–weight loss–function	−0.0002(−0.004, 0.001)	−0.0002(−0.002, 0.0003)	−0.0001(−0.002, 0.0003)
Symptom–DQ change–weight loss–function	0.0001(−0.002, 0.005)	−0.0003(−0.003, 0.0004)	0.0001(−0.002, 0.002)
Symptom–DQ change–PA change–function	0.0004(−0.008, 0.010)	−0.002(−0.007, 0.004)	0.0002(−0.006, 0.006)
Symptom–DQ change–PA change–weight loss–function	0.00001(−0.0003, 0.0006)	−0.0001(−0.0007, 0.0001)	0.0001(−0.0002, 0.0002)
Total indirect	−0.028(−0.093, 0.020)	−0.026(−0.061, 0.003)	−0.019(−0.057, 0.015)
Total effects	−0.658(−0.883, −0.434)	−0.351(−0.487, −0.215)	−0.241(−0.375, −0.107)
Adjusted R^2	0.51	0.59	0.67

B=unstandardized coefficients;

[a]Post-intervention score.

[b]Pre-intervention score.

[c]Change scores; higher (positive) values indicate improvement, i.e., more physical activity.