Obesity

# Behavioral Predictors of Weight Regain in Postmenopausal Women: Exploratory Results from the Breast Cancer and Exercise Trial in Alberta

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**Objective:** This secondary analysis assessed associations between changes in energy balance and sleep behaviors and the risk of weight regain following exercise-induced weight loss.

**Methods:** Of 400 participants initially randomized in the Breast Cancer and Exercise Trial in Alberta (BETA), 227 lost weight following the moderate- to vigorous-intensity exercise intervention (−4.2 ± 3.6 kg) and were included in this analysis. Self-reported energy intake (EI), sleep duration, quality and timing, and objective measurements of physical activity (PA) and sedentary time were collected at the end of the intervention and the end of follow-up. Linear regression models assessed associations between changes in these behaviors and risk of weight regain during follow-up.

**Results:** Participants regained 43% of the weight lost during follow-up. Reductions in moderate to vigorous PA ($\beta = -1.00$; 95% CI = −1.74 to −0.25 h/d; $P = 0.01$) and steps per day ($\beta = -0.0003$; 95% CI = −0.0005 to −0.0001 steps/d; $P = 0.004$); increases in sedentary time ($\beta = 0.54$; 95% CI = 0.67 to 1.02 h/d; $P = 0.03$), EI ($\beta = 0.001$; 95% CI = 0.0003 to 0.002 kcal; $P = 0.01$), and fat intake ($\beta = 0.004$; 95% CI = 0.001 to 0.006 kcal; $P = 0.002$); and delayed sleep timing midpoint ($\beta = 0.02$; 95% CI = 0.004 to 0.03 min; $P = 0.01$) were associated with weight regain during follow-up.

**Conclusions:** These exploratory results suggest that reductions in moderate to vigorous PA; increases in EI, fat intake, and sedentary time; and delayed sleep timing midpoint were significantly associated with risk of weight regain.

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## Introduction

To promote successful weight-loss maintenance, a minimum of 200 to 300 min/wk of moderate-intensity physical activity (PA) is recommended (1,2). These recommendations are supported by findings from observational (3-7) and intervention (8-17) studies that have consistently indicated that successful weight-loss maintenance is associated with greater levels of PA participation. Specifically, intervention studies have reported that participants who maintained weight loss following diet-only (13,16), exercise-only (8), or diet plus exercise and/or lifestyle (10-12,14,15,17) interventions achieved greater levels of PA compared with those who regained weight during a postintervention follow-up period. Some of these intervention studies have also reported that reductions in energy intake and/or modifications in diet composition were associated with improved weight-loss maintenance following intervention completion (8,11,14).

The menopausal transition in particular is associated with weight and fat mass gains over time (18,19), which may leave postmenopausal women at an increased risk of weight regain following weight loss. Indeed, Sénéchal et al. (20) reported that participants who gained more weight since menopause had an increased risk of weight regain following a caloric restriction intervention. Although this study did not observe statistically significant associations of energy intake and daily energy expenditure assessed at the end of follow-up with weight regain (20), a second study reported that changes in PA participation assessed with accelerometry were significantly associated with weight regain following diet plus exercise interventions (15).

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These studies were, however, of shorter duration (15-20 weeks) and had small sample sizes (19-34 participants), suggesting that additional larger-scale studies are needed to complement these findings in postmenopausal women.

In addition to direct modifications in energy balance, observational studies have also begun to investigate the role of sedentary time in successful weight-loss maintenance, reporting that lower levels of sedentary and/or screen time are associated with weight-loss maintenance (5,7,21,22). However, no study to date has assessed the association of changes in sedentary time with the risk of weight regain following an exercise-only intervention. Additionally, observational studies have reported that better sleep quality (23,24), having a morning chronotype (23), and/or having a longer sleep duration (23,24) are associated with successful long-term weight-loss maintenance. Having a later sleep timing midpoint (defined as having a later bedtime and/or wake time, independently of sleep duration) also was associated with greater fast food intake and late-night energy intake (25), in addition to lower moderate to vigorous PA and increased sedentary time (26). Alterations in habitual sleep timing may lead to circadian disruptions that alter the metabolic and hormonal control of energy intake, such as increases in postprandial glucose and insulin levels and decreases in leptin levels (27). No study to date has assessed changes in sleep timing midpoint within the context of successful weight-loss maintenance. Furthermore, only one intervention study to date assessed the associations between changes in sleep duration and changes in weight following a very low-calorie diet in 98 men and women, reporting that decreases in sleep duration following the weight-loss intervention were associated with greater weight regain during follow-up (28). Therefore, additional studies are needed to assess the associations between changes in sleep behaviors and the risk of weight regain, especially following exercise-only interventions in postmenopausal women.

The Breast Cancer and Exercise Trial in Alberta (BETA) investigated the effects of a 12-month exercise intervention on biomarkers associated with breast cancer risk, as well as changes in study outcomes 1 year later in postmenopausal women (29-31). This trial collected objective measurements of PA and sedentary time at baseline, prior to the end of the intervention (12 months), and at the end of follow-up (24 months) (29-31). Self-reported energy and macronutrient intake, as well as sleep duration, sleep quality, and sleep timing, also was collected at each time point. The objective of this secondary analysis was to assess the strength of the associations between changes in these behaviors (PA and sedentary time assessed as hours per day, number of bouts and steps per day, energy and macronutrient intake, and sleep behaviors) and risk of weight regain during the follow-up period in participants who experienced exercise-induced weight loss. We hypothesized that greater weight regain during the follow-up period would be associated with reductions in PA time and steps per day coupled with increases in sedentary time and increases in energy and fat intake, as well as reductions in sleep duration, poorer sleep quality, and a delayed sleep timing midpoint.

# Methods

## Participants and exercise intervention

The design and methods for BETA have been described in detail elsewhere (29-31). This two-center, two-arm, 12-month randomized controlled exercise intervention trial as well as 12-month follow-up assessments was conducted in Calgary and Edmonton (Alberta, Canada) between June 2010 and June 2014. The study protocol was approved by the Alberta Cancer Research Ethics Committee, the Conjoint Health Research Ethics Board of the University of Calgary, and the Health Research Ethics Board of the University of Alberta. Written informed consent was provided by all participants prior to study participation. Participants did not receive a stipend for study participation. A total of 400 women were randomized to either the "moderate" (150 min/wk of exercise) or "high" (300 min/wk of exercise) volumes of aerobic exercise interventions. Inclusion criteria included the following: being aged between 50 and 74 years, being postmenopausal as confirmed with a follicle-stimulating hormone test, being moderately inactive (<90 min/wk of exercise or, if exercising between 90 and 120 min/wk, having cardiorespiratory fitness ($VO_{2peak}$) <34 mL/kg/min as measured by a submaximal fitness test), having BMI ≤ 40 kg/m$^2$, and being able to do unrestricted exercise as assessed by a physician screening. Exclusion criteria included use of hormone replacement therapy for at least 6 months prior to entry into the trial, having a previous cancer diagnosis, being a current smoker, and planning to undertake a dietary weight-loss program.

During the 12-month exercise intervention, participants were asked to exercise 5 d/wk at 65% to 75% of heart rate reserve for either 30 minutes ("moderate") or 60 minutes ("high") per session. These exercise sessions were supervised by certified exercise trainers at fitness facilities in Calgary and Edmonton on at least 3 d/wk, and 2 d/wk of exercise could be unsupervised and completed at a location of the participants' choosing (29). During the 12-month follow-up period, PA time was not monitored, and participants did not receive an exercise prescription or have access to the training facilities and exercise trainers (31). However, participants were aware that all outcome assessments would be repeated at the 24-month time point. Because this exploratory analysis aimed to assess predictors of weight regain following exercise-induced weight loss, all participants who experienced any amount of weight loss (>0-kg decrease in weight) during the 12-month exercise intervention, independently of randomization group, were included in the present analysis ($n$ = 227). We decided to include all participants who experienced any degree of weight loss in the present analysis because the expected amount of weight loss from exercise-only interventions is much more modest compared with diet-only or diet plus exercise and/or lifestyle interventions (2.4 kg vs. 4.9 and 7.9 kg, respectively) (32). Indeed, 71% of participants in the present analysis lost <5 kg during the exercise intervention.

## Predictors, outcome, and covariates

All measurements in BETA were completed at baseline, prior to the end of the intervention (12 months), and at the end of follow-up (24 months). Supporting Information Table S1 summarizes the predictor and outcome measures, as well as covariates at each time point included in the present analyses. The primary outcome was changes in body weight from 12 to 24 months measured to the nearest 0.1 kg with a Health-o-Meter Professional 402KL Physician Balance Beam Scale (Performance Health, Mississauga, Ontario, Canada). Predictors of weight regain were selected based on scientific plausibility (3,5,23,28,33-35). These included objective measurements of moderate to vigorous PA time (hours per day and number of bouts ≥10 min/d), light PA time (hours per day), total number of steps per day, and sedentary time (hours per day and number of bouts ≥60 min/d) over 7 days with a waist-worn accelerometer (ActiGraph GT3X+, ActiGraph LLC, Pensacola, Florida). The methods and calculations used to derive PA and sedentary time variables, as well as to account for potentially influential non-wear time, from the accelerometry-derived activity counts for this study are described in more detail elsewhere (36). Briefly, the ActiGraph Vertical Axis calculations were used to derive PA and sedentary time outcomes (hours per day) from the accelerometry-measured activity counts (37). Moderate to vigorous PA bouts were defined as ≥ 10 minutes without any continuous sedentary time or light PA lasting ≥ 1 minute. Sedentary bouts were defined as ≥ 60 minutes without any moderate to vigorous PA time during this bout or light PA lasting ≥ 1 minute. Additional predictors of weight regain included the following: total energy, carbohydrate, fat, and protein intake (kilocalories) assessed with the Canadian Diet History Questionnaire-II and the Diet*Calc Analysis Program (version 1.4.3; National Cancer Institute Applied Research Program, Bethesda, Maryland); sleep duration (hours per day), sleep quality (total questionnaire score), and sleep timing midpoint (wake time − one-half of total sleep duration) assessed with the Pittsburgh Sleep Quality Index; and weight loss during the intervention (changes in body weight from baseline to 12 months) measured with a balance beam scale.

Study covariates included in all statistical analyses were age, marital status (married or common law vs. unmarried or other), ethnicity (Caucasian vs. other), education (> high school vs. ≤ high school), study site (Calgary vs. Edmonton), randomization group (moderate vs. high), and weight loss during the exercise intervention (kilograms; when not the predictor of interest). Accelerometer wear time (hours per day) and sleep duration (hours per day) were also added as covariates to the

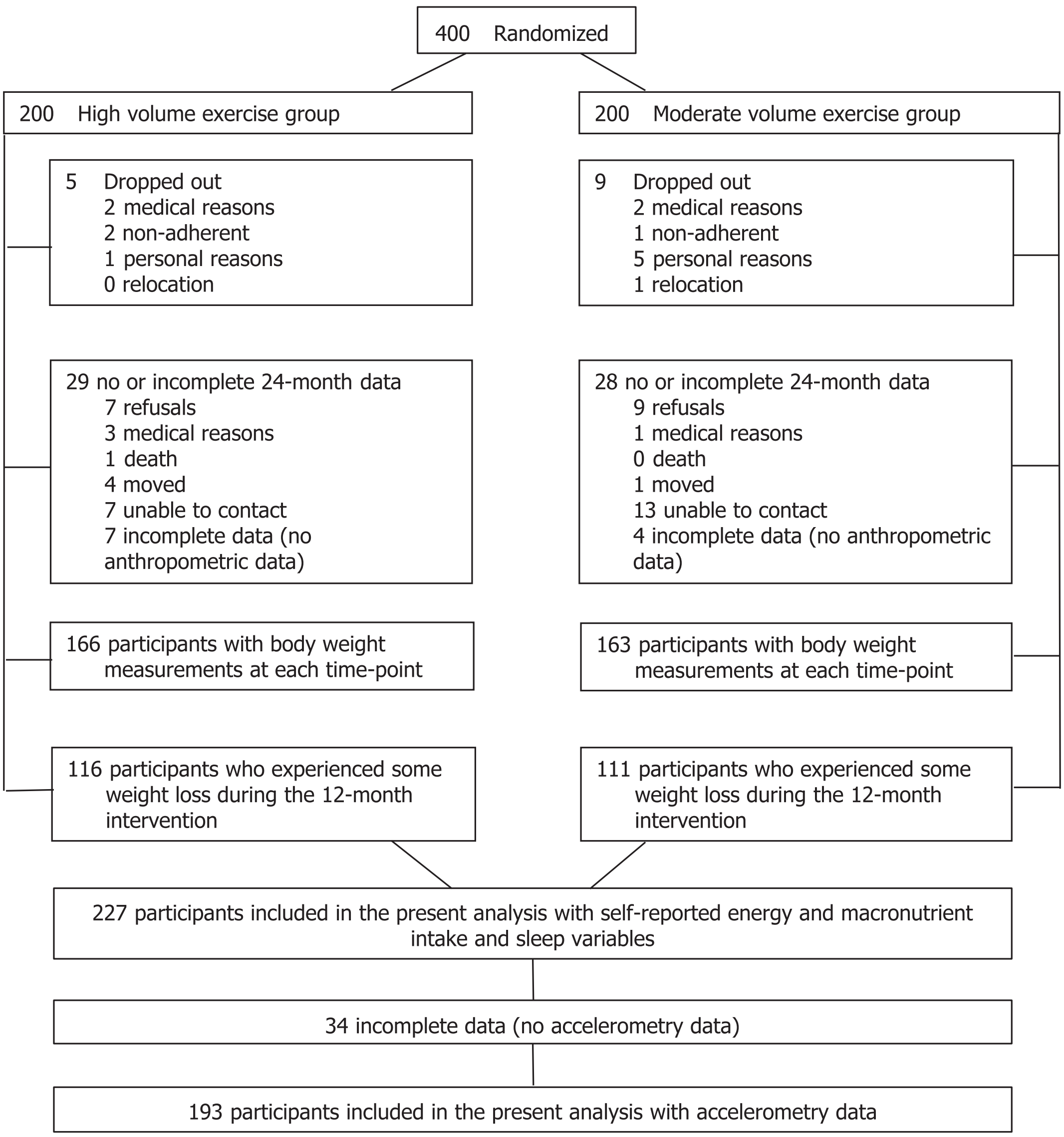



**Figure 1** Study flowchart for the present analysis. The Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014.

statistical models that included accelerometer data or sleep quality and sleep timing midpoint as predictors, respectively.

## Statistical analyses

All analyses were performed using Stata software version 14 (StataCorp, College Station, Texas). Descriptive data were presented as means ± standard deviations (SD) for continuous variables and as counts and percentages for categorical variables. Statistical significance was set at $P<0.05$.

Linear regression models were used to estimate multivariable-adjusted beta coefficients (β) and 95% confidence intervals (CI) of changes in steps per day, PA and sedentary time and bouts, energy and macronutrient intake, sleep behaviors, and weight loss during the intervention with changes in body weight during the follow-up period in participants who experienced exercise-induced weight loss during the 12-month intervention ($n=227$). We decided to combine participants from both randomization groups and include all participants who experienced any amount of weight loss (>0 kg) during the intervention to maximize statistical power in our analyses while still controlling for covariates related to the intervention that may impact the tested associations (i.e., randomization group, amount of exercise-induced weight loss during the interventions). Each predictor variable was interchangeably added to the linear regression model. Multinomial logistic regression analyses were also conducted to assess mean differences in the change of these predictors from 12 to 24 months between participants who continued to lose weight or maintained weight loss as the referent group and participants who regained (1) between 0.1 and 2.5 kg, (2) between 2.6 and 4.9 kg, and (3) ≥5 kg during follow-up. As an exploratory aim, the linear regression analyses were repeated with changes in predictors from baseline to 24 months and absolute predictor values at 24 months.

Effect modification was first assessed by adding the interaction terms for each behavioral predictor of interest by covariate (age, marital status, ethnicity, education, study site, and randomization group) to the multivariable-adjusted models. Stratified analyses were conducted if the interaction term reached statistical significance ($P<0.05$).

# Results

The BETA study flowchart presenting the number of referred or eligible participants and reasons for exclusion from randomization has been previously reported (30,31). Of the 329 participants who had body weight measurements at each time point, 227 participants experienced some exercise-induced weight loss during the 12-month intervention and were included in the present analysis (Figure 1). Data for self-reported energy and macronutrient intake and sleep variables were available for all participants, whereas accelerometry data were available for 193 participants (Figure 1). Baseline demographic characteristics, in addition to mean weight loss during the exercise intervention, adherence to the exercise intervention, and weight change during follow-up,

**TABLE 1** Descriptive characteristics of participants who lost weight during 12-month exercise intervention, the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014

| | Participants with sleep and energy intake data ($n=227$) | Participants with accelerometry data ($n=193$) |
|---|---|---|
| Weight loss during exercise intervention (kg), mean ± SD | −4.2 ± 3.6 | −4.0 ± 3.0 |
| Weight change during follow-up period (kg), mean ± SD | 1.8 ± 3.6 | 1.7 ± 3.4 |
| Baseline age (y), mean ± SD | 60.0 ± 5.0 | 60.1 ± 5.0 |
| Baseline body weight (kg), mean ± SD | 76.8 ± 12.3 | 76.5 ± 12.0 |
| Exercise intervention adherence (% of prescribed min/wk of exercise), mean ± SD | 90.2 ± 18.3 | 91.9 ± 15.6 |
| Study site | | |
| Calgary, *n* (%) | 174 (76.7%) | 150 (77.7%) |
| Edmonton, *n* (%) | 53 (23.3%) | 43 (22.3%) |
| Randomization group | | |
| 150 min/wk (moderate volume), *n* (%) | 111 (48.9%) | 95 (49.2%) |
| 300 min/wk (high volume), *n* (%) | 116 (51.1%) | 98 (50.8%) |
| Marital status | | |
| Married or common law, *n* (%) | 166 (73.1%) | 143 (74.1%) |
| Unmarried/other, *n* (%) | 61 (26.9%) | 50 (25.9%) |
| Education | | |
| ≤High school, *n* (%) | 46 (20.3%) | 42 (21.8%) |
| >High school, *n* (%) | 181 (79.7%) | 151 (78.2%) |
| Ethnicity | | |
| Caucasian, *n* (%) | 202 (89.0%) | 172 (89.1%) |
| Other, *n* (%) | 25 (11.0%) | 21 (10.9%) |

All participants with accelerometry data ($n=193$) also had sleep and energy intake data.

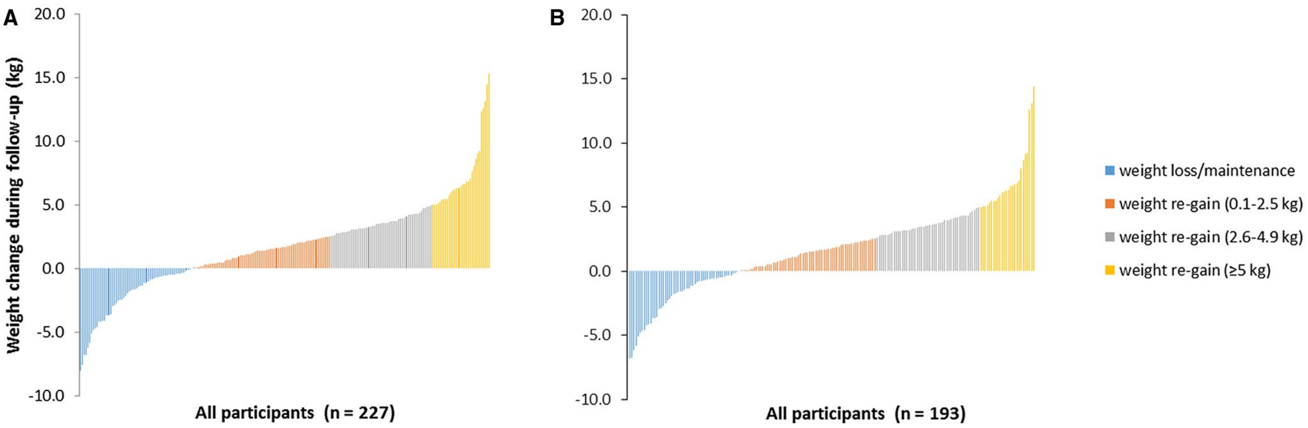



**Figure 2** Distribution of weight change during the follow-up period in participants with (**A**) sleep and energy intake data and (**B**) accelerometry data in the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014. [Color figure can be viewed at wileyonlinelibrary.com]

are presented in Table 1. On average, participants regained 43% of the amount of weight lost during the exercise intervention, indicating that some weight loss was sustained during follow-up. However, large interindividual variations in the quantity of weight change during follow-up were noted (Figure 2). Specifically, 28% of participants continued to lose weight or maintained weight loss during follow-up, whereas 32%, 26%, and 14% regained 0.1 to 2.5 kg, 2.6 to 4.9 kg, and ≥5 kg, respectively.

A greater amount of weight loss during the intervention was associated with greater weight regain during follow-up (β = −0.44; 95% CI: −0.56 to −0.32; $P$ < 0.0001). Indeed, participants who regained weight during follow-up had an increasingly larger amount of weight loss during the intervention (Table 2). Decreases in moderate to vigorous PA time and steps per day (Figure 3), as well as increases in sedentary time (Figure 4), were significantly associated with weight regain during follow-up. Increases in total energy and fat intake (Figure 5), as well as a delayed sleep timing midpoint (Figure 6), were also associated with weight regain during follow-up. Results from the multinomial logistic regressions revealed that significant increases in sedentary time, energy, fat, and protein intake were noted in participants who regained ≥5 kg during follow-up versus those who continued to lose weight or maintained weight loss (Table 2). Our exploratory analyses revealed similar results for moderate to vigorous PA (time, steps per day, and number of bouts), sedentary time and bouts, and sleep timing midpoint when adding absolute predictor values at 24 months to the linear regression model, whereas only reductions in steps per day and moderate to vigorous PA bouts from baseline to 24 months were associated with weight regain during follow-up (Supporting Information Table S2).

The moderate to vigorous PA time × education interaction term was statistically significant when added to the multivariable-adjusted model ($P$ = 0.04); however, the association between reductions in moderate to vigorous PA time and weight regain during follow-up in the ≤ high school education group only reached a statistical trend (β = −2.21; 95% CI: −4.59 to 0.17; $P$ = 0.07) compared with the > high school education group (β = −0.58; 95% CI: −1.37 to 0.20; $P$ = 0.14). The steps per day × randomized group and number of moderate to vigorous PA bouts × randomization group interaction terms were also statistically significant ($P$ = 0.01), with stratified analyses revealing greater reductions in steps per day (β = −0.0004; 95% CI: −0.0007 to −0.0002; $P$ = 0.002 vs. β = −0.00006; 95% CI: −0.0003 to 0.0002; $P$ = 0.60) and bouts of moderate to vigorous PA time (β = −2.97; 95% CI: −5.17 to −0.77; $P$ = 0.01 vs. β = 0.35; 95% CI: −1.35 to 2.06; $P$ = 0.68) in participants randomized to the moderate versus high exercise volume groups. The light PA time × marital status interaction term was also statistically significant ($P$ = 0.02), with stratified analyses indicating a nonsignificant positive association in unmarried or other participants (β = 0.89; 95% CI: −0.61 to 2.39; $P$ = 0.24) and a nonsignificant negative association in married or common law participants (β = −0.68; 95% CI: −1.51 to 0.15; $P$ = 0.11). The energy intake × education interaction term was associated with weight change during follow-up ($P$ = 0.01). Similar results were noted for the carbohydrate intake × education ($P$ = 0.01) and protein intake × education ($P$ = 0.02) interactions terms. Stratified analyses revealed that increases in energy intake were associated with weight regain during follow-up in participants with ≤ high school education (β = 0.005; 95% CI: 0.001 to 0.008; $P$ = 0.01) but not in those reporting > high school education (β = 0.001; 95% CI: −0.0003 to 0.002; $P$ = 0.17). Similar results were noted for protein intake (≤ high school education: β = 0.020; 95% CI: 0.001 to 0.039; $P$ = 0.04), with a statistical trend for carbohydrate intake (≤ high school education: β = 0.004; 95% CI: −0.001 to 0.001; $P$ = 0.09). The energy intake × ethnicity interaction term was also statistically significant ($P$ = 0.04), with stratified analyses revealing a significant positive association between energy intake and weight change in Caucasian participants (β = 0.002; 95% CI: 0.003 to 0.003; $P$ = 0.01) but not participants of other ethnic backgrounds (β = −0.0005; 95% CI: −0.002 to 0.001; $P$ = 0.61). Lastly, the sleep duration × marital status interaction term was statistically significant ($P$ = 0.03), with a statistical trend for an association between reductions in sleep duration and weight regain during follow-up in unmarried or other (β = −0.97; 95% CI: −2.03 to 0.08; $P$ = 0.07) but not married/common law (β = 0.04; 95% CI: −0.46 to 0.54; $P$ = 0.88) participants. No other evidence of effect modification was observed (results not shown).

**TABLE 2** Mean differences in change of behavioral predictors from 12 to 24 months between participants who continued to lose weight or maintained weight loss (referent group) compared with participants who regained weight, the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014

| Changes in behavioral predictors from 12 to 24 mo | Mean ± SD | Multinomial logistic regression results, β (95% CI) | Multinomial logistic regression *P* value[a] |
|---|---|---|---|
| *Weight loss during the intervention (kg)* | | | |
| Weight loss or maintenance | −3.0 ± 2.0 | Referent | Referent |
| Regained 0.1-2.5 kg | −3.6 ± 2.6 | −0.08 (−0.23 to 0.07) | 0.29 |
| Regained 2.6-4.9 kg | −4.3 ± 3.3 | −0.18 (−0.33 to −0.03) | **0.02** |
| Regained ≥5 kg | −7.5 ± 5.8 | −0.36 (−0.52 to −0.20) | **<0.0001** |
| *Moderate to vigorous PA time (h/d)* | | | |
| Weight loss or maintenance (ref) | −0.29 ± 0.52 | Referent | Referent |
| Regained 0.1-2.5 kg | −0.21 ± 0.63 | 0.25 (−0.42 to 0.92) | 0.46 |
| Regained 2.6-4.9 kg | −0.44 ± 0.64 | −0.48 (−1.17 to 0.22) | 0.18 |
| Regained ≥5 kg | −0.54 ± 0.69 | −0.78 (−1.65 to 0.08) | 0.08 |
| *Bouts of moderate to vigorous PA time (number/d)*[b] | | | |
| Weight loss or maintenance (ref) | | | |
| Regained 0.1-2.5 kg | −0.22 ± 0.29 | Referent | Referent |
| Regained 2.6-4.9 kg | −0.27 ± 0.35 | −0.22 (−1.62 to 1.18) | 0.76 |
| Regained ≥5 kg | −0.10 ± 0.35 | 1.30 (−0.19 to 2.78) | 0.09 |
| | −0.24 ± 0.33 | −0.10 (−1.94 to 1.74) | 0.91 |
| *Steps per day* | | | |
| Weight loss or maintenance (ref) | −1800 ± 2486 | Referent | Referent |
| Regained 0.1-2.5 kg | −1962 ± 2660 | 0.00001 (−0.0002 to 0.0002) | 0.95 |
| Regained 2.6-4.9 kg | −934 ± 2181 | 0.0002 (−0.00002 to 0.0004) | 0.07 |
| Regained ≥5 kg | −2295 ± 2436 | −0.0001 (−0.0004 to 0.0002) | 0.46 |
| *Light PA time (h/d)* | | | |
| Weight loss or maintenance (ref) | −0.01 ± 0.77 | Referent | Referent |
| Regained 0.1-2.5 kg | −0.11 ± 0.67 | −0.26 (−0.86 to 0.35) | 0.4 |
| Regained 2.6-4.9 kg | −0.19 ± 0.61 | −0.47 (−1.12 to 0.17) | 0.15 |
| Regained ≥5 kg | −0.20 ± 0.60 | −0.71 (−1.55 to 0.13) | 0.1 |
| *Sedentary time (h/d)* | | | |
| Weight loss or maintenance (ref) | 0.22 ± 1.09 | Referent | Referent |
| Regained 0.1-2.5 kg | 0.16 ± 0.98 | 0.02 (−0.40 to 0.44) | 0.92 |
| Regained 2.6-4.9 kg | 0.44 ± 1.01 | 0.41 (−0.03 to 0.85) | 0.07 |
| Regained ≥5 kg | 0.76 ± 1.46 | 0.64 (0.08 to 1.19) | **0.02** |
| *Bouts of sedentary time (number/d)*[b] | | | |
| Weight loss or maintenance (ref) | 0.37 ± 1.12 | Referent | Referent |
| Regained 0.1-2.5 kg | 0.13 ± 0.95 | 0.25 (−0.64 to 0.14) | 0.21 |
| Regained 2.6-4.9 kg | 0.26 ± 1.14 | −0.09 (−0.48 to 0.31) | 0.66 |
| Regained ≥5 kg | 0.43 ± 1.12 | −0.03 (−0.52 to 0.47) | 0.92 |
| *Energy intake (kcal)* | | | |
| Weight loss or maintenance (ref) | −110 ± 395 | Referent | Referent |
| Regained 0.1-2.5 kg | −4 ± 507 | 0.001 (−0.0002 to 0.002) | 0.16 |
| Regained 2.6-4.9 kg | 21 ± 300 | 0.001 (−0.0003 to 0.002) | 0.14 |
| Regained ≥5 kg | 191 ± 441 | 0.002 (0.001 to 0.003) | **0.002** |
| *Carbohydrate intake (kcal)* | | | |
| Weight loss or maintenance (ref) | −554 ± 250 | Referent | Referent |
| Regained 0.1-2.5 kg | −507 ± 214 | 0.001 (−0.001 to 0.003) | 0.24 |
| Regained 2.6-4.9 kg | −511 ± 186 | 0.001 (−0.001 to 0.003) | 0.2 |

**TABLE 2** (continued).

| Changes in behavioral predictors from 12 to 24 mo | Mean ± SD | Multinomial logistic regression results, β (95% CI) | Multinomial logistic regression *P* value[a] |
|---|---|---|---|
| Regained ≥5 kg | −525 ± 195 | 0.001 (−0.001 to 0.003) | 0.5 |
| *Fat intake (kcal)* | | | |
| Weight loss or maintenance (ref) | −45 ± 205 | Referent | Referent |
| Regained 0.1-2.5 kg | −19 ± 173 | 0.001 (−0.001 to 0.003) | 0.44 |
| Regained 2.6-4.9 kg | 16 ± 134 | 0.002 (−0.0005 to 0.004) | 0.12 |
| Regained ≥5 kg | 96 ± 261 | 0.004 (0.001 to 0.007) | **0.004** |
| *Protein intake (kcal)* | | | |
| Weight loss or maintenance (ref) | −10 ± 69 | Referent | Referent |
| Regained 0.1-2.5 kg | −4 ± 75 | 0.001 (−0.004 to 0.006) | 0.76 |
| Regained 2.6-4.9 kg | 1 ± 60 | 0.001 (−0.004 to 0.007) | 0.68 |
| Regained ≥5 kg | 26 ± 72 | 0.008 (0.001 to 0.015) | **0.03** |
| *Sleep duration (h/d)* | | | |
| Weight loss or maintenance (ref) | −0.02 ± 0.89 | Referent | Referent |
| Regained 0.1-2.5 kg | −0.05 ± 0.79 | −0.04 (−0.43 to 0.34) | 0.82 |
| Regained 2.6-4.9 kg | −0.24 ± 1.03 | −0.26 (−0.67 to 0.16) | 0.23 |
| Regained ≥5 kg | −0.13 ± 1.24 | −0.03 (−0.53 to 0.47) | 0.9 |
| *Sleep quality (total PSQI score, range 0-21)* | | | |
| Weight loss or maintenance (ref) | 0.3 ± 2.5 | Referent | Referent |
| Regained 0.1-2.5 kg | 0.2 ± 2.0 | −0.01 (−0.19 to 0.17) | 0.93 |
| Regained 2.6-4.9 kg | 0.6 ± 2.6 | 0.01 (−0.19 to 0.21) | 0.89 |
| Regained ≥5 kg | 0.5 ± 2.6 | 0.06 (−0.21 to 0.34) | 0.64 |
| *Sleep timing midpoint (min/d)*[c] | | | |
| Weight loss or maintenance (ref) | 3.4 ± 31.7 | Referent | Referent |
| Regained 0.1-2.5 kg | −3.5 ± 32.6 | −0.01 (−0.02 to 0.004) | 0.23 |
| Regained 2.6-4.9 kg | 10.9 ± 28.2 | 0.01 (−0.002 to 0.02) | 0.12 |
| Regained ≥5 kg | 17.3 ± 54.1 | 0.01 (−0.001 to 0.03) | 0.06 |

[a]Results adjusted for the following covariates: age, marital status, education, ethnicity, study site, randomization group, weight loss during exercise intervention (except when the predictor of interest), accelerometer wear time (accelerometry data only), and sleep duration (sleep quality and sleep timing results only). $P \leq 0.05$ are bolded.
[b]Moderate- to vigorous-intensity PA bouts defined as ≥ 10 minutes without any continuous sedentary time or light-intensity PA lasting ≥ 1 minute. Sedentary bouts defined as ≥ 60 minutes without any moderate- to vigorous-intensity PA time during this bout or light-intensity PA lasting ≥ 1 minute.
[c]Positive value indicates delayed sleep timing midpoint at 24 vs. 12 months.
PA, physical activity; PSQI, Pittsburgh Sleep Quality Index.

## Discussion

This secondary analysis aimed to assess the strength of the associations between changes in energy balance and sleep behaviors and the risk of weight regain following exercise-induced weight loss in postmenopausal women. The present analyses explored changes in some novel behaviors (e.g., sedentary time, moderate to vigorous PA and sedentary time bouts, and sleep behaviors) measured following an exercise-only intervention that may predict the risk of weight regain. Furthermore, results from this large-scale intervention complement previous findings on PA as a potential risk factor for weight regain following an intervention in postmenopausal women (15,20). Of the 227 participants who experienced weight loss during the 12-month BETA exercise intervention, mean weight regain was 43%, which is similar to other intervention studies that have assessed weight regain during follow-up in postmenopausal women (15,20,38-40). Furthermore, a greater amount of weight loss during the intervention was associated with greater weight regain during follow-up, which corroborates recent findings from a meta-regression (41).

Our results first suggest that reductions in moderate to vigorous PA time and steps per day were associated with weight regain during follow-up. Specifically, a 1-hour decrease in moderate to vigorous PA time was associated with a 1-kg increase in body weight during follow-up in the fully-adjusted linear regression model. However, these associations were no longer statistically significant in the logistic regression models, which may be attributable to the reduction in statistical power given the smaller number of participants per weight-change group. Greater levels of PA have been consistently associated with weight-loss maintenance post intervention (8,10-17), regardless of the mode of weight loss. Although the impact of PA on actual weight loss is modest compared with dietary interventions (3,32), these findings highlight the importance of maintaining, or even adding, high levels of moderate to vigorous PA and steps per day post intervention to promote weight-loss maintenance.

Increases in sedentary time were associated with weight regain during follow-up, with results from our fully adjusted linear regression model indicating a 1-kg increase in body weight with every 30-minute increase in sedentary time. Participants who regained ≥5 kg, in particular, had

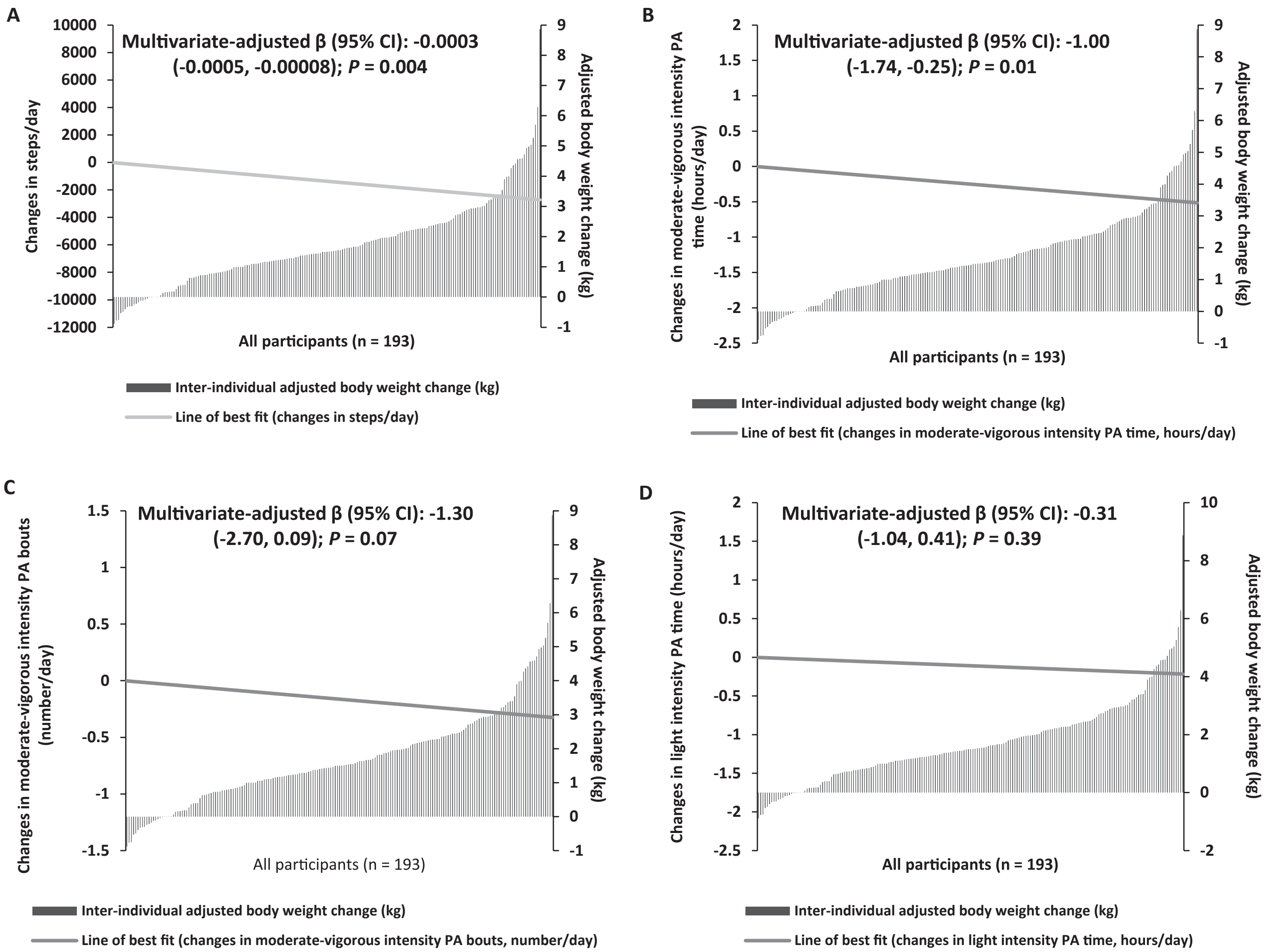



**Figure 3** Strength of the associations between changes in (**A**) steps per day, (**B**) moderate- to vigorous-intensity PA time, (**C**) number of moderate- to vigorous-intensity PA bouts, and (**D**) light-intensity PA time and the changes in body weight from 12 to 24 months (during follow-up) for 193 participants in the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014. Negative values represent decreases in PA and steps per day, as well as weight loss during the follow-up period. Positive values represent increases in PA and steps per day, as well as weight gain during the follow-up period. Multivariable-adjusted β and 95% confidence intervals (CI) were adjusted for the following covariates: age, marital status, education, ethnicity, study site, randomization group, weight loss during the exercise intervention, and differences in accelerometer wear time between 12- and 24-month time points. The changes in steps per day and PA variables (24-month – 12-month values) are represented by the line of best fit, whereas the body weight-change variable was calculated as individual participant β values derived from the multivariable-adjusted linear regression model. β, beta coefficient; PA, physical activity.

a greater increase in sedentary time compared with those who lost or maintained weight during follow-up. Initial observational studies have reported that less time spent being sedentary, including sitting and television viewing time, was associated with successful weight-loss maintenance (5,7,21,22). Using isotemporal substitution modelling, Buman et al. (42) noted that a 30-minute displacement of sedentary time toward light or moderate to vigorous PA was associated with 2%-4% or 2%-15% lower levels of biomarkers of disease risk, respectively. Therefore, lower sedentary time may not only be associated with successful weight-loss maintenance but also meaningful reductions in health risk factors associated with this behavior (42,43). Future studies are needed to assess the efficacy of sedentary time reduction interventions for weight-loss maintenance.

Increases in energy and fat intake were also associated with greater weight regain during follow-up in the linear and logistic regression models. Specifically, participants who continued to lose weight or maintained weight loss during follow-up reported a decrease in energy intake of ≈ 100 kcal/d, whereas an increase of ≈ 200 kcal/d was reported by participants who regained ≥ 5 kg. A reduction in energy intake has been previously associated with successful weight-loss maintenance following diet plus exercise and/or lifestyle (11,14) and diet-only (33) interventions, thus supporting our findings. The only other exercise-only intervention to assess risk factors of weight-loss maintenance also reported that participants who maintained the highest exercise levels had greater decreases in dietary and fat intake during follow-up (8). Effect modification by education was also noted, indicating that energy,

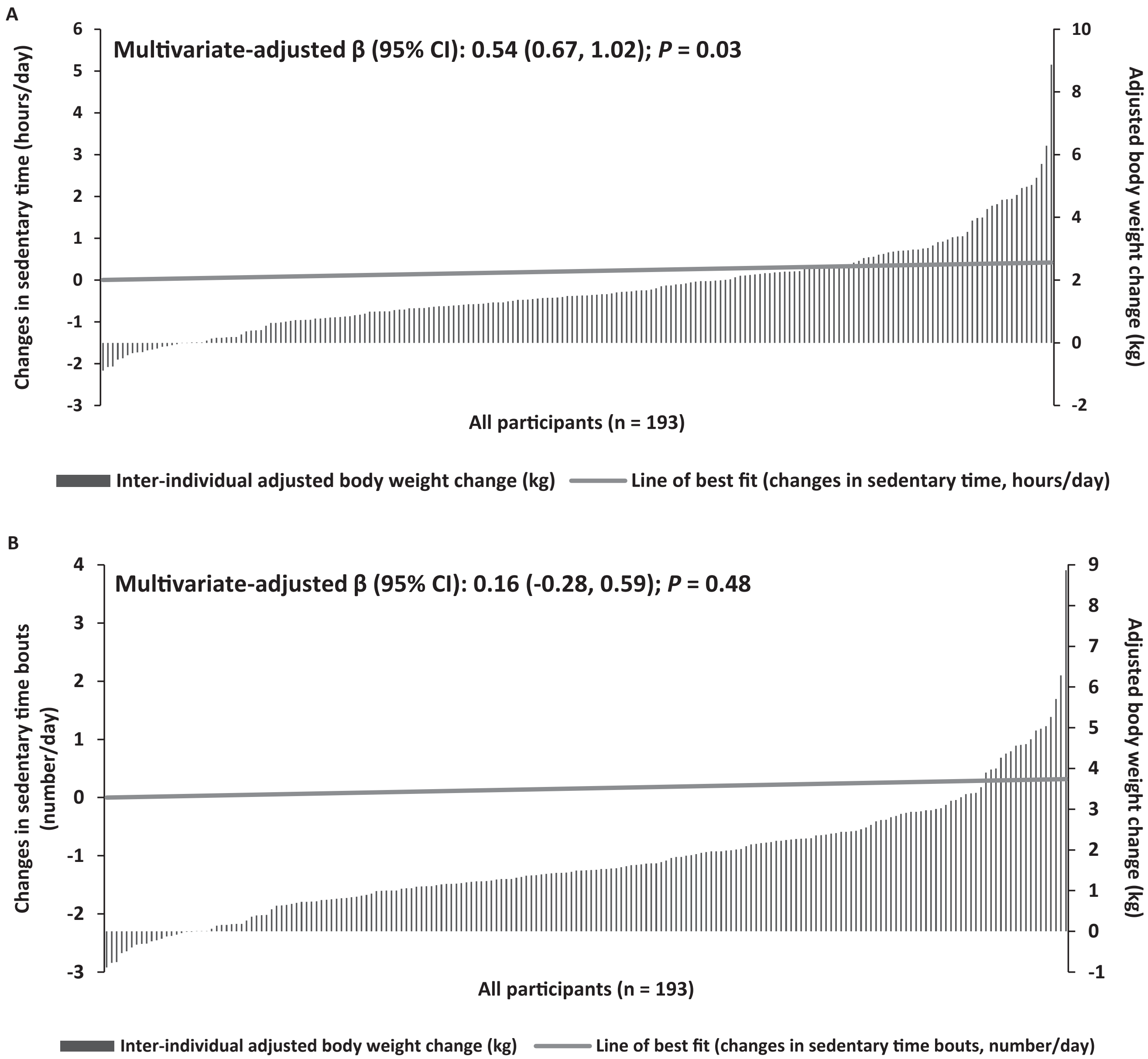



**Figure 4** Strength of the associations between changes in (**A**) sedentary time and (**B**) number of sedentary time bouts and changes in body weight from 12 to 24 months (during follow-up) for 193 participants in the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014. Negative values represent decreases in sedentary time and bouts, as well as weight loss during the follow-up period. Positive values represent increases in sedentary time and bouts, as well as weight gain during the follow-up period. Multivariable-adjusted β and 95% confidence intervals (CI) were adjusted for the following covariates: age, marital status, education, ethnicity, study site, randomization group, weight loss during the exercise intervention, and differences in accelerometer wear time between 12- and 24-month time points. The changes in sedentary time/bouts (24-month – 12-month values) are represented by the line of best fit, whereas the body weight-change variable was calculated as individual participant β values derived from the multivariable-adjusted linear regression model. β, beta coefficient; PA, physical activity.

protein, and a trend for carbohydrate intake were associated with weight regain in participants with ≤ high school education. Previous findings have indicated that a lower (or primary) education is associated with greater energy-dense food intake and between-meal snacking (44,45). Although we noted statistically significant results for energy and fat intake, these results should be interpreted with caution given the small caloric intake β associated with risk of weight regain (i.e., 0.001-0.004 increase in caloric intake is associated with every 1-kg increase in body weight). These trivial effects of energy intake on risk of weight regain could be associated with the exercise-only intervention design where no changes in energy intake may be expected as a result of this intervention, but they may also result from the use of a food frequency questionnaire to assess energy intake over the past year. Indeed, food frequency questionnaires only capture habitual energy intake over an

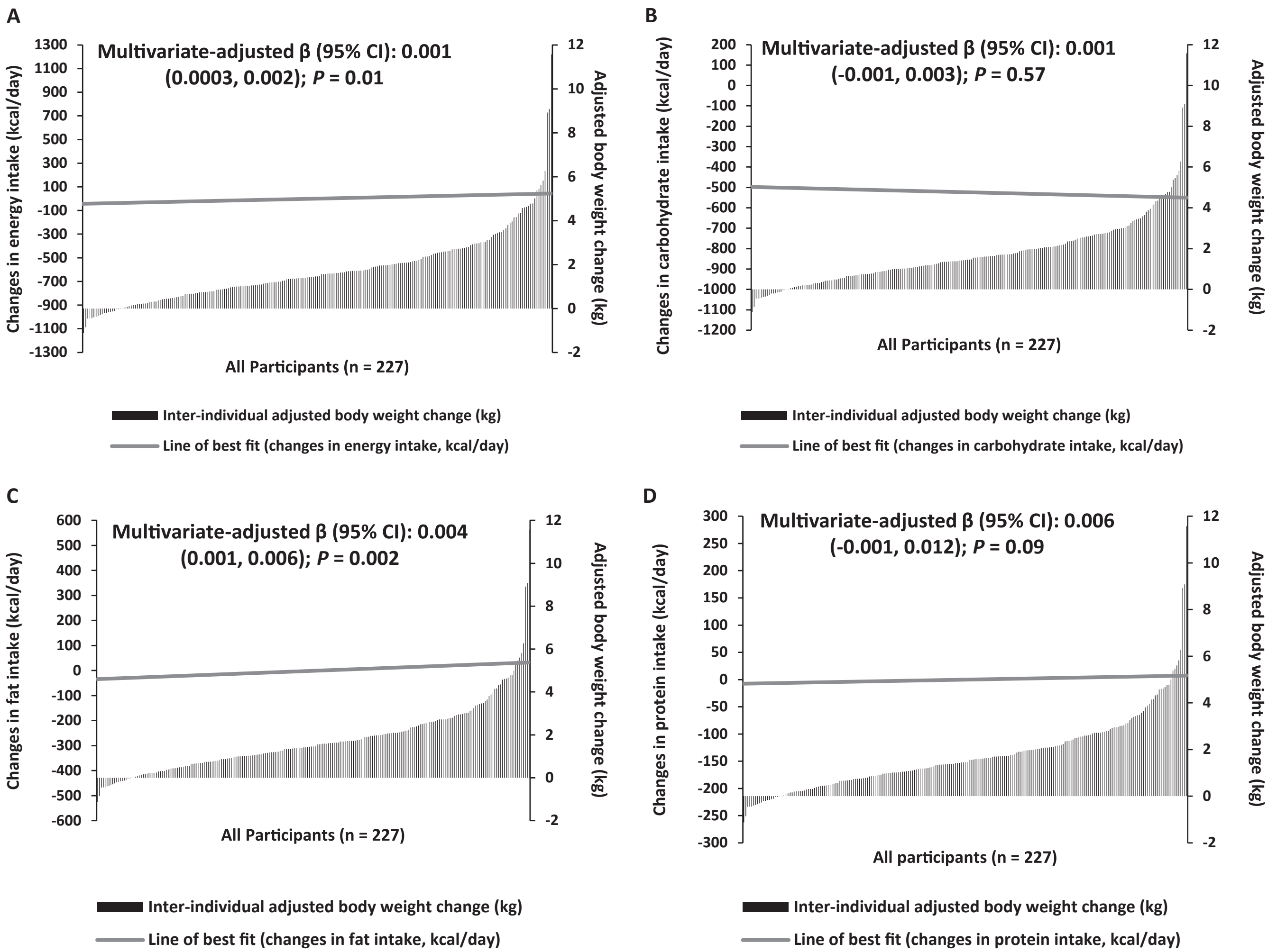
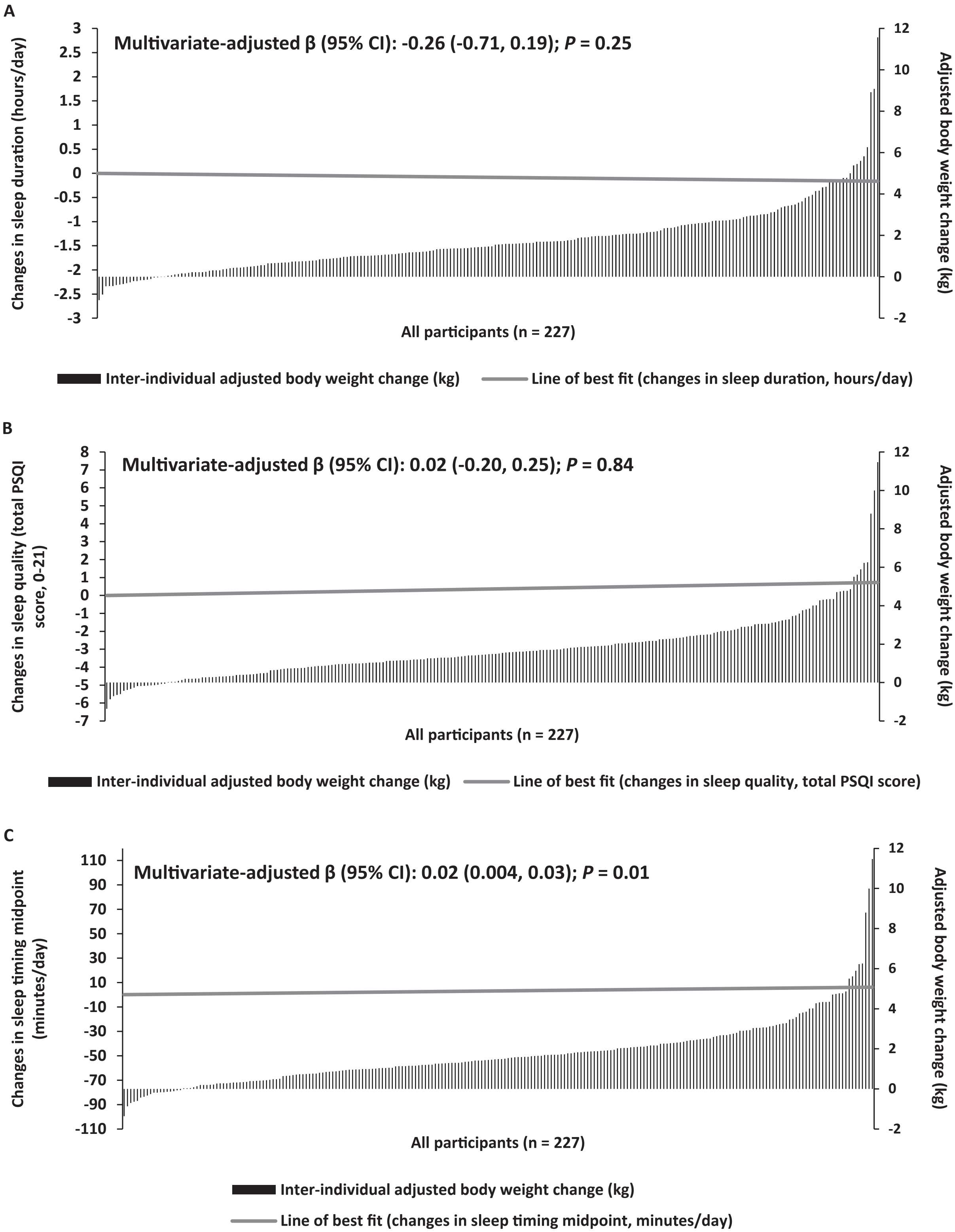



**Figure 5** Strength of the associations between changes in (**A**) energy, (**B**) carbohydrate, (**C**) fat, and (**D**) protein intake and changes in body weight from 12 to 24 months (during follow-up) for 227 participants in the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014. Negative values represent decreases in energy and macronutrient intake, as well as weight loss during the follow-up period. Positive values represent increases in energy and macronutrient intake, as well as weight gain during the follow-up period. Multivariable-adjusted β and 95% confidence intervals (CI) were adjusted for the following covariates: age, marital status, education, ethnicity, study site, randomization group, and weight loss during the exercise intervention. The changes in energy and macronutrient intake variables (24-month – 12-month values) are represented by the line of best fit, whereas the body weight-change variable was calculated as individual participant β values derived from the multivariable-adjusted linear regression model. β, beta coefficient.

extended period of time (1 y), which may greatly reduce the degree of variability and/or change in energy intake captured within the context of an intervention and follow-up period.

Lastly, delays in sleep timing midpoint were associated with risk of weight regain during follow-up in the linear regression model. Although not significantly different than participants who lost or maintained weight during follow-up, participants who regained ≥5 kg had a 17-minute delay in sleep timing midpoint at follow-up compared with end of intervention. Our exploratory analyses also revealed a stronger positive association between 24-month sleep timing midpoint and the risk of weight regain. These results suggest that a later sleep timing midpoint, rather than changes or delays in sleep timing midpoint, may be a stronger predictor of weight regain. To our knowledge, this study is the first to investigate the association between changes in sleep timing midpoint and the risk of weight regain. Having a later sleep timing midpoint has been associated with greater fast food intake and late-night energy intake (25), as well as lower moderate to vigorous PA and sedentary time (26), which may undermine weight-maintenance efforts. Additional studies are needed to confirm our findings.

Our results are mostly generalizable to healthy postmenopausal women. Other limitations include the large number of analyses, which may increase the risk of false-positive findings, the small numbers of participants within certain covariate groups (e.g., unmarried or other group and ≤high school education), which undermined our ability to report statistically significant group differences following stratified analyses, and the use of self-reported measurement tools for energy intake and sleep variables. Specifically, participants were asked to remove the accelerometer before going to bed each day, which limited our




ability to use objective measurements of sleep in the present analyses. Furthermore, the use of a food frequency questionnaire to assess energy intake has inherent limitations, such as misreporting and measurement error (e.g., recall bias, modifying dietary habits or responses on this questionnaire through self-reflection and/or to reduce response burden) (46). Lastly, BETA was not designed to be a weight-loss intervention or to examine the effectiveness of the prescribed exercise intervention in promoting weight loss or successful weight-loss maintenance.

**Figure 6** Strength of the associations between changes in (**A**) sleep duration, (**B**) sleep quality, and (**C**) sleep timing midpoint and changes in body weight from 12 to 24 months (during follow-up) for 227 participants in the Breast Cancer and Exercise Trial in Alberta (BETA), Alberta, Canada, 2010-2014. Negative values represent decreases in sleep duration, improvements in sleep quality, and an earlier sleep timing midpoint, as well as weight loss during the follow-up period. Positive values represent increases in sleep duration, a poorer sleep quality, and a delay in sleep timing midpoint, as well as weight gain during the follow-up period. The multivariable-adjusted β and 95% confidence intervals (CI) were adjusted for the following covariates: age, marital status, education, ethnicity, study site, randomization group, weight loss during the exercise intervention, and changes in sleep duration between 12- and 24-month time points (sleep quality and sleep timing midpoint regression models only). The changes in sleep behavior variables (24-month – 12-month values) are represented by the line of best fit, whereas the body weight-change variable was calculated as individual participant β values derived from the multivariable-adjusted linear regression model. β, beta coefficient; PSQI, Pittsburgh Sleep Quality Index.

## Conclusion

These exploratory results suggest that increases in energy intake, fat intake, and sedentary time, as well as reductions in moderate to vigorous PA time and steps per day and a delayed sleep timing midpoint, may increase the risk of weight regain following exercise-induced weight loss in postmenopausal women. Specifically, the larger β associated with reductions in moderate to vigorous PA and increases in sedentary time were the most meaningful in predicting risk of weight regain during follow-up in these participants, which may naturally reflect the removal of the exercise intervention. These findings add to current knowledge on the behavioral factors that should be targeted in weight-maintenance programs following exercise-induced weight loss, with a particular emphasis on PA and sedentary behaviors. **O**

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The data sets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.



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