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Substituting sedentary time with sleep or physical activity and subsequent weight-loss maintenance

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Abstract

Objective: In this study, the associations between the substitution of sedentary time with sleep or physical activity at different intensities and subsequent weight-loss maintenance were examined.

Methods: This prospective study included 1152 adults from the NoHoW trial who had achieved a successful weight loss of ≥5% during the 12 months prior to baseline and had BMI ≥25 kg/m^2 before losing weight. Physical activity and sleep were objectively measured during a 14-day period at baseline. Change in body weight was included as the primary outcome. Secondary outcomes were changes in body fat percentage and waist circumference. Cardiometabolic variables were included as exploratory outcomes.

Results: Using isotemporal substitution models, no associations were found between activity substitutions and changes in body weight or waist circumference. However, the substitution of sedentary behavior with moderate-to-vigorous physical activity was associated with a decrease in body fat percentage during the first 6 months of the trial (−0.33% per 30 minutes higher moderate-to-vigorous physical activity [95% CI: −0.60% to −0.07%], $p = 0.013$).

Conclusions: Sedentary behavior had little or no influence on subsequent weight-loss maintenance, but during the early stages of a weight-loss maintenance program,

substituting sedentary behavior with moderate-to-vigorous physical activity may prevent a gain in body fat percentage.

INTRODUCTION

Despite public health policies and interventions, the global prevalence of obesity is still rising [1, 2]. Many existing approaches are effective for initial weight loss, but most individuals with obesity are not successful in maintaining their weight loss in the long term [3].

Less sedentary behavior (SB), higher levels of physical activity (PA), and sufficient sleep are all factors that may improve weight-loss maintenance [4–8]. However, effects of a change in one specific activity on body weight likely depend on displacement of other activities [9], and few studies have directly addressed these substitutions in relation to weight-loss maintenance [10].

Because total time in any given day is fixed at 24 hours, time spent on one activity cannot be changed without affecting the time spent on remaining activities. For instance, an increase in the daily duration of SB must be at the expense of either sleep, light physical activity (LPA), or moderate-to-vigorous physical activity (MVPA). The isotemporal substitution model was developed as a modeling strategy to estimate the effects of substituting time from one activity with an equal amount of time from another activity using compositional data [10].

Few longitudinal studies have explored the role of activity substitutions in weight-loss maintenance or weight change in general [10, 11]. Mekary and colleagues examined associations between different activity substitutions and 6-year weight-loss maintenance among 4558 healthy women who had lost more than 5% of their weight prior to baseline. Based on self-reported activity data, they found that substitution of TV watching for either slow walking, brisk walking, or jogging/running was associated with less weight gain [10]. Though not specifically focused on weight-loss maintenance, Pelclová and colleagues also showed that an increase in SB at the expense of LPA and MVPA during a 7-year period was associated with an increase in both body mass index (BMI) and body fat percentage during the same period [11]. However, because of the absence of temporal separation in exposures and outcomes, these analyses are more vulnerable to reverse causality.

In contrast to the lack of longitudinal studies, cross-sectional associations between activity substitutions and body weight or different cardiometabolic markers have been suggested in numerous studies [11–19]. As an example, results from the Whitehall II epidemiological cohort suggested that when replacing accelerometer-measured SB with other activities, only substitution with MVPA was associated with improved metabolic risk factors [19]. More specifically, the study showed that replacing SB with an equal amount of MVPA was associated with lower BMI, glycated hemoglobin (HbA1c), and triglycerides and was associated with higher levels of high-density lipoprotein (HDL) cholesterol [19].

In addition to the lack of evidence from prospective studies, as pointed out by Grgic and colleagues in a systematic scoping review of isotemporal substitution studies, many of the currently published studies have not considered substitution for sleep duration, which is a major limitation to our current knowledge [9].

Using baseline activity data, we conducted isotemporal substitution models to investigate the relationship between SB and subsequent weight-loss maintenance over 6, 12, and 18 months, when SB was substituted with either sleep, LPA, or MVPA. In addition to change in body weight (primary outcome), we included measures of change in body fat percentage and waist circumference as secondary outcomes. Changes in cardiometabolic markers (blood pressure [BP], low-density lipoprotein [LDL], HDL, triglycerides, and HbA1c) were included as exploratory outcomes.

Study Importance

What is already known?

- Weight-loss maintenance is the greatest challenge in successful treatment of obesity.
- Less sedentary behavior, higher levels of physical activity, and sufficient sleep are all factors suggested to improve weight-loss maintenance.
- Few longitudinal studies have explored how substituting sedentary behavior with sleep or physical activity at different intensities is associated with weight-loss maintenance.

What does this study add?

- No associations between activity substitutions and changes in body weight or waist circumference were found.
- Substituting sedentary behavior with moderate-to-vigorous physical activity was associated with a subsequent decrease in body fat percentage during the first 6 months of the study.
- Exploratory analyses suggested that substituting sedentary behavior with light or moderate-to-vigorous physical activity improved the subsequent overall cardiometabolic risk profile.

How might these results change the direction of research or the focus of clinical practice?

- Although our results do suggest health benefits of substituting sedentary behavior with higher levels of physical activity during a weight-loss maintenance effort, the effect of activity substitutions on weight change is likely marginal at best.

METHODS

Study population

NoHoW was a weight-loss maintenance trial conducted in the UK, Denmark, and Portugal. A detailed description of NoHoW can be found elsewhere [20]. At baseline, between March 2017 and March 2018, participants were randomly allocated to one of four arms: (1) control arm with self-monitoring only (self-weighing and activity tracker); (2) self-monitoring plus self-regulation and motivation; (3) self-monitoring plus emotion regulation; or (4) combined self-monitoring, self-regulation, motivation, and emotion regulation. In addition to the primary follow-up visit at month 12, measurements on trial outcomes were also collected at months 6 and 18. Participants were 18 years or older, had achieved a verified and clinically significant weight loss of ≥5% within the 12 months prior to inclusion, and had BMI ≥25 kg/m^2 before losing weight. The exclusion criteria were as follows: achieved weight loss due to illness or surgical procedures; pregnancy/breastfeeding; involvement in other research intervention studies that confound the aims of the intervention; inability to follow written material or telephone conversations in the English, Danish, or Portuguese language (depending on the trial center); diagnosis of an eating disorder; diagnosis of any condition that may interfere with increasing mild to moderate PA and that is unstable (i.e., untreated or unable to be controlled by medication); recent diagnosis of type 1 diabetes; extensive travel plans (e.g., more than 4 weeks); or living in the same household as existing participant in the trial [20]. A total of 1627 participants were enrolled in the NoHoW trial. The trial was registered with the ISRCTN registry (ISRCTN88405328) on December 22, 2016. The trial was conducted in accordance with the Helsinki Declaration. Ethical approval was granted by local institutional ethics committees at the Universities of Leeds (17-0082; February 27, 2017), Lisbon (17/2016; February 20, 2017), and the Capital Region of Denmark (H-16030495; March 8, 2017).

The present study was based on information collected at baseline and 6-month, 12-month, and 18-month follow-up visits. We further excluded participants without valid information on activity and sleep at baseline ($n = 306$), with missing information on baseline covariates ($n = 28$), or with no follow-up information on the primary outcome (body weight) at the 6-, 12-, or 18-month visit ($n = 141$). A study flowchart can be found in Supporting Information Figure S1.

Measurements

PA and sleep

Activity and sleep were collected using the Fitbit Charge 2, a wrist-worn activity tracker with a triaxial accelerometer, providing us with validated information on PA and sleep [21–23]. In the present study, we used the 14 days of data recorded from day 3 to day 16 of the intervention as the baseline measure. Days 1 and 2 were excluded to ensure all devices had been properly set up. Similarly, we used 14 days of data close to each visit at month 6 and month 12. To reduce biases associated with missing data and maximize data retention, we used a scaling methodology previously developed using NoHoW data and described in detail elsewhere [24]. This means that all participants had exactly 24 hours of data available for each of the included days. In accordance with the 24-hour activity cycle [25], daily averages of hours spent on either SB (not including sleep), sleep, LPA, or MVPA were calculated for eligible participants based on activity categories provided by Fitbit [22]. MVPA was not directly provided by Fitbit but was calculated by summing the two Fitbit categories "fairly active" and "very active."

Body weight, waist circumference, and body fat percentage

At baseline and 6-, 12-, and 18-month visits, body weight was measured to the nearest 0.1 kg, and height was measured at baseline to the nearest 0.1 cm using the Seca 704 s combined stadiometer and electronic scale. Waist circumference was measured using a tape measure to the nearest 0.1 cm, midway between the lowest rib and the iliac crest with the subject standing. Waist circumference was taken twice, and if the two measures differed by more than 1 cm, a third measurement was taken. The median waist circumference was used in the present study. Body composition was estimated from bioelectrical impedance using the ImpediMed SFB7 device (ImpediMed Ltd) (software version 5.4.0), following the manufacturer's instructions [26]. All outcomes were included as continuous variables.

BP and biomarkers

At baseline and 6-, 12-, and 18 month visits, BP was measured in a sitting position using an automatic sphygmomanometer (Microlife BP A2). Blood lipids and HbA1c were measured at baseline and month 12 in a fasted state (a minimum of approximately 10 hours) by a fingerprick test using the point-of-care instrument Alere Afinion AS100 analyzer [20, 27, 28]. These outcomes were included in exploratory analyses as continuous variables.

Covariates

Participants provided verified information on weight loss during the 12 months prior to inclusion at baseline (by a health professional, weight loss counselor/friend, weight-loss program record booklet, diary, smartphone app, or before/after photographs). Weight loss was included in the analyses as a continuous variable (kilograms). Intervention group allocation was included as a categorical variable and was described in detail earlier. Participants were asked to report their smoking status, and this information was used to categorize participants as current, previous, or never smokers. Information on highest level of education was provided and categorized according to the

International Standard Classification of Education (ISCED) [29] as high, medium, low, or other (including educations not classified by the ISCED). Age (years), gender, and information on center/country of residence were also included.

Statistical methods

A detailed statistical analysis plan was circulated with all authors prior to conducting any statistical analyses (online Supporting Information).

Linear regression models were constructed to explore substitution effects on study outcomes. The 24-hour activity cycle distributes activities into four categories (SB, sleep, LPA, or MVPA). To examine substitution of SB for other activities, our substitution models were parameterized by including information on all the other activities in the model (e.g., weight change = sleep + LPA + MVPA + covariates). Assuming some degree of variability between individuals in total time (SB + sleep + LPA + MVPA), it would also be appropriate to include this information in the model. However, because of the previously described scaling methodology, the total time was exactly 24 hours for all included individuals.

The estimated corresponding regression coefficients can be interpreted as the effect of substituting one unit of SB for sleep, LPA, or MVPA, since all activities included in the model can be taken as constant [10]. However, since we were using baseline measures of activity and sleep to predict subsequent changes in the outcomes (body weight, body fat percentage, and cardiometabolic markers), a more precise interpretation of the regression coefficients is that they represent the estimated change in outcome for 1-unit higher sleep, LPA, or MVPA and concomitantly lower SB [30]. To ensure that the presented results reflected a clinically meaningful and achievable substitution [31], all regression coefficients presented were transformed to reflect substitutions in units of 30 minutes.

In the primary set of analyses, we used baseline activity data to examine the associations of substituting SB with an equal amount of time from sleep, LPA, or MVPA and subsequent 6-, 12-, and 18-month change in study outcomes. However, for the primary and secondary outcomes, any statistically significant associations between baseline activity data and subsequent changes in study outcomes during the first 6-month period were also replicated in analyses with information on exposure variables at months 6 or 12 and information on subsequent 6-month changes in outcome measures between months 6 and 12 or between months 12 and 18. This was done to assess a potential influence of activity and sleep patterns over the entire trial period.

Both crude and adjusted analyses are presented. The crude models contain information on the outcome measures of interest (body weight, waist circumference, body fat percentage, or cardiometabolic markers), exposures (sleep, LPA, and MVPA), and baseline measures of outcomes. In the adjusted model, we added information on weight loss during the 12 months prior to inclusion, intervention group, smoking status at baseline, level of education, gender, age, country of residence and number, of valid days with Fitbit data. Moreover, gender and intervention interactions were examined by adding product terms to the adjusted models, and stratified analyses were conducted if statistically significant interactions were identified.

All statistical tests were two-sided, with a significance level of 0.05. Bonferroni adjusted p values were calculated and they are presented for analyses related to exploratory outcomes. It was chosen to adjust these analyses for the number of exposures (sleep, LPA, and MVPA) × number of outcomes (systolic BP, diastolic BP, LDL, HDL, triglycerides, and HbA1c). No correction for multiple testing was done for primary and secondary outcomes, but these results should still be interpreted with caution in the context of multiplicity. All statistical analyses were performed using Stata/SE 16 (StataCorp LLC).

Sensitivity analysis

The algorithms that Fitbit uses to predict activity categories and sleep are not publicly available. We identified some irregularities during inspection of data, suggesting that Fitbit may have introduced some minor changes to the algorithms during an update in September 2017, affecting the sleep estimates. Thus, sensitivity analyses exploring effect modification by enrollment date (before or after September 12, 2017) were also conducted for the primary and secondary outcomes by adding product terms to the models, and stratified analyses were conducted if statistically significant interactions were identified.

RESULTS

A total of 809 women and 343 men, with a mean BMI of 29.5 (SD: 5.2) and an initial weight loss of −11.5 kg (SD: 6.6), were included in the present study. Baseline characteristics of participants across tertiles of SB can be found in Table 1. Information on activity, sleep, and key study outcomes can be found in Table 2. Information on all exploratory outcomes can be found in Supporting Information Table S1.

In the adjusted model, no associations between baseline activity substitutions and subsequent change in body weight or waist circumference were found. However, substitution of baseline SB with MVPA was associated with a decreased body fat percentage during the first 6-month period (−0.33% per 30 minutes higher MVPA [95% CI: −0.60 to −0.07], $p = 0.013$). The same direction of the coefficient was seen at months 12 and 18, although associations were not statistically significant (Table 3). Likewise, when replicating the analyses using activity and sleep data from months 6 or 12 and subsequent 6-month change in body fat percentage between months 6 and 12 or between months 12 and 18, the same direction of the coefficients was found, but again associations were not statistically significant (Figure 1).

In analyses examining baseline substitution of SB with LPA and subsequent changes in body weight and body fat percentage, we found evidence of effect modification by gender, indicating that more

TABLE 1 Baseline characteristics of participants in the NoHoW study across tertiles of sedentary behavior

	All ($N = 1152$)	T1 ($n = 384$)	T2 ($n = 384$)	T3 ($n = 384$)
Gender, % women	70.2	76.0	73.2	61.5
Age (y)	45.4 (11.7)	43.9 (11.6)	44.8 (11.4)	47.6 (11.8)
Height (cm)	168.9 (8.6)	168.7 (8.4)	168.4 (7.8)	169.5 (9.4)
BMI (kg/m^2)	29.5 (5.2)	28.5 (4.3)	29.3 (5.0)	30.8 (6.0)
Initial weight loss (kg)	−11.5 (6.6)	−11.4 (6.1)	−11.3 (6.4)	−11.9 (7.1)
Smoking status, %				
Current	7.4	7.5	7.3	7.3
Previous	39.4	37.0	39.8	41.4
Never	53.2	55.5	52.9	51.3
Educational status, %				
Low	9.2	10.7	9.1	7.8
Medium	19.2	23.7	17.5	16.4
High	67.5	61.2	69.8	71.6
Other	4.1	4.4	3.6	4.2
Intervention group, %				
Control	24.9	28.4	22.4	24.0
Self-regulation and motivation	25.2	24.2	24.2	27.1
Emotion regulation	24.3	21.4	26.6	25.0
Emotion regulation + self- regulation and motivation	25.6	26.0	26.8	23.9
Country, %				
UK	33.9	34.1	33.9	33.9
Denmark	35.6	35.9	35.4	35.4
Portugal	30.5	30.0	30.7	30.7

Note: Results are presented as mean (SD) unless otherwise stated.
T1, first tertile of sedentary behavior (range: 407 to 644 minutes); T2, second tertile of sedentary behavior (range: 644 to 710 minutes); T3, third tertile of sedentary behavior (range: 710 to 1180 minutes).

LPA at the expense of SB was associated with a subsequent 6-month increase in body weight (0.26 kg per 30 minutes higher LPA [95% CI: 0.01 to 0.52], $p = 0.039$) and body fat percentage (0.31% per 30 minutes higher LPA [95% CI: 0.04% to 0.59%], $p = 0.027$) among men only (Supporting Information Figure S2). Moreover, in analyses examining baseline substitution of SB with sleep and subsequent changes in body weight, we found some evidence of effect modification by study arm, indicating that more sleep at the expense of SB was associated with a decrease in subsequent 6-month body weight (−0.54 kg per 30 minutes higher sleep duration [95% CI: −0.87 to −0.22], $p = 0.001$) in the control group only (Supporting Information Figure S3). We found no evidence of effect modification by gender or intervention group in analyses of 12- or 18-month changes in body weight and body fat percentage (all p values for interaction >0.05). Likewise, we found no evidence of gender or intervention group interactions when replicating analyses using activity and sleep data from months 6 or 12 and subsequent 6-month changes in study outcomes between months 6 and 12 or between months 12 and 18 (all p values for interaction >0.05). We also found no evidence for effect modification by enrollment date (before or after September 12, 2017) on the primary or secondary outcomes (all p values for interaction >0.05).

None of the associations related to the exploratory outcomes was statistically significant when Bonferroni corrections was implemented (Supporting Information Tables S2 and S3), but some associations were observed in the analyses without Bonferroni corrections. Specifically, we found that baseline substitution of SB with LPA was associated with a subsequent decrease in systolic BP during the first 6 months of the trial (−0.34 mm Hg per 30 minutes higher LPA [95% CI: −0.67 to −0.01], $p = 0.043$) and during the entire 18-month trial period (−0.44 mm Hg per 30 minutes higher LPA [95% CI: −0.83 to −0.06], $p = 0.024$) (Supporting Information Table S2). Substitution of SB with MVPA was associated with a decrease in subsequent 12-month LDL (−0.04 mmol/L per 30 minutes higher LPA [95% CI: −0.08 to −0.00], $p = 0.029$) but an increase in 12-month HbA1c (0.01% per 30 minutes higher LPA [95% CI: 0.00 to 0.03], $p = 0.039$) (Supporting Information Table S3).

DISCUSSION

Using data from a large weight-loss maintenance trial of European women and men, we found that substitution of baseline SB with MVPA was associated with a decrease in body fat percentage during

TABLE 2 Information on Fitbit data and outcome measures among men and women from the NoHoW study

Parameter	*n*	Mean (SD)
Fitbit data		
Valid days at baseline	1152	12.4 (1.9)
Valid days at month 6	798	11.6 (2.4)
Valid days at month 12	667	11.7 (2.5)
SB (min/d) at baseline	1152	678 (86)
SB (min/d) at month 6	798	695 (86)
SB (min/d) at month 12	667	699 (85)
Sleep (min/d) at baseline	1152	428 (57)
Sleep (min/d) at month 6	798	417 (52)
Sleep (min/d) at month 12	667	414 (51)
LPA (min/d) at baseline	1152	276 (64)
LPA (min/d) at month 6	798	266 (61)
LPA (min/d) at month 12	667	265 (63)
MVPA (min/d) at baseline	1152	57 (36)
MVPA (min/d) at month 6	798	63 (44)
MVPA (min/d) at month 12	667	62 (42)
Primary outcome		
Body weight at baseline (kg)	1152	84.4 (16.9)
Change in body weight at month 6 (kg)	1131	−0.3 (4.6)
Change in body weight at month 12 (kg)	1037	0.2 (6.0)
Change in body weight at month 18 (kg)	967	1.3 (6.6)
Secondary outcomes		
Body fat percentage at baseline	1136	37.7 (9.1)
Change in body fat percentage at month 6	1104	−0.6 (5.5)
Change in body fat percentage at month 12	1004	−0.5 (5.4)
Change in body fat percentage at month 18	936	0.2 (5.6)
Waist circumference at baseline (cm)	1149	94.0 (14.0)
Change in waist circumference at month 6 (cm)	1126	−0.3 (5.4)
Change in waist circumference at month 12 (cm)	1029	−0.1 (6.6)
Change in waist circumference at month 18 (cm)	956	0.4 (6.7)

Abbreviations: LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior.

the first 6 months of the trial but was not associated with 6-, 12-, or 18-month change in body weight. We found some evidence of effect modification by both gender and intervention group. Subgroup analyses suggested that more baseline LPA at the expense of SB was associated with a subsequent 6-month increase in body weight and body fat percentage among men only, whereas more baseline sleep at the expense of SB was associated with reduced subsequent 6-month body weight in the control group only. Lastly, our results suggest that substituting SB with LPA or MVPA may improve the overall cardiometabolic risk profile during weight-loss maintenance.

Previous studies have already explored the importance of early prognostic markers related to weight-loss maintenance or weight regain [5], including different activity and sleep correlates of weight-loss maintenance [32, 33]. Other studies have suggested that reduced SB plays a beneficial role in weight loss among individuals with obesity [34], and that PA has beneficial effects on regulation of energy balance, even with some degree of dietary compensation for the higher energy expenditure [35]. However, there is a lack of studies examining the role of activity substitutions for weight-loss maintenance. The current evidence is based on one study by Mekary and colleagues examining associations between different activity substitutions and 6-year weight-loss maintenance among 4558 healthy, premenopausal women who had lost more than 5% of their weight before baseline examinations [10]. Their results suggested that substituting TV watching with slow walking, brisk walking, and especially jogging or running resulted in less weight gain. While we were unable to directly replicate this finding, we found that substituting baseline SB with MVPA was associated with reduced body fat percentage during the first 6 months of the trial. While not statistically significant, similar directions of the coefficients were observed in analyses with body weight as outcome. It is worth noting that the study by Mekary and colleagues was based on self-reported data of PA and it did not account for sleep duration, which is a general major limitation in previous studies on activity substitutions and health outcomes [9]. Though not specifically focused on weight-loss maintenance, Pelclová and colleagues also found that an increase in SB at the expense of LPA and MVPA (assessed by accelerometers) during a 7-year period was associated with an increase in BMI and body fat percentages during the same period among 176 elderly women from three Central European countries [11], which to some extent also supports our finding. We also found some evidence for effect modification by gender, indicating that more baseline LPA at the expense of SB was associated with a subsequent 6-month increase in body weight and body fat percentages among men only. Although we found no previous studies supporting or affirming this finding, some previous studies have shown gender differences in the health benefits of different PA intensities. For example, LPA has been found to provide protection from cardiovascular disease to a greater extent among women than men [36], perhaps indicating that men and women are predisposed to engage in different intensities and types of PA. Likewise, in subgroup analyses we found that more baseline sleep at the expense of SB was associated with reduced subsequent 6-month body weight in the control group only. While we see no obvious reason that this should apply only for participants in the control group, several studies have suggested potential mechanisms by which insufficient sleep can hinder successful weight-loss maintenance, including metabolic changes affecting glucose metabolism, appetite and reward, caloric intake, and energy expenditure [37].

In analyses without correction for multiple testing, our data also showed associations related to the exploratory outcomes. We found that baseline substitution of SB with LPA was associated with a subsequent reduction in systolic BP during the first 6 months of the trial

TABLE 3 Baseline substitution of 30-minute SB with sleep, LPA, or MVPA and subsequent change in body weight, body fat percentage, and waist circumference

	Change at 6 months				Change at 12 months				Change at 18 months			
	n	β[a]	(95% CI)	*p*	*n*	β[a]	(95% CI)	*p*	*n*	β[a]	(95% CI)	*p*
Change in body weight (kg)												
Substituting SB with sleep												
Crude[b]	1131	−0.15	(−0.29 to −0.00)	**0.047***	1037	−0.06	(−0.26 to 0.14)	0.544	967	0.00	(−0.23 to 0.23)	0.977
Adjusted[c]	1131	−0.15	(−0.30 to 0.01)	0.063	1037	−0.12	(−0.34 to 0.09)	0.250	967	−0.09	(−0.33 to 0.15)	0.473
Substituting SB with LPA												
Crude	1131	0.02	(−0.11 to 0.15)	0.724	1037	0.02	(−0.15 to 0.20)	0.815	967	0.16	(−0.05 to 0.36)	0.127
Adjusted	1131	0.02	(−0.12 to 0.15)	0.797	1037	0.04	(−0.15 to 0.22)	0.702	967	0.19	(−0.02 to 0.39)	0.078
Substituting SB with MVPA												
Crude	1131	−0.12	(−0.36 to 0.11)	0.304	1037	−0.06	(−0.38 to 0.25)	0.690	967	0.08	(−0.28 to 0.44)	0.673
Adjusted	1131	−0.18	(−0.42 to 0.06)	0.134	1037	−0.12	(−0.45 to 0.20)	0.452	967	0.03	(−0.34 to 0.39)	0.895
Change in body fat percentage												
Substituting SB with sleep												
Crude	1104	−0.09	(−0.26 to 0.08)	0.279	1004	0.09	(−0.09 to 0.27)	0.331	936	0.05	(−0.15 to 0.24)	0.628
Adjusted	1104	−0.14	(−0.31 to 0.03)	0.097	1004	−0.06	(−0.23 to 0.12)	0.530	936	−0.03	(−0.23 to 0.16)	0.742
Substituting SB with LPA												
Crude	1104	0.09	(−0.06 to 0.24)	0.233	1004	0.04	(−0.12 to 0.20)	0.616	936	0.19	(0.02 to 0.36)	**0.026***
Adjusted	1104	−0.03	(−0.18 to 0.12)	0.681	1004	−0.01	(−0.17 to 0.14)	0.872	936	0.12	(−0.05 to 0.29)	0.166
Substituting SB with MVPA												
Crude	1104	−0.30	(−0.57 to −0.03)	**0.030***	1004	−0.08	(−0.36 to 0.21)	0.588	936	−0.05	(−0.35 to 0.26)	0.762
Adjusted	1104	−0.33	(−0.60 to −0.07)	**0.013***	1004	−0.18	(−0.45 to 0.09)	0.195	936	−0.15	(−0.45 to 0.14)	0.309
Change in waist circumference (cm)												
Substituting SB with sleep												
Crude	1126	−0.17	(−0.34 to −0.00)	**0.049***	1029	−0.09	(−0.31 to 0.13)	0.414	956	−0.11	(−0.34 to 0.12)	0.359
Adjusted	1126	−0.11	(−0.28 to 0.07)	0.237	1029	−0.11	(−0.34 to 0.12)	0.343	956	−0.08	(−0.32 to 0.17)	0.528
Substituting SB with LPA												
Crude	1126	−0.04	(−0.19 to 0.11)	0.575	1029	0.02	(−0.17 to 0.21)	0.860	956	0.13	(−0.07 to 0.34)	0.199
Adjusted	1126	−0.06	(−0.21 to 0.09)	0.457	1029	0.04	(−0.16 to 0.23)	0.713	956	0.18	(−0.03 to 0.39)	0.089
Substituting SB with MVPA												
Crude	1126	−0.18	(−0.44 to 0.09)	0.197	1029	−0.13	(−0.47 to 0.22)	0.473	956	0.08	(−0.28 to 0.45)	0.649
Adjusted	1126	−0.25	(−0.53 to 0.02)	0.067	1029	−0.23	(−0.58 to 0.12)	0.201	956	−0.05	(−0.42 to 0.32)	0.797

Abbreviations: LPA, light physical activity; MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior.

[a]Results presented as changes in outcomes (95% CI) for each 30-minute substitution of sleep, LPA, or MVPA with SB.

[b]Model with information on outcome, all activities except SB, baseline measure of outcome, and height.

[c]Additionally adjusted for weight loss during the 12 months prior to inclusion, intervention group, smoking status, level of education, gender, age, country of residence, and number of valid days with Fitbit data.

*Bold values are statistically significant at $p < 0.05$.

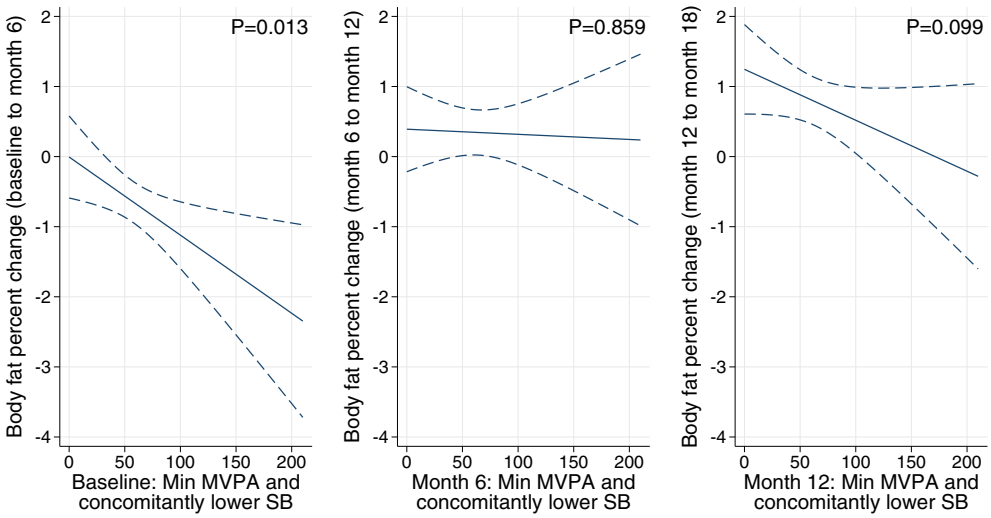

FIGURE 1 Substitution of SB with MVPA at baseline, month 6, or month 12 and subsequent 6-month changes in body fat percentage. Models with information on outcome, all activities except SB, baseline measure of outcome, height, weight loss during the 12 months prior to inclusion, intervention group, smoking status, level of education, gender, age, country of residence, and number of valid days with Fitbit data. MVPA, moderate-to-vigorous physical activity; SB, sedentary behavior [Color figure can be viewed at wileyonlinelibrary.com]

and during the entire 18-month trial period, which is in line with cross-sectional results based on the Tobago health study [38]. Similarly, substituting SB with MVPA was associated with subsequent reduction in 12-month LDL, corresponding to previous cross-sectional results from the Whitehall II epidemiological cohort [19]. We also found an association between substitution of baseline SB with MVPA and a subsequent 12-month increase in HbA1c. This result is inconsistent with results from the Whitehall II epidemiological cohort [19], in which replacing sedentary time with an equal amount of MVPA was associated with lower HbA1c at a cross-sectional level. Moreover, as some studies have suggested that increases in PA are associated with significant reductions in both fasting glucose and HbA1c [39, 40], our finding may represent a false-positive result and it will need to be replicated using data from other cohorts. On the other hand, studies have also found that athletes generally show a consistent trend toward higher HbA1c values [41], indicating that the relationship between PA and HbA1c is not straightforward and is likely dependent on the context.

Our study has several strengths, including the prospective design, which reduces the risk of reverse causation. Activity and sleep were measured using the Fitbit Charge 2 during 14-day periods around each follow-up visit, thus providing us with objectively measured information on the 24-hour activity cycle throughout the trial [21, 22]. Body weight, waist circumference, body fat percentages, and all the cardiometabolic markers were objectively measured using validated instruments [20, 27, 28, 42], and we had information on lifestyle and sociodemographic factors, allowing us to adjust for potential confounding factors.

The study also has some limitations. Although we adjusted our analyses for several potential confounders, as in most observational studies, it is still likely that some unmeasured or residual confounding remained. In this regard, improved diet quality has been found associated with less weight gain, especially in individuals with overweight [43], and our analyses were not adjusted for any measure of diet quality.

The Fitbit app allowed participants to monitor themselves, and this could potentially also have affected both activity and sleep habits. Moreover, as Fitbit estimates activity using accelerometer and heart rate data, we cannot rule out that there is some degree of misclassification between the different activity categories. In addition, we did not have a valid measure of resistance training, which may be a limitation because there is some evidence to suggest that resistance training can attenuate regain of body fat percentages during weight-loss maintenance [44].

When applying Bonferroni correction, we found no statistically significant associations for the exploratory outcomes. Similarly, we cannot rule out that the association between substitution of SB with MVPA and reduced body fat percentages during the first 6 months of the trial is a false positive result. However, although our study results are potentially exposed to type I errors due to multiple testing, most of our findings demonstrated a coherent trend aligning with results from previous studies, thus reducing the likelihood that our findings are false positive.

Finally, we conducted our analyses in a population of individuals with overweight or obesity, who had achieved a clinically significant weight loss prior to enrollment. Additionality, 75% of the participants received a digital intervention based on self-regulation, motivation, and/or emotion regulation tools designed to improve weight-loss maintenance. Thus, generalization of our results should be considered with caution.

In conclusion, our results suggest that SB has little or no influence on subsequent long-term weight-loss maintenance, but during the early stages of a weight-loss maintenance effort, substituting SB with MVPA may improve body composition. Moreover, substituting SB

with LPA or MVPA may improve the overall cardiometabolic risk profile during weight-loss maintenance, but because of multiple testing, these results should be interpreted very cautiously, and replications are needed to form robust conclusions on these outcomes.O

AUTHOR CONTRIBUTIONS

Study conceptualization: Sofus C. Larsen, Berit L. Heitmann; data curation: Sofus C. Larsen, Graham Horgan, Ruairi O'Driscoll, Leigh C. Ward; formal analysis: Sofus C. Larsen; funding acquisition: Berit L. Heitmann, R. James Stubbs, Sofus C. Larsen; investigation: Sofus C. Larsen, Ruairi O'Driscoll, Marie-Louise K. Mikkelsen, Antonio L. Palmeira, Cristiana Duarte, Inês Santos, Jorge Encantado, Jake Turicchi; supervision: Graham Horgan, Berit L. Heitmann; writing–original draft: Sofus C. Larsen; writing–review & editing: Ruairi O'Driscoll, Graham Horgan, Marie-Louise K. Mikkelsen, Ina O. Specht, Jeanett F. Rohde, Jake Turicchi, Inês Santos, Jorge Encantado, Cristiana Duarte, Leigh C. Ward, Antonio L. Palmeira, R. James Stubbs, Berit L. Heitmann.

CONFLICT OF INTEREST

R. James Stubbs consults for Slimming World UK via Consulting Leeds, a wholly owned subsidiary of the University of Leeds. All other authors declared no conflict of interest.

DATA AVAILABILITY STATEMENT

The data presented in this study are available from https://easo.org/the-nohow-dataset/ on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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