

# Changes in physical activity, sedentary behaviour and body composition: longitudinal analysis in the PREDIMED-Plus trial

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## Research

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# Abstract

## Background:

The optimal distribution between physical activity (PA) levels and sedentary behaviour (SB) for the greatest benefits for body composition among older adults with overweight/obesity and chronic health conditions remains unclear. We aimed to determine the prospective association between changes in PA and in SB with concurrent changes in body composition. To examine whether reallocating inactive time into different physical activity levels was associated with 12-month change to body composition in older adults.

## Methods:

A subsample (n=1564) of men and women (age: 55-75 years) with overweight/obesity and metabolic syndrome from the PREDIMED-Plus trial was included in the present analysis. Participants were followed-up at 6- and 12-months. Physical Activity and SB were assessed using validated questionnaires. Out of 1564 participants, 388 wore an accelerometer to objectively measure inactive time and PA over a 7-day period. At each time point, participants' body composition was measured using dual-energy X-ray absorptiometry (DXA). Standard covariate-adjusted and isothermal substitution modelling were applied to linear mixed-effects models.

## Results:

Increasing 30 minutes of total PA and MVPA were associated with significant reductions in body fat ( $\beta$  -0.07% and -0.08%) and VAT (-13.9g, and -15.6g) at 12-months (all  $p$ -values <0.001). Reallocating 30 minutes of inactive time to MVPA was associated with reductions in body fat and VAT, and with an increase in muscle mass and muscle-to-fat mass ratio (all  $p$ -values <0.001).

## Conclusions:

At 12 months, increasing total PA and MVPA and reducing total and TV-viewing SB were associated with improved body composition in participants with overweight or obesity, and metabolic syndrome. This was also observed when reallocating 30 minutes of inactive time by total PA, LPA and MVPA, with the greatest benefits observed for MVPA.

## Trial registration:

The trial was registered at the International Standard Randomized Controlled Trial (ISRCTN: <http://www.isrctn.com/ISRCTN89898870>) with number 89898870 and registration date of 24 July 2014, retrospectively registered.

## Background

The relationship between physical activity (PA), sedentary behaviour (SB) and markers of obesity and body composition has been researched extensively in the literature [1–5]. However, the optimal distribution between SB and PA levels for the greatest benefits for body composition among older adults with overweight

and obesity remains unclear [1, 6–10]. Up-to-date, only a few studies have been conducted in older adults with chronic conditions [4, 11] and scarce research has used longitudinal or objectively measured data [8, 12–15].

Age-related changes in body composition include decline in muscle mass and accumulation of fat in central body regions[16], leading to physical impairment and morbidity. Greater visceral adipose tissue (VAT) seems to play particular role in the development of chronic diseases, such as insulin resistance, type 2 diabetes (T2D) and cardiovascular disease (CVD) [12, 17, 18]. Understanding how increments in PA and reductions in SB may minimize the adverse effects of aging in body composition, would shed light as to what are the best strategies to help improve health and quality of life in older people.

Different PA choices (time and intensity) may affect body composition differently, depending partly on SB displacement. Isotemporal substitution models (ISM) have been recommended as one of the most appropriate statistical analysis to explore the associations between reallocating activity patterns (time spent in PA and SB) and health outcomes, attending the time boundaries of a day [19, 20]. Scarce research using ISM to explore the associations between activity patterns and body composition has been conducted in elderly cohorts; and most research had been conducted using a cross-sectional design[21, 22] or used anthropometry to assess body composition[15]. Therefore, studies using device-based longitudinal measures for activity patterns and regional body composition are warranted.

This novel study aimed to provide new evidence about the associations between SB and PA with directly quantified body composition in an aging population with the metabolic syndrome, using a longitudinal study design. The specific objectives of the present study were a) to determine the association of concurrent changes in self-reported PA levels and SB with body composition changes measured with dual-energy X-ray absorptiometry (DXA) at 12-months follow-up; b) to assess the impact of replacing accelerometer-derived inactive time data (IT), as a proxy measure of SB, by PA and time in bed, on body composition changes.

## Methods

### Study overview and sample

The present study reports longitudinal data from a subsample (n = 1564) of participants from the PREDIMED-Plus study (Spain; <http://www.predimedplus.com/>) This clinical trial aims to prevent CVD in older adults and has been described elsewhere [23, 24]. In brief, men (55–75 years) and women (60–75 years), with a body mass index (BMI)  $\geq 27$  and  $< 40$  kg/m<sup>2</sup> and  $\geq 3$  components of the metabolic syndrome (MetS) were eligible [25]. Participants were recruited into the study between 2013 and 2016 and were randomised into control or intervention arm. Members of the same households were randomized by clusters, with the couple as the unit of randomization. Participants in the intervention arm received a multicomponent weight loss intervention. Those in the control group received recommendations about an unrestricted caloric MedDiet and usual care (the trial is still ongoing).

Longitudinal data collected at baseline, 6 and 12 months from 1564 participants recruited across 7 centres were included in this analysis. Figure 1 in supplementary material shows the number of participants at each

time point (**S1 Fig**). All participants provided written informed consent. The study's protocol was approved by the Research Ethic Committees from all recruiting centres according to the ethical standards of the Declaration of Helsinki. The trial was registered at the International Standard Randomized Controlled Trial (ISRCTN: <http://www.isrctn.com/ISRCTN89898870>). The study's longitudinal database generated in March-25th 2019 was used for this analysis.

## **Exposure assessment**

### **Self-reported physical activity and sedentary behaviours**

Leisure time PA performed during a conventional month was assessed using the validated self-reported REGICOR questionnaire [26]. Time spent on SB over the last year was measured using the validated self-reported Nurses' Health Study questionnaire [27]. Time spent in PA was calculated as a product of the frequency and duration of 6 types of activities categorized into three intensities: light PA (LPA) (< 4 Metabolic Equivalent Tasks, METs) – walking at a slow/normal pace; moderate (4–5.5 METs) – brisk walking, gardening; and vigorous ( $\geq 6.0$  METs) – walking in the countryside, climbing stairs, exercise or playing sports [28]. Moderate-to-vigorous PA (MVPA) was calculated as the sum of moderate and vigorous PA, total PA was determined by adding up all the activities. Time spent in total SB (counting number of hours per day spent seated position) and in TV-viewing was calculated as the sum of time spent in each activity during weekdays\*5 and weekend-days\*2. Data for these questionnaires were collected by trained interviewers in all-time points. Questionnaire results are analysed in bouts of 30 min/day.

### **Accelerometer measured physical activity and inactive time**

Inactive time, used as a proxy measure for sedentary time, is defined as any activity that requires less than 1.5 METs during waking hours. Participants were asked to wear an accelerometer (GENEActiv, ActivInsights Ltd, Kimbolton, United Kingdom) on their non-dominant wrist continuously for 7 days. Data extracted from the GENEActiv was clustered as IT in bouts of 1 minute (< 1.5 METs), LPA (1.5-3 METs), MVPA (> 3 METs) and time in bed (time difference between going to bed and leaving) [29–31]. Details of how the PA and IT were processed have been described [32] previously. Accelerometer measures were taken at baseline, 6- and 12-months follow-up. Accelerometer results are presented in bouts of 30 min/day.

### **Body composition assessment**

Baseline, 6- and 12-months follow-up data of total and regional body composition were taken using third-generation DXA scanners from GE Healthcare (Madison, WI, USA), using the EnCore™ software. Total body fat mass and total body muscle mass were expressed as percentage of DXA-derived total body mass (sum of total bone, fat and muscle mass (g)). VAT was determined using the validated CoreScan software application [33]. The muscle-to-fat mass ratio was calculated dividing total muscle mass (g) by total fat mass (g), and multiplied by 100. DXA scans were performed by trained operators following a standard protocol and subject positioning provided by the manufacturer. DXA scanners were phantom calibrated daily according to the manufacturer guidelines.

### **Other covariates**

Baseline data for sex, age, smoking habits (categorized as never, current or former), educational level (categorized as higher education/technician, secondary education or not-completed primary education/primary education), medical conditions (T2D) and medication use (antidiabetic treatment) were self-reported. Body weight (kg) and height (m) were measured in light clothing and without shoes using a calibrated scale and a wall-mounted stadiometer. Weight and height were measured twice the mean value was used in the analysis. Glycated hemoglobin (HbA1c, %) was determined using standard biochemical analyses with blood samples collected after an overnight fast. Type 2 diabetes was defined as meeting any of the following criteria: self-reported diabetes at inclusion or baseline, HbA1c  $\geq$  6.5% or use of antidiabetic medication at baseline, such as insulin, metformin (in case of diagnosed diabetes or HbA1c  $\geq$  6.5%), and other medication for diabetes. A validated food frequency questionnaire [34] and the Spanish food composition tables [35] were used to estimate total energy intake (kcal/day).

## Statistical analyses

Characteristics of the study participants at baseline and at follow-up are presented as mean and standard deviations (SD) for continuous variables, and absolute numbers (percentages) for categorical variables.

Main analyses were run in completers-only. Linear mixed-effect models with random intercepts at recruiting centre, family and patient level were used to explore the associations between concurrent changes in self-reported PA (total, light and moderate-to vigorous, in bouts of 30 min/day) and SB (total and TV-viewing, in bouts of 30 min/day) with body composition changes (percentage of body fat, percentage of muscle mass, g of VAT) at 12-months follow-up. Changes in repeatedly measured variables were calculated as the difference between results from each follow-up assessment (changes from 0 to 6 months follow-up and from 6 months to 12 months follow-up). Firstly, minimally adjusted models were run controlling for age (years), sex, intervention arm (intervention or control group) and follow-up point (months). Multivariable-adjusted models were further adjusted for baseline variables, such as educational level, smoking status, T2D (all categorical) and height (m), as well as changes in repeatedly measured total energy intake (kcal/day), total PA (30 min/day bouts) for SB exposures, and total SB (30 min/day bouts) for PA exposures.

Analyses using objectively measured PA and IT in the subsample of participants providing DXA scans and accelerometry data (n = 388) were also performed. Linear mixed-effect models using the ISM were used to explore the impact of replacing 30 minute of IT by 30 minute of time in bed, LPA or MVPA on body composition changes at 12-months follow-up. These models were performed with random intercepts at recruiting centre, family and patient level. Prior to running the minimally- and multivariable-adjusted models (the same covariates as described above), all activity patterns at baseline, 6 and 12 months follow-up (time in bed, IT, LPA and MVPA) were divided by 30, which was considered as the unit of time equivalent to 30 min/day (according to the PA guidelines [36–38]). To account for the 24-hour day finite time[20], a variable representing the total accelerometer wear time was constructed by adding up time in bed, IT, LPA and MVPA. This was entered simultaneously in all ISMs. Analyses followed the published guidelines for ISM [39].

Sensitivity analyses using the last observation carried forward (LOCF) method were used to estimate missing data at follow-up on both exposure and outcome variables. Models were repeated after excluding

data measured at 6 months (due to high number of missing data). These analyses were also performed in the subsample of participants (n = 388) providing accelerometer data

Lastly, potential effect modifications by sex (men or women), were checked by adding an interaction term between sex and all exposures. Stratified analyses were conducted when a significant interaction was detected ( $p < 0.05$ ). All analyses were conducted with Stata v15.0. program. All p-values  $< 0.05$  were deemed as statistically significant.

## Results

Table 1 shows participants' characteristics at baseline, 6 and 12 months. On average, participants at baseline were 65 years old, with a BMI of 32.5 kg/m<sup>2</sup> and 48% were women. At 12 months, participants (intervention and control groups) reduced their waist circumference, BMI, and total energy intake compared to baseline. At 6 and 12 months, participants accrued more total PA, LPA and MVPA and less total and TV-viewing SB compared to baseline. Reductions of percentage body fat and VAT and increased percentage of muscle mass and muscle-to-fat mass ratio were also observed at 12-months. Similar results were observed in those providing accelerometry data (See Additional file 1: Table S1).

Table 2 shows the  $\beta$ -coefficients (95% CIs) for the associations between concurrent changes in self-reported leisure time PA, self-reported SB, (both per 30-minute bouts) and body composition. After adjustment for potential confounders, increasing 30 minute of total PA was significantly associated with a decrease in body fat ( $\beta$  -0.07%, 95% CIs -0.10;-0.04%) and VAT (-13.9g; -21.5;-6.23) and increased muscle mass (0.07%; 0.04;0.10) and muscle-to-fat mass ratio (0.41; 0.15;0.67). Increments of 30 minute of MVPA was linked to significantly reduced body fat (-0.08%, -0.11;-0.04%) and VAT (-15.6g; -24.1;-7.25); and with increased muscle mass (0.07%; 0.04;0.10) and muscle-to-fat mass ratio (0.44; 0.15;0.72). Overall, 30 more minute of total and TV-viewing SB were associated with significantly greater body fat and lower muscle mass. No significant associations were observed for LPA.

Table 3 shows the  $\beta$ -coefficients (95% CIs) for the ISM, Figure 2 shows the ISM with the changes in body composition standardized as z-scores to aid comparability. After adjusting for potential confounders, reallocating 30 min/day of IT with time in bed, LPA and MVPA was associated with lower VAT ( $\beta$  -23.8g, -11.2g and -92.4g) and body fat ( $\beta$  -0.09%, -0.13% and -0.54%,) and with an increased muscle mass ( $\beta$  0.08%, 0.12% and 0.51%) and muscle-to-fat mass ratio ( $\beta$  0.89, 0.90 and 3.74), with the strongest associations seen in MVPA.

No major differences were observed when repeating the models in the whole sample after replacing missing data using the LOCF method. (See Additional file 1: Table S2). No significant differences were found when repeating ISM in the subsample after replacing missing data using the LOCF method. (See Additional file 1: Table S3). No major differences were found when linear mixed-effect models were performed in the subsample providing accelerometer data (n=388). (See Additional file 1: Table S4). No modification effect by sex was observed. Results were consistent after repeating the models with completers only, excluding the 6 months' data.

## Discussion

Results from this longitudinal study suggest that increasing total PA and MVPA were associated with an improved body composition phenotype in a sample of older adults with overweight or obesity and the MetS. Greater total SB, and to a lesser extent TV-viewing sedentary time were associated with a worsen body composition. Overall, this study highlights that replacing 30 minute a day of IT with an equal amount of MVPA, LPA and time in bed resulted in significantly improved markers of body composition.

These findings are consistent with previous cross-sectional research in adult populations [3, 32, 40], which have found a hazardous relationship between SB and markers of body composition, including body fat, VAT and muscle mass [3, 9, 32, 40, 41]. The present results showed that greater SB is associated with greater body fat and lower muscle mass in an aging population, resulting in greater cardiometabolic risk and disability. In line with our findings, other authors found that increasing total PA and MVPA improves body composition [3, 8, 40] and reduce the accumulation of VAT [8, 10, 42, 43], yet no effects associated to LPA and body composition have been reported with the present results based on self-reported data.

Limited research using the ISM in older adults is available and only, isolated reports in general adult populations with chronic conditions, such as the MetS [44, 45], or using data from DXA scans are available[32]. However, no research using the same methods as this study in older adults has been found, limiting the opportunities for comparison. Cross-sectional research conducted in adults ( $\geq 18$  years)[46, 47] showed similar beneficial effects of replacing a unit of time spent inactive with equal amounts of LPA, MVPA or sleep in body composition markers using anthropometric measures. However, if this relationship persists over time remains unclear.

Our results showed that replacing IT for LPA is associated with improved body composition changes (body fat and muscle mass), although the greatest benefit has been observed with MVPA. Similar results have been observed in previous cross-sectional research in adults[32] and in longitudinal studies performed with children [48, 49]. Therefore, the present results build on previous knowledge in other populations and indicate that replacing IT with any other activity behaviour has a beneficial impact on body composition in older adults with an incremental effect according to the intensity level. Indeed, replacing 30 min/day of IT with equal amounts of time in bed, LPA and MVPA was associated with a decrease in body fat of -0.09%, 0.13%, and - 0.54%, respectively. Therefore, these results showed the close interactions between IT, PA and health, and highlight the need for them to be treated jointly. These research also highlights that to promote the greater body composition changes MVPA is the most effective form of PA [8, 17, 32, 40, 43, 50], yet, increasing LPA in older adults with chronic conditions would also be of benefit for an improved health profile [13, 40, 47, 51–54]. Overall, small beneficial changes in body composition were observed when replacing IT by time in bed, which is similar to previous research [32, 52] which could be due to measurement errors, thus further research using gold standard measures to assess sleep in older adults are recommended.

Marked strengths of this study were the use of a longitudinal design in a large cohort of older men and women, with overweight/obesity and MetS across different communities in Spain using objective measurements. However, this study involved a homogeneous sample of Caucasian men and women within narrow ranges of BMI, age and with worsen metabolic health profile, limiting the opportunities for

extrapolation into other ethnicities and with healthier individuals. Therefore, it is recommended for future research to be replicated in different ethnic groups with different lifestyles and fat distribution. It is important to highlight the novelty of the present study, with repeated measures of body composition using gold standard methods, such as DXA [55, 56], and the measurement of exposure variables with validated questionnaires and with accelerometer data in a subsample. Several complex and sophisticated statistical analyses were performed to assess our results. Some limitations to highlight are the use of questionnaires to obtain data on PA and SB within the larger sample, although these were validated methods and have facilitated the access to a larger sample size. It is important to mention that the GENEactiv is not able to differentiate between sitting and standing position or to differentiate time in bed from sleeping [29–31], thus further similar research using other monitors capable to differentiate between these behaviours is recommended. Finally, there was a considerable loss of data from the DXA scan at 6 and 12 months' visits. Nevertheless, results were mostly consistent when imputing missing data in those subjects using the LOCF method.

## Conclusions

Results from this longitudinal study indicate that increments in PA and reductions of SB over 12 months follow-up were associated with an improved body composition profile in older adults with overweight or obesity and MetS. Replacing IT with any PA and time in bed were associated with improvements on body composition. Based on the present results the promotion of MVPA would provide the greatest health benefits in older adults, followed by LPA. Taking this into account, interventions promoting LPA might be more appealing in terms of feasibility and sustainability, as it will help increase attrition rates, reduce participant and delivery burden as they will not need continuous supervision, making them a low-cost and easy option to be implemented at home or care homes. Future intervention trials are needed to confirm causality of the effect of PA and SB on body composition changes in older adults with chronic conditions.

## List Of Abbreviations

PA; Physical activity

SB; Sedentary behaviour

VAT; Visceral adipose tissue

T2D; Type 2 diabetes

CVD; Cardiovascular disease

ISM; Isotemporal substitution model

DXA; Dual-energy X-ray absorptiometry

IT; Inactive Time

BMI; Body mass index

MetS; Metabolic syndrome

MedDiet; Mediterranean Diet

LPA; Light physical activity

MVPA; Moderate-to-vigorous physical activity

MET; Metabolic equivalent task

HbA1c, %; Glycated hemoglobin

SD; standard deviation

LOCF; Last observation carried forward

## **Declarations**

### **Ethics approval and consent to participate**

Research Ethics Committees from all recruitment centers approved the study protocol, according to the ethical standards of the Declaration of Helsinki. All participants provided written informed consent. All centers have the ethics approval and consent from all the ethic committees. The trial was registered at the International Standard Randomized Controlled Trial (ISRCTN: <http://www.isrctn.com/ISRCTN89898870>) with number 89898870 and registration date of 24 July 2014, retrospectively registered.

### **Consent for publication**

Not applicable.

### **Availability of data and material**

There are restrictions on the availability of data for the PREDIMED-Plus trial, due to the signed consent agreements around data sharing, which only allow access to external researchers for studies following the project purposes. Requestors wishing to access the PREDIMED-Plus trial data used in this study can make a request to the PREDIMED-Plus trial Steering Committee chair: [jordi.salas@urv.cat](mailto:jordi.salas@urv.cat). The request will then be passed to members of the PREDIMED-Plus Steering Committee for deliberation.

### **Competing interests**

The authors declare that they have no competing interests.

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### **Authors' contributions**

AMGP, JK and DR conceived of the study. AMGP, JK and DR completed the statistical analysis. AMGP, JK, VVM and DR drafted the manuscript. DR supervised the study. All authors were involved in oversight of recruitment, data collection, revision of the manuscript and read and approved the final manuscript.

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## Tables

**Table 1.** Socio-demographic , lifestyle and body composition characteristics of participants at baseline, 6 and 12 months follow-up

Parameters	n	Baseline	n	6 months	n	12 months
		Mean (SD)		Mean (SD)		Mean (SD)
Socio-demographic characteristics						
Age (years)	1564	65.3 (5.0)				
Sex, Women, n (%)	1564	751 (48)				
Type 2 Diabetes, n (%)	1564	469 (30)				
Height (m)	1564	1.63 (0.10)				
Waist circumference (cm)	1564	107 (9.31)	1444	105 (9.52)	1404	105 (9.72)
Body mass index (kg/m <sup>2</sup> )	1564	32.5 (3.34)	1502	32.0 (3.49)	1496	31.8 (3.50)
Current smokers, n (%)	1564	197 (12.6)				
Higher education, n (%)	1564	333 (21.3)				
Total energy intake (kcal/day)	1564	2426 (581)	1428	2294 (467)	1400	2268 (454)
Lifestyle: physical activity and sedentary behaviour (self-reported)						
Total PA (h/day)	1564	1.22 (1.01)	1447	1.40 (1.06)	1406	1.41 (1.06)
LPA (h/day)	1564	0.47 (0.56)	1447	0.48 (0.59)	1406	0.49 (0.59)
MVPA (h/day)	1564	0.76 (0.90)	1447	0.92 (0.96)	1406	0.92 (0.97)
Total SB (h/day)	1564	5.86 (1.86)	1446	5.63 (1.77)	1406	5.51 (1.75)
TV-viewing SB (h/day)	1564	3.12 (1.64)	1446	2.91 (1.52)	1406	2.87 (1.44)
Body composition determined by DXA						
Percentage of body fat*	1564	40.5 (6.90)	1048	39.7 (7.06)	1234	39.6 (7.04)
VAT (kg)	1529	2.30 (0.89)	1035	2.17 (0.86)	1223	2.21 (0.88)
Percentage of muscle mass*	1564	56.5 (6.56)	1048	57.2 (6.70)	1234	57.2 (6.68)
Muscle-to-fat mass ratio**	1564	147 (44.1)	1048	152 (48.3)	1234	153 (48.1)

Values are mean (SD) for continuous variables, and n (percentage) for categorical variables. Abbreviation: DXA; dual-energy X-ray absorptiometry, VAT; visceral adipose tissue, PA; physical activity, LPA; light physical activity, MVPA; moderate-to-vigorous physical activity, SB; sedentary behaviour.\*Percentage of body fat and percentage of muscle mass were calculated taking into account muscle mass, fat mass and bone mass measured with a whole body DXA scan. \*\*muscle-to-fat mass ratio was calculated (total muscle mass in g / total fat mass in g)\*100.

**Table 2.** Association of concurrent changes in self-reported leisure time physical activity and sedentary behaviour in bouts of 30 min with body composition: analyses in completers-only.

	Percentage of body fat		VAT (g)		Percentage of muscle mass		Muscle-to-fat mass ratio	
	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value
<b>Physical activity</b>								
<b>Total PA</b>								
Minimally-adjusted	-0.08 (-0.11;-0.05)	<0.001	-15.1 (-22.7;-7.49)	<0.001	0.08 (0.05;0.11)	<0.001	0.46 (0.20;0.71)	0.001
Multivariable-adjusted	-0.07 (-0.10;-0.04)	<0.001	-13.9 (-21.5;-6.23)	<0.001	0.07 (0.04;0.10)	<0.001	0.41 (0.15;0.67)	0.002
<b>LPA</b>								
Minimally-adjusted	-0.02 (-0.07;0.02)	0.298	-1.69 (-13.2;9.87)	0.775	0.02 (-0.02;0.07)	0.311	0.10 (-0.29;0.49)	0.629
Multivariable-adjusted	-0.03 (-0.07;0.02)	0.264	-2.23 (-13.8;9.36)	0.706	0.02 (-0.02;0.07)	0.283	0.11 (-0.28;0.50)	0.585
<b>MVPA</b>								
Minimally-adjusted	-0.09 (-0.12;-0.06)	<0.001	-17.4 (-25.8;-9.05)	<0.001	0.08 (0.05;0.12)	<0.001	0.50 (0.22;0.78)	0.001
Multivariable-adjusted	-0.08 (-0.11;-0.04)	<0.001	-15.6 (-24.1;-7.25)	<0.001	0.07 (0.04;0.10)	<0.001	0.44 (0.15;0.72)	0.003
<b>Sedentary Behaviour</b>								
<b>Total SB</b>								
Minimally-adjusted	0.04 (0.02;0.06)	<0.001	5.46 (0.78;10.1)	0.022	-0.04 (-0.06;-0.02)	<0.001	-0.17 (-0.32;-0.01)	0.040
Multivariable-adjusted	0.03 (0.01;0.05)	<0.001	4.37 (-0.35;9.08)	0.070	-0.03 (-0.05;-0.01)	<0.001	-0.14 (-0.30;0.02)	0.097
<b>TV-viewing SB</b>								
Minimally-adjusted	0.03 (0.01;0.05)	0.007	0.56 (-5.17;6.29)	0.848	-0.03 (-0.05;-0.01)	0.007	-0.10 (-0.29;0.09)	0.305
Multivariable-adjusted	0.03 (0.01;0.05)	0.014	-0.01 (-5.74;5.72)	0.996	-0.03 (-0.05;-0.01)	0.012	-0.08 (-0.28;0.11)	0.390

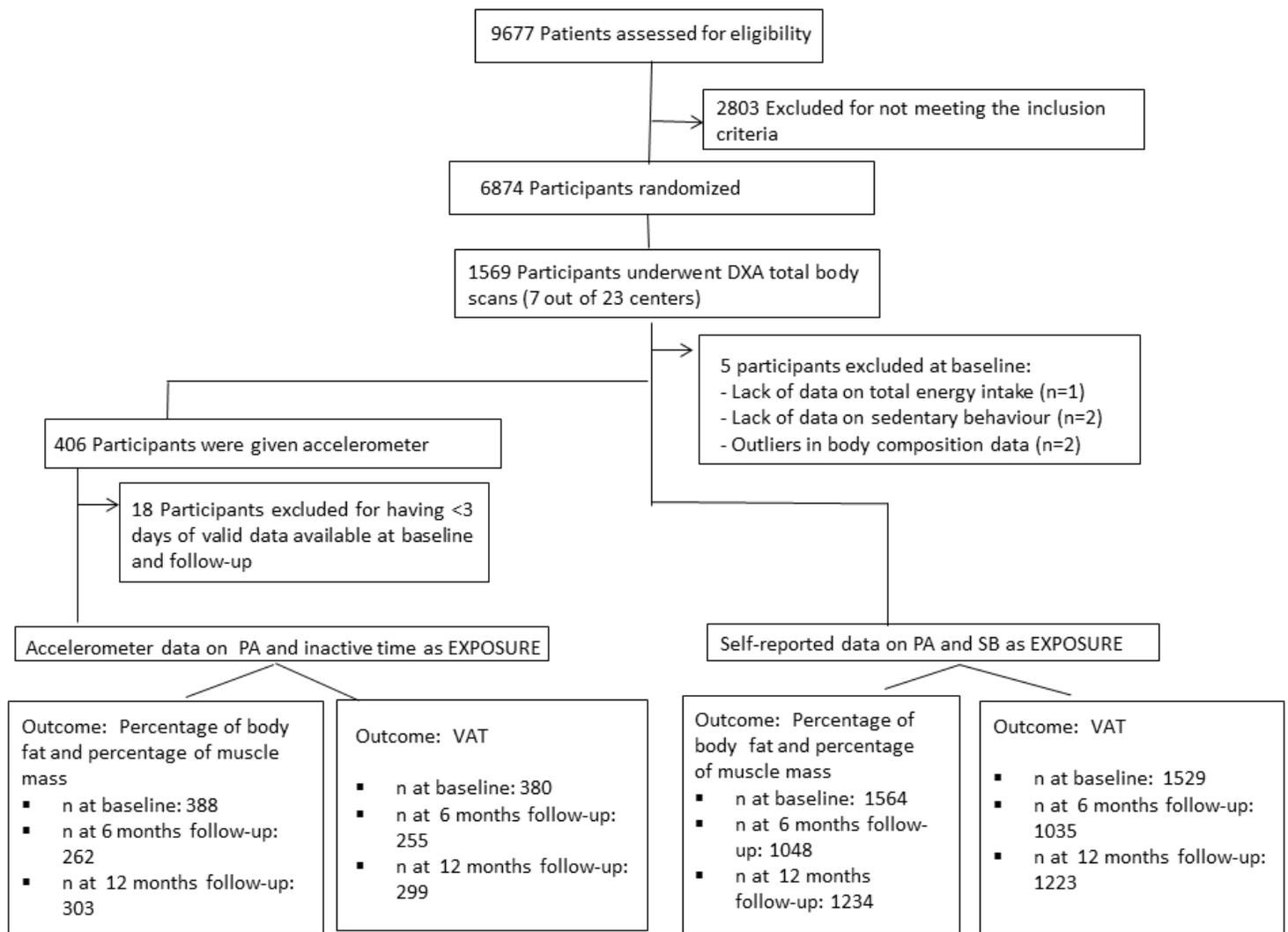
Values shows the  $\beta$ -coefficients (95% CIs). These represent the change in outcome variables (percentage of body fat, VAT (g), percentage of muscle mass and muscle-to-fat mass ratio), when increasing 30 min/day of each exposure variable (total PA, LPA, MVPA, total SB and TV-viewing SB). Mixed-effects linear models with random intercepts at recruiting center, family and patient level were used. Analyses included only completers. Minimally-adjusted model: age, sex, intervention arm, time and total wear time. Multivariable-adjusted model was further adjusted for baseline variables, such as educational level, smoking, diabetes, height, as well as repeatedly measured total energy intake. Abbreviation: VAT; visceral adipose tissue, PA; physical activity, LPA; light physical activity, MVPA; moderate-to-vigorous physical activity, SB; sedentary behaviour. The n of each outcome at baseline was: for percentage of body fat n= 1564, for VAT n=1529, for percentage of muscle mass n=1564, and for muscle-to-fat mass ratio n=1564; at 6 months was: for percentage of body fat n= 1048, for VAT n=1035, for percentage of muscle mass n=1048, and for muscle-to-fat mass ratio n=1048; at 12 months was: percentage of body fat n= 1234, for VAT n=1223, for percentage of muscle mass n=1234, and for muscle-to-fat mass ratio n=1234.

**Table 3.** Isotemporal substitution of inactive time (30 min/day) with time in bed and physical activity measured with accelerometer in body composition changes: Longitudinal analyses in completers-only.

	Percentage of body fat		VAT (g)		Percentage of muscle mass		Muscle-to-fat mass ratio	
	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value	$\beta$ (95% CI)	<i>p</i> -value
<b>Inactive time with Time in bed</b>								
Minimally-adjusted	-0.10 (-0.20;0.00)	0.051	-26.9 (-46.5;-7.27)	0.007	0.09 (-0.01;0.19)	0.067	0.93 (0.03;1.83)	0.042
Multivariable-adjusted	-0.09 (-0.19;0.01)	0.079	-23.8 (-43.3;-4.27)	0.017	0.08 (-0.02;0.18)	0.097	0.89 (-0.01;1.79)	0.052
<b>Inactive time with LPA</b>								
Minimally-adjusted	-0.13 (-0.25;-0.00)	0.044	-11.8 (-36.1;12.6)	0.343	0.12 (0.00;0.24)	0.046	0.87 (-0.24;1.97)	0.124
Multivariable-adjusted	-0.13 (-0.25;-0.00)	0.042	-11.2 (-35.4;13.0)	0.363	0.12 (0.00;0.25)	0.042	0.90 (-0.20;2.01)	0.110
<b>Inactive time with MVPA</b>								
Minimally-adjusted	-0.53 (-0.76;-0.29)	<0.001	-98.7 (-146;-52.0)	<0.001	0.50 (0.27;0.73)	<0.001	3.51 (1.43;5.60)	0.001
Multivariable-adjusted	-0.54 (-0.78;-0.31)	<0.001	-92.4 (-139;45.6)	<0.001	0.51 (0.28;0.74)	<0.001	3.74 (1.64;5.85)	<0.001

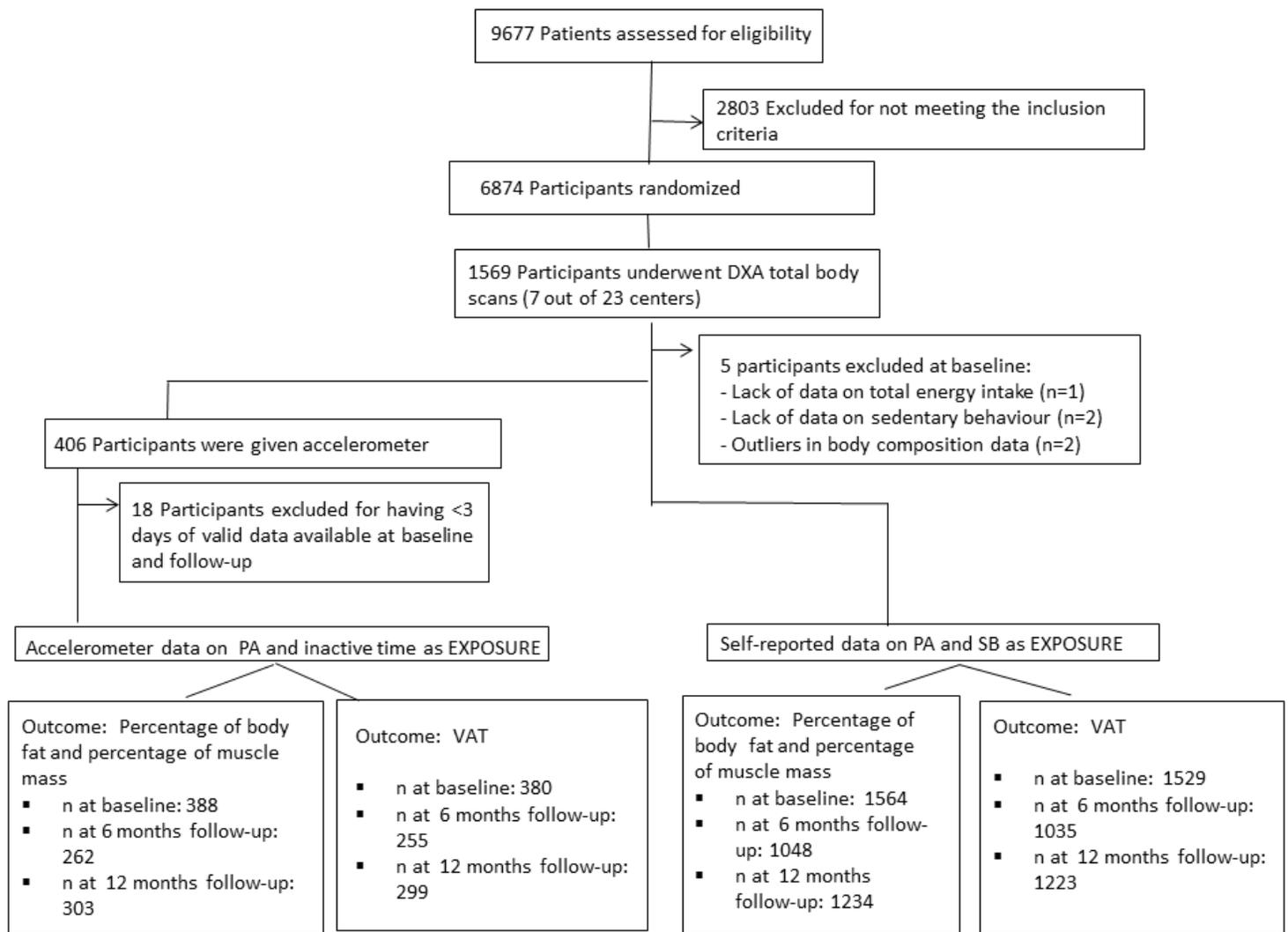
Values shows the  $\beta$ -coefficients (95% CIs). These represent the change in outcome variables when substituting 30 min/day of inactive time with time in bed and physical activity. Isotemporal mixed-effect linear models with random intercepts at recruiting center, family and patient level were used. Analyses included only completers. Minimally-adjusted model: age, sex, intervention arm, time and total wear time. Multivariable-adjusted model was further adjusted for baseline variables, such as educational level, smoking, diabetes, height, as well as repeatedly measured total energy intake. Abbreviation: VAT; visceral adipose tissue, LPA; light physical activity, MVPA; moderate-vigorous physical activity. The n of each outcome at baseline was: for percentage of body fat n= 388, for VAT n=380, for percentage of muscle mass n=388, and for muscle-to-fat mass ratio n=388; at 6 months was: for percentage of body fat n= 262, for VAT n=255, for percentage of muscle mass n=262, and for muscle-to-fat mass ratio n=262; at 12 months was: for percentage of body fat n= 303, for VAT n=299, for percentage of muscle mass n=303, and for muscle-to-fat mass ratio n=303.

## Figures



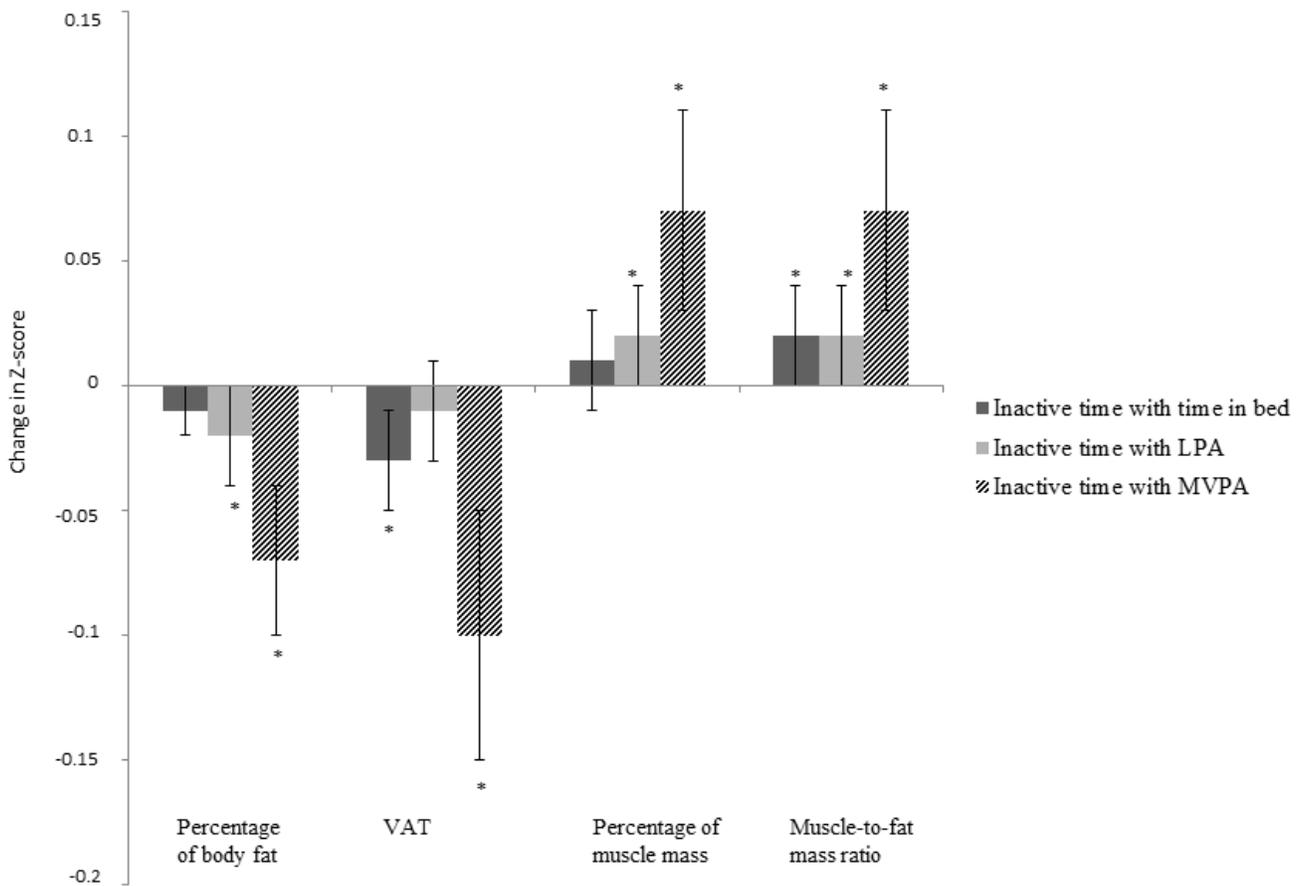
**Figure 1**

Flow Chart of the study sample.



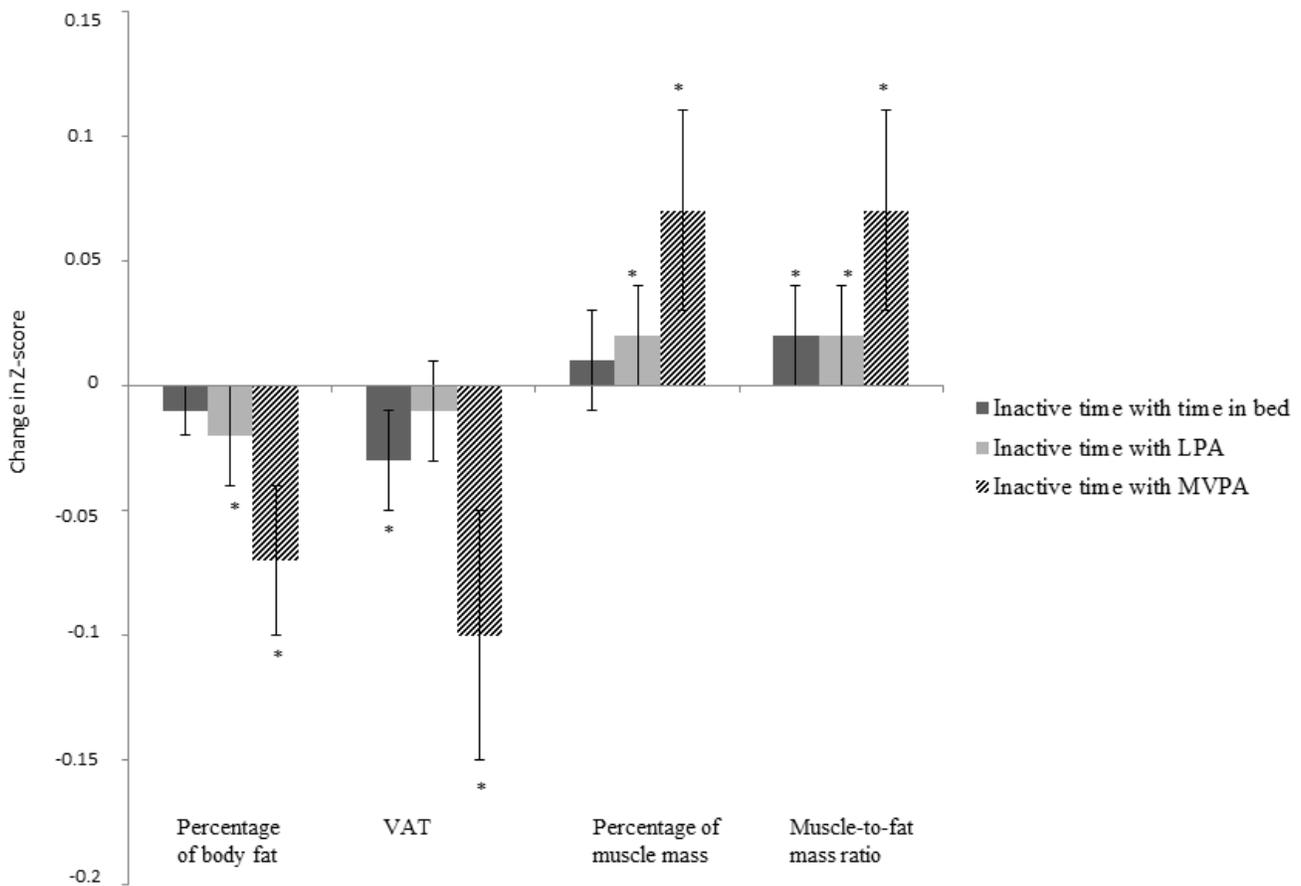
**Figure 1**

Flow Chart of the study sample.



**Figure 2**

Isotemporal substitution of inactive time (30 min/day) with time in bed and physical activity on standardized body composition (z-score): analyses in completers-only. Values shown are  $\beta$  (95% CI). These represent the change in outcome variables (z-scores) when substituting 30 min/day of inactive time with time in bed and physical activity. Abbreviations: LPA: light physical activity; MVPA: moderate-vigorous physical activity; VAT: visceral adipose tissue. Mixed-effect linear models with random intercepts at recruiting center, family and patient level were used to assess isotemporal substitution of inactive time with time in bed, LPA and MVPA, adjusting for age, sex, intervention arm, time, educational level, smoking, diabetes, height, repeatedly measured total energy intake and total wear time. \*indicates p-value <0.05.



**Figure 2**

Isotemporal substitution of inactive time (30 min/day) with time in bed and physical activity on standardized body composition (z-score): analyses in completers-only. Values shown are  $\beta$  (95% CI). These represent the change in outcome variables (z-scores) when substituting 30 min/day of inactive time with time in bed and physical activity. Abbreviations: LPA: light physical activity; MVPA: moderate-vigorous physical activity; VAT: visceral adipose tissue. Mixed-effect linear models with random intercepts at recruiting center, family and patient level were used to assess isotemporal substitution of inactive time with time in bed, LPA and MVPA, adjusting for age, sex, intervention arm, time, educational level, smoking, diabetes, height, repeatedly measured total energy intake and total wear time. \*indicates p-value <0.05.

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