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An Eight-Week Prospective Cohort Study

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Association between weight loss and spontaneous changes in physical inactivity in overweight/obese individuals with knee osteoarthritis: an 8-week prospective cohort study

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ABSTRACT

OBJECTIVE: To describe spontaneous changes in time spent physically inactive measured continuously by accelerometry during an 8-week weight loss intervention in overweight/obese individuals with knee osteoarthritis.

METHOD: This study was designed as an observational cohort study including individuals with concomitant overweight/obesity and symptomatic knee osteoarthritis from an osteoarthritis outpatient clinic. Participants completed an 8-week dietary intervention previously shown to induce substantial weight loss. The main outcome was accelerometer-based measurement of physical inactivity for 24 hours daily during the 8-week intervention period presented as change in the average daily time spent inactive (sitting, reclined or sleeping) from one week prior to intervention to the last week of the intervention.

RESULTS: A total of 124 participants completed the dietary intervention and had valid accelerometer recordings. The mean weight loss was 12.7 kg [95% CI -13.2 to -12.1; P<.0001] after 8 weeks corresponding to a decrease in BMI of 4.3 kg/m² [95%CI -4.5 to -4.2; P<.0001]. Significant improvements in osteoarthritis symptoms (assessed by the Knee Injury and Osteoarthritis Outcome Score) was found across all subscales; for KOOS pain an
improvement of 12.8 points [95% CI, 10.6 to 15.0; P<.0001] was observed. No statistically
significant change occurred in the average daily time spent inactive from baseline to follow-
up (mean change: 8.8 minutes/day [95% CI, -12.1 to 29.7; P=0.41]).

CONCLUSION: Physical inactivity remains stable despite a clinically significant weight loss
and improvements in knee osteoarthritis symptoms. Change in inactivity does not seem to
occur spontaneously, suggesting that focused efforts to reduce inactive behaviors are
needed.

SIGNIFICANCE AND INNOVATIONS

- Physical inactivity remains stable during an 8-week intensive dietary intervention
  period despite a clinically significant weight loss and improvements in knee
  osteoarthritis symptoms.
- This indicates that changes in physical inactivity must be stimulated by other efforts
  (e.g. education, motivation, etc.) following a weight loss to reduce overall health
  risks associated with sedentary behavior and increase the chance of long-term
  weight loss maintenance.

INTRODUCTION

Physical inactivity (lack of moderate-to-vigorous activity) is associated with increased risks of
developing non-communicable diseases such as heart diseases, diabetes and even
premature death(1-3). Physical inactivity increases with age in all World Health Organization
(WHO) regions(3) and thereby has a marked impact on the disease burden related to
chronic diseases.
One of the contributors to physical inactivity in the aging population is osteoarthritis (OA) of the hips or knees(4). OA is characterized by pain during activity resulting in reluctance to move due to pain(5). In fact, OA symptoms are negatively associated with physical activity (moderate-to-vigorous intensity)(6) and most adults with OA in both the US and Europe have a sedentary life style (sitting or reclined most of the day)(7, 8). Altogether, individuals with OA are very susceptible to development of chronic disease related to physical inactivity.

Obesity is also well-established as associated with physical inactivity(9) and obesity is linked to the onset and progression of knee OA(10). Obesity and knee OA often share pathogenetic phenotypes and the onset or progression of one condition increases the risk of developing the other, and a vicious circle may be triggered(11). It is therefore not surprising that individuals with the combination of obesity and knee OA are generally very physically inactive and efforts should be made to reduce physical inactivity in this population.

Current treatment guidelines recommend weight loss as a primary treatment of concomitant overweight/obesity and knee OA(12-14). Weight loss interventions are well-documented with beneficial effects on pain, physical functioning, and quality of life(15-17). In an observational non-intervention cohort study weight loss above 10 lbs. (4.5 kilograms) over 2 years were associated with a minor reduction in time spent on sedentary behavior (7 minutes/day), whereas a weight gain above 10 lbs. was associated with more time spent on sedentary behavior (25.8 minutes/day)(18). This suggest that a moderate change in weight (minimum 4.5 kilograms) is related to a change in time spent on sedentary behavior after 2 years. As sedentary behavior is linked to overweight/obesity(19) and severity of knee OA.
symptoms, an assessment of whether an intensive weight loss intervention aiming at a 10% weight loss and symptomatic improvements associates with a spontaneous decrease in time spent physically inactive (sitting, reclined or sleeping) is relevant.

The terms “physical inactivity”, “physical activity” and “sedentary behavior” are used throughout the literature to describe the participants daily habits. In this paper the term “physical inactivity” will be used to describe time spent sitting, reclined and sleeping during a 24-hour period. “Physical activity” will be used to describe time spent on moderate-to-vigorous activity during wakening hours (10-15 hours) and “sedentary behavior” will represent time spent sitting or reclined during wakening hours (10-15 hours).

As part of a run-in period of a trial with focus of weight maintenance, the objective of this study was to explore if weight loss in overweight/obese individuals with knee OA was associated with a spontaneous change in physical inactivity during an 8-week intensive dietary intervention period. We hypothesized that weight loss is associated with a spontaneous decrease in daily time spent physically inactive.

METHODS
This study is a prospective cohort study conducted from November 2016 to November 2017. The study is a sub-study of a randomized trial “Effect of liraglutide on body weight and pain in overweight or obese patients with knee osteoarthritis” (registered at www.clinicaltrials.gov: NCT02905864), in which participants underwent an 8-week intensive dietary intervention prior to a random allocation to either liraglutide or placebo. For the purpose of this sub-study we focused on the pre-allocation phase (before randomization to
liraglutide or placebo), and took advantage of the initial 8-week intensive dietary intervention proven to induce a significant weight loss(21).

A detailed protocol was developed for this sub-study (supplementary file 1), that was pre-registered before commencement of any study related activities (www.clinicaltrials.gov: NCT02910544). The protocol was approved by the local health research ethics committee (H-16019969), and all participants provided written informed consent.

Participants were recruited from the Osteoarthritis outpatient’s clinic by a rheumatologist at the Parker Institute at the Copenhagen University Hospital Bispebjerg-Frederiksberg. The key inclusion criteria included: A clinical diagnosis of knee OA according to ACR(22), radiographic changes (Kellgren-Lawrence (KL) grade 1, 2, or 3), Body Mass Index (BMI) ≥ 27 kg/m², and motivation for weight loss (judged subjectively by the including rheumatologist during an interview). The key exclusion criteria included: Planned knee surgery, previous or planned surgical treatment for obesity, and current medical or dietary obesity treatment. The rest of the inclusion and exclusion criteria can be found at www.clinicaltrials.gov: NCT02905864. In this study participants with a BMI of 30 kg/m² or more were considered obese and participants with a BMI equal to or more than 27 kg/m² were considered overweight.

WEIGHT LOSS INTERVENTION

The intensive dietary intervention (IDI) comprised of a full meal replacement diet for 8 weeks. The meal replacements consisted of soups, shakes, porridges, and bars (Cambridge
Weight Plan UK), resulting in an energy intake of 800-1000 kcal/day. Further, weekly educational group sessions (2 hours per session; 6-8 participants per group) that focused on healthy diet and motivational support were provided. The program has been proven to result in a significant weight loss (>10% reduction in bodyweight) among overweight/obese knee OA patients (21). Two dietitians (with 11 and 14 years of experience) were responsible for the educational group sessions and supplied the participants with the meal replacement products.

BODY WEIGHT
The participant’s body weight was measured at baseline (1 week prior to the IDI) and at the end of the 8-week IDI, by a study nurse using a decimal weighting scale (TANITA BW-800, Tanita Europe BV, The Netherlands), with the participant fasting and wearing underwear or light clothing only. Further, body weight was measured at each weekly group session in the IDI period with the participant wearing normal clothing, but without shoes.

PHYSICAL INACTIVITY MEASUREMENTS
Measurements of physical inactivity in daily life were obtained objectively by using a single-use miniature tri-axial accelerometer (dimensions: 50x21x5 mm, weight: 8g; SENS-MOTION® activity measurement system, version 1.7.1). The accelerometer measured activity continuously at 12.5 Hz for 24 hours and had battery capacity for at least 20 weeks of continuous use. The accelerometer was placed within a small water proof Band-Aid (Medipore™, 3M, Soft Cloth Surgical Tape on Liner), and worn discretely on the lateral side of the thigh. The accelerometer had an onboard memory and was connected to a dedicated
smartphone application via Bluetooth and the collected data was uploaded to a secured web-server for storage and subsequent analysis. To avoid loss of data (due to full memory) a connection to a smartphone with the dedicated application had to take place at least once weekly. The discretely worn accelerometer did not interfere with the participant’s daily habits(23). The accelerometer was water proof and therefore not necessary to remove during bathing, swimming, and showering.

The participants had the accelerometer mounted one week before commencing the IDI and were asked to wear it constantly until the follow-up visit at the end of the IDI (a total period of 9 weeks). During that period the participants could change the Band-Aid if needed, and we have previously shown that replacing the accelerometer on the opposite thigh does not affect the measurements(23). An explanation of the purpose of the device was given to participants and an instruction sheet and additional Band-Aids were provided.

The accelerometer has an inbuilt algorithm that categorizes data based on intensity thresholds and gravity vectors into inactivity (sitting, reclined or sleeping), standing, walking, cycling, and other activities in 10-second epochs. The algorithm provides valid and reliable data on time spent physically inactive (sitting, reclined or sleeping), standing, and movement (e.g. walking, running, cycling, and other activities) in knee OA patients. We have previously investigated the agreement between actual observations and the algorithm, which showed that algorithm detected 99% of the actual time periods spent physically inactive (standard deviation (SD) 3%), 95% (SD 6%) for standing, and 97% (SD 9%) for movement. Day to day reliability for physical inactivity was 96% (SD 8%), 99% (SD 1%) for
KNEE OA SYMPTOMS

Knee OA symptoms were assessed by the patient reported outcome questionnaire “Knee injury and Osteoarthritis Outcome Score” (KOOS)(24) 1 week prior to the IDI and right after the IDI period. The KOOS questionnaire was developed to assess the patients’ opinion about their knee problems and consists of 5 subscales; pain, other symptoms, function in daily living (ADL), function in sport and recreation (sport/rec), and knee related quality of life (QoL). Answers are given on 5-point Likert scales scoring from 0 to 4. A normalized score is calculated (0-100) for each subscale with 100 indicating no symptoms and 0 indicating extreme symptoms. KOOS has a high test-retest reliability, and is regarded a valid tool when assessing patients with knee OA(25, 26). A change between 8 to 12 points is considered clinically relevant(27).

STATISTICAL ANALYSES

The analyses were performed on the per protocol (PP) population defined as participants with baseline and 8-week follow-up data on body weight, as well as complete and valid accelerometer data from the initial week (the week prior to the IDI) and the last week of the IDI period at the least. Data was deemed valid if a minimum of 24 consecutive hours of wear-time in both the baseline period and the follow-up period was detected.
The main outcome of this study was change in average daily time spent physically inactive (minutes/day) from baseline (defined as the daily average during the one week prior to the IDI), to the 8-week follow-up (the daily average of the last week of the 8-week IDI). Similar averages were calculated for time spent standing and moving (see above), changes in body weight, and changes in knee OA symptoms assessed by the KOOS questionnaire. The changes from baseline were analyzed using analysis of covariance (ANCOVA) adjusting for the baseline value. The analyses were repeated with further adjustment for age and gender.

The individual time course patterns of body weight (weekly measurements) and physical activity (daily measurements) were plotted, and the linear trends in the time-courses were analyzed by repeated measures mixed linear models with time (day or week) as fixed factor and participant as random factor.

The main trial was powered to include at least 150 participants. Such a sample provided the current sub-study with a power of 0.999 to detect a change in the average weekly time spent physically inactive of at least 30 minutes per day at a two-sided significance level of 0.05.

We set the statistical significance at the conventional level of 0.05. All analyses were performed using commercially available statistical software (SAS, version 9.4; SAS Institute Inc).
RESULTS

Study participants flow are presented in figure 1. A total of 168 participants were enrolled in the IDI and all had baseline assessments; 8 (5%) participants withdrew and 36 (21%) participants had accelerometer malfunction resulting in invalid data either at baseline or at follow-up. Data loss was caused by either: batteries not being attached properly (25%), lack of connection between smartphone and device (30.6%), data not stored (30.6%), and accelerometer misplacements (13.9%). A total of 124 participants had valid accelerometer recordings throughout the observation period and thus, constituted the per-protocol population. There were no statistically significant differences between the included and excluded participants (assessed by t-tests). Baseline characteristics of the participants are presented in table 1.

The average number of visits to the dietitian for the 124 participants was 7.4 (SD 0.75) out of 8 possible visits and the average weight loss was 12.7 kg [95% Confidence Interval (CI): -13.2 to -12.1; P=<.0001] corresponding to a decrease in BMI of 4.3 points [95% CI: -4.5 to -4.2; P=<.0001].

No changes occurred in the average time (minutes/day) spent physically inactive from baseline to follow-up (mean difference: 8.8 minutes [95% CI: -12.1 to 29.7]; P=0.41). Likewise, no change occurred in the average time spent standing or moving (Table 2). There were statistically significant and clinically relevant improvements in the patient reported knee OA symptoms following the weight loss intervention (Table 2). The age and gender adjusted analyses did only change the results slightly (Table 2).
The individual time course patterns of the changes in body weight, time spent physically inactive, time spent standing, and time spent moving are presented in figure 2. The figure demonstrates substantial day-to-day variability in each of the measurements, however, no trends towards systematic changes were detected as illustrated by the linear regression fits.

DISCUSSION

Being overweight and obese is associated with knee OA onset, progression and severity of symptoms, all of which is linked to a physically inactive behavior that is a serious threat to overall health. Weight loss could therefore prove beneficial in terms of a spontaneous decrease in time spent physically inactive in a population of overweight/obese knee OA patients. However, our results show that despite a significant weight loss paralleled by clinically relevant symptomatic improvements, there were neither changes in time spent physically inactive nor were there signs of increased time spent moving.

The WHO recommends 30 minutes of physical activity 5 times weekly (28) but do not have any concrete recommendations about relevant reductions in physical inactivity. Accordingly, we powered our study for detection of a 30 minutes reduction in daily time spent physically inactive as a best estimate of a clinically relevant change, but no such reduction was detected in the cohort. Indeed, our 95% CI respects this pragmatic margin and shows that weight loss does not lead to reduced time spent physically inactive. When looking at changes in daily time spent moving the absence of change supports the fact that overweight/obese patient with knee OA maintain their daily habits despite a significant weight loss and reduction in symptoms. Therefore, our results show, very robustly, that
changes in daily habits do not occur spontaneously in connection to weight loss among knee OA patients.

The lack of change in time spent physically inactive may be related to the focus of the intervention. The participants volunteered to the study to achieve a weight loss with the purpose of reducing their symptoms; not to decrease physical inactivity. However, as previous non-interventional studies have linked weight changes with changes in physical activity(18, 29), we expected that a focused dietary intervention yielding a substantial weight loss, would result in significant changes in physical inactivity. Our results suggest that emphasis on changes in sedentary behavior is important in relation to a weight loss intervention, to reduce health risk and increase the chances of a long-lasting weight loss(18, 29).

Few studies have assessed accelerometer based recordings of changes in physical activity following physical activity interventions in OA populations, and the overall effect of the interventions show little to no changes in physical activity level(30). Getting patients with knee OA to increase their overall physical activity level seems to be a challenge we have not yet successfully met. An 8-week intervention for patients with knee OA combining several modalities (exercise and education-behavior change) showed an increase in the time spent exercising after 12 months(31). However, whether this extends to a change in daily time spent physically inactive is uncertain. Together with other studies(31, 32), this confirms that to change knee OA patients’ daily habits a specific focus on this matter is necessary.
This is the first study to report 9 weeks of 24-hour measurements of physical inactivity in patients with knee OA participating in an IDI. Previous studies have typically measured physical activity for 10 hours per day for up to 7 days (33-35). We utilized a validated wearable sensor that enabled us to monitor physical inactivity continuously (24 hours per day) for 9 weeks without data loss (23), which exceeds the recommended 10 hours of wear-time with a 90-minute non-wear threshold (36). Further, the 24-hour recording ensures capture of all activities performed, which gives a precise estimate of total time spent sitting or reclined. Thus, our estimates of time spent physically inactive most likely have better credibility than previous estimates.

Our study has some limitations. Due to the nature of the underlying main trial, we did not record physical inactivity after the 8-week IDI period. The low energy diet (800-1000 kcal/day) can result in a feeling of low energy, which may have prevented a spontaneous decrease in physical inactivity during the intervention. However, we saw no such trends, and spontaneous changes after the IDI is unlikely. Further it is likely that this patient group, that have dealt with overweight/obesity and knee OA for many years, have had a general low activity level for a long period of their lives (37, 38), making it less likely that they spontaneously change behavior. Another limitation is the frequency of accelerometer malfunctions (21% of participants). However, the excluded participants were not different from the PP population (table 1), and the PP population consisted of 124 participants, which provides a strong statistical power to detect even minor changes in time spent physically inactive. It is unlikely that the results would have been different had there been fewer accelerometer malfunctions.
We observed a significant day-to-day variability in the individual physical inactivity levels. We are uncertain about the meaning of this observation, as daily observations over a prolonged period have not been published before. It is possible that this may be caused by the awareness of having daily habits measured (the Hawthorne effect)(39). However, this would be expected to result in a reduced physically inactive behavior – at least in the initial phase, which we did not observe.

The generalizability of the results regarding time spent moving is limited as we did not assess the intensity of the movements. It is possible that the types of movement did change towards higher intensities, while the total time spent moving remained unchanged. However, we focused on time spent physically inactive as this as a risk factor for poor health outcomes independently of time and intensity of any movement (41-43). It is also important to notice that despite a substantial weight loss, the average participant would still be classified as obese after the 8-week period (mean BMI at follow-up approximately 32). However, the combined weight loss and improvements in knee OA symptoms was hypothesized to induce spontaneous decrease in physical inactivity despite still being overweight/obese. Our data oppose that notion based on the findings in this study and the hypothesis is rejected.

CONCLUSION

We found that time spent physically inactive remains stable throughout an 8-week intensive dietary intervention among overweight/obese individuals with knee OA despite a substantial weight loss and clinically relevant changes in knee OA symptoms. This indicates

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that changes in physical inactivity must be stimulated by other efforts (e.g. education of the importance of reducing time spent physically active etc.) to reduce overall health risks associated with sedentary behavior and increase the chance of long-term weight loss maintenance.

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FUNDING

The main trial was an investigator-initiated study, initiated by the Parker Institute and supported by Novo Nordisk A/S and Cambridge Weight Plan UK. This sub-study did not receive any specific grants but is part of CB’s PhD, which is supported by The Danish Physical Therapy Association, The Oak foundation, The Danish Rheumatism Association(R141-A4030), and “Muskellaboratoriefonden” v/Bente Danneskiold-Samsøe. None of the funders had a role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon the approval of Novo or Cambridge Weight Plan UK.
TRANSPARENCY DECLARATION

The last author (MH) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA SHARING

No additional data available.

ETHICAL APPROVAL

The protocol was approved by the local health research ethics committee (H-16019969).

COMPETING INTEREST

CB has no competing interests in this study.

RC has no competing interests related to this study. Professor Christensen reports that he has previously received travel grants from the Cambridge Manufacturing Company to attend scientific meetings.

LEK has no competing interests related to this study.

HG has no competing interests related to this study.

HB has no competing interests related to this study.

AO has no competing interests related to this study.

MUR has no competing interests related to this study.
MH has no competing interests related to this study. Professor Henriksen reports that he has previously received travel grants from the Cambridge Manufacturing Company to attend scientific meetings.

CONTRIBUTION

CB, RC, LEK, HG, HB, and MH contributed to the design of the study. CB, HB, AO, MUR collected the data. CB analyzed the data, and CB and MH made initial interpretations. CB drafted the work and RC, LEK, HG, HB, AO, MUR, and MH critically revised the manuscript. All authors have approved the final version of the manuscript and are accountable for all aspects of the work.
Table 1. Baseline characteristics of the per-protocol (PP) population, intention to treat (ITT) and drop outs presented as mean and standard deviation (SD).

<table>
<thead>
<tr>
<th></th>
<th>Mean(SD)</th>
<th>Excluded from analyses(^a)</th>
<th>ITT n=168</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PP n=124</td>
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<tr>
<td>Gender, no. (%)</td>
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</tr>
<tr>
<td>Female</td>
<td>78 (62.9)</td>
<td>31 (70.45)</td>
<td>109 (64.9)</td>
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<tr>
<td>Male</td>
<td>46 (37.1)</td>
<td>13 (29.55)</td>
<td>59 (35.1)</td>
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<td>Age (years)</td>
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<td>57 (11.0)</td>
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<tr>
<td>Body weight (kg)</td>
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<td>103.2 (20.2)</td>
<td>106.0 (19.6)</td>
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<tr>
<td>Height (cm)</td>
<td>170.8 (8.7)</td>
<td>169.7 (9.7)</td>
<td>170.5 (8.9)</td>
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<tr>
<td>BMI (kg/m(^2))</td>
<td>36.6 (5.8)</td>
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<tr>
<td>Physical activity measures</td>
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<tr>
<td>Inactivity (min/day)</td>
<td>1081.3 (115.7)</td>
<td>1075.7 (108.9)</td>
<td>1079.9 (113.6)</td>
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<tr>
<td>Standing (min/day)</td>
<td>111.1 (53.0)</td>
<td>133.0 (68.5)</td>
<td>116.9 (58.0)</td>
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<tr>
<td>Movement (min/day)</td>
<td>228.8 (71.2)</td>
<td>214.8 (89.1)</td>
<td>225.1 (76.3)</td>
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<tr>
<td>KOOS, 0-100</td>
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<td></td>
</tr>
<tr>
<td>Function (ADL)</td>
<td>68.1 (18.5)</td>
<td>66.4 (15.2)</td>
<td>67.7 (17.6)</td>
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<td>Quality of life (QoL)</td>
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<td>39.5 (16.2)</td>
<td>42.3 (17.8)</td>
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<tr>
<td>Pain</td>
<td>63.7 (17.2)</td>
<td>63.7 (14.2)</td>
<td>63.7 (16.5)</td>
</tr>
<tr>
<td>Sport/Rec</td>
<td>36.5 (25.3)</td>
<td>31.3 (22.1)</td>
<td>35.1 (24.5)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>67.7 (17.3)</td>
<td>67.5 (16.9)</td>
<td>67.6 (17.2)</td>
</tr>
</tbody>
</table>

Abbreviation: KOOS, Knee Injury and Osteoarthritis Outcome Score; Inactivity, sum of time spent sitting or lying down; Movement, sum of time spent walking and other movements; BMI, body mass index.

\(^a\) Withdrew from the main trial (n=8), device malfunction (n=36).
Table 2. Change from baseline to follow-up (8 weeks) in the per-protocol population (n=124).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean change (95% CI)</th>
<th>P value</th>
<th>Mean change adjusted for age and gender (95% CI)</th>
<th>P value</th>
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<tr>
<td>Change in time spent</td>
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<td>Physically Inactive (min/day)</td>
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<td>Standing (min/day)</td>
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<tr>
<td>Moving (min/day)</td>
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<tr>
<td>Body weight (kg)</td>
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<tr>
<td>BMI (kg/m^2)</td>
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<tr>
<td>Change in KOOS (0-100)</td>
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<td>Quality of life (QoL)</td>
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<td>Pain</td>
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<tr>
<td>Sport/Rec</td>
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<td>Symptoms</td>
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<tr>
<td>Function (ADL)</td>
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Abbreviation: KOOS, Knee Injury and Osteoarthritis Outcome Score; BMI, body mass index

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FIGURE CAPTIONS

**Figure 1.** Diagram showing patient flow through the study.

**Figure 2.** Individual trajectories for changes from baseline over the 8-week intensive dietary intervention in (A) weekly measured body weight, (B) daily time spent physically inactive (minutes/day), (C) daily time spent standing (minutes/day), and (D) daily time spent moving (minutes/day).
Figure 1. Diagram showing patient flow through the study.

Pre-screened (n=339)

- Pre-screening not approved (n=117)

Assessed for eligibility (n=222)

- Excluded (n=54)
  - Not meeting inclusion criteria (n=8)
  - Withdraw of consent (n=12)
  - Waiting list (n=29)
  - Not meeting eligibility criteria (n=5)

Enrolled (n=168)

- Withdraw of consent (n=6)

Completed the intensive dietary intervention (n=162)

- Withdraw of consent prior to randomization (n=2)
- Accelerometer malfunction (n=36)

PP population (n=124)