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Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: A six-month randomized controlled trial

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ABSTRACT

Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF).

Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain-related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance imaging.

Results Pain-related disability increased during the intervention in both groups. Back pain intensity increased significantly more in the control group than in the intervention group in which back pain intensity remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain-related disability, ODI, or paraspinal GU and FF were observed. The change in daily steps associated positively with the change in paraspinal muscle GU.

Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening regardless of paraspinal muscle GU or FF.

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Keywords: sedentary behaviour, accelerometry, back pain, disability, insulin sensitivity, muscle fat fraction

What is already known on this topic

- Lack of physical activity and high sedentary behaviour may lead to insulin resistance and fat infiltration of the back muscles which may contribute to back pain and disability.
- Whether reducing sedentary behaviour can improve back muscle insulin sensitivity or fat infiltration, back pain, or pain-related disability, is not currently known.

What this study adds

- Reducing sedentary behaviour may prevent back pain from increasing even if no improvements in disability, back muscle insulin sensitivity or fat infiltration are achieved.
- Increasing daily steps may improve back muscle insulin sensitivity.

How this study might affect research, practice or policy

- Clinicians should consider patients' sedentary behaviour habits and consider guiding them towards reducing sedentary time to prevent or reduce back pain.
- Pain-related rehabilitation outcomes may not be related to the physiological risk factors (such as insulin resistance or muscle fat infiltration) for pain.

INTRODUCTION

Sedentary behaviour (SB) has emerged as a plausible intervention target for back pain alleviation (1–4). Whilst randomized controlled trials suggest that reducing SB could improve pain-related disability without affecting pain intensity (5,6), the evidence remains limited. Moreover, the mechanisms by which SB modification could affect back pain remain poorly understood. Insulin resistance and fatty infiltration of the paraspinal muscles associate with back pain (7–11), and previous evidence shows that insufficient physical activity (PA) associates with increased paraspinal muscle fat fraction (FF) and successfully reducing SB improves muscle insulin sensitivity (12,13).

Thus, we aimed to investigate the effects of a six-month SB reduction intervention on back pain, disability, and paraspinal muscle FF and insulin sensitivity (glucose uptake, GU). Additionally, we assessed the back pain related factors cross-sectionally.

METHODS

This study consists of secondary analyses of a six-month randomized controlled trial that was conducted at the Turku PET Centre (Turku, Finland) between April 2017 and March 2020 (Clinicaltrials.gov NCT03101228, 05/04/2017). The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study (16/1801/2017). All participants gave their informed consent before entering the study, and the study was conducted according to the Declaration of Helsinki.

Participants

As reported earlier (12,14), volunteers were recruited from the community. Inclusion criteria were: age 40–65 years, body mass index (BMI) 25–40 kg/m^2, self-reported physical inactivity (<120 min/week of moderate-to-vigorous physical activity [MVPA]), accelerometer-measured sedentary time ≥10 h or ≥60 % of accelerometer wear time, and metabolic syndrome (15). Exclusion criteria included diagnosed diabetes or fasting blood glucose ≥7.0 mmol/l, abundant alcohol consumption according to the national guidelines, the use of any tobacco products, diagnosed depressive or bipolar disorder, inability to understand written Finnish, and any condition that would endanger the participant or study procedures (e.g., previous exposure to ionizing radiation).

Measurements

Back pain intensity and pain-related disability were assessed by two questions and 10-cm visual analogue scales (VAS): 1) Have you had back pain within the last month? Mark the intensity of the worst perceived pain during the month on the line below; and 2) Has the perceived pain caused you disability at your work

or everyday tasks within the last month? Mark the intensity of the greatest extent of disability that you experienced during the month on the line below. A higher value (0–10 cm) indicates higher pain intensity and disability. Additionally, back pain-related disability was assessed using the Oswestry disability index (ODI), which provides a value of 0–100%, and a higher value represents higher disability (16).

Paraspinal muscle (i.e., erector spinae and transversospinales) FF was assessed using the two-point Dixon magnetic resonance (MR) imaging method (Philips 3T Ingenuity TF, Philips Healthcare, Amsterdam, The Netherlands and Siemens Magnetom Skyra Fit 3T system, Siemens Healthcare, Erlangen, Germany) (17). Paraspinal muscle GU was measured using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET; GE D690 PET/CT, GE Healthcare, Milwaukee, WI) during hyperinsulinemic euglycemic clamp (HEC) as described previously (12,18). Both the FF and GU were analyzed separately for the transversospinal and erector spinae muscles at the level of L3-4. The measurements were performed using Carimas (version 2.10, https://www.carimas.fi).

Physical activity (PA) and SB were measured using accelerometers for four weeks during screening (UKK AM30, UKK Terveyspalvelut Oy, Tampere, Finland) and the whole six-month intervention period (Movesense, Suunto, Vantaa, Finland, with ExSed application, UKK Terveyspalvelut Oy, Tampere, Finland). The accelerometer data was analyzed using six-second epochs, and the raw acceleration data was analyzed using the mean amplitude deviation (to assess SB, standing, light PA [LPA], and moderate-to-vigorous PA [MVPA]) and angle for posture estimation (to differentiate SB and standing) methods as described previously (3,18–20).

Height was measured using a wall-mounted stadiometer, and body mass and body fat percentage were measured by air displacement plethysmography (Cosmed USA, Concord, CA) after at least four hours of fasting. Waist circumference was measured using a measuring tape midway between the lowest rib and the iliac crest.

Intervention

After the screening, eligible volunteers were randomized into the intervention and control groups in a 1:1 ratio by a statistician using random permuted block randomization (block size 44) in SAS (version 9.4 for Windows, SAS Institute, Inc., Cary, NC). The randomization was performed for men and women separately.

As described in more detail previously (18), participants in the intervention group were advised to reduce their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by subtracting 1 h of SB from the amount during screening. Correspondingly, 1 h was added to standing, LPA, and MVPA goals distributing the time based on individual preferences. However, a maximum of 20 minutes was added to MVPA, and increasing intentional physical exercise training was discouraged. For the control

group, the daily SB and PA goals were set equal to the screening values. All participants could monitor their daily SB and PA and the fulfilment of the goals using a mobile phone application (ExSed) connected to the accelerometer.

Patient involvement

Patients were not involved in designing or conducting this study.

Equity, diversity and inclusion

Both the study participants and researchers include self-identified men and women in a relatively balanced fashion. The research group consists of both junior and senior researchers.

Statistical methods

Baseline characteristics are presented as mean (standard deviation, SD) if not stated otherwise. Intervention effects are presented as model-based mean (95% confidence interval, 95% CI). Baseline correlations were analyzed using the Spearman rank correlation. The main analyses of intervention effects were performed using linear mixed models for repeated measurements. The outcome of interest was the dependent variable, and independent variables included group, time, sex, and group x time in all analyses. Additionally, FF analyses were adjusted for age, and pain questionnaire analyses were adjusted for self-reported regular pain medication status (yes/no) and BMI, because this improved the distribution of the residuals. The normal distribution of the residuals was visually inspected, and log10 or square root transformations were performed as necessary. Tukey-Kramer adjustment for multiple comparisons was used. Compound symmetry or unstructured covariance structure was chosen based on the Akaike information criterion. Statistical significance was set at $p<0.05$ (two-tailed). The main analyses were performed in SAS (version 9.4 for Windows, SAS Institute Inc., Cary, NC) and the correlation analyses were performed using JMP Statistics (version 16, SAS Institute Inc., Cary, NC).

The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming an increase of 0.7 (SD 0.55) µmol/100g/min in the intervention group (10% increase) and an increase of 0.05 µmol/100g/min in the control group, we calculated that 16 participants per group would be sufficient for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity ($\alpha=0.05$, $1-\beta=0.9$). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin sensitivity would behave similar to quadriceps femoris and thus, the study would be sufficiently powered to detect statistically significant changes in paraspinal muscle insulin sensitivity.

RESULTS

Baseline characteristics

Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and MR imaging. The baseline characteristics are presented in Table 1.

Baseline correlations

All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated positively with erector spinae and transversospinal FF (r_s=0.53, 0.55, respectively). Erector spinae GU correlated positively with MVPA and step count (r_s=0.36 and 0.40, respectively) and negatively with SB (r_s=-0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s=0.42 and 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and transversospinal FF correlated with MVPA (r_s=-0.30 and -0.36, respectively). Increased body adiposity (BMI and body fat percentage) associated with lower paraspinal muscle GU and higher FF.

Pain-related disability correlated positively with standing time (r_s=0.27). Furthermore, the ODI score correlated negatively with MVPA (r_s=-0.28) and step count (r_s=-0.26). Finally, the ODI score correlated positively with body fat percentage (r_s=0.33). Back pain intensity did not correlate with any PA, SB, or paraspinal muscle-related variables.

Intervention effects

Accelerometry

The intervention effects on SB and PA have been reported previously (18). During the six-month study period, the intervention group reduced SB by 40 min/day on average. Subsequently, MVPA increased in the intervention group by 20 min/day, with no statistically significant changes in the control group. LPA increased on average by 10 min/day without statistically significant between-group differences. Both groups increased their daily step counts with a statistically significantly higher increase in the intervention group (+3300 vs. +1600 steps/day in the intervention and control groups, respectively).

Pain and disability questionnaires

The pain and disability questionnaire results are presented in Figure 1. In the intervention group, back pain did not change whereas it increased statistically significantly in the control group (group x time p=0.030). Pain-related disability increased over time in both groups (time p=0.017), but no statistically significant between-group differences in the changes in pain-related disability or ODI were observed.

Paraspinal muscle FF and GU

Transversospinal FF was higher in the control group throughout the study (p=0.011), but no statistically significant changes were observed in paraspinal muscle FF or GU in either group (Figure 2).

Explorative analyses

As previously done (12,18), when the study group was divided according to the measured changes in SB or daily steps no statistically significant changes in any pain-related outcomes were observed (group x time p>0.05 for all; data not shown). Furthermore, no statistically significant differences were observed in paraspinal muscle FF or GU when the group was divided according to the measured change in SB (group x time p>0.05 for all; data not shown). However, with the step-based groups (i.e., an increase of >2500 steps/day vs. <2500 steps/day increase, or decrease), the changes in erector spinae and transversospinal GU were statistically significantly different between groups in favor of the more active group (group x time p=0.033) (Supplementary Figure 2).

In the whole study group, the changes in BMI, body fat percentage, and body mass correlated positively with the change in ODI (Table 2). None of the changes in PA or SB correlated with the changes in pain-related outcomes. The change in BMI correlated negatively with the change in erector spinae and transversospinal GU (r_s=-0.34 and -0.40, respectively). In line with the analyses based on high vs. low step count increase, the changes in steps correlated positively with the changes in paraspinal muscle GU but not with the changes in FF.

DISCUSSION

In the present study, we show that an intervention aimed at reducing SB by 1 h/day for six months may prevent the worsening of back pain intensity which was observed in the control group. However, the change in back pain intensity was not associated with changes in paraspinal muscle (i.e., erector spinae or transversospinales) FF, GU, or the changes in PA, SB, pain-related disability, or ODI score. Additionally, no intervention effects on paraspinal muscle FF or GU were observed, although increases in daily steps associated with improved paraspinal muscle GU.

Pain and physical behaviours

In this study, back pain intensity increased by about two-fold in the control group, on average. Although the baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS in the intervention and control groups, respectively), the change in the control group represents a substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain intensity are achieved. However, we did not observe any intervention effects on pain-related disability or ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This might be explained by the relatively low pain intensity that might not be severe enough to cause disability.

The reason for back pain intensity increase in the control group remains elusive. One explanation for the increase could be related to the open-label nature of this study. Although not formally documented, many control participants were disappointed to be included in the control group instead of the intervention group. These negative emotions may have affected pain intensity (22). This phenomenon, in conjunction with the possible benefits from the increased PA in the intervention group, could explain the difference between groups. The fact that the explorative analyses with SB or step-based *post hoc* group divisions showed no between-group differences in pain-related outcomes further emphasizes that the sole allocation to either intervention or control group may have affected the perception of pain. However, the cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the cross-sectional correlations and the correlations of changes during the study suggest that maintaining a healthier body composition could decrease disability, as body fat percentage correlated positively with the ODI score (see Table 2 and Supplementary Table 1).

Contrary to our results, a previous six-month randomized controlled trial involving adults with low back pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity measured using VAS did not differ between groups in the study (5). The study sample was comparable to ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, the aforementioned study did not aim to change only SB but also included behavioral counseling in the self-management of pain. Furthermore, the reduction in SB was notably higher in the previous study compared to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. Additionally, the intensity of longstanding pain might not always be related to the disability (23).

As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with pain-related disability at baseline in our study (3). However, no correlation between the change in standing time and the change in pain-related disability was observed. Related to this finding, a recent randomized controlled trial observed that, within three months, increasing occupational standing may increase multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer present (4). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that standing may exacerbate pain acutely, but habitual standing may not be detrimental.

Paraspinal muscle FF and GU

We did not observe any intervention effects on either erector spinae or transversospinal FF. This finding is consistent with a recent systematic review of six intervention studies, concluding that paraspinal FF cannot be reduced even with exercise training (24). This demonstrates that even though paraspinal muscle FF is strongly associated with back pain (7–9), successful back pain prevention or treatment can be independent of FF. This may be explained in part by the effect of time, i.e., age, which correlated with paraspinal FF (r_s=0.55 and 0.53 for transversospinal and erector spinae FF; see Supplementary Table 1) and was a significant contributor in the linear models investigating paraspinal FF ($p<0.001$ for both muscle groups) in this study. In accordance, the effectiveness of back pain rehabilitation is not related to specific strength or mobility goals of the rehabilitation (25), emphasizing other than structural aspects in treating experienced pain and disability. Therefore, back pain risk factors (such as paraspinal muscle FF) should not be the direct targets of rehabilitation as much as the psychological and cognitive aspects of pain perception and the individual preferences for physical exercise (26). However, as lower paraspinal muscle FF associated with higher amounts of MVPA and lower body adiposity, the results suggest that maintaining healthy body composition and MVPA levels might help prevent fat infiltration of the paraspinal muscles.

We have previously reported the intervention effects on hamstrings and quadriceps femoris GU (12) which seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses revealed no intervention effects on any of these muscles. However, the secondary analyses of the present study and the previously published study show the association between increased PA (e.g., steps) and improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal muscle GU correlated with the changes in any pain-related outcomes (Table 2). Moreover, as paraspinal muscle GU but not FF was associated with steps, the results suggest that GU can improve despite no changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI correlated negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI.

Clinical implications

The present study highlights that clinicians should assess patients' SB habits and consider interventions to reduce SB if back pain is an issue. Furthermore, as observed before with strength or mobility goals for rehabilitation (25), the possible improvements in pain or disability seem to not be related to paraspinal muscle GU or FF.

Strengths and weaknesses

The strengths of this study include the robust measurement of PA, standing, and SB with accelerometers during the whole six-month study. Moreover, the accelerometer data was analyzed using validated algorithms (19,20). Furthermore, the ODI is a validated questionnaire (16), and VAS is commonly used for pain assessment, and it associates with functional outcomes (27). However, a weakness in this study is the use of non-validated questions with the VAS. Another key strength is the muscle specific GU assessment with the HEC protocol combined with FDG-PET imaging (28). Further, the two-point Dixon is a highly reproducible method for FF assessment (29).

One limitation of the present study is the sample size. For the GU assessments, the sample size was likely adequate (12), but as the pain-related outcomes were not the primary outcomes of the whole trial, the statistical power might have been inadequate. Additionally, the study sample was not chosen based on pain status which may have increased heterogeneity in the sample, and thus decreased the statistical power.

Conclusion

An intervention aimed at reducing SB by 1 h/day for six months may prevent increases in back pain intensity in adults with metabolic syndrome and physical inactivity. However, this effect does not seem to be related to paraspinal muscle insulin sensitivity or fat infiltration. Instead, increasing daily step count may lead to improved paraspinal muscle insulin sensitivity.

Author contributions

I.H., K.K., T.Va. and T.S. conception and design of the study. T.S., S.L., T.G., K.L. and N.H. acquisition of data. T.S., J.N., H.V-Y., H.S., T.G., S.L., T.Ve., V.S., J.H., E.L. and I.H. analysis and interpretation of data. J.N. drafted the manuscript and all authors edited and revised the manuscript. All authors approved the final version of the manuscript.

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Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The other authors report no conflicts of interest. The results are presented clearly and honestly without fabrication, falsification, or inappropriate data manipulation.

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Figure legends

Figure 1. Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. VAS = visual analogue scale. *=Tukey's p=0.026

Figure 2. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are

adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

Table 1. Study participant characteristics at the baseline. Unless otherwise stated, the results are presented as mean (SD).

	Intervention	n	**Control**	n
Men, n (%)	13 (39)	33	14 (45)	31
Age, yrs	59 (6)	33	57 (8)	31
Anthropometrics & metabolism				
BMI, kg/m^2	31.5 (4.0)	33	31.7 (4.6)	31
Body fat, %	43.1 (8.0)	33	43.1 (8.0)	31
Waist circumference, cm	111.1 (11.6)	33	110.7 (11.1)	31
fP-Glucose, mmol/l	5.9 (0.5)	33	5.8 (0.4)	31
fP-Insulin, mU/l *	9 (7, 13)	33	11 (7, 17)	30
HbA1c, mmol/l	37.0 (2.8)	33	36.3 (2.7)	31
Transversospinal FF, %*	23.7 (15.6, 33.8)	22	23.8 (19.6, 34.0)	21
Erector spinae FF, %*	17.5 (13.3, 26.8)	22	18.0 (14.4, 23.4)	21
Transversospinal GU, µmol/100 cm^3/min*	2.8 (2.3, 3.2)	23	2.5 (2.0, 3.3)	20
Erector spinae GU, µmol/100 cm^3/min*	2.9 (2.0, 3.3)	23	2.4 (1.9, 3.9)	20
QF GU, µmol/100 cm^3/min*	2.0 (1.4, 2.7)	23	1.9 (1.2, 3.2)	20
Hamstring GU, µmol/100 cm^3/min*	3.0 (2.0, 4.6)	23	2.8 (1.4, 4.0)	20
Whole-body GU, µmol/kg /min*	15.3 (10.7, 21.0)	33	13.9 (9.8, 21.0)	31
Pain & disability				
Regular medication for pain, n (%)	3 (9)	33	4 (13)	31
VAS Back pain, 0-10 cm*	0.3 (0.1, 3.5)	33	0.5 (0.1, 3.0)	29
VAS Pain-related disability, 0-10 cm*	0.4 (0.1, 2.2)	33	0.7 (0.2, 2.6)	30
Oswestry disability index, %*	6.0 (1.0, 13.0)	33	6.7 (2.0, 16.0)	31
Physical activity				
Accelerometry, h/day	14.5 (1.0)	33	14.6 (1.0)	31
Sedentary time, h/day	10.0 (0.9)	33	10.1 (1.1)	31
Standing time, h/day	1.8 (0.6)	33	1.8 (0.6)	31
LPA, h/day	1.7 (0.4)	33	1.8 (0.5)	31
MVPA, h/day	0.96 (0.31)	33	0.97 (0.34)	31
Breaks in sedentary time, n/day	28 (8)	33	29 (8)	31
Steps, n/day	5204 (1910)	33	5091 (1760)	31

BMI, Body mass index; FF, fat fraction; GU, insulin-stimulated glucose uptake; QF, Quadriceps femoris muscle; fP-Glucose, fasting plasma glucose; fP-Insulin, fasting plasma insulin; HbA1c, glycated hemoglobin; VAS, visual analogue scale; LPA, light physical activity; MVPA moderate to vigorous physical activity. * presented as median (Q1, Q3).

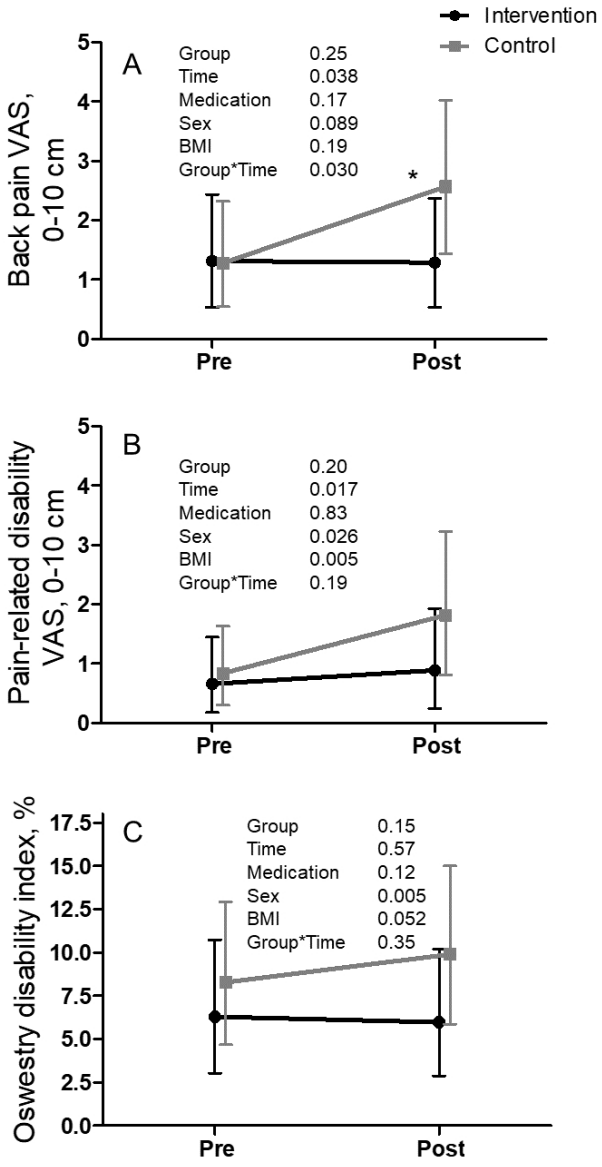
Table 2. Spearman's rank correlation coefficients between changes (Δ values) in the measured outcomes before and after the 6-month intervention period.

	Δ ES FF	Δ Tra. GU	Δ ES GU	Δ QF GU	Δ Ham. GU	Δ WB GU	Δ BMI	Δ WC	Δ Body fat %	Δ Weight	Δ Glucose	Δ Insulin	Δ HbA1c	Δ SB%	Δ Standing%	Δ LPA%	Δ PA%	Δ Steps	Δ Breaks in SB	Δ BP	Δ PRD	Δ ODI
Δ Tra. FF	0.55 **	0.16	0.10	0.43 *	0.18	0.04	-0.20	-0.18	0.15	-0.23	0.08	-0.26	-0.41 *	0.00	-0.01	-0.02	0.02	0.05	-0.03	-0.06	0.22	0.06
Δ ES FF	1	0.03	0.05	0.15	0.22	-0.04	-0.04	-0.18	0.02	-0.08	-0.15	-0.12	-0.29	-0.11	0.12	0.07	0.13	0.22	0.24	-0.11	0.17	-0.05
Δ Tra. GU		1	0.91 **	0.56 **	0.70 **	0.72 **	-0.40 *	-0.12	-0.32	-0.38 *	-0.11	-0.20	-0.05	-0.25	0.10	0.22	0.33	0.39 *	0.12	-0.07	0.21	0.03
Δ ES GU			1	0.49 **	0.82 **	0.76 **	-0.34 *	-0.15	-0.33	-0.32	-0.17	-0.19	-0.05	-0.30	0.22	0.20	0.29	0.41 *	0.05	0.04	0.26	0.07
Δ QF GU				1	0.67 **	0.47 **	-0.45 **	-0.04	-0.09	-0.45 **	0.08	-0.18	-0.33 *	-0.41 *	0.19	0.42 *	0.50 **	0.42 *	0.06	0.04	0.03	-0.17
Δ Ham. GU					1	0.77 **	-0.46 **	-0.26	-0.27	-0.45 **	-0.06	-0.19	-0.14	-0.53 **	0.39 *	0.39 *	0.48 **	0.52 **	0.16	0.08	0.20	0.05
Δ WB GU						1	-0.53 **	-0.33 *	-0.08	-0.53 **	-0.28 *	-0.30 *	-0.06	-0.41 **	0.32 *	0.32 *	0.36 **	0.30 *	0.14	-0.14	-0.13	-0.12
Δ BMI							1	0.47 **	0.29 *	1.0**	0.15	0.29 *	0.33 *	0.35 *	-0.22	-0.31 *	-0.35 *	-0.36 **	-0.24	0.10	0.19	0.37 **
Δ WC								1	0.16	0.47 **	0.09	0.24	0.17	0.21	0.02	-0.24	-0.31 *	-0.28	-0.16	0.05	0.09	0.13

Δ Body fat %									1	0.28*	-0.04	-0.04	0.18	0.12	-0.17	0.08	-0.09	0.02	-0.29*	-0.13	-0.05	0.18	0.26*
Δ Weight										1	0.15	0.31*	0.35**	0.37**	-0.24	-0.32*	-0.20	-0.36**	-0.36**	-0.25	0.08	0.16	0.35**
Δ Glucose											1	0.27*	0.10	-0.07	0.18	-0.09	-0.10	-0.14	-0.23	0.17	0.00	-0.15	
Δ Insulin												1	0.24	0.23	-0.22	-0.21	-0.19	-0.21	-0.16	-0.17	-0.25	-0.05	
Δ HbA1c													1	0.21	0.00	-0.12	-0.26	-0.41**	-0.28*	0.04	-0.02	0.14	
Δ SB%														1	-0.76**	-0.66**	-0.77**	-0.60**	-0.37**	-0.08	-0.05	0.21	
Δ Standing %															1	0.21	0.24	0.30*	0.15	0.22	0.06	-0.15	
Δ LPA %																1	0.87**	0.44**	0.34*	0.10	0.09	-0.10	
Δ MVPA%																	0.81**	0.73**	0.44**	-0.10	-0.07	-0.24	
Δ PA%																	1	0.64**	0.41**	-0.10	-0.08	-0.23	

Δ Steps																	1	0.57**	-0.07	-0.11	-0.26
Δ Breaks in SB																		1	0.07	0.10	0.04
Δ BP																			1	0.67**	0.48**
Δ PRD																				1	0.61**

Δ Change in the measured outcome, Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05, **significant at the level of p<0.01.



Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain intensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026

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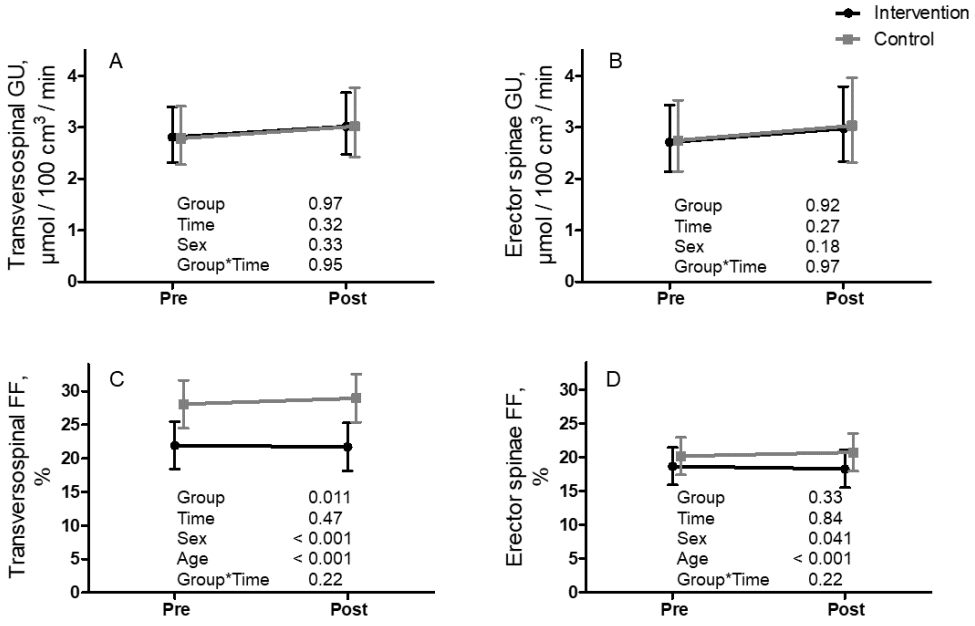

Figure 2. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

732x479mm (38 x 38 DPI)

Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: A six-month randomized controlled trial

Supplementary file

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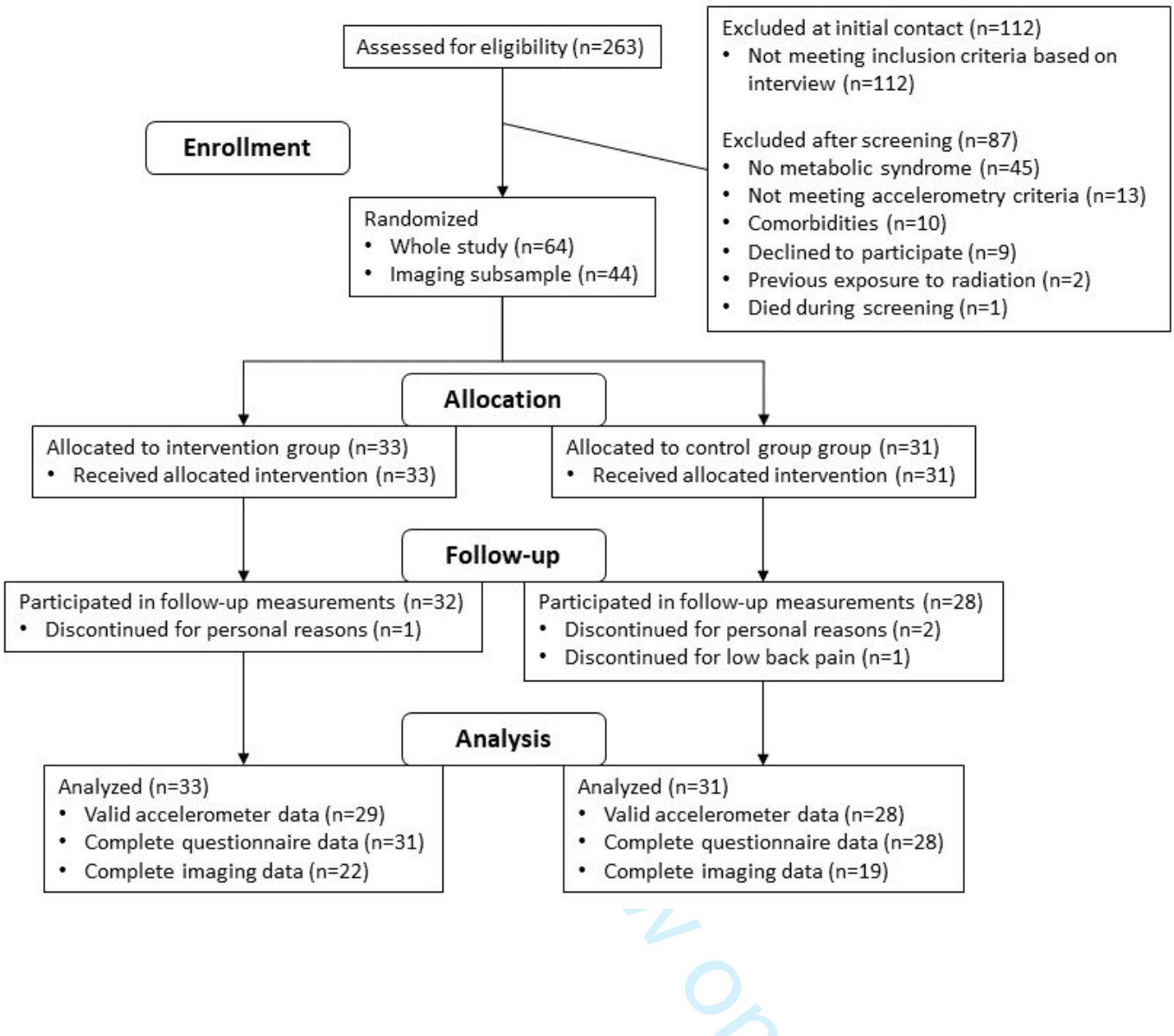
Supplementary Figure 1. Study flow diagram.

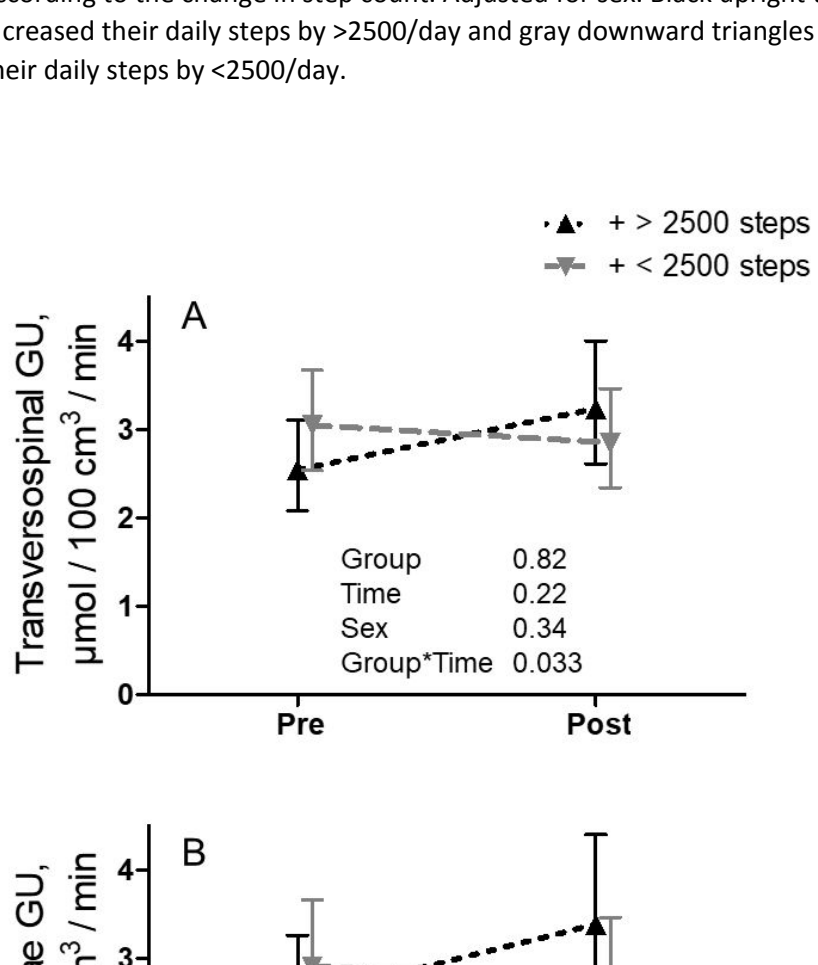


Supplementary Table 1. Baseline Spearman's rank correlation coefficients

	Tra. FF	ES FF	Tra. GU	ES GU	QF GU	Ham. GU	WB GU	BMI	WC	Body fat %	Weight	Glucose	Insulin	HbA1c	SB %	Standing %	LPA %	MVPA %	PA %	Steps /day	Breaks	BP	PRD	ODI
Age	0.55**	0.53**	-0.01	0.00	-0.02	-0.04	0.04	-0.04	0.06	0.03	-0.12	-0.01	-0.06	0.23	0.07	-0.09	0.09	-0.25*	-0.07	-0.26*	-0.01	0.10	0.02	0.12
Tra. FF	1	0.79**	-0.14	-0.10	0.02	-0.04	0.06	0.15	0.15	0.37*	-0.01	-0.15	-0.15	0.15	0.00	0.08	0.17	-0.36*	-0.11	-0.27	0.0	0.11	0.07	0.19
ES FF		1	-0.24	-0.22	-0.06	-0.10	-0.09	0.24	0.26	0.39*	0.12	0.00	0.04	0.20	0.07	-0.05	0.13	-0.30*	-0.05	-0.27	-0.0	-0.05	-0.09	0.06
Tra. GU			1	0.90**	0.69**	0.71**	0.67**	-0.41**	-0.54**	-0.13	-0.45**	-0.48**	-0.54**	-0.49**	-0.28	0.28	0.01	0.42**	0.24	0.44*	-0.1	-0.04	-0.14	-0.23
ES GU				1	0.79**	0.84**	0.85**	-0.51**	-0.69**	-0.18	-0.52**	-0.36*	-0.65**	-0.54**	-0.31*	0.28	0.10	0.36*	0.30	0.40*	-0.1	-0.04	-0.18	-0.24
QF GU					1	0.92**	0.86**	-0.47**	-0.67**	-0.10	-0.48**	-0.26	-0.65**	-0.43**	-0.42**	0.43**	0.15	0.28	0.28	0.33*	-0.1	-0.11	-0.13	-0.23
Ham. GU						1	0.93**	-0.53**	-0.72**	-0.19	-0.56**	-0.27	-0.68**	-0.48**	-0.46**	0.45**	0.21	0.34*	0.35*	0.36*	-0.1	-0.07	-0.08	-0.21
WB GU							1	-0.53**	-0.71**	-0.12	-0.60**	-0.34**	-0.69**	-0.29*	-0.43**	0.46**	0.19	0.18	0.23	0.30*	-0.1	0.07	0.03	-0.10
BMI								1	0.76**	0.54**	0.80**	0.15	0.61**	0.08	0.29*	-0.16	-0.09	-0.26*	-0.23	-0.37*	0.04**	0.00	-0.02	0.15
WC									1	0.23	0.80**	0.25*	0.64**	0.26*	0.38**	-0.31*	-0.17	-0.32*	-0.29*	-0.42*	0.06**	-0.03	0.00	0.08
BF %										1	0.11	-0.17	0.15	0.05	0.02	0.21	0.13	-0.29*	-0.09	-0.28*	0.0	0.18	0.16	0.33**
Weight											1	0.27*	0.68**	0.17	0.40**	-0.35**	-0.24	-0.18	-0.28*	-0.33*	-0.1*	-0.13	-0.12	-0.01
Glucose												1	0.24	0.12	0.06	-0.32**	0.17	0.10	0.16	0.01	-0.0	-0.15	-0.16	-0.14
Insulin													1	0.25*	0.41**	-0.49**	-0.15	-0.11	-0.19	-0.26*	-0.0*	-0.16	-0.08	0.06
HbA1c														1	0.14	-0.18	0.10	-0.10	-0.01	-0.10	-0.06	0.01	-0.07	0.10
SB															1	-0.79**	-0.62**	-0.55**	-0.75**	-0.54*	-0.06**	0.03	-0.19	0.07
Standing																1	0.28*	0.19	0.30*	0.22	0.2	0.06	0.27*	0.06
LPA																	1	0.28*	0.83**	0.21	0.1**	0.06	0.04	-0.03
MVPA																		1	0.73**	0.93*	0.1*	-0.20	-0.03	-0.28*
PA																			1	0.65*	0.2**	-0.09	-0.01	-0.21
Steps																				1	0.2*	-0.18	-0.03	-0.26*
Breaks																					1	0.09	0.14	-0.04
BP																						1	0.61**	0.71**
PRD																							1	0.71**

Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05. **significant at the level of p<0.01.

Supplementary Figure 2. Changes in A) transversospinal glucose uptake (GU) and B) erector spinae GU according to the change in step count. Adjusted for sex. Black upright triangles represent the group that increased their daily steps by >2500/day and gray downward triangles represent the group that increased their daily steps by <2500/day.



Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

Design and conduct			
1. Clear description of the goal of research, study objective(s), study design, and study population	Yes	Unclear	No
2. Clear description of outcomes, exposures/treatments and covariates, and their measurement methods	Yes	Unclear	No
3. Validity of study design	Yes	Unclear	No
4. Clear statement and justification of sample size	Yes	Unclear	No
5. Clear declaration of design violations and acceptability of the design violations	Yes	Unclear	No
6. Consistency between the paper and its previously published protocol	Yes	Unclear	No
Data analysis			
7. Correct and complete description of statistical methods	Yes	Unclear	No
8. Valid statistical methods used and assumptions outlined	Yes	Unclear	No
9. Appropriate assessment of treatment effect or interaction between treatment and another covariate	Yes	Unclear	No
10. Correct use of correlation and associational statistical testing	Yes	Unclear	No
11. Appropriate handling of continuous predictors	Yes	Unclear	No
12. Confidence intervals do not include impossible values	Yes	Unclear	No
13. Appropriate comparison of baseline characteristics between the study arms in randomized trials	Yes	Unclear	No
14. Correct assessment and adjustment of confounding	Yes	Unclear	No
15. Avoiding model extrapolation not supported by data	Yes	Unclear	No
16. Adequate handling of missing data	Yes	Unclear	No
Reporting and presentation			
17. Adequate and correct description of the data	Yes	Unclear	No
18. Descriptive results provided as occurrence measures with confidence intervals, and analytic results provided as association measures and confidence intervals along with P-values	Yes	Unclear	No
19. Confidence intervals provided for the contrast between groups rather than for each group	Yes	Unclear	No
20. Avoiding selective reporting of analyses and P-hacking	Yes	Unclear	No
21. Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, and reporting the P-values rather their range	Yes	Unclear	No
22. Providing sufficient numerical results that could be included in a subsequent meta-analysis	Yes	Unclear	No
23. Acceptable presentation of the figures and tables	Yes	Unclear	No
Interpretation			
24. Interpreting the results based on association measures and 95% confidence intervals along with P-values, and correctly interpreting large P-values as indecisive results, not evidence of absence of an effect	Yes	Unclear	No
25. Using confidence intervals rather than post-hoc power analysis for interpreting the results of studies	Yes	Unclear	No
26. Correctly interpreting occurrence or association measures	Yes	Unclear	No
27. Distinguishing causation from association and correlation	Yes	Unclear	No
28. Results of pre-specified analyses are distinguished from the results of exploratory analyses in the interpretation	Yes	Unclear	No
29. Appropriate discussion of the study methodological limitations	Yes	Unclear	No
30. Drawing only conclusions supported by the statistical analysis and no generalization of the results to subjects outside the target population	Yes	Unclear	No

Mansournia MA, *et al. Br J Sports Med* 2021; 55:1–2. doi: 10.1136/bjsports-2020-10365

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	1	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	4	
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	4-6	
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	5-6	
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	-	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	5-6	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	4	

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	4, 5	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	4-5	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	5-6	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	7	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

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Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: Secondary analysis of a six-month randomized controlled trial

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Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: Secondary analysis of a six-month randomized controlled trial

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ABSTRACT

Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF).

Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain-related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance imaging.

Results Pain-related disability increased during the intervention in both groups. Back pain intensity increased significantly more in the control group than in the intervention group in which back pain intensity remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain-related disability, ODI, or paraspinal GU and FF were observed. In the whole study group, the change in daily steps associated positively with the change in paraspinal muscle GU.

Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening regardless of paraspinal muscle GU or FF.

Strengths and limitations of this study

- The strengths of this study include the randomized controlled study design and the use of accelerometers to monitor physical activities and sedentary behaviours throughout the six-month study.
- Moreover, the imaging modalities (positron emission tomography with hyperinsulinemic-euglycemic clamp for muscle-specific insulin resistance and magnetic resonance imaging for muscle-specific fat fraction) may be considered as the gold standard measures.
- However, this is a secondary analysis of the whole study, and thus the power calculations were not done for back pain or disability.
- Further, no specific back pain related eligibility criteria were applied.

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INTRODUCTION

Physical activity (PA) associates with a decreased risk for low back pain (1,2). Conversely, observational studies suggest an association between high sedentary behaviour (SB) and increased low back pain or pain-related disability (1,3). A meta-analysis of 16 longitudinal studies reported that higher SB associated with higher pain-related disability but not with back pain intensity (1). On the other hand, a meta-analysis of cross-sectional studies found a positive association between non-occupational and occupational SB and back pain (3). Moreover, we have previously observed cross-sectionally that higher SB associated with lower pain-related disability (4). Thus, it is clear that the observational evidence is mixed. However, different study settings (i.e., cross-sectional or longitudinal) represent different time frames and the possibility of reverse causality cannot be ruled out.

Previous three to six-month interventional studies among fifty-year-old office workers suggest that reducing SB might improve pain-related disability without affecting back pain intensity (5,6). However, the mechanisms by which SB modification could affect back pain or disability remain poorly understood.

Insulin resistance and fatty infiltration of the paraspinal muscles associate with back pain (7–11) and successfully reducing SB improves muscle insulin sensitivity (12). Moreover, lower levels of PA associate with higher fat content of the transversospinal muscles (13). Taken together, these findings make SB a plausible target for an intervention to maintain or improve back health.

Thus, we aimed to investigate the effects of a six-month SB reduction intervention on back pain, disability, and paraspinal muscle FF and insulin sensitivity (glucose uptake, GU). Additionally, we assessed the back pain related factors cross-sectionally.

METHODS

This study consists of secondary analyses of a six-month randomized controlled trial that was conducted at the Turku PET Centre (Turku, Finland) between April 2017 and March 2020 (Clinicaltrials.gov NCT03101228, 05/04/2017). The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study (16/1801/2017). All participants gave their informed consent before entering the study, and the study was conducted according to the Declaration of Helsinki.

Participants

As reported earlier (12,14), volunteers were recruited from the community. Inclusion criteria were: age 40–65 years, body mass index (BMI) 25–40 kg/m^2, self-reported physical inactivity (<120 min/week of moderate-to-vigorous physical activity [MVPA]), accelerometer-measured sedentary time ≥10 h or ≥60 % of

accelerometer wear time, and metabolic syndrome (15). Exclusion criteria included diagnosed diabetes or fasting blood glucose ≥7.0 mmol/l, abundant alcohol consumption according to the national guidelines, the use of any tobacco products, diagnosed depressive or bipolar disorder, inability to understand written Finnish, and any condition that would endanger the participant or study procedures (e.g., previous exposure to ionizing radiation).

Measurements

Back pain intensity and pain-related disability were assessed by two questions and 10-cm visual analogue scales (VAS): 1) Have you had back pain within the last month? Mark the intensity of the worst perceived pain during the month on the line below; and 2) Has the perceived pain caused you disability at your work or everyday tasks within the last month? Mark the intensity of the greatest extent of disability that you experienced during the month on the line below. A higher value (0–10 cm) indicates higher pain intensity and disability. Additionally, back pain-related disability was assessed using the Oswestry disability index (ODI), which provides a value of 0–100%, and a higher value represents higher disability (16).

Paraspinal muscle (i.e., erector spinae and transversospinales) FF was assessed using the two-point Dixon magnetic resonance (MR) imaging method (Philips 3T Ingenuity TF, Philips Healthcare, Amsterdam, The Netherlands and Siemens Magnetom Skyra Fit 3T system, Siemens Healthcare, Erlangen, Germany) (17). Paraspinal muscle GU was measured using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET; GE D690 PET/CT, GE Healthcare, Milwaukee, WI) during hyperinsulinemic euglycemic clamp (HEC) as described previously (12,18). Both the FF and GU were analyzed separately for the transversospinal and erector spinae muscles at the level of L3-4. The measurements were performed using Carimas (version 2.10, https://www.carimas.fi).

PA and SB were measured using accelerometers for four weeks during screening (UKK AM30, UKK Terveyspalvelut Oy, Tampere, Finland) to determine the baseline values and throughout the six-month intervention period (Movesense, Suunto, Vantaa, Finland, with ExSed application, UKK Terveyspalvelut Oy, Tampere, Finland) to monitor and facilitate behaviour change. The accelerometer variables during the intervention period were analyzed as means over the whole six-month period. The participants were advised to wear the device on the right hip during waking hours (except when the device could be exposed to water) and remove it when sleeping at night. Accelerometer weartime of 10–19 h/day was considered valid, and measurement exceeding 19 h/day was substracted from SB. The accelerometer data was analyzed using six-second epochs, and the raw acceleration data was analyzed using the mean amplitude deviation (to assess sedentariness, light PA [LPA], and moderate-to-vigorous PA [MVPA]) and angle for posture estimation (to differentiate SB and standing) methods as described previously (4,18–20).

Height was measured using a wall-mounted stadiometer, and body mass and body fat percentage were measured by air displacement plethysmography (Cosmed USA, Concord, CA) after at least four hours of fasting. Waist circumference was measured using a measuring tape midway between the lowest rib and the iliac crest. Pain medication use was self-reported by the participants and categorized into using medication or not.

Intervention

After the screening, eligible volunteers were randomized into the intervention and control groups in a 1:1 ratio by a statistician using random permuted block randomization (block size 44) in SAS (version 9.4 for Windows, SAS Institute, Inc., Cary, NC). The randomization was performed for men and women separately.

As described in more detail previously (18), participants in the intervention group were advised to reduce their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by subtracting 1 h of SB from the amount during screening. Correspondingly, 1 h was added to standing, LPA, and MVPA goals distributing the time based on individual preferences. However, a maximum of 20 minutes was added to MVPA, and increasing intentional physical exercise training was discouraged. The ways for replacing SB were discussed individually and included, for example, using standing desks, taking the stairs instead of the lift, and lightly walking. For the control group, the daily SB and PA goals were set equal to the screening values. All participants could monitor their daily SB and PA and the fulfilment of the goals using a mobile phone application (ExSed) connected to the accelerometer.

Patient involvement

Patients were not involved in designing or conducting this study.

Equity, diversity and inclusion

Both the study participants and researchers include self-identified men and women in a relatively balanced fashion. The research group consists of both junior and senior researchers.

Statistical methods

Baseline characteristics are presented as mean (standard deviation, SD) if not stated otherwise. Intervention effects are presented as model-based mean (95% confidence interval, 95% CI). Baseline correlations were analyzed using the Spearman rank correlation. The main analyses of intervention effects were performed using linear mixed models for repeated measurements. The outcome of interest was the dependent variable, and independent variables included group, time, sex, and group x time in all analyses. Random intercepts for individual effect was also included. Additionally, FF analyses were adjusted for age, and pain questionnaire analyses were adjusted for self-reported regular pain medication status (yes/no)

and BMI, because this improved the distribution of the residuals. The normal distribution of the residuals was visually inspected, and log10 or square root transformations were performed as necessary. Tukey-Kramer adjustment for multiple comparisons was used. Compound symmetry or unstructured covariance structure was chosen based on the Akaike information criterion. Statistical significance was set at $p<0.05$ (two-tailed). The main analyses were performed in SAS (version 9.4 for Windows, SAS Institute Inc., Cary, NC) and the correlation analyses were performed using JMP Statistics (version 16, SAS Institute Inc., Cary, NC).

The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming an increase of 0.7 (SD 0.55) µmol/100g/min in the intervention group (10% increase) and an increase of 0.05 µmol/100g/min in the control group, we calculated that 16 participants per group would be sufficient for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity ($\alpha=0.05$, $1-\beta=0.9$). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin sensitivity would behave similar to quadriceps femoris and thus, the study would be sufficiently powered to detect statistically significant changes in paraspinal muscle insulin sensitivity.

RESULTS

Baseline characteristics

Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and MR imaging. The baseline characteristics are presented in Table 1.

Baseline correlations

All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated positively with erector spinae and transversospinal FF (r_s=0.53, 0.55, respectively). Erector spinae GU correlated positively with MVPA and step count (r_s=0.36 and 0.40, respectively) and negatively with SB (r_s=-0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s=0.42 and 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and

transversospinal FF correlated with MVPA (r_s=-0.30 and -0.36, respectively). Increased body adiposity (BMI and body fat percentage) associated with lower paraspinal muscle GU and higher FF.

Pain-related disability correlated positively with standing time (r_s=0.27). Furthermore, the ODI score correlated negatively with MVPA (r_s=-0.28) and step count (r_s=-0.26). Finally, the ODI score correlated positively with body fat percentage (r_s=0.33). Back pain intensity did not correlate with any PA, SB, or paraspinal muscle-related variables.

Intervention effects

Accelerometry

The intervention effects on SB and PA have been reported previously (18). In comparison to the control group, the intervention group reduced their SB by 40 min/day and subsequently increased their MVPA by 20 min/day, on average over the six-month intervention period; no statistically significant changes were observed in the control group. LPA increased by 10 min/day in both groups without statistically significant between-group differences. No statistically significant changes in standing time or the number of breaks in SB were observed in either group. Step count increased in both groups but the increase was statistically significantly higher in the intervention group (from 5150 to 6749 steps/day in the control group vs. 5326 to 8632 steps/day in the intervention group).

Pain and disability questionnaires

The pain and disability questionnaire results are presented in Figure 1, and the changes in each participant's back pain by group are presented in Figure 2. In the intervention group, back pain did not change whereas it increased statistically significantly in the control group (group x time p=0.030). Pain-related disability increased over time in both groups (time p=0.017), but no statistically significant between-group differences in the changes in pain-related disability or ODI were observed.

Paraspinal muscle FF and GU

Transversospinal FF was higher in the control group throughout the study (p=0.011), but no statistically significant changes were observed in paraspinal muscle FF or GU in either group (Figure 3).

Explorative analyses

As previously done (12,18), when the study group was divided according to the measured changes in SB or daily steps no statistically significant changes in any pain-related outcomes were observed (group x time p>0.05 for all; data not shown). Furthermore, no statistically significant differences were observed in paraspinal muscle FF or GU when the group was divided according to the measured change in SB (group x time p>0.05 for all; data not shown). However, with the step-based groups (i.e., an increase of >2500

steps/day vs. <2500 steps/day increase, or decrease), the changes in erector spinae and transversospinal GU were statistically significantly different between groups in favour of the more active group (group x time p=0.033) (Supplementary Figure 2).

In the whole study group, the changes in BMI, body fat percentage, and body mass correlated positively with the change in ODI (r_s=0.37, 0.26, and 0.35, respectively; Table 2). None of the changes in PA or SB correlated with the changes in pain-related outcomes. The change in BMI correlated negatively with the change in erector spinae and transversospinal GU (r_s=-0.34 and -0.40, respectively). In line with the analyses based on high vs. low step count increase, the changes in steps correlated positively with the changes in paraspinal muscle GU (r_s=0.39 and 0.41 for the transversospinales and erector spinae, respectively) but not with the changes in FF.

DISCUSSION

In the present study, we show that an intervention aimed at reducing SB by 1 h/day for six months may prevent the worsening of back pain intensity which was observed in the control group. However, the change in back pain intensity was not associated with changes in paraspinal muscle (i.e., erector spinae or transversospinales) FF, GU, or the changes in PA, SB, pain-related disability, or ODI score. Additionally, no intervention effects on paraspinal muscle FF or GU were observed, although increases in daily steps associated with improved paraspinal muscle GU.

Pain and physical behaviours

In this study, back pain intensity increased by about two-fold in the control group, on average. Although the baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS in the intervention and control groups, respectively), the change in the control group represents a substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain intensity are achieved. However, we did not observe any intervention effects on pain-related disability or ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This might be explained by the relatively low pain intensity that might not be severe enough to cause disability.

The reason for back pain intensity increase in the control group remains elusive. One explanation for the increase could be related to the open-label nature of this study. Although not formally documented, many control participants were disappointed to be included in the control group instead of the intervention group. These negative emotions may have affected pain intensity (22). This phenomenon, in conjunction with the possible benefits from the increased PA in the intervention group, could explain the difference between groups. The fact that the explorative analyses with SB or step-based *post hoc* group divisions

showed no between-group differences in pain-related outcomes further emphasizes that the sole allocation to either intervention or control group may have affected the perception of pain. However, the cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the cross-sectional correlations and the correlations of changes during the study suggest that maintaining a healthier body composition could decrease disability, as body fat percentage correlated positively with the ODI score (see Table 2 and Supplementary Table 1).

Contrary to our results, a previous six-month randomized controlled trial involving adults with low back pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity measured using VAS did not differ between groups in the study (5). The study sample was comparable to ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, the aforementioned study did not aim to change only SB but also included behavioural counselling in the self-management of pain. Furthermore, the reduction in SB was notably higher in the previous study compared to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. Additionally, the intensity of longstanding pain might not always be related to the disability (23).

It should be acknowledged that back pain is often a recurring and varying, and sometimes a longstanding complaint (24). For this reason, future studies should assess pain and disability more frequently than only at baseline and at the end of the intervention, as in the current study. However, the six-month duration of this study should be sufficient to reveal the effects of a SB reduction intervention, as in a previous study the ODI score tended to decrease up until three months before plateauing (5).

As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with pain-related disability at baseline in our study (4). However, no correlation between the change in standing time and the change in pain-related disability was observed. Related to this finding, a recent randomized controlled trial observed that, within three months, increasing occupational standing may increase multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer present (25). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that standing may exacerbate pain acutely, but habitual standing may not be detrimental.

Paraspinal muscle FF and GU

We did not observe any intervention effects on either erector spinae or transversospinal FF. This finding is consistent with a recent systematic review of six intervention studies, concluding that paraspinal FF cannot

be reduced even with exercise training (26). This demonstrates that even though paraspinal muscle FF is strongly associated with back pain (7–9), successful back pain prevention or treatment can be independent of FF. This may be explained in part by the effect of time, i.e., age, which correlated with paraspinal FF (r_s=0.55 and 0.53 for transversospinal and erector spinae FF; see Supplementary Table 1) and was a significant contributor in the linear models investigating paraspinal FF (p<0.001 for both muscle groups) in this study. In accordance, the effectiveness of back pain rehabilitation is not related to specific strength or mobility goals of the rehabilitation (27), emphasizing other than structural aspects in treating experienced pain and disability. Therefore, back pain risk factors (such as paraspinal muscle FF) should not be the direct targets of rehabilitation as much as the psychological and cognitive aspects of pain perception and the individual preferences for physical exercise (28). However, as lower paraspinal muscle FF associated with higher amounts of MVPA and lower body adiposity, the results suggest that maintaining healthy body composition and MVPA levels might help prevent fat infiltration of the paraspinal muscles.

We have previously reported the intervention effects on hamstrings and quadriceps femoris GU (12) which seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses revealed no intervention effects on any of these muscles. However, the secondary analyses of the present study and the previously published study show the association between increased PA (e.g., steps) and improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal muscle GU correlated with the changes in any pain-related outcomes (Table 2). Moreover, as paraspinal muscle GU but not FF was associated with steps, the results suggest that GU can improve despite no changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI correlated negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI.

Clinical implications

The present study highlights that being in a SB reduction intervention which elicits changes to PA, standing, and SB might work as a protective strategy against back pain. Furthermore, as observed before with strength or mobility goals for rehabilitation (27), the possible improvements in pain or disability seem to not be related to paraspinal muscle GU or FF.

Strengths and weaknesses

The strengths of this study include the robust measurement of PA, standing, and SB with accelerometers during the whole six-month study. Moreover, the accelerometer data was analyzed using validated algorithms (19,20). Furthermore, the ODI is a validated questionnaire (16), and VAS is commonly used for pain assessment, and it associates with functional outcomes (29). However, a weakness in this study is the

use of non-validated questions with the VAS. Another key strength is the muscle specific GU assessment with the HEC protocol combined with FDG-PET imaging (30). Further, the two-point Dixon is a highly reproducible method for FF assessment (31).

One limitation of the present study is the sample size. For the GU assessments, the sample size was likely adequate (12), but as the pain-related outcomes were not the primary outcomes of the whole trial, the statistical power might have been inadequate. Additionally, the study sample was not chosen based on pain status which may have increased heterogeneity in the sample, and thus decreased the statistical power.

Conclusion

An intervention aimed at reducing SB by 1 h/day for six months may prevent increases in back pain intensity in adults with metabolic syndrome and physical inactivity. However, this effect does not seem to be related to paraspinal muscle insulin sensitivity or fat infiltration. Instead, increasing daily step count may lead to improved paraspinal muscle insulin sensitivity.

Author contributions

I.H., K.K., T.Va. and T.S. conception and design of the study. T.S., S.L., T.G., K.L. and N.H. acquisition of data. T.S., J.N., H.V-Y., H.S., T.G., S.L., T.Ve., V.S., J.H., E.L. and I.H. analysis and interpretation of data. J.N. drafted the manuscript and all authors edited and revised the manuscript. All authors approved the final version of the manuscript. I.H. acted as the guarantor.

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Data availability statement

Data are available upon reasonable request from the corresponding author.

Ethical approval

The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study (16/1801/2017).

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The other authors report no conflicts of interest. The results are presented clearly and honestly without fabrication, falsification, or inappropriate data manipulation.

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Figure legends

Figure 1. Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain intensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026

Figure 2. Changes in each participant's back pain during the intervention. Blue bars represent participants in the intervention group and red bars represent participants in the control group. Of the six participants

with no changes in back pain, four were in the intervention and two in the control group. A higher value indicates higher pain intensity. VAS = visual analogue scale.

Figure 3. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

Table 1. Study participant characteristics at the baseline. Unless otherwise stated, the results are presented as mean (SD).

	Intervention	n	**Control**	n
Men, n (%)	13 (39)	33	14 (45)	31
Age, yrs	59 (6)	33	57 (8)	31
Anthropometrics & metabolism				
BMI, kg/m^2	31.5 (4.0)	33	31.7 (4.6)	31
Body fat, %	43.1 (8.0)	33	43.1 (8.0)	31
Waist circumference, cm	111.1 (11.6)	33	110.7 (11.1)	31
fP-Glucose, mmol/l	5.9 (0.5)	33	5.8 (0.4)	31
fP-Insulin, mU/l *	9 (7, 13)	33	11 (7, 17)	30
HbA1c, mmol/l	37.0 (2.8)	33	36.3 (2.7)	31
Transversospinal FF, %*	23.7 (15.6, 33.8)	22	23.8 (19.6, 34.0)	21
Erector spinae FF, %*	17.5 (13.3, 26.8)	22	18.0 (14.4, 23.4)	21
Transversospinal GU, µmol/100 cm^3/min*	2.8 (2.3, 3.2)	23	2.5 (2.0, 3.3)	20
Erector spinae GU, µmol/100 cm^3/min*	2.9 (2.0, 3.3)	23	2.4 (1.9, 3.9)	20
QF GU, µmol/100 cm^3/min*	2.0 (1.4, 2.7)	23	1.9 (1.2, 3.2)	20
Hamstring GU, µmol/100 cm^3/min*	3.0 (2.0, 4.6)	23	2.8 (1.4, 4.0)	20
Whole-body GU, µmol/kg /min*	15.3 (10.7, 21.0)	33	13.9 (9.8, 21.0)	31
Pain & disability				
Regular medication for pain, n (%)	3 (9)	33	4 (13)	31
VAS Back pain, 0-10 cm*	0.3 (0.1, 3.5)	33	0.5 (0.1, 3.0)	29
VAS Pain-related disability, 0-10 cm*	0.4 (0.1, 2.2)	33	0.7 (0.2, 2.6)	30
Oswestry disability index, %*	6.0 (1.0, 13.0)	33	6.7 (2.0, 16.0)	31
Physical activity				
Accelerometry, h/day	14.5 (1.0)	33	14.6 (1.0)	31
Sedentary time, h/day	10.0 (0.9)	33	10.1 (1.1)	31
Standing time, h/day	1.8 (0.6)	33	1.8 (0.6)	31
LPA, h/day	1.7 (0.4)	33	1.8 (0.5)	31
MVPA, h/day	0.96 (0.31)	33	0.97 (0.34)	31
Breaks in sedentary time, n/day	28 (8)	33	29 (8)	31
Steps, n/day	5204 (1910)	33	5091 (1760)	31

BMI, Body mass index; FF, fat fraction; GU, insulin-stimulated glucose uptake; QF, Quadriceps femoris muscle; fP-Glucose, fasting plasma glucose; fP-Insulin, fasting plasma insulin; HbA1c, glycated hemoglobin; VAS, visual analogue scale; LPA, light physical activity; MVPA moderate to vigorous physical activity. * presented as median (Q1, Q3).

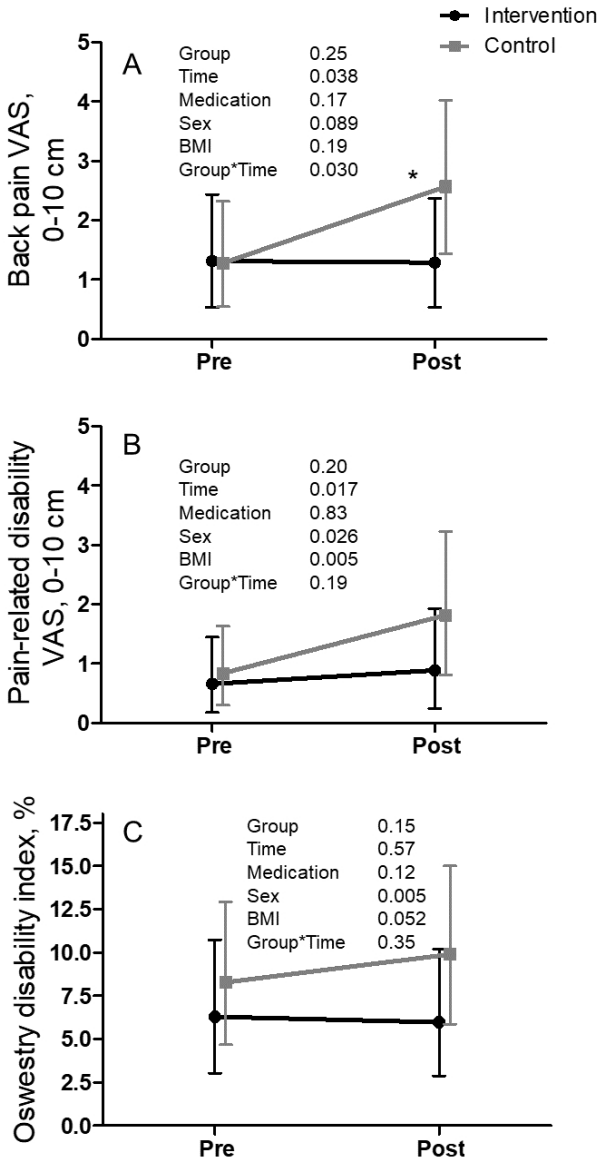
Table 2. Spearman's rank correlation coefficients between changes (Δ values) in the measured outcomes before and after the 6-month intervention period.

	Δ ES FF	Δ Tra. GU	Δ ES GU	Δ QF GU	Δ Ham.	Δ WB GU	Δ BMI	Δ WC	Δ Body	Δ Weigh	Δ Glucos	Δ Insulin	Δ HbA1c	Δ SB%	Δ Standi	Δ LPA%	Δ MVPA	Δ PA%	Δ Steps	Δ Breaks	Δ BP	Δ PRD	Δ ODI
Δ Tra. FF	0.55**	0.16	0.10	0.43*	0.18	0.04	-0.20	-0.18	0.15	-0.23	0.08	-0.26	-0.41*	0.00	-0.01	-0.02	-0.02	0.02	0.05	-0.03	-0.06	0.22	0.06
Δ ES FF	1	0.03	0.05	0.15	0.22	-0.04	-0.04	-0.18	0.02	-0.08	-0.15	-0.12	-0.29	-0.11	0.12	0.07	0.13	0.13	0.22	0.24	-0.11	0.17	-0.05
Δ Tra. GU		1	0.91**	0.56**	0.70**	0.72**	-0.40*	-0.12	-0.32	-0.38*	-0.11	-0.20	-0.05	-0.25	0.10	0.22	0.33	0.33	0.39*	0.12	-0.07	0.21	0.03
Δ ES GU			1	0.49**	0.82**	0.76**	-0.34*	-0.15	-0.33	-0.32	-0.17	-0.19	-0.05	-0.30	0.22	0.20	0.29	0.29	0.41*	0.05	0.04	0.26	0.07
Δ QF GU				1	0.67**	0.47**	-0.45**	-0.04	-0.09	-0.45**	0.08	-0.18	-0.33*	-0.41*	0.19	0.42*	0.46**	0.50**	0.42*	0.06	0.04	0.03	-0.17
Δ Ham. GU					1	0.77**	-0.46**	-0.26	-0.27	-0.45**	-0.06	-0.19	-0.14	-0.53**	0.39*	0.39*	0.46**	0.48**	0.52**	0.16	0.08	0.20	0.05
Δ WB GU						1	-0.53**	-0.33*	-0.08	-0.53**	-0.28*	-0.30*	-0.06	-0.41**	0.32*	0.32*	0.22	0.36**	0.30*	0.14	-0.14	-0.13	-0.12
Δ BMI							1	0.47**	0.29*	1.0**	0.15	0.29*	0.33*	0.35*	-0.22	-0.31*	-0.27	-0.35*	-0.36**	-0.24	0.10	0.19	0.37**
Δ WC								1	0.16	0.47**	0.09	0.24	0.17	0.21	0.02	-0.24	-0.27	-0.31*	-0.28	-0.16	0.05	0.09	0.13
Δ Body fat %									1	0.28*	-0.04	-0.04	0.18	0.12	-0.17	0.08	-0.09	0.02	-0.29*	-0.13	-0.05	0.18	0.26*
Δ Weight										1	0.15	0.31*	0.35**	0.37**	-0.24	-0.32*	-0.26	-0.36**	-0.36**	-0.25	0.08	0.16	0.35**

Δ Glucose											1	0.27*	0.10	-0.07	0.18	-0.09	-0.04	-0.10	-0.14	-0.23	0.17	0.00	-0.15
Δ Insulin												1	0.24	0.23	-0.22	-0.21	-0.08	-0.19	-0.21	-0.16	-0.17	-0.25	-0.05
Δ HbA1c													1	0.21	0.00	-0.12	-0.24	-0.26	-0.41**	-0.28*	0.04	-0.02	0.14
Δ SB%														1	-0.76**	-0.66**	-0.58**	-0.77**	-0.60**	-0.37**	-0.08	-0.05	0.21
Δ Standing%															1	0.21	0.11	0.24	0.30*	0.15	0.22	0.06	-0.15
Δ LPA%																1	0.51**	0.87**	0.44**	0.34*	0.10	0.09	-0.10
Δ MVPA%																	1	0.81**	0.73**	0.44**	-0.10	-0.07	-0.24
Δ PA%																		1	0.64**	0.41**	-0.10	-0.08	-0.23
Δ Steps																			1	0.57**	-0.07	-0.11	-0.26
Δ Breaks in SB																				1	0.07	0.10	0.04
Δ BP																					1	0.67**	0.48**
Δ PRD																						1	0.61**

Δ Change in the measured outcome, Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris

muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05, **significant at the level of p<0.01.



Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain intensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026

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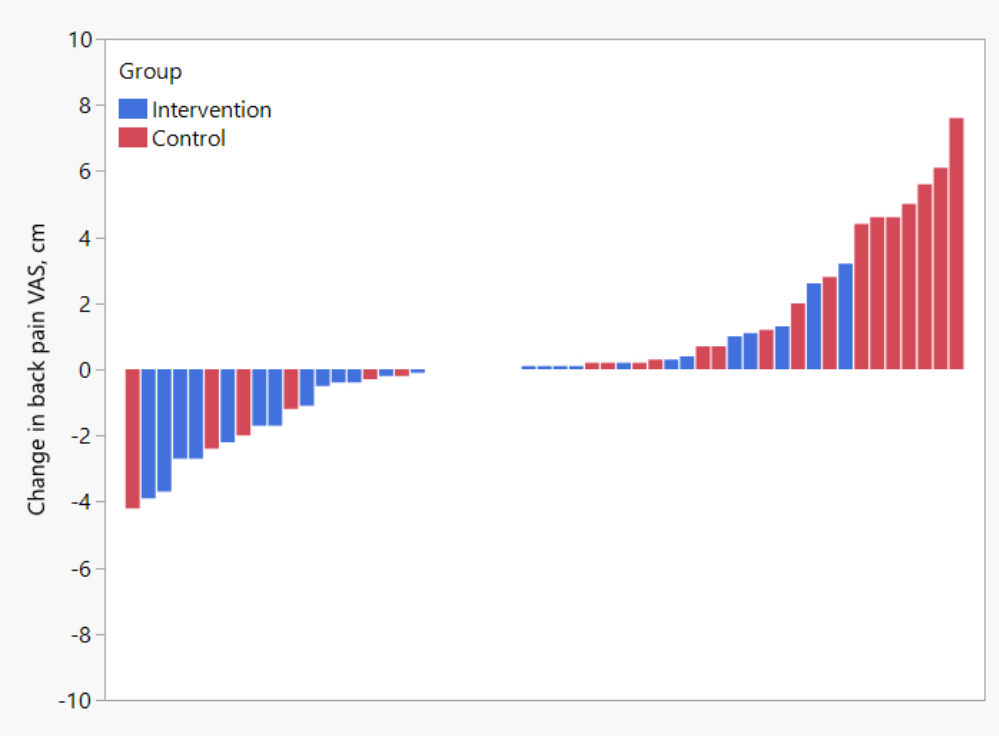

Changes in each participant's back pain during the intervention. Blue bars represent participants in the intervention group and red bars represent participants in the control group. Of the six participants with no changes in back pain, four were in the intervention and two in the control group. A higher value indicates higher pain intensity. VAS = visual analogue scale.

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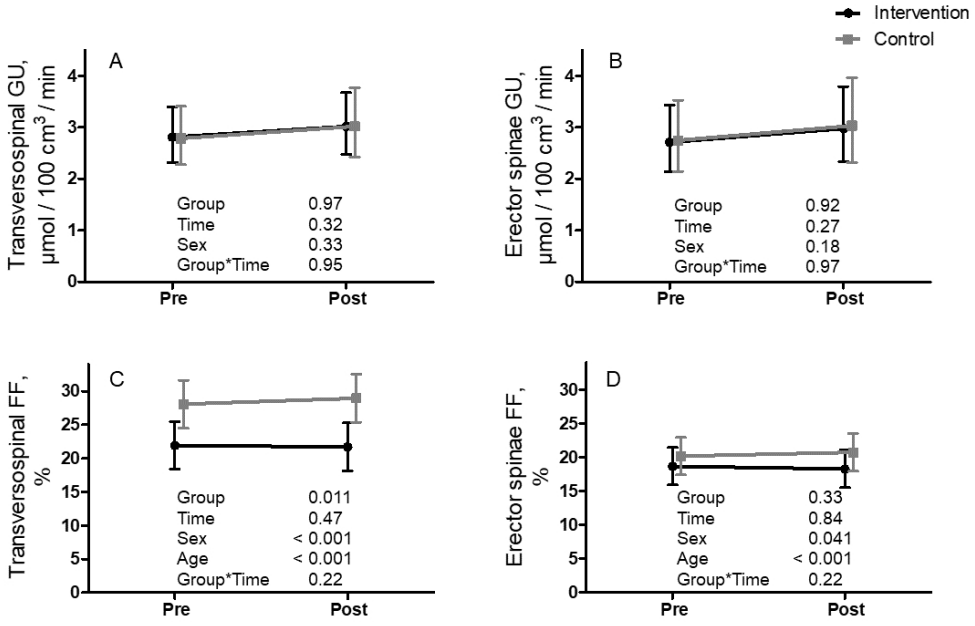

Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

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Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: Secondary analysis of a six-month randomized controlled trial

Supplementary file

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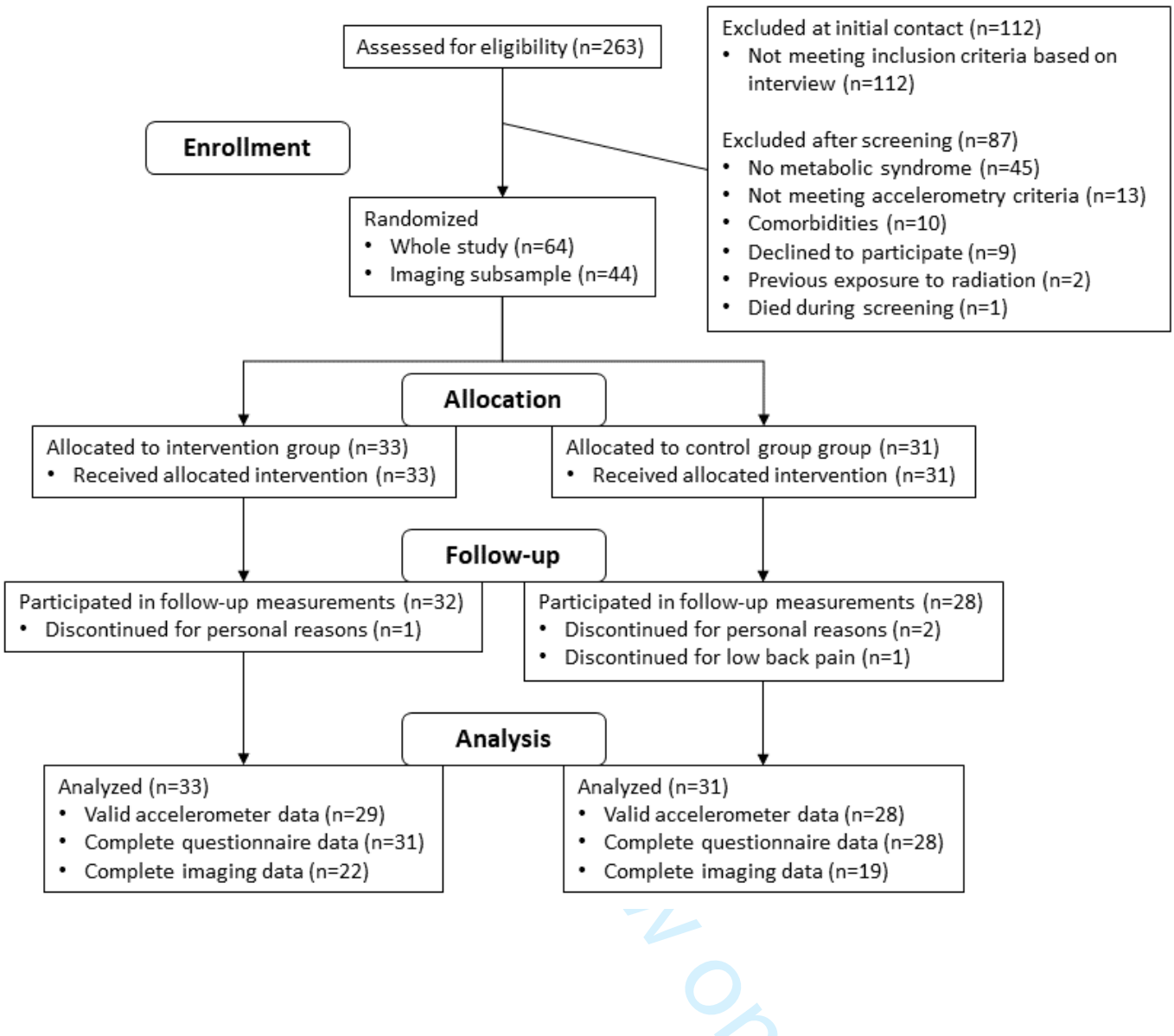
Supplementary Figure 1. Study flow diagram.

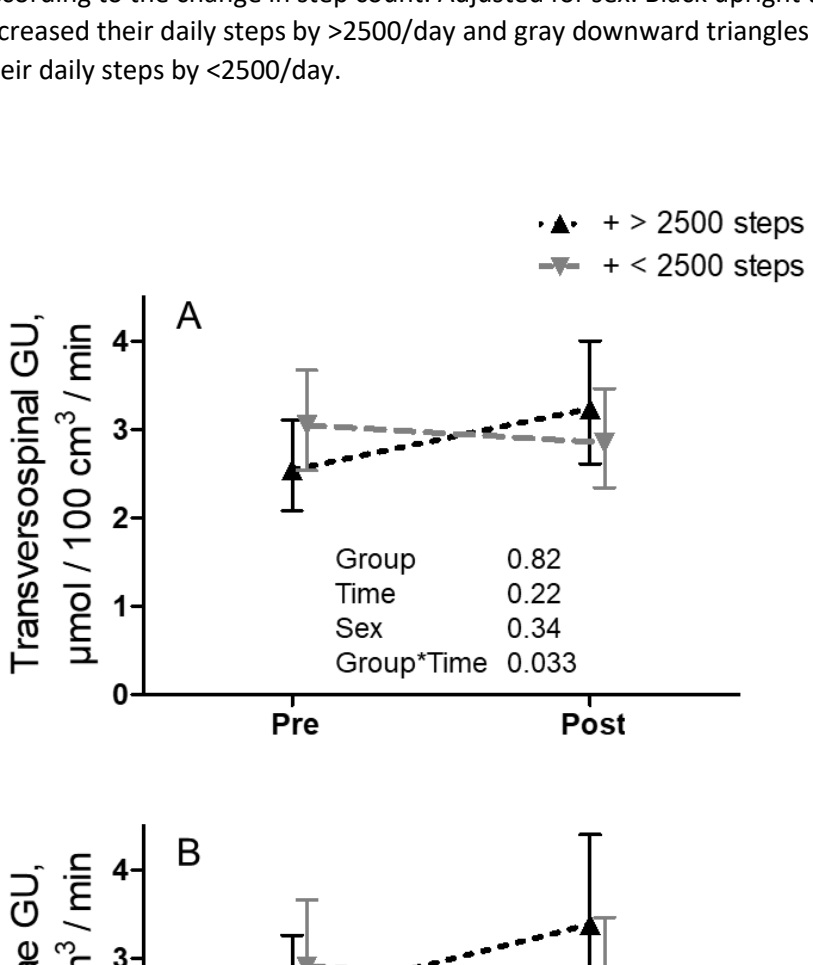


Supplementary Table 1. Baseline Spearman's rank correlation coefficients

	Tra. FF	ES FF	Tra. GU	ES GU	QF GU	Ham. GU	WB GU	BMI	WC	Body fat %	Weight	Glucose	Insulin	HbA1c	SB %	Standing %	LPA %	MVPA %	PA %	Steps /day	Breaks	BP	PRD	ODI
Age	0.55**	0.53**	-0.01	0.00	-0.02	-0.04	0.04	-0.04	0.06	0.03	-0.12	-0.01	-0.06	0.23	0.07	-0.09	0.09	-0.25*	-0.07	-0.26*	-0.3**	0.10	0.02	0.12
Tra. FF	1	0.79**	-0.14	-0.10	0.02	-0.04	0.06	0.15	0.15	0.37*	-0.01	-0.15	-0.15	0.15	0.00	0.08	0.17	-0.36*	-0.11	-0.27	-0.3*	0.11	0.07	0.19
ES FF		1	-0.24	-0.22	-0.06	-0.10	-0.09	0.24	0.26	0.39*	0.12	0.00	0.04	0.20	0.07	-0.05	0.13	-0.30*	-0.05	-0.27	-0.3*	-0.05	-0.09	0.06
Tra. GU			1	0.90**	0.69**	0.71**	0.67**	-0.41**	-0.54**	-0.13	-0.45**	-0.48**	-0.54**	-0.49**	-0.28	0.28	0.01	0.42**	0.24	0.44*	0.3*	-0.04	-0.14	-0.23
ES GU				1	0.79**	0.84**	0.85**	-0.51**	-0.69**	-0.18	-0.52**	-0.36*	-0.65**	-0.54**	-0.31*	0.28	0.10	0.36*	0.30	0.40*	0.3*	-0.04	-0.18	-0.24
QF GU					1	0.92**	0.86**	-0.47**	-0.67**	-0.10	-0.48**	-0.26	-0.65**	-0.43**	-0.42**	0.43**	0.15	0.28	0.28	0.33*	0.3*	-0.11	-0.13	-0.23
Ham. GU						1	0.93**	-0.53**	-0.72**	-0.19	-0.56**	-0.27	-0.68**	-0.48**	-0.46**	0.45**	0.21	0.34*	0.35*	0.36*	0.3*	-0.07	-0.08	-0.21
WB GU							1	-0.53**	-0.71**	-0.12	-0.60**	-0.34**	-0.69**	-0.29*	-0.43**	0.46**	0.19	0.18	0.23	0.30*	0.3*	0.07	0.03	-0.10
BMI								1	0.76**	0.54**	0.80**	0.15	0.61**	0.08	0.29*	-0.16	-0.09	-0.26*	-0.23	-0.37*	-0.4**	0.00	-0.02	0.15
WC									1	0.23	0.80**	0.25*	0.64**	0.26*	0.38**	-0.31*	-0.17	-0.32*	-0.29*	-0.42**	-0.4**	-0.03	0.00	0.08
BF %										1	0.11	-0.17	0.15	0.05	0.02	0.21	0.13	-0.29*	-0.09	-0.28*	-0.2*	0.18	0.16	0.33**
Weight											1	0.27*	0.68**	0.17	0.40**	-0.35**	-0.24	-0.18	-0.28*	-0.33*	-0.3*	-0.13	-0.12	-0.01
Glucose												1	0.24	0.12	0.06	-0.32**	0.17	0.10	0.16	0.01	-0.2*	-0.15	-0.16	-0.14
Insulin													1	0.25*	0.41**	-0.49**	-0.15	-0.11	-0.19	-0.26*	-0.2*	-0.16	-0.08	0.06
HbA1c														1	0.14	-0.18	0.10	-0.10	-0.01	-0.10	-0.1	0.01	-0.07	0.10
SB															1	-0.79**	-0.62**	-0.55**	-0.75**	-0.54**	-0.5**	0.03	-0.19	0.07
Standing																1	0.28*	0.19	0.30*	0.22	0.2	0.06	0.27*	0.06
LPA																	1	0.28*	0.83**	0.21	0.3**	0.06	0.04	-0.03
MVPA																		1	0.73**	0.93**	0.2*	-0.20	-0.03	-0.28*
PA																			1	0.65**	0.3**	-0.09	-0.01	-0.21
Steps																				1	0.2*	-0.18	-0.03	-0.26*
Breaks																					1	0.09	0.14	-0.04
BP																						1	0.61**	0.71**
PRD																							1	0.71**

Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05. **significant at the level of p<0.01.

Supplementary Figure 2. Changes in A) transversospinal glucose uptake (GU) and B) erector spinae GU according to the change in step count. Adjusted for sex. Black upright triangles represent the group that increased their daily steps by >2500/day and gray downward triangles represent the group that increased their daily steps by <2500/day.



Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

Design and conduct				
1.	Clear description of the goal of research, study objective(s), study design, and study population	Yes	Unclear	No
2.	Clear description of outcomes, exposures/treatments and covariates, and their measurement methods	Yes	Unclear	No
3.	Validity of study design	Yes	Unclear	No
4.	Clear statement and justification of sample size	Yes	Unclear	No
5.	Clear declaration of design violations and acceptability of the design violations	Yes	Unclear	No
6.	Consistency between the paper and its previously published protocol	Yes	Unclear	No
Data analysis				
7.	Correct and complete description of statistical methods	Yes	Unclear	No
8.	Valid statistical methods used and assumptions outlined	Yes	Unclear	No
9.	Appropriate assessment of treatment effect or interaction between treatment and another covariate	Yes	Unclear	No
10.	Correct use of correlation and associational statistical testing	Yes	Unclear	No
11.	Appropriate handling of continuous predictors	Yes	Unclear	No
12.	Confidence intervals do not include impossible values	Yes	Unclear	No
13.	Appropriate comparison of baseline characteristics between the study arms in randomized trials	Yes	Unclear	No
14.	Correct assessment and adjustment of confounding	Yes	Unclear	No
15.	Avoiding model extrapolation not supported by data	Yes	Unclear	No
16.	Adequate handling of missing data	Yes	Unclear	No
Reporting and presentation				
17.	Adequate and correct description of the data	Yes	Unclear	No
18.	Descriptive results provided as occurrence measures with confidence intervals, and analytic results provided as association measures and confidence intervals along with P-values	Yes	Unclear	No
19.	Confidence intervals provided for the contrast between groups rather than for each group	Yes	Unclear	No
20.	Avoiding selective reporting of analyses and P-hacking	Yes	Unclear	No
21.	Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, and reporting the P-values rather their range	Yes	Unclear	No
22.	Providing sufficient numerical results that could be included in a subsequent meta-analysis	Yes	Unclear	No
23.	Acceptable presentation of the figures and tables	Yes	Unclear	No
Interpretation				
24.	Interpreting the results based on association measures and 95% confidence intervals along with P-values, and correctly interpreting large P-values as indecisive results, not evidence of absence of an effect	Yes	Unclear	No
25.	Using confidence intervals rather than post-hoc power analysis for interpreting the results of studies	Yes	Unclear	No
26.	Correctly interpreting occurrence or association measures	Yes	Unclear	No
27.	Distinguishing causation from association and correlation	Yes	Unclear	No
28.	Results of pre-specified analyses are distinguished from the results of exploratory analyses in the interpretation	Yes	Unclear	No
29.	Appropriate discussion of the study methodological limitations	Yes	Unclear	No
30.	Drawing only conclusions supported by the statistical analysis and no generalization of the results to subjects outside the target population	Yes	Unclear	No

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TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	1	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	4	
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	4-6	
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	5-6	
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	-	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	5-6	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	4	

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	4, 5	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	4-5	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	5-6	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	7	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

BMJ Open

Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: A secondary analysis of a six-month randomized controlled trial

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Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: A secondary analysis of a six-month randomized controlled trial

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ABSTRACT

Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF).

Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain-related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance imaging.

Results Pain-related disability increased during the intervention in both groups. Back pain intensity increased significantly more in the control group than in the intervention group in which back pain intensity remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain-related disability, ODI, or paraspinal GU and FF were observed. In the whole study group, the change in daily steps associated positively with the change in paraspinal muscle GU.

Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening regardless of paraspinal muscle GU or FF.

Strengths and limitations of this study

- The strengths of this study include the use of accelerometers to monitor physical activities and sedentary behaviours throughout the six-month study.
- Moreover, the imaging modalities (positron emission tomography with hyperinsulinemic-euglycemic clamp for muscle-specific insulin resistance and magnetic resonance imaging for muscle-specific fat fraction) may be considered as the gold standard measures.
- However, this is a secondary analysis of the whole study, and thus the power calculations were not done for back pain or disability.
- Further, no specific back pain related eligibility criteria were applied.

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Keywords: sedentary behaviour, accelerometry, back pain, disability, insulin sensitivity, muscle fat fraction

INTRODUCTION

Physical activity (PA) associates with a decreased risk for low back pain (1,2). Conversely, observational studies suggest an association between high sedentary behaviour (SB) and increased low back pain or pain-related disability (1,3). A meta-analysis of 16 longitudinal studies reported that higher SB associated with higher pain-related disability but not with back pain intensity (1). On the other hand, a meta-analysis of cross-sectional studies found a positive association between non-occupational and occupational SB and back pain (3). Moreover, we have previously observed cross-sectionally that higher SB associated with lower pain-related disability (4). Thus, it is clear that the observational evidence is mixed. However, different study settings (i.e., cross-sectional or longitudinal) represent different time frames and the possibility of reverse causality cannot be ruled out.

Previous three to six-month interventional studies among fifty-year-old office workers suggest that reducing SB might improve pain-related disability without affecting back pain intensity (5,6). However, the mechanisms by which SB modification could affect back pain or disability remain poorly understood.

Insulin resistance and fatty infiltration of the paraspinal muscles associate with back pain (7–11) and successfully reducing SB improves muscle insulin sensitivity (12). Moreover, lower levels of PA associate with higher fat content of the transversospinal muscles (13). Taken together, these findings make SB a plausible target for an intervention to maintain or improve back health.

Thus, we aimed to investigate the effects of a six-month SB reduction intervention on back pain, disability, and paraspinal muscle FF and insulin sensitivity (glucose uptake, GU). Additionally, we assessed the back pain related factors cross-sectionally.

METHODS

This study consists of secondary analyses of a six-month randomized controlled trial that was conducted at the Turku PET Centre (Turku, Finland) between April 2017 and March 2020 (Clinicaltrials.gov NCT03101228, 05/04/2017). The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study (16/1801/2017). All participants gave their informed consent before entering the study, and the study was conducted according to the Declaration of Helsinki.

Participants

As reported earlier (12,14), volunteers were recruited from the community. Inclusion criteria were: age 40–65 years, body mass index (BMI) 25–40 kg/m^2, self-reported physical inactivity (<120 min/week of moderate-to-vigorous physical activity [MVPA]), accelerometer-measured sedentary time ≥10 h or ≥60 % of

accelerometer wear time, and metabolic syndrome (15). Exclusion criteria included diagnosed diabetes or fasting blood glucose ≥7.0 mmol/l, abundant alcohol consumption according to the national guidelines, the use of any tobacco products, diagnosed depressive or bipolar disorder, inability to understand written Finnish, and any condition that would endanger the participant or study procedures (e.g., previous exposure to ionizing radiation).

Measurements

Back pain intensity and pain-related disability were assessed by two questions and 10-cm visual analogue scales (VAS): 1) Have you had back pain within the last month? Mark the intensity of the worst perceived pain during the month on the line below; and 2) Has the perceived pain caused you disability at your work or everyday tasks within the last month? Mark the intensity of the greatest extent of disability that you experienced during the month on the line below. A higher value (0–10 cm) indicates higher pain intensity and disability. Additionally, back pain-related disability was assessed using the Oswestry disability index (ODI), which provides a value of 0–100%, and a higher value represents higher disability (16).

Paraspinal muscle (i.e., erector spinae and transversospinales) FF was assessed using the two-point Dixon magnetic resonance (MR) imaging method (Philips 3T Ingenuity TF, Philips Healthcare, Amsterdam, The Netherlands and Siemens Magnetom Skyra Fit 3T system, Siemens Healthcare, Erlangen, Germany) (17). Paraspinal muscle GU was measured using ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET; GE D690 PET/CT, GE Healthcare, Milwaukee, WI) during hyperinsulinemic euglycemic clamp (HEC) as described previously (12,18). Both the FF and GU were analyzed separately for the transversospinal and erector spinae muscles at the level of L3-4. The measurements were performed using Carimas (version 2.10, https://www.carimas.fi).

PA and SB were measured using accelerometers for four weeks during screening (UKK AM30, UKK Terveyspalvelut Oy, Tampere, Finland) to determine the baseline values and throughout the six-month intervention period (Movesense, Suunto, Vantaa, Finland, with ExSed application, UKK Terveyspalvelut Oy, Tampere, Finland) to monitor and facilitate behaviour change. The accelerometer variables during the intervention period were analyzed as means over the whole six-month period. The participants were advised to wear the device on the right hip during waking hours (except when the device could be exposed to water) and remove it when sleeping at night. Accelerometer weartime of 10–19 h/day was considered valid, and measurement exceeding 19 h/day was subtracted from SB as measurement exceeding 19 h/day likely means that the participant slept with the device on. For example, if the measurement on one day was 20.5 h, 1.5 h was subtracted from the measured SB, resulting in 19 h of analyzed wear time. The accelerometer data was analyzed using six-second epochs, and the raw acceleration data was analyzed using the mean amplitude deviation (to assess sedentariness, light PA [LPA], and moderate-to-vigorous PA

[MVPA]) and angle for posture estimation (to differentiate SB and standing) methods as described previously (4,18–20).

Height was measured using a wall-mounted stadiometer, and body mass and body fat percentage were measured by air displacement plethysmography (Cosmed USA, Concord, CA) after at least four hours of fasting. Waist circumference was measured using a measuring tape midway between the lowest rib and the iliac crest. Pain medication use was self-reported by the participants and categorized into using medication or not.

Intervention

After the screening, eligible volunteers were randomized into the intervention and control groups in a 1:1 ratio by a statistician using random permuted block randomization (block size 44) in SAS (version 9.4 for Windows, SAS Institute, Inc., Cary, NC). The randomization was performed for men and women separately.

As described in more detail previously (18), participants in the intervention group were advised to reduce their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by subtracting 1 h of SB from the amount during screening. Correspondingly, 1 h was added to standing, LPA, and MVPA goals distributing the time based on individual preferences. However, a maximum of 20 minutes was added to MVPA, and increasing intentional physical exercise training was discouraged. The ways for replacing SB were discussed individually and included, for example, using standing desks, taking the stairs instead of the lift, and lightly walking. For the control group, the daily SB and PA goals were set equal to the screening values. All participants could monitor their daily SB and PA and the fulfilment of the goals using a mobile phone application (ExSed) connected to the accelerometer.

Patient involvement

Patients were not involved in designing or conducting this study.

Equity, diversity and inclusion

Both the study participants and researchers include self-identified men and women in a relatively balanced fashion. The research group consists of both junior and senior researchers.

Statistical methods

Baseline characteristics are presented as mean (standard deviation, SD) if not stated otherwise. Intervention effects are presented as model-based mean (95% confidence interval, 95% CI). Baseline correlations were analyzed using the Spearman rank correlation. The main analyses of intervention effects were performed using linear mixed models for repeated measurements. The outcome of interest was the dependent variable, and independent variables included group, time, sex, and group x time in all analyses.

Random intercepts for individual effect was also included. Additionally, FF analyses were adjusted for age, and pain questionnaire analyses were adjusted for self-reported regular pain medication status (yes/no) and BMI, because this improved the distribution of the residuals. The normal distribution of the residuals was visually inspected, and log10 or square root transformations were performed as necessary. Tukey-Kramer adjustment for multiple comparisons was used. Compound symmetry or unstructured covariance structure was chosen based on the Akaike information criterion. Statistical significance was set at $p<0.05$ (two-tailed). The main analyses were performed in SAS (version 9.4 for Windows, SAS Institute Inc., Cary, NC) and the correlation analyses were performed using JMP Statistics (version 16, SAS Institute Inc., Cary, NC).

The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming an increase of 0.7 (SD 0.55) µmol/100g/min in the intervention group (10% increase) and an increase of 0.05 µmol/100g/min in the control group, we calculated that 16 participants per group would be sufficient for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity ($\alpha=0.05$, $1-\beta=0.9$). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin sensitivity would behave similar to quadriceps femoris and thus, the study would be sufficiently powered to detect statistically significant changes in paraspinal muscle insulin sensitivity.

RESULTS

Baseline characteristics

Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and MR imaging. The baseline characteristics are presented in Table 1.

Baseline correlations

All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated positively with erector spinae and transversospinal FF ($r_s=0.53$, 0.55, respectively). Erector spinae GU correlated positively with MVPA and step count ($r_s=0.36$ and 0.40, respectively) and negatively with SB ($r_s=$-

0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s=0.42 and 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and transversospinal FF correlated with MVPA (r_s=-0.30 and -0.36, respectively). Increased body adiposity (BMI and body fat percentage) associated with lower paraspinal muscle GU and higher FF.

Pain-related disability correlated positively with standing time (r_s=0.27). Furthermore, the ODI score correlated negatively with MVPA (r_s=-0.28) and step count (r_s=-0.26). Finally, the ODI score correlated positively with body fat percentage (r_s=0.33). Back pain intensity did not correlate with any PA, SB, or paraspinal muscle-related variables.

Intervention effects

Accelerometry

The intervention effects on SB and PA have been reported previously (18). In comparison to the control group, the intervention group reduced their SB by 40 min/day and subsequently increased their MVPA by 20 min/day, on average over the six-month intervention period; no statistically significant changes were observed in the control group. LPA increased by 10 min/day in both groups without statistically significant between-group differences. No statistically significant changes in standing time or the number of breaks in SB were observed in either group. Step count increased in both groups but the increase was statistically significantly higher in the intervention group (from 5150 to 6749 steps/day in the control group vs. 5326 to 8632 steps/day in the intervention group).

Pain and disability questionnaires

The pain and disability questionnaire results are presented in Figure 1, and the changes in each participant's back pain by group are presented in Figure 2. In the intervention group, back pain did not change whereas it increased statistically significantly in the control group (group x time p=0.030). Pain-related disability increased over time in both groups (time p=0.017), but no statistically significant between-group differences in the changes in pain-related disability or ODI were observed.

Paraspinal muscle FF and GU

Transversospinal FF was higher in the control group throughout the study (p=0.011), but no statistically significant changes were observed in paraspinal muscle FF or GU in either group (Figure 3).

Explorative analyses

As previously done (12,18), when the study group was divided according to the measured changes in SB or daily steps no statistically significant changes in any pain-related outcomes were observed (group x time p>0.05 for all; data not shown). Furthermore, no statistically significant differences were observed in

paraspinal muscle FF or GU when the group was divided according to the measured change in SB (group x time p>0.05 for all; data not shown). However, with the step-based groups (i.e., an increase of >2500 steps/day vs. <2500 steps/day increase, or decrease), the changes in erector spinae and transversospinal GU were statistically significantly different between groups in favour of the more active group (group x time p=0.033) (Supplementary Figure 2).

In the whole study group, the changes in BMI, body fat percentage, and body mass correlated positively with the change in ODI (r_s=0.37, 0.26, and 0.35, respectively; Supplementary Table 2). None of the changes in PA or SB correlated with the changes in pain-related outcomes. The change in BMI correlated negatively with the change in erector spinae and transversospinal GU (r_s=-0.34 and -0.40, respectively). In line with the analyses based on high vs. low step count increase, the changes in steps correlated positively with the changes in paraspinal muscle GU (r_s=0.39 and 0.41 for the transversospinales and erector spinae, respectively) but not with the changes in FF.

DISCUSSION

In the present study, we show that an intervention aimed at reducing SB by 1 h/day for six months may prevent the worsening of back pain intensity which was observed in the control group. However, the change in back pain intensity was not associated with changes in paraspinal muscle (i.e., erector spinae or transversospinales) FF, GU, or the changes in PA, SB, pain-related disability, or ODI score. Additionally, no intervention effects on paraspinal muscle FF or GU were observed, although increases in daily steps associated with improved paraspinal muscle GU.

Pain and physical behaviours

In this study, back pain intensity increased by about two-fold in the control group, on average. Although the baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS in the intervention and control groups, respectively), the change in the control group represents a substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain intensity are achieved. However, we did not observe any intervention effects on pain-related disability or ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This might be explained by the relatively low pain intensity that might not be severe enough to cause disability.

The reason for back pain intensity increase in the control group remains elusive. One explanation for the increase could be related to the open-label nature of this study. Although not formally documented, many control participants were disappointed to be included in the control group instead of the intervention group. These negative emotions may have affected pain intensity (22). This phenomenon, in conjunction

with the possible benefits from the increased PA in the intervention group, could explain the difference between groups. The fact that the explorative analyses with SB or step-based *post hoc* group divisions showed no between-group differences in pain-related outcomes further emphasizes that the sole allocation to either intervention or control group may have affected the perception of pain. However, the cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the cross-sectional correlations and the correlations of changes during the study suggest that maintaining a healthier body composition could decrease disability, as body fat percentage correlated positively with the ODI score (see Supplementary Tables 1 and 2).

Contrary to our results, a previous six-month randomized controlled trial involving adults with low back pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity measured using VAS did not differ between groups in the study (5). The study sample was comparable to ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, the aforementioned study did not aim to change only SB but also included behavioural counselling in the self-management of pain. Furthermore, the reduction in SB was notably higher in the previous study compared to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. Additionally, the intensity of longstanding pain might not always be related to the disability (23).

It should be acknowledged that back pain is often a recurring and varying, and sometimes a longstanding complaint (24). For this reason, future studies should assess pain and disability more frequently than only at baseline and at the end of the intervention, as in the current study. However, the six-month duration of this study should be sufficient to reveal the effects of a SB reduction intervention, as in a previous study the ODI score tended to decrease up until three months before plateauing (5).

As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with pain-related disability at baseline in our study (4). However, no correlation between the change in standing time and the change in pain-related disability was observed. Related to this finding, a recent randomized controlled trial observed that, within three months, increasing occupational standing may increase multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer present (25). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that standing may exacerbate pain acutely, but habitual standing may not be detrimental.

Paraspinal muscle FF and GU

We did not observe any intervention effects on either erector spinae or transversospinal FF. This finding is consistent with a recent systematic review of six intervention studies, concluding that paraspinal FF cannot be reduced even with exercise training (26). This demonstrates that even though paraspinal muscle FF is strongly associated with back pain (7–9), successful back pain prevention or treatment can be independent of FF. This may be explained in part by the effect of time, i.e., age, which correlated with paraspinal FF (r_s=0.55 and 0.53 for transversospinal and erector spinae FF; see Supplementary Table 1) and was a significant contributor in the linear models investigating paraspinal FF ($p<0.001$ for both muscle groups) in this study. In accordance, the effectiveness of back pain rehabilitation is not related to specific strength or mobility goals of the rehabilitation (27), emphasizing other than structural aspects in treating experienced pain and disability. Therefore, back pain risk factors (such as paraspinal muscle FF) should not be the direct targets of rehabilitation as much as the psychological and cognitive aspects of pain perception and the individual preferences for physical exercise (28). However, as lower paraspinal muscle FF associated with higher amounts of MVPA and lower body adiposity, the results suggest that maintaining healthy body composition and MVPA levels might help prevent fat infiltration of the paraspinal muscles.

We have previously reported the intervention effects on hamstrings and quadriceps femoris GU (12) which seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses revealed no intervention effects on any of these muscles. However, the secondary analyses of the present study and the previously published study show the association between increased PA (e.g., steps) and improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal muscle GU correlated with the changes in any pain-related outcomes (Supplementary Table 2). Moreover, as paraspinal muscle GU but not FF was associated with steps, the results suggest that GU can improve despite no changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI correlated negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI.

Clinical implications

The present study highlights that being in a SB reduction intervention which elicits changes to PA, standing, and SB might work as a protective strategy against back pain. Furthermore, as observed before with strength or mobility goals for rehabilitation (27), the possible improvements in pain or disability seem to not be related to paraspinal muscle GU or FF.

Strengths and weaknesses

The strengths of this study include the robust measurement of PA, standing, and SB with accelerometers during the whole six-month study. Moreover, the accelerometer data was analyzed using validated

algorithms (19,20). Furthermore, the ODI is a validated questionnaire (16), and VAS is commonly used for pain assessment, and it associates with functional outcomes (29). However, a weakness in this study is the use of non-validated questions with the VAS. Another key strength is the muscle specific GU assessment with the HEC protocol combined with FDG-PET imaging (30). Further, the two-point Dixon is a highly reproducible method for FF assessment (31).

One limitation of the present study is the sample size. For the GU assessments, the sample size was likely adequate (12), but as the pain-related outcomes were not the primary outcomes of the whole trial, the statistical power might have been inadequate. Additionally, the study sample was not chosen based on pain status which may have increased heterogeneity in the sample, and thus decreased the statistical power.

Conclusion

An intervention that reduced SB by mainly replacing it with PA may prevent against increases to back pain intensity in adults with metabolic syndrome and physical inactivity. Replacing the SB by walking over six months may contribute to improved paraspinal muscle insulin sensitivity, and these factors warrant continued investigation in the context of pain and disability.

Author contributions

I.H., K.K., T.Va. and T.S. conception and design of the study. T.S., S.L., T.G., K.L. and N.H. acquisition of data. T.S., J.N., H.V-Y., H.S., T.G., S.L., T.Ve., V.S., J.H., E.L. and I.H. analysis and interpretation of data. J.N. drafted the manuscript and all authors edited and revised the manuscript. All authors approved the final version of the manuscript. I.H. acted as the guarantor.

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Data availability statement

Data are available upon reasonable request from the corresponding author.

Ethical approval

The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study (16/1801/2017).

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The other authors report no conflicts of interest. The results are presented clearly and honestly without fabrication, falsification, or inappropriate data manipulation.

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Figure legends

Figure 1. Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain intensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026

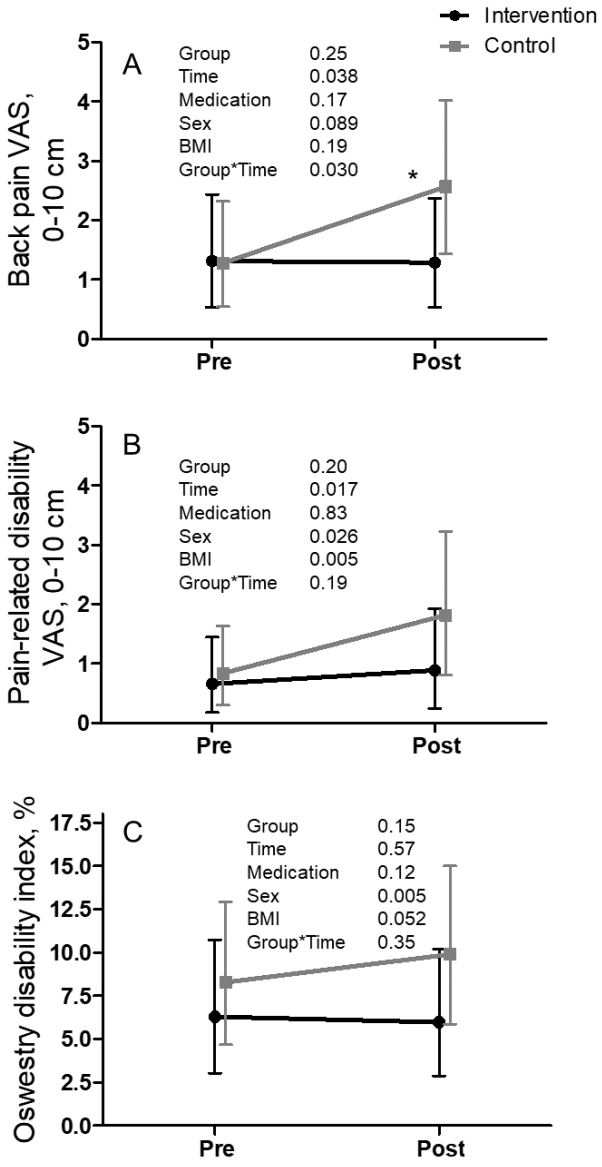
Figure 2. Changes in each participant's back pain during the intervention. Blue bars represent participants in the intervention group and red bars represent participants in the control group. Of the six participants with no changes in back pain, four were in the intervention and two in the control group. A higher value indicates higher pain intensity. VAS = visual analogue scale.

Figure 3. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

Table 1. Study participant characteristics at the baseline. Unless otherwise stated, the results are presented as mean (SD).

	Intervention	n	**Control**	n
Men, n (%)	13 (39)	33	14 (45)	31
Age, yrs	59 (6)	33	57 (8)	31
Anthropometrics & metabolism				
BMI, kg/m^2	31.5 (4.0)	33	31.7 (4.6)	31
Body fat, %	43.1 (8.0)	33	43.1 (8.0)	31
Waist circumference, cm	111.1 (11.6)	33	110.7 (11.1)	31
fP-Glucose, mmol/l	5.9 (0.5)	33	5.8 (0.4)	31
fP-Insulin, mU/l *	9 (7, 13)	33	11 (7, 17)	30
HbA1c, mmol/l	37.0 (2.8)	33	36.3 (2.7)	31
Transversospinal FF, %*	23.7 (15.6, 33.8)	22	23.8 (19.6, 34.0)	21
Erector spinae FF, %*	17.5 (13.3, 26.8)	22	18.0 (14.4, 23.4)	21
Transversospinal GU, µmol/100 cm^3/min*	2.8 (2.3, 3.2)	23	2.5 (2.0, 3.3)	20
Erector spinae GU, µmol/100 cm^3/min*	2.9 (2.0, 3.3)	23	2.4 (1.9, 3.9)	20
QF GU, µmol/100 cm^3/min*	2.0 (1.4, 2.7)	23	1.9 (1.2, 3.2)	20
Hamstring GU, µmol/100 cm^3/min*	3.0 (2.0, 4.6)	23	2.8 (1.4, 4.0)	20
Whole-body GU, µmol/kg /min*	15.3 (10.7, 21.0)	33	13.9 (9.8, 21.0)	31
Pain & disability				
Regular medication for pain, n (%)	3 (9)	33	4 (13)	31
VAS Back pain, 0-10 cm*	0.3 (0.1, 3.5)	33	0.5 (0.1, 3.0)	29
VAS Pain-related disability, 0-10 cm*	0.4 (0.1, 2.2)	33	0.7 (0.2, 2.6)	30
Oswestry disability index, %*	6.0 (1.0, 13.0)	33	6.7 (2.0, 16.0)	31
Physical activity				
Accelerometry, h/day	14.5 (1.0)	33	14.6 (1.0)	31
Sedentary time, h/day	10.0 (0.9)	33	10.1 (1.1)	31
Standing time, h/day	1.8 (0.6)	33	1.8 (0.6)	31
LPA, h/day	1.7 (0.4)	33	1.8 (0.5)	31
MVPA, h/day	0.96 (0.31)	33	0.97 (0.34)	31
Breaks in sedentary time, n/day	28 (8)	33	29 (8)	31
Steps, n/day	5204 (1910)	33	5091 (1760)	31

BMI, Body mass index; FF, fat fraction; GU, insulin-stimulated glucose uptake; QF, Quadriceps femoris muscle; fP-Glucose, fasting plasma glucose; fP-Insulin, fasting plasma insulin; HbA1c, glycated hemoglobin; VAS, visual analogue scale; LPA, light physical activity; MVPA moderate to vigorous physical activity. * presented as median (Q1, Q3).



Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain intensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026

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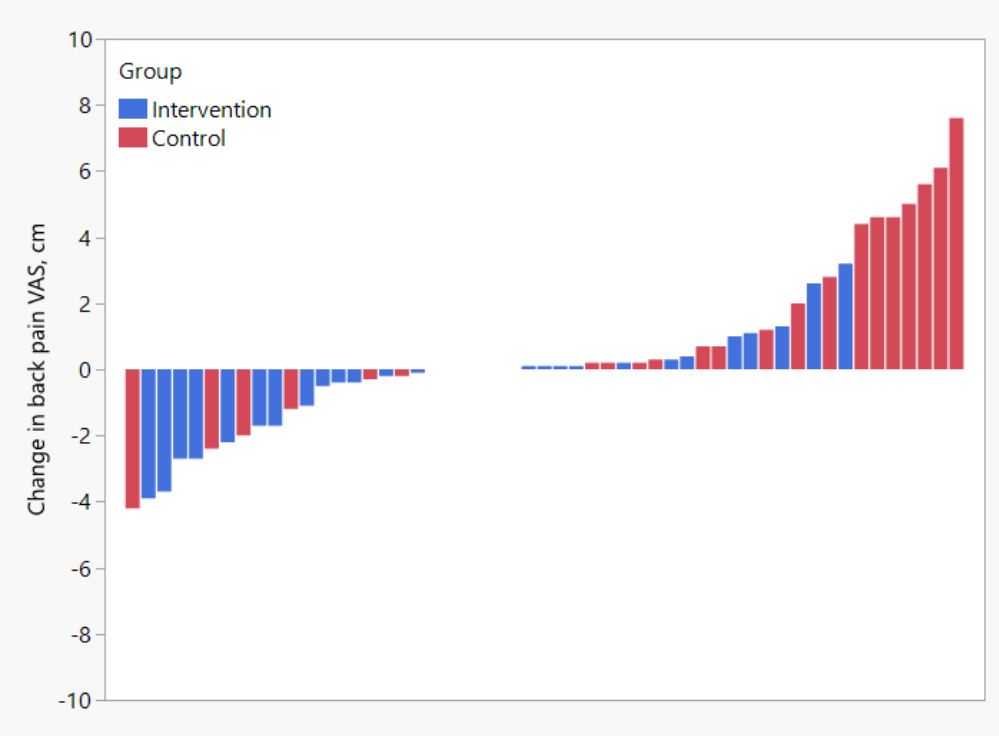

Changes in each participant's back pain during the intervention. Blue bars represent participants in the intervention group and red bars represent participants in the control group. Of the six participants with no changes in back pain, four were in the intervention and two in the control group. A higher value indicates higher pain intensity. VAS = visual analogue scale.

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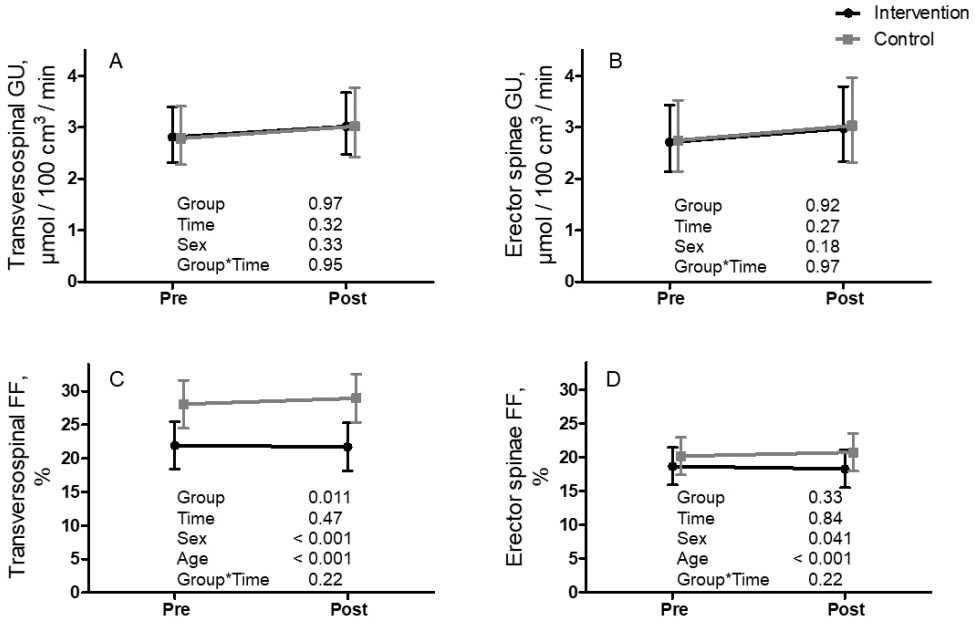

Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent the intervention group and gray squares represent the control group. The presented estimates are model-based means and 95% confidence intervals.

732x479mm (38 x 38 DPI)

Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat fraction and their associations: A secondary analysis of a six-month randomized controlled trial

Supplementary file

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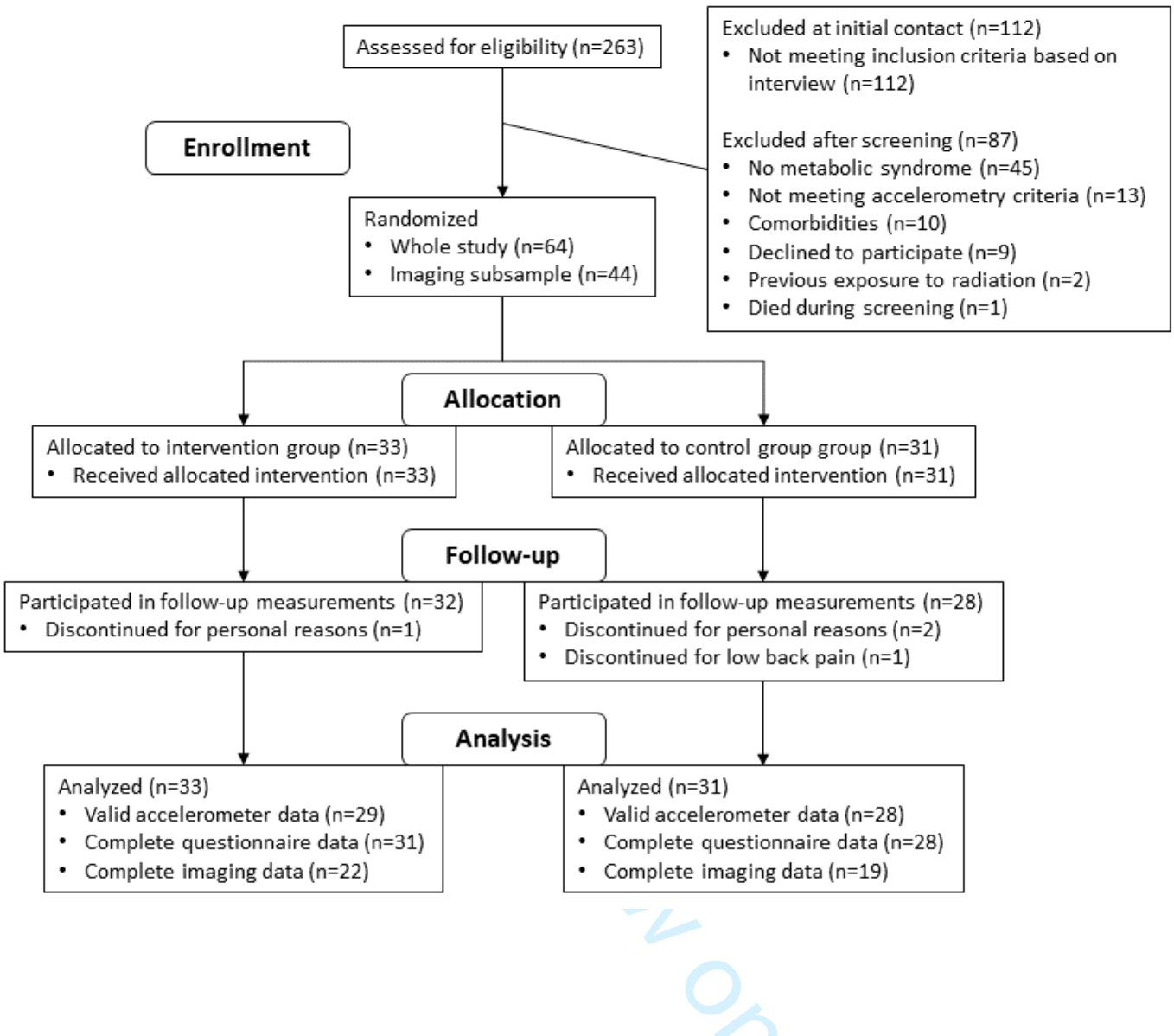
Supplementary Figure 1. Study flow diagram.



Supplementary Table 1. Baseline Spearman's rank correlation coefficients

	Tra. FF	ES FF	Tra. GU	ES GU	QF GU	Ham. GU	WB GU	BMI	WC	Body fat %	Weight	Glucose	Insulin	HbA1c	SB %	Standing %	LPA %	MVPA %	PA %	Steps /day	Breaks	BP	PRD	ODI
Age	0.55**	0.53**	-0.01	0.00	-0.02	-0.04	0.04	-0.04	0.06	0.03	-0.12	-0.01	-0.06	0.23	0.07	-0.09	0.09	-0.25*	-0.07	-0.26*	-0.3**	0.10	0.02	0.12
Tra. FF	1	0.79**	-0.14	-0.10	0.02	-0.04	0.06	0.15	0.15	0.37*	-0.01	-0.15	-0.15	0.15	0.00	0.08	0.17	-0.36*	-0.11	-0.27	-0.3*	0.11	0.07	0.19
ES FF		1	-0.24	-0.22	-0.06	-0.10	-0.09	0.24	0.26	0.39*	0.12	0.00	0.04	0.20	0.07	-0.05	0.13	-0.30*	-0.05	-0.27	-0.3*	-0.05	-0.09	0.06
Tra. GU			1	0.90**	0.69**	0.71**	0.67**	-0.41**	-0.54**	-0.13	-0.45**	-0.48**	-0.54**	-0.49**	-0.28	0.28	0.01	0.42**	0.24	0.44*	0.3*	-0.04	-0.14	-0.23
ES GU				1	0.79**	0.84**	0.85**	-0.51**	-0.69**	-0.18	-0.52**	-0.36*	-0.65**	-0.54**	-0.31*	0.28	0.10	0.36*	0.30	0.40*	0.3*	-0.04	-0.18	-0.24
QF GU					1	0.92**	0.86**	-0.47**	-0.67**	-0.10	-0.48**	-0.26	-0.65**	-0.43**	-0.42**	0.43**	0.15	0.28	0.28	0.33*	0.3*	-0.11	-0.13	-0.23
Ham. GU						1	0.93**	-0.53**	-0.72**	-0.19	-0.56**	-0.27	-0.68**	-0.48**	-0.46**	0.45**	0.21	0.34*	0.35*	0.36*	0.3*	-0.07	-0.08	-0.21
WB GU							1	-0.53**	-0.71**	-0.12	-0.60**	-0.34**	-0.69**	-0.29*	-0.43**	0.46**	0.19	0.18	0.23	0.30*	0.3*	0.07	0.03	-0.10
BMI								1	0.76**	0.54**	0.80**	0.15	0.61**	0.08	0.29*	-0.16	-0.09	-0.26*	-0.23	-0.37*	-0.4**	0.00	-0.02	0.15
WC									1	0.23	0.80**	0.25*	0.64**	0.26*	0.38**	-0.31*	-0.17	-0.32*	-0.29*	-0.42*	-0.4**	-0.03	0.00	0.08
BF %										1	0.11	-0.17	0.15	0.05	0.02	0.21	0.13	-0.29*	-0.09	-0.28*	-0.2*	0.18	0.16	0.33**
Weight											1	0.27*	0.68**	0.17	0.40**	-0.35**	-0.24	-0.18	-0.28*	-0.33*	-0.3*	-0.13	-0.12	-0.01
Glucose												1	0.24	0.12	0.06	-0.32**	0.17	0.10	0.16	0.01	-0.2*	-0.15	-0.16	-0.14
Insulin													1	0.25*	0.41**	-0.49**	-0.15	-0.11	-0.19	-0.26*	-0.2*	-0.16	-0.08	0.06
HbA1c														1	0.14	-0.18	0.10	-0.10	-0.01	-0.10	-0.1	0.01	-0.07	0.10
SB															1	-0.79**	-0.62**	-0.55**	-0.75**	-0.54**	-0.5**	0.03	-0.19	0.07
Standing																1	0.28*	0.19	0.30*	0.22	0.2	0.06	0.27*	0.06
LPA																	1	0.28*	0.83**	0.21	0.3**	0.06	0.04	-0.03
MVPA																		1	0.73**	0.93**	0.2*	-0.20	-0.03	-0.28*
PA																			1	0.65*	0.3**	-0.09	-0.01	-0.21
Steps																				1	0.2*	-0.18	-0.03	-0.26*
Breaks																					1	0.09	0.14	-0.04
BP																						1	0.61**	0.71**
PRD																							1	0.71**

Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05. **significant at the level of p<0.01.

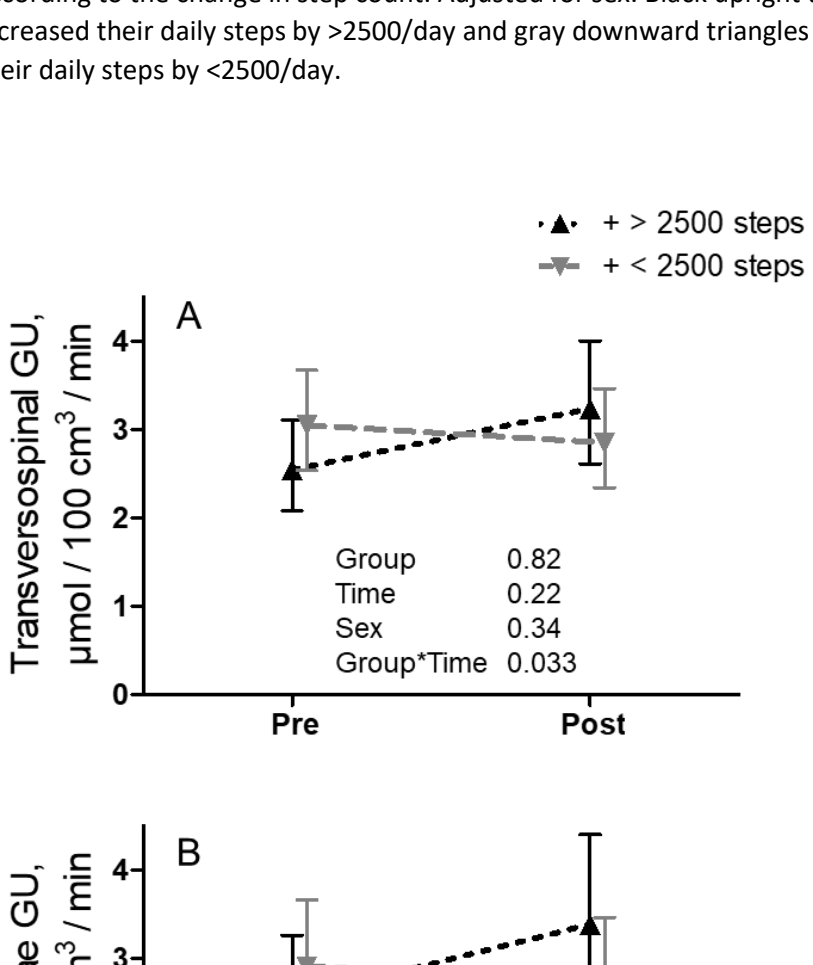
Supplementary Table 2. Spearman's rank correlation coefficients between changes (Δ values) in the measured outcomes before and after the 6-month intervention period.

	Δ ES FF	Δ Tra. GU	Δ ES GU	Δ QF GU	Δ Ham.	Δ WB GU	Δ BMI	Δ WC	Δ Body	Δ Weigh	Δ Glucos	Δ Insulin	Δ HbA1c	Δ SB%	Δ Standi	Δ LPA%	Δ MVPA	Δ PA%	Δ Steps	Δ Breaks	Δ BP	Δ PRD	Δ ODI
Δ Tra. FF	0.55**	0.16	0.10	0.43*	0.18	0.04	-0.20	-0.18	0.15	-0.23	0.08	-0.26	-0.41*	0.00	-0.01	-0.02	-0.22	0.02	0.05	-0.03	-0.06	0.22	0.06
Δ ES FF	1	0.03	0.05	0.15	0.22	-0.04	-0.04	-0.18	0.02	-0.08	-0.15	-0.12	-0.29	-0.11	0.12	0.07	0.08	0.13	0.22	0.24	-0.11	0.17	-0.05
Δ Tra. GU		1	0.91**	0.56**	0.70**	0.72**	-0.40*	-0.12	-0.32	-0.38*	-0.11	-0.20	-0.05	-0.25	0.10	0.22	0.20	0.33	0.39*	0.12	-0.07	0.21	0.03
Δ ES GU			1	0.49**	0.82**	0.76**	-0.34*	-0.15	-0.33	-0.32	-0.17	-0.19	-0.05	-0.30	0.22	0.20	0.27	0.29	0.41*	0.05	0.04	0.26	0.07
Δ QF GU				1	0.67**	0.47**	-0.45**	-0.04	-0.09	-0.45**	0.08	-0.18	-0.33*	-0.41*	0.19	0.42*	0.36**	0.50**	0.42*	0.06	0.04	0.03	-0.17
Δ Ham. GU					1	0.77**	-0.46**	-0.26	-0.27	-0.45**	-0.06	-0.19	-0.14	-0.53**	0.39*	0.39*	0.43**	0.48**	0.52**	0.16	0.08	0.20	0.05
Δ WB GU						1	-0.53**	-0.33*	-0.08	-0.53**	-0.28*	-0.30*	-0.06	-0.41**	0.32*	0.32*	0.22	0.36**	0.30*	0.14	-0.14	-0.13	-0.12
Δ BMI							1	0.47**	0.29*	1.0**	0.15	0.29*	0.33*	0.35*	-0.22	-0.31*	-0.17	-0.35*	-0.36**	-0.24	0.10	0.19	0.37**
Δ WC								1	0.16	0.47**	0.09	0.24	0.17	0.21	0.02	-0.24	-0.17	-0.31*	-0.28	-0.16	0.05	0.09	0.13
Δ Body fat %									1	0.28*	-0.04	-0.04	0.18	0.12	-0.17	0.08	-0.09	0.02	-0.29*	-0.13	-0.05	0.18	0.26*
Δ Weight										1	0.15	0.31*	0.35**	0.37**	-0.24	-0.32*	-0.26	-0.36**	-0.36**	-0.25	0.08	0.16	0.35**
Δ Glucose											1	0.27*	0.10	-0.07	0.18	-0.09	-0.04	-0.10	-0.14	-0.23	0.17	0.00	-0.15

Δ Insulin												1	0.24	0.23	-0.22	-0.21	-0.28	-0.19	-0.21	-0.16	-0.17	-0.25	-0.05
Δ HbA1c													1	0.21	0.00	-0.12	-0.34*	-0.26	-0.41**	-0.28*	0.04	-0.02	0.14
Δ SB%														1	-0.76**	-0.66**	-0.88**	-0.77**	-0.60**	-0.37**	-0.08	-0.05	0.21
Δ Standing %															1	0.21	0.47**	0.24	0.30*	0.15	0.22	0.06	-0.15
Δ LPA%																1	0.76**	0.87**	0.44**	0.34*	0.10	0.09	-0.10
Δ MVPA%																		0.81**	0.73**	0.44**	-0.10	-0.07	-0.24
Δ PA%																		1	0.64**	0.41**	-0.10	-0.08	-0.23
Δ Steps																			1	0.57**	-0.07	-0.11	-0.26
Δ Breaks in SB																				1	0.07	0.10	0.04
Δ BP																					1	0.67**	0.48**
Δ PRD																						1	0.61**

Δ Change in the measured outcome, Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity measured with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability measured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05, **significant at the level of p<0.01.

Supplementary Figure 2. Changes in A) transversospinal glucose uptake (GU) and B) erector spinae GU according to the change in step count. Adjusted for sex. Black upright triangles represent the group that increased their daily steps by >2500/day and gray downward triangles represent the group that increased their daily steps by <2500/day.



Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

Design and conduct				
1.	Clear description of the goal of research, study objective(s), study design, and study population	Yes	Unclear	No
2.	Clear description of outcomes, exposures/treatments and covariates, and their measurement methods	Yes	Unclear	No
3.	Validity of study design	Yes	Unclear	No
4.	Clear statement and justification of sample size	Yes	Unclear	No
5.	Clear declaration of design violations and acceptability of the design violations	Yes	Unclear	No
6.	Consistency between the paper and its previously published protocol	Yes	Unclear	No
Data analysis				
7.	Correct and complete description of statistical methods	Yes	Unclear	No
8.	Valid statistical methods used and assumptions outlined	Yes	Unclear	No
9.	Appropriate assessment of treatment effect or interaction between treatment and another covariate	Yes	Unclear	No
10.	Correct use of correlation and associational statistical testing	Yes	Unclear	No
11.	Appropriate handling of continuous predictors	Yes	Unclear	No
12.	Confidence intervals do not include impossible values	Yes	Unclear	No
13.	Appropriate comparison of baseline characteristics between the study arms in randomized trials	Yes	Unclear	No
14.	Correct assessment and adjustment of confounding	Yes	Unclear	No
15.	Avoiding model extrapolation not supported by data	Yes	Unclear	No
16.	Adequate handling of missing data	Yes	Unclear	No
Reporting and presentation				
17.	Adequate and correct description of the data	Yes	Unclear	No
18.	Descriptive results provided as occurrence measures with confidence intervals, and analytic results provided as association measures and confidence intervals along with P-values	Yes	Unclear	No
19.	Confidence intervals provided for the contrast between groups rather than for each group	Yes	Unclear	No
20.	Avoiding selective reporting of analyses and P-hacking	Yes	Unclear	No
21.	Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, and reporting the P-values rather their range	Yes	Unclear	No
22.	Providing sufficient numerical results that could be included in a subsequent meta-analysis	Yes	Unclear	No
23.	Acceptable presentation of the figures and tables	Yes	Unclear	No
Interpretation				
24.	Interpreting the results based on association measures and 95% confidence intervals along with P-values, and correctly interpreting large P-values as indecisive results, not evidence of absence of an effect	Yes	Unclear	No
25.	Using confidence intervals rather than post-hoc power analysis for interpreting the results of studies	Yes	Unclear	No
26.	Correctly interpreting occurrence or association measures	Yes	Unclear	No
27.	Distinguishing causation from association and correlation	Yes	Unclear	No
28.	Results of pre-specified analyses are distinguished from the results of exploratory analyses in the interpretation	Yes	Unclear	No
29.	Appropriate discussion of the study methodological limitations	Yes	Unclear	No
30.	Drawing only conclusions supported by the statistical analysis and no generalization of the results to subjects outside the target population	Yes	Unclear	No

Mansournia MA, *et al. Br J Sports Med* 2021; 55:1–2. doi: 10.1136/bjsports-2020-10365

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	1	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	4	
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	4-6	
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	5-6	
	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	-	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	5-6	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	4	

	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	4, 5	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	4-5	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	5-6	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	7	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).