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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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| 1 2 | | |
|--|----|---|
| 2 3 | 1 | Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat |
| 4 5 6 | 2 | fraction and their associations: A six-month randomized controlled trial |
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| 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 | 17 | ⁺ Jooa Norha and Tanja Sjöros contributed equally to this work. |

| 1 | | |
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| 2 3 4 | 18 | ABSTRACT |
| 5 6 | 19 | Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, |
| 7 | 20 | this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and |
| 8 9 | 21 | related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) |
| 10 11 | 22 | insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF). |
| 12 13 | 23 | Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into |
| 14 15 | 24 | intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day |
| 16 17 | 25 | (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain- |
| 18 | 26 | related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) |
| 19 20 | 27 | questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission |
| 21 22 | 28 | tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance |
| 23 | 29 | imaging. |
| 24 25 26 | 30 | Results Pain-related disability increased during the intervention in both groups. Back pain intensity |
| 27 | 31 | increased significantly more in the control group than in the intervention group in which back pain intensity |
| 28 29 | 32 | remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain- |
| 30 31 | 33 | related disability, ODI, or paraspinal GU and FF were observed. The change in daily steps associated |
| 31 32 33 | 34 | positively with the change in paraspinal muscle GU. |
| 34 35 | 35 | Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening |
| 36 | 36 | regardless of paraspinal muscle GU or FF. |
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| 39 40 | 57 | |
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| 45 46 | 40 | Keywords: sedentary behaviour, accelerometry, back pain, disability, insulin sensitivity, muscle fat fraction |
| 47 | 41 | |
| 48 49 | 71 | |
| 50 51 | 42 | What is already known on this topic |
| 52 | 43 | - Lack of physical activity and high sedentary behaviour may lead to insulin resistance and fat |
| 53 54 | 44 | infiltration of the back muscles which may contribute to back pain and disability. |
| 55 56 | 45 | - Whether reducing sedentary behaviour can improve back muscle insulin sensitivity or fat |
| 57 58 | 46 | infiltration, back pain, or pain-related disability, is not currently known. |
| 59 60 | 47 | What this study adds |
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|--------------|----|--|
| 3 | 48 | - Reducing sedentary behaviour may prevent back pain from increasing even if no improvements in |
| 4 5 | 49 | disability, back muscle insulin sensitivity or fat infiltration are achieved. |
| 6 7 | 50 | - Increasing daily steps may improve back muscle insulin sensitivity. |
| 8 9 10 | 51 | How this study might affect research, practice or policy |
| 11 | 52 | - Clinicians should consider patients' sedentary behaviour habits and consider guiding them towards |
| 12 13 | 53 | reducing sedentary time to prevent or reduce back pain. |
| 14 15 | 54 | - Pain-related rehabilitation outcomes may not be related to the physiological risk factors (such as |
| 16 | 55 | insulin resistance or muscle fat infiltration) for pain. |
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56 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.

68 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.

74 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/m², 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).

83 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 ¹⁸F-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, <u>https://www.carimas.fi</u>). 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 28 101 (Movesense, Suunto, Vantaa, Finland, with ExSed application, UKK Terveyspalvelut Oy, Tampere, Finland). ₃₀ 102 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 33 104 [MVPA]) and angle for posture estimation (to differentiate SB and standing) methods as described previously (3,18-20). 37 106 Height was measured using a wall-mounted stadiometer, and body mass and body fat percentage were ₃₉ 107 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 42 109 iliac crest. Intervention 47 111 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 50 113 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 54 115 their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by 56 116 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

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| 3 4 | 119 | group, the daily SB and PA goals were set equal to the screening values. All participants could monitor their |
| 5 | 120 | daily SB and PA and the fulfilment of the goals using a mobile phone application (ExSed) connected to the |
| 6 7 8 | 121 | accelerometer. |
| 9 10 | | Patient involvement |
| 12 | 123 | Patients were not involved in designing or conducting this study. |
| 14 15 | 124 | Equity, diversity and inclusion |
| | 125 | Both the study participants and researchers include self-identified men and women in a relatively balanced |
| 17 18 19 | | fashion. The research group consists of both junior and senior researchers. |
| 20 21 | 127 | Statistical methods |
| 22 23 | 128 | Baseline characteristics are presented as mean (standard deviation, SD) if not stated otherwise. |
| | 129 | Intervention effects are presented as model-based mean (95% confidence interval, 95% CI). Baseline |
| | 130 | correlations were analyzed using the Spearman rank correlation. The main analyses of intervention effects |
| 27 28 | 131 | were performed using linear mixed models for repeated measurements. The outcome of interest was the |
| 29 | 132 | dependent variable, and independent variables included group, time, sex, and group x time in all analyses. |
| 30 31 | 133 | Additionally, FF analyses were adjusted for age, and pain questionnaire analyses were adjusted for self- |
| 32 33 | 134 | reported regular pain medication status (yes/no) and BMI, because this improved the distribution of the |
| 34 | | residuals. The normal distribution of the residuals was visually inspected, and log10 or square root |
| | 136 | transformations were performed as necessary. Tukey-Kramer adjustment for multiple comparisons was |
| 37 38 | 137 | used. Compound symmetry or unstructured covariance structure was chosen based on the Akaike |
| 39 | 138 | information criterion. Statistical significance was set at p<0.05 (two-tailed). The main analyses were |
| | 139 | performed in SAS (version 9.4 for Windows, SAS Institute Inc., Cary, NC) and the correlation analyses were |
| 42 43 44 | | performed using JMP Statistics (version 16, SAS Institute Inc., Cary, NC). |
| 45 | 141 | The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power |
| 46 47 | 142 | calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined |
| 48 49 | 143 | based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming |
| 50 | | an increase of 0.7 (SD 0.55) μ mol/100g/min in the intervention group (10% increase) and an increase of |
| 51 52 | 145 | 0.05 μ mol/100g/min in the control group, we calculated that 16 participants per group would be sufficient |
| 53 54 | | for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity |
| 55 | 147 | (α =0.05, 1- β =0.9). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 |
| 56 57 | 148 | participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin |
| | 149 | 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. |
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| 2 3 4 | 151 | |
| 5 6 | 152 | RESULTS |
| 7 8 9 | 153 | Baseline characteristics |
| 10 | 154 | Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were |
| 11 12 | 155 | randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary |
| 13 14 | 156 | Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain |
| 15 | 157 | (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample |
| 16 17 | 158 | of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and |
| 18 19 | 159 | MR imaging. The baseline characteristics are presented in Table 1. |
| 20 | 160 | Baseline correlations |
| | 161 | All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated |
| | 162 | positively with erector spinae and transversospinal FF (r_s =0.53, 0.55, respectively). Erector spinae GU |
| 26 27 | 163 | correlated positively with MVPA and step count (r_s =0.36 and 0.40, respectively) and negatively with SB (r_s =- |
| 28 29 | 164 | 0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s =0.42 and |
| 30 | 165 | 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and |
| 31 32 | 166 | transversospinal FF correlated with MVPA (r_s =-0.30 and -0.36, respectively). Increased body adiposity (BMI |
| 33 34 | | and body fat percentage) associated with lower paraspinal muscle GU and higher FF. |
| | 168 | Pain-related disability correlated positively with standing time (r_s =0.27). Furthermore, the ODI score |
| 37 38 | 169 | correlated negatively with MVPA (r_s =-0.28) and step count (r_s =-0.26). Finally, the ODI score correlated |
| 39 40 | 170 | positively with body fat percentage (r $_{ m s}$ =0.33). Back pain intensity did not correlate with any PA, SB, or |
| 40 41 42 | 171 | paraspinal muscle-related variables. |
| 43 44 | 172 | Intervention effects |
| 45 46 47 | 173 | Accelerometry |
| 48 | 174 | The intervention effects on SB and PA have been reported previously (18). During the six-month study |
| 49 50 | 175 | period, the intervention group reduced SB by 40 min/day on average. Subsequently, MVPA increased in the |
| 51 | 176 | intervention group by 20 min/day, with no statistically significant changes in the control group. LPA |
| 52 53 | 177 | increased on average by 10 min/day without statistically significant between-group differences. Both |
| 54 55 | 178 | groups increased their daily step counts with a statistically significantly higher increase in the intervention |
| 56 57 | 179 | group (+3300 vs. +1600 steps/day in the intervention and control groups, respectively). |
| 58 59 60 | | Pain and disability questionnaires |

Page 9 of 29

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| The pain and disability questionnaire results are presented in Figure 1. In the intervention group, back pa |
|---|
| 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 c |
| 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 > |
| 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 tim |
| 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 n |
| 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 o |
| 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 |

185 Paraspinal muscle FF and GU

13 186 Transversospinal FF was higher in the control group thro 187 significant changes were observed in paraspinal muscle

17 188 **Explorative analyses**

19 189 As previously done (12,18), when the study group was d 20 daily steps no statistically significant changes in any pain 21 190 22 191 p>0.05 for all; data not shown). Furthermore, no statistic 23 24 192 paraspinal muscle FF or GU when the group was divided 25 26 193 time p>0.05 for all; data not shown). However, with the 27 28 ¹⁹⁴ steps/day vs. <2500 steps/day increase, or decrease), th 29 195 GU were statistically significantly different between group 30 31 196 p=0.033) (Supplementary Figure 2).

33 197 In the whole study group, the changes in BMI, body fat p 34 35 198 with the change in ODI (Table 2). None of the changes in 36 ₃₇ 199 related outcomes. The change in BMI correlated negativ 38 200 transversospinal GU (r_s=-0.34 and -0.40, respectively). Ir 39 40 201 count increase, the changes in steps correlated positivel 41 ₄₂ 202 with the changes in FF.

44 203 DISCUSSION

46 204 In the present study, we show that an intervention aime 47 48 205 prevent the worsening of back pain intensity which was 49 50 206 change in back pain intensity was not associated with ch 51 207 transversospinales) FF, GU, or the changes in PA, SB, pai 52 53 208 intervention effects on paraspinal muscle FF or GU were 54 55 209 associated with improved paraspinal muscle GU.

⁵⁷ 210 Pain and physical behaviours

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211 In this study, back pain intensity increased by about two-fold in the control group, on average. Although the 212 baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS 213 in the intervention and control groups, respectively), the change in the control group represents a 214 substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening 10 215 with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain 11 216 intensity are achieved. However, we did not observe any intervention effects on pain-related disability or 12 13 217 ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This 14 15 218 might be explained by the relatively low pain intensity that might not be severe enough to cause disability. 16

17 219 The reason for back pain intensity increase in the control group remains elusive. One explanation for the 18 19 220 increase could be related to the open-label nature of this study. Although not formally documented, many 20 221 control participants were disappointed to be included in the control group instead of the intervention 21 22 222 group. These negative emotions may have affected pain intensity (22). This phenomenon, in conjunction 23 24 223 with the possible benefits from the increased PA in the intervention group, could explain the difference 25 224 between groups. The fact that the explorative analyses with SB or step-based post hoc group divisions 26 27 225 showed no between-group differences in pain-related outcomes further emphasizes that the sole 28 29 226 allocation to either intervention or control group may have affected the perception of pain. However, the 30 227 cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count 31 32 228 associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the 33 34 229 cross-sectional correlations and the correlations of changes during the study suggest that maintaining a 35 230 healthier body composition could decrease disability, as body fat percentage correlated positively with the 36 37 231 ODI score (see Table 2 and Supplementary Table 1). 38

39 ₄₀ 232 Contrary to our results, a previous six-month randomized controlled trial involving adults with low back 41 233 pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an 42 43 234 intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity 44 45 235 measured using VAS did not differ between groups in the study (5). The study sample was comparable to 46 236 ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our 47 48 237 study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was 49 50 238 longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, 51 239 the aforementioned study did not aim to change only SB but also included behavioral counseling in the self-52 53 240 management of pain. Furthermore, the reduction in SB was notably higher in the previous study compared 54 55 241 to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. Additionally, the 56 242 intensity of longstanding pain might not always be related to the disability (23). 57

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243 As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with 244 pain-related disability at baseline in our study (3). However, no correlation between the change in standing 245 time and the change in pain-related disability was observed. Related to this finding, a recent randomized 246 controlled trial observed that, within three months, increasing occupational standing may increase 10 247 multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer 248 present (4). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that 249 standing may exacerbate pain acutely, but habitual standing may not be detrimental.

250 Paraspinal muscle FF and GU

18 251 We did not observe any intervention effects on either erector spinae or transversospinal FF. This finding is 252 consistent with a recent systematic review of six intervention studies, concluding that paraspinal FF cannot 253 be reduced even with exercise training (24). This demonstrates that even though paraspinal muscle FF is 23 254 strongly associated with back pain (7–9), successful back pain prevention or treatment can be independent 255 of FF. This may be explained in part by the effect of time, i.e., age, which correlated with paraspinal FF 256 (r_s=0.55 and 0.53 for transversospinal and erector spinae FF; see Supplementary Table 1) and was a 28 257 significant contributor in the linear models investigating paraspinal FF (p<0.001 for both muscle groups) in ₃₀ 258 this study. In accordance, the effectiveness of back pain rehabilitation is not related to specific strength or 259 mobility goals of the rehabilitation (25), emphasizing other than structural aspects in treating experienced 33 260 pain and disability. Therefore, back pain risk factors (such as paraspinal muscle FF) should not be the direct ₃₅ 261 targets of rehabilitation as much as the psychological and cognitive aspects of pain perception and the 262 individual preferences for physical exercise (26). However, as lower paraspinal muscle FF associated with 38 263 higher amounts of MVPA and lower body adiposity, the results suggest that maintaining healthy body ₄₀ 264 composition and MVPA levels might help prevent fat infiltration of the paraspinal muscles.

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42 265 We have previously reported the intervention effects on hamstrings and quadriceps femoris GU (12) which 43 44 266 seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses 45 267 revealed no intervention effects on any of these muscles. However, the secondary analyses of the present 46 47 268 study and the previously published study show the association between increased PA (e.g., steps) and 48 49 269 improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant 50 270 moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle 51 52 271 GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal 53 54 272 muscle GU correlated with the changes in any pain-related outcomes (Table 2). Moreover, as paraspinal 55 273 muscle GU but not FF was associated with steps, the results suggest that GU can improve despite no 56 ⁵⁷ 274 changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI correlated 58 59 275 negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI. 60

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276 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.

281 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.

295 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.

301 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.
 the manuscript.

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| 19 20 315 21 | collecting, analyzing, or interpreting the data, or preparing the manuscript. |
| 22 316 23 | Conflicts of interest |
| ²⁴ 317 25 | The authors declare the following financial interests/personal relationships which may be considered as |
| 26 318 | potential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The |
| 27 28 319 | other authors report no conflicts of interest. The results are presented clearly and honestly without |
| ²⁹ 320 30 | fabrication, falsification, or inappropriate data manipulation. |
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| 46 47 4 | 06 | Figu | ire legends |
| 48 49 4 | 07 | Figu | re 1. Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry |
| 50 51 4 | | - | bility index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black |
| 52 53 4 | | | s represent the intervention group and gray squares represent the control group. The presented |
| 53 ⁻ 54 4 | | | mates are model-based means and 95% confidence intervals. VAS = visual analogue scale. *=Tukey's |
| 55 56 4 | | | .026 |
| 57 | | μ-0 | .020 |
| ⁵⁸ 4 59 | 12 | Figu | re 2. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) |
| 60 4 | 13 | tran | sversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are |

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| 2 3 | 414 | adjusted for sox and EE analyses (namels C and D) are additionally adjusted for age. Black data represent |
| 4 5 | 414 | 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- |
| 5 6 7 | 416 | based means and 95% confidence intervals. |
| 7 8 | 410 | based means and 55% confidence intervals. |
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Table 1. Study participant characteristics at the baseline. Unless otherwise stated, the results arepresented as mean (SD).

| | | Intervention | n | Control | n |
|--------------------------------|----------------------------|-------------------|----|-------------------|----|
| Men, n (%) | | 13 (39) | 33 | 14 (45) | 31 |
| Age, yrs | | 59 (6) | 33 | 57 (8) | 31 |
| Anthropometrics & | netabolism | | | | |
| 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) | 22 |
| Erector spinae FF, % | | 17.5 (13.3, 26.8) | 22 | 18.0 (14.4, 23.4) | 2 |
| Transversospinal GU | | 2.8 (2.3, 3.2) | 23 | 2.5 (2.0, 3.3) | 20 |
| µmol/100 cm ³ /min* | | | | | |
| Erector spinae GU, | | 2.9 (2.0, 3.3) | 23 | 2.4 (1.9, 3.9) | 20 |
| µmol/100 cm ³ /min* | | | | | |
| 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, μm | ol/kg/min* | 15.3 (10.7, 21.0) | 33 | 13.9 (9.8, 21.0) | 3 |
| Pain & disability | | | | | |
| Regular medication f | or pain, n (%) | 3 (9) | 33 | 4 (13) | 3 |
| VAS Back pain, 0-10 | cm* | 0.3 (0.1, 3.5) | 33 | 0.5 (0.1, 3.0) | 29 |
| VAS Pain-related disa | bility, 0-10 cm* | 0.4 (0.1, 2.2) | 33 | 0.7 (0.2, 2.6) | 30 |
| Oswestry disability ir | idex, %* | 6.0 (1.0, 13.0) | 33 | 6.7 (2.0, 16.0) | 31 |
| Physical activity | | 9 | | | |
| Accelerometry, h/da | y | 14.5 (1.0) | 33 | 14.6 (1.0) | 3 |
| Sedentary time, h/da | | 10.0 (0.9) | 33 | 10.1 (1.1) | 32 |
| Standing time, h/day | | 1.8 (0.6) | 33 | 1.8 (0.6) | 32 |
| LPA, h/day | | 1.7 (0.4) | 33 | 1.8 (0.5) | 32 |
| MVPA, h/day | | 0.96 (0.31) | 33 | 0.97 (0.34) | 31 |
| Breaks in sedentary t | ime, 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).

| Page | 18 | of 2 | 9 |
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| | Δ ES FF | Δ Tra. GU | A ES GU | A QF GU | Δ Ham. GU | efficien □ 0 0 0 0 0 0 0 0 0 0 0 0 0 | Δ BMI | Δ WC | Δ Body fat % | Δ Weight | Δ Glucose | Δ Insulin | Δ HbA1c | ∆ SB% | Δ Standing% | Δ LPA% | n 28 Septen ing∀d0/\USes | Δ PA% | Δ Steps | Δ Breaks in SB | Δ BP | Δ PRD | A ODI |
|---------------------|------------|-----------|---------|------------|------------|--|-----------------|----------------|-----------------|-----------------|----------------|----------------|----------------|-----------------|----------------|----------------|--|----------------|-----------------|-------------------|-----------|-----------|------------|
| ∆ 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 | emen ted to | | 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 | Downloaded fr it Superieur (AE) text and data | 0.13 | 0.22 | 0.24 | - 0.11 | 0.17 | - 0.05 |
| ∆ 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 | r (ABES) . 2 Ida mining, AI | 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 | g, Al trainir | 0.29 | 0.41 * | 0.05 | 0.04 | 0.26 | 0.07 |
| ∆ 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 * | 9.46 bmj. | 0.50 ** | 0.42 * | 0.06 | 0.04 | 0.03 | - 0.17 |
| ∆ Ha m. GU | | | | | 1 | 0.77 | - 0.46 ** | - 0.26 | - 0.27 | - 0.45 ** | - 0.06 | - 0.19 | - 0.14 | - 0.53 ** | 0.39 * | 0.39 | similår technotogies. | 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 * | e Z, 2025 at 2 hotogies. | 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 * | - Agence | - 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 | - Bibliographique de | - 0.31 * | - 0.28 | - 0.16 | 0.05 | 0.09 | 0.13 |

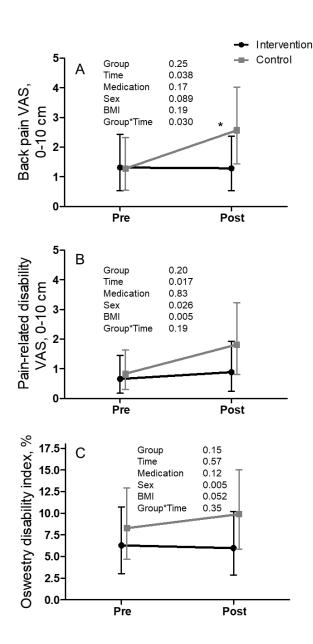
BMJ Open Table 2. Spearman's rank correlation coefficients between changes (Δ values) in the measured outcomes before and acter the 6-month intervention period.

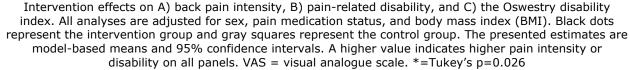
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| Δ SB% | | | 0.77 0.60 ** ** | 0.37 0.08 | - 0.05 | 0 |
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Δ Change in the measured outcome, Tra., transversospinal muscles; FF, fat fraction measured with magnetic reso GU, insulin-stimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission 🐺 🗟 graphy; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fater centage; 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; Bb thick pain measured with visual analogue scale; ODI, Oswestry disability index. ** significant at the level of p<0.01.





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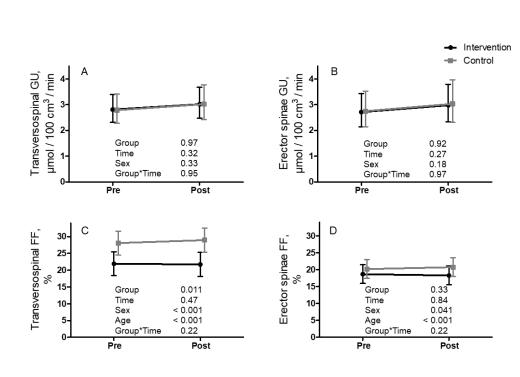


Figure 2. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black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

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BMJ Open

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

Jooa Norha^{1*†}, Tanja Sjöros^{1†}, Taru Garthwaite¹, Saara Laine¹, Tiina Verho¹, Virva Saunavaara^{1,2}, Kirsi Laitinen³, Noora Houttu³, Jussi Hirvonen^{4, 5} Henri Vähä-Ypyä⁶, Harri Sievänen⁶, Eliisa Löyttyniemi⁷, Tommi Vasankari^{4, 6}, Kari K. Kalliokoski¹, Ilkka H. A. Heinonen¹

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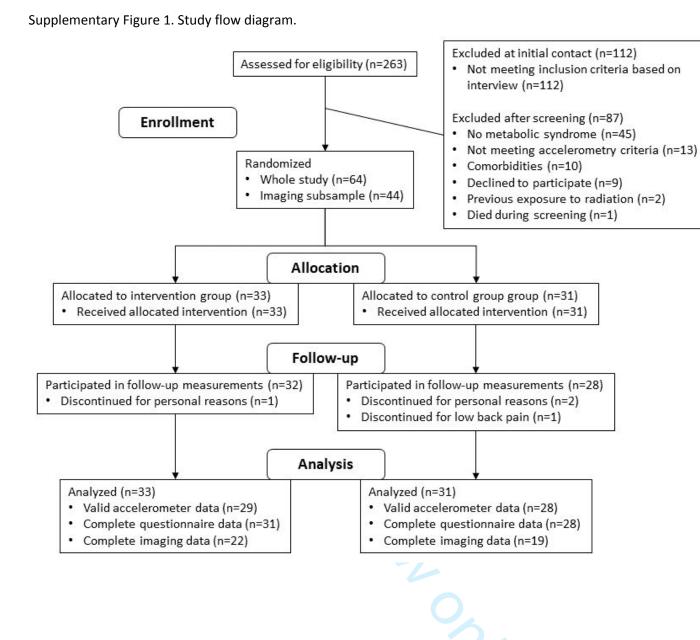
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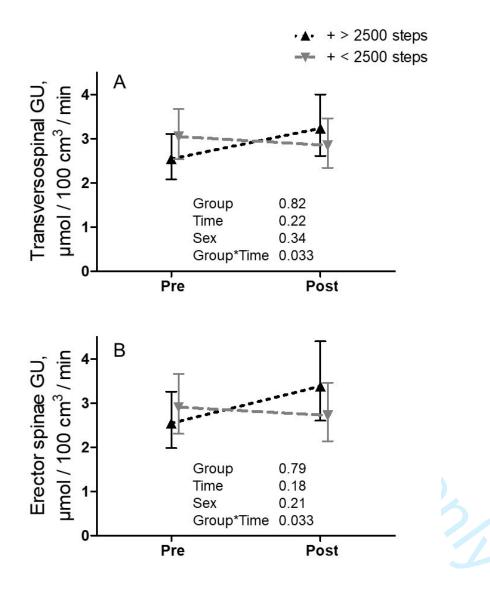
Supplementary Table 1. Baseline Spearman's rank correlation coefficients

| | Tra. FF | ES FF | Tra. GU | ES GU | QF GU | Ham. GU | WB GU | BMI | WC | Body fat % | Weight | Glucos e | Insulin | HbA1c | SB % | Standi ng % | LPA % | MVPA % | PA % | steps -0.26 | -084305 | BP | PRD | IDO |
|----------|---------|--------|---------------------|---------------------|--------|---------------------|--------|---------|---------|---------------|---------|-------------|---------|---------|---------|----------------|---------|-----------|---------|--|-----------------|-------|----------------------|-----|
| 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 5' | 0.10 | 0.02 | 0.1 |
| Tra. FF | 1 | 0.79** | - <mark>0.14</mark> | - <mark>0.10</mark> | 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 | 0.60 | 0.11 | 0.07 | 0.1 |
| ES FF | | 1 | -0.24 | -0.22 | -0.06 | - <mark>0.10</mark> | -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 9 | -0 6 8 | -0.05 | -0.09 | 0.0 |
| 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 | -0.27 uses 0.44*es re | Ens. | -0.04 | -0.14 | -0. |
| 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°a | | -0.04 | -0.18 | -0. |
| 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 ·d | 2027 ennie | -0.11 | -0.13 | -0. |
| 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 6 | in F Dia | -0.07 | -0.08 | -0. |
| | | | | | | - | | | | | | | | | | | | | 0.00 | X. | wn | 1000 | | |
| 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 nd | pad | 0.07 | 0.03 | -0 |
| BMI | | | | | | | | 1 | 0.76** | 0.54** | 0.80** | 0.15 | 0.61** | 0.08 | 0.29* | -0.16 | -0.09 | -0.26* | -0.23 | 0.40 ss related to text and data minin | Ed f | 0.00 | -0.02 | 0. |
| WC | | | | | | | | | 1 | 0.23 | 0.80** | 0.25* | 0.64** | 0.26* | 0.38** | -0.31* | -0.17 | -0.32* | -0.29* | -0.42 3 . | BES nom | -0.03 | 0.00 | 0. |
| 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. |
| Weight | | | | | | | | | | | 1 | 0.27* | 0.68** | 0.17 | 0.40** | -0.35** | -0.24 | -0.18 | -0.28* | -0.33 | -031 | -0.13 | -0.12 | -0 |
| Glucose | | | | | | | | | | | - | 1 | 0.24 | 0.12 | 0.06 | -0.32** | 0.17 | 0.10 | 0.16 | 0.01 aini | -0.02 | -0.15 | -0.16 | -0 |
| Insulin | | | | | | | | | | | - | | 1 | 0.25* | 0.41** | -0.49** | -0.15 | -0.11 | -0.19 | -0.260 | -0 9 0 | -0.16 | -0.08 | 0.0 |
| HbA1c | | | | | | | | | | - | | | - | 1 | 0.14 | -0.18 | 0.10 | -0.10 | -0.01 | -0.10 d | -0 1 6 | 0.01 | -0.07 | 0.: |
| SB | | | | | | | | | | | | | | - - | 1 | -0.79** | -0.62** | -0.55** | -0.75** | -0.54 <u>S</u> . B | -0.86** | 0.03 | -0.19 | 0. |
| Standing | | | | | | | | | | - | | | | | | 1 | 0.28* | 0.19 | 0.30* | 0.22 a | 0.26 | 0.06 | 0.27* | 0. |
| LPA | | | | | | | | - | | | | | | | | | 1 | 0.28* | 0.83** | 0.21 7 | 0.35** | 0.06 | 0.04 | -0 |
| MVPA | | | | | | | | | | | | | | | | | | 1 | 0.73** | 0.93 h | | -0.20 | -0.03 | -0 |
| PA | | | | | | | | | | | | | | - | | | | | 1 | 0.65 0 | 0.30" N | -0.09 | - <mark>0.0</mark> 1 | -0 |
| Steps | | | | | | | | | | | | | | | | | | | | gies. | 0.25 | -0.18 | -0.03 | -0 |
| Breaks | | | | | | | | | | | | | | | | | | | | | 1 A | 0.09 | 0.14 | -0 |
| BP | | | | | | | | | | | | | | | | | | <u> </u> | | | ge | 1 | 0.61** | 0. |
| PRD | | | | | | | | | | | - | | | | | | | | | - | enc | + | 1 | 0. |

Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulin-stimula d glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadriceps femoris muscle; Ham., hamstring muscles; WB, whole-body; Hall, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; LPA, light physical activity deasured 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. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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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.



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Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

| 1. | Clear description of the goal of research, study objective(s), study design, and study population | Yes _s | Unclear |] |
|------------|--|------------------|---------|---|
| 2. | population Clear description of outcomes, exposures/treatments and covariates, and their measurement | Yes | Unclear |] |
| 2 | methods Validity of study design | Yes | Unclear | 1 |
| 3. 4. | Clear statement and justification of sample size | Yes | Unclear | 1 |
| 5. | Clear declaration of design violations and acceptability of the design violations | Yes | Unclear | 1 |
| 6. | Consistency between the paper and its previously published protocol | Yes | Unclear | 1 |
| Data an | | | | |
| 7. | Correct and complete description of statistical methods | Yes | Unclear | 1 |
| 8. | Valid statistical methods used and assumptions outlined | Yes | Unclear | 1 |
| 9. | Appropriate assessment of treatment effect or interaction between treatment and another | Yes | Unclear | 1 |
| | covariate | 105 | Uncieda | 1 |
| 10. | Correct use of correlation and associational statistical testing | Yes | Unclear | 1 |
| 11. | Appropriate handling of continuous predictors | Yes | Unclear | ľ |
| 12. | Confidence intervals do not include impossible values | Yes | Unclear | l |
| 13. | Appropriate comparison of baseline characteristics between the study arms in randomized | Yes | Unclear | 1 |
| 14 | trials Correct assessment and adjustment of confounding | Yes | Unclear | 1 |
| 14. | Avoiding model extrapolation not supported by data | Yes | Unclear | 1 |
| 15. 16. | Adequate handling of missing data | Yes | Unclear | 1 |
| | and presentation | 105 | Oncical | 1 |
| 17. | Adequate and correct description of the data | Yes | Unclear | 1 |
| 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 | 1 |
| 19. | Confidence intervals provided for the contrast between groups rather than for each group | Yes | Unclear | 1 |
| 20. | Avoiding selective reporting of analyses and P-hacking | Yes | Unclear | l |
| 21. | Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, | Yes | Unalaar | r |
| | and reporting the P-values rather their range | 1 05 | Unclear | 1 |
| 22. | Providing sufficient numerical results that could be included in a subsequent meta-analysis | Yes | Unclear | 1 |
| 23. | Acceptable presentation of the figures and tables | Yes | Unclear | ľ |
| Interpre | tation | | | |
| 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 | 1 |
| 25. | Using confidence intervals rather than post-hoc power analysis for interpreting the results of | V | 11 | |
| | studies | Yes | Unclear | 1 |
| 26. | Correctly interpreting occurrence or association measures | Yes | Unclear | Ì |
| 27. | Distinguishing causation from association and correlation | Yes | Unclear | l |
| 28. | Results of pre-specified analyses are distinguished from the results of exploratory analyses in the interpretation | Yes | Unclear | 1 |
| 29. | Appropriate discussion of the study methodological limitations | -Yes | Unclear | |
| | Drawing only conclusions supported by the statistical analysis and no generalization of the results | Yes | Uncical | 1 |

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 Page 28 of 29

 Mursourniu MA, et al. Br.J.Sports Med 2021; 55:1–2. doi: 10.1136/bjsports-2020-1036F
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|------------|-------------------------------------|--|---------------------|---|------------------------------|
| | DieR | The TIDieR (Template for Intervention Description and | d Replicat | tion) Checklist*: | |
| | or Intervention and Replication | Information to include when describing an intervention and the | e location | of the information | |
| ltem | Item | | ding | Where lo | ocated ** |
| number | | | for uses relat | grimary paper | Other [†] (details) |
| | BRIEF NAME | | ed to | 024. [| |
| 1. | | e or a phrase that describes the intervention. | text and | 11 Superie | |
| 2. | Describe any rat | ionale, theory, or goal of the elements essential to the intervention. | data mir | 44 ded from | |
| 3. | Materials: Descriprovided to partic | be any physical or informational materials used in the intervention, includ cipants or used in intervention delivery or in training of intervention provid ion on where the materials can be accessed (e.g. online appendix, URL). | ling those lers. | 4-64 | |
| 4. | Procedures: Des | cribe each of the procedures, activities, and/or processes used in the interabling or support activities. | Di | en.bmj.com/ 0 | |
| 5. | - | ry of intervention provider (e.g. psychologist, nursing assistant), describe round and any specific training given. | + | - - - - - - - - - - - - - - - - - - - | |
| 6. | | des of delivery (e.g. face-to-face or by some other mechanism, such as ir intervention and whether it was provided individually or in a group. | ,, nternet or | at5-6 Agence | |
| 7. | Describe the type | e(s) of location(s) where the intervention occurred, including any necessa relevant features. | ary | 4 Bibliographique | |
| TIDieR che | cklist | For peer review only - http://bmjopen.bmj.com/site/about/guide | elines.xhtml | hique de | I |

 WHEN and HOW MUCH
 Including the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.

 TAILORING
 Tailor including the number of sessions in the intervention was delivered and over what period of time including the number of sessions intensity or dose.

 8. 4 5 TAILORING If the intervention was planned to be personalised, titrated or adapted, then describe what, why, 4-5 9. ber 2024. when, and how. **MODIFICATIONS** nt Su If the intervention was modified during the course of the study, describe the changes (what, why, 10.* N/A vnloaded perieur (*/* t and data when, and how). **HOW WELL** Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any 5-6 11. http://bh strategies were used to maintain or improve fidelity, describe them. , ĝu AI trainin 12.[‡] Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned. ** 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 and elaboration 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 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 a 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 claecklist for that study design (see www.equator-network.org). For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml de **TIDieR** checklist

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44 45 46 Page 30 of 29

BMJ Open

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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| Date Submitted by the Author: | 12-Aug-2024 |
| Complete List of Authors: | Norha, Jooa; Turku University Hospital; University of Turku, Turku PET Centre Sjöros, Tanja; Turku PET Centre Garthwaite, Taru; Turku PET Centre Laine, Saara; Turku PET Centre Verho, Tiina; Turku University Hospital Saunavaara, Virva; Turku University Hospital; Turku University Hospital, Department of Medical Physics Laitinen, Kirsi; University of Turku Houttu, Noora; Institute of Biomedicine; Functional Foods Forum University of Turku Hirvonen, Jussi; Tampere University; Turku University Hospital, Department of Radiology Vähä-Ypyä, Henri; Ukk Instituutti Sievänen, Harri; UKk-Institute Löyttyniemi, Eliisa; University of Turku Vasankari, Tommi ; Ukk Instituutti Kalliokoski, Kari; University of Turku, Turku PET Centre Heinonen, Ilkka; Turku PET Centre |
| Primary Subject Heading : | Rehabilitation medicine |
| Secondary Subject Heading: | Sports and exercise medicine |
| Keywords: | Back pain < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, Clinical Trial, Overweight, Magnetic Resonance Imaging |
| | |

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| 1 2 | | |
|----------------------------|----|---|
| 3 | 1 | Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat |
| 4 5 6 | 2 | fraction and their associations: Secondary analysis of a six-month randomized controlled trial |
| 7 | 3 | Jooa Norha1* [†] , Tanja Sjöros1 [†] , Taru Garthwaite ¹ , Saara Laine1, Tiina Verho1, Virva Saunavaara1,2, Kirsi |
| 8 9 | 4 | Laitinen ³ , Noora Houttu ³ , Jussi Hirvonen ^{4, 5} Henri Vähä-Ypyä ⁶ , Harri Sievänen ⁶ , Eliisa Löyttyniemi ⁷ , Tommi |
| 10 11 12 | 5 | Vasankari ^{4, 6} , Kari K. Kalliokoski ¹ , Ilkka H. A. Heinonen ¹ |
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| 37 38 | 17 | + Jooa Norha and Tanja Sjöros contributed equally to this work. |
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| 2 3 | 18 | ABSTRACT |
| 4 | 10 | |
| 5 6 | 19 | Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, |
| 7 8 | 20 | this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and |
| 9 | 21 | related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) |
| 10 11 | 22 | insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF). |
| 12 13 | 23 | Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into |
| 14 15 | 24 | intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day |
| 16 17 | 25 | (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain- |
| 17 | 26 | related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) |
| 19 20 | 27 | questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission |
| 21 22 | 28 | tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance |
| 23 | 29 | imaging. |
| 24 25 | 30 | Results Pain-related disability increased during the intervention in both groups. Back pain intensity |
| 26 27 | 31 | increased significantly more in the control group than in the intervention group in which back pain intensity |
| 28 29 | 32 | remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain- |
| 30 | 33 | related disability, ODI, or paraspinal GU and FF were observed. In the whole study group, the change in |
| 31 32 | 34 | daily steps associated positively with the change in paraspinal muscle GU. |
| 33 34 | 35 | Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening |
| 35 36 | 36 | regardless of paraspinal muscle GU or FF. |
| 37 38 | | 7 |
| 39 | 37 | Strengths and limitations of this study |
| 40 41 | 38 | - The strengths of this study include the randomized controlled study design and the use of |
| 42 43 | 39 | accelerometers to monitor physical activities and sedentary behaviours throughout the six-month |
| 44 | 40 | study. |
| 45 46 | 41 | - Moreover, the imaging modalities (positron emission tomography with hyperinsulinemic- |
| 47 48 | 42 | euglycemic clamp for muscle-specific insulin resistance and magnetic resonance imaging for |
| 49 | 43 | muscle-specific fat fraction) may be considered as the gold standard measures. |
| 50 51 | 44 | - However, this is a secondary analysis of the whole study, and thus the power calculations were not |
| 52 53 | 45 | done for back pain or disability. |
| 54 55 | 46 | - Further, no specific back pain related eligibility criteria were applied. |
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| 3 4 | 53 | INTRODUCTION |
| 5 6 | 54 | Physical activity (PA) associates with a decreased risk for low back pain (1,2). Conversely, observational |
| 7 | 55 | studies suggest an association between high sedentary behaviour (SB) and increased low back pain or pain- |
| 8 9 | 56 | related disability (1,3). A meta-analysis of 16 longitudinal studies reported that higher SB associated with |
| 10 11 | 57 | higher pain-related disability but not with back pain intensity (1). On the other hand, a meta-analysis of |
| 12 13 | 58 | cross-sectional studies found a positive association between non-occupational and occupational SB and |
| 14 | 59 | back pain (3). Moreover, we have previously observed cross-sectionally that higher SB associated with |
| 15 16 | 60 | lower pain-related disability (4). Thus, it is clear that the observational evidence is mixed. However, |
| 17 18 | 61 | different study settings (i.e., cross-sectional or longitudinal) represent different time frames and the |
| 19 20 | 62 | possibility of reverse causality cannot be ruled out. |
| 21 22 | 63 | Previous three to six-month interventional studies among fifty-year-old office workers suggest that |
| 23 | 64 | reducing SB might improve pain-related disability without affecting back pain intensity (5,6). However, the |
| 24 25 26 | 65 | mechanisms by which SB modification could affect back pain or disability remain poorly understood. |
| 27 | 66 | Insulin resistance and fatty infiltration of the paraspinal muscles associate with back pain (7–11) and |
| 28 29 | 67 | successfully reducing SB improves muscle insulin sensitivity (12). Moreover, lower levels of PA associate |
| 30 31 | 68 | with higher fat content of the transversospinal muscles (13). Taken together, these findings make SB a |
| 32 33 | 69 | plausible target for an intervention to maintain or improve back health. |
| 34 35 | 70 | Thus, we aimed to investigate the effects of a six-month SB reduction intervention on back pain, disability, |
| 36 37 | 71 | and paraspinal muscle FF and insulin sensitivity (glucose uptake, GU). Additionally, we assessed the back |
| 38 | 72 | pain related factors cross-sectionally. |
| 39 40 41 | 73 | |
| 42 43 | 74 | METHODS |
| 44 45 | 75 | This study consists of secondary analyses of a six-month randomized controlled trial that was conducted at |
| 46 47 | 76 | the Turku PET Centre (Turku, Finland) between April 2017 and March 2020 (Clinicaltrials.gov NCT03101228, |
| 48 | 77 | 05/04/2017). The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the |
| 49 50 | 78 | study (16/1801/2017). All participants gave their informed consent before entering the study, and the |
| 51 52 53 | 79 | study was conducted according to the Declaration of Helsinki. |
| 53 54 55 | 80 | Participants |
| 56 57 | 81 | As reported earlier (12,14), volunteers were recruited from the community. Inclusion criteria were: age 40- |
| 58 | 82 | 65 years, body mass index (BMI) 25–40 kg/m ² , self-reported physical inactivity (<120 min/week of |
| 59 60 | 83 | moderate-to-vigorous physical activity [MVPA]), accelerometer-measured sedentary time ≥10 h or ≥60 % of |
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3 84 accelerometer wear time, and metabolic syndrome (15). Exclusion criteria included diagnosed diabetes or 4 85 fasting blood glucose ≥7.0 mmol/l, abundant alcohol consumption according to the national guidelines, the 5 6 86 use of any tobacco products, diagnosed depressive or bipolar disorder, inability to understand written 8 87 Finnish, and any condition that would endanger the participant or study procedures (e.g., previous 9 88 exposure to ionizing radiation). 10

12 89 Measurements 13

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14 90 Back pain intensity and pain-related disability were assessed by two questions and 10-cm visual analogue 15 16 91 scales (VAS): 1) Have you had back pain within the last month? Mark the intensity of the worst perceived 17 18 92 pain during the month on the line below; and 2) Has the perceived pain caused you disability at your work 19 93 or everyday tasks within the last month? Mark the intensity of the greatest extent of disability that you 20 21 94 experienced during the month on the line below. A higher value (0–10 cm) indicates higher pain intensity 22 23 95 and disability. Additionally, back pain-related disability was assessed using the Oswestry disability index 24 96 (ODI), which provides a value of 0-100%, and a higher value represents higher disability (16). 25

27 97 Paraspinal muscle (i.e., erector spinae and transversospinales) FF was assessed using the two-point Dixon 28 98 magnetic resonance (MR) imaging method (Philips 3T Ingenuity TF, Philips Healthcare, Amsterdam, The 29 30 99 Netherlands and Siemens Magnetom Skyra Fit 3T system, Siemens Healthcare, Erlangen, Germany) (17). 31 32 100 Paraspinal muscle GU was measured using ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-33 101 PET; GE D690 PET/CT, GE Healthcare, Milwaukee, WI) during hyperinsulinemic euglycemic clamp (HEC) as 34 35 102 described previously (12,18). Both the FF and GU were analyzed separately for the transversospinal and 36 37 103 erector spinae muscles at the level of L3-4. The measurements were performed using Carimas (version 38 ₃₉ 104 2.10, <u>https://www.carimas.fi</u>).

41 105 PA and SB were measured using accelerometers for four weeks during screening (UKK AM30, UKK 42 43 106 Terveyspalvelut Oy, Tampere, Finland) to determine the baseline values and throughout the six-month 44 107 intervention period (Movesense, Suunto, Vantaa, Finland, with ExSed application, UKK Terveyspalvelut Oy, 45 46 108 Tampere, Finland) to monitor and facilitate behaviour change. The accelerometer variables during the 47 48 109 intervention period were analyzed as means over the whole six-month period. The participants were 49 110 advised to wear the device on the right hip during waking hours (except when the device could be exposed 50 51 111 to water) and remove it when sleeping at night. Accelerometer weartime of 10–19 h/day was considered 52 53 112 valid, and measurement exceeding 19 h/day was substracted from SB. The accelerometer data was 54 113 analyzed using six-second epochs, and the raw acceleration data was analyzed using the mean amplitude 55 56 114 deviation (to assess sedentariness, light PA [LPA], and moderate-to-vigorous PA [MVPA]) and angle for 57 posture estimation (to differentiate SB and standing) methods as described previously (4,18–20). 58 115 59

Page 7 of 31

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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.

² 121 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.

125 As described in more detail previously (18), participants in the intervention group were advised to reduce 22 126 their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by 127 subtracting 1 h of SB from the amount during screening. Correspondingly, 1 h was added to standing, LPA, 128 and MVPA goals distributing the time based on individual preferences. However, a maximum of 20 minutes 27 129 was added to MVPA, and increasing intentional physical exercise training was discouraged. The ways for 130 replacing SB were discussed individually and included, for example, using standing desks, taking the stairs 131 instead of the lift, and lightly walking. For the control group, the daily SB and PA goals were set equal to the 32 132 screening values. All participants could monitor their daily SB and PA and the fulfilment of the goals using a ₃₄ 133 mobile phone application (ExSed) connected to the accelerometer.

36 134 Patient involvement

⁸ 135 Patients were not involved in designing or conducting this study.

41 136 Equity, diversity and inclusion

43 137 Both the study participants and researchers include self-identified men and women in a relatively balanced
 44 45 138 fashion. The research group consists of both junior and senior researchers.

47 139 Statistical methods48

49 140 Baseline characteristics are presented as mean (standard deviation, SD) if not stated otherwise. 50 51 141 Intervention effects are presented as model-based mean (95% confidence interval, 95% CI). Baseline 52 53 142 correlations were analyzed using the Spearman rank correlation. The main analyses of intervention effects 54 143 were performed using linear mixed models for repeated measurements. The outcome of interest was the 55 56 144 dependent variable, and independent variables included group, time, sex, and group x time in all analyses. 57 58 145 Random intercepts for individual effect was also included. Additionally, FF analyses were adjusted for age, 59 146 and pain questionnaire analyses were adjusted for self-reported regular pain medication status (yes/no) 60

147 and BMI, because this improved the distribution of the residuals. The normal distribution of the residuals 148 was visually inspected, and log10 or square root transformations were performed as necessary. Tukey-149 Kramer adjustment for multiple comparisons was used. Compound symmetry or unstructured covariance 150 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, 10 151 11 152 NC) and the correlation analyses were performed using JMP Statistics (version 16, SAS Institute Inc., Cary, 12 13 153 NC). 14

15 The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power 154 16 17 155 calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined 18 19 156 based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming 20 157 an increase of 0.7 (SD 0.55) µmol/100g/min in the intervention group (10% increase) and an increase of 21 22 158 0.05 µmol/100g/min in the control group, we calculated that 16 participants per group would be sufficient 23 24 159 for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity 25 160 (α =0.05, 1- β =0.9). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 26 27 161 participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin 28 29 162 sensitivity would behave similar to quadriceps femoris and thus, the study would be sufficiently powered to 30 163 detect statistically significant changes in paraspinal muscle insulin sensitivity. 31

165 RESULTS

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Baseline characteristics 166

40 167 Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were 41 ₄₂ 168 randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary 43 169 Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain 44 45 170 (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample 46 47 171 of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and 48 172 MR imaging. The baseline characteristics are presented in Table 1. 49

Baseline correlations 51 173

53 174 All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated 54 55 175 positively with erector spinae and transversospinal FF (r_s =0.53, 0.55, respectively). Erector spinae GU 56 176 correlated positively with MVPA and step count (r_s =0.36 and 0.40, respectively) and negatively with SB (r_s =-57 58 177 0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s=0.42 and 59 60 178 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and

Page 9 of 31

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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 10 positively with body fat percentage (r_s =0.33). Back pain intensity did not correlate with any PA, SB, or 11 12 paraspinal muscle-related variables.

14 **Intervention effects** 15

17 186 Accelerometry

19 The intervention effects on SB and PA have been reported previously (18). In comparison to the control 20 group, the intervention group reduced their SB by 40 min/day and subsequently increased their MVPA by 21 188 22 20 min/day, on average over the six-month intervention period; no statistically significant changes were 23 24 observed in the control group. LPA increased by 10 min/day in both groups without statistically significant 25 26 191 between-group differences. No statistically significant changes in standing time or the number of breaks in 27 SB were observed in either group. Step count increased in both groups but the increase was statistically 28 29 significantly higher in the intervention group (from 5150 to 6749 steps/day in the control group vs. 5326 to 30 31 194 8632 steps/day in the intervention group).

33 Pain and disability questionnaires 34

35 ₃₆ 196 The pain and disability questionnaire results are presented in Figure 1, and the changes in each 37 participant's back pain by group are presented in Figure 2. In the intervention group, back pain did not 38 39 198 change whereas it increased statistically significantly in the control group (group x time p=0.030). Pain-40 41 199 related disability increased over time in both groups (time p=0.017), but no statistically significant between-42

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group differences in the changes in pain-related disability or ODI were observed. 43

45 201 Paraspinal muscle FF and GU

47 202 Transversospinal FF was higher in the control group throughout the study (p=0.011), but no statistically 48 significant changes were observed in paraspinal muscle FF or GU in either group (Figure 3). 49

51 204 **Explorative analyses** 52

53 205 As previously done (12,18), when the study group was divided according to the measured changes in SB or 54 55 206 daily steps no statistically significant changes in any pain-related outcomes were observed (group x time 56 57 207 p>0.05 for all; data not shown). Furthermore, no statistically significant differences were observed in 58 208 paraspinal muscle FF or GU when the group was divided according to the measured change in SB (group x 59 60 209 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).

213 In the whole study group, the changes in BMI, body fat percentage, and body mass correlated positively 9 10 214 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 11 12 215 correlated with the changes in pain-related outcomes. The change in BMI correlated negatively with the 13 14 216 change in erector spinae and transversospinal GU (r_s =-0.34 and -0.40, respectively). In line with the analyses 15 217 based on high vs. low step count increase, the changes in steps correlated positively with the changes in 16 17 218 paraspinal muscle GU (r_s =0.39 and 0.41 for the transversospinales and erector spinae, respectively) but not 18 19 219 with the changes in FF.

²¹ 220 **DISCUSSION**

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23 ₂₄ 221 In the present study, we show that an intervention aimed at reducing SB by 1 h/day for six months may 25 222 prevent the worsening of back pain intensity which was observed in the control group. However, the 26 27 223 change in back pain intensity was not associated with changes in paraspinal muscle (i.e., erector spinae or 28 224 transversospinales) FF, GU, or the changes in PA, SB, pain-related disability, or ODI score. Additionally, no 29 30 225 intervention effects on paraspinal muscle FF or GU were observed, although increases in daily steps 31 32 226 associated with improved paraspinal muscle GU. 33

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35227Pain and physical behaviours

36 In this study, back pain intensity increased by about two-fold in the control group, on average. Although the 228 37 38 229 baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS 39 40 230 in the intervention and control groups, respectively), the change in the control group represents a 41 42 231 substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening 43 232 with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain 44 45 233 intensity are achieved. However, we did not observe any intervention effects on pain-related disability or 46 47 234 ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This 48 235 might be explained by the relatively low pain intensity that might not be severe enough to cause disability. 49

51 236 The reason for back pain intensity increase in the control group remains elusive. One explanation for the 52 237 increase could be related to the open-label nature of this study. Although not formally documented, many 53 ⁵⁴ 238 control participants were disappointed to be included in the control group instead of the intervention 55 56 239 group. These negative emotions may have affected pain intensity (22). This phenomenon, in conjunction 57 240 with the possible benefits from the increased PA in the intervention group, could explain the difference 58 59 241 between groups. The fact that the explorative analyses with SB or step-based post hoc group divisions 60

Page 11 of 31

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3 242 showed no between-group differences in pain-related outcomes further emphasizes that the sole 4 243 allocation to either intervention or control group may have affected the perception of pain. However, the 5 6 244 cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count 7 8 245 associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the 9 10 246 cross-sectional correlations and the correlations of changes during the study suggest that maintaining a 11 247 healthier body composition could decrease disability, as body fat percentage correlated positively with the 12 13 248 ODI score (see Table 2 and Supplementary Table 1). 14

15 249 Contrary to our results, a previous six-month randomized controlled trial involving adults with low back 16 17 250 pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an 18 19 251 intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity 20 252 measured using VAS did not differ between groups in the study (5). The study sample was comparable to 21 22 253 ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our 23 24 254 study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was 25 255 longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, 26 27 256 the aforementioned study did not aim to change only SB but also included behavioural counselling in the 28 29 257 self-management of pain. Furthermore, the reduction in SB was notably higher in the previous study 30 258 compared to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. 31 32 259 Additionally, the intensity of longstanding pain might not always be related to the disability (23). 33

34 260 It should be acknowledged that back pain is often a recurring and varying, and sometimes a longstanding 35 36 261 complaint (24). For this reason, future studies should assess pain and disability more frequently than only 37 38 262 at baseline and at the end of the intervention, as in the current study. However, the six-month duration of 39 ₄₀ 263 this study should be sufficient to reveal the effects of a SB reduction intervention, as in a previous study the 41 264 ODI score tended to decrease up until three months before plateauing (5). 42

43 44 265 As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with 45 266 pain-related disability at baseline in our study (4). However, no correlation between the change in standing 46 47 267 time and the change in pain-related disability was observed. Related to this finding, a recent randomized 48 49 268 controlled trial observed that, within three months, increasing occupational standing may increase 50 269 multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer 51 52 270 present (25). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that 53 54 271 standing may exacerbate pain acutely, but habitual standing may not be detrimental.

⁵⁶ 272 Paraspinal muscle FF and GU ⁵⁷

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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

25 288 seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses 26 27 289 revealed no intervention effects on any of these muscles. However, the secondary analyses of the present 28 29 290 study and the previously published study show the association between increased PA (e.g., steps) and 30 291 improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant 31 32 292 moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle 33 34 293 GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal 35 294 muscle GU correlated with the changes in any pain-related outcomes (Table 2). Moreover, as paraspinal 36 37 295 muscle GU but not FF was associated with steps, the results suggest that GU can improve despite no 38 39 296 changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI correlated 40 ₄₁ 297 negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI.

43 298 Clinical implications

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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.

53 303 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.

317 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.

3 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. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

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| 4 | 38 | Dat | a availability statement |
| 5 6 33 7 | 39 | Data | a are available upon reasonable request from the corresponding author. |
| | 40 | Ethi | ical approval |
| 10 34 11 | 41 | The | Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study |
| 12 34 13 | 42 | (16/ | /1801/2017). |
| 14 34 15 | 43 | Con | flicts of interest |
| 16 17 ³⁴ | | The | authors declare the following financial interests/personal relationships which may be considered as |
| 18 34 19 | 45 | pote | ential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The |
| 20 34 | 46 | othe | er authors report no conflicts of interest. The results are presented clearly and honestly without |
| 21 22 ³⁴ | 47 | fabr | rication, falsification, or inappropriate data manipulation. |
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45 46 438 Figure legends

- 48 439 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
- 53 442 estimates are model-based means and 95% confidence intervals. A higher value indicates higher pain 54
- 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 the second se
- in the intervention group and red bars represent participants in the control group. Of the six participants
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| 2 | 446 | with no changes in back pain, four were in the intervention and two in the control group. A higher value |
| 4 5 | 447 | indicates higher pain intensity. VAS = visual analogue scale. |
| 6 | | |
| 7 8 | 448 | Figure 3. Intervention effects on A) transversospinal muscle glucose uptake (GU), B) erector spinae GU, C) |
| 9 | 449 | transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are |
| 10 11 | | adjusted for sex, and FF analyses (panels C and D) are additionally adjusted for age. Black dots represent |
| 12 13 | 451 | the intervention group and gray squares represent the control group. The presented estimates are model- |
| 14 | 452 | based means and 95% confidence intervals. |
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³ 453 Table 1. Study participant characteristics at the baseline. Unless otherwise stated, the results are
 ⁴ 454 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/I * | 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, | 2.8 (2.3, 3.2) | 23 | 2.5 (2.0, 3.3) | 20 |
| µmol/100 cm³/min* | | | | |
| Erector spinae GU, | 2.9 (2.0, 3.3) | 23 | 2.4 (1.9, 3.9) | 20 |
| µmol/100 cm³/min* | | | | |
| 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).

Page 19 of 31

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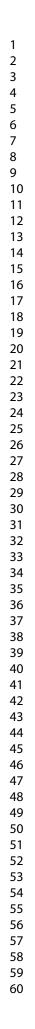
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| | Δ ES FF | Δ Tra. GU | Δ ES GU | Δ QF GU | ∆ Ham. | Δ WB GU | Δ BMI | Δ WC | Δ Bodv | Δ Weigh | Δ Glucos | ∆ Insulin | Δ HbA1c | Δ SB% | Δ Standi | Δ LPA% | 5 on 28 S VdAW Iuding to | Δ ΡΑ% | Δ Steps | Δ Breaks | Δ BP | Δ PRD | A ODI |
| ∆ Tra. FF | 0.55 ** | 0.1 6 | 0.10 | 0.43 * | 0.18 | 0.04 | -0.20 | - 0.18 | 0.1 5 | -0.23 | 0.08 | - 0.26 | - 0.41 * | 0.00 | -0.01 | -0.02 | r⊌ses re | 0.02 | 0.05 | -0.03 | - 0.0 6 | 0.22 | 0.0 |
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| ∆ Tra. GU | | 1 | 0.91 ** | 0.56 ** | 0.70 ** | 0.72 ** | - 0.40* | - 0.12 | - 0.3 2 | - 0.38 [*] | - 0.11 | - 0.20 | - 0.05 | -0.25 | 0.10 | 0.22 | ownload Superieu St and c |).33 | 0.39* | 0.12 | - 0.0 7 | 0.21 | 0. |
| Δ ES GU | | | 1 | 0.49 ** | 0.82 ** | 0.76 ** | - 0.34* | - 0.15 | - 0.3 3 | -0.32 | - 0.17 | - 0.19 | - 0.05 | -0.30 | 0.22 | 0.20 | ded from h ur (ABES) data minir |).29 | 0.41* | 0.05 | 0.0 4 | 0.26 | 0. |
| Δ QF GU | | | | 1 | 0.67 ** | 0.47 ** | - 0.45* * | - 0.04 | - 0.0 9 | - 0.45* * | 0.08 | - 0.18 | - 0.33 * | - 0.41* | 0.19 | 0.42* | 0 🚰 6* 葺 0 | 0.50* | 0.42* | 0.06 | 0.0 4 | 0.03 | - 0. |
| ∆ Ham. GU | | | | | 1 | 0.77 ** | - 0.46* * | - 0.26 | - 0.2 7 | - 0.45* * | - 0.06 | - 0.19 | - 0.14 | - 0.53* * | 0.39* | 0.39* | ່ 🖁 🔒 🕻 |).48* | 0.52* * | 0.16 | 0.0 8 | 0.20 | 0. |
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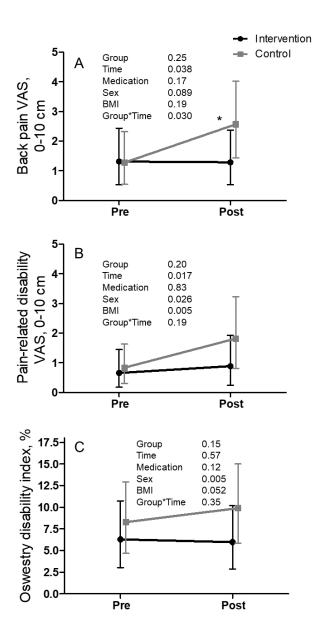
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BMJ Open BMJ Open muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemoglobin; SB, sedentary behavior measured with accelerometry; IPA, light physical activity measured with accelerometry; BA, physical activity (IPA+MVPA) measured with accelerometry; BA 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; B, b ck pain measured with visual

Page 22 of 31

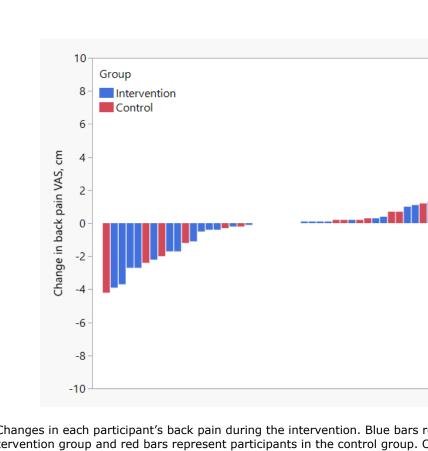
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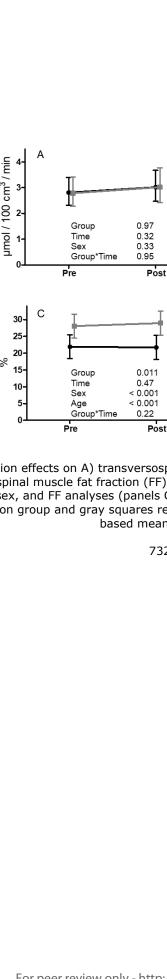
Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented 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

467x884mm (38 x 38 DPI)



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.

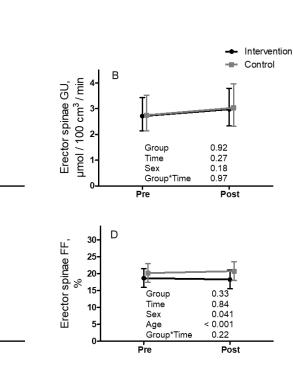
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Transversospinal GU,

Transversospinal FF,

%



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 modelbased means and 95% confidence intervals.

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BMJ Open

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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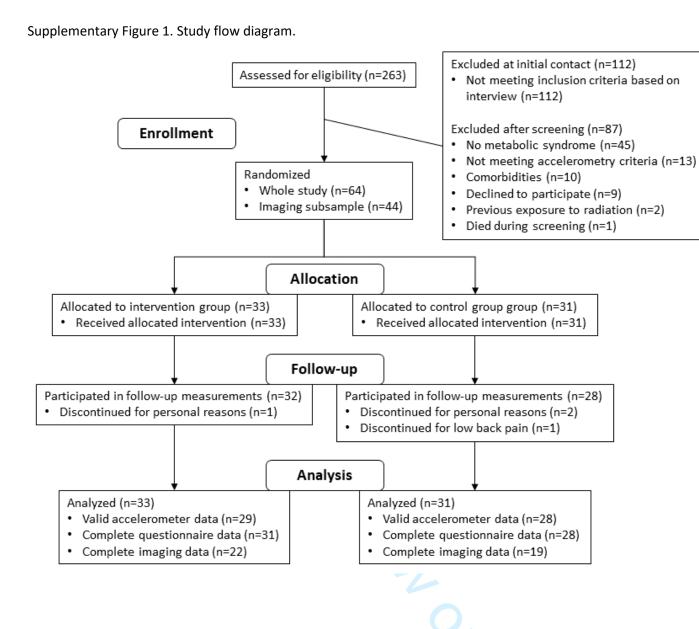
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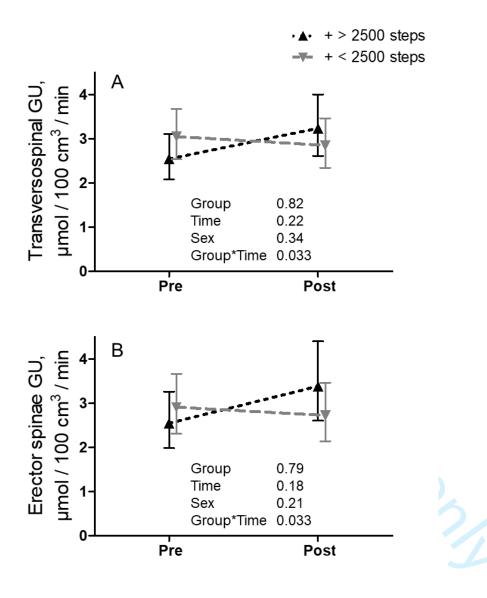
Supplementary Table 1. Baseline Spearman's rank correlation coefficients

| | Tra. FF | ES FF | Tra. GU | ES GU | QF GU | Ham. GU | WB GU | BMI | WC | Body fat % | Weight | Glucos e | Insulin | HbA1c | SB % | Standi ng % | LPA % | MVPA % | PA % | Steps ndðVur |)84305 ⁴ | ВР | PRD | IQO |
|----------|---------|--------|---------|--------|--------|------------|--------|---------|---------|---------------|---------|-------------|---------|---------|---------|----------------|---------|-----------|---------|----------------------|---------------------|----------|--------|------|
| 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 2 5' | 0.10 | 0.02 | 0.1 |
| 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 | -0.270 | 0.66 | 0.11 | 0.07 | 0.1 |
| 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 | 060 | -0.05 | -0.09 | 0.0 |
| 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 *65 | Ens. | -0.04 | -0.14 | -0.1 |
| 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°at | | -0.04 | -0.18 | -0. |
| 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 | 0.44 S related to to | | -0.11 | -0.13 | -0. |
| 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 8 | ut Dio Su | -0.07 | -0.08 | -0. |
| 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°nd | /nkpa perie | 0.07 | 0.03 | -0. |
| BMI | | | | | | | | 1 | 0.76** | 0.54** | 0.80** | 0.15 | 0.61** | 0.08 | 0.29* | -0.16 | -0.09 | -0.26* | -0.23 | 0.30 nd data | ud €d Id | 0.00 | -0.02 | 0.1 |
| WC | | | | | | | | | 1 | 0.23 | 0.80** | 0.25* | 0.64** | 0.26* | 0.38** | -0.31* | -0.17 | -0.32* | -0.29* | -0.42 3 | HT Com | -0.03 | 0.00 | 0.0 |
| 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 | 0.3 |
| Weight | | | | | | | | | | | 1 | 0.27* | 0.68** | 0.17 | 0.40** | -0.35** | -0.24 | -0.18 | -0.28* | 0.33 | -0.31 | -0.13 | -0.12 | -0. |
| Glucose | | | | | | | | | | | | 1 | 0.24 | 0.12 | 0.06 | -0.32** | 0.17 | 0.10 | 0.16 | 0.01 ain | -0.22 | -0.15 | -0.16 | -0. |
| nsulin | | | | | | | | | | | | | 1 | 0.25* | 0.41** | -0.49** | -0.15 | -0.11 | -0.19 | -0.260 | -0 <u>9</u> 0 | -0.16 | -0.08 | 0.0 |
| HbA1c | | | | | | | | | | | | | | 1 | 0.14 | -0.18 | 0.10 | -0.10 | -0.01 | -0.10 d | -0 3 6 | 0.01 | -0.07 | 0.1 |
| SB | | | | | | | | | | | | | | - | 1 | -0.79** | -0.62** | -0.55** | -0.75** | -0.54 | -0.86 | 0.03 | -0.19 | 0.0 |
| Standing | | | | | | | | | | | | | | | | 1 | 0.28* | 0.19 | 0.30* | 0.22 a | 0.26 | 0.06 | 0.27* | 0.0 |
| | | | | | | | | | | | | | | | | - | 1 | 0.28* | 0.83** | 0.21 G | 0.3 5 | 0.06 | 0.04 | -0. |
| MVPA | | | | | | | | | | | | | | | | | | 1 | 0.73** | 0.93 . | 0.2 | -0.20 | -0.03 | -0. |
| PA | | | | | | | | | | | | | | | | | | | 1 | 0.65 | 0.30** | -0.09 | -0.01 | -0. |
| Steps | | | | | | | | | | | | | | | | | | | | 1 S. | 2025 | -0.18 | -0.03 | -0. |
| Breaks | | | | | | | | | | | | | | | | | | | | | 1 | 0.09 | 0.14 | -0. |
| BP | | | | | | | | | | | | | | | | | | | | | | 1 | 0.61** | 0.7 |
| PRD | | | | | | | | | | | | | | | | | | | | | enc | <u> </u> | 1 | 0.7 |

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

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d by copyrig 1jopen-2024 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.



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Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

| 1 | . Clear description of the goal of research, study objective(s), study design, and study population | Yes _s | Unclear | |
|--------|---|------------------|---------|---|
| 2 | Clear description of outcomes, exposures/treatments and covariates, and their measurement | Yes | Unclear | |
| 3 | methods Validity of study design | Yes | Unclear | 1 |
| 4 | | Yes | Unclear | |
| 5 | | Yes | Unclear | |
| 6 | | Yes | Unclear | |
| | analysis | | | |
| 7 | | Yes | Unclear | |
| 8 | | Yes | Unclear | |
| 9 | Appropriate assessment of treatment effect or interaction between treatment and another covariate | Yes | Unclear | |
| 1 | 0. Correct use of correlation and associational statistical testing | Yes | Unclear | |
| 1 | 1. Appropriate handling of continuous predictors | Yes | Unclear | |
| 1 | 2. Confidence intervals do not include impossible values | Yes | Unclear | |
| 1 | 3. Appropriate comparison of baseline characteristics between the study arms in randomized | Yes | Unclear | |
| | trials | | | |
| | 4. Correct assessment and adjustment of confounding | Yes | Unclear | |
| | 5. Avoiding model extrapolation not supported by data | Yes | Unclear | |
| | 6. Adequate handling of missing data <i>ting and presentation</i> | Yes | Unclear | |
| - | 7. Adequate and correct description of the data | Yes | Unclear | |
| 1 | 8. Descriptive results provided as occurrence measures with confidence intervals, and analytic | Yes | Unclear | |
| | results provided as association measures and confidence intervals along with P-values | 105 | Unclear | |
| 1 | 9. Confidence intervals provided for the contrast between groups rather than for each group | Yes | Unclear | |
| 2 | 20. Avoiding selective reporting of analyses and P-hacking | Yes | Unclear | |
| 2 | 1. Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, | Yes | Unclear | |
| | and reporting the P-values rather their range | 105 | onereur | |
| 2 | 2. Providing sufficient numerical results that could be included in a subsequent meta-analysis | Yes | Unclear | |
| 2 | 3. Acceptable presentation of the figures and tables | Yes | Unclear | |
| Interp | pretation | | | |
| 2 | 4. 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 | |
| 2 | 5. Using confidence intervals rather than post-hoc power analysis for interpreting the results of studies | Yes | Unclear | |
| 'n | 6. Correctly interpreting occurrence or association measures | Yes | Unclear | |
| | 7. Distinguishing causation from association and correlation | Yes | Unclear | |
| | 8. Results of pre-specified analyses are distinguished from the results of exploratory analyses in the | | | |
| | interpretation | Yes | Unclear | |
| | 9. Appropriate discussion of the study methodological limitations | Yes | Unclear | |
| 3 | 0. Drawing only conclusions supported by the statistical analysis and no generalization of the results | Yes | Unclear |] |

| | BMJ Open Mansournia MA, et al. Br.J Sports Med 2021; 55:1–2. doi: 10.1 | Page 30 of 31 |
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| | Mansournia MA, et al. Br J Sports Med 2021; 55:1-2. doi: 10.1 | 1136/bjsports-2020-10365 |
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| TE | DieR | The TIDieR (Template for Intervention Descript | tion and Replication) Checklist*: | |
| | for Intervention and Replication | Information to include when describing an interventior | n and the location | |
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| 3. | Materials: Descr | ibe any physical or informational materials used in the interventic | on, including those 4-6 | |
| | provided to partie | cipants or used in intervention delivery or in training of interventic | on providers. | |
| | Provide informat | tion on where the materials can be accessed (e.g. online appendi | lix, URL). | |
| 4. | Procedures: Des | scribe each of the procedures, activities, and/or processes used i | <u>9</u> | |
| | including any en | abling or support activities. | | |
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| 5. | For each catego | ry of intervention provider (e.g. psychologist, nursing assistant), o | describe their | |
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| | HOW | | describe their similar technologies. | |
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| | | e intervention and whether it was provided individually or in a grou | A | |
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| | infractructure or | relevant features. | | |

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| | WHEN and HOW MUCH | <u> </u> | 24-084305 4 5 | |
| 8. | Describe the number of times the intervention was delivered and over what period of time including | <u> </u> | | _ |
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| 9. | If the intervention was planned to be personalised, titrated or adapted, then describe what, why, | Ensi | otem4-5 | |
| | when, and how. | eign relat | ber | |
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| 10. [‡] | If the intervention was modified during the course of the study, describe the changes (what, why, | nt Su | 9 N/A | |
| | when, and how). | t and | vnlo | |
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| 11. | Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any | ABE: | fron5-6 | |
| | strategies were used to maintain or improve fidelity, describe them. | | http | |
| 12. [‡] | Actual: If intervention adherence or fidelity was assessed, describe the extent to which the | Al tra | http://b | |
| | intervention was delivered as planned. | aini | njop | |
| sufficie | s - use N/A if an item is not applicable for the intervention being described. Reviewers – use '?' if informat ontly reported. | similar | com/ o | |
| | published papers (provide citation details) or a website (provide the URL). eting the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be describ | chno | notil the study is a | complete |
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| * We stron | gly recommend using this checklist in conjunction with the TIDieR guide (see BMJ 2014;348:g1687) which contains a | n ex | anation and elal | poration for each item. |
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| studies ar | e covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist | t. Wł | gen a randomised | trial is being reported, the |
| | ecklist should be used in conjunction with the CONSORT statement (see <u>www.consort-statement.org</u>) as an extension | | 0 | |
| When a clinical trial protocol is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as a generation of Item 11 of the SPIRIT 2013 | | | | |
| | t (see <u>www.spirit-statement.org</u>). For alternate study designs, TIDieR can be used in conjunction with the appropria | te c <u>i</u> | ecklist for that st | udy design (see |
| www.equ | ator-network.org). | - | nique | |
| TIDieR ch | ecklist For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtm | I | le de l | |

Page 32 of 31

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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| Secondary Subject Heading: | Sports and exercise medicine |
| Keywords: | Back pain < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, Clinical Trial, Overweight, Magnetic Resonance Imaging |
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| 1 | Effects of reducing sedentary behaviour on back pain, paraspinal muscle insulin sensitivity and muscle fat |
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| 2 | fraction and their associations: A secondary analysis of a six-month randomized controlled trial |
| 3 | Jooa Norha ^{1*†} , Tanja Sjöros ^{1†} , Taru Garthwaite ¹ , Saara Laine ¹ , Tiina Verho ¹ , Virva Saunavaara ^{1,2} , Kirsi |
| 4 | Laitinen ³ , Noora Houttu ³ , Jussi Hirvonen ^{4, 5} Henri Vähä-Ypyä ⁶ , Harri Sievänen ⁶ , Eliisa Löyttyniemi ⁷ , Tommi |
| 5 | Vasankari ^{4, 6} , Kari K. Kalliokoski ¹ , Ilkka H. A. Heinonen ¹ |
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| 15 | *Corresponding author: Jooa Norha, Turku PET Centre, University of Turku and Turku University Hospital, |
| 16 | P.O. Box 52, 20521 Turku, Finland, tel. +358 443312942, E-mail: <u>jooa.norha@utu.fi</u> |
| 17 | ⁺ Jooa Norha and Tanja Sjöros contributed equally to this work. |
| | 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 |

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| 2 3 4 | 18 | ABSTRACT |
| 5 6 | 19 | Objectives Sedentary behaviour (SB) is a plausible intervention target for back pain mitigation. Therefore, |
| 7 | 20 | this study aimed to investigate the effects of a six-month SB reduction intervention on back pain and |
| 8 9 | 21 | related disability outcomes, and paraspinal muscle (i.e., erector spinae and transversospinales separately) |
| 10 11 | 22 | insulin sensitivity (glucose uptake, GU) and muscle fat fraction (FF). |
| 12 13 | 23 | Methods Sixty-four adults with overweight or obesity and metabolic syndrome were randomized into |
| 14 15 | 24 | intervention (n=33) and control (n=31) groups. The intervention group aimed to reduce SB by 1 h/day |
| 16 17 | 25 | (measured with accelerometers) and the control group continued as usual. Back pain intensity and pain- |
| 18 | 26 | related disability were assessed using 10 cm visual analogue scales and the Oswestry disability index (ODI) |
| 19 20 | 27 | questionnaire. Paraspinal muscle GU was measured using 18-fluorodeoxyglucose positron emission |
| 21 22 | 28 | tomography during hyperinsulinemic-euglycemic clamp. FF was measured using magnetic resonance |
| 23 | 29 | imaging. |
| 24 25 26 | 30 | Results Pain-related disability increased during the intervention in both groups. Back pain intensity |
| 27 | 31 | increased significantly more in the control group than in the intervention group in which back pain intensity |
| 28 29 | 32 | remained unchanged (group x time p=0.030). No statistically significant between-group changes in pain- |
| 30 31 | 33 | related disability, ODI, or paraspinal GU and FF were observed. In the whole study group, the change in |
| 32 33 | 34 | daily steps associated positively with the change in paraspinal muscle GU. |
| 34 35 | 35 | Conclusion An intervention focusing on SB reduction may be feasible for preventing back pain worsening |
| 36 37 | 36 | regardless of paraspinal muscle GU or FF. |
| 38 39 | 37 | Strengths and limitations of this study |
| 40 41 | 38 | - The strengths of this study include the use of accelerometers to monitor physical activities and |
| 42 43 | 39 | sedentary behaviours throughout the six-month study. |
| 44 45 | 40 | - Moreover, the imaging modalities (positron emission tomography with hyperinsulinemic- |
| 46 | 41 | euglycemic clamp for muscle-specific insulin resistance and magnetic resonance imaging for |
| 47 48 | 42 | muscle-specific fat fraction) may be considered as the gold standard measures. |
| 49 50 | 43 | - However, this is a secondary analysis of the whole study, and thus the power calculations were not |
| 51 | 44 | done for back pain or disability. |
| 52 53 | 45 | - Further, no specific back pain related eligibility criteria were applied. |
| 54 55 | 46 | |
| 56 57 | 47 | Abstract word count: 226 |
| 58 59 | | |
| 60 | 48 | Manuscript word count: 3636 |

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|----------------|----|---|
| 3 4 | 49 | Keywords: sedentary behaviour, accelerometry, back pain, disability, insulin sensitivity, muscle fat fraction |
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| 3 4 | 52 | INTRODUCTION |
| 5 6 | 53 | Physical activity (PA) associates with a decreased risk for low back pain (1,2). Conversely, observational |
| 7 8 | 54 | studies suggest an association between high sedentary behaviour (SB) and increased low back pain or pain- |
| 9 | 55 | related disability (1,3). A meta-analysis of 16 longitudinal studies reported that higher SB associated with |
| 10 11 | 56 | higher pain-related disability but not with back pain intensity (1). On the other hand, a meta-analysis of |
| 12 13 | 57 | cross-sectional studies found a positive association between non-occupational and occupational SB and |
| 14 | 58 | back pain (3). Moreover, we have previously observed cross-sectionally that higher SB associated with |
| 15 16 | 59 | lower pain-related disability (4). Thus, it is clear that the observational evidence is mixed. However, |
| 17 18 | 60 | different study settings (i.e., cross-sectional or longitudinal) represent different time frames and the |
| 18 19 20 | 61 | possibility of reverse causality cannot be ruled out. |
| 20 21 22 | 62 | Previous three to six-month interventional studies among fifty-year-old office workers suggest that |
| 23 | 63 | reducing SB might improve pain-related disability without affecting back pain intensity (5,6). However, the |
| 24 25 26 | 64 | mechanisms by which SB modification could affect back pain or disability remain poorly understood. |
| 26 27 | 65 | Insulin resistance and fatty infiltration of the paraspinal muscles associate with back pain (7–11) and |
| 28 29 | 66 | successfully reducing SB improves muscle insulin sensitivity (12). Moreover, lower levels of PA associate |
| 30 31 | 67 | with higher fat content of the transversospinal muscles (13). Taken together, these findings make SB a |
| 31 32 33 | 68 | plausible target for an intervention to maintain or improve back health. |
| 34 35 | 69 | Thus, we aimed to investigate the effects of a six-month SB reduction intervention on back pain, disability, |
| 36 | 70 | and paraspinal muscle FF and insulin sensitivity (glucose uptake, GU). Additionally, we assessed the back |
| 37 38 | 71 | pain related factors cross-sectionally. |
| 39 40 | 72 | |
| 41 42 | 73 | METHODS |
| 43 44 | | |
| 45 | 74 | This study consists of secondary analyses of a six-month randomized controlled trial that was conducted at |
| 46 47 | 75 | the Turku PET Centre (Turku, Finland) between April 2017 and March 2020 (Clinicaltrials.gov NCT03101228, |
| 48 49 | 76 | 05/04/2017). The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the |
| 50 | 77 | study (16/1801/2017). All participants gave their informed consent before entering the study, and the |
| 51 52 53 | 78 | study was conducted according to the Declaration of Helsinki. |
| 55 54 55 | 79 | Participants |
| 56 | 80 | As reported earlier (12,14), volunteers were recruited from the community. Inclusion criteria were: age 40- |
| 57 58 | 81 | 65 years, body mass index (BMI) 25–40 kg/m ² , self-reported physical inactivity (<120 min/week of |
| 59 60 | 82 | 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 ¹⁸F-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 37 102 erector spinae muscles at the level of L3-4. The measurements were performed using Carimas (version ₃₉ 103 2.10, <u>https://www.carimas.fi</u>).

41 104 PA and SB were measured using accelerometers for four weeks during screening (UKK AM30, UKK 43 105 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, 46 107 Tampere, Finland) to monitor and facilitate behaviour change. The accelerometer variables during the 48 108 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 51 110 to water) and remove it when sleeping at night. Accelerometer weartime of 10–19 h/day was considered 53 111 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 56 113 20.5 h, 1.5 h was subtracted from the measured SB, resulting in 19 h of analyzed wear time. The 58 114 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

Page 7 of 31

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118 Height was measured using a wall-mounted stadiometer, and body mass and body fat percentage were 8 119 measured by air displacement plethysmography (Cosmed USA, Concord, CA) after at least four hours of 9 10 120 fasting. Waist circumference was measured using a measuring tape midway between the lowest rib and the 11 12 121 iliac crest. Pain medication use was self-reported by the participants and categorized into using medication 13 14 122 or not.

¹⁶ 123 Intervention 17

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.

24 127 As described in more detail previously (18), participants in the intervention group were advised to reduce 25 26 128 their daily SB by 1 h/day for the six-month study period. Daily SB goals were calculated individually by 27 ₂₈ 129 subtracting 1 h of SB from the amount during screening. Correspondingly, 1 h was added to standing, LPA, 29 130 and MVPA goals distributing the time based on individual preferences. However, a maximum of 20 minutes 30 31 131 was added to MVPA, and increasing intentional physical exercise training was discouraged. The ways for 32 132 replacing SB were discussed individually and included, for example, using standing desks, taking the stairs 33 34 133 instead of the lift, and lightly walking. For the control group, the daily SB and PA goals were set equal to the 35 36 134 screening values. All participants could monitor their daily SB and PA and the fulfilment of the goals using a 37 ₃₈ 135 mobile phone application (ExSed) connected to the accelerometer.

40 136 Patient involvement

⁴²₄₃ 137 Patients were not involved in designing or conducting this study.

44 45 138 Equity, diversity and inclusion

47 139 Both the study participants and researchers include self-identified men and women in a relatively balanced
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49 140 fashion. The research group consists of both junior and senior researchers.

51 141 Statistical methods52

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
 Intervention effects are presented as model-based mean (95% confidence interval, 95% CI).

57 144 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

⁶⁰ 146 dependent variable, and independent variables included group, time, sex, and group x time in all analyses.

147 Random intercepts for individual effect was also included. Additionally, FF analyses were adjusted for age, 148 and pain questionnaire analyses were adjusted for self-reported regular pain medication status (yes/no) 149 and BMI, because this improved the distribution of the residuals. The normal distribution of the residuals 150 was visually inspected, and log10 or square root transformations were performed as necessary. Tukey-10 151 Kramer adjustment for multiple comparisons was used. Compound symmetry or unstructured covariance 11 152 structure was chosen based on the Akaike information criterion. Statistical significance was set at p<0.05 12 13 153 (two-tailed). The main analyses were performed in SAS (version 9.4 for Windows, SAS Institute Inc., Cary, 14 15 154 NC) and the correlation analyses were performed using JMP Statistics (version 16, SAS Institute Inc., Cary, 16 155 NC). 17 18

19 156 The total sample size (n=64) was calculated according to whole-body insulin sensitivity-based power 20 calculations (reported elsewhere) (18). The sample size for the imaging subsample (n=44) was determined 157 21 22 158 based on power calculations for quadriceps femoris insulin sensitivity (reported elsewhere) (12). Assuming 23 24 159 an increase of 0.7 (SD 0.55) µmol/100g/min in the intervention group (10% increase) and an increase of 25 160 0.05 µmol/100g/min in the control group, we calculated that 16 participants per group would be sufficient 26 27 161 for detecting a statistically significant between-group change in quadriceps femoris insulin sensitivity 28 29 162 (α =0.05, 1- β =0.9). To ensure sufficient sample size despite possible drop-outs and technical challenges, 44 30 163 participants were recruited for the imaging subsample. We hypothesize that paraspinal muscle insulin 31 32 164 sensitivity would behave similar to quadriceps femoris and thus, the study would be sufficiently powered to 33 34 165 detect statistically significant changes in paraspinal muscle insulin sensitivity.

₃₉ 167 RESULTS

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41 168 **Baseline characteristics**

43 Of 263 volunteers, 151 were screened, and 64 fulfilled the inclusion criteria. In total, 64 participants were 169 44 45 170 randomized into the intervention (n=33, 39% men) or control (n=31, 45% men) groups (see Supplementary 46 47 171 Figure 1 for the study flow diagram). Four participants dropped out during the study: one for low back pain 48 172 (in the control group) and three for personal reasons (two in the control group). Additionally, a subsample 49 50 173 of 44 randomized participants (intervention n=23, 39% men; control n=21, 48% men) underwent PET and 51 52 174 MR imaging. The baseline characteristics are presented in Table 1.

⁵⁴ 175 **Baseline correlations** 55

56 176 All of the baseline correlation coefficients are presented in Supplementary Table 1. Age correlated 57 58 177 positively with erector spinae and transversospinal FF (r_s =0.53, 0.55, respectively). Erector spinae GU 59 60 178 correlated positively with MVPA and step count (r_s =0.36 and 0.40, respectively) and negatively with SB (r_s =- Page 9 of 31

BMJ Open

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| 3 | 179 | 0.31). Correspondingly, transversospinal GU correlated positively with MVPA and step count (r_s =0.42 and |
| 4 5 | 180 | 0.40, respectively), but no correlation with SB was found (p=0.065). Similarly, both erector spinae and |
| 6 7 | 181 | transversospinal FF correlated with MVPA (r_s =-0.30 and -0.36, respectively). Increased body adiposity (BMI |
| 8 9 | 182 | and body fat percentage) associated with lower paraspinal muscle GU and higher FF. |
| 10 11 | 183 | Pain-related disability correlated positively with standing time (r_s =0.27). Furthermore, the ODI score |
| 12 13 | 184 | correlated negatively with MVPA (r_s =-0.28) and step count (r_s =-0.26). Finally, the ODI score correlated |
| | 185 | positively with body fat percentage (r_s =0.33). Back pain intensity did not correlate with any PA, SB, or |
| 15 16 | 186 | paraspinal muscle-related variables. |
| 17 18 19 | 187 | Intervention effects |
| 20 21 | 188 | Accelerometry |
| 22 23 | 189 | The intervention effects on SB and PA have been reported previously (18). In comparison to the control |
| 24 | | group, the intervention group reduced their SB by 40 min/day and subsequently increased their MVPA by |
| | 191 | 20 min/day, on average over the six-month intervention period; no statistically significant changes were |
| 27 28 | 192 | observed in the control group. LPA increased by 10 min/day in both groups without statistically significant |
| 29 30 | 193 | between-group differences. No statistically significant changes in standing time or the number of breaks in |
| 31 | 194 | SB were observed in either group. Step count increased in both groups but the increase was statistically |
| 32 33 | 195 | significantly higher in the intervention group (from 5150 to 6749 steps/day in the control group vs. 5326 to |
| 34 35 | 196 | 8632 steps/day in the intervention group). |
| 36 37 38 | 197 | Pain and disability questionnaires |
| 39 | 198 | The pain and disability questionnaire results are presented in Figure 1, and the changes in each |
| 40 41 | 199 | participant's back pain by group are presented in Figure 2. In the intervention group, back pain did not |
| 42 43 | 200 | change whereas it increased statistically significantly in the control group (group x time p=0.030). Pain- |
| 44 | 201 | related disability increased over time in both groups (time p=0.017), but no statistically significant between- |
| 45 46 47 | 202 | group differences in the changes in pain-related disability or ODI were observed. |
| 48 49 | | Paraspinal muscle FF and GU |
| 50 51 | 204 | Transversospinal FF was higher in the control group throughout the study (p=0.011), but no statistically |
| 52 53 | | significant changes were observed in paraspinal muscle FF or GU in either group (Figure 3). |
| 54 55 | 206 | Explorative analyses |
| | 207 | As previously done (12,18), when the study group was divided according to the measured changes in SB or |
| 58 59 | 208 | daily steps no statistically significant changes in any pain-related outcomes were observed (group x time |
| | 209 | p>0.05 for all; data not shown). Furthermore, no statistically significant differences were observed in |

2 3 210 paraspinal muscle FF or GU when the group was divided according to the measured change in SB (group x 4 211 time p>0.05 for all; data not shown). However, with the step-based groups (i.e., an increase of >2500 5 6 212 steps/day vs. <2500 steps/day increase, or decrease), the changes in erector spinae and transversospinal 7 8 213 GU were statistically significantly different between groups in favour of the more active group (group x 9 10 214 time p=0.033) (Supplementary Figure 2).

12 215 In the whole study group, the changes in BMI, body fat percentage, and body mass correlated positively 13 14 216 with the change in ODI ($r_s=0.37$, 0.26, and 0.35, respectively; Supplementary Table 2). None of the changes 15 217 in PA or SB correlated with the changes in pain-related outcomes. The change in BMI correlated negatively 16 17 218 with the change in erector spinae and transversospinal GU (r_s =-0.34 and -0.40, respectively). In line with the 18 19 219 analyses based on high vs. low step count increase, the changes in steps correlated positively with the 20 220 changes in paraspinal muscle GU (r_s =0.39 and 0.41 for the transversospinales and erector spinae, 21 22 221 respectively) but not with the changes in FF. 23

²⁴ ₂₅ 222 **DISCUSSION**

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27 223 In the present study, we show that an intervention aimed at reducing SB by 1 h/day for six months may 28 224 prevent the worsening of back pain intensity which was observed in the control group. However, the 29 30 225 change in back pain intensity was not associated with changes in paraspinal muscle (i.e., erector spinae or 31 32 226 transversospinales) FF, GU, or the changes in PA, SB, pain-related disability, or ODI score. Additionally, no 33 ₃₄ 227 intervention effects on paraspinal muscle FF or GU were observed, although increases in daily steps 35 228 associated with improved paraspinal muscle GU. 36

Pain and physical behaviours

40 230 In this study, back pain intensity increased by about two-fold in the control group, on average. Although the 41 42 231 baseline median back pain was relatively low among all participants (median 0.3 cm and 0.5 cm on the VAS 43 232 in the intervention and control groups, respectively), the change in the control group represents a 44 45 233 substantial relative change in pain intensity (21). Considering this, preventing back pain from worsening 46 47 234 with a SB reduction-focused intervention could be clinically meaningful, even if no improvements in pain 48 235 intensity are achieved. However, we did not observe any intervention effects on pain-related disability or 49 50 236 ODI score, meaning that the changes in back pain intensity were unrelated to functional outcomes. This 51 52 237 might be explained by the relatively low pain intensity that might not be severe enough to cause disability. 53

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

Page 11 of 31

BMJ Open

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242 with the possible benefits from the increased PA in the intervention group, could explain the difference 243 between groups. The fact that the explorative analyses with SB or step-based post hoc group divisions 244 showed no between-group differences in pain-related outcomes further emphasizes that the sole 245 allocation to either intervention or control group may have affected the perception of pain. However, the 10 246 cross-sectional correlations in this study show that a higher amount of MVPA and a higher step count 247 associated with better function, measured with the ODI (Supplementary Table 1). Moreover, both the 248 cross-sectional correlations and the correlations of changes during the study suggest that maintaining a 15 249 healthier body composition could decrease disability, as body fat percentage correlated positively with the 250 ODI score (see Supplementary Tables 1 and 2).

19 251 Contrary to our results, a previous six-month randomized controlled trial involving adults with low back 252 pain (mean ODI score about 24%) observed a statistically significant improvement in ODI with an 253 intervention that resulted in an average SB reduction of 1.4 h/day (5). Moreover, back pain intensity 24 254 measured using VAS did not differ between groups in the study (5). The study sample was comparable to 255 ours in terms of age, SB, and BMI, but two-thirds of the participants met the PA guidelines, whereas in our 256 study, this was an exclusion criterion. Additionally, an inclusion criterion in the previous study was 29 257 longstanding low back pain, while we did consider pain history in the inclusion or exclusion criteria. Further, 258 the aforementioned study did not aim to change only SB but also included behavioural counselling in the 259 self-management of pain. Furthermore, the reduction in SB was notably higher in the previous study 34 260 compared to ours (1.4 vs. 0.7 h/day) (5). These factors can explain the differences in the findings. 261 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).

47 267 As reported earlier (albeit with n=72 from the screening data), standing time correlated positively with 48 49 268 pain-related disability at baseline in our study (4). However, no correlation between the change in standing 50 269 time and the change in pain-related disability was observed. Related to this finding, a recent randomized 51 52 270 controlled trial observed that, within three months, increasing occupational standing may increase 53 54 271 multisite musculoskeletal pain, but in the longer term (12 months), the increase in pain was no longer 55 272 present (25). Thus, as cross-sectional correlations represent shorter rather than longer term, it seems that 56 57 273 standing may exacerbate pain acutely, but habitual standing may not be detrimental. 58

⁵⁹₆₀ 274 **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 Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

276 be reduced even with exercise training (26). This demonstrates that even though paraspinal muscle FF is 277 278 strongly associated with back pain (7–9), successful back pain prevention or treatment can be independent 10 279 of FF. This may be explained in part by the effect of time, i.e., age, which correlated with paraspinal FF 11 280 (r_s=0.55 and 0.53 for transversospinal and erector spinae FF; see Supplementary Table 1) and was a 12 13 281 significant contributor in the linear models investigating paraspinal FF (p<0.001 for both muscle groups) in 14 15 282 this study. In accordance, the effectiveness of back pain rehabilitation is not related to specific strength or 16 283 mobility goals of the rehabilitation (27), emphasizing other than structural aspects in treating experienced 17 18 284 pain and disability. Therefore, back pain risk factors (such as paraspinal muscle FF) should not be the direct 19 20 285 targets of rehabilitation as much as the psychological and cognitive aspects of pain perception and the 21 286 individual preferences for physical exercise (28). However, as lower paraspinal muscle FF associated with 22 23 287 higher amounts of MVPA and lower body adiposity, the results suggest that maintaining healthy body 24 25 288 composition and MVPA levels might help prevent fat infiltration of the paraspinal muscles. 26 27 289 We have previously reported the intervention effects on hamstrings and quadriceps femoris GU (12) which 28 29 290 seem to have responded similarly to the intervention as the paraspinal muscles. The main analyses 30 291 revealed no intervention effects on any of these muscles. However, the secondary analyses of the present 31 32 292 study and the previously published study show the association between increased PA (e.g., steps) and 33 34 293 improved muscle GU (12). Additionally, the paraspinal and thigh muscle GU have statistically significant 35 294 moderate-to-strong correlations of 0.69–0.84 (see Supplementary Table 1). Furthermore, paraspinal muscle 36

37 295 GU was not cross-sectionally associated with any pain-related outcomes, nor was the change in paraspinal 38 39 296 muscle GU correlated with the changes in any pain-related outcomes (Supplementary Table 2). Moreover, 40 ₄₁ 297 as paraspinal muscle GU but not FF was associated with steps, the results suggest that GU can improve 42 298 despite no changes in FF. Finally, as observed before with whole-body GU (18), the change in BMI 43 44 299 correlated negatively with paraspinal muscle GU, indicating lower insulin sensitivity with increasing BMI. 45

46 300 **Clinical implications** 47

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48 49 301 The present study highlights that being in a SB reduction intervention which elicits changes to PA, standing, 50 302 and SB might work as a protective strategy against back pain. Furthermore, as observed before with 51 52 303 strength or mobility goals for rehabilitation (27), the possible improvements in pain or disability seem to 53 54 304 not be related to paraspinal muscle GU or FF.

56 305 Strengths and weaknesses 57

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58 306 The strengths of this study include the robust measurement of PA, standing, and SB with accelerometers 59 60 307 during the whole six-month study. Moreover, the accelerometer data was analyzed using validated

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| 2 3 4 | 308 | algorithms (19,20). Furthermore, the ODI is a validated questionnaire (16), and VAS is commonly used for |
| 4 5 | 309 | pain assessment, and it associates with functional outcomes (29). However, a weakness in this study is the |
| 6 7 | 310 | use of non-validated questions with the VAS. Another key strength is the muscle specific GU assessment |
| , 8 9 | 311 | with the HEC protocol combined with FDG-PET imaging (30). Further, the two-point Dixon is a highly |
| - | 312 | reproducible method for FF assessment (31). |
| | 313 | One limitation of the present study is the sample size. For the GU assessments, the sample size was likely |
| 14 | 314 | adequate (12), but as the pain-related outcomes were not the primary outcomes of the whole trial, the |
| 15 16 | 315 | statistical power might have been inadequate. Additionally, the study sample was not chosen based on |
| 17 18 | 316 | pain status which may have increased heterogeneity in the sample, and thus decreased the statistical |
| 19 | 317 | power. |
| 20 21 | 318 | |
| 22 23 | 510 | |
| 24 | 319 | Conclusion |
| | 320 | An intervention that reduced SB by mainly replacing it with PA may prevent against increases to back pain |
| 27 28 | 321 | intensity in adults with metabolic syndrome and physical inactivity. Replacing the SB by walking over six |
| 29 30 | 322 | months may contribute to improved paraspinal muscle insulin sensitivity, and these factors warrant |
| 31 | 323 | continued investigation in the context of pain and disability. |
| 32 33 | 374 | |
| 34 35 | 01. | |
| 36 | 325 | Author contributions |
| 37 38 | 326 | 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. |
| 39 40 | 327 | 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 |
| 41 42 | 328 | the manuscript and all authors edited and revised the manuscript. All authors approved the final version of |
| 12 | 329 | the manuscript. I.H. acted as the guarantor. |
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| 52 | | Medicine at Turku University Hospital and Turku PET Centre for assistance in the data collection. |
| 53 54 | | |
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| 58 59 | 337 | University Foundation, the Finnish Diabetes Research Foundation, Turku University Hospital Foundation, |
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| | | |

3 338 and the Päivikki and Sakari Sohlberg foundation (220068). The funding bodies did not take part in designing 4 339 the study, collecting, analyzing, or interpreting the data, or preparing the manuscript. 5 6 7 340 Data availability statement 8 9 Data are available upon reasonable request from the corresponding author. 341 10 11 12 342 **Ethical approval** 13 ¹⁴ 343 The Ethics Committee of the Hospital District of Southwest Finland gave its approval for the study 15 16 344 (16/1801/2017). 17 18 345 **Conflicts of interest** 19 20 346 The authors declare the following financial interests/personal relationships which may be considered as 21 22 347 potential competing interests: T.S. received a speaker fee from Pihlajalinna Plc, Tampere, Finland. The 23 24 348 other authors report no conflicts of interest. The results are presented clearly and honestly without 25 349 fabrication, falsification, or inappropriate data manipulation. 26 27 28 350 29 30 351 References 31 32 Alzahrani H, Alshehri MA, Alzhrani M, Alshehri YS, Al Attar WSA. The association between sedentary 352 33 34 353 behavior and low back pain in adults: a systematic review and meta-analysis of longitudinal studies. 35 354 PeerJ. 2022 Mar 28;10:e13127. 36 37 355 Park SM, Kim HJ, Jeong H, Kim H, Chang BS, Lee CK, et al. Longer sitting time and low physical activity 2. 38 356 are closely associated with chronic low back pain in population over 50 years of age: a cross-sectional ³⁹ 357 study using the sixth Korea National Health and Nutrition Examination Survey. Spine J Off J North Am 40 358 Spine Soc. 2018;18(11):2051-8. 41 42 359 3. Dzakpasu FQS, Carver A, Brakenridge CJ, Cicuttini F, Urquhart DM, Owen N, et al. Musculoskeletal pain 43 44 360 and sedentary behaviour in occupational and non-occupational settings: a systematic review with 45 361 meta-analysis. Int J Behav Nutr Phys Act. 2021 Dec 13;18(1):159. 46 47 362 4. Norha J, Hautala AJ, Sjöros T, Laine S, Garthwaite T, Knuuti J, et al. Standing time and daily proportion 48 363 of sedentary time are associated with pain-related disability in a one month accelerometer 49 364 measurement in adults with overweight or obesity. Scand J Pain. 2022 Apr 26;22(2):317–24. 50 51 365 Barone Gibbs B, Hergenroeder AL, Perdomo SJ, Kowalsky RJ, Delitto A, Jakicic JM. Reducing sedentary 5. 52 366 behaviour to decrease chronic low back pain: the stand back randomised trial. Occup Environ Med. 53 367 2018;75(5):321-7. 54 55 368 Danguah IH, Kloster S, Holtermann A, Aadahl M, Tolstrup JS. Effects on musculoskeletal pain from 56 ₅₇ 369 "Take a Stand!" - a cluster-randomized controlled trial reducing sitting time among office workers. 58 370 Scand J Work Environ Health. 2017;43(4):350-7. 59 60

Page 15 of 31

BMJ Open

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| | 440 | Figu | ure legends |
| 52 53 | 441 | Figu | re 1. Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry |
| 54 | 442 | disa | bility index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black |
| 55 56 | 443 | dot | s represent the intervention group and gray squares represent the control group. The presented |
| 57 58 | 444 | esti | mates are model-based means and 95% confidence intervals. A higher value indicates higher pain |
| | 445 | inte | ensity or disability on all panels. VAS = visual analogue scale. *=Tukey's p=0.026 |

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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) ¹² 451 transversospinal muscle fat fraction (FF), and D) erector spinae FF. GU analyses (panels A and B) are 14 452 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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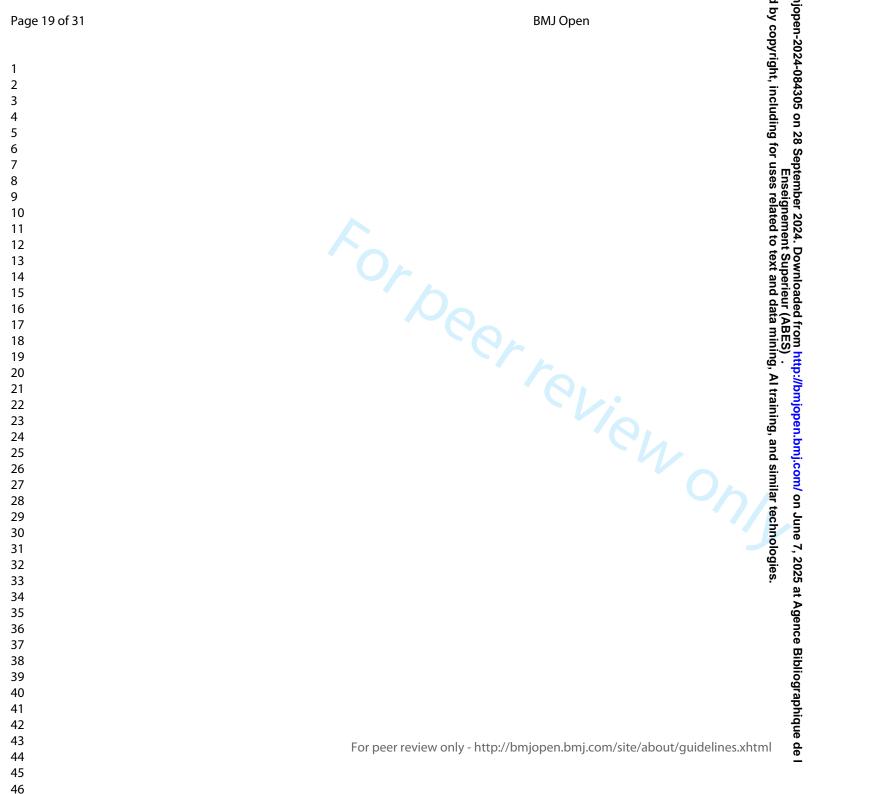
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| 2 3 455 4 5 456 | Table 1. Study participant characteristics at the basel presented as mean (SD). | ine. Unless c | otherwise stated | , the results | are |
|--------------------------|---|---------------|------------------|---------------|-----|
| 6 7 | Intervention | n | Control | n | |

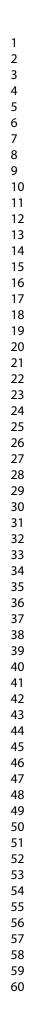
| 7 | | Intervention | 11 | Control | 11 |
|--------------|--|------------------------|-------|---------------------|---------|
| 8 | Men, n (%) | 13 (39) | 33 | 14 (45) | 31 |
| 9 | Age, yrs | 59 (6) | 33 | 57 (8) | 31 |
| 10 11 | Anthropometrics & metabolism | | | | |
| 12 | BMI, kg/m ² | 31.5 (4.0) | 33 | 31.7 (4.6) | 31 |
| 13 | Body fat, % | 43.1 (8.0) | 33 | 43.1 (8.0) | 31 |
| 14 15 | Waist circumference, cm | 111.1 (11.6) | 33 | 110.7 (11.1) | 31 |
| 15 | fP-Glucose, mmol/l | 5.9 (0.5) | 33 | 5.8 (0.4) | 31 |
| 17 | fP-Insulin, mU/I * | 9 (7, 13) | 33 | 11 (7, 17) | 30 |
| 18 | HbA1c, mmol/l | 37.0 (2.8) | 33 | 36.3 (2.7) | 31 |
| 19 20 | Transversospinal FF, %* | 23.7 (15.6, 33.8) | 22 | 23.8 (19.6, 34.0) | 21 |
| 20 | Erector spinae FF, %* | 17.5 (13.3, 26.8) | 22 | 18.0 (14.4, 23.4) | 21 |
| 22 | Transversospinal GU, | 2.8 (2.3, 3.2) | 23 | 2.5 (2.0, 3.3) | 20 |
| 23 24 | µmol/100 cm ³ /min* | | | | |
| 24 25 | Erector spinae GU, | 2.9 (2.0, 3.3) | 23 | 2.4 (1.9, 3.9) | 20 |
| 26 | µmol/100 cm³/min* | | | | |
| 27 | QF GU, µmol/100 cm ³ /min* | 2.0 (1.4, 2.7) | 23 | 1.9 (1.2, 3.2) | 20 |
| 28 29 | Hamstring GU, µmol/100 cm ³ /min* | 3.0 (2.0, 4.6) | 23 | 2.8 (1.4, 4.0) | 20 |
| 30 | Whole-body GU, µmol/kg/min* | 15.3 (10.7, 21.0) | 33 | 13.9 (9.8, 21.0) | 31 |
| 31 | Pain & disability | | | | |
| 32 | Regular medication for pain, n (%) | 3 (9) | 33 | 4 (13) | 31 |
| 33 34 | VAS Back pain, 0-10 cm* | 0.3 (0.1, 3.5) | 33 | 0.5 (0.1, 3.0) | 29 |
| 35 | VAS Pain-related disability, 0-10 cm* | 0.4 (0.1, 2.2) | 33 | 0.7 (0.2, 2.6) | 30 |
| 36 | Oswestry disability index, %* | 6.0 (1.0, 13.0) | 33 | 6.7 (2.0, 16.0) | 31 |
| 37 38 | Physical activity | 7 | | | |
| 30 39 | Accelerometry, h/day | 14.5 (1.0) | 33 | 14.6 (1.0) | 31 |
| 40 | Sedentary time, h/day | 10.0 (0.9) | 33 | 10.1 (1.1) | 31 |
| 41 | Standing time, h/day | 1.8 (0.6) | 33 | 1.8 (0.6) | 31 |
| 42 43 | LPA, h/day | 1.7 (0.4) | 33 | 1.8 (0.5) | 31 |
| 44 | MVPA, h/day | 0.96 (0.31) | 33 | 0.97 (0.34) | 31 |
| 45 | Breaks in sedentary time, n/day | 28 (8) | 33 | 29 (8) | 31 |
| 46 47 | Steps, n/day | 5204 (1910) | 33 | 5091 (1760) | 31 |
| 47 49 457 | BMI. Body mass index: FF. fat fraction: | GU. insulin-stimulated | eluco | se uptake: OF, Ouad | lriceps |

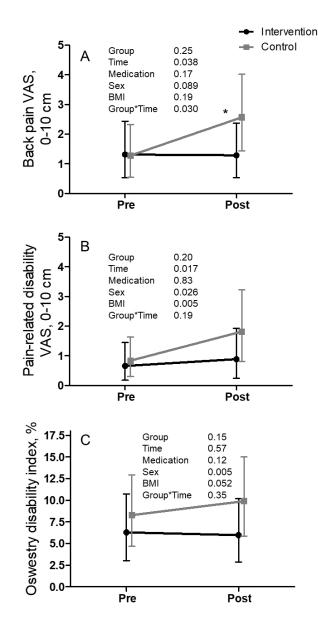
₄₈ 457 BMI, Body mass index; FF, fat fraction; GU, insulin-stimulated glucose uptake; QF, Quadric femoris muscle; fP-Glucose, fasting plasma glucose; fP-Insulin, fasting plasma insulin; HbA 49 458 ⁵⁰ 459 glycated hemoglobin; VAS, visual analogue scale; LPA, light physical activity; MVPA moder 52 460 vigorous physical activity. * presented as median (Q1, Q3).



Page 20 of 31

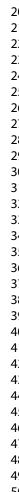
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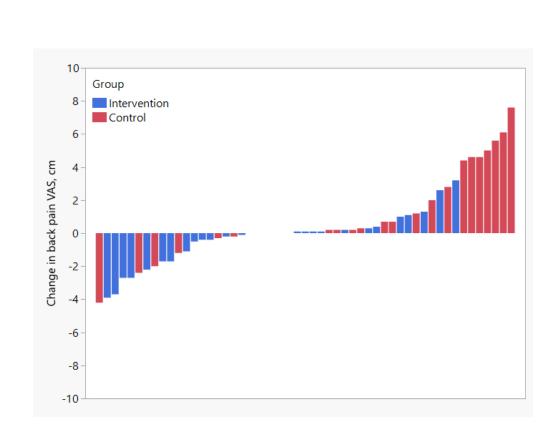




Intervention effects on A) back pain intensity, B) pain-related disability, and C) the Oswestry disability index. All analyses are adjusted for sex, pain medication status, and body mass index (BMI). Black dots represent the intervention group and gray squares represent the control group. The presented 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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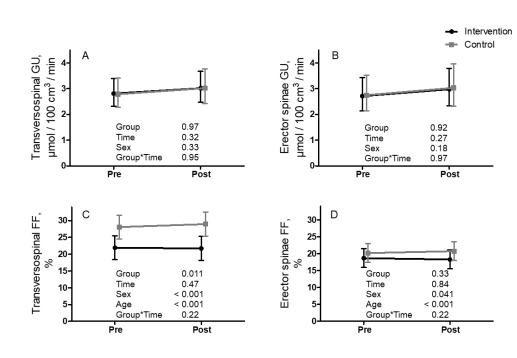




Changes in each participant's back pain during the intervention. Blue bars represent participants in the intervention group and red bars represent participants in the control group. Of the six participants with no changes in back pain, four were in the intervention and two in the control group. A higher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

184x136mm (96 x 96 DPI)





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: A secondary analysis of a six-month randomized controlled trial

Supplementary file

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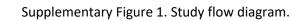
5 Department of Radiology, University of Turku and Turku University Hospital, Turku, Finland

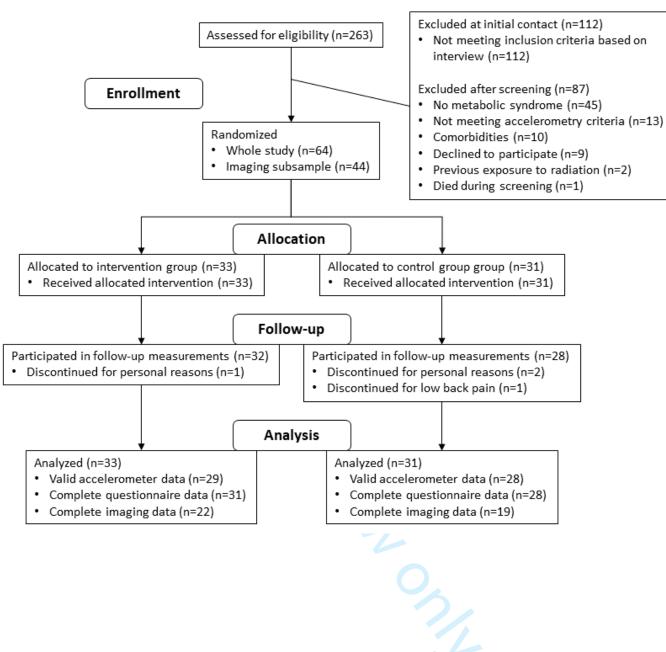
6 The UKK Institute for Health Promotion Research, Tampere, Finland

7 Department of Biostatistics, University of Turku and Turku University Hospital, Turku, Finland

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Supplementary Table 1. Baseline Spearman's rank correlation coefficients

| | | | | | | | | | | | | | | | | | | | | ght, | ļ. | | | |
|----------|---------|--------|---------|--------|--------|------------|--------|---------|---------|---------------|---------|-------------|---------|---------|---------|----------------|---------|-----------|---------|---|-------------------------------|-------|--------|-----|
| | Tra. FF | ES FF | Tra. GU | ES GU | QF GU | Ham. GU | WB GU | BMI | WC | Body fat % | Weight | Glucos e | Insulin | HbA1c | SB % | Standi ng % | KPA % | MVPA % | PA % | , including | 84305 o | BP | PRD | IQO |
| 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 | -025 | 0.10 | 0.02 | 0.1 |
| 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 | 0.255 | 0.11 | 0.07 | 0.1 |
| 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 9 | -0 % q 0 -0_ | -0.05 | -0.09 | 0.0 |
| 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 [•] es | tem nse | -0.04 | -0.14 | -0. |
| 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° a | | -0.04 | -0.18 | -0. |
| 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 | 0.44 s related to t | 2024 ennie | -0.11 | -0.13 | -0. |
| 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 | | -0.07 | -0.08 | -0. |
| 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 | 0.36 ext and data minin -0.37 data minin | | 0.07 | 0.03 | -0 |
| 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 | ade: euro | 0.00 | -0.02 | 0. |
| WC | | | | | | | | | 1 | 0.23 | 0.80** | 0.25* | 0.64** | 0.26* | 0.38** | -0.31* | -0.17 | -0.32* | -0.29* | -0.42 3 | | -0.03 | 0.00 | 0. |
| BF % | | | | | | | | | | 1 | 0.11 | -0.17 | 0.15 | 0.05 | 0.02 | 0.21 | 0.13 | -0.29* | -0.09 | -0.28 | | 0.18 | 0.16 | 0. |
| Weight | | | | | | | | | | - | 1 | 0.27* | 0.68** | 0.17 | 0.40** | -0.35** | -0.24 | -0.18 | -0.28* | -0.33 | -0.31 | -0.13 | -0.12 | -0 |
| Glucose | | | | | | | | | | | | 1 | 0.24 | 0.12 | 0.06 | -0.32** | 0.17 | 0.10 | 0.16 | 0.01 ain | -0.92 -0.92 | -0.15 | -0.16 | -0 |
| Insulin | | | | | | | | | | | | | 1 | 0.25* | 0.41** | -0.49** | -0.15 | -0.11 | -0.19 | -0.260 | -0 9 0' | -0.16 | -0.08 | 0. |
| HbA1c | | | | | | | | | | | | | | 1 | 0.14 | -0.18 | 0.10 | -0.10 | -0.01 | -0.10 <mark>0</mark> | -0 3 6 | 0.01 | -0.07 | 0. |
| SB | | | | | | | | | | | | | | | 1 | -0.79** | -0.62** | -0.55** | -0.75** | -0.54 <mark>26.</mark> B | -0.86** | 0.03 | -0.19 | 0. |
| Standing | | | | | | | | | | | | | | | | 1 | 0.28* | 0.19 | 0.30* | 0.22 a | 0.26 | 0.06 | 0.27* | 0. |
| LPA | | | | | | | | | | | | | | | | | 1 | 0.28* | 0.83** | 0.21 F | 0.33** | 0.06 | 0.04 | -0 |
| MVPA | | | | | | | | | | | | | | | | | | 1 | 0.73** | 0.93 Ch | 0. În e | -0.20 | -0.03 | -0. |
| PA | | | | | | | | | | | | | | | | | | | 1 | 0.65 .0 | 0.30** | -0.09 | -0.01 | -0. |
| Steps | | | | | | | | | | | | | | | | | | | | 1 S. | | -0.18 | -0.03 | -0 |
| Breaks | | | | | | | | | | | | | | | | | | | | | 1 ₽ 1 ₽ | 0.09 | 0.14 | -0 |
| BP | | | | | | + | | | | | | | | | | | | | | | Age | 1 | 0.61** | 0.1 |
| PRD | | | | | | | | | | - | | - | | | | | | | | + | nc | + | 1 | 0. |

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

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

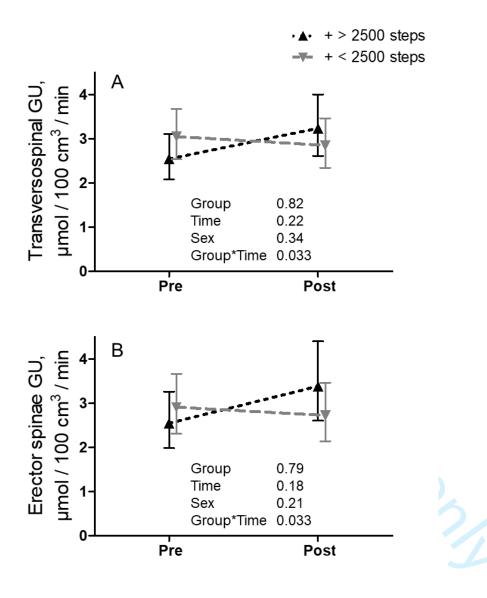
| | Δ ES FF | Δ Tra. GU | Δ ES GU | Δ QF GU | ∆ Ham. | Δ WB GU | Δ BMI | Δ WC | Δ Body | ∆ Weigh | Δ Glucos | ∆ Insulin | Δ HbA1c | Δ SB% | ∆ Standi | A LPA% | 084305 Qn | Δ PA% | Δ Steps | Δ Breaks | ΔBP | Δ PRD | A ODI |
|-----------------|------------|--------------|------------|------------|------------|------------|-------------------------|------------|-----------|-------------|-------------|--------------|------------|-------------|-------------|------------|--------------------------------------|-------------|-------------|-------------|-----------|-------|-----------|
| ∆ Tra. FF | 0.55* * | 0.1 6 | 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 | -01292 | 0.02 | 0.05 | -0.03 | - 0.06 | 0.22 | 0.06 |
| Δ ES FF | 1 | 0.0 3 | 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 | 3 Septe#aber 2024. [Enseignement | 0.13 | 0.22 | 0.24 | - 0.11 | 0.17 | -0.05 |
| ∆ 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 | 024. Down ment Supe | 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 | nlaaded fr oefieur (AE | 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* ų | 。 「昭和 http 小BES). | 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. [®] mjope | 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* g | | 0.36** | 0.30* | 0.14 | - 0.14 | -0.13 | -0.12 |
| ΔΒΜΙ | | | | | | | 1 | 0.47* * | 0.29 * | 1.0** | 0.15 | 0.29* | 0.33* | 0.35* | -0.22 | -0.31* | -0 2 7 | -0.35* | - 0.36** | -0.24 | 0.10 | 0.19 | 0.37 * |
| ΔWC | | | | | | | | 1 | 0.16 | 0.47** | 0.09 | 0.24 | 0.17 | 0.21 | 0.02 | -0.24 | -0 6 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 | 2025 ⁹ at Age | 0.02 | -0.29* | -0.13 | - 0.05 | 0.18 | 0.26 |
| ∆ Weight | | | | | | | | | | 1 | 0.15 | 0.31* | 0.35* * | 0.37** | -0.24 | -0.32* | -0 2 6 B : | - 0.36** | - 0.36** | -0.25 | 0.08 | 0.16 | 0.35 * |
| ∆ Glucose | | | | | | | | | | | 1 | 0.27* | 0.10 | -0.07 | 0.18 | -0.09 | bliographique | -0.10 | -0.14 | -0.23 | 0.17 | 0.00 | -0.1 |

| 7 of 31 | | | | | | | BMJ | Open | | | | | jopen-2(bv cop | | | | | | |
|--------------------|--|--|---|-----|----|---|-----|------|------|------|-------------|-------|---|-------------|-------------|-------------|-----------|------------------------|----------|
| Δ Insulin | | | | | | | | 1 | 0.24 | 0.23 | -0.22 | -0.21 | njopen-2024-0843 | -0.19 | -0.21 | -0.16 | - 0.17 | -0.25 | -0.(|
| Δ HbA1c | | | | | | | | | 1 | 0.21 | 0.00 | | 3024* -,324* cludina 1 | -0.26 | - 0.41** | -0.28* | 0.04 | -0.02 | 0.1 |
| Δ SB% | | | | | | | | | | 1 | - 0.76** | - | 8 Septemb - Ensei | - 0.77** | - 0.60** | - 0.37** | - 0.08 | -0.05 | 0.2 |
| Δ Standing % | | | | | | | | | | | 1 | 0.21 | * Ginemei Ginemei | 0.24 | 0.30* | 0.15 | 0.22 | 0.06 | -0 |
| Δ LPA% | | | 0 | r . | | | | | | | | 1 | : Downloaded from to Superieur (ABES) | 0.87** | 0.44** | 0.34* | 0.10 | 0.09 | -0 |
| Δ MVPA% | | | | K | 20 | 0 | | | | | | | aded fror eur (ABE | 0.81** | 0.73** | 0.44** | - 0.10 | -0.07 | -0 |
| Δ ΡΑ% | | | | | | | 1 | 0. | | | | ę | n http://br S) . nina. Al tr | 1 | 0.64** | 0.41** | - 0.10 | -0.08 | -0 |
| Δ Steps | | | | | | | | V | 6 | | | ę | mjopen.br | | 1 | 0.57** | - 0.07 | -0.11 | -0 |
| Δ Breaks in SB | | | | | | | | | | V | | | omj.com/ o | | | 1 | 0.07 | 0.10 | 0. |
| ΔΒΡ | | | | | | | | | | | | | on June 7 | | | | 1 | 0.67 [*] * | 0.4 * |
| ΔPRD | | | | | | | | | | | | | 7, 2025 ologies. | | | | | 1 | 0. * |

Δ Change in the measured outcome, Tra., transversospinal muscles; FF, fat fraction measured with magnetic resonance imaging; ES, erector spinae muscle; GU, insulinstimulated glucose uptake measured with euglycemic hyperinsulinemic clamp and positron emission tomography; QF, quadri geps femoris muscle; Ham., hamstring muscles; WB, whole-body; BMI, body mass index; WC, waist circumference; BF%, body fat percentage; Hba1c, glycated hemo accelerometry; LPA, light physical activity measured with accelerometry; MVPA, moderate-to-vigorous physical activity meas $\mathbf{\bar{e}}$ ed with accelerometry; PA, physical activity (LPA+MVPA) measured with accelerometry; BP, back pain measured with visual analogue scale; PRD, pain-related disability neasured with visual analogue scale; ODI, Oswestry disability index. *significant at the level of p<0.05, **significant at the level of p<0.01. aphique

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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.



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Appendix. CHAMP: CHecklist for statistical Assessment of Medical Papers

| 1 | . Clear description of the goal of research, study objective(s), study design, and study population | Yes _s | Unclear | |
|--------|---|------------------|---------|---|
| 2 | Clear description of outcomes, exposures/treatments and covariates, and their measurement | Yes | Unclear | |
| 3 | methods Validity of study design | Yes | Unclear | 1 |
| 4 | | Yes | Unclear | |
| 5 | | Yes | Unclear | |
| 6 | | Yes | Unclear | |
| | analysis | | | |
| 7 | | Yes | Unclear | |
| 8 | | Yes | Unclear | |
| 9 | Appropriate assessment of treatment effect or interaction between treatment and another covariate | Yes | Unclear | |
| 1 | 0. Correct use of correlation and associational statistical testing | Yes | Unclear | |
| 1 | 1. Appropriate handling of continuous predictors | Yes | Unclear | |
| 1 | 2. Confidence intervals do not include impossible values | Yes | Unclear | |
| 1 | 3. Appropriate comparison of baseline characteristics between the study arms in randomized | Yes | Unclear | |
| | trials | | | |
| | 4. Correct assessment and adjustment of confounding | Yes | Unclear | |
| | 5. Avoiding model extrapolation not supported by data | Yes | Unclear | |
| | 6. Adequate handling of missing data <i>rting and presentation</i> | Yes | Unclear | |
| - | 7. Adequate and correct description of the data | Yes | Unclear | |
| 1 | 8. Descriptive results provided as occurrence measures with confidence intervals, and analytic | Yes | Unclear | |
| | results provided as association measures and confidence intervals along with P-values | 105 | Unclear | |
| 1 | 9. Confidence intervals provided for the contrast between groups rather than for each group | Yes | Unclear | |
| 2 | 20. Avoiding selective reporting of analyses and P-hacking | Yes | Unclear | |
| 2 | 1. Appropriate and consistent numerical precisions for effect sizes, test statistics, and P-values, | Yes | Unclear | |
| | and reporting the P-values rather their range | 105 | onereur | |
| 2 | 2. Providing sufficient numerical results that could be included in a subsequent meta-analysis | Yes | Unclear | |
| 2 | 3. Acceptable presentation of the figures and tables | Yes | Unclear | |
| Interp | pretation | | | |
| 2 | 4. 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 | |
| 2 | 5. Using confidence intervals rather than post-hoc power analysis for interpreting the results of studies | Yes | Unclear | |
| 'n | 6. Correctly interpreting occurrence or association measures | Yes | Unclear | |
| | 7. Distinguishing causation from association and correlation | Yes | Unclear | |
| | 8. Results of pre-specified analyses are distinguished from the results of exploratory analyses in the | | | |
| | interpretation | Yes | Unclear | |
| | 9. Appropriate discussion of the study methodological limitations | Yes | Unclear | |
| 3 | 0. Drawing only conclusions supported by the statistical analysis and no generalization of the results | Yes | Unclear |] |

| | BMJ Open Mansournia MA, et al. Br.J Sports Med 2021; 55:1–2. doi: 10.1 | Page 30 of 31 |
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| number | | | Ensei uses r | grimary paper bage or appendix wmber) | Other † (details) | |
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| 1. | | e or a phrase that describes the intervention. | Superie text and | 001 | | |
| 2. | Describe any rat WHAT | onale, theory, or goal of the elements essential to the intervention | on. data mini | 44 | | |
| 3. | provided to partic | be any physical or informational materials used in the intervention cipants or used in intervention delivery or in training of intervention for on where the materials can be accessed (e.g. online append | on, including those | 4-6 | | |
| 4. | Procedures: Des | cribe each of the procedures, activities, and/or processes used i abling or support activities. | , jo | en | | |
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| | WHEN and HOW MUCH | <u> </u> | 24-0843005 4 5 | |
| 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. | 3 | on 28 | |
| | TAILORING | for c | S Sel | |
| 9. | If the intervention was planned to be personalised, titrated or adapted, then describe what, why, | Ensi | otem4-5 | |
| | when, and how. | eign relat | ber | |
| | MODIFICATIONS | emei ted t | 2024 | |
| 10. [‡] | If the intervention was modified during the course of the study, describe the changes (what, why, | nt Su o tex | N/A | |
| | when, and how). | t and | vnlo | |
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| 11. | Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any | ABE: a mir | fron5-6 | |
| | strategies were used to maintain or improve fidelity, describe them. | | h http | |
| 12. [‡] | Actual: If intervention adherence or fidelity was assessed, describe the extent to which the | Al tra | http://b7 | |
| | intervention was delivered as planned. | aini | njop | |
| sufficie | - use N/A if an item is not applicable for the intervention being described. Reviewers – use '?' if information the provided in the primary paper, give details of where this information is available. This may i | similar | com/ o | |
| | published papers (provide citation details) or a website (provide the URL). eting the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be describ | chno | natil the study is c | omplete |
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| * We stron | gly recommend using this checklist in conjunction with the TIDieR guide (see BMJ 2014;348:g1687) which contains a | n ex | anation and elab | oration for each item. |
| * The focus | of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a stud | y. Oť | ► Ber elements and | methodological features of |
| studies ar | e covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklis | t. Wł | gen a randomised | trial is being reported, the |
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| | t (see <u>www.spirit-statement.org</u>). For alternate study designs, TIDieR can be used in conjunction with the appropria | te c <u>i</u> | ecklist for that stu | ıdy design (see |
| www.equ | ator-network.org). | - | nique | |
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Page 32 of 31