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The impact of physical activity level on the short- and long-term pain relief from supervised exercise therapy and education: A study of 12,796 Danish patients with knee osteoarthritis

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ABSTRACT

Objectives: It is unknown if people with knee osteoarthritis (OA) who are already physically active benefit from exercise therapy. To study the impact of physical activity level on pain relief, post-intervention and 12 months following exercise therapy and education.

Method: The analyses included 12,796 patients with knee OA from the Good Life with osteoArthritis in Denmark (GLA:D®) program. GLA:D® consists of 12 sessions of supervised neuromuscular exercise and two sessions of education delivered by trained physical therapists. The impact of physical activity level on change in knee pain intensity (0 to 100) immediately post-intervention and at 12 months was estimated using a mixed-effects model adjusted for age, sex, body mass index, educational level and comorbidity. Physical activity level was assessed using the University of California, Los Angeles activity scale.

Results: Physically inactive patients had worse baseline pain compared to patients with low to very high physical activity level (6 to 15 points worse; p<0.001). Pain decreased by 13.4 points (95%CI; 9.7 to 17.1) following the treatment program and by 12.8 points (7.7 to 18.0) at 12 months in the inactive patients, with similar improvements in patients with higher levels of physical activity (p=0.278 to 0.851).

Conclusion: In patients with knee OA, similar and persistent long-term pain relief was found from supervised exercise therapy and education regardless of the initial physical activity level. Patients with high to very high levels of physical activity can expect pain relief from supervised exercise therapy and education similar to that of more physically inactive patients.

Keywords: Osteoarthritis; Exercise therapy; Physical activity
INTRODUCTION

In addition to improving symptoms, one of the goals from prescribing exercise therapy in patients with knee osteoarthritis (OA) is to increase physical activity level for the benefit of improved overall health\textsuperscript{1}. Therefore, it may seem unnecessary, or even counter-intuitive, to expect benefits from exercise therapy in those who are already physically active. Additionally, greater pain seems to be associated with lower physical activity level in knee OA\textsuperscript{2,3}, suggesting that greater pain relief can be expected from interventions such as exercise therapy in less active patients.

However, little is actually known about the impact of physical activity level on the effects of pain relief following exercise therapy as most randomized trials do not report or insufficiently report physical activity level at baseline\textsuperscript{4}. Knowledge about the effects of exercise therapy in patients with knee OA who engage in different levels of physical activity is important, as it could help personalize treatment advice based on physical activity level and challenge the assumption that exercise therapy is more beneficial to patients with lower physical activity levels.

The purpose was to study the impact of physical activity level on the short- and long-term pain relief following an 8-week supervised exercise therapy and patient education program. The hypothesis was that physically inactive patients would experience greater improvements in knee pain compared to patients who had a higher physical activity level when entering the program.
METHOD

Design

This was a registry-based study evaluating the short- and long-term outcome from the Good Life with osteoArthritis in Denmark (GLA:D®) program – an ongoing nationwide initiative aimed at implementing treatment guidelines for knee and hip OA in clinical practice. GLA:D® is a treatment program consisting of two sessions of patient education followed by 12 60-minute sessions of neuromuscular exercise (twice weekly for 6 weeks) supervised by physical therapists certified to deliver the treatment program, and evaluate the effects using pre-defined and validated outcomes at baseline, immediately after the treatment program and at 12 months. A detailed description of GLA:D®, including patient characteristics, treatment and outcomes, was published previously and so were details of the neuromuscular exercise program.

This report conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting observational studies. Ethics approval of GLA:D® is not needed, according to the local ethics committee of the North Denmark Region. The GLA:D® registry has previously been approved by the Danish Data Protection Agency and all patients consented to submitting their data to the GLA:D® registry.

Participants

Patients with knee or hip joint pain or functional impairments that result in contact with the health care system who do not meet one or both of the exclusion criteria listed below were eligible for GLA:D®.

Exclusion criteria were: 1) another reason for the joint symptoms than OA as evaluated by the physical therapist, e.g. inflammatory joint disease or patellar tendinopathy; 2) other symptoms that are more pronounced than the OA symptoms, e.g. chronic, generalized pain, or fibromyalgia.
For the current report, patients with knee OA fulfilling the eligibility criteria above and with available data from baseline (pain intensity and physical activity level) and at least one of the two follow-ups (pain intensity) were included.

**Outcome variable**

Change in self-reported mean pain intensity during the last month in the most affected knee. Pain was evaluated at baseline, immediately after the 8 weeks of supervised exercise therapy and patient education and at 12 months on a 100-point visual analogue scale (VAS) with the terminal descriptors being ‘no pain’ (0) and ‘maximum pain’ (100)⁸.

**Exposures**

Two self-reported measures of physical activity were applied. The primary measure of physical activity was The University of California, Los Angeles (UCLA) activity scale⁹. The scale has ten descriptive activity levels ranging from inactive and dependent on others (level 1) to regular participation in impact sports (level 10). For analytic purposes, the ten physical activity levels reported were grouped into five categories with two levels in each category (physically inactive, low physical activity level (e.g. walking and limited housework), moderate physical activity level (e.g. swimming and unlimited housework), high physical activity level (e.g. prolonged biking and fitness) and very high physical activity level (e.g. running, tennis and skiing).

To support the findings from the primary analyses, a secondary analysis using the following question was applied: “How often do you usually exercise at a level where you get short of breath or sweat?” with seven response categories ranging from Never (response category 1) to Every day (response category 7). Participants were grouped into four categories based on their response: physically inactive (i.e. participants did not sweat or were not short of breath more often than twice
a month, response category 1-3), physically active once weekly (i.e. participants did sweat or were short of breath once weekly, response category 4), physically active 2-3 times weekly (i.e. participants did sweat or were short of breath 2-3 times a week, response category 5) and physically active >3 times weekly (i.e. participants did sweat or were short of breath more than 3 times a week, response category 6-7).

**Statistical analysis**

For this analysis data collected in GLA:D between January 2013 and end of December 2016 was used. The impact of physical activity level on change in knee pain intensity was estimated using linear mixed effects models with patients, nested by clinics, as a random factor and follow-up time (baseline, immediately after the treatment program, and at 12 months) and physical activity level as fixed factors. Each of the two measures of physical activity was analysed separately. Crude and adjusted analyses were conducted. The analyses were adjusted for age (continuous), sex (male/female), Body Mass Index (BMI (Kg/m²); continuous), the number of comorbidities (discrete), and educational level (categorical). Sensitivity analyses were conducted including only patients who had radiographically-confirmed knee OA and including only patients who had not undergone a TKR.

A p-value less than 0.05 (two-sided) was considered significant. All analyses were carried out in Stata 15.1 (StataCorp, College Station, TX, USA).
RESULTS

Table 1 presents the characteristics of the 12,796 patients with knee OA included in the analyses according to their baseline physical activity level. The follow-up rate in GLA:D® is 84% immediately after the treatment program and 70% at 12 months. Out of 10,902 patients (85%) who self-reported that they previously had a radiographic examination of their knee, 9,886 patients (91%) self-reported that they had radiographically-confirmed knee OA.

***** Table 1 HERE******

Primary analysis: Physical activity assessed with the UCLA score

At baseline, physically inactive participants had higher knee pain intensity compared to participants with higher physical activity levels (p<0.001; Table 2).

Knee pain intensity improved in all five physical activity groups (P<0.05). The crude analysis demonstrated that knee pain intensity decreased by 13.7 points (95%CI 10.0 to 17.5) immediately following supervised exercise therapy and patient education and by 13.4 points (95%CI 8.2 to 18.5) at 12 months in the inactive group. Physical activity level was not associated with the outcome (p=0.197 to 0.962; Table 2). The adjusted analysis demonstrated similar results, with knee pain intensity decreasing by 13.4 points (95%CI 9.4 to 17.1) immediately following supervised exercise therapy and patient education and by 12.8 points (95%CI 7.7 to 18.0) at 12 months in the inactive group. Physical activity level was not associated with a decrease in knee pain intensity (p=0.278 to 0.851; Table 2).

Secondary analyses: Physical activity assessed using the question “How often do you usually exercise at a level where you get short of breath or sweat?”
The results from the secondary analysis supported the primary analysis. At baseline, physically inactive participants had higher knee pain intensity compared to participants with higher physical activity levels (p<0.001; Table 2).

Knee pain intensity improved in all four physical activity groups (P<0.05). The crude analysis demonstrated that knee pain intensity decreased by 13.4 points (95%CI 12.5 to 14.3) immediately following supervised exercise therapy and patient education and by 13.1 points (95%CI 11.9 to 14.3) at 12 months. Physical activity level was not associated with a decrease in knee pain intensity (p=0.218 to 0.941; Table 2). The adjusted analysis demonstrated similar results, with knee pain intensity decreasing by 13.3 points (95%CI 12.4 to 14.2) immediately following supervised exercise therapy and patient education and by 12.8 points (95%CI 11.6 to 14.1) at 12 months. Physical activity level was not associated with a decrease in knee pain intensity (p=0.189 to 0.985; Table 2).

Sensitivity analyses resulted in similar findings (data not shown).
DISCUSSION

While physically inactive patients had worse baseline knee pain intensity than patients with higher levels of physical activity, and thus greater potential for improvement, similar improvements in pain were seen across this large-scale sample of patients with knee OA. Our finding supports the use of supervised exercise therapy and patient education as effective treatment for patients with knee OA, regardless of their physical activity level.

We found that physically inactive patients had worse knee pain intensity than patients with higher levels of physical activity. In contrast, a cross-sectional study of 1,788 participants with, or at high risk of, knee OA did not find that the presence of knee pain was associated with physical activity level. The difference might relate to differences in how physical activity (self-reported vs. wearing an activity monitor) and knee pain (pain intensity vs. pain categorized into three intensities) was measured, cultural differences between Denmark and the United States, or differences in population characteristics that are known to affect physical activity pattern (such as sex, age and BMI).

Interestingly, our analyses revealed a trend towards lower baseline pain intensity with higher physical activity levels, supporting previous findings of an inverse association between pain and physical activity level. Due to the cross-sectional nature of this finding, it is unclear whether worse pain or lower levels of physical activity comes first. However, a recent study suggests that maintaining at least low levels of physical activity throughout middle age is associated with a lower incidence of later joint symptoms, underscoring the importance of physical activity for patients with knee OA.

We are unaware of previous studies investigating the impact of baseline physical activity level on pain relief from exercise therapy in patients with knee OA. We were unable to confirm our hypothesis that physically inactive patients would experience greater knee pain relief after an 8-week supervised exercise therapy and education program, compared to patients with a higher
physical activity level when entering the program. Despite worse baseline knee pain intensity in
inactive patients, and thus greater potential for improvement, the treatment program resulted in
similar clinically relevant improvements in all patients, regardless of their baseline physical activity
level. This confirms recent findings in patients with systolic heart failure, demonstrating similar risk
of all-cause mortality and hospitalization and functional response to exercise therapy in patients
with higher baseline physical activity level compared to those with lower levels\textsuperscript{13}. Our findings are
important, as they challenge the clinical assumption that exercise therapy is more effective in
patients with lower physical activity levels and suggest that supervised exercise therapy is equally
effective even in patients with a high or very high physical activity level.

A few limitations should be mentioned. First, the two measures of physical activity were self-
reported. Self-reported physical activity is known to be associated with various degrees of
measurement error depending on the physical activity in focus and the time period assessed\textsuperscript{14}. Second, the uncontrolled design of our study has most likely resulted in an overestimation of the
specific treatment effects\textsuperscript{15}. Third, a more narrow definition of OA and other outcomes in addition
to pain, such as functional limitations and muscle strength, might have given a different result.
Fourth, the analyses were based on registry-based data collected in clinical practice reflecting wider
variations in treatment protocols and collection of data compared to those in clinical trials.
However, our large sample of patients with knee OA taken from a nationwide clinical registry
supports the generalizability of the findings to clinical practice.

In conclusion, regardless of initial physical activity level, similar and persistent long-term pain
relief was found from supervised exercise therapy and patient education in patients with knee OA.
Patients with high to very high levels of physical activity can expect pain relief from exercise
therapy and patient education similar to that of more physically inactive patients.
ACKNOWLEDGEMENTS
The authors would like to thank the clinicians and patients involved in collecting data for GLA:D®.

AUTHOR CONTRIBUTIONS
Study conception and design. Skou, Bricca, Roos
Recruitment of patients: Skou, Roos
Acquisition of data. Skou, Roos
Analysis and interpretation of data. Skou, Bricca, Roos
Drafting the article or revising it critically for important intellectual content. Skou, Bricca,
Roos
Final approval of the article. Skou, Bricca, Roos

All authors had full access to all the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

FUNDING/SUPPORT
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ROLE OF THE FUNDER/SPONSOR
The funders did not have any role in this study other than to provide funding.

COMPETING INTEREST
Dr. Roos is deputy editor of Osteoarthritis and Cartilage, the developer of the Knee injury and Osteoarthritis Outcome Score (KOOS) and several other freely available patient-reported outcome
measures and co-founder of Good Life with Osteoarthritis in Denmark (GLA:D®), a not-for profit initiative hosted at University of Southern Denmark aimed at implementing clinical guidelines for osteoarthritis in clinical practice.

Dr. Skou is associate editor of the Journal of Orthopaedic & Sports Physical Therapy, has received grants from The Lundbeck Foundation, personal fees from Munksgaard, all of which are outside the submitted work. He is co-founder of GLA:D®.

The authors report no other conflict of interest.
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8. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis care & research 2011;63 Suppl 11:S240-52.


### TABLE 1. Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>All individuals n=12796</th>
<th>Physically inactive n=237</th>
<th>Low physical activity level n=3725</th>
<th>Moderate physical activity level n=3807</th>
<th>High physical activity level n=4138</th>
<th>Very high physical activity level n=889</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>64 (10)</td>
<td>62 (11)</td>
<td>65 (10)</td>
<td>64 (10)</td>
<td>64 (10)</td>
<td>60 (10)</td>
</tr>
<tr>
<td><strong>Sex, n (%)</strong></td>
<td>Men</td>
<td>3446 (27%)</td>
<td>74 (31%)</td>
<td>810 (21%)</td>
<td>804 (21%)</td>
<td>1317 (32%)</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>9350 (73%)</td>
<td>163 (69%)</td>
<td>2915 (78%)</td>
<td>3003 (79%)</td>
<td>2821 (68%)</td>
</tr>
<tr>
<td><strong>BMI (kg/m²) (mean and SD) a</strong></td>
<td>28 (5)</td>
<td>32 (7)</td>
<td>30 (5)</td>
<td>29 (5)</td>
<td>28 (5)</td>
<td>27 (4)</td>
</tr>
<tr>
<td><strong>Pain intensity (0-100) (mean and SD)</strong></td>
<td>49 (22)</td>
<td>62 (22)</td>
<td>54 (22)</td>
<td>48 (21)</td>
<td>45 (21)</td>
<td>42 (21)</td>
</tr>
<tr>
<td><strong>Pain medication n (%)</strong></td>
<td>Yes</td>
<td>7803 (61%)</td>
<td>162 (68%)</td>
<td>2558 (69%)</td>
<td>2314 (61%)</td>
<td>2339 (57%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>4993 (39%)</td>
<td>75 (32%)</td>
<td>1667 (31%)</td>
<td>1493 (39%)</td>
<td>1799 (43%)</td>
</tr>
<tr>
<td><strong>Educational level, n (%) b</strong></td>
<td>Primary school 237 (2%)</td>
<td>60 (3%)</td>
<td>42 (3%)</td>
<td>52 (2%)</td>
<td>69 (1%)</td>
<td>14 (1%)</td>
</tr>
<tr>
<td></td>
<td>Secondary school 3716 (29%)</td>
<td>888 (40%)</td>
<td>485 (32%)</td>
<td>773 (31%)</td>
<td>1287 (25%)</td>
<td>283 (20%)</td>
</tr>
<tr>
<td></td>
<td>Short-term education** 3800 (30%)</td>
<td>557 (25%)</td>
<td>404 (27%)</td>
<td>802 (32%)</td>
<td>1610 (32%)</td>
<td>427 (30%)</td>
</tr>
<tr>
<td></td>
<td>Middle-term education*** 4131 (32%)</td>
<td>584 (27%)</td>
<td>476 (32%)</td>
<td>761 (30%)</td>
<td>1754 (34%)</td>
<td>556 (39%)</td>
</tr>
<tr>
<td></td>
<td>Long-term education**** 888 (7%)</td>
<td>116 (5%)</td>
<td>89 (6%)</td>
<td>143 (6%)</td>
<td>398 (8%)</td>
<td>139 (10%)</td>
</tr>
<tr>
<td><strong>Number of comorbidities, n (%)</strong>**</td>
<td>0</td>
<td>5699 (45%)</td>
<td>73 (31%)</td>
<td>1393 (38%)</td>
<td>1667 (44%)</td>
<td>2060 (50%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>4097 (32%)</td>
<td>72 (30%)</td>
<td>1172 (32%)</td>
<td>1277 (34%)</td>
<td>1329 (32%)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1990 (16%)</td>
<td>44 (19%)</td>
<td>728 (20%)</td>
<td>592 (16%)</td>
<td>540 (13%)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1010 (8%)</td>
<td>48 (20%)</td>
<td>432 (12%)</td>
<td>271 (7%)</td>
<td>209 (5%)</td>
</tr>
<tr>
<td><strong>Compliance with exercise therapy, n (%)</strong></td>
<td>&gt; 12 sessions 2898 (38%)</td>
<td>43 (38%)</td>
<td>797 (38%)</td>
<td>897 (38%)</td>
<td>972 (37%)</td>
<td>189 (37%)</td>
</tr>
<tr>
<td></td>
<td>10 to 12 sessions 3490 (45%)</td>
<td>51 (44%)</td>
<td>974 (46%)</td>
<td>1084 (46%)</td>
<td>1172 (45%)</td>
<td>209 (40%)</td>
</tr>
<tr>
<td></td>
<td>7 to 9 sessions 714 (9%)</td>
<td>15 (13%)</td>
<td>194 (9%)</td>
<td>206 (9%)</td>
<td>245 (9%)</td>
<td>54 (10%)</td>
</tr>
<tr>
<td></td>
<td>1 to 6 sessions 309 (4%)</td>
<td>2 (2%)</td>
<td>89 (4%)</td>
<td>85 (4%)</td>
<td>108 (4%)</td>
<td>25 (5%)</td>
</tr>
<tr>
<td></td>
<td>Did not attend 285 (4%)</td>
<td>4 (3%)</td>
<td>71 (3%)</td>
<td>66 (3%)</td>
<td>104 (4%)</td>
<td>40 (8%)</td>
</tr>
<tr>
<td><strong>Compliance with patient education, n (%)</strong></td>
<td>Theory session 1 6811 (89%)</td>
<td>99 (86%)</td>
<td>1879 (88%)</td>
<td>2098 (90%)</td>
<td>2292 (88%)</td>
<td>446 (86%)</td>
</tr>
<tr>
<td></td>
<td>Theory session 2 6542 (85%)</td>
<td>96 (83%)</td>
<td>1811 (85%)</td>
<td>2002 (86%)</td>
<td>2209 (85%)</td>
<td>424 (82%)</td>
</tr>
<tr>
<td><strong>High compliance, n (%)</strong></td>
<td>Both educational session and a minimum of 10 exercise sessions 5092 (70%)</td>
<td>72 (69%)</td>
<td>1411 (70%)</td>
<td>1587 (72%)</td>
<td>1707 (69%)</td>
<td>315 (64%)</td>
</tr>
<tr>
<td><strong>Low-to-moderate compliance, n (%)</strong></td>
<td>Not both educational sessions and/or less than 10 exercise sessions 2207 (30%)</td>
<td>33 (31%)</td>
<td>610 (30%)</td>
<td>627 (28%)</td>
<td>762 (31%)</td>
<td>175 (36%)</td>
</tr>
</tbody>
</table>

---

* = at least one of the following medications: Paracetamol, NSAID (oral or topical), Morphine or other opioids; **= under 3 years after secondary school; ***= 3-4 years after secondary school; ****= at least 5 years after secondary school; *****= Hypertension, cardiovascular diseases, lung diseases, diabetes, stomach diseases, kidney diseases, blood diseases, cancer, depression, rheumatoid arthritis, neurological disorders, other medical diseases. Missing values: *: n= 5; b: n=24.
## TABLE 2. Knee pain differences at baseline, and changes immediately after supervised exercise therapy and education and at 12 months stratified by physical activity level*

<table>
<thead>
<tr>
<th>Physical activity level (UCLA classification)</th>
<th>Unadjusted pain intensity (mm) (n=12796)</th>
<th>Adjusted** pain intensity (mm) (n=12767)</th>
<th>Adjusted*** pain intensity (mm) (n=12781)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain intensity at baseline (mm) Mean (95%CI)</td>
<td>Pain intensity following treatment (mm) Mean (95%CI)</td>
<td>Pain intensity at 12 months pain intensity (mm) Mean (95%CI)</td>
</tr>
<tr>
<td>Physically inactive (Reference)</td>
<td>62.0 (58.8 to 65.2)</td>
<td>48.3 (41.3 to 55.2)</td>
<td>47.6 (40.3 to 57.0)</td>
</tr>
<tr>
<td>Difference at baseline Mean (95%CI)</td>
<td>-7.3 (-10.2 to -4.5)</td>
<td>-1.4 (-5.2 to 2.4)</td>
<td>-2.2 (-7.5 to 3.1)</td>
</tr>
<tr>
<td>Low physical activity level</td>
<td>-13.0 (-15.8 to -10.2)</td>
<td>-0.1 (-3.9 to 3.7)</td>
<td>0.9 (-4.3 to 6.2)</td>
</tr>
<tr>
<td>Moderate physical activity level</td>
<td>-16.0 (-18.9 to -13.2)</td>
<td>1.5 (-2.3 to 5.3)</td>
<td>0.8 (-4.4 to 6.1)</td>
</tr>
<tr>
<td>Very high physical activity level</td>
<td>-19.2 (-22.3 to -16.0)</td>
<td>2.7 (-1.4 to 6.8)</td>
<td>1.2 (-4.5 to 7.0)</td>
</tr>
<tr>
<td>Adjusted*** pain intensity (mm) (n=12813)</td>
<td>Baseline pain intensity (mm) Mean (95%CI)</td>
<td>Following treatment pain intensity (mm) Mean (95%CI)</td>
<td>At 12 months pain intensity (mm) Mean (95%CI)</td>
</tr>
<tr>
<td>Physically inactive (Reference)</td>
<td>51.9 (50.0 to 53.8)</td>
<td>38.5 (36.5 to 40.4)</td>
<td>38.8 (36.7 to 41.0)</td>
</tr>
<tr>
<td>Difference at baseline Mean (95%CI)</td>
<td>-6.0 (-8.9 to -3.2)</td>
<td>-1.7 (-5.4 to 2.1)</td>
<td>-2.5 (-7.7 to 2.8)</td>
</tr>
<tr>
<td>Low physical activity level</td>
<td>-10.6 (-13.4 to -7.8)</td>
<td>-0.4 (-4.1 to 3.4)</td>
<td>0.6 (-4.6 to 5.8)</td>
</tr>
<tr>
<td>Moderate physical activity level</td>
<td>-12.3 (-15.2 to -9.6)</td>
<td>1.2 (-2.6 to 5.0)</td>
<td>0.5 (-4.7 to 5.7)</td>
</tr>
<tr>
<td>Very high physical activity level</td>
<td>-14.7 (-17.8 to -11.6)</td>
<td>2.4 (-1.7 to 6.5)</td>
<td>0.8 (-4.8 to 6.5)</td>
</tr>
</tbody>
</table>

### Physical activity level (How often...?)***

<table>
<thead>
<tr>
<th>Physically inactive (Reference)</th>
<th>Baseline pain intensity (mm) Mean (95%CI)</th>
<th>Following treatment pain intensity (mm) Mean (95%CI)</th>
<th>At 12 months pain intensity (mm) Mean (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physically active once weekly</td>
<td>-2.3 (-3.4 to -1.2)</td>
<td>-0.8 (-2.2 to 0.5)</td>
<td>0.8 (-1.1 to 2.6)</td>
</tr>
<tr>
<td>Physically Active 2-3 times weekly</td>
<td>-4.0 (-5.0 to -3.0)</td>
<td>0.2 (-1.0 to 1.4)</td>
<td>-0.7 (-2.3 to 0.8)</td>
</tr>
<tr>
<td>Physically Active &gt;3 times weekly</td>
<td>-3.1 (-4.2 to -1.9)</td>
<td>0.7 (-1.4 to 1.6)</td>
<td>-0.6 (-2.6 to 1.4)</td>
</tr>
</tbody>
</table>

**Adjusted** pain intensity (mm) (n=12784)
<table>
<thead>
<tr>
<th>Activity Level</th>
<th>Baseline pain intensity (mm) Mean (95%CI)</th>
<th>Following treatment pain intensity (mm) Mean (95%CI)</th>
<th>At 12 months pain intensity (mm) Mean (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physically inactive (Reference)</td>
<td>44.7 (34.6 to 54.7)</td>
<td>31.1 (21.1 to 41.1)</td>
<td>31.6 (21.5 to 41.7)</td>
</tr>
<tr>
<td>Physically active once weekly</td>
<td>Difference at baseline Mean (95%CI)</td>
<td>Difference in change following treatment Mean (95%CI)</td>
<td>Difference in change at 12 months Mean (95%CI)</td>
</tr>
<tr>
<td></td>
<td>-1.8 (-3.0 to -0.7)</td>
<td>0.1 (-1.5 to 1.5)</td>
<td>1.3 (-0.9 to 3.4)</td>
</tr>
<tr>
<td>Physically Active 2-3 times weekly</td>
<td>-3.0 (-4.0 to -2.0)</td>
<td>0.8 (-0.5 to 2.0)</td>
<td>-0.5 (-2.2 to 1.3)</td>
</tr>
<tr>
<td>Physically Active &gt;3 times weekly</td>
<td>-1.9 (-3.2 to -0.6)</td>
<td>0.4 (-1.3 to 2.0)</td>
<td>0.2 (-2.1 to 2.5)</td>
</tr>
</tbody>
</table>

*The numbers in the inactive rows (reference) are the actual numbers, while the numbers in the other rows are differences between that group and the reference. Negative values correspond to lower pain intensity as compared to the reference. **Adjusted for baseline characteristics of age, sex, BMI, educational level and comorbidity index. Twenty-nine participants were not included in the adjusted analysis due to missing data in educational level (n=24) and BMI (n=5). ***= “How often do you usually exercise at a level where you get short of breath or sweat?”*