Osteoarthritis and Cartilage



Changes in physical activity and the association between pain and physical activity — a longitudinal analysis of 17,454 patients with knee or hip osteoarthritis from the GLA: D^{\otimes} registry



L. Baumbach † ‡ *, D.T. Grønne ‡, N.C. Møller §, S.T. Skou ‡ ||, E.M. Roos ‡

- † Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Germany
- ‡ Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Denmark
- § Research Unit for Exercise Epidemiology, Centre of Research in Childhood Health, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark. Denmark
- || The Research Unit PROgrez, Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Denmark

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SUMMARY

Objective: Investigate change in physical activity following an 8-week education and exercise therapy program for patients with knee/hip osteoarthritis, focusing on those with low physical activity level. Furthermore, to evaluate associations between changes in pain intensity and physical activity.

Method: Data from the Good Life with osteoArthritis in Denmark (GLA:D®) registry, at baseline, immediately after completion, and 12 months after entering the program was used. Measures of interest were UCLA activity scale (1−10) and Visual Analog Scale for pain intensity (0−100 mm). Changes in physical activity levels (low 1−4, moderate 5−6, and high 7−10) over three time points were investigated. Asymmetric fixed effects regression models were used to evaluate the association between clinically relevant change in pain (≥15 mm) and change in physical activity level from baseline to 12 months.

Results: 37% with low activity level at baseline (n = 4,836) and 69% of all patients (n = 17,454) reached or maintained at least a moderate physical activity level at follow-ups.

Surprisingly, both an improvement ($\beta = 1.44$, P < 0.001) and a worsening ($\beta = 1.18$, P < 0.001) in pain intensity was associated with increased physical activity in low activity patients. For all patients a similar trend was observed ($\beta = 0.51$, P < 0.001 and $\beta = 0.11$, P = 0.215, respectively).

Conclusion: In low active knee or hip OA patients, a third of patients participating in an education and exercise therapy program reached and maintained at least a moderate physical activity level for 1 year. The improvement in physical activity was not dependent on pain reduction.

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Introduction

Physical activity is defined as "any bodily movement produced by skeletal muscles that requires energy expenditure" (1) and is important to improve and maintain general health^{2,3}. For patients with knee and hip osteoarthritis (OA), exercise and physical activity are recommended as initial treatments to improve joint related

E-mail address: l.baumbach@uke.de (L. Baumbach).

pain and functioning⁴⁻⁶. Physical inactivity is a risk factor for several typical OA comorbidities, such as hypertension, diabetes and depression². Nonetheless, most patients with OA do not meet the recommended levels for physical activity⁷⁻⁹.

Increasing physical activity is difficult in general^{10–12}, and joint pain is a suggested specific barrier in people with hip or knee OA^{13,14}. Possibly physical activity could be improved in patients with hip or knee OA after participating in a patient education and exercise therapy program but it is unknown if such improvements would be maintained for an extended period in real world clinical practice.

Studying the role of joint pain is important to understand potential underlying mechanisms for change in physical activity. Such

^{*} Address correspondence and reprint requests to: L. Baumbach, Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany. Tel.: 49-40-7410-59047.

knowledge can inform physical activity initiatives in people with OA. Cross sectional studies have found a negative association between these two factors^{8,9}. However, available studies assume that an increase in pain leads to the same effect on physical activity as a decrease in pain8,9. Since pain is often perceived as an acute warning sign, an asymmetric correlation effect could be plausible as well. In other words, it is possible that the correlation of increasing pain with decreasing physical activity is stronger than the correlation of decreasing pain with increasing physical activity. Evidence for such an effect is, however, missing.

The Good life with osteoArthritis in Denmark (GLA:D®) registry enables the evaluation of physical activity changes and investigating the association between change in pain intensity and change in physical activity over three time points in real-world clinical practice. The patients with knee or hip OA included in the registry all participated in a standardized patient education and supervised exercise therapy program. Shedding light on the program's ability to sustainably increase physical activity levels is of interest for policy makers and clinicians, particularly in patients with low physical activity level at baseline as these patients would have the greatest benefit from increasing their activity level. In addition, further knowledge on the association between change in pain, decrease or increase, and change in physical activity would support better understanding of pain as a barrier to increase physical activity in patients with knee or hip OA.

The primary objective of this study was to describe the change in physical activity levels from baseline to immediately after and to 12 months after entering GLA:D®. The secondary objective was to examine associations between clinically relevant improvement and worsening in pain and change in physical activity, to better understand the role of pain as a potential barrier for physical activity. We focused on patients with low physical activity but also present analyses for patients with moderate and high physical activity levels as well as for the total sample.

Methods

Data source

This was a registry-based study using data from the GLA:D[®] initiative. GLA:D[®] was introduced in 2013 and consists of a 2-day education course for therapists, a treatment program comprising two patient education sessions and twelve exercise therapy sessions (twice weekly) lasting for 8–12 weeks, and data collection in the GLA:D[®] registry. The treatment program is delivered in primary care to patients with symptomatic knee or hip OA.

The GLA:D® registry holds information from three timepoints; baseline, immediately after the program, and at 12 months follow-up. It covers a range of patient characteristics at baseline, including demographic information such as age, sex, educational level, and presence of comorbidities, as well as outcomes collected at baseline and follow-ups, including physical activity level and function, knee or hip pain intensity, intake of pain medication, and quality of life. The GLA:D® initiative is described in further detail elsewhere 15.

Study sample

We included all patients who participated in the GLA:D® program in Denmark between 2013 and 2019 and provided information on the University of California, Los Angeles (UCLA) activity scale at baseline. Restriction of the inclusion period meant that patients had the opportunity to provide the 12 months measurement before the COVID-19 pandemic, thereby avoiding the potential influence of the pandemic on the results. Participants in the GLA:D® program had symptomatic OA as evaluated by the treating

therapist ¹⁶. Patients were not eligible for the GLA:D® program if they did not understand Danish, had another pain condition with more pronounced symptoms than the knee or hip OA (e.g., fibromyalgia, chronic generalized pain), or had a reason other than OA for their joint symptoms (e.g., inflammatory joint disease, tendinopathy). Furthermore, we excluded patients who did not provide data on the UCLA activity scale after the program and at 12 months follow-up, as well as those who received a knee or hip joint replacement during the study period.

Variables

The outcome of interest was self-reported physical activity level obtained using the UCLA activity scale (1–10, low to high) at baseline, immediately after the program, and at 12 months follow-up 17 . The scale was developed to access the activity level of patients undergoing knee and hip arthroplasty 18 and it has been used for measuring changes in self-reported physical activity 17 . Patients were asked to consider their physical activity during the last 4 weeks. To evaluate change of physical activity over three timepoints, the variable was used both as continuous and as categorical. For the latter it was categorized into low $^{1-4}$, moderate 5,6 , and high physical activity level $^{7-10}$ (Table I). The cut points were informed by the existing literature 19,20 .

The independent variable of interest was knee/hip pain intensity, which was measured at baseline, immediately after the program. and at 12 months follow-up. Pain was assessed on a visual analog scale (VAS) ranging from 0 (no pain) to 100 mm (worst pain imaginable). Participants replied to the question: "Please mark the line at the point which best describes your average knee/hip pain during the past month: 0 indicates no pain and 100 indicates worst pain imaginable" ¹⁰. For the evaluation of the within patient association between change in pain and change in physical activity, we identified three time-varying co-variates as relevant, based on a theoretically driven directed acyclic graph (DAG): change in back pain, change in number of painful hip and knee joints, and change in selfefficacy (Supplementary Fig. S1). Highest level of back pain during the previous month was obtained on a numeric rating scale (NRS) ranking from 0 (no pain) to 10 (worst pain imaginable) and treated as continuous variable. This variable was not added to the registry until 12th of July, 2018 and therefore not available for the full cohort. The number of painful hip and knee joints was based on reported complaints in each joint respectively; ranking from 1 (=complaints only in the index joint, due to which they participated in the GLA:Dprogram) to 4 (=complaints in both hips and both knees). Self-efficacy was measured using the "other symptoms Arthritis Self-Efficacy Scale" (ASES) ranging from 10 (low) to 100 (high). In addition to these time varying covariates, we also considered 'high compliance' defined as having attended at least 10 of the 12 exercise therapy sessions delivered in the GLA:D® program.

Statistical methods

Baseline patient characteristics are described for those with low, moderate and high physical activity at baseline, and for the total sample. Baseline characteristics for included and excluded patients are provided.

Increases and decreases by at least one physical activity unit on the UCLA scale ^{1–10} from baseline to immediately after the program and to 12 months follow-up are visualized for patients categorized as low, moderate, and high physical activity levels at baseline, and for the total sample. Changes in physical activity levels (low, moderate, high) are displayed using Sankey diagrams. The absolute numbers and proportions of patients changing between these three levels, stratified for baseline physical activity level, are presented.

Activity level

Low activity level

- 1) Wholly inactive: dependent on others; cannot leave residence
- 2) Mostly inactive: very restricted to minimum activities of daily living
- 3) Sometimes participates in mild activities such as walking, limited housework and limited shopping
- 4) Regularly participates in mild activities

Moderate activity level

- 5) Sometimes participates in moderate activities such as swimming, and can do unlimited housework or shopping
- 6) Regularly participates in moderate activities

High activity level

- 7) Regularly participates in active events such as bicycling
- 8) Regularly participates in very active events such as bowling or golf
- 9) Sometimes participates in impact sports such as jogging, tennis, skiing, acrobatics, ballet, heavy labor, or backpacking
- 10) Regularly participates in impact sports

Table I



University of California, Los Angeles (UCLA) activity scale as first published by Amstutz et al. (1984), with the incorporation of the physical activity levels low, moderate and high activity of the present study

Since we were mostly interested in the influence of the direction of change in pain on changes in physical activity, we applied asymmetric fixed effect regressions²¹. An advantage of this method is that observed or unobserved time-constant variables do not bias the estimates, as only within-individual changes are investigated^{21,22}. Thus, time-constant variables, such as sex, do not influence the results and are therefore not included as main effects in these models. The depended continuous variable was physical activity, which was measured with the UCLA scale (1–10, low to high).

The independent variable (pain) was categorized into those experiencing a clinically relevant improvement or worsening of at least 15 mm on the VAS^{23,24}. Those changing less than 15 mm in either direction were not included in the analyses since this change was not considered clinically relevant. We only included data from baseline and 12 months for two reasons; to avoid including patients more than once since a patient could report change in different directions immediately after and 12 months after entering the program, and since we focused on sustainable changes in physical activity. The analysis was repeated for subjects with low, moderate, and high activity at baseline, and for the total sample. To account for the potential influence of compliance with the program on the association between pain and physical activity it was also repeated for those with high compliance. All models were complete case analyses and adjusted for the three time-varying co-variates; back pain, number of painful hip and knee joints, and self-efficacy.

Since the covariate back pain was not added until 5 years after the cohorts inception which resulted in a high number of missing values, we decided to perform supplementary asymmetric fixed effects regression analysis, adjusting only for self-efficacy, and the number of painful knee and hip joints. Furthermore, we performed linear fixed effects regression models in which the dependent variable pain intensity was treated as a continuous variable. These models included data provided at baseline, immediately after the program, and at 12 months follow-up. Similarly, the analyses were repeated in patients with low, moderate, and high physical activity at baseline, to the total sample, and finally to those with high compliance only.

The analyses were performed in STATA 16.1 (StataCorp., College Station, Texas, USA) and R Version 1.4.1106.

For reporting the results of this study we applied the STROBE (Strengthening the reporting of observational studies in epidemiology) checklist²⁵.

Results

A flow chart of the patients included in the study is provided in Supplementary Fig. S2. Characteristics of included patients stratified for physical activity level at baseline, and for the total sample, are presented in Table II.

Compared to included, excluded patients had slightly lower educational level, somewhat higher pain and lower self-efficacy but no other apparent differences in characteristics (Supplementary Table S1).

Of the low active patients, 47% were able to increase their physical activity level by at least one UCLA activity scale unit during the 12 months. Most improved immediately after the program and at least maintained that improvement until 12 months while others did not improve until at 12 months [Fig. 1(a)]. Similarly, 38% of all patients increased their physical activity by at least one UCLA unit during the follow-up of the GLA:D® program [Fig. 1(d)]. Detailed information on changes in those with low, moderate, and high physical activity levels at baseline as well as for the total sample are given in Fig. 1(b)—(d).

On a group level, pain decreased with 14 mm (95% CI -14.19; -13.30) and physical activity increased with 0.36 (95% CI 0.32; 0.39) UCLA points from baseline to immediately after GLAD®. At 12 months follow-up, the mean pain decrease compared to baseline was 11 mm (95% CI -11.59; -10.65) and the UCLA increase was 0.26 (95% CI 0.22; 0.30) (Table II).

To evaluate to what the extent a sufficient (at least moderate) level of the physical activity was achieved or maintained, the change in proportions of patients with low, moderate, and high physical activity level at baseline and the total sample are presented in Fig. 2(a)–(d). Of the 4,836 low activity patients at baseline, 2,626 (54%) were classified as at least moderate physically active immediately after the program, and 37% (n = 1,792) maintained an at least moderate physical activity level also to 12 months after GLA:D[®]. Among all patients, 59% (n = 10,287) reported at least

Characteristics at baseline	Low physical activity level $n = 4,836 (28\%)$	Moderate physical activity level $n = 6,296 (36\%)$	High physical activity level	Total sample $n = 17,454 (100\%)$	
			n = 6,322 (36%)		
Age (years), mean (SD)	65.46 (9.7)	65.05 (9.1)	64.3 (8.6)	64.89 (9.1)	
Sex (female), n (%)	3,706 (76.6)	4,807 (76.4)	4.064 (64.3)	12,577 (72.1)	
BMI (kg/m ²), mean (SD) * $n = 52$	29.37 (5.7)	28.22 (5.2)	26.95 (4.4)	28.08 (5.2)	
Educational level, n (%) * n = 36					
Primary school	979 (20.3)	862 (13.7)	771 (12.2)	2,612 (15.0)	
Secondary school	568 (11.8)	651 (10.4)	652 (10.3)	1,871 (10.7)	
Short-term education	1067 (22.1)	1267 (20.2)	1155 (18.3)	3,489 (20.0)	
Middle-term education	1778 (36.8)	2747 (43.7)	2792 (44.3)	7,317 (42.0)	
Long-term education	434 (9.0)	757 (12.9)	938 (14.9)	2,129 (12.2)	
Number of comorbidities, n (%) $^{\#,*}n = 3,289$	• •				
0, n (%)	1,268 (31.8)	1,893 (39.1)	2,452 (45.9)	5,613 (39.6)	
1, n (%)	1,431 (35.9)	1,774 (36.6)	1,882 (35.3)	5,087 (35.9)	
2, n (%)	851 (21.4)	830 (17.1)	729 (13.7)	2,410 (17.0)	
3+, n (%)	435 (10.9)	350 (7.2)	270 (5.1)	1,055 (7.4)	
Time since osteoarthritis (months), median (IQR) $^{\#,*}n = 2,110$	14 (6, 48)	18 (6, 48)	18 (6, 48)	18 (6, 48)	
Seasonal start, n (%)					
Spring	1,082 (22.4)	1,279 (20.3)	1,428 (22.6)	3,789 (21.7)	
Summer	967 (20.0)	1,244 (19.8)	1,343 (21.2)	3,554 (20.4)	
Autumn	1,309 (27.1)	1,893 (30.1)	1,836 (29.0)	5,038 (28.9)	
Winter	1,478 (30.6)	1,880 (29.9)	1,715 (27.1)	5,073 (29.1)	
Self-efficacy, mean (SD) $*n = 6$ (10 low to 100 high)	66.63 (18.0)	72.68 (16.3)	75.91 (15.6)	72.18 (17.0)	
Fear of movement, n (%) * n = 22	826 (17.1)	792 (12.6)	734 (11.6)	2,351 (13.5)	
Number of painful hip and knees, mean (SD) $*n = 70$	1.68 (0.7)	1.65 (0.6)	1.62 (0.6)	1.65 (0.6)	
VAS back pain, n (%) (0 low to 10 high) $^{\#,*}n = 14,676$	3.07 (2.7)	2.52 (2.6)	2.22 (2.5)	2.59 (2.6)	
VAS knee/hip pain intensity, mean (SD) (0 low to 100 high) $*n = 25$	50.9 (21.8)	44.4 (21.0)	41.5 (21.1)	45.1 (21.6)	
Walking speed (m/sec), mean (SD) $*n = 806$	1.39 (0.3)	1.51 (0.3)	1.62 (0.3)	1.52 (0.3)	
Knee/Hip-related quality of life (KOOS/HOOS), mean (SD) $*n = 70$	42.72 (15.0)	42.92 (14.4)	50.26 (14.5)	47.33 (14.9)	
Mean change in VAS knee/hip pain intensity, (95% CI) (-100 incre	ase to 100 decrease)				
From baseline to immediately after GLA:D®	-15.4	-13.6	-12.7	-13.74	
•	(-16.24; -14.50)	(-14.31; -12.87)	(-13.36; -11.94)	(-14.19; -13.30)	
From immediately after to 12 months after GLA:D®	2.14 (1.21; 3.06)	3.08 (2.30; 3.82)	2.57 (1.83; 3.29)	2.64 (2.16; 3.08)	
From baseline to 12 months after GLA:D®	-13.2	-10.5	-10.1	-11.1	
	(-14.16; -12.32)	(-11.30; -9.75)	(-10.85; -9.33)	(-11.59; -10.65)	
Mean change on UCLA activity scale (95% CI) (-9 decrease to 9 inc	crease)	•	•	,	
From baseline to immediately after GLA:D®	1.43 (1.38; 1,48)	0.40 (0.36; 0.43)	-0.50 (-0.55; -0.46)	0.36 (0.32; 0.39)	
From immediately after to 12 months after GLA:D®	-0.02 (-0.09; 0.04)	-0.08(-0.13; -0.03)	-0.16(-0.22; -0.11)	-0.09 (-0.13; -0.0	
From baseline to 12 months after GLA:D®	1.41 (1,36; 1.46)	0.31 (0.28; 0.35)	-0.67(-0.71; -0.62)	0.26 (0.22; 0.30)	

CI = confidence interval, HOOS = hip injury and osteoarthritis outcome score, IQR = interquartile range, KOOS = knee injury and osteoarthritis outcome score, UCLA = University of California, Los Angeles, VAS = visual analog scale.

Table II

Osteoarthritis and Cartilage

Characteristics of patients with low, moderate and high physical activity level at baseline, and of the total sample

a moderate activity level at all three time points. When considering only the two time points after the program, 69% of the total sample were able to achieve or maintain at least a moderate physical activity level during the whole first year after GLA:D[®].

For the second aim of the study, we evaluated the within-individual association of change in pain with change in physical activity. A clinically relevant improvement in hip/knee pain from baseline to 12 months was seen in 2,134 (44%), 2,503 (40%), 2,389 (38%), and 7,026 (40%) of low, moderate, high activity patients and the total sample, respectively. A clinically relevant worsening in hip/knee pain was reported by 599 (12%), 820 (13%), 808 (13%), and 2,227 (13%), respectively. Neither improvement nor worsening in pain was observed in 2,103 (43%), 2,973 (42%), 3,125 (49%) and 8,201 (47%), respectively.

Results from the asymmetric fixed effects regression analyses are presented in Table III. We tested the residuals' distributions and confirmed normality. We found statistically significant associations

between a clinically relevant improvement in pain and increased physical activity in the low activity patients ($\beta = 1.44$, P < 0.001). Similar findings were observed for moderate activity patients, the total sample, and for patients with high compliance to the GLA:D®-program, but not for patients with high physical activity at baseline.

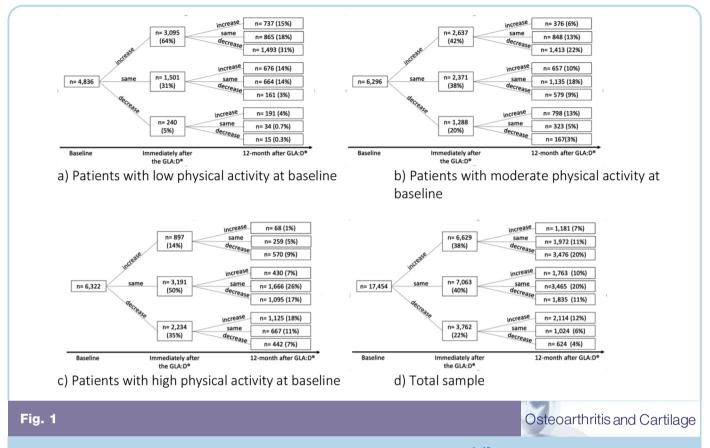
For low activity patients, the association between a clinically relevant worsening in pain and physical activity was positive ($\beta = 1.18$, P < 0.001). No associations were observed between clinically relevant worsening in pain and physical activity in moderate activity patients, the total sample, or among patients with high program compliance. Highly active patients had a negative association ($\beta = -0.93$, P < 0.001).

The supplementary asymmetric fixed effects regressions adjusted only for self-efficacy and number of painful knee and hip joints revealed similar results (Supplementary Table 2).

Supplementary fixed effects regression analyses, in which the independent pain variable was treated as continuous showed

^{*} Missing values.

[#] most missing values due to a restricted data collection period.



a-d. Increase and decrease of physical activity by at least one unit on the UCLA activity scale¹⁻¹⁰ for patients with a) low activity levels, b) moderate activity levels, c) high activity levels, and d) for the total sample.

statistically significant negative associations between change in pain and change in physical activity in low, and moderate activity patients, the total sample and those with high compliance (Supplementary Table 3). For patients with high physical activity levels at baseline the association was not statistically significant.

Discussion

A statistically higher physical activity level was observed after completion of the GLA:D® program. More than half (55%) of participants with low physical activity before GLA:D® reached at least a moderate physical activity level following the program, and 37 percent maintained their moderate physical activity level for at least 1 year. The majority (72%) already had at least a moderate activity level when starting the GLA:D® program. Still, 1 in 4 of all participants increased their physical activity following GLA:D®, and two thirds maintained at least a moderate physical activity level from immediately after to 12 months after the program. Interestingly, the increase in physical activity was not dependent on a simultaneous decrease in pain. Self-reported physical activity increased in both low activity patients, those experiencing a clinically relevant pain decrease and in those experiencing a clinically relevant pain increase.

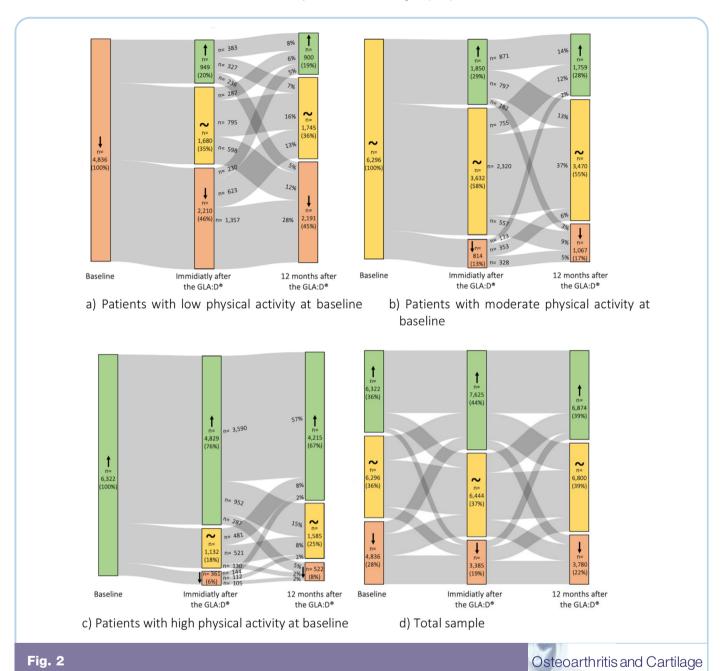
We confirmed that physical activity increases from before to after participation in a patient education and exercise therapy program delivered in a clinical setting. We observed a statistically significant increase of 0.36 UCLA points (baseline to immediately

after the program) and 0.26 (baseline to 12 month follow up), respectively, in the total sample. This observation is well in line with the finding of a meta-analysis, which suggested that interventions aimed at improving physical activity level lead to small, but statistically significant improvements in patients with knee or hip OA¹¹.

In line with a Swedish study²⁶ we found that physical activity decreased from immediately after the program to the 12-month follow-up, confirming strategies to support people in maintaining increased physical activity over time are needed²⁷.

Patients with low physical activity would benefit the most from increased physical activity and we therefore had a focus on this group. We found that 47% of the low active participants, who never decreased their physical activity during follow-ups, increased their physical activity with on average 2.59 UCLA points over the first year after entering the GLA:D®-program. The threshold for minimal important change for UCLA has not been established. However, any improvement is desirable from a general health perspective 1.

A drawback of analyzing the low active patients separately is that they are 'bound to improve' and thus regression to the mean could play a bigger part in the improvement seen compared to in the full group or other subgroups. We however note that only 1% reported a baseline UCLA score of 1, thus the other 99% had the possibility of reporting a decline as well. For transparency, we also report the results for moderate and high physically active patients as well as for the total sample.



a-d. Changes in the number of patients with self-reported low (\downarrow) , moderate (\sim) , and high (\uparrow) physical activity level at baseline, immediately after, and at 12 months after entering the GLA:D[®] program in a) patients with low physical activity level at baseline, b) patients with moderate physical activity level at baseline, c) patients with high physical activity level at baseline, and d) the total sample.

Our findings confirm the negative association between change in pain intensity and change in physical activity reported in previous cross-sectional and longitudinal studies ^{8,9} for all groups but the high active group. However, the cross-sectional reports focused on group-based associations between pain and physical activity, while we studied within-individual associations over time. Surprisingly we also found that patients who experienced a clinically relevant worsening of pain improved their physical activity, albeit not to the same degree as those whose pain decreased. Consequently, pain

might not be an absolute barrier to physical activity in patients with hip and knee OA. Future studies are needed to verify our findings and should include further unobserved confounding factors, which could explain these observations better.

Our statistical approach allowed us to incorporate clinical relevance when analyzing the association with change in pain. By categorizing pain as improved or deteriorated by at least 15 mm in the asymmetric fixed effects regression models, we obtained larger effect estimates for the change in physical activity. In the total

Variable	Sample						
	Low physical activity level	Moderate physical activity level	High physical activity level	Total sample	High compliance		
Clinically relevant improvement in knee/hip	1.44 (0.11)	0.52 (0.08)	-0.74 (0.12)	0.51 (0.06)	0.54 (0.07)		
VAS pain (- 15 mm on the VAS 0-100)	[1.21; 1.66] <i>P</i> < 0.001	[0.37; 0.68] <i>P</i> < 0.001	[-0.98; -0.49] P < 0.001	[0.38; 0.63] <i>P</i> < 0.001	[0.41; 0.67] <i>P</i> < 0.001		
Clinically relevant worsening in knee/hip	1.18 (0.17)	0.04 (0.10)	-0.93(0.17)	0.11 (0.09)	0.12 (0.09)		
VAS pain ($+15$ mm, on the VAS 0 -100)	[0.86; 1.51] <i>P</i> < 0.001	[-0.16; 0.24] P = 0.699	[-1.26; -0.61] P < 0.001	[-0.06; 0.27] P = 0.215	[-0.06; 0.30] P = 0.185		
Self-efficacy, (10 low to 100 high)	0.02 (0.00) [0.01; 0.02] <i>P</i> < 0.001	0.01 (0.00) $[0.00; 0.01] P$ $= 0.008$	0.01 (0.00) [0.00; 0.02] P = 0.018	0.01 (0.00) [0.01; 0.02] <i>P</i> < 0.001	0.01 (0.00) [0.01; 0.02] <i>P</i> < 0.001		
VAS back pain, (0 low to 10 high)	-0.06 (0.03) [-0.12; 0.00] P = 0.059	0.01 (0.02) $[-0.03; 0.05] P$ $= 0.622$	0.03 (0.03) $[-0.03; 0.09] P$ $= 0.354$	-0.01 (0.02) [-0.04; 0.02] P = 0.692	0.01 (0.02) [-0.02; -0.04] P = 0.599		
Number of painful hip and knees	-0.25 (0.07)	-0.15 (0.05)	0.01 (0.08)	-0.12 (0.04)	-0.13 (0.04)		
	[-0.39; -0.11] P < 0.001	[-0.25; -0.06] P = 0.002	[-0.14; 0.16] P = 0.896	[-0.19; -0.05] P = 0.002	[-0.21; -0.06] P = 0.001		
Constant	3.51 (0.31) [2.90; 4.13] <i>P</i> < 0.001	5.44 (0.22) [5.00; 5.87] <i>P</i> < 0.001	6.84 (0.38) [6.08; 7.59] <i>P</i> < 0.001	5.19 (0.18) [4.83; 5.54] <i>P</i> < 0.001	5.03 (0.20) [4.64; 5.41] <i>P</i> < 0.001		
Observations	2491	4284	2295	9070	7891		
Number of participants	1766	2912	1616	6294	5470		
R-squared	0.28	0.07	0.12	0.06	0.07		

P = P-value; VAS = visual analog scale, number of id refers to the number of included participants.

Table III



Unstandardized beta-coefficients are displayed with robust standard errors in parentheses and confidence intervals in squared parentheses for changes in physical activity gained through adjusted asymmetric fixed effects regression analyses including data from baseline and from 12 months after entering the program

sample a clinically relevant reduction in pain of at least 15 mm was associated with an increase of half a point in UCLA activity score. In the linear fixed effects regression models, a decrease in pain was only associated with an increase in physical activity of 0.01 (P < 0.01; see supplement). This lower effect estimate in the linear fixed effects regression model might partly be explained by combining patients increasing their physical activity when pain worsens with those patients whose pain improves. Consequently, we suggest that future studies consider to investigate the association between pain and physical activity respecting the direction of change in pain to better understand the role of pain in physical activity.

Strengths and limitations

The large sample of patients recruited from real-world clinical practice settings is a major strength of our study. Likewise, the use of asymmetric fixed effects regression models allowed us to conduct robust analyses 21,22 , while traditional statistical models relay on rather unstable assumptions or produce inconsistent estimates when time-constant unobserved factors are correlated with the regressors $^{22,28-30}$.

The UCLA activity scale was developed for patients undergoing knee or hip arthroplasty and has been used when evaluating changes in physical activity ^{17,18}. Despite this, the use may be problematic as it is a self-reported measure, and as such prone to recall and social desirability biases. However, these biases are likely to be time-constant, and as we investigate within-individual change, the biases are less likely to manifest a significant influence

on the estimates. Furthermore, the UCLA does not assess the duration of the activities and only broadly covers activity frequency and intensity. Such details may matter, but were not assessed. The UCLA activity scale is also prone to a celling effect in highly active patients. In addition, the categorizing of the UCLA activity scale might have induced a loss of information because of too high discretization. This is however unlikely to affect our conclusions, as we focused on the changes of physical activity and not on maximizing the accuracy of physical activity scores. Finally, the clinical relevance of the UCLA activity scale estimates is difficult to judge, for a lack of knowledge and scientific agreement regarding what change in physical activity is to be considered clinically relevant.

Another limitation is the lack of a control group, prohibiting us from attributing the whole observed increase in physical activity to program participation, likely unobserved confounding factors and a regression to the mean contribute to the improvement seen. Still, our focus on within-individual changes control for this to some degree, and from a clinical perspective the increase of physical activity is real, regardless of its origin. Finally, temporal factors such as BMI unaccounted for might have influenced our results and, while unlikely, in theory a chance in physical activity could precede the change in pain. Thus, reverse causation cannot be fully dismissed.

The generalizability of our results is limited: Findings only apply to patients with knee or hip osteoarthritis who participated at a patient education and exercise therapy program. Furthermore, our excluded participants had slightly worse health characteristics. Finally, some of our statistically significant findings might be due to the large sample size, and should be verified in future studies focusing on the clinical relevance of changes in physical activity.

Conclusion

A bit more than half of patients with knee or hip OA with an initially low physical activity level achieved at least a moderate physical activity level immediately after completing a supervised patient education and exercise therapy program, 37% maintained at least a moderate activity at 1 year. Surprisingly, both improvement and worsening in pain was associated with increased physical activity in low activity patients. This contrasts with findings in all patients, where only pain improvement was associated with increased physical activity. The importance of pain in changes in physical activity warrants further study, especially in low active patients.

Contributions

Study conception and design: Baumbach, Skou, Grønne, Møller, Roos.

Acquisition of data: Roos, Skou.

Analysis and interpretation of data: Baumbach, Skou, Grønne, Møller. Roos.

Drafting the article or revising it critically for important intellectual content: Baumbach, Skou, Grønne, Møller, Roos.

Final approval of the article: Baumbach, Skou, Grønne, Møller, Roos.

Conflict of interest

Dr. Roos is the developer of the KOOS and several other freely available patient-reported outcome measures and co-founder of Good Life with Osteoarthritis in Denmark ($GLA:D^{\circledast}$), 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 personal fees from Munksgaard and TrustMe-Ed, all of which are outside the submitted work. He is co-founder of the Good Life with osteoArthritis in Denmark (GLA:D) program, a not-for-profit initiative to implement clinical guidelines in primary care.

 $\operatorname{\mathsf{MSc}}$ Grønne, Dr. Møller and Dr. Baumbach declare no conflict of interest.

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Supplementary data

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