Pain Medicine, 2023, **00**, 1–9
https://doi.org/10.1093/pm/pnad167
Advance access publication 21 December 2023
Original Research Article

Weekly pain trajectories among people with knee or hip osteoarthritis participating in a digitally delivered first-line exercise and education treatment

Ali Kiadaliri, PhD[1,2,*], Helena Hörder, RPT, PhD[1], L. Stefan Lohmander, MD, PhD[1,2], Leif E. Dahlberg, MD, PhD[1,2]

[1]Department of Clinical Sciences Lund, Orthopaedics, Lund University, 221 85 Lund, Sweden
[2]Joint Academy®, 211 34 Malmö, Sweden

[*]*Corresponding author*. Department of Clinical Sciences Lund, Clinical Epidemiology Unit, Skåne University Hospital, Remissgatan 4, SE-221 85 Lund, Sweden. Email: Ali.kiadaliri@med.lu.se

Abstract

Objective: Digital self-management programs are increasingly used in the management of osteoarthritis (OA). Little is known about heterogeneous patterns in response to these programs. We describe weekly pain trajectories of people with knee or hip OA over up to 52-week participation in a digital self-management program.

Methods: Observational cohort study among participants enrolled between January 2019 and September 2021 who participated at least 4 and up to 52 weeks in the program ($n = 16\,274$). We measured pain using Numeric Rating Scale (NRS 0–10) and applied latent class growth analysis to identify classes with similar trajectories. Associations between baseline characteristics and trajectory classes were examined using multinomial logistic regression and dominance analysis.

Results: We identified 4 pain trajectory classes: "mild-largely improved" (30%), "low moderate-largely improved" (34%), "upper moderate-improved" (24%), and "severe-persistent" (12%). For classes with decreasing pain, the most pain reduction occurred during first 20 weeks and was stable thereafter. Male sex, older age, lower body mass index (BMI), better physical function, lower activity impairment, less anxiety/depression, higher education, knee OA, no walking difficulties, no wish for surgery and higher physical activity, all measured at enrolment, were associated with greater probabilities of membership in "mild-largely improved" class than other classes. Dominance analysis suggested that activity impairment followed by wish for surgery and walking difficulties were the most important predictors of trajectory class membership.

Conclusions: Our results highlight the importance of reaching people with OA for first-line treatment prior to developing severe pain, poor health status and a wish for surgery.

Keywords: digital treatment; first-line treatment; osteoarthritis; pain; trajectory; Sweden.

Introduction

Osteoarthritis (OA) is a leading cause of chronic pain and functional disability among older adults.[1,2] With no cure for OA, exercise and education is recommended as first-line treatment to reduce symptoms in all persons with OA.[3] First line treatment can be delivered face-to-face or digitally and while both formats are effective in reducing pain and improving physical function,[4,5] a recent systematic review and individual patient data meta-analysis suggested that the magnitude of their overall effect is small and of questionable clinical importance.[6] However, there are variations in response to exercise treatment and hence it is crucial to identify subgroups of persons with OA who are most likely to benefit.[6,7] In this line, the recent decade has witnessed a rapid increase in using data-driven methods including mixture models to explore heterogeneity in longitudinal patterns of pain in OA.[8] Moreover, the European League Against Rheumatism declared the identification of phenotypes and different subgroups in OA as a top epidemiologic research priority.[9]

However, most previous studies either investigated trajectories of pain and other outcomes among general OA cohort regardless of the treatment received or among those received total joint replacement.[8,10] Two exceptions are the study by Lee et al. exploring pain and function over up to 12-weeks following exercise interventions and our previous study in a similar population as the present study investigating work and activity limitations over a year following participation in a digital self-management program for OA.[11,12] Furthermore, most previous studies were conducted in small to moderate sample sizes and/or included few data points (generally 5–6 data points),[8] which might limit the ability to accurately capture fluctuations in the outcomes. In addition, despite explosion in digital delivery of OA treatments, there is limited knowledge on pain trajectories among participants of these treatments.

In the present study, we aimed to explore trajectories of weekly measured pain over up to 52 weeks among participants of a digital first-line exercise and education treatment for hip and knee OA in Sweden. We also investigated the relative importance of participants' sociodemographic and clinical characteristics at baseline in predicting membership in trajectory subgroups.

Methods

This was an observational longitudinal study using data obtained from the participants of a digitally delivered first-

Received: 15 August 2023. **Revised:** 27 November 2023. **Accepted:** 5 December 2023

line exercise and education program for hip and knee OA, known as Joint Academy®, in Sweden. All participants gave digital consent prior to data extraction and analysis for research.

Digital program

Inspired by the Swedish first-line face-to-face management program for OA– "Better management of patients with OsteoArthritis"[13]– the digital self-management program was introduced in Sweden in 2016, described in details elsewhere.[14] The digital program is targeted towards exercise, physical activity and education and is delivered as a smartphone application. It includes lessons on OA, physical activity, and self-management, followed by short quizzes on the topics. These lessons are packed within themes (1–5 lessons in each theme) with one theme provided per week for the first 6 weeks of the program and then every other week over participation period. Participants also receive individualized exercises adjusted with their progression in the program. The participants are supervised by their physical therapist including possibility to chat asynchronously during the entire duration of the program.[14] The participants are receiving the digital treatment throughout their participation in the program. Physical therapists participating in the program are certified in OA knowledge.

Participants

Data for all consecutive participants with hip or knee OA enrolled in the digital program between January 2019 and September 2021 were extracted ($n = 16\,914$). Participants were referred to the program by their local orthopaedic surgeon or physiotherapist, or joined via online advertisements and campaigns placed on search engines and social networks. Most (around 95%) participants in the programme had a prior radiographic and/or clinical diagnosis of hip or knee OA from a physical therapist or physician. For individuals without a prior diagnosis, clinical OA was confirmed by a physiotherapist via phone through responding to a series of diagnostic questions based on criteria outlined by NICE and Swedish National Guidelines.[15] If the diagnosis remained uncertain, participants were referred for a physical visit. Of these participants, 640 (3.8%) persons participated less than 4 weeks in the program and were excluded. Given that a minimum of 3 observations are required for estimating trajectory,[16] we selected a 4-week threshold to make sure that individuals participated enough to benefit from the program.

Outcome

Participants rated their knee/hip pain over the previous week at enrolment (baseline) and every week after enrolment up to 52 weeks using the numeric rating scale (NRS) for pain.[17] We used an 11-point NRS ranging from 0 (no pain) to 10 (the worst possible pain). For interpretation, we considered NRS pain 1–4 as *mild*, 5–6 as *moderate*, and 7–10 as *severe* pain.[18] For changes over time, we used 1-unit reduction in NRS pain as a minimal important change according to a recent study conducted among the participants of the same digital intervention.[19]

Baseline covariates

We included in our analysis the following explanatory variables obtained at enrolment, all self-reported by the participants: Sex, age, BMI, index joint (knee or hip), education, place of residence (living in three metropolitan municipalities of Stockholm, Gothenburg, or Malmö: Yes/no), physical function, physical activity, overall health (11-point NRS, "mark on the scale how good or bad your current health is?" with 0 = worst imaginable and 10 = best imaginable), activity impairment (11-point NRS, "during the past 7 days, how much did knee/hip osteoarthritis affect your ability to do your regular daily activities, other than work at a job?", with 0 = no effect and 10 = it completely prevented me from doing my daily activities),[20] EQ-5D-5L anxiety/depression dimension, fear of moving (yes/no), wish for surgery ("are your symptoms so severe that you wish to undergo surgery in your knee/hip?": yes/no), patient acceptable symptom state (PASS, "considering your hip/knee function, do you feel that your current state is satisfactory?": yes/no), walking difficulties, and self-reported doctor diagnosed diabetes, lung diseases, balance troubles, rheumatoid arthritis, and cardiovascular diseases.

Physical function was measured using the 30-second chair stand test (30CST),[21] and physical activity was measures based on time spent in a typical week on daily physical activity that is not exercise, such as walking, cycling or gardening.[22]

Data analysis

Patient characteristics at enrolment are reported as mean (standard deviation [SD]) for continuous variables and number/proportions for categorical variables. We computed standardized difference to compare baseline characteristics of participants included and excluded from the analyses and applied a threshold of 0.1 to define important difference.[23]

To identify classes with distinct pain trajectories, we used latent class growth analysis (LCGA). LCGA assumes the presence of a fixed but unknown number of classes with distinct trajectories within the underlying population and model the mean development of an outcome over time within every class.[24] LCGA exhibits no individual-level random variation within each class (ie individuals within each class follow exactly the same trajectory) and allows for class- and time-specific random errors (this is different from group-based trajectory modelling which assumes the same random errors for all classes and all time points).[24]

We modelled time in each class using cubic B-spline functions.[25] We estimated models with 1–7 classes and selected the optimal number of classes based on a combination of sample size–adjusted Bayesian information criterion (SABIC, smaller values indicating better fit), average posterior probability of assignment (APPA, > 0.7 for each class), the odds of correct classification (OCC, > 5 for each class), class size ($\geq 5\%$ of participants in the smallest class), and relative entropy (values closer to 1 reflect better fit with values >0.80 considered to provide well-separated classes).[26] The OCC reflects the improvement over chance in a model's assignment accuracy, and it is calculated as:

$$OCC_k = \frac{APPA_k/(1 - APPA_k)}{\widehat{\pi}_k/(1 - \widehat{\pi}_k)},$$

where $\widehat{\pi}_k$ is the model-estimated proportion for class k. This implies that the OCC represents the ratio of 2 odds. The numerator is the odds of correct classification of subjects into class k based on the maximum probability classification rule

(the APPA).[24,26] For example, for a class with an APPA of 0.80, there will be an odds of 4 to 1 for correct classification (0.8/[1–0.8]). The denominator is the odds of correct classification based on random assignment given $\hat{\pi}_k$. If we assume an estimated class membership proportion of 0.25 in previous example for class k, it means that random assignment of individuals into group k would correctly classify 25% of individuals and hence the odds of correct classification based on random assignment is 1 in 3 (0.25/[1–0.25]). For this example, the OCC for class *k* will be 12 [(4/1)/(1/3)]. An OCC value close to 1 suggests that the maximum probability assignment rule has predictive power not beyond random chance.[24,26] We also considered model parsimony, class interpretability, and distinctive features of identified classes (ie, when a class was divided into 2 or more classes with very similar trajectories, we selected the model with lower number of classes). After estimating the selected model, each participant was assigned to the class with the highest posterior probability of membership. We then used multinomial logistic regression to explore the associations between the baseline covariates and identified trajectories. We also employed dominance analysis to determine the relative importance of each baseline covariate in predicting class membership.[27] LCGA was conducted using "lcmm" package in R, which is based on maximum likelihood assuming missing at random to account for missing data.[28] Multinomial logistic regression and dominance analysis were implemented using Stata's "mlogit" and "domin" commands.[27]

Sensitivity analysis

While maximum likelihood approach used in the study can handle missing at random data, it is biased if the data are missing not at random. For instance, there is a possibility that people discontinue the treatment because of worsening pain. If this is the case, then it can influence the identified trajectory classes. For instance, this might underestimate the number of subjects in the worsening or severe pain trajectories.[29] We explored the plausibility of missing at random using 2 strategies. First, we used standardized difference to compare the baseline characteristics of participants with no missing weekly response (complete case) with (i) those with at least one missing response and (ii) those who dropped out early ($\leq$12 weeks). Similarity between these groups supports plausibility of missing at random assumption. Second, we estimated LCGA among those with no missing values (complete case analysis) and compared this with our full sample analysis.[30] We also conducted a subgroup analysis by OA joint (ie, knee/hip OA). It might be argued that 4 weeks of participation in the program may not be sufficient enough to capture the changes in pain, hence we conducted an additional analysis among those who participated for at least 6 weeks in the program given that 6-week participation in education and exercise therapy has resulted in significant effects on patient symptoms in previous studies.[31] However, this latter analysis resulted in almost identical results to our main analysis and hence data are not shown.

Results

A total of 16 274 participants, mean (SD) age 64.2 (9.1), and 75.1% females, participated for at least 4 weeks into the digital program and were included. Of these, 9698 (59.6%) participants had knee OA and 6576 (40.4%) had hip OA. While the baseline characteristics of these individuals were generally comparable to those excluded because of less than 4 weeks participation particularly reporting the same level of baseline NRS pain, those included were younger, had less co-existing conditions and were more likely to have knee OA (Table 1). Among participants, around 94%, 68% and 31% provided a minimum of 12, 24, and 48 responses, respectively. Among those included, 6199 (38%), 5885 (36%), and 4190 (26%) reported an NRS pain of $\leq$4, 5–6, and $\geq$7 at baseline, respectively.

While most fit statistics continued to improve with increasing number of classes up to a 6-class model (model with 7-class didn't converge), we selected a 4-class model as the optimal model given that 5- and 6-class models divided participants with moderate baseline pain in subclasses with very similar trajectories (Figure 1 and Figure SA1–SA2 and Table SA1). Around 12% of participants were assigned to a class with severe pain at baseline that persisted, 24% to a class with upper moderate pain at baseline that improved, 34% to a class with low moderate pain at baseline that largely improved, and 30% to a class with mild pain at baseline that largely improved (individual trajectories within each class is shown in Figure SA3). Individuals assigned to classes with higher levels of pain generally reported poorer patient-reported outcomes at baseline, had lower level of education, higher proportion of people with BMI $\geq$ 30, more wish for surgery, and lower level of physical activity (Table 2). Patterns of weekly responses suggested a larger proportion of missing responses in the class "severe pain-persistent" (Figure 1 and Table SA2).

Multinomial logistic regression suggested that male sex, older age, lower BMI, better physical function, lower activity impairment, less anxiety/depression, higher education, knee OA, no walking difficulties, no wish for surgery and higher physical activity, all measured at enrolment, were associated with greater probabilities of membership in "mild-largely improved" class than other classes (Table 3). McFadden pseudo-R^2 from this model revealed that the baseline covariates could explain around 10.7% of variations in pain trajectories with activity impairment accounting for the largest portion of this explained variance (Figure 2). Wish for surgery and walking difficulties were the 2nd and 3rd most important predictors of pain trajectory class membership. On the other hand, age, place of residence, and sex had the least importance in predicting trajectory class membership.

Sensitivity analysis

There were little meaningful differences between persons with at least one missing response on pain ($n = 12\,781$) or those who dropped out early (n = 1065) and those with complete responses ($n = 3493$) (Table SA3). Estimated LCGA in persons with complete responses yielded similar results to our main analysis with a 4-class model selected as the optimal model and very similar distribution of participants across classes (Table SA4 and Figure SA4).

The subgroup analysis among participants with knee or hip OA suggested that in both groups a 4-class model was the optimal model and the participants followed comparable trajectories (Tables SA5–SA6 and Figures SA5–SA6). The main difference was a higher proportion of people with hip OA assigned to the class "severe pain-persistent," which was in line with the main analysis (ie lower odds of assigning to

Table 1. Baseline characteristics of persons enrolled in the digital program.

Variable	Included ($n = 16\,274$)	Excluded ($n = 640$)	Absolute standardized difference
Female, *n* (%)	12 218 (75.1)	462 (72.2)	0.066
Age, mean (SD)	64.2 (9.1)	66.1 (10.4)	0.192
BMI, mean (SD)	27.1 (4.7)	27.3 (5.4)	0.027
NRS pain, mean (SD)	5.1 (1.9)	5.1 (2.1)	0.005
Physical function, mean (SD)	12.7 (4.3)	12.1 (4.5)	0.131
EQ-5D-5L anxiety/depression, n (%)			
No problem	7997 (49.1)	308 (48.1)	0.020
Slight problems	6303 (38.7)	230 (35.9)	0.058
Moderate problems	1600 (9.8)	79 (12.3)	0.080
Severe problems	374 (2.3)	23 (3.6)	0.077
Overall health, mean (SD)	6.6 (1.8)	6.5 (2.0)	0.042
Activity impairment, mean (SD)	3.9 (2.4)	4.2 (2.4)	0.097
Diabetes, *n* (%)	932 (5.7)	57 (8.9)	0.122
Lung diseases, *n* (%)	1717 (10.6)	72 (11.3)	0.022
Balance troubles, *n* (%)	556 (3.4)	34 (5.3)	0.093
Rheumatoid arthritis, *n* (%)	748 (4.6)	50 (7.8)	0.134
Cardiovascular diseases, *n* (%)	1247 (7.7)	72 (11.3)	0.123
Education, *n* (%)			
Less than high school	1419 (8.7)	64 (10.0)	0.0440
High school	5863 (36.0)	235 (36.7)	0.0144
College/university	8992 (55.3)	341 (53.3)	0.0396
Index joint, *n* (%)			
Knee	9698 (59.6)	311 (48.6)	0.222
Hip	6576 (40.4)	329 (51.4)	0.222
Fear of moving, *n* (%)	2492 (15.3)	99 (15.5)	0.004
Walking difficulties, *n* (%)	10 655 (65.5)	418 (65.3)	0.003
Patient acceptable symptom state, *n* (%)	2804 (17.2)	133 (20.8)	0.091
Living in Stockholm/Gothenburg/Malmö, *n* (%)	3175 (19.5)	137 (21.4)	0.047
Wish for surgery, *n* (%)	2503 (15.4)	124 (19.4)	0.106
Physical activity, *n* (%)			
Less than 30 minutes	1154 (7.1)	56 (8.8)	0.061
30–60 minutes	2535 (15.6)	146 (22.8)	0.184
61 to 90 minutes	2419 (14.9)	99 (15.5)	0.017
91 to 150 minutes	2881 (17.7)	103 (16.1)	0.043
151 to 300 minutes	3779 (23.2)	108 (16.9)	0.159
More than 300 minutes	3506 (21.5)	128 (20.0)	0.038
Follow up responses, *n* (%)			
5–12	1268 (7.8)	–	–
13–24	4339 (26.7)	–	–
25–36	3353 (20.6)	–	–
37–52	7314 (44.9)	–	–

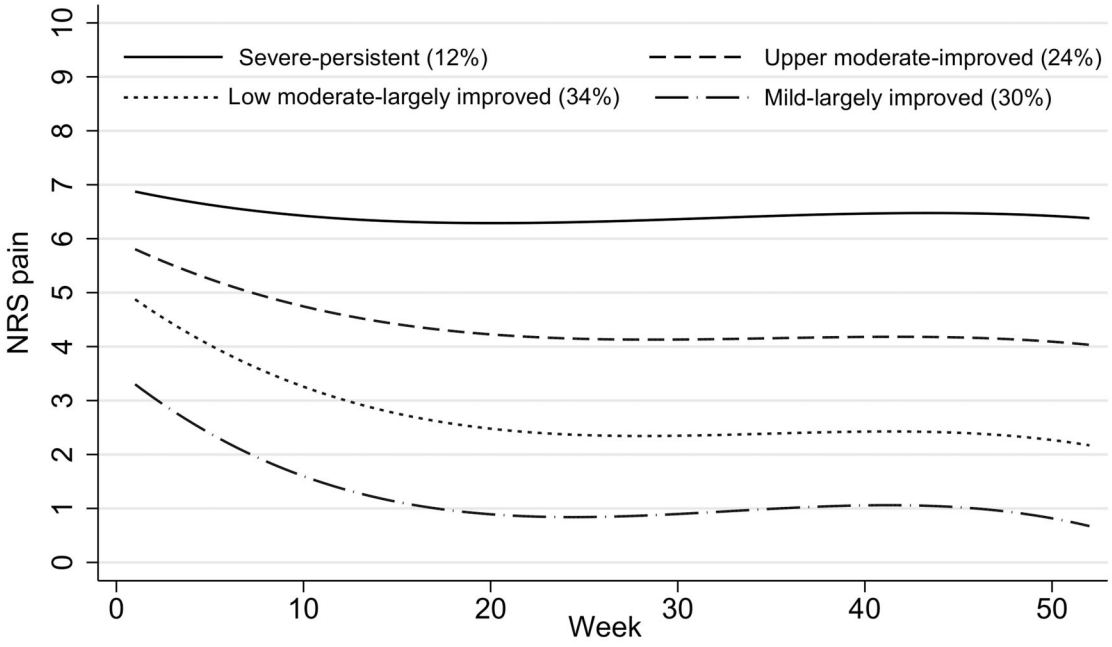
Overall health = 0–10 (worst to best), NRS Pain = 0–10 (higher value indicates more pain), Activity impairment = 0–100 (higher value indicates higher impairment). BMI: Body mass index; NRS: Numeric Rating Scale; SD: Standard deviation.

the class "severe pain-persistent" for people with knee than hip OA).

Discussion

In a large cohort of participants in a digital self-management program for OA, we identified four distinct trajectories of NRS pain over up to 52-week participation in the program: Mild-largely improved, low moderate-largely improved, upper moderate-improved, and severe-persistent. Participants with hip OA and poorer physical and mental health who wished for surgery at baseline were more likely to follow a severe-persistent pain trajectory. Among baseline covariates, activity impairment followed by wish for surgery and walking difficulties were the most important predictors of trajectory class membership.

Previous studies consistently documented the presence of subgroups with distinct trajectories of pain and other health-related outcomes in OA population.[8,12,32] The number of pain trajectory classes identified in previous studies ranged between 3 and 6 classes with mostly non-progressive pain severity including a (small) class with severe-persistent pain.[8] While the presence of a small class with severe-persistent pain in this study is consistent with previous research, we observed a large portion (88%) of our sample that experienced improvement in their pain intensity, which is inconsistent with most previous studies. This might be due to differences in sample characteristics (eg, OA severity), pain measurement instrument (NRS vs VAS, WOMAC), and number of measurements and their intervals (weekly vs monthly/annually). Another plausible explanation is that most previous studies were conducted among OA cohorts including those on no specific treatment, while the individuals included in the present study were participating in a self-management program which could have contributed to pain improvement. Indeed, our finding here is similar to the study by Lee et al. among knee OA patients participating in exercise interventions, where 3 out of 4 identified classes (91% of the sample) experienced improvements in pain, and 1 class (9% of sample) reported high persistent pain.[11] Moreover, in a previous study in the same population as the present study, 3 out 3 trajectory classes of work impairment and 4 out of 5 classes of activity impairment experienced improving trajectories



Week #	10	20	30	40	50
Severe-persistent, n (%)	1739 (88.8)	1304 (66.6)	941 (48.0)	682 (34.8)	478 (24.4)
Upper moderate-improved, n (%)	3640 (92.7)	2966 (75.5)	2237 (57.0)	1693 (43.1)	1269 (32.3)
Low moderate-largely improved, n (%)	5293 (94.9)	4240 (76.0)	3233 (58.0)	2543 (45.6)	1898 (34.0)
Mild-largely improved, n (%)	4501 (93.6)	3394 (70.5)	2487 (51.7)	1926 (40.0)	1480 (30.8)

Figure 1. Trajectory classes of NRS pain from baseline up to 1-year follow-up (numbers in parentheses report percentages of participants in each class). The table displays the number (%) of weekly responses in each trajectory class.

following participation in the digital treatment.[12] In studies among individuals undergoing knee/hip arthroplasty, classes with improving pain generally accounted for a larger proportion of cohorts.[10] Self-selection might be another explanation, as those participating in the digital program are possibly healthier, more educated, and more motivated to take an active role in their disease management than the general OA population. For instance, the proportion of females, those with a college/university degree, and with no walking difficulties is higher in the digital program than those participating in the Swedish face-to-face first-line intervention.[33]

The observed improvements following participation in the self-management program in the present study are encouraging and highlight the importance of providing core first line treatments to all persons with OA as recommended by clinical guidelines.[34] In particular, the persistent pain in spite of treatment in people with severe pain at baseline might suggest the importance of initiating self-management program as early as possible when people have lower pain, better health status, and do not wish to undergo surgery.[35] However, given heterogeneity in severity and progression pattern of OA, there is no guarantee that participants with severe-persistent pain trajectory would have experienced improvements if they had reached earlier. It should also be noted that physical activity and exercise have health benefits beyond pain relief and hence our results do not suggest that individuals with severe baseline pain should be dropped from participation in self-management programs, but some modifications might be needed for this subgroup (eg, longer intervention, booster sessions, etc).[31] For instance, co-existing conditions are common in OA especially among those with higher pain and exercise therapy is effective in managing many of these conditions.[31] Particularly, physical activity is highly beneficial for improving symptoms of depression and anxiety which were more common among those with severe-persistent pain in our study.[36] Furthermore, exercise therapy provides similar level of pain relief as other non-surgical OA treatments (eg, analgesic medication) regardless of OA severity and pain level, but with safety advantages over those alternatives.[31]

The predictors of severe persistent pain in the present study including female sex, younger age, higher BMI, poorer health status, anxiety, depression, and lower education were similar to those reported in previous research.[8] Activity impairment was the most important predictor of trajectory class membership. This is in line with a previous study in the same population where baseline pain was the most important predictor of activity impairment trajectory class,[12] highlighting significant interrelations between pain and activity limitations. Wish for surgery was the second most important predictor of severe persistent pain trajectory. While the role of wish for surgery in pain trajectory class hasn't been investigated, a recent study among participants in the face-to-face self-management program in Sweden reported that wish for surgery was associated with lower odds of experiencing clinically relevant pain reduction.[35] The authors suggested that wish for surgery might be associated with more disease severity, lower expectations and hence a lower motivation for self-management programs.[35] The participants with severe-persistent pain also had higher levels of anxiety/depression at baseline which might have negatively influenced their response to the treatment through engagement level, pain sensitization and symptom amplification.[11] The covariates included in the present study could explain around 11% of variance in pain trajectory class membership with activity impairment, wish for

Table 2. Baseline characteristics of the participants in pain trajectory classes.

Variable	MLI ($n = 4811$)	LMLI ($n = 5577$)	UMI ($n = 3927$)	SP ($n = 1959$)
Female, *n* (%)	3576 (74.3)	4173 (74.8)	2981 (75.9)	1488 (76.0)
Age, mean (SD)	64.4 (9.1)	64.3 (9.1)	64.2 (9.0)	63.7 (9.5)
BMI, mean (SD)	26.2 (4.1)	26.9 (4.5)	27.7 (5.0)	28.7 (5.4)
BMI $\geq$ 30, *n* (%)	779 (16.2)	1182 (21.2)	1078 (27.5)	675 (34.5)
Pain, mean (SD)	3.7 (1.8)	5.0 (1.6)	5.9 (1.4)	7.0 (1.3)
Physical function, mean (SD)	13.3 (4.4)	12.9 (4.3)	12.3 (4.3)	11.6 (4.3)
EQ-5D-5L anxiety/depression, *n* (%)				
No problem	2930 (60.9)	2752 (49.4)	1627 (41.4)	688 (35.1)
Slight problems	1592 (33.1)	2248 (40.3)	1681 (42.8)	782 (39.9)
Moderate problems	248 (5.2)	495 (8.9)	506 (12.9)	351 (17.9)
Severe problems	41 (0.9)	82 (1.5)	113 (2.9)	138 (7.1)
Overall health, mean (SD)	7.0 (1.8)	6.6 (1.8)	6.3 (1.8)	6.0 (2.0)
Activity impairment, mean (SD)	27.4 (21.9)	38.4 (21.7)	46.1 (21.5)	56.8 (21.1)
Diabetes, *n* (%)	221 (4.6)	308 (5.5)	238 (6.1)	165 (8.4)
Lung diseases, *n* (%)	446 (9.3)	587 (10.5)	448 (11.4)	236 (12.1)
Balance troubles, *n* (%)	151 (3.1)	173 (3.1)	150 (3.8)	82 (4.2)
Rheumatoid arthritis, *n* (%)	168 (3.5)	251 (4.5)	203 (5.2)	126 (6.4)
Cardiovascular diseases, *n* (%)	315 (6.6)	434 (7.8)	307 (7.8)	191 (9.8)
Education, *n* (%)				
Less than high school	353 (7.3)	442 (7.9)	363 (9.2)	261 (13.3)
High school	1509 (31.4)	1959 (35.1)	1584 (40.3)	811 (41.4)
College/university	2949 (61.3)	3176 (57.0)	1980 (50.4)	887 (45.3)
Knee as the index joint, *n* (%)	2943 (61.2)	3381 (60.6)	2315 (59.0)	1059 (54.1)
Fear of movement, *n* (%)	687 (14.3)	820 (14.7)	635 (16.2)	350 (17.9)
Walking difficulties, *n* (%)	2273 (47.3)	3643 (65.3)	2995 (76.3)	1744 (89.0)
Patient acceptable symptom state, *n* (%)	1380 (28.7)	859 (15.4)	408 (10.4)	157 (8.0)
Living in Stockholm/Gothenburg/Malmö, *n* (%)	947 (19.7)	1090 (19.5)	751 (19.1)	387 (19.8)
Wish for surgery, *n* (%)	214 (4.5)	588 (10.5)	854 (21.8)	847 (43.2)
Physical activity, *n* (%)				
Less than 30 minutes	198 (4.1)	344 (6.2)	358 (9.1)	254 (13.0)
30–60 minutes	621 (12.9)	839 (15.0)	703 (17.9)	372 (19.0)
61 to 90 minutes	685 (14.2)	821 (14.7)	605 (15.4)	308 (15.7)
91 to 150 minutes	852 (17.7)	1040 (18.7)	670 (17.1)	319 (16.3)
151 to 300 minutes	1226 (25.5)	1367 (24.5)	832 (21.2)	354 (18.1)
More than 300 minutes	1229 (25.6)	1166 (20.9)	759 (19.3)	352 (18.0)

BMI: Body mass index; LMLI: Low moderate-largely improved; MLI: Mild-largely improved; SP: Severe-persistent; UMI: Upper moderate-improved.

surgery, walking difficulties, PASS, and anxiety/depression accounting for 82% of this explained variance. Hence, these variables might be useful to implement some modifications in the digital self-management program in order to improve the treatment response among participants. Albeit, to better predict pain trajectory class membership, there is need to identify and measure other important predictors. For instance, previous studies suggested that duration of symptoms and Kellgren & Lawrence radiographic grade of OA are associated with pain trajectory class and hence might improve predicting pain trajectory.[8]

A unique feature of this study was using weekly pain data for up to 52 weeks which reflect the symptom fluctuations more accurately than monthly or yearly measurement intervals commonly used in previous research.[32] Using dominance analysis to explore the relative importance of pain trajectory class membership beyond the average associations is another unique contribution of the present study. The large sample size is another strength of the present study. We also acknowledge several limitations of the current study. Data used in the study are self-reported and hence prone to biases. Participation in the digital program is voluntary and this self-selection into the digital intervention limit the generalizability of the findings. The lack of a control group means that the observed pain improvements cannot be fully attributed to the digital program and other factors such as natural course of disease and context effects are included in the observed outcomes. It should be noted that while regression to the mean (RTM) is a concern in longitudinal studies without a control group,[37] our findings (ie larger improvements among participants with milder pain at baseline and persistent pain among those with severe baseline pain) does not support RTM. In addition, we lack the data on possible concurrent additional treatments (eg, pain medications, other face-to-face/digital treatments) which could have influenced pain trajectories among the participants. The use of a single pain dimension (ie, intensity), may not provide full information regarding symptom progression and health outcomes. The choice of the final model in LCGA is to some extent subjective which calls for caution in interpreting the results. We did not have data on some potentially important predictors of pain trajectory class membership such as lifestyle factors (eg, smoking, alcohol use), duration of the OA symptoms, and Kellgren & Lawrence radiographic OA grade.

Conclusion

The present exploratory study adds to the growing body of evidence documenting significant variations in longitudinal patterns of pain and treatment response in persons with OA.

Table 3. Relative risk ratios (95% CI) for NRS pain trajectory classes from multinomial logit model (mild-largely improved class as the reference).

Variable	LMLI	UMI	SP
Female (male=ref)	1.06 (0.96, 1.16)	1.18 (1.06, 1.32)	1.28 (1.11, 1.48)
Age (per 5-year)	1.01 (0.99, 1.03)	1.02 (0.99, 1.05)	0.98 (0.95, 1.02)
BMI	1.01 (1.00, 1.02)	1.03 (1.02, 1.04)	1.04 (1.03, 1.06)
Physical function	1.00 (0.99, 1.01)	0.99 (0.98, 1.00)	0.97 (0.96, 0.99)
EQ-5D-5L anxiety/depression			
No problem	Ref (=1.00)	Ref (=1.00)	Ref (=1.00)
Slight problems	1.19 (1.09, 1.30)	1.28 (1.16, 1.42)	1.16 (1.01, 1.33)
Moderate problems	1.34 (1.13, 1.59)	1.67 (1.39, 2.00)	1.75 (1.41, 2.17)
Severe problems	1.15 (0.77, 1.71)	1.65 (1.11, 2.45)	2.43 (1.61, 3.68)
Overall health	0.94 (0.92, 0.97)	0.93 (0.90, 0.95)	0.93 (0.90, 0.97)
Activity impairment	1.17 (1.15, 1.20)	1.28 (1.25, 1.31)	1.50 (1.45, 1.54)
Diabetes (no=ref)	1.07 (0.88, 1.28)	1.03 (0.83, 1.26)	1.27 (0.99, 1.62)
Lung diseases (no=ref)	1.03 (0.90, 1.18)	1.04 (0.89, 1.21)	1.00 (0.83, 1.21)
Balance troubles (no=ref)	0.75 (0.59, 0.94)	0.80 (0.82, 1.03)	0.72 (0.52, 0.99)
Rheumatoid arthritis (no=ref)	1.11 (0.90, 1.37)	1.15 (0.91, 1.44)	1.26 (0.96, 1.66)
Cardiovascular diseases (no=ref)	1.10 (0.94, 1.30)	1.04 (0.86, 1.24)	1.26 (1.01, 1.57)
Education			
Less than high school	Ref (=1.00)	Ref (=1.00)	Ref (=1.00)
High school	1.07 (0.97, 1.26)	1.06 (0.89, 1.26)	0.73 (0.59, 0.90)
College/university	0.92 (0.79, 1.08)	0.74 (0.62, 0.88)	0.48 (0.39, 0.59)
Knee as the index joint (hip=ref)	0.92 (0.85, 1.00)	0.81 (0.73, 0.89)	0.60 (0.53, 0.68)
Fear of movement (no=ref)	0.82 (0.73, 0.92)	0.80 (0.70, 0.91)	0.75 (0.63, 0.89)
Walking difficulties (no=ref)	1.37 (1.25, 1.49)	1.65 (1.48, 1.83)	2.58 (2.18, 3.05)
Patient acceptable symptom state (no=ref)	0.64 (0.57, 0.70)	0.52 (0.46, 0.59)	0.59 (0.48, 0.72)
Living in Stockholm/Gothenburg/Malmö (no=ref)	1.08 (0.97, 1.19)	1.14 (1.01, 1.28)	1.30 (1.12, 1.51)
Wish for surgery (no=ref)	1.68 (1.42, 1.98)	3.19 (2.70, 3.77)	6.73 (5.63, 8.03)
Physical activity			
Less than 30 minutes	Ref (=1.00)	Ref (=1.00)	Ref (=1.00)
30–60 minutes	0.89 (0.72, 1.09)	0.80 (0.64, 0.99)	0.70 (0.54, 0.90)
61 to 90 minutes	0.84 (0.68, 1.04)	0.71 (0.57, 0.89)	0.66 (0.51, 0.86)
91 to 150 minutes	0.90 (0.74, 1.11)	0.70 (0.56, 0.87)	0.64 (0.50, 0.83)
151 to 300 minutes	0.86 (0.71, 1.05)	0.66 (0.53, 0.82)	0.58 (0.45, 0.75)
More than 300 minutes	0.77 (0.63, 0.94)	0.65 (0.52, 0.80)	0.62 (0.48, 0.80)
McFadden pseudo-R^2		0.107	

BMI: Body mass index; LMLI: Low moderate-largely improved; SP: Severe-persistent; UMI: Upper moderate-improved.

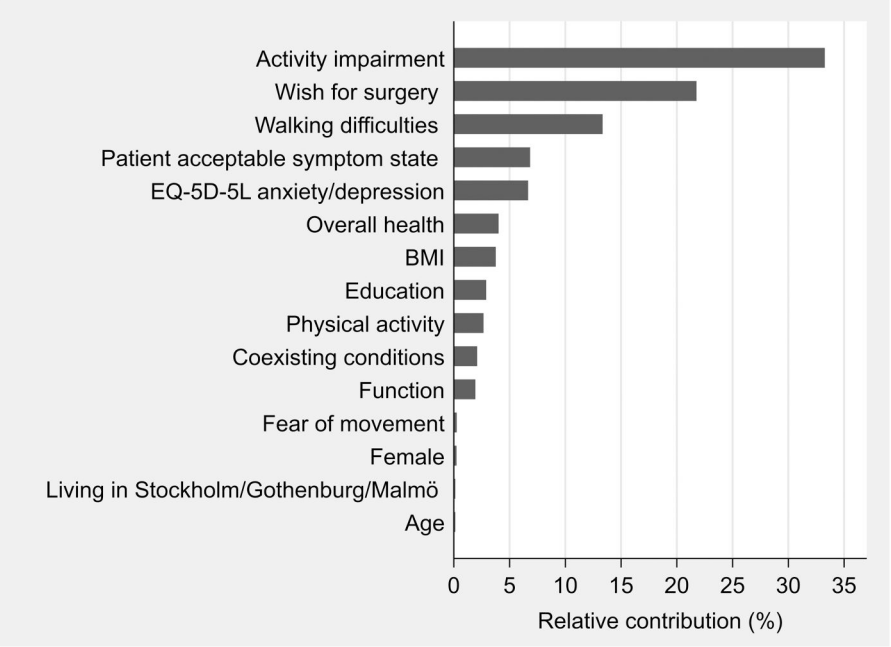


Figure 2. The relative contributions of baseline characteristics to the explained variance of pain trajectory class membership (coexisting conditions includes the index joint, diabetes, lung diseases, balance troubles, rheumatoid arthritis, and cardiovascular diseases).

Our findings suggest the importance of early provision of core first line treatments for OA prior to developing severe pain, activity limitations, walking difficulties, poor health status and a wish for surgery. It also provides insights on some important predictors of pain trajectory classes which can be used for modification of the digital program. For a better prediction of pain trajectory, further detailed data needs to be collected.

Acknowledgments

Authors' contributions: All authors contributed to the study design. A.K. performed the statistical analysis and drafted the manuscript. L.E.D. participated in acquisition of data. H.H., L.S.L., and L.E.D. participated in revising the manuscript critically for important intellectual content. All authors contributed to the interpretation of the results and approved the final manuscript for submission.

Ethics: The study was approved by the Swedish Ethical Review Authority (Dnr: 2021–01713, 2021–06–16) and performed in accordance with the Declaration of Helsinki. Digital informed consent was obtained from participants at enrolment.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

Funding

Support for this study was provided by the Greta and Johan Kock Foundation, Faculty of Medicine–Lund University, the Promobilia Foundation, and STF Bistånd. The funding sources had no role in the study design, collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Conflicts of interest: A.K. and L.S.L. act as part-time advisors for Joint Academy®; H.H was a former part-time employee at Joint Academy® when the study was conducted, L.E.D. is the founder and chief medical officer at Joint Academy®.

References

1. Hunter DJ, Schofield D, Callander E. The individual and socioeconomic impact of osteoarthritis. Nat Rev Rheumatol. 2014; 10(7):437-441. https://doi.org/10.1038/nrrheum.2014.44
2. Kiadaliri AA, Lohmander LS, Moradi-Lakeh M, Petersson IF, Englund M. High and rising burden of hip and knee osteoarthritis in the Nordic region, 1990-2015. Acta Orthop. 2018; 89(2):177-183. https://doi.org/10.1080/17453674.2017.1404791
3. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019; 27(11):1578-1589. https://doi.org/10.1016/j.joca.2019.06.011
4. Safari R, Jackson J, Sheffield D. Digital self-management interventions for people with osteoarthritis: systematic review with meta-analysis. J Med Internet Res. 2020; 22(7):e15365. https://doi.org/10.2196/15365
5. Sasaki R, Honda Y, Oga S, et al. Effect of exercise and/or educational interventions on physical activity and pain in patients with hip/knee osteoarthritis: a systematic review with meta-analysis. PLoS One. 2022; 17(11):e0275591. https://doi.org/10.1371/journal.pone.0275591
6. Holden MA, Hattle M, Runhaar J, et al. Moderators of the effect of therapeutic exercise for knee and hip osteoarthritis: a systematic review and individual participant data meta-analysis. Lancet Rheumatol. 2023; 5(7):e386-e400. https://doi.org/10.1016/S2665-9913(23)00122-4
7. Hunter DJ, Hall M. Time to revisit the therapeutic benefits of exercise for osteoarthritis? The Lancet Rheumatol. 2023; 5(7): e365-e367. https://doi.org/10.1016/S2665-9913(23)00135-2
8. Wieczorek M, Rotonda C, Guillemin F, Rat AC. What Have we learned from trajectory analysis of clinical outcomes in knee and hip osteoarthritis before surgery? Arthritis Care Res (Hoboken). 2020; 72(12):1693-1702. https://doi.org/10.1002/acr.24069
9. Conaghan PG, Kloppenburg M, Schett G, Bijlsma JW; EULAR Osteoarthritis Ad Hoc Committee. Osteoarthritis research priorities: a report from a EULAR ad hoc expert committee. Ann Rheum Dis. 2014; 73(8):1442-1445. https://doi.org/10.1136/annrheumdis-2013-204660
10. Wieczorek M, Rotonda C, Guillemin F, Rat AC. What have we learned about the course of clinical outcomes after total knee or hip arthroplasty? Arthritis Care Res (Hoboken). 2020; 72(11):1519-1529. https://doi.org/10.1002/acr.24045
11. Lee AC, Harvey WF, Han X, et al. Pain and functional trajectories in symptomatic knee osteoarthritis over up to 12 weeks of exercise exposure. Osteoarthritis Cartilage. 2018; 26(4):501-512. https://doi.org/10.1016/j.joca.2018.01.016
12. Kiadaliri A, Lohmander LS, Ignjatovic MM, Nero H, Dahlberg LE. Digital self-management of hip and knee osteoarthritis and trajectories of work and activity impairments. BMC Musculoskelet Disord. 2023; 24(1):207. https://doi.org/10.1186/s12891-023-06322-z
13. Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. Better management of patients with osteoarthritis: development and nationwide implementation of an evidence-based supported osteoarthritis self-management programme. Musculoskelet Care. 2015; 13(2):67-75. https://doi.org/10.1002/msc.1085
14. Dahlberg LE, Grahn D, Dahlberg JE, Thorstensson CA. A web-based platform for patients with osteoarthritis of the hip and knee: a pilot study. JMIR Res Protoc. 2016; 5(2):e115. https://doi.org/10.2196/resprot.5665
15. National Collaborating Centre for Chronic Conditions (UK). Osteoarthritis: National Clinical Guideline for Care and Management in Adults. London: Royal College of Physicians (UK); 2008. https://www.ncbi.nlm.nih.gov/pubmed/21290638
16. Nguena Nguefack HL, Page MG, Katz J, et al. Trajectory modelling techniques useful to epidemiological research: a comparative narrative review of approaches. Clin Epidemiol. 2020; 12:1205-1222. https://doi.org/10.2147/CLEP.S265287
17. 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 Res (Hoboken). 2011; 63(suppl 11): S240-52. https://doi.org/10.1002/acr.20543
18. Kapstad H, Hanestad BR, Langeland N, Rustoen T, Stavem K. Cutpoints for mild, moderate and severe pain in patients with osteoarthritis of the hip or knee ready for joint replacement surgery. BMC Musculoskelet Disord. 2008; 9:55. https://doi.org/10.1186/1471-2474-9-55
19. Cronstrom A, Ingelsrud LH, Nero H, et al. Interpretation threshold values for patient-reported outcomes in patients participating in a digitally delivered first-line treatment program for hip or knee osteoarthritis. Osteoarthr Cartil Open. 2023; 5(3):100375. https://doi.org/10.1016/j.ocarto.2023.100375
20. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993; 4(5):353-365. https://doi.org/10.2165/00019053-199304050-00006

21. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. Res Q Exerc Sport. 1999; 70(2):113-119. https://doi.org/10.1080/02701367.1999.10608028
22. Olsson SJ, Ekblom O, Andersson E, Borjesson M, Kallings LV. Categorical answer modes provide superior validity to open answers when asking for level of physical activity: a cross-sectional study. Scand J Public Health. 2016; 44(1):70-76. https://doi.org/10.1177/1403494815602830
23. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med. 2015; 34(28):3661-3679. https://doi.org/10.1002/sim.6607
24. van der Nest G, Lima Passos V, Candel M, van Breukelen GJP. An overview of mixture modelling for latent evolutions in longitudinal data: modelling approaches, fit statistics and software. Adv Life Course Res. 2020; 43:100323. https://doi.org/10.1016/j.alcr.2019.100323
25. Francis B, Elliott A, Weldon M. Smoothing group-based trajectory models through b-splines. J Dev Life Course Criminol. 2016; 2(1):113-133. https://doi.org/10.1007/s40865-016-0025-6
26. Nagin DS. Group-Based Modeling of Development. Harvard University Press; 2005. https://doi.org/ 10.4159/9780674041318
27. Luchman JN. Determining relative importance in Stata using dominance analysis: domin and domme. Stata J. 2021; 21(2):510-538. https://doi.org/10.1177/1536867x211025837
28. Proust-Lima C, Philipps V, Liquet B. Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. J Stat Soft. 2017; 78(2):1-56. https://doi.org/10.18637/jss.v078.i02
29. Losina E, Collins JE. Forecasting the future pain in hip OA: can we rely on pain trajectories? Osteoarthritis Cartilage. 2016; 24(5):765-767. https://doi.org/10.1016/j.joca.2016.01.989
30. Jackson H, Engelman M, Bandeen-Roche K. Robust respondents and lost limitations: the implications of nonrandom missingness for the estimation of health trajectories. J Aging Health. 2019; 31(4):685-708. https://doi.org/10.1177/0898264317747079
31. Skou ST, Pedersen BK, Abbott JH, Patterson B, Barton C. Physical activity and exercise therapy benefit more than just symptoms and impairments in people with hip and knee osteoarthritis. J Orthop Sports Phys Ther. 2018; 48(6):439-447. https://doi.org/10.2519/jospt.2018.7877
32. Thomas MJ. Expanding and explaining symptoms in knee osteoarthritis trajectories: Fluctuations, flares, and future directions. Osteoarthritis Cartilage. 2023; 31(6):725-726. https://doi.org/10.1016/j.joca.2023.03.014
33. Jonsson T, Dell'Isola A, Lohmander LS, Wagner P, Cronstrom A. Comparison of face-to-face vs digital delivery of an osteoarthritis treatment program for hip or knee osteoarthritis. JAMA Netw Open. 2022; 5(11):e2240126. https://doi.org/10.1001/jamanetworkopen.2022.40126
34. Arden NK, Perry TA, Bannuru RR, et al. Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. Nat Rev Rheumatol. 2021; 17(1):59-66. https://doi.org/10.1038/s41584-020-00523-9
35. Jonsson T, Eek F, Hansson EE, Dahlberg LE, Dell'Isola A. Factors associated with clinically relevant pain reduction after a self-management program including education and exercise for people with knee and/or hip osteoarthritis: data from the BOA register. PLoS One. 2023; 18(2):e0282169. https://doi.org/10.1371/journal.pone.0282169
36. Singh B, Olds T, Curtis R, et al. Effectiveness of physical activity interventions for improving depression, anxiety and distress: An overview of systematic reviews. Br J Sports Med. 2023; 57(18):1203-1209. https://doi.org/10.1136/bjsports-2022-106195
37. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. Int J Epidemiol. 2005; 34(1):215-220. https://doi.org/10.1093/ije/dyh299