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Defining hip pain trajectories in early symptomatic hip osteoarthritis – 5 year results from a nationwide prospective cohort study (CHECK)

A.N. Bastick † *, S.P.J. Verkleij †, J. Damen †, J. Wesseling ‡, W.K.H.A. Hilberdink §, P.J.E. Bindels †, S.M.A. Bierma-Zeinstra †

† *Department of General Practice, Erasmus MC, University Medical Center Rotterdam, The Netherlands*
‡ *Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, The Netherlands*
§ *Allied Health Care Center for Rheumatology and Rehabilitation (AHCRR), Groningen, The Netherlands*

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SUMMARY

Objective: To define distinct hip pain trajectories in individuals with early symptomatic hip osteoarthritis (OA) and to determine risk factors for these pain trajectories.
Method: Data were obtained from the nationwide prospective Cohort Hip and Cohort Knee (CHECK) study. Participants with hip pain or stiffness and a completed 5-year follow-up were included. Baseline demographic, anamnestic, physical examination characteristics were assessed. Outcome was annually assessed by the Numeric Rating Scale (NRS) for pain. Pain trajectories were retrieved by latent class growth analysis (LCGA). Multinomial logistic regression was used to calculate risk ratios.
Results: 545 participants were included. Four distinct pain trajectories were uncovered by LCGA. We found significant differences in baseline characteristics, including body mass index (BMI); symptom severity; pain coping strategies and in criteria for clinical hip OA (American College of Rheumatology (ACR)). Lower education, higher activity limitation scores, frequent use of pain transformation as coping strategy and painful internal hip rotation were more often associated with trajectories characterized by more severe pain. No association was found for baseline radiographic features.
Conclusion: We defined four distinct pain trajectories over 5 years follow-up in individuals with early symptomatic hip OA, suggesting there are differences in symptomatic progression of hip OA. Baseline radiographic severity was not associated with the pain trajectories. Future research should be aimed at measuring symptomatic progression of hip OA with even more frequent symptom assessment.

Introduction

Osteoarthritis (OA) of the hip is a painful and disabling condition. The prevalence and incidence of hip OA are increasing and will continue to increase due to the current aging of the general population[1]. Several studies have been performed to determine predictors for hip OA progression, however only few studies have used pain as a definition of progression[2–4]. Furthermore, consensus is not yet met on the apparent correlation between severity of radiographic hip OA and severity of perceived pain[5]. The latter could imply that there may be differences in risk factors or patient characteristics for both radiographic hip OA progression and pain progression in hip OA. In addition, pain due to hip OA is known to fluctuate and consequently multiple assessments of pain over a longer time period would provide a better indication of the course of pain than one single assessment[4]. This course of pain, or pain trajectory, would consequently be a more accurate representation of clinical disease progression. Physicians, mainly general practitioners (GP), are frequently consulted by patients with suspected hip OA. In most cases, they present themselves in the beginning stages of the disease. Hence the ability to predict pain trajectories in an early stage of the disease could guide the clinician in choosing preventive activities for further pain progression. Therefore, the objective of our study was to define distinct hip pain trajectories in individuals with early symptomatic hip OA and to determine which

* Address correspondence and reprint requests to: A.N. Bastick, Department of General Practice, Room NA-1923, Erasmus MC, University Medical Center Rotterdam, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands. Tel: 31-(0)-10-704-3737; Fax: 31-(0)-10-704-4766.
E-mail addresses: a.bastick@erasmusmc.nl (A.N. Bastick), s.p.j.verkleij@gmail.com (S.P.J. Verkleij), j.damen@erasmusmc.nl (J. Damen), J.Wesseling@umcutrecht.nl (J. Wesseling), info@pcrr.nl (W.K.H.A. Hilberdink), p.bindels@erasmusmc.nl (P.J.E. Bindels), s.bierma-zeinstra@erasmusmc.nl (S.M.A. Bierma-Zeinstra).

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baseline characteristics are associated with these trajectories. To our knowledge, only one study has previously been published defining pain trajectories in patients with hip OA[4].

Method

Study design and population

The data for the current study were acquired from the Cohort Hip and Cohort Knee (CHECK) study[6]. CHECK is a prospective, 10-year follow-up cohort of 1002 participants with assumed early symptomatic OA of the knee and/or hip in The Netherlands. The CHECK inclusion period ran from October 2002 until September 2005. Inclusion criteria for the CHECK study were: pain and/or stiffness of the knee and/or hip; age between 45 and 65 years; and never, or less than 6 months prior to recruitment of the study, consulted a physician for these symptoms. Participants were excluded from CHECK if they had other pathological conditions that could explain the existing complaints (e.g., other rheumatic disease, previous hip or knee joint replacement, congenital dysplasia, osteochondritis dissecans, intra-articular fractures, septic arthritis, Perthes' disease, ligament or meniscus damage, plica syndrome, Baker's cyst); co morbidity that would not allow physical evaluation during 10 years follow-up; malignancy in the past 5 years; and inability to understand the Dutch language. For the analyses of the current study we included all participants from CHECK who reported hip pain and/or stiffness at baseline. If a participant had two affected hips, we included the hip with the worst score based on pain, Kellgren and Lawrence (KL) score and physical examination findings. The latter included hip pain during internal and external rotation and flexion, and internal and external range of motion (ROM). If all findings were identical in both hips, we arbitrarily included the right hip.

Baseline characteristics

The study included a baseline medical history assessment, physical examination and radiographs of the hip and knee. The medical history was taken through questionnaires in which self-reported data were assessed. The following diseases were assessed as co morbidity: asthma, chronic sinusitis, cardio-vascular disease, high blood pressure, gastric ulcer, gallstones, liver disease, renal disease, diabetes, thyroid gland disease, epilepsy, cancer (during follow-up), severe skin disease, and other chronic musculoskeletal diseases. The Western Ontario and McMaster osteoarthritis index (WOMAC) was used to measure pain, stiffness and physical functioning with a higher score indicating worse health (range 0–100). Pain-coping behavior was assessed with a six scale Pain-Coping Inventory (PCI): pain transformation (i.e., reinterpreting pain); distraction; reducing demands; retreating; worrying; and resting[6,7]. All six items are scored according to a four-point Likert scale ranging from 1 (hardly ever) to 4 (very often) in terms of frequency with which strategies are applied when dealing with pain. Clinical hip OA was determined according to the American College of Rheumatology (ACR) criteria, which are: hip pain and all of the following criteria under (1) or (2): (1) hip internal rotation greater than or equal to 15°, pain present on internal rotation of the hip, morning stiffness of the hip for less than or equal to 60 min and age greater than 50 years; (2) hip internal rotation less than 15° and hip flexion less than or equal to 115°[8].

Radiographs

Standardized weight-bearing anteroposterior view (AP) radiographs of the pelvis were made along with a weight-bearing single faux profile (FP) radiograph of the hip[9]. Radiographs were scored for individual OA features according to criteria described by Altman[10]. Radiographic OA severity was defined by the KL classification[11]. Superior or medial hip joint space narrowing (JSN), superior or inferior acetabular osteophytes (OP), superior or inferior femoral OP, inferior acetabular OP and femoral subchondral sclerosis were scored as absent or present. On the FP radiographs, superior or posterior JSN was scored as absent (i.e., normal) or present.

Outcome variable

Pain was assessed annually through questionnaires during the 5 years of follow-up using the Numeric Rating Scale (NRS) for pain ranging from 0 to 10, with a higher score indicating more pain. The participants were asked to score the pain they experienced in their most painful joint over the last week. Using latent class growth analysis (LCGA) pain trajectories based on the annually assessed NRS were identified (see Statistical analysis), blinded to all other characteristics. If participants underwent hip replacement surgery (HRS) during follow-up, their pain scores were scored as missing from the moment of surgery. If a participant missed more than two pain assessments, he or she was excluded from the analyses.

Statistical analysis

LCGA was used to identify the different pain trajectory groups. LCGA is a technique that uncovers heterogeneity in a population and makes it possible to distinguish groups of people who are similar in their growth trajectories longitudinally. It was tested whether the course of pain was best described by linear, quadratic or cubic trajectories. The most optimal model was determined on a combination of indices of fit, the interpretability of the model, i.e., are the uncovered groups each sufficiently large (threshold approximately 15% of the study population, or 90 participants) to enable further statistical analyses and whether the trajectories were visually distinguishable from each other to the clinical physician, i.e., can we uncover groups with progressing and decreasing trajectories or trajectories with variable paths, thus are the trajectories truly distinct (in accordance with the aim of this study). The following indices of fit used were: Bayesian Information Criterion (BIC); Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (LRT) and the bootstrap LRT; and entropy indices.

Baseline characteristics were calculated per obtained pain trajectory group using descriptive statistics. After checking for collinearity setting the cut-off value for Pearson's correlation coefficient (R) at 0.70, we performed univariable multinomial logistic regression analyses to test whether differences were statistically different and to obtain crude risk estimates, setting the group with the mildest pain trajectory as the reference group. All variables from the univariable analyses with $P < 0.10$ were ultimately included in a final multivariable multinomial logistic regression model (P-removal $P < 0.05$), again setting the group with the mildest pain trajectory as the reference group. Risk ratios (RR) and 95% confidence intervals (CI) were obtained for belonging to a trajectory characterized by greater pain compared to the reference group.

The LCGA was performed using *Mplus 6.1 ed. 1998–2010*. All other analyses were performed using *SPSS Statistical Package PASW 20.0*.

Results

Baseline characteristics

At baseline, 588 of the 1002 participants reported hip pain and therefore fulfilled our inclusion criteria. 43 (7%) participants missed

more than two annual pain assessments or were lost to follow-up. The baseline values of body mass index (BMI), NRS, age, sex and KL of the 43 lost to follow-up did not differ significantly from the study population. The total study population after 5 years therefore consisted of 545 participants. The mean age was 55.7 ± 5.2 years and 81% was female. 140 participants (26%) fulfilled the ACR criteria for clinical hip OA. See Tables I and II for a detailed description of the study population. The variables 'NRS at the moment of questionnaire' and the 'WOMAC pain subscale' were positively correlated ($R > 0.70$) and were excluded from the multivariable analyses. There were no other strong correlations. After 5 years follow-up 38 study participants (7%) had undergone HRS.

Outcome variable

The most optimal and clinically relevant model retrieved by LCGA was a quadratic four-group model (lower BIC 12360 with best entropy indices 0.74 and LRT P-value < 0.05). The quadratic three-group model had BIC 12412, entropy 0.75 but LRT P-value > 0.05; the five-group model BIC 12340, entropy 0.70 and LRT P-value > 0.05. The model uncovered sufficiently large groups of participants with extreme trajectories, which were considered highly informative and clinically relevant: group A ($N = 231$) showed a constant mild pain trajectory during follow-up; group B ($N = 94$) showed moderate pain and moderate pain regression during follow-up; group C ($N = 132$) also showed moderate pain, but showed pain progression; and group D ($N = 88$) showed a constant severe pain trajectory. Detailed depictions of the individual trajectories are presented in Fig. 1. Average fitted lines of these four pain trajectories are depicted in Fig. 2.

Multinomial logistic regression analyses

The means of all baseline characteristics per pain trajectory group are presented in Table II. Variables with P-value < 0.10 from the univariable analyses have been made bold, however all of these variables also had P-value < 0.05. Statistically significant differences were found for various demographic and anamnestic features, including baseline pain and function severity scores, use of pain coping strategies, clinical findings for the hip and in fulfilling criteria for clinical hip OA. Distribution of JSN on the AP view differed significantly amongst the groups. No other significant differences in baseline radiographic severity scores were found. The crude risk estimates from the univariable multinomial regression analyses are presented in Table III.

The results from the final multivariable model are shown in Table IV (Nagelkerke $R^2 = 0.41$). The trajectory group with the mildest trajectory (group A) was set as the reference group. Baseline education level, WOMAC physical function, frequent use of coping strategy pain transformation and painful internal hip rotation showed significant associations.

Discussion

This study is one of the first to uncover distinct pain trajectories over 5 years follow-up in individuals with early symptomatic hip OA. We identified a substantial group (group A) of 231 participants (42% of the study population) with a constant mild pain trajectory. Another group (group B) comprised of 94 participants (17% of the study population) and showed a moderate pain trajectory. Thus, 60% of our study population showed a constant mild, or moderate pain trajectory during 5 years follow-up. It therefore seems justifiable to maintain a wait-and-see policy for participants from these trajectory groups in managing their disease. It seems more important to identify participants with pain trajectories characterized by greater pain and/or pain progression, i.e., groups C and D. The results from the multivariable analyses indicate that these participants had a lower education, higher activity limitation scores, frequent use of the pain coping strategy pain transformation and painful internal hip rotation more often were associated with trajectories characterized by greater pain compared to the mild pain trajectory group. No association was found for baseline radiographic features in multivariable analyses. Noteworthy is group B with a moderate decrease pain trajectory. At baseline, these participants had higher pain scores, however no other variables, including painful internal hip rotation, from the multivariable analyses showed associations. This implies that clinicians should reassess patients within the first year of follow-up whom initially have hip pain, but have no painful internal hip rotation during physical examination, to better establish which pain trajectory the patient is likely to be in. Baseline differences were also found between the trajectory groups in BMI, co morbidity count, symptom severity, use of pain coping strategies, morning stiffness of the hip <60 min, painful movement of the hip during examination, fulfilling the ACR criteria for clinical hip OA and JSN on the AP radiograph.

Table I
Baseline characteristics of the study population

Baseline characteristic/factor	Total population ($N = 545$)	Lost to follow-up ($N = 43$)	P-value
Demographics block			
Age (years)	55.7 ± 5.2	56.6 ± 6.4	0.29
Sex (% female)	81%	81%	0.92
Body Mass Index (kg/m^2)	26.2 ± 4.2	25.4 ± 3.6	0.24
Baseline NRS in the past week	3.7 ± 2.1	3.7 ± 2.0	0.99
WOMAC subscales score			
Pain	27.2 ± 17.0	27.4 ± 17.9	0.93
Joint stiffness	34.7 ± 20.8	36.6 ± 25.8	0.56
Physical function	25.3 ± 17.5	25.5 ± 19.7	0.96
Clinical hip OA*	26%	23%	0.73
KL grade			
Distribution, % hips with grade 0/1	67/33	100/0	0.06
THA after 5 years follow-up (total no.)	38 (7%)	–	–

Values are: mean values ± the standard deviation or percentages %.
THA: Total Hip Arthroplasty.
Differences in distribution between groups assessed with Analysis of Variance (ANOVA) or Pearson's χ^2 test when appropriate.
* According to the ACR criteria for clinical hip OA[8].

Table II
Baseline characteristics of the four pain trajectory groups retrieved by LCGA

Pain trajectory groups	A (mild pain) $N = 231$	B (moderate decrease) $N = 94$	C (moderate progression) $N = 132$	D (severe pain) $N = 88$
Baseline characteristic/factor				
Age (years)	56 ± 5	56 ± 6	55 ± 6	56 ± 5
Sex (% female)	77%	86%	81%	84%
Body Mass Index (kg/m^2)	25 ± 4	26 ± 4	27 ± 5	27 ± 5
Highest achieved education level				
Primary or secondary school	67%	79%	82%	78%
University/college	33%	21%	18%	22%
Ethnicity (% Caucasian vs other)	100%	98%	98%	97%
Participants with >1 co morbidity	38%	54%	59%	66%
Baseline NRS at moment of questionnaire	1.9 (1.0–3.0)	4.3 (3.0–5.0)	3.1 (2.0–4.0)	5.7 (5.0–7.0)
Baseline NRS in the past week	2.2 (1.0–3.0)	5.5 (4.0–7.0)	3.4 (2.0–5.0)	6.1 (5.0–7.0)
PCI subscales score				
Pain transformation	2.0 (1.5–2.5)	2.3 (1.8–2.8)	2.3 (1.8–2.8)	2.5 (2.0–3.0)
Distraction	2.1 (1.6–2.6)	2.3 (1.8–2.6)	2.3 (1.8–2.6)	2.5 (2.2–2.9)
Reducing demands	1.9 (1.7–2.0)	2.1 (1.7–2.7)	2.0 (1.7–2.3)	2.2 (1.7–2.7)
Retreating	1.5 (1.1–1.9)	1.5 (1.1–1.9)	1.5 (1.1–1.7)	1.6 (1.3–1.9)
Worrying	1.5 (1.2–1.7)	1.6 (1.3–1.9)	1.5 (1.2–1.8)	1.8 (1.4–2.1)
Resting	1.7 (1.4–2.0)	1.9 (1.6–2.4)	1.9 (1.6–2.6)	2.1 (1.6–2.6)
WOMAC subscales score				
Pain	17 (8.8–25)	40 (25–45)	37 (20–40)	51 (30–55)
Joint stiffness	25 (13–38)	44 (25–50)	51 (25–50)	54 (38–63)
Physical function	15 (5.9–21)	30 (19–40)	27 (15–37)	44 (31–56)
Use of pain medication (% yes)	41%	40%	34%	40%
≤2 times/week physical activity ≥ 0.5 h/day	61%	54%	56%	44%
Do you drink alcohol (% yes)	82%	77%	76%	73%
Smoker, or previous smoker (% yes)	12%	15%	12%	22%
Additional supplements or vitamins (% yes)	58%	51%	53%	55%
Knee pain ipsilateral knee	52%	64%	68%	68%
Morning stiffness of the hips < 60 min	48%	50%	65%	66%
Pain internal hip rotation	44%	50%	59%	69%
Pain external hip rotation	22%	23%	42%	43%
Pain flexion hip	42%	48%	58%	64%
Pain adduction hip	25%	34%	43%	58%
Pain abduction hip	34%	31%	49%	64%
ROM internal hip rotation hip (°)	30 ± 9	30 ± 10	28 ± 9	27 ± 9
ROM external hip rotation (°)	28 ± 8	27 ± 9	27 ± 9	27 ± 10
ROM flexion hip (°)	120 ± 11	117 ± 11	114 ± 11	113 ± 12
Pain flexion ipsilateral knee	15%	12%	27%	28%
Bouchard swelling digitorum 2–5 left/right	19%	28%	19%	28%
Heberden node digitorum 2–5 left/right	49%	53%	50%	53%
Clinical hip OA*	21%	21%	29%	38%
KL grade hip				
% Hips with grade 0/1	65/35	76/27	64/36	63/37
JSN score > 0 (AP) hip	38%	25%	38%	45%
JSN score > 0 (FP) hip	20%	11%	14%	22%
Osteophyte score > 0 hip	41%	33%	48%	38%
THA after 5 years follow-up (absolute no.)	9	10	4	15

Values are: mean values ± the standard deviation; mean (interquartile range); or percentages %.
THA: Total Hip Arthroplasty.
Differences in distribution between groups assessed with multinomial logistic regression analysis setting the group with mildest pain trajectory as the reference group.
Bold indicates *P*-value < 0.10 from the univariable multinomial logistic regression analyses. All variables made bold also had *P*-value < 0.05.
* According to the ACR criteria for clinical hip OA[8].

Previous studies have not found strong, significant associations between BMI and clinical or radiographic hip OA progression[12,13]. Frequent usage of the pain coping strategy pain transformation, an active pain coping strategy which reflects a patient's effort to reinterpret and transform the pain, had a significant association with the pain trajectories[7]. It is important for patients to have proper knowledge of their condition and its prognosis. Only then will they be able to learn to optimally manage and cope with their conditions[14]. The ACR, the Osteoarthritis Research Society International (OARSI) and the National Institute for Health and Clinical Excellence (NICE) all recommend patient education interventions for the treatment of hip OA.[15–17]

In the trajectory groups with greater pain, individuals had significantly more hip pain during active movements of the hip joint. Pain during internal hip rotation proved to have a strong association with these pain trajectories. These findings indicate strong similarities between criteria for symptomatic hip OA progression and diagnostic ACR criteria for hip OA described by Altman *et al.*[8] In a previous article by Lievense *et al.*, the authors longitudinally studied the prognosis of hip pain in a population similar to ours[3]. They found that baseline painful internal hip rotation significantly contributed to the prediction of HRS after 3 years (odds ratio (OR) 3.5), adjusted for factors assessed during history taking and regardless of radiographic hip OA severity. Moreover,

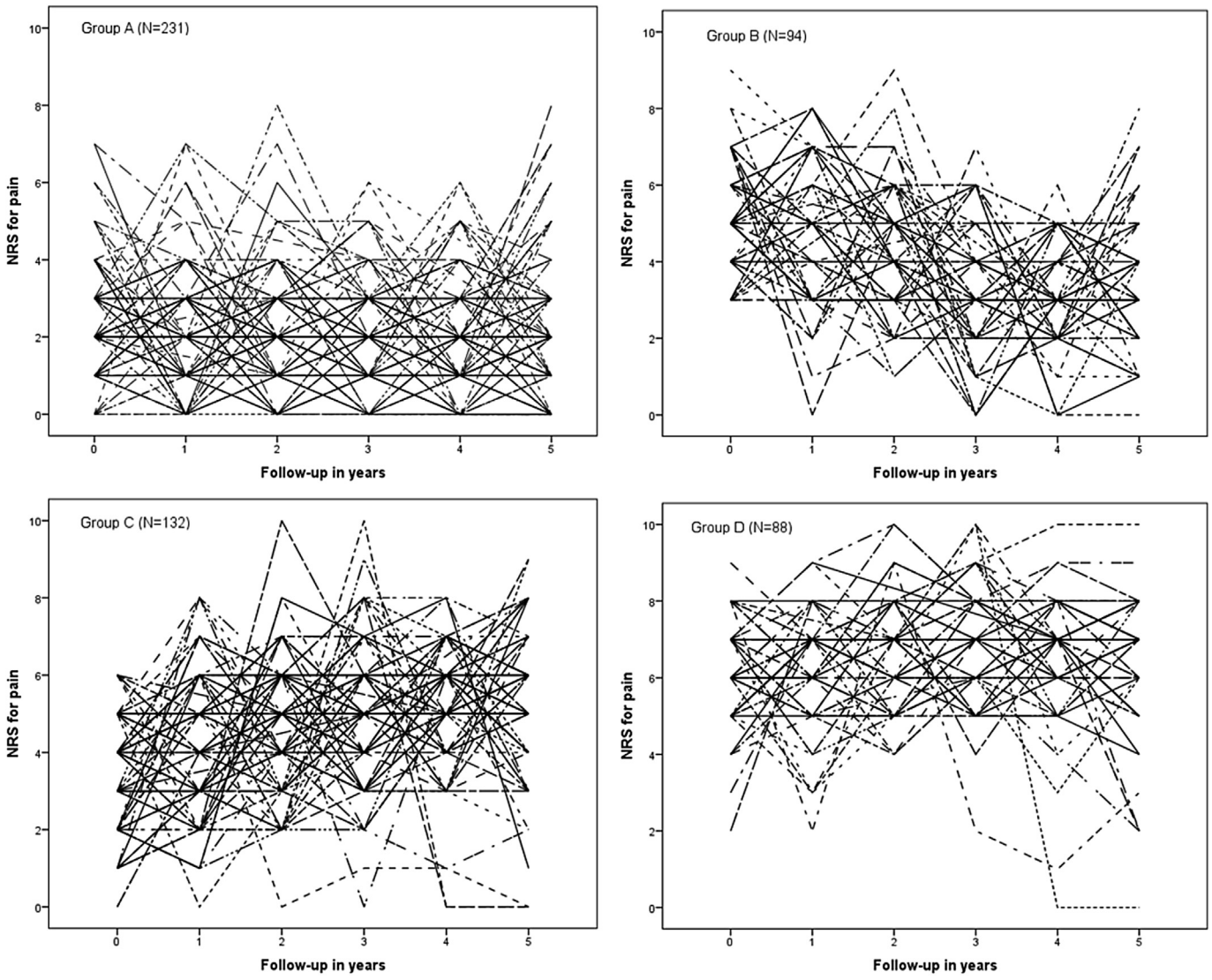

Fig. 1. Detailed depictions of the pain trajectories of the four group model obtained by LCGA.

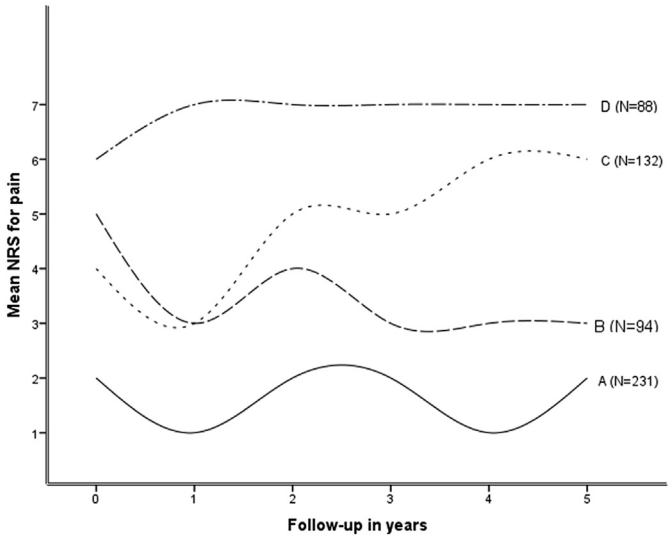

Fig. 2. Average fitted lines of the pain trajectories obtained by LCGA as depicted in Fig. 1.

their univariable analysis showed a significant association between painful hip adduction and HRS after 6 years (OR 3.6). They also presented significant associations between hip ROM in all directions and HRS after 3 and 6 years. In our study population, the baseline means of the ROM differed significantly between the trajectory groups. Birrell *et al.* previously reported similar findings[18]. They found that a lower range of internal rotation and range of flexion were significantly associated with an increased hazard of HRS.

To our knowledge, only one other study by Verkleij *et al.* has been published determining pain trajectories in hip OA[4]. The authors defined five distinct pain trajectories in a study population ($N = 222$) with clinically and radiographically defined hip OA according to ACR criteria over a 2 year follow-up period. Main baseline risk factors (in univariable analyses) for trajectories characterized by greater pain compared to the mild pain group were BMI, education level, radiographic severity, morning stiffness and decreased ROM. These findings are very similar to our results, however we found no association for radiographic severity. The latter is likely to be caused by the fact that their study population was in a more advanced stage of the disease at baseline compared to our study population.

Table III
Univariable crude risk estimates. RR for belonging in each trajectory relative to reference trajectory (mild, group A) ($N = 231$)

Pain trajectory groups	B (moderate decrease) $N = 94$	C (moderate progression) $N = 132$	D (severe pain) $N = 88$
Baseline characteristic/factor			
Age (years)†	1.02 (0.97–1.04)	1.00 (0.95–1.04)	1.04 (0.99–1.09)
Sex (% female)	1.86 (0.96–3.60)	1.27 (0.74–2.17)	1.57 (0.82–3.01)
Body Mass Index (kg/m^2)†	**1.07 (1.00–1.14)**	**1.10 (1.04–1.16)**	**1.12 (1.05–1.19)**
Highest achieved education level			
University/college	ref.	ref.	ref.
Primary or secondary school	**2.07 (1.17–3.64)**	**2.03 (1.24–3.32)**	**4.42 (2.17–9.02)**
Ethnicity (% Caucasian vs other)	5.00 (0.45–55.6)	5.38 (0.55–52.6)	8.13 (0.83–76.9)
Participants with >1 co morbidity	**3.16 (1.89–5.32)**	**2.42 (1.56–3.77)**	**1.94 (1.19–3.16)**
Baseline NRS at moment of questionnaire†	**2.57 (2.13–3.10)**	**1.66 (1.43–1.93)**	**4.45 (3.47–5.72)**
PCI subscales score†			
Pain transformation	**1.65 (1.07–2.54)**	**1.84 (1.25–2.70)**	**2.23 (1.38–3.59)**
Distraction	**1.51 (1.02–2.23)**	**1.42 (1.00–2.01)**	**2.18 (1.44–3.31)**
Reducing demands	**1.58 (1.05–2.37)**	1.36 (0.94–1.96)	**2.08 (1.37–3.14)**
Retreating	0.59 (0.30–1.13)	**0.42 (0.23–0.77)**	**0.36 (0.18–0.74)**
Worrying	**2.62 (1.24–5.54)**	1.68 (0.83–3.40)	**7.17 (3.28–15.7)**
Resting	1.87 (0.97–3.63)	**2.59 (1.42–4.72)**	**3.36 (1.67–6.76)**
WOMAC subscales score†			
Pain	**1.09 (1.07–1.11)**	**1.07 (1.05–1.09)**	**1.14 (1.11–1.17)**
Joint stiffness	**1.04 (1.03–1.06)**	**1.04 (1.02–1.05)**	**1.07 (1.06–1.09)**
Physical function	**1.08 (1.06–1.11)**	**1.07 (1.05–1.09)**	**1.15 (1.12–1.17)**
Use of pain medication (% yes)	1.04 (0.64–1.71)	1.35 (0.86–2.12)	1.02 (0.62–1.70)
≤2 times/week physical activity ≥ 0.5 h/day	1.28 (0.79–2.10)	1.19 (0.77–1.85)	**1.98 (1.20–3.29)**
Do you drink alcohol (% yes)	1.38 (0.76–2.51)	1.46 (0.86–2.49)	1.70 (0.95–3.07)
Smoker, or previous smoker (% yes)	1.31 (0.65–2.63)	1.02 (0.53–1.98)	**2.07 (1.08–3.95)**
Additional supplements or vitamins (% yes)	0.74 (0.45–1.20)	0.82 (0.53–1.26)	0.89 (0.54–1.47)
Knee pain ipsilateral knee	1.65 (1.00–2.72)	**1.96 (1.24–3.09)**	**1.98 (1.16–3.39)**
Morning stiffness of the hips < 60 min	1.10 (0.68–1.79)	**2.08 (1.33–3.25)**	**2.16 (1.29–3.62)**
Pain internal hip rotation	1.18 (0.74–1.88)	**1.88 (1.22–2.92)**	**2.69 (1.60–4.50)**
Pain external hip rotation	1.27 (0.66–2.43)	**2.87 (1.69–4.85)**	**2.72 (1.49–4.98)**
Pain flexion hip	1.30 (0.80–4.01)	**1.90 (1.23–2.93)**	**2.40 (1.44–4.02)**
Pain adduction hip	1.63 (0.90–2.96)	**2.20 (1.31–3.70)**	**4.39 (2.42–7.94)**
Pain abduction hip	0.88 (0.49–1.57)	**1.91 (1.18–3.11)**	**3.37 (1.89–6.02)**
ROM internal hip rotation hip (°)	1.01 (0.98–1.03)	**0.98 (0.95–1.00)**	**0.97 (0.95–1.00)**
ROM external hip rotation (°)	1.00 (0.97–1.04)	0.99 (0.96–1.03)	0.99 (0.95–1.02)
ROM flexion hip (°)	**0.97 (0.95–0.99)**	**0.95 (0.93–0.97)**	**0.95 (0.93–0.97)**
Pain flexion ipsilateral knee	0.72 (0.35–1.49)	**2.02 (1.20–3.40)**	**2.18 (1.20–3.94)**
Bouchard swelling digitorum 2–5 left/right	0.64 (0.36–1.12)	1.04 (0.60–1.81)	0.62 (0.35–1.1)
Heberden node digitorum 2–5 left/right	0.86 (0.53–1.39)	0.97 (0.63–1.50)	0.84 (0.51–1.37)
Clinical hip OA*	1.00 (0.56–1.81)	1.50 (0.92–2.46)	**2.23 (1.31–3.80)**
KL grade hip			
% Hips with grade 0/1	0.61 (0.36–1.07)	1.09 (0.68–1.75)	1.10 (0.63–1.92)
JSN score > 0 (AP) hip	**1.78 (1.02–3.11)**	0.99 (0.62–1.57)	0.70 (0.41–1.21)
JSN score > 0 (FP) hip	2.14 (0.99–4.62)	1.54 (0.83–2.89)	0.91 (0.48–1.74)
Osteophyte score > 0 hip	1.39 (0.82–2.36)	0.76 (0.48–1.20)	1.13 (0.65–1.98)

THA: Total Hip Arthroplasty.
Numbers indicate RR with corresponding 95% CI in brackets.
RR obtained by multinomial logistic regression.
Bold indicates $P < 0.05$.
* According to the ACR criteria for clinical hip OA[8].
† RR per unit increase.

One of the limitations to our study is that although patients were asked where the pain was located (knee and/or hip; left and/or right), the NRS and WOMAC scales were assessed on the joint with the most severe pain. Hence, an individual with both hip and knee or bilateral symptoms could have more pain in his or her knee, or contralateral hip and consequently have a high NRS. It is possible that the NRS therefore would not fully correspond with the pain the individual experiences in the included hip. On the other hand, it might be difficult for an individual to score his or her NRS separately for affected joints. Nevertheless, the above-mentioned could have led to misclassification bias in our outcome measure. Also for this reason, we decided to apply a person-specific approach in our analyses as opposed to a hip-specific approach. A second limitation to our study is that we used the NRS that was assessed annually during the follow-up period to create the different pain trajectories; however an even more frequent NRS assessment would lead to an even more precise estimation of the pain trajectories. Thirdly, we excluded participants from the analyses if they missed more than two pain assessments, which could have led informative censoring. Fourthly, we included all participants with hip pain due to early symptomatic hip OA at baseline, however only 26% of these individuals actually fulfilled the ACR criteria for hip OA at baseline. Performing our analyses only on participants fulfilling the ACR criteria would have made our study population too small. Nevertheless, an important part of the participants in our study suffered from an aggravation of hip pain symptoms making them a clinically relevant group for follow-up. Lastly, we tested a relatively

Table IV
Multivariable model. RR for belonging in each trajectory relative to reference trajectory (mild, group A) ($N = 231$)

Pain trajectory groups	B (moderate decrease) $N = 94$	C (moderate progression) $N = 132$	D (severe) $N = 88$
Baseline characteristic/factor			
Highest achieved education level			
University/college	ref.	ref.	ref.
Primary or secondary school	1.59 (0.86–2.95)	**1.75 (1.00–3.06)**	**3.35 (1.37–8.20)**
PCI subscale pain transformation*	1.51 (0.99–2.30)	**1.47 (1.00–2.16)**	**1.89 (1.13–3.17)**
WOMAC physical function subscale†	**1.07 (1.06–1.10)**	**1.06 (1.04–1.08)**	**1.14 (1.11–1.17)**
Painful internal rotation hip	1.16 (0.67–2.00)	**1.78 (1.08–2.92)**	**2.57 (1.29–5.13)**

Numbers indicate RR with corresponding 95% CI in brackets.
RR obtained by multinomial logistic regression.
Nagelkerke $R^2 = 0.41$ for the model.
Bold indicates $P < 0.05$.
* RR per unit increase. A higher score indicates more frequent usage of pain transformation.
† RR per unit increase. A higher WOMAC score indicates more limitations due to physical health.

large number of variables in the analysis which could have lead to a type I error. Most variables in the analysis however are all part of the standard clinical examination and are assumed to relate to disease severity or overall health. In addition we used data reduction methods, testing for co-linearity, and by entering variables based on univariable *P*-values.

In conclusion, we defined four distinct pain trajectories over 5 years follow-up in individuals with early symptomatic hip OA. Individuals whom are less educated, have higher activity limitation scores, use the pain coping strategy pain transformation frequently and have painful internal hip rotation have an increased risk for being in a trajectory with more severe pain. Moreover, individuals whom were at risk for pain progression showed differences in pain coping strategies, more often had morning stiffness of the hip at baseline, and fulfilled existing criteria for clinical hip OA during physical examination. Baseline radiographic severity was not associated with the pain trajectories. We would like to emphasize that radiography does not provide benefit over clinical diagnosis of early symptomatic hip OA. Also, the majority of the study population (58%, groups A and B combined) had a relatively mild pain trajectory throughout the entire follow-up period, which endorses current recommendations in OA guidelines for conservative treatment in the early stages of the disease. Re-assessment of clinical symptoms due to hip OA should take place within the first year of follow-up. Future research should be aimed at measuring symptomatic progression of hip OA with even more frequent symptom assessment.

Authors' contributions

ANB was responsible for concept, design, analyses and drafting of the article. SPJV was responsible for part of the statistical analysis and gave feedback on the article. JD, JW and WKHAH were responsible in collection and assembly of data and gave feedback on the article. PJEB gave critical expert feedback on the article. SMABZ participated in concept, design and analyses of the article and gave critical expert feedback and the final approval on the article. ANB takes responsibility for the integrity of the work as a whole from inception to finished article.

Competing interests

The authors have no conflicts of interest to disclose.

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References

1. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. Rheum Dis Clin North Am 2008 Aug;34(3):515–29.
2. van Dijk GM, Dekker J, Veenhof C, van den Ende CH, Carpa Study G. Course of functional status and pain in osteoarthritis of the hip or knee: a systematic review of the literature. Arthritis Rheum 2006 Oct 15;55(5):779–85.
3. Lievense AM, Koes BW, Verhaar JA, Bohnen AM, Bierma-Zeinstra SM. Prognosis of hip pain in general practice: a prospective followup study. Arthritis Rheum 2007 Dec 15;57(8):1368–74.
4. Verkleij SP, Hoekstra T, Rozendaal RM, Waarsing JH, Koes BW, Luijsterburg PA, *et al*. Defining discriminative pain trajectories in hip osteoarthritis over a 2-year time period. Ann Rheum Dis 2012 Sep;71(9):1517–23.
5. Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000 Jun;27(6):1513–7.
6. Wesseling J, Dekker J, van den Berg WB, Bierma-Zeinstra SM, Boers M, Cats HA, *et al*. CHECK (Cohort Hip and Cohort Knee): similarities and differences with the Osteoarthritis Initiative. Ann Rheum Dis 2009 Sep;68(9):1413–9.
7. Kraaimaat FW, Evers AW. Pain-coping strategies in chronic pain patients: psychometric characteristics of the pain-coping inventory (PCI). Int J Behav Med 2003;10(4):343–63.
8. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, *et al*. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991 May;34(5):505–14.
9. Lequesne MG, Laredo JD. The faux profil (oblique view) of the hip in the standing position. Contribution to the evaluation of

osteoarthritis of the adult hip. Ann Rheum Dis 1998 Nov;57(11):676–81.
10. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis Cartilage 2007; 15(Suppl A):A1–A56.
11. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957 Dec;16(4):494–502.
12. Wright AA, Cook C, Abbott JH. Variables associated with the progression of hip osteoarthritis: a systematic review. Arthritis Rheum 2009 Jul 15;61(7):925–36.
13. Lievense AM, Bierma-Zeinstra SM, Verhagen AP, Verhaar JA, Koes BW. Prognostic factors of progress of hip osteoarthritis: a systematic review. Arthritis Rheum 2002 Oct 15;47(5):556–62.
14. Mazzuca SA. Does patient education in chronic disease have therapeutic value? J Chronic Dis 1982;35(7):521–9.
15. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000 Sep;43(9):1905–15.
16. National Collaborating Centre for Chronic Conditions. Osteoarthritis: National Clinical Guideline for Care and Management in Adults. London: Royal College of Physicians (UK); 2008. National Institute for Health and Clinical Excellence (NICE) Clinical Guideline 59.
17. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, *et al*. OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008 Feb;16(2):137–62.
18. Birrell F, Afzal C, Nahit E, Lunt M, Macfarlane GJ, Cooper C, *et al*. Predictors of hip joint replacement in new attenders in primary care with hip pain. Br J Gen Pract 2003 Jan;53(486): 26–30.