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The clinical and radiographic course of early knee and hip osteoarthritis over 10 years in CHECK (Cohort Hip and Cohort Knee)

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SUMMARY

Objective: To describe the radiographic and symptomatic course in subjects with hip or knee complaints suspected of early osteoarthritis (OA).
Design: CHECK (Cohort Hip and Cohort Knee) is a multicenter, prospective observational cohort study of 1,002 subjects with first complaints in knee(s) and/or hip(s) (age 56 ± 5 years; 79% female; body mass index (BMI) 26 ± 4 kg/m^2). Visits took place at baseline and at 2, 5, 8, and 10 year follow-up. At each visit, questionnaires were administered, physical examination performed, and X-ray images obtained. Clinical OA was defined according to the clinical American College of Rheumatism (ACR) criteria. Radiographic OA (ROA) was defined as Kellgren and Lawrence score (K&L) ≥2.
Results: 83% of the subjects reported knee pain, 59% hip pain, and 42% reported both hip and knee pain at baseline. 85% of the subjects completed 10-year follow-up. Pain scores remained rather stable over time, although individual scores fluctuated. A total of 138 subjects never fulfilled the clinical American College of Rheumatology (ACR) criteria. 60% ($n = 601$) had ROA in one or both knees, and 51% ($n = 513$) had ROA in one or both hips at 10 years. Only 13.5% of the subjects did not develop ROA after 10 years. Most joint replacements ($n = 52$ (57%)) took place in subjects with multiple affected joints.
Conclusions: The symptomatic course in subjects with hip or knee complaints suspected of OA remained fairly stable on population level, though individual scores fluctuated. The radiological course was progressive, with joint replacements particularly in subjects with both hip and knee OA.

Introduction

Hip and knee osteoarthritis (OA) are leading causes of global disability. Globally, hip and knee OA were ranked as the eleventh highest contributor to global disability in 2010[1]. Moreover, the number of people living with hip and/or knee OA is anticipated to increase substantially over the coming decades and OA is expected to become the most prevalent chronic disease in the Netherlands in 2040[2].

Although primary OA is a slowly progressive disease, it also is known that symptoms within a person may vary over time. Studies presenting the long-term OA course, with repeated assessments over the years, are scarce. Recently three large observational OA cohorts reported on 5–7 years symptomatic trajectories, based on repeated assessments[3–8]. All these reports focused on either the hip or the knee and described one dimension of the symptoms. In clinical practice symptoms are not always restricted to one joint. OA of hip and knee can occur together and may have impact on each other. Evenly, bilateral disease is not uncommon. Moreover, the clinical course from first presentation of both hip and knee OA together is not yet described, and would be very informative for health care providers, especially for those that provide the primary care for these patients.

In the present paper we present the overall 10-years course after first presentation of complaints of hip or knee that were indicative for OA. We present the course of symptoms, the (co-)occurrence of

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painful joints, Radiographic OA (ROA), clinical OA, and joint replacement, as well as pain trajectories.

Methods

Selection and description of the population

The current study includes data from CHECK (Cohort Hip and Cohort Knee)[9,10], a prospective, longitudinal cohort study. General practitioners (GPs) referred potentially eligible patients with pain and/or stiffness in their hip(s) and/or knee(s) to one of the 10 participating medical centers throughout the Netherlands. In addition, subjects were recruited through local newspapers and the Dutch Arthritis Foundation's website. Eligibility was then checked by experienced study physicians in the medical centers. The protocol was approved by each center's Medical Ethical Committee.

In- and exclusion criteria

Subjects were eligible if they were aged 45–65 years at the time of inclusion and had either consulted their GP with pain and/or stiffness in their hip(s) and/or knee(s) for the first time within 6 months before the date of inclusion or had never consulted a health care provider for these complaints before.

Exclusion criteria were 1) other pathological conditions that could explain the joint complaints (for details see box 1 in Wesseling *et al.*[9]), 2) comorbidity that would not allow completion of the 10-year follow-up, 3) malignancy in the past 5 years or 4) inability to understand the Dutch language.

Measurements

At baseline (T0) and 2 (T2), 5 (T5), 8 (T8) and 10 years (T10) of follow-up, all subjects filled-in a questionnaire and visited one of the participating medical centers for physical examination and radiography.

Demographics

Collected baseline demographics included age, ethnicity, sex, menopausal status in women, education level, smoking status, and physical activity level ('Are you physically active for more than 30 min per day on 3 or more days per week?'). body mass index (BMI) (kg/m^2) was calculated using self-reported body weight and height.

Questionnaires

For OA related complaints, subjects filled-in The Western Ontario and McMaster Osteoarthritis Index (WOMAC) questionnaire[11]. From this, validated subscales for pain, function and stiffness were calculated and rescaled to 0–100, with higher scores indicating worse symptoms.

Numeric rating scales (NRS) (0–10) were filled in by the subjects for current hip and/or knee pain intensity and for average hip and/or knee pain intensity over the past week.

Health status was evaluated using the Short Form 36 (SF-36) questionnaire[12]. The physical component summary was calculated from the scales relating to role limitations due to physical health and bodily pain. The mental component summary was calculated from the scales relating to role limitations due to emotional problems and social functioning. Scores ranged from 0 to 100, with a higher score indicating a better health-related quality of life.

Health-related quality of life was evaluated using the EuroQol (EQ-5D) questionnaire about problems with mobility, self-care, and usual activities, pain and discomfort, and anxiety and depression[13].

Self-reported comorbidities were collected for: chronic lung disease, severe cardiac disease or stroke, hypertension, diabetes mellitus, back disorders, and for disorders of neck, shoulder, elbow, wrist and/or hand. Also self-reported pain medication use was obtained.

Physical examination

Hips were examined for active range of motion and pain at internal rotation and flexion. Knees were examined for warmth, bony enlargement, bony tenderness, and crepitus.

Radiography

For the hips, weight-bearing anteroposterior (AP) radiographs of the pelvis and weight-bearing single faux profile radiographs of both hips were obtained.

Radiographs of the tibiofemoral joints (TFJ) were made in a semi-flexed (7–10°), weight-bearing posteroanterior (PA) view[14]. Radiographs of the patellofemoral joints were made by a single standing mediolateral view in 30° flexion and a skyline (inferior superior) view in 30° flexion.

All AP hip and PA knee radiographs were centrally graded (sequence known) according to the Kellgren & Lawrence (K&L) classification system[15]. See Damen *et al.* for an extensive description of the methods[16]. A hip or knee prostheses (HP or KP) was defined when present at the radiographs.

Statistics

Course of patient-reported clinical outcomes

Baseline, T2, T5, T8 and T10 values of WOMAC and SF-36 subscales, NRS for current pain intensity, and NRS for pain over the past week were calculated for all available subjects (mean and standard deviation (sd)). Also, frequencies for each of the EQ-5D items were determined for all available subjects at each time point.

Course of clinical American College of Rheumatology (ACR) criteria

Both hips and both knees of all subjects were assessed for fulfilling the clinical American College of Rheumatism (ACR) criteria for hip and knee OA at baseline, T2, T5, T8 and T10. The clinical ACR criteria for hip OA were: hip pain plus internal rotation $<15°$ and flexion of the hip $\leq 115°$ or hip pain plus internal rotation $\geq 15°$, pain at internal rotation, stiffness ≤ 60 min, and age >50 years[17]. The clinical ACR criteria for knee OA were: knee pain and at least three of the following features: age >50 years, stiffness <30 min, crepitus, bony tenderness, bony enlargement and no palpable warmth[18]. A hierarchical figure was made to display the course of OA during follow-up.

Pain trajectories

Based on NRS for pain over the past week for all subjects at all time points, trajectories of pain were evaluated using latent class growth analysis (LCGA) in M+ software (Mplus version 7.4; Múthen and Múthen, Los Angeles, USA). Entropy, Bayesian Information Criteria (BIC), and Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (LRT) were used to determine the best fit for 2 to 6 groups with linear, quadratic, cubic, and free variance. NRS for subjects undergoing HP or KP were defined missing from the first time point at which radiographs showed HP/KP onwards. For the best fitted model, the number of subjects with only hip complaints at baseline, subjects with only knee complaints at baseline, subjects with both hip and knee complaints at baseline, proportion of females, and the number of hip and knee replacements during follow-up were compared.

Radiographic hip and knee OA over time

The prevalence of ROA, defined as KL grade ≥ 2, was determined for all hips and all knees of all subjects at all time points and

visualized in a proportional Venn-diagrams. The prevalence and overlap between ROA in the left and the right joint were presented at each time point for hips and knees separately. Additionally, the prevalence and overlap with hip ROA was added to the diagrams presenting knee ROA, as were the prevalence and overlap with knee ROA to the diagrams presenting hip ROA. HP and/or KP, occurring in between radiographs, were added to the diagram in the area where the subject belonged to in the last assessment before joint replacement was performed.

Results

Supplementary Fig. 1 shows the flow chart of the 1,002 included subjects. 145 Subjects were lost to follow-up. Baseline characteristics of the population are presented in Table I. At baseline, the mean age was 56 years (sd = 5) and mean BMI was 26 kg/m^2 (sd = 4).

The majority of the population was female (79%), of whom the majority was postmenopausal (77%). 59% of the study population reported hip complaints and 83% reported knee complaints. The mean total WOMAC score was 25 (sd = 16) and the mean NRS for hip and/or knee pain over the past week was 3.6 (sd = 2.1). 16% of the population fulfilled the clinical ACR criteria for hip OA and 42% fulfilled the clinical ACR criteria for knee OA. 159 subjects had ROA in at least one knee and 164 subjects had ROA in at least one hip (for distribution of ROA per time point see Supplementary file Table S2). The median duration of complaints at baseline is 14 months (range 1–240).

Course of patient-reported clinical outcomes

At baseline, 46% of the subjects reported bilateral knee pain and 21% reported bilateral hip pain. These numbers gradually decreased to 32% (95%CI 29–35) and 18% (95%CI 15–21), respectively, over the 10-year follow-up (Supplementary Table S1). A stable 13% (95%CI 11–15) of the subjects reports pain all four joints over the 10-year follow-up. The mean WOMAC pain scale remained stable, around 23 (range: 21–25) (Table II).

The other WOMAC subscales, stiffness and function, were relatively stable as well, as were NRS for pain 'in the past week', the SF-36 and the EQ-5D (Table II).

Course of clinical American College of Rheumatology (ACR) criteria

At baseline, 520 subjects (52%) fulfilled the clinical ACR criteria for knee and/or hip OA. Of these, only 91 (18% (95%CI 15–21)) fulfilled the criteria at every follow-up time point [Fig. 1(a)]. Differences are seen in fulfilment of knees and hips separately; 17% (95%CI 13–21) fulfilled the ACR criteria for knee OA and 4% (95%CI 1–7) fulfilled the ACR criteria for hip OA at all time points [Fig. 1(b) and 1(c)]. A total of 482 subjects did not fulfill the clinical ACR criteria at baseline. Of these, 138 (29% (95%CI 26–32)) never fulfilled the criteria in the 10-year follow-up. The majority of the population fulfilled the criteria (71% (95%CI 68–74)) at some time point.

Pain trajectories

Fig. 2 shows the pain trajectories in six groups with cubic variance. This model showed the best combination of fit indices. The model with three groups and cubic variance showed a similar goodness of fit, but was deemed less clinically relevant. In the six-group model, the 'always high pain trajectory' (red line, n = 176) included a high percentage of females and total joint replacements (KPs > HPs). The 'always low pain trajectory' (brown line, n = 289) included the highest percentage of subjects with only knee complaints. The 'decreasing pain trajectory' (blue line, n = 37) included the highest percentage of subjects with only hip complaints. The 'fluctuating high pain trajectories' (green and pink lines, n = 88 and n = 142, respectively) included a high percentage of females and subjects with both knee and hip complaints.

Table I
Baseline characteristics

Characteristic	N (%)
Age in years, mean (sd)	56 (5)
Females, *n* (%)	792 (79)
Post menopausal, *n* (%)	475 (77)
Caucasian, *n* (%)	976 (98)
BMI in kg/m^2, mean (sd)	26 (4)*
Academic or higher vocational education, *n* (%)	267 (28)*
Physical active (>30 min) 3 times a week or more, *n* (%)	524 (54)*
Smoking every day, *n* (%)	90 (9)*
Co-morbidity	
Chronic lung disease, *n* (%)	90 (9)*
Severe cardiac disease, or stroke, *n* (%)	18 (2)*
Hypertension, *n* (%)	198 (20)*
Diabetes mellitus, *n* (%)	35 (4)*
Back disorder, *n* (%)	172 (18)*
Neck, shoulder, elbow, wrist or hand disorder*, *n* (%)	218 (22)*
Using any pain medication, *n* (%)	372 (38)
Knee complaints any knee, *n* (%)	829 (83)
Morning stiffness any knee, *n* (%)	533 (54)
Crepitus any knee, *n* (%)	466 (47)
Joint line tenderness any knee, *n* (%)	440 (44)
Bony enlargement any knee, *n* (%)	43 (4)
Hip complaints any hip, *n* (%)	588 (59)
Morning stiffness any hip, *n* (%)	348 (36)*
Painful internal rotation any hip, *n* (%)	380 (38)
Painful flexion any hip, *n* (%)	387 (39)
Complaints in hip and knee, *n* (%)	418 (42)
Complaints only in knee, *n* (%)	414 (41)
Complaints only in hip, *n* (%)	170 (17)
WOMAC total (0–100), mean (sd)	25 (16)*
WOMAC pain (0–100), mean (sd)	25 (17)*
WOMAC function (0–100), mean (sd)	24 (17)*
WOMAC stiffness (0–100), mean (sd)	33 (21)*
NRS hip and/or knee pain past week (0–10), mean (sd)	3.6 (2.1)*
ACR criteria any hip, *n* (%)	160 (16)
ACR criteria any knee, *n* (%)	424 (42)
Highest KL score knee based on retrospective scoring, *n* (%)	
KL 0	486 (49)
KL 1	343 (34)
KL 2	157 (16)
KL 3	2 (<1)
Highest KL score hip based on retrospective scoring, *n* (%)	
KL 0	537 (54)
KL 1	290 (29)
KL 2	153 (15)
KL 3	11 (1)
Duration of complaints in months†, median	14
<6 months, *n* (%)	66 (8)
6–12 months, *n* (%)	214 (25)
12–24 months, *n* (%)	230 (26)
2 years or more, *n* (%)	363 (42)

N: number of subjects; sd: standard deviation; WOMAC: Western Ontario and McMaster Osteoarthritis Index (100 = most severe); NRS: Numerical Rating Scale (10 = most severe); KL: Kellgren & Lawrence.
* 2–3% missing.
† 13% missing.

Radiographic hip and knee OA over time

The Venn diagrams in Fig. 3 show the overlap in hip and knee ROA within subjects per follow-up moment. At baseline, 54 (5.4%) had bilateral hip ROA and 48 (4.8%) had bilateral knee ROA. At

Table II
10-year course of the subscales of WOMAC, Numeric rating scales (NRS) pain, SF36 and EQ5D

	T0	T2	T5	T8	T10
	Mean SD range	Mean SD range	Mean SD range	Mean SD range	Mean SD range
WOMAC pain	**25** 17 0–55	**23** 18 0–55	**24** 19 0–60	**21** 18 0–55	**22** 19 0–55
WOMAC stiffness	**33** 21 0–75	**31** 21 0–63	**32** 23 0–75	**29** 23 0–75	**31** 24 0–75
WOMAC function	**24** 17 1–56	**22** 18 0–59	**24** 19 0–59	**23** 19 0–59	**23** 19 0–60
NRS pain past week	**3.5** 2.1 1.0–7.0	**3.4** 2.3 0.0–7.0	**3.5** 2.4 0.0–8.0	**3.2** 2.4 0.0–7.0	**3.5** 2.5 0.0–8.0
SF36 – PCS	**43.5** 8.6 14.3–67.0	**44.4** 9.1 11.9–71.3	**44.2** 9.4 9.6–67.3	**43.5** 9.5 10.4–62.3	**42.9** 9.8 7.9–67.6
SF36 - MCS	**51.3** 8.9 8.7–67.3	**50.7** 10.1 15.5–67.8	**51.5** 9.3 7.4–71.0	**51.7** 9.5 2.8–68.7	**52.1** 9.0 3.3–68.2
EQ-5D*					
Mobility (%)	**45.1**	**41.1**	**43.7**	**43.3**	**46.4**
Self-care (%)	**3.7**	**5.1**	**7.6**	**7.9**	**7.8**
Daily (%)	**43.1**	**37.9**	**39.3**	**38.5**	**39.7**
Pain (%)	**83.5**	**80.7**	**78.1**	**77.4**	**76.0**
Mood (%)	**18.6**	**16.6**	**16.8**	**15.5**	**14.4**
Global health assessment (VAS)	**76.1** 13.0 0–100	**75.2** 13.4 12–100	**75.3** 13.8 5–100	**75.1** 13.2 0–100	**74.9** 12.8 10–100

T0 = Baseline; T2 = measurements on time-point 2 (2 years after baseline); T5 = measurements 5 years after baseline; T8 = measurements 8 years after baseline; T10 = measurements 10 years after baseline; SD = standard deviation; WOMAC = Western Ontario and McMaster Osteoarthritis Index; NRS = Numeric Rating Scale; SF36 = Short Form Health Survey (36 items); PCS = physical component summary score; MCS = Mental Component summary score; EQ-5D = EuroQol 5D; VAS = visual analogue scale (0–100).

* Percentage of people reporting problems is presented.

T10, 513 (60.4% (95%CI 57–64)) had hip ROA in at least one hip and 603 (70.9% (95%CI 68–74)) had knee ROA in at least one knee. Of those with hip ROA at T10, 270 (54.0% (95%CI 50–58)) had bilateral knee ROA. Of the subjects with knee ROA at T10, 251 (42.6% (95%CI 39–47)) had bilateral hip ROA at T10. The percentage of subjects with both knee and hip ROA increased from 4.6% at baseline to 49.4% (95%CI 46–53) at T10. Only 115 (14.3% (95%CI 12–17)) subjects did not develop knee or hip ROA. Most HPs and KPs occurred between T2 and T5 (29 HPs and 11 KPs). 41.4% of the HPs between T2 and T5 took place in subjects also having knee ROA.

Discussion

The current study shows that on average there was little to no progression of complaints during a 10-year follow-up period in a large group of subjects with early symptoms of knee and/or hip OA. More than half of the population fulfilled the clinical ACR criteria for hip or knee OA at baseline, but 14% never fulfilled the clinical ACR criteria for OA at any point over 10 years. Groups of subjects with different pain trajectories seem to exist; the largest groups being 'always high pain' and 'always low pain'. Despite slow progression of pain, 71% had knee ROA at 10-year follow-up, compared to 16% at baseline, and 60% had hip ROA at 10-year follow-up, compared to 17% at baseline. Most HPs and KPs occurred between 2 and 5-year follow-up, especially in subjects with ROA in more than one joint.

Previous longitudinal OA studies show that OA symptoms follow a relatively stable long-term course[3–8], but that subgroups of hip and knee OA patients with different pain trajectories can be distinguished[3–8]. These studies mostly identified subgroups with mild progression, fast progression, no progression, and/or improvement in pain among knee OA patients and subjects with knee pain and at risk for knee OA[4,5,7,8]. The current study confirms that pain in hip and knee OA follows a stable 10-year course. Still, LCGA did identify two groups of subjects with relatively strongly fluctuating pain (together 22% of the total number of subjects). Likewise, in another study, 18% of community-dwelling adults over 55 years with hip or knee pain reported highly unstable total WOMAC scores[19]. No subgroup with fast pain progression was identified in our study, which contrasts with other studies showing fast progression of pain in 5–28% of the subjects[6,8]. This difference might be due to differences in populations (only knee vs both knee and hip) and/or time intervals between measurements (annually, 1.5 year or 2 years). Moreover, CHECK comprises a group of relatively young subjects with early OA symptoms who had visited a GP or physician for their symptoms for the first time within 6 months or had not yet visited a GP or physician for their symptoms (although in 50% of the subjects the duration of complaints lasted more than 14 months), as opposed to most other OA cohorts of overall older subjects with more severe complaints[10,20].

The clinical ACR criteria for knee and hip OA were developed by the ACR and are often used to classify patients in clinical studies. There is not yet consensus about criteria for early knee OA. For this reason we used the ACR criteria, but the high percentage of knees of first time presenters fulfill the criteria for knee OA is remarkable. The higher proportion of subjects meeting

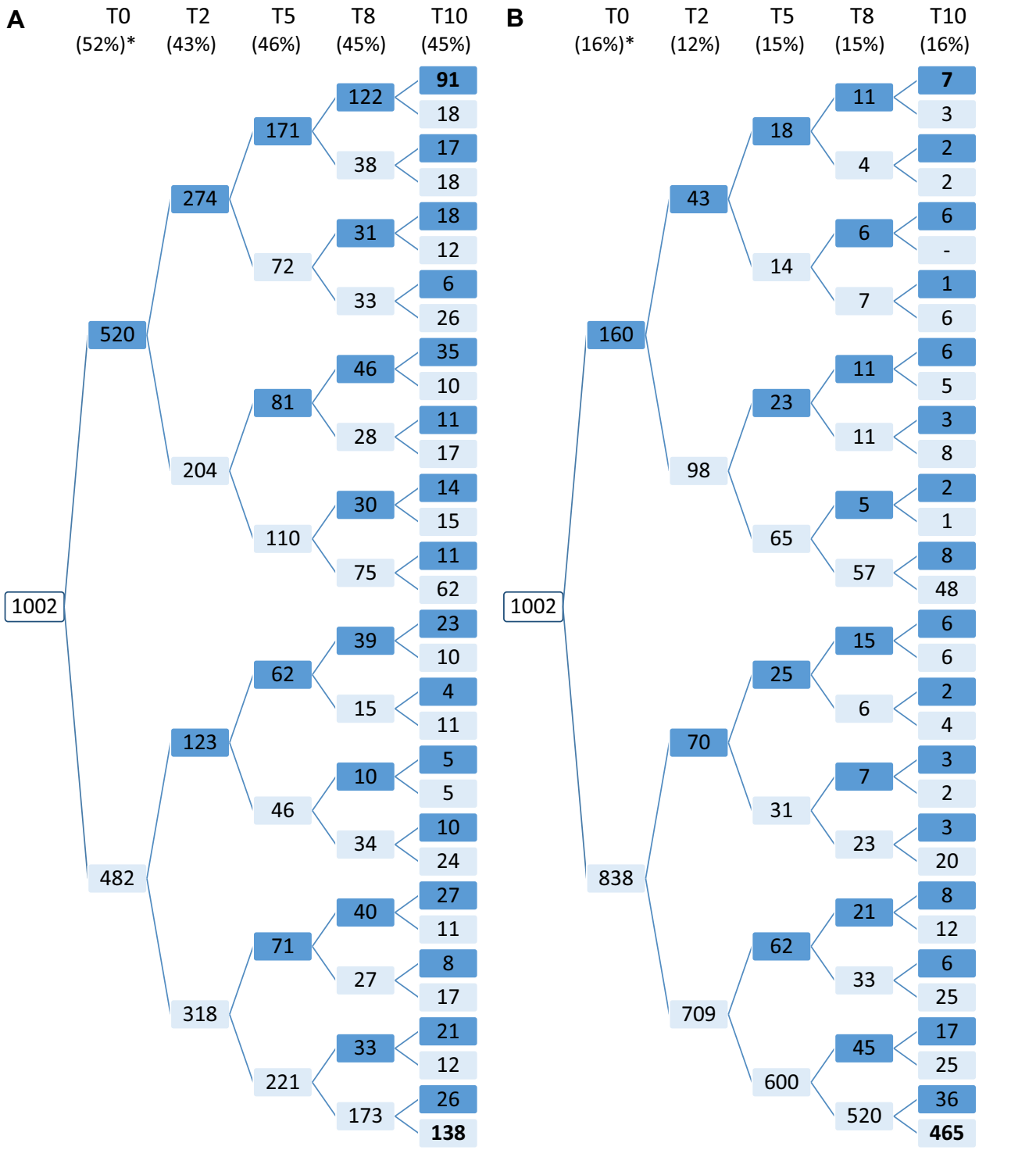


Fig. 1. a: Course of American College of Rheumatism (ACR) criteria for hip or knee OA. Dark blue = Fulfilling the ACR criteria for hip or knee OA; light blue = not fulling the ACR criteria for hip or knee OA. * Percentage of subjects fulfilling the criteria. b: Course of ACR criteria for hip OA. Dark blue = Fulfilling the ACR criteria for hip OA; light blue = not fulling the ACR criteria for hip OA. * Percentage of subjects fulfilling the criteria. c: Course of ACR criteria for knee OA. Dark blue = Fulfilling the ACR criteria for knee OA; light blue = not fulling the ACR criteria for knee OA. * Percentage of subjects fulfilling the criteria.

the ACR criteria for knee OA (42%) than for hip OA (16%) at baseline might be explained by the differences in the combination of features to meet the ACR criteria for knee and hip OA. There is a possibility that the criteria for the knee are more sensitive than the criteria for the hip in early OA. Another explanation might be that more people with hip complaints have other diagnosis than hip OA compared to people with knee complaints. The ACR criteria were applied on all patients in the current study on each

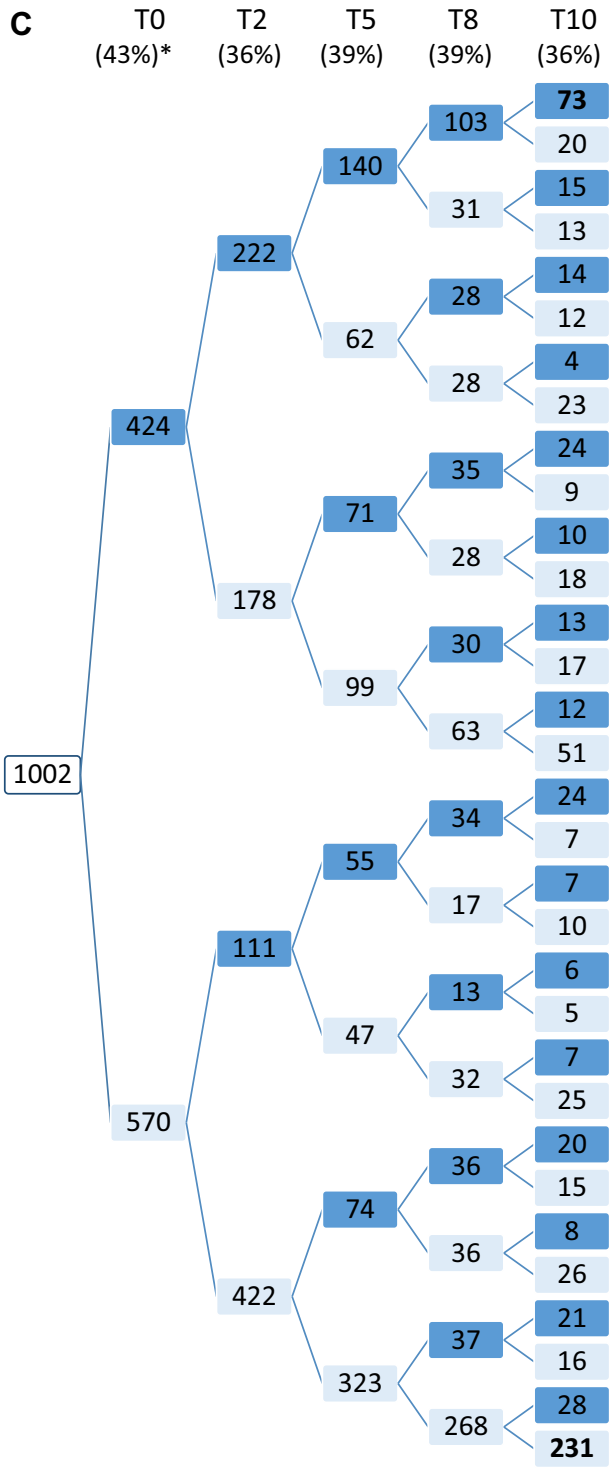


Fig. 1. (*continued*).

time point. Only 17.5% of the patients that fulfilled the criteria at baseline fulfilled the ACR criteria at every follow-up measurement. Moreover, the majority of the study population fulfilled the criteria only intermittently. Peat *et al.* already showed that the ACR criteria for knee OA seem to reflect advanced disease and not early, mild OA[21]. This is strengthened by the current study findings and questions the applicability of the ACR criteria in early OA. Yet, of the total study population, only 14% ($n = 138$) did not fulfill the ACR criteria at any of the time points. The intermittent fulfilment of the ACR criteria is likely due to the fluctuating character of pain in patients with OA[19,22–24].

CHECK subjects were included because of early hip and/or knee complaints. At baseline, almost 70% of the study population experienced pain in at least two of the four joints. Venn

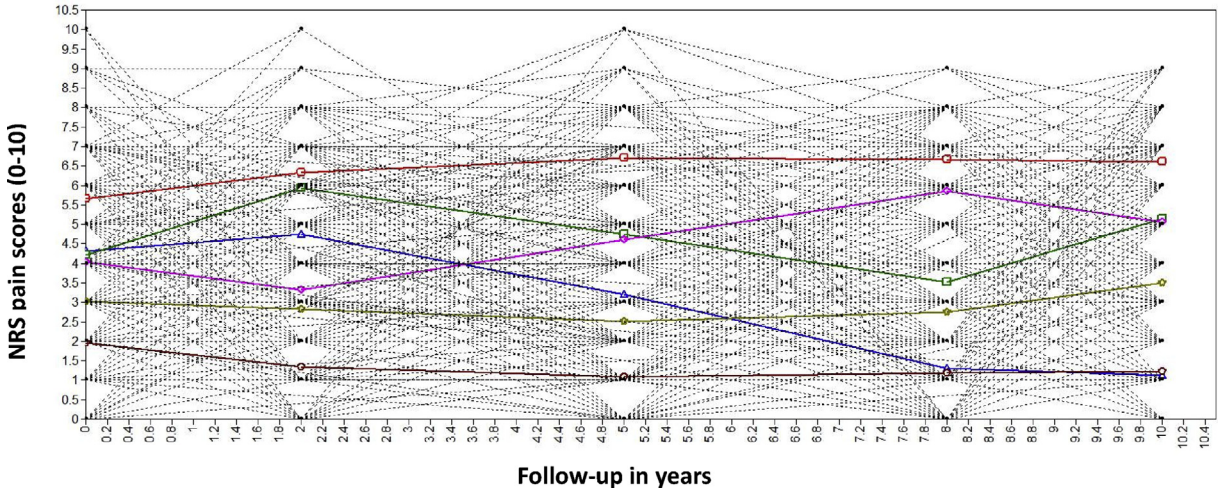


Fig. 2. Pain trajectories – 6 groups; - Always high pain trajectory associated to high percentage females and high numbers of THPs (red group); Always low pain trajectory associated to more knee only patients (brown group); Decreasing pain trajectory associated to more hip only patients (blue group); Fluctuating high pain trajectories associated to high percentage females and more knee and hip patients (green and pink groups).

diagrams showed that almost 12% of the subjects had ROA in at least two joints at baseline. The Venn diagrams also show a clear trend towards more HPs and KPs in the subjects with ROA in more than one joint. Previous studies showed similar results. In a cohort of subjects who underwent HP/KP, 82.7% had at least two troublesome hips and/or knees before HP/KP[25] and 85% reported a pain in another joint than the index knee in a knee OA cohort[26]. Both studies showed that pain in multiple joints negatively influences outcomes after HP/KP. The amount of HP and KP reflects the surgical patterns in the Netherlands[27] and is not influenced by the duration of complaints at baseline (data not shown).

Strengths and limitations

This is the first study presenting the course of early signs of knee and hip OA over 10-years. CHECK includes a rich collection of measurements, including symptomatic and radiographic measurements at relatively short-term time intervals. Additionally, the loss-to-follow-up was only 14% after 10 years. This might have been further enhanced with phone calls. Data from CHECK are, on request, available to all researchers worldwide (http://check-onderzoek.nl/). We used available data for the presented analyses. This might have affected the results but this is very unlikely since the baseline characteristics of the missing subjects were not different from the baseline characteristics of the study population with complete follow-up (Supplementary file Table S3).

Intervals between measurements in CHECK are somewhat longer (2–3 years) than in the OAI (annual measurements) and CAS-K study (1.5 year between measurements). Although the longer time intervals limit the ability to show short term dynamics in pain, the results of the present study do show a complete overview of the course of early hip and knee complaints. Another limitation is the self-reported BMI, although in the age category and BMI range of the current study population the difference between self-reported BMI and measured BMI is minimal[28].

One might argue that combining hip and knee complaints, for example in the ACR criteria and the pain trajectories is another limitation. However, as is shown by the Venn diagrams, hip and knee complaints are often intertwined. Therefore, presenting hip and knee data separately would not do justice to the complex reality of OA in clinical practice and thus the authors decided to present the results for the population as a whole.

Radiographs of baseline T2 and T5 were scored together, with known sequence (but blinded to clinical status)[9,16]. Radiographs of T5 (re-read) and T8 (new read) were scored together, with knowledge of the previous scores and previous radiographs available for the readers. T10 was scored with knowledge of all previous scores and all previous radiographs available. After T10 was scored, the chronologic order of the K&L scores over all time points was evaluated and joints where there was a decrease in K&L score over time were re-evaluated for all time points. Therefore a shift was seen in reporting the prevalence of ROA (K&L $\geq$ 2), from none of the subjects at baseline in previous scorings[9] to 17% having hip ROA and 17% having knee ROA at baseline in the present scoring. Earlier research showed that more and constant progression was measured when reading radiographs in sequence compared to random reading[29]. The shift might be due to knowledge of the 'future' definite OS or JSN, but might also be due to subjectivity of the reader.

Implications of the findings

The present study failed to identify a group that progressively worsened in complaints, but showed two groups which highly fluctuated in complaints. In-depth analysis of these groups might give some information about flares or inflammation, for example in combinations with physical examination variables, other symptoms than pain, and biochemical markers. Furthermore, the relatively high number of HPs and KPs in this early OA population was surprising given the stable pattern in pain and function during follow-up. This raises the question whether these HPs/KPs may have occurred during flare-ups of pain in these patients.

As a whole, the present study showed fairly stable pain scores over time, with some subgroups of subjects that fluctuate in pain over time. The majority fulfilled the ACR criteria for hip and/or knee OA at least once over 10 years. A large overlap in hip and knee complaints and ROA was observed. In addition, more than half of the subjects had ROA at 10-year follow-up. Numbers of joint replacements were highest in subjects developing both hip and knee ROA.

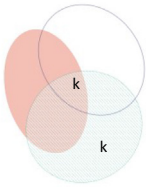
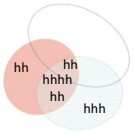
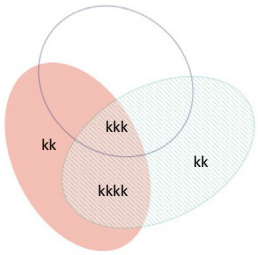
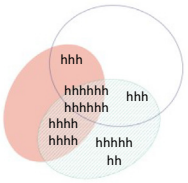
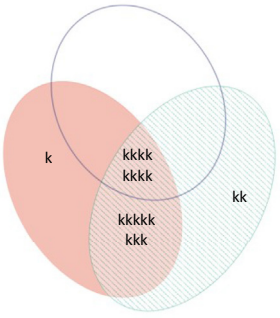
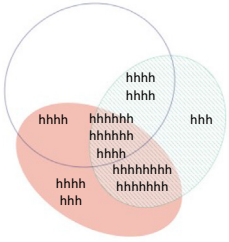
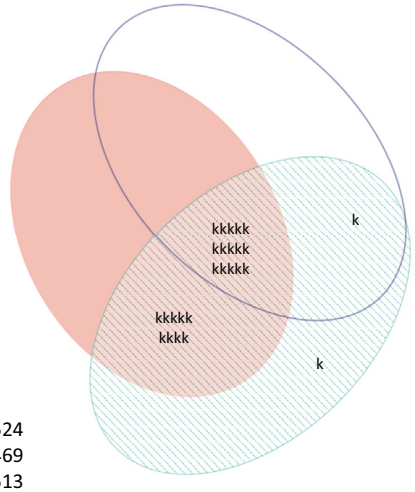
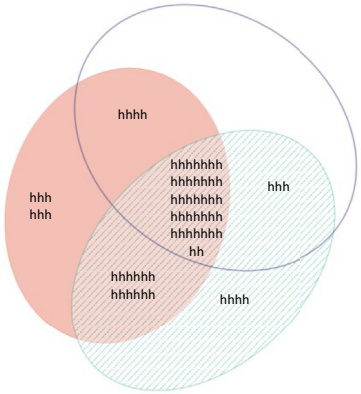
Left knee OA=orange; right knee OA=blue stripes; white=OA in at least one of both hips; k= KP	*Left hip OA =orange; right hip OA=blue stripes; white=OA in at least one of both knees; h=HP*
Baseline (N=1002) RKOA N=102 LKOA N=105 HOA N=164	 RHOA N=107 LHOA N=111 KOA N=159 
T2 (N=947) RKOA N=202 LKOA N=179 HOA N=215	 RHOA N=154 LHOA N=139 KOA N=266 
T5 (N=899) RKOA N=336 LKOA N=275 HOA N=283	 RHOA N=204 LHOA N=196 KOA N=396 
T8 (N=865) RKOA N=380 LKOA N=336 HOA N=335	 RHOA N=239 LHOA N=246 KOA N=481 
T10 (N=850) RKOA N=524 LKOA N=469 HOA N=513	 RHOA N=424 LHOA N=396 KOA N=603 

Fig. 3. Proportional Venn-diagrams showing participants with radiographic knee and/or hip OA and total knee and hip replacements. Figure shows respectively left and right knee OA with overlap of hip OA in one or two joints (left side of figure) and left and right hip OA with overlap of knee OA in one or two joints (right side of figure), including HPs and KPs in each of the (overlapping) groups; OA = osteoarthritis; HP = Hip Prosthesis; KP = Knee Prosthesis; RKOA = Right knee OA; LKOA = left knee OA; HOA = hip OA in one of both hips; RHOA = right hip OA; LHOA = left hip OA; KOA = knee OA in one of both knees.

Author contribution

DS, JR, JHW, MvM, SBZ have contributed to the concept and design of the work. DS, JR, JHW, WEvS, MvM, and SBZ have all contributed to the analysis and interpretation of the data and the drafts of the article and revising it critically. All authors approved the final version and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

DS, JR, JHW, WEvS, MvM have no competing interests.

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Supplementary data

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