Characteristics associated between the incidence of hip osteoarthritis and early hip complaints (CHECK study) within 10 years

Annemaria C. van Berkel, MD1, Dieuwke Schiphof, PhD1, Jan H. Waarsing, PhD2, Jos Runhaar, PhD1, John M. van Ochten, PhD1, Patrick J.E. Bindels PhD, professor1, Sita M.A. Bierma-Zeinstra, PhD, professor1,2

1 Department of General Practice, Erasmus Medical Center, Rotterdam, The Netherlands, 2 Department of Orthopaedics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

Correspondence:

Annemaria C. van Berkel (ORCID ID: 0000-0002-7624-3979), Erasmus Medical Center Rotterdam, Department of General Practice, room Na-1923; PO-box 2040, 3000 CB Rotterdam, the Netherlands. E-mail: a.vanberkel@erasusmc.nl

© The Author(s) 2021. Published by Oxford University Press on behalf of the British Society for Rheumatology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
ABSTRACT

Objective: To determine which baseline characteristics, especially clinically variables like pain, stiffness, physical functioning and disease variables, are associated with incident hip osteoarthritis (OA) within 10-years in first presenters with hip complaints.

Methods: Data were obtained from the nationwide prospective Cohort Hip and Cohort Knee (CHECK) study (n=1002). Incident hip OA was defined as fulfilling the clinical ACR criteria for hip OA, a Kellgren and Lawrence score ≥2 with hip pain, or received a hip replacement during follow-up. Baseline measurements were used of participants with hip complaints and without hip OA. Principal component analysis (PCA) was used to reduce the number of correlated variables. Associations between baseline characteristics (including PCA components) and incident hip OA were investigated using logistic regression analysis, adjusted for age, sex and BMI.

Results: In total 312 participants (85% female and 98% Caucasian) were included, 181 developed hip OA. PCA resulted in four components. Incident hip OA was associated with i) component 1 [general presence of pain and symptoms] [OR=1.46 (95%CI 1.08-1.98)], ii) component 3 [relatively high levels of pain during shopping/walking combined with less difficulty with putting socks on/off and rising from bed] [OR=1.58 (95%CI 1.18-2.12)] and iii) knee pain [OR=0.34 (95%CI 0.17-0.66)].

Conclusion: In first presenters with hip complaints, use of a few history taking variables might allow better recognition of those at higher odds for incident hip OA within 10-year.

Keywords: hip osteoarthritis; hip pain; primary health care; cohort study; WOMAC
Key messages:

1) History taking and not physical exam variables are associated with incident hip osteoarthritis.

2) Specific questions about daily life activities are associated with incident hip OA.

3) These questions are about pain while walking/shopping, difficulties putting socks on/off and rising from bed.
Introduction

Osteoarthritis (OA) of the hip is increasing in the Western society. In the Netherlands in 2017, 31,200 patients were newly diagnosed with hip OA and 431,400 were registered with OA of the hip (prevalence: 25.15 per 1,000 persons) (1). This number will increase with further ageing of the population (2). The number of patients with any type of OA is estimated to increase to 41% in 2040 (1). Although most patients with hip complaints (such as pain or stiffness) are diagnosed and treated in primary care, general practitioners (GPs) and other primary care practitioners, e.g. physiotherapists, currently lack evidence-based tools to enable them to predict the prognosis of early hip complaints. Better knowledge of the progression of early hip OA has the potential to improve effective management. Variables reported to predict hip OA progression leading to hip replacement (HR) include severe pain, disability, and restriction in range of motion (particularly internal rotation) (3, 4). However, it remains unknown which hip complaints represent the early symptoms of hip OA.

A widely used and disease-specific standardized questionnaire for hip (and knee) OA is the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (5). This instrument evaluates symptomatology (pain, stiffness) and physical function. Time to complete this questionnaire is approximately 12 min and interpretation takes around 5-10 min (6). However, a GP may lack time to complete the WOMAC for each person with hip complaints; moreover, the score cannot be used as a diagnostic tool. The question arose whether it would be possible to use only a few WOMAC items, together with other anamnestic and physical examination measurements, to identify persons at higher odds for incident hip OA.
Therefore, in the present study we aimed to identify baseline characteristics (demographic, history taking (including WOMAC-questions) and physical examination measurements) which are associated with the incidence of hip OA (occurring within 10 years) among first presenters with hip complaints, but free of hip OA at presentation.

Methods

General design

Data for this study were derived from the Cohort Hip and Cohort Knee (CHECK) study; details on this cohort are published elsewhere (7). In short, the CHECK study is a prospective, 10-year follow-up cohort in the Netherlands of 1,002 first presenters with hip and/or knee complaints. Individuals entered the cohort between October 2002 and September 2005.

Inclusion criteria for the CHECK study were: i) stiffness and/or pain of the knee and/or hip, ii) aged 45-65 years, and iii) participants had not yet consulted their GP for these symptoms, or iv) the first consultation was within 6 months before entry. Exclusion criteria were: i) other pathological conditions that could explain the existing complaints, such as other rheumatic disease (e.g. rheumatoid arthritis, ankylosing spondylitis, infectious arthritis and polymyalgia rheumatica), previous hip/knee joint replacement, congenital dysplasia, osteochondritis dissecans, intra-articular fractures, septic arthritis, Perthes’ disease, ligament or meniscus damage, plica syndrome or Baker’s cyst, ii) co-morbidity that would not allow physical evaluation during the 10-year follow-up, iii) malignancy in the past 5 years, and iv) inability to understand the Dutch language. Details for follow-up rate for each follow-up visit are published elsewhere (8). The Medical Ethics committees of all participating centres approved the study and all participants gave written informed consent.
Determinants

Information on pain and other hip symptoms, physical functioning of the lower limb, comorbidity, quality of life, and psychosocial factors was collected by using (self-reported) questionnaires and physical examination. Demographic variables used were age, sex, ethnicity, height and weight to calculate body mass index (BMI), education level, alcohol use, smoking, use of pain medication (none, paracetamol, aspirin, non-steroid anti-inflammatory drug, other), and number of times a week participants were physically active for at least 30min. The number of comorbidities was defined by the presence of self-reported complaints: asthma, chronic sinusitis, cardiovascular disease, high blood pressure, gastric ulcer, gallstones, liver disease, renal disease, diabetes, chronic cystitis, prolapse (only women), thyroid gland disease, epilepsy, cancer, migraine, vertigo, severe skin disease, and other chronic musculoskeletal diseases (including lower back pain). The WOMAC questionnaire was used to measure stiffness, pain, and physical functioning, with a higher score indicating worse health.

The following additional questions were also used to assess pain and physical functioning: i) pain level getting in/out of a car, during shopping, during heavy physical activities (range 0-5; higher scores indicating more pain); ii) difficulty with walking 1 km, walking 2 km, taking a shower, heavy activities, ascending/descending stairs while carrying something, and keeping up with others (range 0-5; higher scores indicating more difficulty). Pain in the most affected joint during the previous week was assessed with a numeric rating scale (NRS) for pain (range 0-10; higher scores indicating more pain). During physical examination the participants were asked if they had morning stiffness of the hip, hip pain and knee pain, and pain during internal rotation of the hip; the degree of flexion and internal rotation of the hip was measured using a goniometer (9).
**Outcome variables**

Clinical hip OA was determined according to the clinical American College of Rheumatology (ACR) criteria: hip pain and all of the following criteria under [1] or [2]: [1] hip internal rotation ≥15°, pain present with internal rotation of the hip, morning stiffness of the hip ≤60 min, and age >50 years; [2] hip internal rotation <15°, and hip flexion ≤115° (10).

In addition, at baseline and at 2, 5, 8 and 10 years, standardized radiographs were taken in anteroposterior view, pelvic view or unilateral faux profile view of the hips. Radiographs were centrally scored according to the Kellgren and Lawrence (K&L) criteria (11). Radiographs taken at 2, 5, 8 and 10-year follow-up were scored retrospectively and with known sequence. In the hip all radiograph features showed good inter-observer reliability (0.71-0.91) (12). Radiographic hip OA (ROA) was defined as K&L score ≥2. During each follow-up moment hip pain was asked (yes/no), we defined hip pain if a participants answered this question with yes. Information on HR was obtained from the radiographs. In this study, (incident) hip OA was defined as one or more of the following three definitions: 1) fulfilling the clinical ACR criteria for hip OA (ACR-group); 2) having ROA together with hip pain (ROA&pain-group), or 3) having received a HR during follow-up (HR-group).

**Study population**

At baseline, participants who reported hip pain without hip OA (according to the definitions above) were included in the analysis. Participants with missing data on hip OA status at baseline or at 10-year follow-up or participants who met one of our hip OA criteria at baseline were excluded. Subgroups were defined based on the hip OA definitions.
**Statistical analysis**

Descriptive statistics were used to describe baseline characteristics of the study population. Principal component analysis (PCA) was used to reduce the number of variables that were correlated (13). It creates new variables (components) which are a linear combination of the “most important” variables in the original dataset. The principle components are the underlying structure in the data. An Eigen value is a number, explaining how much variance there is in the data in that direction. The Eigenvector with the highest Eigen value is therefore the first component. The variance explained reflects an amount of questions which are represented into this component (13). One could say the each PC ‘groups’ together variables that are correlated. Each WOMAC question, self-reported NRS score for pain (previous week), and pain and physical functioning-related outcomes [patient-reported outcomes measurements (PROM)] were entered in the PCA. Components with Eigen values >1 were selected.

Univariate multinomial logistic regression analysis was used to test whether the baseline variable (the components (created by PCA), using any pain medication, comorbidities, variables obtained during physical examination, age, BMI and sex) was associated with incidence of hip OA and to obtain crude odds ratios (OR). All variables from the univariate analyses with P<0.20 were included in a multivariate multinomial logistic regression model (BMI, age and sex added as confounder) to analyse the independent association between the baseline variables and the incidence of hip OA. Non-significant (p>0.05) covariates were removed via backward stepwise elimination until significant variables (p<0.05) and the confounders remained in the final model. To prevent overfitting of our main model, we used the rule of thumb that logistic models should be used with a minimum of 10 outcome events per variable (14). The ORs represent the odds that the outcome (incident hip OA) will be
present in the participants with the particular variable at baseline, compared to the outcome in the participants without the particular variable at baseline. The same steps and exactly the same analyses were used for each of the OA outcomes separately for the ACR-group, the ROA&pain-group, and for the HR-group. Statistical analyses were performed using SPSS version 24.0 for Windows (SPSS Inc).

**Results**

Of all participants in the CHECK study, 588 reported hip pain at baseline. Of those 588 participants 358 did not have hip OA (eligible participants), 222 met our hip OA criteria, and 8 had missing data at baseline. Of the 358 eligible participants, 312 had available data on hip OA status at the 10-year follow-up (Figure 1). Table 1 presents the characteristics of the study population (n=312). At baseline, mean age was 54.9 (SD 5.4) years, mean BMI was 26.1 (SD 3.9) kg/m², 84.9% was female and 98% was Caucasian (Table 1). Of the 312 participants, 131 did not meet any of our OA criteria at any time point and 181 developed hip OA during the 10-year follow-up (Figure 1). In addition, 10 (3%) participants met all 3 of our definitions and 43 (10%) participants met 2 of our definitions during follow-up (Supplementary Figure S1). Noteworthy is the small cross over between the ACR-group and the ROA&pain-group.

**Separate outcomes**

**ACR-group:** of the 588 participants, 424 did not fulfil the clinical hip OA criteria at baseline, 160 participants met the ACR criteria, and 4 participants had missing data. Of the 424 eligible participants, 350 had available data on clinical hip OA status at 10-year follow-up (Supplementary Figure S2). At baseline, mean age was 55.0 (SD 5.3) years, mean BMI was
26.2 (SD 3.9) kg/m² and 82.6% was female (Supplementary Table S1). During follow-up, 144 fulfilled the clinical hip OA criteria (41.1%) (Supplementary Figure S2).

**ROA & pain-group**: of the 588 participants, 472 did not have ROA at baseline, 110 had ROA, and 8 had no radiograph of the hips. Of the 472 eligible participants, 388 had available data on ROA and hip pain at 10-year follow-up (Supplementary Figure S3). At baseline, mean age was 55.2 (SD 5.2) years, mean BMI was 26.3 (SD 4.2) kg/m², and 86.1% was female (Supplementary Table S1). During follow-up, 144 participants (37.1%) had ROA combined with hip pain (Supplementary Figure S3).

**HR-group**: of the 588 participants, two participants had missing radiograph (Supplementary Figure S4). At baseline, mean age was 55.8 (SD 5.3) years, mean BMI was 26.1 (SD 4.0) kg/m², and 80.8% was female (Supplementary Table S1). Of the 584 participants without a HR at baseline, 69 (11.7%) had a HR during follow-up (Supplementary Figure S4).

**Principal component analysis**

As expected, scores on the WOMAC, answers to the additional questions used to assess pain/physical functioning, and the NRS pain score were highly correlated (data not shown). PCA was performed to reduce the number of the correlated variables. Four components had an “Eigen value” ≥1 (Supplementary Table S2). All the WOMAC questions, questions used to assess pain/physical functioning and the NRS pain score were included in the first component (general presence of pain and symptoms), explaining 56% of the variance (Eigen value=19.7). The second component explained 5% of the variance (Eigen value=1.8). Participants with a positive value component 2 had relatively high levels of pain during rest (pain resting, pain lying in bed and nocturnal pain) and relatively more difficulty lying in bed,
together with less difficulty during climbing stairs while carrying something. Participants with negative values for component 2 had relatively more difficulty climbing stairs while carrying something compared to pain during rest and difficulty lying in bed. The third component also explained 5% of the variance (Eigen value=1.7). Participants with positive values for component 3 had relatively high levels of pain during shopping/walking combined with less difficulty with putting socks on/off and rising from bed. Participants with negative values for component 3 had relatively more difficulty with putting socks on/off and rising from bed compared to pain during shopping/walking. The fourth and last component, explaining 3% of the variance (Eigen value=1.2), was specifically attributable to pain during climbing stairs.

*Variables associated with incident hip OA*

The univariate and the final multivariate associations for incidence of hip OA within 10 years are presented in Table 2. Factors associated with incidence of hip OA were component 1 [OR=1.46 (95%CI 1.08-1.98)] and component 3 [OR=1.58 (95%CI 1.18-2.12)]. The presence of knee pain was protective for incident hip OA [OR=0.34 (95%CI 0.17-0.66)] (Table 2).

*Separate outcomes:* Age was associated with incidence of ROA&p [OR=1.09 (95%CI 1.04-1.15)] and with receiving a HR (HR-group) [OR=1.07 (95%CI 1.01-1.14)], but not with incidence of clinical hip OA (ACR-group) [OR=1.00 (95%CI 0.94-1.04)]. Component 3 was associated with incidence of clinical hip OA (ACR-group) [OR=1.59 (95%CI 1.21-2.09)] and with ROA&p [OR=1.36 (95%CI 1.04-1.78)], but not with receiving a HR. Similar to the main analysis, knee pain was negatively associated with clinical OA, ROA combined with hip pain and receiving a HR: [OR=0.42 (95%CI 0.23-0.79), [OR=0.42 (95%CI 0.23-0.79)] and [OR=0.23 (95%CI 0.12-0.44)], respectively. Similar to the main analysis, component 1 was associated with clinical OA and receiving a HR: [OR=1.62 (95%CI 1.23-2.14)] and [OR=1.85 (95%CI 1.34-
Component 2 was only associated with receiving a HR [OR=1.64 (95%CI 1.19-2.25)]. The number of comorbidities was negatively associated with receiving a HR [OR=0.55 (95% CI 0.40-0.75)]. Furthermore, flexion $<115^\circ$ was positively associated with incident ROA & pain [OR=1.76 (95%CI 1.01-3.07)]. Univariate and final multivariate associations for the incidence of the separate outcomes within 10 years are presented in Supplementary Tables S4-S6.

Discussion

This study is one of the first to describe which baseline variables are associated with incidence of hip OA during a 10-year follow-up in first presenters with hip complaints in primary care. The PCA analysis showed that the data may be reduced to four independent underlying dimensions (components). In this cohort study it was observed that component 3 was positively associated with incidence of hip OA in first presenters with hip complaints when the different definitions of hip OA were combined. Component 3 could be interpreted as follows: participants with positive values have relatively high levels of pain during shopping/walking combined with less difficulty with putting socks on/off and rising from bed; participants with negative values have relatively more difficulty with putting socks on/off and rising from bed compared to pain during shopping/walking.

Comparison of main findings with other studies

To the best of our knowledge, no previous studies in primary care have examined the association between baseline characteristics (history taking, WOMAC questions and physical examination) and incident hip OA as outcome measurement. Studies on incident hip OA are scarce. Most studies have examined associations between history taking or physical
examination variables and progression of hip OA. Those studies showed that restrictions in movement (range of motion), particularly internal rotation, are predictors for progression of hip OA (4, 15).

Decades ago, studies showed that in general most diagnoses were made based on history taking, (16, 17) and that physical examination and laboratory tests made a smaller contribution to the diagnosis. The studies reported that the physicians’ confidence in the correct diagnosis increased after physical examination and laboratory tests, but led to fewer diagnoses. The present study showed that mainly the patients’ history variables are associated with incident hip OA, compared to physical examination variables. No association was found between elements of physical examination and incident hip OA; this is in line with others (16, 17). An earlier study examined the functional impact of hip pain in older persons and found that those reporting hip pain were more likely to report disability in shopping than persons without hip pain (18). Our finding of an association between component 3 and incident hip OA is in line with this. Also, our finding that fewer comorbidities and higher age are associated with receiving a HR is also in line with others. Better health and higher age are reported to be associated with a greater probability of undergoing total joint replacement (19). Persons with fewer comorbidities are more likely to have an operation, because they have a better long-term outcome after HR (20). Older age and number of comorbidities were also associated with the risk of an adverse event or complication (21).

**Interpretation main results**

Independent associations were found for component 1 (general presence of pain and symptoms) and component 3 with incident hip OA. This can indicate that asking more specific questions, is just as good as asking all questions about general presence of pain and
symptoms. Because of the amount of questions represented in component 1, GPs probably will prefer the feasible limited number of questions from component 3. Component 3 included questions about making a painful movement with the hip, i.e. internal rotation combined with flexion, which might be important for diagnosing hip OA (22). The contrast in the component is worth consideration: if a participant has a relatively high level of pain during shopping/walking and has (relatively) no difficulty putting socks on/off and rising from bed, that participant is at increased odds on incident hip OA during the 10-year follow-up. Component 3 can also be interpreted as follows: participants with a negative value (thus, participants with relatively more difficulty putting socks on/off and rising from bed, compared to their relative pain levels during walking/shopping) are protected against incident hip OA. However, the mechanisms underlying the association between component 3 and incident hip OA (or related outcomes) remains unclear. We can speculate on the mechanism that pain during walking is prodromal symptom of hip OA and that difficulty with putting socks on is a symptom of later stage OA, which is in line with earlier research on knee OA (23). Further research is needed to explain the mechanisms of this component. In the HR-group, the association between component 2 (have relatively higher levels of rest pain and relatively more difficulty lying in bed combined with less difficulty with climbing stairs while carrying something) and receiving a HR, might be explained by the fact that having rest pain is often an indication for the need for a HR (24). The negative association of the presence of knee pain at baseline with incident hip OA, and in all sub analyses, might be explained as pain in the hip due to (future) knee OA or knee complaints. Therefore, those participants with hip pain at baseline might develop knee OA, and not hip OA, within 10 years. All of our results need to be validated in another separate but similar population before they can be useful in clinical applications as real prognostic factors.
Strengths and weaknesses

The strengths of this study include its prospective population-based design with a large number of participants from 10 centres across the Netherlands, indicating that the CHECK population is highly representative for patients with (very) early onset of hip OA in primary care (25). Also, the richness of data and possibility to identify hip OA with different definitions is a strength. However, there are also some limitations. Although participants were asked where the pain was located (knee and/or hip; left and/or right), they were not asked to specify for which joint they filled in the NRS and the WOMAC questionnaire.

Although we aimed to minimize this limitation by selecting only those participants reporting hip pain (with/without knee pain) at baseline, hip pain may not have been the main problem. Finally, the model of incident HR might be over-fitted, i.e. although this HR-group included only 69 cases, we decided to use the same variables in this model as in the other three models. Our study sample contained mainly females (about 80%) and Caucasian participants, which might be due to the way of recruitment (26). The majority of females implies that our model is mainly built on female participants. Restricting the analysis to females only yielded a similar model. For men, however, the sample was too small to build a separate model.

In conclusion, a few variables obtained from history taking were associated with incident hip OA, specific questions representing the components: Do you have pain during walking/shopping, do you have difficulty putting on/off socks, and do you have difficulty rising from bed). When a person reports pain during shopping/walking and does not (yet) have difficulty rising from bed and putting socks on/off, the primary care practitioner might be alerted to these early symptoms of hip OA and treat and monitor the patient accordingly.
However, the prognostic factors need to be validated in a separate but similar cohort of patients.
Acknowledgements and affiliations:

The authors thank all participants of the CHECK cohort and all collaborators from the different sites for their valuable contribution. CHECK is funded by the Dutch Arthritis Association and is led by a steering committee comprising 16 members with expertise in different fields of osteoarthritis chaired by Professor JWJ Bijlsma and coordinated by J Wesseling. Involved are: Erasmus MC University Medical Center Rotterdam; Academic Hospital Maastricht; Jan van Breemen Institute/VU Medical Center Amsterdam; Kennemer Gasthuis Haarlem; Martini Hospital Groningen/Allied Health Care Center for Rheumatology and Rehabilitation Groningen; Medical Spectrum Twente Enschede/Twenteborg Hospital Almelo; St Maartenskliniek Nijmegen; Leiden University Medical Center; University Medical Center Utrecht; and Wilhelmina Hospital Assen.

This work was previously presented at OARSI 2019: A.C. Berkel van, D. Schiphof, J. Waarsing, J. Runhaar, J. van Ochten, P. Bindels, S. Bierma-Zeinstra. Characteristics associated with incidence of hip osteoarthritis within 10 years in people with early hip complaints in the check study. 2019. DOI: https://doi.org/10.1016/j.joca.2019.02.107

Authors’ contributions

AB, DS, SBZ contributed to the conception and design of this study. AB, DS, JW and SBZ contributed to the analysis of data. All authors contributed to the interpretation of data. Article draughts were written by AB and critically revised by all authors. The final version of the article was approved by all authors.

Role of funding

CHECK is funded by the Dutch Arthritis Foundation.
Competing interests

The authors have declared no competing interests.

Data availability statement

Datasets analysed during the current study are available from the corresponding author on reasonable request.
References

1. Volksgezondheidenzorg. Dutch Public Health and Health Care; [updated 2019. Available from: https://www.volksgezondheidenzorg.info/onderwerp/artrose/cijfers-context/huidige-situatie#node-prevalenti-en-aantal-nieuwe-gevallen-van-artrose
2. Neogi T, Zhang Y. Epidemiology of osteoarthritis. Rheum Dis Clin North Am. 2013;39(1):1-19.
3. 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;53(486):26-30.
4. 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;57(8):1368-74.
5. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol. 1988;15(12):1833-40.
6. Rheumatology ACo. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [updated 2015. Available from: https://www.rheumatology.org/I-Am-A/Rheumatologist/Research/Clinician-Researchers/Western-Ontario-McMaster-Universities-Osteoarthritis-Index-WOMAC.
7. Wesseling J, Boers M, Viergever MA, Hilberdink WK, Lafeber FP, Dekker J, et al. Cohort Profile: Cohort Hip and Cohort Knee (CHECK) study. Int J Epidemiol. 2016;45(1):36-44.
8. Schiphof D, Runhaar J, Waarsing JH, van Spil WE, van Middelkoop M, Bierma-Zeinstra SMA. The clinical and radiographic course of early knee and hip osteoarthritis over 10 years in CHECK (Cohort Hip and Cohort Knee). Osteoarthritis Cartilage. 2019;27(10):1491-500.
9. Norkin CC. Measurement of joint motion: a guide to goniometry: F.A. Davis Company; 1995.
10. Altmann 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;34(5):505-14.
11. Bierma-Zeinstra S, Bohnen A, Ginai A, Prins A, Verhaar J. Validity of American College of Rheumatology criteria for diagnosing hip osteoarthritis in primary care research. J Rheumatol. 1999;26(5):1129-33.
12. Damen J, Schiphof D, Wolde ST, Cats HA, Bierma-Zeinstra SM, Oei EH. Inter-observer reliability for radiographic assessment of early osteoarthritis features: the CHECK (cohort hip and cohort knee) study. Osteoarthritis Cartilage. 2014;22(7):969-74.
13. Stevens J. Applied Multivariate Statistics for the Social Sciences, Sixth Edition: Taylor & Francis Ltd; 2016.
14. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996;49(12):1373-9.
15. Birrell F, Croft P, Cooper C, Hosie G, Macfarlane G, Silman A, et al. Predicting radiographic hip osteoarthritis from range of movement. Rheumatology (Oxford). 2001;40(5):506-12.
16. Hampton JR, Harrison MJ, Mitchell JR, Prichard JS, Seymour C. Relative contributions of history-taking, physical examination, and laboratory investigation to diagnosis and management of medical outpatients. Br Med J. 1975;2(5969):486-9.
17. Peterson MC, Holbrook JH, Von Hales D, Smith NL, Staker LV. Contributions of the history, physical examination, and laboratory investigation in making medical diagnoses. West J Med. 1992;156(2):163-5.
18. Cecchi F, Molino-Lova R, Di Iorio A, Conti AA, Mannoni A, Lauretani F, et al. Measures of physical performance capture the excess disability associated with hip pain or knee pain in older persons. J Gerontol A Biol Sci Med Sci. 2009;64(12):1316-24.
19. Hawker GA, Guan J, Croxford R, Coyte PC, Glazier RH, Harvey BJ, et al. A prospective population-based study of the predictors of undergoing total joint arthroplasty. Arthritis Rheum. 2006;54(10):3212-20.
20. Gandhi R, Dhotar H, Davey JR, Mahomed NN. Predicting the longer-term outcomes of total hip replacement. J Rheumatol. 2010;37(12):2573-7.
21. Dowsey MM, Liew D, Stoney JD, Choong PF. The impact of obesity on weight change and outcomes at 12 months in patients undergoing total hip arthroplasty. Med J Aust. 2010;193(1):17-21.
22. Cibulka MT, White DM, Woehrle J, Harris-Hayes M, Enseki K, Fagerson TL, et al. Hip pain and mobility deficits—hip osteoarthritis: clinical practice guidelines linked to the international classification of functioning, disability, and health from the orthopaedic section of the American Physical Therapy Association. J Orthop Sports Phys Ther. 2009;39(4):A1-25.
23. Case R, Thomas E, Clarke E, Peat G. Prodromal symptoms in knee osteoarthritis: a nested case-control study using data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2015;23(7):1083-9.
24. Dreinhofer KE, Dieppe P, Sturmer T, Grober-Gratz D, Floren M, Gunther KP, et al. Indications for total hip replacement: comparison of assessments of orthopaedic surgeons and referring physicians. Ann Rheum Dis. 2006;65(10):1346-50.
25. Holla JF, Steultjens MP, van der Leeden M, Roorda LD, Bierma-Zeinstra SM, den Broeder AA, et al. Determinants of range of joint motion in patients with early symptomatic osteoarthritis of the hip and/or knee: an exploratory study in the CHECK cohort. Osteoarthritis Cartilage. 2011;19(4):411-9.
26. Manjer J, Elmstahl S, Janzon L, Berglund G. Invitation to a population-based cohort study: differences between subjects recruited using various strategies. Scand J Public Health. 2002;30(2):103-12.
Figure 1. Systematic overview of the study cohort. Of the total cohort (n=1002), at baseline 588 reported hip pain. OA+ indicates meeting at least one of the following criteria: 1) the clinical ACR criteria, 2) ROA together with hip pain, or 3) received HR and OA- indicates that none of the criteria were met for hip OA. In total, 181 participants developed hip OA during follow-up.
| Baseline characteristics                                    | Total included group at baseline at risk for incident hip OA | After 10-years follow-up incident hip OA | After 10-years follow-up no incident hip OA |
|--------------------------------------------------------------|--------------------------------------------------------------|------------------------------------------|-------------------------------------------|
| Number of participants                                      | 312                                                         | 181                                      | 131                                       |
| Age (years)                                                 | 54.9±5.4                                                   | 55.1±5.7                                 | 54.6±4.9                                  |
| Female (n, %)                                                | 265 (84.9)                                                 | 149 (82.3)                               | 116 (86.1)                                |
| Caucasian (n, %)                                            | 307 (98.4)                                                 | 177 (97.8)                               | 130 (99.2)                                |
| Body mass index (kg/m²)                                     | 26.2±3.9 ▲▲ ▲                                           | 26.5±3.9 ▲▲ ▲                           | 25.7±4.1 ▲                               |
| Education level (n, %)                                      |                                                             |                                          |                                            |
| Primary                                                     | 53 (17.5)                                                 | 33 (19.1)                                | 20 (15.5)                                 |
| Secondary                                                   | 137 (45.4)                                                 | 88 (50.9)                                | 49 (38.0)                                 |
| High                                                        | 112 (37.1)                                                 | 52 (30.1)                                | 60 (46.5)                                 |
| Smoke(d) every day (n, %)                                   | 134 (42.9) ▲▲ ▲                                          | 82 (46.6) ▲                               | 52 (40.9) ▲                               |
| Use of alcohol (n, %)                                       | 242 (80.1) ▲                                              | 139 (79.0) ▲                             | 103 (81.7) ▲                             |
| Use of any pain medication (n, %)                           | 128 (42.0) ▲                                              | 83 (47.2) ▲                              | 45 (34.4) ▲                               |
| Number of comorbidities                                     | 1.6±1.4 ▲▲ ▲                                              | 1.7±1.6 ▲                               | 1.4±1.3 ▲                                 |
| NRS pain (0-10) past week                                  | 3.5±2.1 ▲▲ ▲                                             | 3.9±2.1 ▲▲ ▲                            | 2.4±1.8 ▲                                 |
| NRS pain (0-10) this moment                                | 3.0±2.0 ▲                                              | 3.5±2.0 ▲▲ ▲                            | 3.0±2.1 ▲                                 |
| Morning stiffness hip<60min(n,%)                            | 134 (42.9) ▲                                              | 85 (47.0)                                | 49 (37.4)                                 |
| Knee pain (n, %)                                            | 230 (73.7)                                                | 125 (69.1)                               | 105 (80.2)                                |
| Physically active (>30 min) ≥3 times/week (n, %)            | 161 (53.8) ▲▲ ▲                                         | 91 (52.3) ▲▲ ▲                         | 70 (56.0) ▲▲ ▲                           |
| WOMAC                                                       |                                                             |                                          |                                            |
| - Pain (0-20)                                               | 5.0±3.2 ▲▲ ▲                                             | 5.6±3.2 ▲▲ ▲                           | 4.2±3.1 ▲                                 |
| - Stiffness (0-8)                                          | 2.6±1.7 ▲▲ ▲                                             | 2.9±1.7 ▲▲ ▲                           | 2.3±1.6 ▲                                 |
| - Physical function (0-68)                                 | 15.7±11.3 ▲▲ ▲                                          | 18.2±11.7 ▲▲ ▲                         | 12.3±10.0 ▲▲ ▲                          |
| -Standardized total score (0-100)                          | 24.2±15.9 ▲▲ ▲                                          | 27.6±16.3 ▲▲ ▲                         | 19.6±14.1 ▲▲ ▲                          |
| Physical examination                                       |                                                             |                                          |                                            |
| Painful internal rotation either hip (n, %)                 | 116 (37.5) ▲                                             | 74 (41.1) ▲                              | 42 (32.6) ▲                               |
| Flexion <115° either hip (n, %)                             | 137 (43.9) ▲                                             | 88 (48.6)                                | 49 (37.4) ▲                               |

Values are: mean ± standard deviation, median (IQR) or percentage, IQR = interquartile range or number and present percentages %. NRS = Numeric Rating Scale. WOMAC = Western Ontario and McMaster osteoarthritis index. ▲ 1-5 participant missing, ▲▲ 6-14 participants missing, * not normally distributed.
Table 2. Univariate and multivariate analysis for the association with incident hip OA within 10-year follow-up.

|                  | Univariate analysis | Multivariate analysis |
|------------------|---------------------|-----------------------|
|                  | OR      | CI (95%)  | P-value | OR      | CI (95%)  | P-value |
| BMI              | 1.06    | 1.00-1.12 | 0.08    | 1.02    | 0.95-1.09 | 0.66    |
| Age              | 1.01    | 0.97-1.06 | 0.50    | 1.04    | 0.99-1.10 | 0.15    |
| Female           | 0.60    | 0.31-1.16 | 0.13    | 0.68    | 0.32-1.42 | 0.30    |
| Number of comorbidities | 1.18    | 1.00-1.39 | 0.05    |         |          |         |
| Use of any pain medication | 1.66    | 1.04-2.66 | 0.03    |         |          |         |
| Component 1      | 1.35    | 1.02-1.78 | 0.04    | 1.46    | 1.08-1.98 | 0.01    |
| Component 2      | 1.14    | 0.87-1.51 | 0.33    |         |          |         |
| Component 3      | 1.39    | 1.07-1.82 | 0.02    | 1.58    | 1.18-2.12 | <0.01   |
| Component 4      | 1.07    | 0.83-1.38 | 0.63    |         |          |         |
| Morning stiffness hip | 1.48    | 0.94-2.34 | 0.09    |         |          |         |
| Pain knee        | 0.55    | 0.32-0.94 | 0.03    | 0.34    | 0.17-0.66 | <0.01   |
| Painful internal rotation either hip | 1.45    | 0.90-2.32 | 0.13    |         |          |         |
| Flexion <115° either hip | 1.58    | 1.00-2.51 | 0.05    |         |          |         |

An OR >1 indicates an increased odds for incidence of hip OA. BMI= body mass index, OR =Odds ratio, CI =confidence interval, component 1 = general presence of pain and symptoms, component 2 = participants with positive scores have relatively high levels of pain at rest (pain resting, pain lying in bed and nocturnal pain) and relatively more difficulty lying in bed, combined with less difficulty climbing stairs while carrying something, component 3 = participants with positive scores have relatively high levels of pain during shopping and walking combined with less difficulty with putting socks on/off and rising from bed, component 4 = pain during climbing stairs.