The course of limitations in activities over 5 years in patients with knee and hip osteoarthritis with moderate functional limitations: risk factors for future functional decline

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SUMMARY

Objective: To describe the course of limitations in activities over 5 years follow-up and identify predictors of future limitations in activities in elderly patients with osteoarthritis (OA) of the hip or knee with moderate functional limitations.

Method: A longitudinal cohort study with 5 years follow-up was conducted. Patients (n = 288) were recruited at rehabilitation centers and hospitals. The main outcome measures were self-reported and performance-based limitations in activities. Prognostic factors were demographic and clinical data, body functions, comorbidity, cognitive functioning, avoidance of activity and social support. Measurements were conducted at baseline, 1, 2, 3 and 5 years follow-up.

Results: Both in patients with knee and hip OA, the course of limitations in activities remained fairly stable over a period of 5 years. Avoidance of activity, increased pain, more comorbidity, a higher age, a longer disease duration, a reduced muscle strength and range of joint motion at baseline predicted more future limitations in activities in patients with knee OA. In patients with hip OA, avoidance of activity, increased pain, more comorbidity, a higher age, a higher

educational level and a reduced range of motion at baseline predicted more future limitations in activities.

Conclusions: The course of limitations in activities remains fairly stable over a period of 5 years in elderly patients with hip or knee OA. However, at individual level there is considerable variation. Predictors of more future limitations in activities include avoidance of activity, increased pain, higher morbidity count, reduced range of motion, and a higher age.

INTRODUCTION

Osteoarthritis (OA) of the hip or knee is a common chronic and degenerative disease[1]. OA causes impairments in body functions and/or structures (such as pain, reduced muscle strength, range of joint motion, and joint instability) and moderate-to-severe limitations in activities, e.g., walking, stair climbing, and transfers (rising from a chair, rising from bed, getting in and out a car)[2e4]. These limitations in activities frequently lead to limitations in participation (e.g., remunerative employment, community life, and recreation and leisure) and a decreased quality of life.

Cross sectional research on determinants of limitations in activities is robust[2,5e14] and several longitudinal studies on the course of limitations in activities over time are performed in elderly patients with knee pain[15e19]. However, van Dijk concluded based on a systematic review of the existing literature that high quality longitudinal research remains limited in elderly patients who are diagnosed (radiographically or using clinical criteria) with knee or hip OA[19]. Existing longitudinal research on functional decline in elderly patients who are diagnosed (radiographically or using clinical criteria) with knee or hip OA showed that limitations in activities seem to deteriorate slowly over time[19e21]. Furthermore, these studies showed that determinants of future limitations in activities include sociodemographic factors (higher age, female sex, ethnicity, lower social class and being retired), impairments in body functions [pain, stiffness, reduced muscle strength, laxity of the knee joint, proprioceptive inaccuracy, poor standing balance and impaired range of motion (ROM)], psychological and social factors (anxiety, depression, fatigue, poor self-efficacy and social support), cognitive decline, comorbidity, overweight, and a lack of regular physical activity[19e21]. However, existing longitudinal studies in elderly patients who are diagnosed (radiographically or using clinical criteria) with knee or hip OA used relatively short follow-up periods (<3 years follow-up). In a systematic review on the clinical course and predictors of future limitations in activities, van Dijk et al. found only one high quality study with a follow-up which was longer than 3 years[19].Therefore, further high quality longitudinal research with longer follow-up periods is needed[19,20].

Knowledge about the course of limitations in activities over time and predictors of future limitations in activities is important for both patients and clinicians. Based on this information clinicians can identify patients who are at risk for future functional decline and prognosticate future limitations in activities. Furthermore, more insight in the course of limitations in activities and predictors of future limitations in

activities is the basis for improving treatments and rehabilitation of patients with OA of the hip or knee[20].
The objectives of the current study are (1) to describe the course of limitations in activities in patients with moderate functional limitations due to OA of the hip and knee over a follow-up period of 5 years, and (2) to identify predictors of future limitations in activities in elderly patients with moderate functional limitations at baseline due to OA of the hip or knee, focusing on demographic and clinical data, impairments in body functions (pain, reduced muscle strength and range of joint motion), comorbidity, cognitive functioning, avoidance of activity, and social support.

METHOD

Design

A 5 years prospective cohort study among 288 patients with knee or hip OA was conducted. Measurements were conducted at baseline, 1, 2, 3 and 5 years follow-up. The study was approved by the Medical Ethics Committee of the VU University Medical Center, Amsterdam, the Netherlands.

Setting and study population

Patients were recruited from three rehabilitation centers and two hospitals (Departments of Orthopedics, Rheumatology or Rehabilitation). Inclusion criteria were: (1) diagnosis of hip or knee OA by medical specialist according to radiological criteria or clinical criteria of the American College of Rheumatology[24,25]; (2) age between 50 and 84 years; (3) referral to hospital or rehabilitation center less than 1 year before inclusion; (4) at least moderate functional problems (Lequesne Algofunctional Index score _ 5)[26] and (5) informed consent. Exclusion criteria were: (1) insufficient understanding of the Dutch language and (2) expected death within 1 year after inclusion, due to terminal illness.

Outcome measurements

Self-reported limitations in activities were measured using the physical functioning subscale of theWestern Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[22,23]. A higher score on the WOMAC (0-68) reflects more limitations in activities.
Performance-based limitations in activities were measured using a 10 m timed walking test[24]. Each patient was asked to walk to the end of a pre-set distance of 10 m, at his or her ‘natural walking speed’. A stopwatch was used to measure in seconds the time patients walked the 10 m distance. If necessary, patients could use an assistive device during the timed walking test. Use of devices was recorded and consequently, devices were also used at 1, 2, 3 and 5 years follow-up. A higher score on the timed walking test reflects more limitations in activities.

Predictors of future limitations in activities

Impairments in body functions

Assisted active ROM was measured in both legs using goniometry, following a standardized protocol[25]. For the hip, internal rotation, external rotation and flexion were measured. For the knee, flexion and extension were measured. Isometric muscle strength of knee extension and hip abduction was measured in both legs with a hand held dynamometer, the MicroFet, using a break-test[26].

Patients were asked to deliver maximum strength against the researcher resistance. A standardized protocol, describing postures, instructions and procedure was used. The measurements of both ROM and muscle strength were repeated twice. The average score was used in the analyses. Patients rated their pain on a visual analog scale (VAS), prior to the physical assessment. A higher score on the VAS reflects more pain.

Comorbidity

Information about comorbidity was gathered in an interview with the patients using the cumulative illness rating scale (CIRS)[24,27]. The CIRS consists of 13 body systems. Scoring is weighted by the severity of the comorbid condition. Severity scores range from 0 (none) to 4 (extremely severe). Because all patients suffered from OA (OA can be regarded as the index disease), they all scored positive on CIRS 10 and for this reason, diseases in CIRS 10 (muscle, bone and skin diseases) were not used in the analyses. The indices of comorbidity derived from the CIRS are the presence of the various disease categories (moderate-to-severe comorbidity; CIRS _ 2), and morbidity count, the number of diseases on which the patients scored a severity of two or higher.

Cognitive functioning

Various aspects of cognitive functioning were measured. Firstly, the 20 item cognitive screening test (CST20) was applied. This test was developed as a screening instrument for cognitive decline in elderly[36]. Scores range from 0 to 20. An indication of cognitive decline was calculated. For patients older than 81 years, cognitive decline is defined by a score on the CST20 of 10 or less; for patients of 81 years or younger, cognitive decline is defined by a score on the CST20 of 12 or less. Secondly, to assess visual selective attention, the abridged Stroop ColorWord test was applied[39,40]. The variables derived from the Stroop test are the number of uncorrected mistakes in part III of the test and the interference score (the time needed for part III minus the time needed for part II).

Avoidance of activity & social support

To assess the level to which patients avoid physical activity when in pain (passive coping strategy), the subscale resting of the Pain Coping Inventory (PCI) was used[28,29]. This subscale consists of five items, which assess the level to which patients avoid physical activity when experiencing pain (e.g., When I am in pain, I rest myself by sitting down or reclining). Scores range from 0 to 4 (1 rarely/never; 2 occasionally; 3 often; 4 very often). The sum of scores on all five items is used as the score for avoidance of activity.

A higher score means more frequent use of avoidance of activity as a coping style, when patients are in pain. Patients rated their social support on the Social Support Scale (SOS)[30]. Scores range from 0 to 60. A higher score indicates that patients experience more social support.

Demographic and clinical data

Demographic and clinical data were collected on age, gender, height, weight, location of OA, duration of complaints, and level of education. Body mass index (BMI) was calculated; obesity was defined as BMI > 30.

All assessments were conducted at the same time and were performed at test locations by a research assistant.

Statistical analysis

Following the method used by Steultjens et al.[13], indices for ROM (hip flexion, hip external rotation, hip internal rotation, knee extension and knee flexion) and muscle strength (hip abduction and knee extension) were calculated using the sum score for left and right for each movement. Prior to this calculation, scores for muscle strength on the MicroFet were divided by body weight.

Multiple imputations (MI) were used to impute any missing data in our study, using the Multivariate Imputation by Chained Equations (MICE) Procedure[31,32]. Ignoring missing data, by restricting the analyses to subjects with complete data, can lead to biased results if missing values are not missing completely at random (MCAR). In our dataset, the missing data was Missing at Random (MAR), i.e., missing data depended on other observed data.

For example, subjects with complete data at 5 years follow-up were younger and had a shorter duration of complaints, a higher level of education, fewer limitations in activities, greater muscle strength, less pain and less comorbidity compared with subject without complete data. MI was done by fitting models to predict missing values for a given variable based on all other observed variables, including the outcome variable. This makes the MAR assumption plausible. Five imputed data sets were created, each of which was analyzed separately. The results of the five analyses were combined using Rubin's rules to produce pooled estimates of mean effects and standard deviations[33,34].

All analyses were performed separately for patients with knee OA and patients with hip OA. Because patients with both knee and hip OA were included in both groups, all analyses were adjusted for having both hip and knee OA. All analyses were performed using generalized estimating equations (GEE)[35e37]. GEE correct for the dependency of individual observations; the relationships are investigated for each individual separately, and the final result is obtained by getting the population average of all individual relationships.

The correction for dependency of the observations is performed by assuming a so-called working correlation structure.

In the current study an unstructured correlation structure was used. To identify predictors of future limitations in activities in elderly patients with OA of the hip or knee, multivariate GEE analyses were performed with potential predictors at baseline as independent variable and limitations of activities (self-reported and performance-based limitations in activities) at 1, 2, 3 and 5 years follow-up assessment as dependent variable. All potential predictors were entered into a multivariable model, after which backward elimination of predictors was used to remove nonsignificant predictors (P to remove _ 0.10). The interpretation of the regression coefficient (B) from the performed GEE analyses is as follows: one unit difference in the predictor at baseline is associated with B units lower or higher future limitations in activities on average over time. All analyses were performed using STATA 10.0.

RESULTS

Patients with OA of the hip or knee who visited the department in the year prior to inclusion (n = 775) were contacted by mail and were asked to participate in the study. Of those patients who volunteered (n = 364), 288 were included. Seventy-six patients were excluded. Reasons of exclusion are shown in Fig. 1. No differences were found between the group of patients that were initially contacted (N = 775) and

the patients that were included in the study (N = 288) with regard to age and gender. Patients that were initially contacted suffered less frequently from both hip and knee OA (6.2% vs 26.5%) and more frequently from knee OA (59.5% vs 48.4%) and hip OA (34.3% vs 25.1%) compared to the study population.
Of the 288 patients that were included in the study, 211 patients (73%) also participated after 5 years (see Fig. 1). Baseline characteristics of completers were compared with non-completers.
Patients who completed the study were younger and had a shorter duration of complaints, a higher level of education, fewer limitations in activities, greater muscle strength, less pain and less comorbidity. The baseline characteristics of the study population are presented in Table I. The majority of the patients (79%) originated from Departments of Orthopedics. The other 21% came from Departments of Rheumatology and Departments of Rehabilitation.
On average, patients had hip and knee complaints for 9.5 years.

[FIGURE 1] [TABLE 1]

Course of limitations of activities

Table II presents the results of the course of self-reported and performance-based limitations in activities over 5 years. The results show a small significant improvement in self-reported limitations in activities over time in patients with knee OA. Self-reported limitations in activities also improved within the first 2 years in patients with hip OA. However, at 3 and 5 years follow-up patients' self-reported limitations in activities deteriorated. No significant change in the course of self-reported limitations in activities was found in patients with hip OA. Both in patients with knee or hip OA, performance-based limitations in activities remained stable over 5 years. However, as indicated by the large standard deviations of the change scores (see Table II), there were considerable withinpatient differences in the course of limitations in activities; some patients improved, while others deteriorated.

Predictors of future limitations in activities in patients with knee OA

The results of the multivariable analyses on predictors of future limitations in activities in patients with knee OA are shown in Table III. The most important predictor at baseline for more future self-reported limitations in activities in patients with knee OA was more avoidance of activity, followed by increased pain, higher morbidity count, a longer duration of complaints and a lower knee extension muscle strength. The results presented in Table III indicate that for example, 1 N/kg more knee extension muscle strength at baseline is associated with 2.25 points lower future self-reported limitations in activities on average over time. Predictors of more future performance-based limitations in activities were more avoidance of activity, a higher age, reduced range of joint motion

[TABLE 2] [TABLE 3]

(knee extension and knee flexion), and a lower knee extension muscle strength at baseline.

Predictors of future limitations in activities in patients with hip OA

The results of the multivariable analyses on predictors of future limitations in activities in patients with hip OA are shown in Table IV. The most important

predictor at baseline for more future self-reported limitations in activities in patients with hip OA was a higher level of education, followed by more avoidance of activity, a higher morbidity count, and increased pain at baseline. Predictors of more future performance-based limitations in activities were more avoidance of activity, a higher age, a higher morbidity count and a reduced ROM (hip flexion) at baseline.

DISCUSSION

The objective of our study was to describe the course of limitations in activities over a follow-up period of 5 years and to identify predictors of future limitations in activities in elderly patients with moderate functional limitations due to OA of the hip or knee. It can be concluded that the course of limitations in activities remains fairly stable over 5 years follow-up in elderly patients with moderate functional limitations at baseline due to hip or knee OA recruited from hospitals and rehabilitations centers.

Only in patients with knee OA, a small significant improvement in self-reported limitations in activities was found during 5 years follow-up. However, this improvement (2.7 points; 9%) was not clinically relevant. Namely Angst et al. demonstrated that in patients with OA changes in limitations of activities of at least 12% can be indicated as clinically important changes[38]. Although the results suggest that the course of limitations in activities is fairly stable in elderly patients with OA, the large standard deviations of change scores over time indicate that there are considerable differences in the course of limitations in activities between patients. In some patients limitations in activities improve over time, while in others limitations in activities deteriorate. These findings underline even more the importance of knowing which factors predict future limitations in activities in elderly patients with OA of the knee or hip, so that clinicians can identify patients who are at risk for functional decline.

The results of the current study show that predictors of future limitations in activities are rather similar for patients with knee OA and patients with hip OA. Both in patients with knee OA and in patients with hip OA, more avoidance of activity, increased pain, higher morbidity count, reduced ROM, and higher age at baseline were identified as predictors of more future limitations in activities.

Besides these factors in patients with knee OA also a longer duration of complaints and a reduced muscle strength (knee extension) at baseline and in patients with hip OA gender (female) and a higher educational level at baseline were identified as predictors of more future limitations in activities. In contrast with earlier research[20], cognitive decline, social support and overweight were not identified as predictors of future limitations in activities, both in patients with knee and hip OA.

Since there is considerable variation between individuals in the course of limitations in activities, clinicians need a tool to identify patients at risk for functional decline. By measuring the predictors found in the current study clinicians can identify which patients are at risk for future functional decline. The results apply to patients with moderate functional limitations at baseline due to hip or knee OA. In patient at risk for future functional decline the treatment [table 4] should focus on modifiable risk factors such as avoidance of activity, pain, range of joint motion and muscle strength, so that further functional decline and the associated negative consequences may be prevented. Based on the results of the current study it would be interesting to

investigate if interventions aiming at these modifiable risk factors can prevent further functional decline.

Although the results of the current study describe the course of limitations in activities over 5 years and give insight in predictors of future functional decline, the mechanism of developing more limitations in activities over time in elderly patients with hip or knee OA remains unclear. Based on the results of the current study, a possible explanation of the mechanism of developing more limitations in activities over time could be that patients avoid activities, because they induce pain. In the short term, pain can probably be reduced by avoidance of physical activity. In the long-term, however, a lack of regular physical activity will result in deterioration of body functions such as muscle strength. Due to deterioration of muscle strength, joints become less stable and reduces the joints' ability to carry load, resulting in even more limitations in activities. Furthermore, a lack of regular physical activity will increase the risk for co morbidities (e.g., obesity, hypertension, diabetes type II) in elderly patients with OA of the knee and hip. Consequently, patients will avoid physical activity even more, resulting in a downwards spiral toward worsening of the course of limitations in activities. On the other hand, a more pathophysiological mechanism can be the explanation of developing more limitations in activities over time in patients with knee or hip OA. As OA progresses, the joint capsule undergoes fribrosis, shortens and loses it compliance; in the long run resulting in greater capsular tension during movements and consequently in a reduced range of joint motion[39e42]. During movement of the joint, greater capsular tension is produced and pain is provoked. Furthermore, there is some evidence which suggests that muscle weakness is directly involved in the pathogenesis of OA[43]. It can be hypothesized that these impairments in body functions due to the pathogenesis of OA are the main trigger for pain and consequently patients tend to avoid physical activity resulting in worsening of the course of limitations in activities. For improvement of the treatment and rehabilitation of patients with OA of the hip or knee more research on the mechanism of developing more limitations in activities over time is needed. Furthermore, research on potential predictors of avoidance of activity in patients with OA is needed, since the results of the current study show that avoidance of activity seems to be an important risk factor for functional decline.

There are a few limitations that need to be mentioned. First of all, because elderly patients were recruited at hospitals and rehabilitations centers and all patients received treatment as usual, such as medication, physiotherapy or surgery the results of our study cannot be generalized to the population of patients with OA of the hip and/or knee in general. However, existing research on the course of limitations in activities among elderly patients with OA who are attending hospitals and rehabilitation centers is limited and information on predictors of future limitations in activities is highly relevant for clinicians treating patients with hip or knee OA. Secondly, a limitation of our study was the way in which avoidance of activity was measured. Namely, the resting subscale of the PCI asks patients if they avoid activity when they experience pain (selfreported behavior). It remains however unclear if, patients who say that they avoid activity when they experience pain are actually less physically active in their daily lives. At last, missing data in our study were MAR; i.e., missing data depended on other observed data (e.g., subjects with complete data at 5 years follow-up were younger and had a shorter duration of complaints, a higher

level of education, fewer limitations in activities, greater muscle strength, less pain and less comorbidity compared with subjects without complete data).
Generally, when missing data are MAR, ignoring missing data or using simple techniques for handling missing data (i.e., complete and available case analyses, the indicator method or overall mean imputation), give biased results[44]. However, more sophisticated techniques (e.g., MI) as used in our study, give unbiased results when missing data are MAR[34,44e50].
In conclusion, the course of limitations in activities appeared to remain fairly stable in elderly patients with moderate functional limitations at baseline due to hip or knee OA recruited from hospitals and rehabilitations centers during 5 years follow-up. However, there was at individual level considerable variation in the course of limitations in activities. Predictors of future limitations in activities in both patients with hip or knee OA include avoidance of activity, increased pain, higher morbidity count, lower muscle strength, and a higher age. These findings can help clinicians prognosticate future limitations in activities in patients with hip or knee OA and identify patients who are at risk for more future limitations in activities.

AUTHOR CONTRIBUTIONS

The authors declare the following contributions to the preparation of the manuscript: Study conception and design (all authors); collection and assembly of data (Pisters and van Dijk); analysis (Pisters, Heymans and Twisk) and interpretation of data (all authors); drafting of the manuscript (Pisters); critical revision of the manuscript for important intellectual content (all authors); final approval of the manuscript (all authors); obtaining of funding (Veenhof). All authors take responsibility for the integrity of the work.

CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

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REFERENCES

1. Miedema HS. Reuma in Nederlands: De cijfers. [Rheumatic Diseases in the Netherlands: The Facts]. Leiden; The Netherlands: TNO Prevention and Health; 1997.
2. Dekker J, Boot B, van der Woude LH, Bijlsma JW. Pain and disability in osteoarthritis: a review of biobehavioral mechanisms.
J Behav Med 1992;15(2):189e214.
3. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med 2000;133(8): 635e46.
4. McAlindon TE, Cooper C, Kirwan JR, Dieppe PA. Determinants of disability in osteoarthritis of the knee. Ann Rheum Dis 1993;52:258e62.

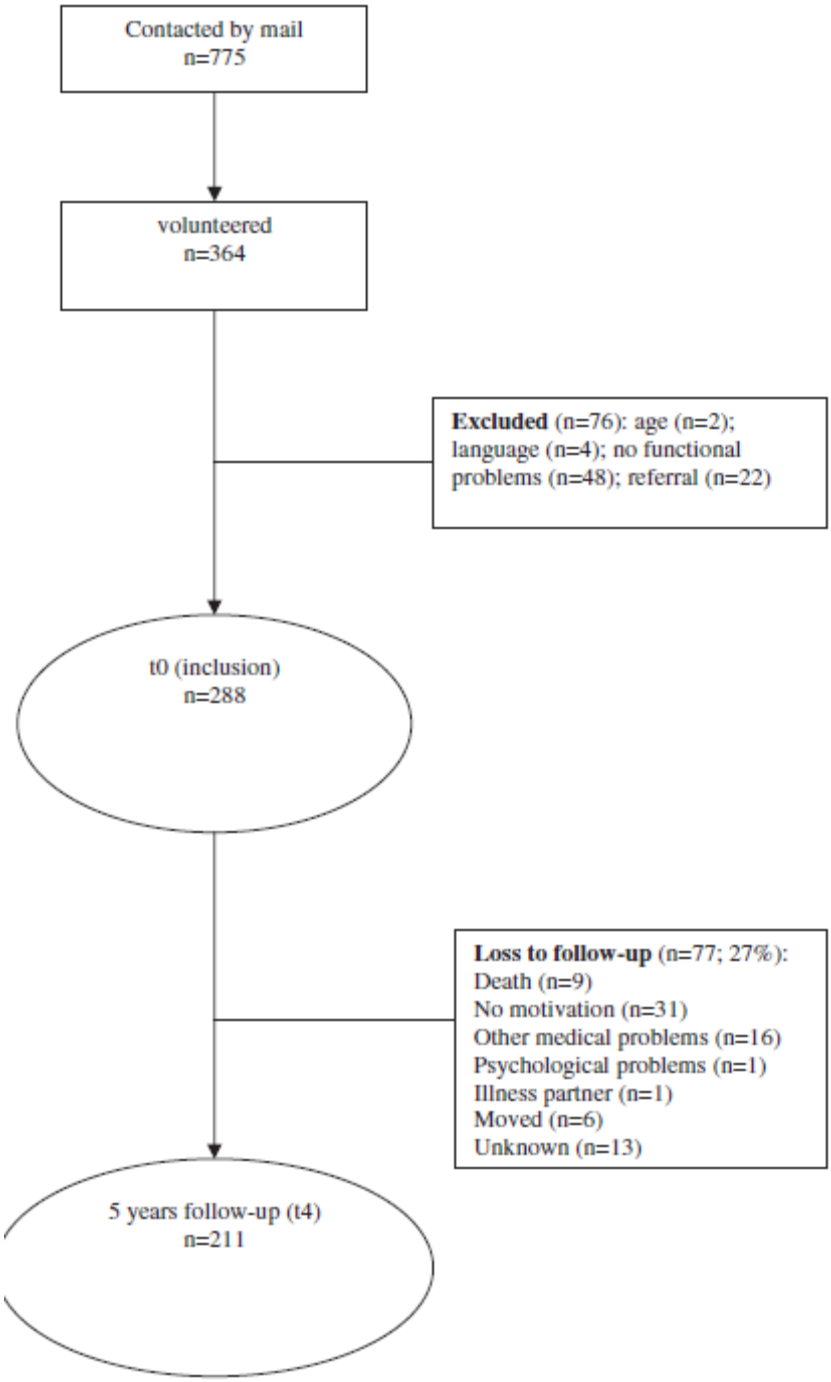
5. Creamer P, Lethbridge-Cejku M, Hochberg MC. Factors associated with functional impairment in symptomatic knee osteoarthritis. Rheumatology (Oxford) 2000;39(5):490e6.
6. Pells JJ, Shelby RA, Keefe FJ, Dixon KE, Blumenthal JA, LaCaille L, et al. Arthritis self-efficacy and self-efficacy for resisting eating: relationships to pain, disability, and eating behavior in overweight and obese individuals with osteoarthritic knee pain. Pain 2008;136(3):340e7.
7. Kee CC. Older adults with osteoarthritis. Psychological status and physical function. J Gerontol Nurs 2003;29(12): 26e34.
8. Salaffi F, Cavalieri F, Nolli M, Ferraccioli G. Analysis of disability in knee osteoarthritis. Relationship with age and psychological variables but not with radiographic score. J Rheumatol 1991; 18(10):1581e6.
9. Summers MN, Haley WE, Reveille JD, Alarcon GS. Radiographic assessment and psychologic variables as predictors of pain and functional impairment in osteoarthritis of the knee or hip.
Arthritis Rheum 1988;31(2):204e9.
10. Odding E, Valkenburg HA, Algra D, Vandenouweland FA, Grobbee DE, Hofman A. Associations of radiological osteoarthritis of the hip and knee with locomotor disability in the Rotterdam Study. Ann Rheum Dis 1998;57(4):203e8.
11. Van Dijk GM, Veenhof C, Schellevis F, Hulsmans H, Bakker JP, Arwert H, et al. Comorbidity, limitations in activities and pain in patients with osteoarthritis of the hip or knee. BMC Musculoskelet Disord 2008;9:95.
12. Van Dijk GM, Veenhof C, Lankhorst GJ, Dekker J. Limitations in activities in patients with osteoarthritis of the hip or knee: the relationship with body functions, comorbidity and cognitive functioning. Disabil Rehabil 2009;31(20): 1685e91.
13. Steultjens MP, Dekker J, van Baar ME, Oostendorp RA, Bijlsma JW. Muscle strength, pain and disability in patients with osteoarthritis. Clin Rehabil 2006;15(3):331e41.
14. van Baar ME, Dekker J, Lemmens JA, Oostendorp RA, Bijlsma JW. Pain and disability in patients with osteoarthritis of hip and knee: the relationship with articular, kinesiological, and psychological characteristics. J Rheumatol 1998;25(1): 125e33.
15. Thorstensson CA, Andersson ML, Jonsson H, Saxne T, Petersson IF. Natural course of knee osteoarthritis in middle-aged subjects with knee pain: 12-year follow-up using clinical and radiographic criteria. Ann Rheum Dis 2009;68(12): 1890e3.
16. Mallen CD, Peat G, Thomas E, Lacey R, Croft P. Predicting poor functional outcome in community-dwelling older adults with knee pain: prognostic value of generic indicators. Ann Rheum Dis 2007;66(11):1456e61.
17. White DK, Felson DT, Niu J, Nevitt MC, Lewis CE, Torner JC, et al. Reasons for functional decline despite reductions in knee pain: the multicenter osteoarthritis study. Phys Ther 2011; 91(12):1e7.
18. Roos EM, Bremander AB, Englund M, Lohmander LS. Change in self-reported outcomes and objective physical function over 7 years in middle-aged subjects with or at high risk of knee osteoarthritis. Ann Rheum Dis 2008;67(4):505e10.
19. Van Dijk GM, Dekker J, Veenhof C, van den Ende CH. Course of functional status and pain in osteoarthritis of the hip or knee: a systematic review of the literature. Arthritis Rheum 2006;55(5):779e85.
20. Dekker J, Van Dijk GM, Veenhof C. Risk factors for functional decline in osteoarthritis of the hip or knee. Curr Opin Rheumatol 2009;21.
21. Van Dijk GM, Veenhof C, Spreeuwenberg P, Coene N, Burger BJ, van Schaardenburg D, et al. Prognosis of limitations in activities in osteoarthritis of the hip or knee: a 3-year cohort study. Arch Phys Med Rehabil 2010;91(1):58e66.
22. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW.
Validation of WOMAC: a health status instrument for measuring clinically important patient relevant outcome to antirheumatic drugs therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15(12):1833e40.
23. Roorda LD, Jones CA, Waltz M, Lankhorst GJ, Bouter LM, van der Eijken JW, et al. Satisfactory cross cultural equivalence of the Dutch WOMAC in patients with hip osteoarthritis waiting for arthroplasty. Ann Rheum Dis 2004;63(1):36e42.
24. Lin YC, Davey RC, Cochrane T. Tests for physical function of the elderly with knee and hip osteoarthritis. Scand J Med Sci Sports 2001;11(5):280e6.

25. Norkin C, White D. Measurement of Joint Motion: A Guide to Goniometry. Philadelphia: FA Davis Company; 1986.
26. Bohannon R. Muscle strength testing with hand-held dynamometers.
In: Amundsen L, Ed. Muscle Trength Testing: Instrumented and Non-instrumented Systems. New York: Churchill Livingstone; 1990:69e88.
27. Conwell Y, Forbes NT, Cox C, Caine ED. Validation of a measure of physical illness burden at autopsy: the Cumulative Illness Rating Scale. J Am Geriatr Soc 1993;41(1):38e41.
28. Kraaimaat FW, Bakker A, Evers AWM. Pijncoping-strategieen bij chronische pijnpatienten: De ontwikkeling van de Pijn-Coping_Inventarisatielijst (PCI). Gedragstherapie 1997;30 (3):185e201 [in Dutch].
29. Perrot S, Poiraudeau S, Kabir M, Bertin P, Sichere P, Serrie A, et al. Active or passive pain coping strategies in hip and knee osteoarthritis? Results of a national survey of 4,719 patients in a primary care setting. Arthritis Rheum 2008; 59(11):1555e62.
30. Feij JA, Doorn CD, Kampen Dv, Berg PTvd, Resing WCM.
Sensation seeking and social support as moderators of the relationship between life events and physical illness/psychological distress. In: Winnubst JAM, Maes S, Eds. Lifestyle Stress and Health. Leiden: DSWO Press; 1992:285e302.
31. Royston P. Multiple imputation of missing values: update of ice. Stata Journal 2005;5(4):527e36.
32. Royston P. Multiple imputation of missing values. Stata Journal 2004;4(3):227e41.
33. Royston P, Carlin JB, White IR. Multiple imputation of missing values: new features for mim. Stata Journal 2009;9:252e64.
34. Rubin DB. Multiple Imputation for Nonresponse in Surveys.
New York: John Wiley & Sons; 1987.
35. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika 1986;73:13e22.
36. Twisk JW. Different statistical models to analyze epidemiological observational longitudinal data: an example from the Amsterdam Growth and Health Study. Int J Sports Med 1997;18(Suppl 3):S216e24.
37. Twisk JW. Applied Longitudinal Data Analysis for Epidemiology: A Practical Guide. Cambridge, England: Cambridge University Press; 2003.
38. Angst F, Aeschlimann A, Stucki G. Smallest detectable and minimal clinically important differences of rehabilitation intervention whit their implications for required sample sizes using WOMAC and SF-36 quality of live measurement instruments in patients with osteoarthritis of the lower extremities.
Arthritis Rheum 2001;45(4):384e91.
39. Smith MD, Triantafillou S, Parker A, Youssef PP, Coleman M.
Synovial membrane inflammation and cytokine production in patients with early osteoarthritis. J Rheumatol 1997;24(2): 365e71.
40. Lloyd-Roberts GC. The role of capsular changes in osteoarthritis of the hip joint. J Bone Joint Surg Br 1953;35- B(4):627e42.
41. Tarasevicius S, Kesteris U, Gelmanas A, Smailys A, Wingstrand H.
Intracapsular pressure and elasticity of the hip joint capsule in osteoarthritis. J Arthroplasty 2007;22(4):596e600.
42. Wingstrand H, Wingstrand A. Biomechanics of the hip joint capsule e a mathematical model and clinical implications. Clin Biomech (Bristol, Avon) 1997;12(5):273e80.
43. Ikeda S, Tsumura H, Torisu T. Age-related quadricepsdominant muscle atrophy and incident radiographic knee osteoarthritis. J Orthop Sci 2005;10(2):121e6.
44. Donders AR, van der Heyden GJ, Stijnen T, Moons KG. Review: a gentle introduction to imputation of missing values. J Clin Epidemiol 2006;59:1087e91.
45. Greenland S, Finkle WD. A critical look at methods for handling missing covariates in epidemiologic regression analyses. Am J Epidemiol 1995;142:1255e64.
46. Vach W. Logistic Regression with Missing Values in the Covariates. New York: Springer; 1994.
47. Schafer JL. Analysis of Incomplete Multivariate Data. London: Chapman & Hall/CRC Press; 1997.
48. Little RA. Regression with missing X's; a review. J Am Stat Assoc 1992;87:1227e37.

49. Clark TG, Altman DG. Developing a prognostic model in the presence of missing data. An ovarian cancer case study. J Clin Epidemiol 2003;56:28e37.
50. Vach W, Blettner M. Missing data in epidemiological studies. In: Armitrage P, Colton T, Eds. Encyclopedia of Biostatistics. Chichester: Wiley; 1998:2641e54.

TABLES AND FIGURES

Fig. 1. Flowchart of exclusion and lost to follow-up.



Pisters, M.F., Veenhof, C., Dijk, G.M. van, Heymans, M.W., Twisk, J.W.R., Dekker, J. The course of limitations in activities over 5 years in patients with knee and hip osteoarthritis with moderate functional limitations: risk factors for future functional decline. Osteoarthritis and Cartilage: 2012, 20(6), 503-510

Table II
Course of self-reported and performance-based limitations in activities in patients with knee OA or hip OA*

		n	Baseline Mean (sd)	1-yr follow-up Mean (sd)	2-yr follow-up Mean (sd)	3-yr follow-up Mean (sd)	5-yr follow-up Mean (sd)	*P*
WOMAC (0-68)								
Mean (sd)	Knee OA	216	30.3 (13.6)	28.4 (14.0)	26.2 (13.9)	27.1 (14.7)	27.6 (14.9)	0.025
Change score (sd)†				−1.8 (11.9)	−2.2 (12.6)	0.9 (11.4)	0.4 (13.1)	
Mean (sd)	Hip OA	149	30.2 (12.9)	27.5 (13.5)	24.3 (14.0)	26.4 (13.7)	27.7 (16.4)	0.523
Change score (sd)†				−2.7 (13.1)	−3.1 (12.4)	2.1 (11.6)	1.4 (13.5)	
Timed walking test (s)								
Mean (sd)	Knee OA	216	10.6 (4.5)	9.9 (2.7)	10.0 (2.6)	10.3 (2.8)	10.5 (3.5)	0.971
Change score (sd)†				−0.7 (4.1)	0.2 (2.5)	0.3 (2.7)	0.2 (3.8)	
Mean (sd)	Hip OA	149	10.4 (4.0)	9.7 (2.7)	9.7 (2.6)	9.9 (2.5)	10.3 (3.9)	0.813
Change score (sd)†				−0.7 (3.8)	0.1 (2.4)	0.2 (2.6)	0.4 (4.0)	

* Analyses were adjusted for having both knee and hip OA.
† Changes between two consecutive measurements.

Table III
Predictors of future limitations in activities in patients with knee OA ($n = 216$); results from the multivariable analyses*

	Self-reported limitations in activities (WOMAC)			Performance-based limitations in activities (timed walking test)		
	B [95% CI]	*B* [95% CI]	*P*	B [95% CI]	*B* [95% CI]	*P*
Muscle strength, knee extension	−2.25 [−4.81; 0.31]	0.11 [0.01; 1.36]	0.08	−0.50 [−1.03; 0.03]	0.60 [0.37; 1.03]	0.06
ROM, knee extension				−0.08 [−0.15; −0.02]	0.92 [0.86; 0.98]	0.02
ROM, knee flexion				−0.04 [−0.08; −0.01]	0.96 [0.92; 0.99]	0.04
Pain	1.79 [1.07; 2.51]	5.99 [2.90; 12.37]	0.00			
Comorbidity (Morbidity count)	1.31 [0.50; 2.11]	3.69 [1.66; 8.23]	0.00			
Avoidance of activity	3.15 [0.67; 5.64]	23.26 [1.93; 280.70]	0.01	1.14 [0.67; 1.61]	3.13 [1.95; 5.03]	0.00
Age				0.04 [0.01; 0.08]	1.05 [1.01; 1.09]	0.02
Duration of complaints	0.11 [−0.001; 0.23]	1.11 [0.99; 1.26]	0.08			

B = coefficient in GEE analysis (Interpretation: One unit difference in the prognostic factors on baseline is associated with B units higher future limitations in activities on average over time; negative signs (B) indicate less future limitations in activities); 95% CI = 95% confidence interval; *B* = standardized Beta coefficient.
* Adjusted for having both hip and knee OA.

Table IV
Predictors of future limitations in activities in patients with hip OA ($n = 149$); results from the multivariable analyses*

	Self-reported limitations in activities (WOMAC)			Performance-based limitations in activities (timed walking test)		
	B [95% CI]	*B* [95% CI]	*P*	B [95% CI]	*B* [95% CI]	*P*
ROM, hip flexion				−0.04 [−0.08; 0.001]	0.96 [0.92; 1.00]	0.06
Pain	0.79 [0.01; 1.56]	2.19 [1.01; 4.75]	0.05			
Comorbidity (Morbidity count)	1.59 [0.59; 2.59]	4.89 [1.80; 13.30]	0.00	0.16 [−0.02; 0.32]	1.17 [1.00; 1.37]	0.05
Avoidance of activity	4.19 [0.99; 7.38]	66.0 [2.71; 1604.6]	0.01	0.99 [0.33; 1.65]	1.40 [1.39; 5.19]	0.00
Age				0.08 [0.04; 0.12]	1.08 [1.04; 1.13]	0.00
Education						
Medium vs lower	5.53 [0.93; 10.13]	251.82 [2.53; 25,069]	0.02			
High vs lower	4.56 [0.50; 8.62]	95.7 [1.67; 5534]	0.03			

B = coefficient in GEE analysis (Interpretation: One unit difference in the prognostic factors on baseline is associated with B units higher future limitations in activities on average over time; negative signs (B) indicate less future limitations in activities).
* Adjusted for having both hip and knee OA.