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Muscle strength, physical performance and physical activity as predictors of future knee replacement: A prospective cohort study

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Abstract

Objective—To investigate associations between lower levels of muscle strength, physical performance and physical activity and the risk of knee replacement (KR) in older adults with frequent knee pain.

Method—Participants from the Multicenter Osteoarthritis Study (MOST) with knee pain on most of the past 30 days at baseline were included (n=1,257; mean (SD) age of 62.2 (8.2)). We examined the association between 1) baseline peak isokinetic knee extensor strength, (60°/sec,

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AUTHOR CONTRIBUTIONS

Study conception and design. Skou, Wise, Segal
Recruitment of patients: Lewis, Felson, Nevitt, Segal
Acquisition of data. Lewis, Felson, Nevitt, Segal
Analysis and interpretation of data. Skou, Wise, Lewis, Felson, Nevitt, Segal
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CONFLICT OF INTEREST

The authors report no conflict of interest.

maximum out of 4 trials), 2) best time to stand in timed chair stand (2 trials of 5 repetitions), and 3) baseline Physical Activity Scale for the Elderly score with incident KR between baseline and the 84-month follow-up.

Results—1,252 (99.6%) participants (1,682 knees) completed the follow-up visits. 331 participants (394 knees) underwent a KR during the 84 months (229 women and 102 men). The crude analysis demonstrated a decreased risk of KR in women ($p < .0001$) with higher knee extensor strength (Hazard Ratio (HR; 95% CI) 0.99 (0.98 to 0.99)). The risk remained significant ($p = 0.03$) when adjusting for age, BMI, race, clinic site, education, occupation, previous knee injury, previous knee surgery, and WOMAC pain (HR (95% CI) 0.99 (0.99 to 1.00)), but not when adjusting for Kellgren-Lawrence grade ($p = 0.97$).

Conclusion—Lower levels of chair stand performance and self-reported physical activity are not associated with an increased risk of KR within 7 years, while the independent effect of knee extensor strength on risk for KR in women is non-significant after adjusting for radiographic severity.

Keywords

Osteoarthritis; Knee; Prognosis; Arthroplasty; Replacement; Muscle Strength; Motor Activity

INTRODUCTION

Due to demographic changes, the burden of symptomatic osteoarthritis (OA) is expected to increase rapidly in the future[1]. Concurrently, the number of knee replacements (KR), an increasingly common treatment for end-stage knee OA[2], is expected to increase by almost 700% in the coming decades[3]. This suggests a need for a paradigm shift towards early-stage treatment strategies[4].

Muscle strength deficits have been demonstrated to be associated with knee joint space narrowing over 2.5 years[5] and worsening knee pain over five years[6], two factors considered in KR decision making. Early identification of those at higher risk of OA progression could be a way to enable treatment at an earlier disease stage. Previous prospective studies aimed at identifying risk factors for OA progression have utilized change in radiographic knee OA, self-reported symptomatic knee OA or KR due to knee OA as criteria for OA progression. While radiographic findings are poorly correlated with symptoms[7] and the validity of self-reported OA can be questioned, KR is considered an acceptable surrogate measure of end-stage knee OA.

Ideally, the identification of patients at higher risk of KR should be done by easily obtainable and modifiable measures, since they could easily be implemented and utilized in clinical practice and further, would represent a target for intervention. Muscle strength, functional performance and physical activity represent such measures. Recently, muscle strength was found to be predictive of KR in women in the Osteoarthritis Initiative (OAI)[8]. A small prospective study found that quadriceps strength and functional performance (Timed Up and Go and Stair Climb Test) at baseline were worse in patients subsequently undergoing KR than in patients not undergoing KR, while neither quadriceps strength nor functional performance were predictors of KR in the adjusted model[9]. However, the follow-up period was only two years, all patients had end-stage knee OA at baseline and the sample size was relatively low (120 patients with 40 undergoing KR). Three previous large-scale prospective studies have looked at physical activity as a risk factor for KR[10–12]. The results were inconsistent with one showing a positive, but small, association between increasing levels of physical activity and KR[11], one showing no association between physical activity and KR[10], and one showing no association between leisure physical activity and KR but an association between intensive physical activity at work and KR[12]. Well-designed prospective large-scale studies with a sufficient follow-up period are needed to clarify the role of muscle strength, functional performance and physical activity in risk for KR in people with knee OA.

The purpose of this study was to determine the extent to which lower levels of muscle strength, physical performance and physical activity are associated with an increased risk of KR. We hypothesized that lower isokinetic knee extensor strength, slower chair stand and lower Physical Activity Scale for the Elderly score (PASE) at baseline were associated with elevated risk for KR within 84 months in the Multicenter Osteoarthritis Study (MOST) in subjects with knee pain on most of the past 30 days at baseline with or without radiographic knee OA.

METHOD

Trial design

MOST is an NIH-funded prospective cohort study of risk factors for incident or progressive knee OA in individuals with or at risk of knee OA. Symptomatic knee OA was defined as daily knee pain/stiffness and Kellgren-Lawrence grade ≥2 on weight bearing, fixed-flexion radiographs. 3,026 subjects (6,052 knees) between the age of 50 and 79 years at enrollment were recruited from the areas in and around Birmingham, Alabama and Iowa City, Iowa, USA. A detailed description of participants and recruitment in MOST was published previously[13].

This report from MOST conforms to The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting observational studies[14]. The appropriate institutional review boards (University of California, San Francisco; Boston University; University of Alabama at Birmingham and University of Iowa) granted approval for the MOST study, and the study was designed to follow the principles of the Helsinki Declaration.

Participants

Participants in MOST were asked about the presence of knee pain or stiffness twice in two separate interviews, one the initial telephone interview and a second time at the baseline clinic visit. If they responded positively in both interviews that they had pain or stiffness on most of the past 30 days they were deemed eligible for this study. Participants with and without radiographic knee OA were included.

Outcome variable

KR was assessed by self-report at baseline and at follow-ups after 15, 30, 60, 72 and 84 months and confirmed by radiograph or by medical record documentation. Only incident KR during follow-up was included in the analysis (77 knees had KR at baseline and was excluded from the analyses).

Predictor variables

Knee extensor strength—Isokinetic knee extensor strength for both limbs were measured by trained and certified staff using a Cybex 350 computerized dynamometer at baseline and 60 months (at 60 months mainly measured on the right side; HUMAC software version 4.3.2/Cybex 300 for Windows 98, Avocent, Huntsville, AL)[15]. After three familiarization trials, the participants completed four repetitions at 60°/sec using a standardized protocol to assure uniformity among test sites. The peak torque (Nm) out of the four repetitions at each time point was used as the strength variable for analyses as this is the variable most closely associated with muscle strength as well as risk for knee OA[15].

Timed chair stand—The timed chair stand (45 cm seat height) was used to assess physical performance at baseline and 60 months[16]. Two trials of five repetitions were completed and the best time to stand five times without using hands at each time point was included in the analysis.

Physical Activity Scale for the Elderly—Physical Activity Scale for the Elderly (PASE) was applied as a measure of physical activity at baseline and 60 months. PASE is a reliable and valid self-reported questionnaire for older people, assessing occupational, household and leisure items of physical activities during the last 7 days[17]. Scores are calculated from weights and frequency values of each type of activity assessed. In MOST, scores ranged from 0 to 573.2 (worst to best).

Statistical analysis

In sex-stratified survival analyses, we examined the association between 1) baseline knee extensor strength, 2) baseline timed chair stand, and 3) baseline PASE score with incident KR (for knee strength: ipsilateral KR) using Cox proportional hazards model to get hazard ratios (HR). The incident KR surgery (including both total and partial replacement) was considered as the end point. The knees without incident KR were censored at the last visit when a subject was contacted during follow-up or the last follow-up visit (84-month visit) in the MOST study, whichever occurred first. The robust sandwich estimate was used to control for the clustered events of the same subject. Crude and adjusted analyses were conducted treating the predictor variables as continuous. The analyses were adjusted for age (continuous), Body Mass Index (BMI; continuous), race, clinic site, education (in three levels: high school graduate or below, some college, college graduate or above), occupation (in three levels: labor, non-labor, “other”), previous knee injury, previous knee surgery, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) knee pain subscale (continuous), and Kellgren-Lawrence (KL) grade.

In a secondary analysis, the association between exposures and the risk of incident KR in two time-periods, 0–30 months and 60–84 months, were applied (combined in the analysis). The two time-periods were chosen since knee extensor strength was assessed at baseline and 60 months, providing the opportunity to assess the risk of KR within a shorter time frame. Because of the gap between the 30- and 60-month visits, Cox proportional hazards model could not be applied in the secondary analysis. Odds ratios (OR) were calculated using logistic regression. Generalized estimating equations was used to account for correlation between multiple observations per participant.

The significance level was set at $p<0.05$ and all analyses were carried out in SAS version V9.2 (SAS Institute Inc., Cary, NC, USA)

RESULTS

Participant characteristics

Of 1,257 participants with knee pain on most of the past 30 days at baseline 1,252 (99.6%) participants (1,682 knees) with a mean (SD) age of 62.2 (8.2) completed the follow-up visits (65.3% were women). Of these 1,108 participants (1,480 knees) had ipsilateral knee strength measurement and 1,173 (1,564 knees) had chair stand time measurement at baseline. 331 participants (394 knees) underwent a KR during the 84 months (229 women and 102 men). Participant characteristics for the primary analysis are presented in Table 1.

1,233 participants (1,658 knees) were followed from 0–30 months visit for KR, and 747 (1,055 knees) were followed from 60–84 months visit for KR. 131 participants (147 knees) underwent a KR from 0–30 months (96 women and 35 men), while 88 (102 knees) underwent a KR from 60–84 months (59 women and 29 men).

Primary analysis

The crude analysis demonstrated a decreased risk of KR from 0–84 months in women ($p < .0001$) with higher knee extensor strength at baseline (HR (95% CI) 0.99 (0.98 to 0.99)). The risk reduction remained statistically significant when adjusting for age, BMI, race, clinic site, education, occupation, previous knee injury, previous knee surgery, and WOMAC knee pain (HR (95% CI) 0.99 (0.99 to 1.00); $p = 0.03$), but not when additionally adjusted for KL grade ($p = 0.97$; Table 2).

No other significant associations were found in the primary analysis.

Secondary analysis

The crude analysis demonstrated a decreased risk of KR in women within the shorter time frames of 0–30 months and 60–84 months with higher knee extensor strength at baseline being associated with reduced risk (HR (95% CI) 0.98 (0.97 to 0.99); $p < .001$). The risk reduction remained statistically significant when adjusting for age, BMI, race, clinic site, education, occupation, previous knee injury, previous knee surgery, and WOMAC knee pain (HR (95% CI) 0.99 (0.98 to 1.00); $p < 0.01$), but not when adjusting for KL grade in addition to the other covariates ($p = 0.27$; Table 3).

The fully adjusted analysis demonstrated an increased risk of KR in men within the shorter time frame (p = 0.05) with higher knee extensor strength at baseline (HR (95% CI) 1.01 (1.00 to 1.02)), but the number of knees with incident KR was low.

The crude analysis demonstrated an increased risk of KR in women within the shorter time frame (p < .01) with higher chair stand time at baseline (HR (95% CI) 1.05 (1.01 to 1.09)). The risk remained statistically significant (p = 0.03) when adjusting for age, BMI, race, clinic site, education, occupation, previous knee injury, and previous knee surgery (HR (95% CI) 1.04 (1.00 to 1.08)), but not when adjusting for WOMAC knee pain (p = 0.27) and KL grade (p = 0.20; Table 3) in addition to the other covariates.

No other significant associations were found in the secondary analysis.

DISCUSSION

We demonstrated that higher knee extensor strength at baseline was associated with a decreased risk of KR in women with knee pain at both short-term (2–2.5years) and long-term (7 years) follow-ups. The association remained significant when adjusting for a range of covariates, including knee pain, but not when adjusting for radiographic severity. Furthermore, we found that worse chair stand time at baseline was associated with an increased risk of KR in women with knee pain within 2–2.5 years, albeit non-significant after adjusting for knee pain and radiographic severity. The study highlights that muscle strength might be a potential predictor of KR in women, but it is not independent of radiographic severity.

This is the first large-scale prospective study assessing the association between both muscle strength, functional performance, physical activity and KR. A previous prospective study of 120 patients with end-stage knee OA demonstrated that quadriceps strength, Timed Up and Go and Stair Climb Test were worse in patients undergoing KR within two years compared to patients that did not[9]. Our study adds to this by demonstrating a significant association between knee extensor strength, timed chair stand and KR in women, but not men, in a larger cohort of persons with or at high risk of knee OA. Consistent with our findings, muscle strength was also predictive of KR in women in OAI[8]. Our study adds to the findings of the OAI study, since it investigates the association during a short and a long follow-up period and since it has more KRs thereby increasing the validity of the findings. Furthermore, in contrast to the OAI study, our study included only those with frequent knee pain strengthening the clinical relevance of the findings. Recently, self-reported functional impairment, closely related to reduced muscle strength in OA[18], has been demonstrated to be a strong predictor of KR within 30 months in MOST[19]. Furthermore, if KR is thought of as a surrogate measure of end-stage knee OA, the results are consistent with previous reports of associations between knee extensor strength and knee joint space narrowing over 2.5 years[5] and worsening knee pain over five years[6] in MOST.

It is still unclear whether the increase in total joint reaction force from muscle contraction actually accelerates degeneration of the joint cartilage[20], as suggested by the increased risk of KR in men within 2–2.5 years with higher knee extensor strength at baseline in our study.

It is likely that this finding is related to chance, since it was only significant in the fully adjusted model, and since the number of knees with incident KR was much less than the required number by rule of thumb (about 10 outcome events per predictor variable). The potential protective role of muscle strength is highlighted by Wang et al. demonstrating that an increase in vastus medialis size is associated with reduced pain, reduced cartilage loss and reduced risk of KR[21], which suggests an effect that is consistent with the finding for women reported here.

Lin et al. found that very high and very low PASE scores were associated with accelerated degenerative changes of the cartilage in asymptomatic, middle-aged persons compared to persons with moderate PASE scores[22]. We did not find an association between physical activity (PASE) and KR, contributing another data point to the inconsistent prior reported results on the association between self-reported physical activity and KR[10–12]. The measurements of physical activity in the existing studies are all based on self-reports using various questionnaires. This suggests a potential explanation for the varying results, since estimates based on self-reports of physical activity are known to be higher than objectively measured physical activity[23]. Recent studies have demonstrated that physical activity, objectively measured using an accelerometer-based device, are protective against onset and progression of disability[24] and incident functional limitations[25] in persons with or at risk of knee OA.

Clinical implications

We investigated the association between KR and potentially modifiable factors, which are relatively easily measured in clinical practice. The clinical implications of our study are that isokinetic knee extensor strength could be a potential clinical measure to identify women at risk of future KR, even though adjusting for radiographic severity made the result non-significant. The shortcoming is that the isokinetic measurement of knee extensor strength is not typically available in clinical settings, which is why our findings need to be confirmed using a clinically available isotonic and isometric measurement, such as a handheld dynamometer. Furthermore, the small magnitude of difference in muscle strength between women having and not having a KR of approximately 9 Nm needs to be taken into consideration when interpreting the clinical implications of the results.

When the results were adjusted for radiographic OA severity, the associations were non-significant, highlighting radiographic severity as an important driver of KR as previously demonstrated[26, 27]. As lower knee extensor strength is a known risk factor for OA incidence[28] and progression[5, 6], adjusting for radiographic severity, an intermediary in the path between lower muscle strength and KR, attenuates the relationship with knee extensor strength. Although associated with an increased risk of KR in women with knee pain within 2–2.5 years it is possible that timed chair stand may not be an independent predictor of KR, since the association was non-significant when adjusting for knee pain and radiographic severity. Since radiographic assessment is associated with some risk due to radiation and cost, and since not all persons with knee pain have had radiographs of their knees, consistent with prior studies[5, 19], muscle strength may be a useful clinical predictor of KR. In fact, since only 0.5 % of radiographs in primary health care reveal treatment-changing pathology[29] and since non-surgical treatment improves pain irrespective of radiographic severity[30] in knee OA, muscle strength could be an important marker at the point of clinical contact to identify women in need of early non-surgical treatment to prevent progression of knee OA.

Strengths and limitations

The diagnosis of symptomatic OA in MOST is based on concurrent symptoms and radiographic changes. While the authors acknowledge that a trauma might have happened before being enrolled in the study or that other causes could explain the pain/stiffness of the participants, it seems likely that OA is the dominant explanation to the symptoms of participants in MOST. By including persons with frequent knee pain from MOST, a large longitudinal cohort of patients with or at elevated risk of knee OA, the findings of this study are generalizable to a clinically relevant group of patients. This cohort is community dwelling and not a clinic sample. However, findings may provide clinicians with the opportunity to identify patients at risk of progression to KR and intervene at an early disease stage with the possibility to prevent or slow the progression of OA. Including participants, both with and without symptomatic knee OA, could affect the conclusions, since different mechanisms of the disease might be involved. However, since an x-ray will not always be available in clinical practice, this enhances the generalizability of the study findings. Another limitation of our study was that isokinetic strength might not represent functional strength used in everyday life; however, functional strength can be difficult to measure in a standardized way. Furthermore, pain during knee extensor strength measurement may inhibit maximum performance thereby introducing bias to the results.

Conclusions

Lower levels of chair stand performance and self-reported physical activity are not associated with an increased risk of KR within 7 years in either men or women. Chair stand performance is predictive of KR within 2–2.5 years in women with frequent knee pain, but not after additionally adjusting for knee pain and radiographic severity. The association of knee extensor strength on risk for KR within 2–2.5 years and 7 years in women with frequent knee pain is independent of pain and other covariates but is non-significant after adjusting for radiographic severity. The study suggests knee extensor strength as a potential clinically relevant parameter to identify women in need of early non-surgical treatment aimed at preventing progression of knee OA. However, further studies are needed to confirm the predictive role of muscle strength as well as the role of other functional tests and physical activity measures.

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REFERENCES

1. Hootman JM, Helmick CG. Projections of US prevalence of arthritis and associated activity limitations. Arthritis Rheum. 2006; 54:226–229. [PubMed: 16385518]

2. Carr AJ, Robertsson O, Graves S, Price AJ, Arden NK, Judge A, et al. Knee replacement. Lancet. 2012; 379:1331–1340. [PubMed: 22398175]
3. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J. Bone Joint Surg. Am. 2007; 89:780–785. [PubMed: 17403800]
4. Hunter DJ. Lower extremity osteoarthritis management needs a paradigm shift. Br. J. Sports Med. 2011; 45:283–288. [PubMed: 21297174]
5. Segal NA, Glass NA, Torner J, Yang M, Felson DT, Sharma L, et al. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. Osteoarthritis Cartilage. 2010; 18:769–775. doi: 10.1016/j.joca.2010.02.002; 10.1016/j.joca.2010.02.002. [PubMed: 20188686]
6. Glass NA, Torner JC, Frey Law LA, Wang K, Yang T, Nevitt MC, et al. The relationship between quadriceps muscle weakness and worsening of knee pain in the MOST cohort: a 5-year longitudinal study. Osteoarthritis Cartilage. 2013; 21:1154–1159. [doi]. [PubMed: 23973125]
7. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskelet. Disord. 2008; 9:116. [PubMed: 18764949]
8. Culvenor A, Wirth W, Ruhdorfer A, Eckstein F. Thigh muscle strength predicts knee replacement risk independent of radiographic disease and pain in women - data from the Osteoarthritis Initiative. Arthritis Rheumatol. 2015 [doi].
9. Zeni JA Jr, Axe MJ, Snyder-Mackler L. Clinical predictors of elective total joint replacement in persons with end-stage knee osteoarthritis. BMC Musculoskelet. Disord. 2010; 11:86. [PubMed: 20459622]
10. Ageberg E, Engstrom G, Gerhardsson de Verdier M, Rollof J, Roos EM, Lohmander LS. Effect of leisure time physical activity on severe knee or hip osteoarthritis leading to total joint replacement: a population-based prospective cohort study. BMC Musculoskelet. Disord. 2012; 13 73,2474-13-73. [doi].
11. Wang Y, Simpson JA, Wluka AE, Teichtahl AJ, English DR, Giles GG, et al. Is physical activity a risk factor for primary knee or hip replacement due to osteoarthritis? A prospective cohort study. J. Rheumatol. 2011; 38:350–357. [doi]. [PubMed: 20952471]
12. Apold H, Meyer HE, Nordsletten L, Furnes O, Baste V, Flugsrud GB. Risk factors for knee replacement due to primary osteoarthritis, a population based, prospective cohort study of 315,495 individuals. BMC Musculoskelet. Disord. 2014; 15 217,2474-15-217. [doi].
13. Segal NA, Nevitt MC, Gross KD, Hietpas J, Glass NA, Lewis CE, et al. The Multicenter Osteoarthritis Study: opportunities for rehabilitation research. PM R. 2013; 5:647–654. [doi]. [PubMed: 23953013]
14. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007; 370:1453–1457. [PubMed: 18064739]
15. Segal NA, Torner JC, Felson D, Niu J, Sharma L, Lewis CE, et al. Effect of thigh strength on incident radiographic and symptomatic knee osteoarthritis in a longitudinal cohort. Arthritis Rheum. 2009; 61:1210–1217. [doi]. [PubMed: 19714608]
16. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J. Gerontol. 1994; 49:M85–M94. [PubMed: 8126356]
17. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. J. Clin. Epidemiol. 1993; 46:153–162. doi: 0895-4356(93)90053-4 [pii]. [PubMed: 8437031]
18. Steultjens MP, Dekker J, van Baar ME, Oostendorp RA, Bijlsma JW. Muscle strength, pain and disability in patients with osteoarthritis. Clin. Rehabil. 2001; 15:331–341. [PubMed: 11386405]
19. Wise BL, Niu J, Felson DT, Hietpas J, Sadosky A, Torner J, et al. Functional Impairment Is a Risk Factor for Knee Replacement in the Multicenter Osteoarthritis Study. Clin. Orthop. Relat. Res. 2015; 473:2505–2513. [doi]. [PubMed: 25754756]

20. Bennell KL, Wrigley TV, Hunt MA, Lim BW, Hinman RS. Update on the role of muscle in the genesis and management of knee osteoarthritis. Rheum. Dis. Clin. North Am. 2013; 39:145–176. doi: 10.1016/j.rdc.2012.11.003; 10.1016/j.rdc.2012.11.003. [PubMed: 23312414]
21. Wang Y, Wluka AE, Berry PA, Siew T, Teichtahl AJ, Urquhart DM, et al. Increase in vastus medialis cross-sectional area is associated with reduced pain, cartilage loss, and joint replacement risk in knee osteoarthritis. Arthritis Rheum. 2012; 64:3917–3925. [doi]. [PubMed: 23192791]
22. Lin W, Alizai H, Joseph GB, Srikhum W, Nevitt MC, Lynch JA, et al. Physical activity in relation to knee cartilage T2 progression measured with 3 T MRI over a period of 4 years: data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2013; 21:1558–1566. [doi]. [PubMed: 23831632]
23. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. Med. Sci. Sports Exerc. 2008; 40:181–188. [doi]. [PubMed: 18091006]
24. Dunlop DD, Song J, Semanik PA, Sharma L, Bathon JM, Eaton CB, et al. Relation of physical activity time to incident disability in community dwelling adults with or at risk of knee arthritis: prospective cohort study. BMJ. 2014; 348:g2472. [doi]. [PubMed: 24782514]
25. White DK, Tudor-Locke C, Zhang Y, Fielding R, LaValley M, Felson DT, et al. Daily walking and the risk of incident functional limitation in knee OA: An observational study. Arthritis Care. Res. (Hoboken). 2014 [doi].
26. Skou ST, Roos EM, Laursen MB, Rathleff MS, Arendt-Nielsen L, Simonsen O, et al. Criteria used when deciding on eligibility for total knee arthroplasty – between thinking and doing. The Knee. 2015
27. Gossec L, Paternotte S, Maillefert JF, Combescure C, Conaghan PG, Davis AM, et al. The role of pain and functional impairment in the decision to recommend total joint replacement in hip and knee osteoarthritis: an international cross-sectional study of 1909 patients. Report of the OARSI-OMERACT Task Force on total joint replacement. Osteoarthritis Cartilage. 2011; 19:147–154. [PubMed: 21044689]
28. Oiestad BE, Juhl CB, Eitzen I, Thorlund JB. Knee extensor muscle weakness is a risk factor for development of knee osteoarthritis. A systematic review and meta-analysis. Osteoarthritis Cartilage. 2015; 23:171–177. [doi]. [PubMed: 25450853]
29. Skou ST, Thomsen H, Simonsen OH. The value of routine radiography in patients with knee osteoarthritis consulting primary health care: a study of agreement. Eur. J. Gen. Pract. 2014; 20:10–16. [doi]. [PubMed: 23992129]
30. Skou ST, Derosche CA, Andersen MM, Rathleff MS, Simonsen O. Nonoperative treatment improves pain irrespective of radiographic severity – a cohort study of 1,414 patients with knee osteoarthritis. Acta Orthop. 2015; 86:1–6. [PubMed: 25582923]

Table 1

Participant characteristics primary analysis

	Participants with FKP[1]			Women with FKP		Men with FKP	
Characteristics	**No KR**	**KR**	**All**	**No KR**	**KR**	**No KR**	**KR**
Age (years), mean (SD)	61.5 (8.4)	64.1 (7.4)	62.2 (8.2)	61.6 (8.2)	64.4 (7.3)	61.2 (8.7)	63.5 (7.6)
BMI (kg/m^2), mean (SD)	31.2 (6.5)	33.0 (6.9)	31.7 (6.7)	31.4 (6.9)	33.3 (6.7)	30.8 (5.7)	32.3 (7.4)
Females, N (%)	589 (64.0)	229 (69.2)	818 (65.3)	______	______	______	______
WOMAC knee pain	6.9 (3.8)	7.7 (3.4)	7.1 (3.7)	7.0 (3.9)	8.1 (3.4)	6.6 (3.6)	6.9 (3.2)
KL grade, N (%)							
0	454 (35.2)	8 (2.0)	462 (27.5)	301 (36.2)	6 (2.3)	153 (33.6)	2 (1.5)
1	199 (15.5)	9 (2.3)	208 (12.4)	126 (15.1)	6 (2.3)	73 (16.0)	3 (2.3)
2	235 (18.2)	45 (11.4)	280 (16.6)	168 (20.2)	34 (12.9)	67 (14.7)	11 (8.5)
3	262 (20.3)	164 (41.6)	426 (25.3)	168 (20.2)	113 (42.8)	94 (20.6)	51 (39.2)
4	138 (10.7)	168 (42.6)	306 (18.2)	69 (8.3)	105 (39.8)	69 (15.1)	63 (48.5)
Symptomatic tibiofemoral OA, N (%)	635 (49.3)	377 (95.7)	1012 (60.2)	405 (48.7)	252 (95.5)	230 (50.4)	125 (96.2)
Knee extensor strength (Nm), mean (SD)	74.3 (38.6)	68.3 (39.7)	73.0 (39.0)	57.3 (24.5)	48.4 (23.3)	107.0 (39.8)	105.1 (37.4)
Chair stand time (s), mean (SD)	12.2 (4.1)	12.7 (3.8)	12.4 (4.1)	12.7 (4.3)	13.1 (3.9)	11.4 (3.8)	11.9 (3.5)
PASE (range 0–573.2), mean (SD)	171.9 (89.8)	162.1 (83.2)	169.3 (88.2)	154.5 (75.4)	146.7 (75.4)	202.9 (103.9)	196.8 (89.6)
Race, N (%)							
White or Caucasian	693 (75.2)	286 (86.4)	979 (78.2)	442 (75.0)	189 (82.5)	251 (75.6)	97 (95.1)
Black or African American	208 (22.6)	43 (13.0)	251 (20.0)	135 (22.9)	39 (17.0)	73 (22.0)	4 (3.9)
Asian	2 (0.2)	1 (0.3)	3 (0.2)	1 (0.2)	1 (0.4)	1 (0.3)	0 (0.0)

Characteristics	Participants with FKP[1]			Women with FKP		Men with FKP	
	No KR	KR	All	No KR	KR	No KR	KR
American Indian or Alaskan Native	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
More than one							
race	9 (1.0)	0 (0.0)	9 (0.7)	6 (1.0)	0 (0.0)	3 (0.9)	0 (0.0)
Other	7 (0.8)	1 (0.3)	8 (0.6)	3 (0.5)	0 (0.0)	4 (1.2)	1 (1.0)
Don’t know/refused	1 (0.1)	0 (0.0)	1 (0.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Education, N (%)							
High School or less	295 (32.0)	113 (34.1)	408 (32.6)	193 (32.8)	75 (32.8)	102 (30.7)	38 (37.3)
Some college	254 (27.6)	92 (27.8)	346 (27.6)	173 (29.4)	68 (29.7)	81 (24.4)	24 (23.5)
College Graduate or Higher	372 (40.4)	126 (38.1)	498 (39.8)	223 (37.9)	86 (37.6)	149 (44.9)	40 (39.2)
Work, N (%)							
Labor	340 (36.9)	126 (38.1)	466 (37.2)	171 (29.0)	75 (32.8)	169 (50.9)	51 (50.0)
Non-labor	393 (42.7)	127 (38.4)	520 (41.5)	284 (48.2)	96 (41.9)	109 (32.8)	31 (30.4)
Other	188 (20.4)	78 (23.6)	266 (21.2)	134 (22.8)	58 (25.3)	54 (16.3)	20 (19.6)
Previous knee injury, N (%)	432 (33.7)	154 (39.5)	586 (35.0)	237 (28.7)	90 (34.6)	195 (42.8)	64 (49.2)
Previous knee surgery, N (%)	203 (15.8)	127 (32.2)	330 (19.6)	101 (12.1)	72 (27.3)	102 (22.4)	55 (42.3)
Clinic site, N (%)							
UAB	567 (61.6)	167 (50.5)	734 (58.6)	361 (61.3)	117 (51.1)	206 (62.0)	50 (49.0)
UIowa	354 (38.4)	164 (49.5)	518 (41.4)	228 (38.7)	112 (48.9)	126 (38.0)	52 (51.0)

[1]FKP=Frequent knee pain; KR=Knee replacement; BMI=Body Mass Index; KL grade= Kellgren-Lawrence grade; PASE=Physical Activity Scale for the Elderly; Symptomatic tibiofemoral OA was defined as daily knee pain/stiffness and Kellgren-Lawrence grade ≥2 on weight bearing, fixed-flexion radiographs; UAB=the University of Alabama at Birmingham; and UIowa=University of Iowa.

Table 2

Associations between the predictor variables and incident knee replacement from 0–84 months[1]

Sex	Predictor (KR/knees included in analysis)	crude model hazard ratio (95% CI)	crude model P-value	adjusted model[1][2] hazard ratio (95% CI)	adjusted model[1][2] P-value	adjusted model[2][2] hazard ratio (95% CI)	adjusted model[2][2] P-value	adjusted model[3][2] hazard ratio (95% CI)	adjusted model[3][2] P-value
Men	Knee extensor strength in Nm (119/511)	1.00 (0.99,1.00)	0.58	1.00 (1.00,1.01)	0.73	1.00 (1.00,1.01)	0.54	1.00 (0.99,1.01)	0.79
	Chair stand time in s. (125/561)	1.02 (0.97,1.06)	0.43	1.00 (0.95,1.05)	0.94	0.99 (0.94,1.05)	0.78	1.01 (0.95,1.07)	0.71
	PASE (130/586)	1.00 (1.00,1.00)	0.18	1.00 (1.00,1.00)	0.67	1.00 (1.00,1.00)	0.59	1.00 (1.00,1.00)	0.81
Women	Knee extensor strength in Nm (220/969)	0.99 (0.98,0.99)	<.0001 *	0.99 (0.98,1.00)	<.01 *	0.99 (0.99,1.00)	0.03 *	1.00 (0.99,1.01)	0.97
	Chair stand time in s. (232/1,003)	1.01 (0.98,1.04)	0.40	0.99 (0.96,1.02)	0.48	0.98 (0.94,1.01)	0.16	0.98 (0.95,1.02)	0.34
	PASE (264/1,096)	1.00 (1.00,1.00)	0.27	1.00 (1.00,1.00)	0.57	1.00 (1.00,1.00)	0.37	1.00 (1.00,1.00)	0.43

[1] PASE= Physical Activity Scale for the Elderly; KR=Knee replacement

[2] Adjusted for: [1] Age, BMI, race, site, education, occupation, knee injury, surgery; [2] Age, BMI, race, site, education, occupation, knee injury, surgery, WOMAC knee pain; [3] Age, BMI, race, site, education, occupation, knee injury, surgery, WOMAC knee pain, Kellgren-Lawrence grade.

Significant ($p < 0.05$) associations are indicated by *.

Table 3

Associations between the predictor variables and incident knee replacement from 0–30 and 60–84 months (combined)[1]

		crude model		adjusted model[1][2]		adjusted model[2][2]		adjusted model[3][2]	
Sex	**Predictor (KR/knee visits included in analysis)**	**odds ratio (95% CI)**	**P-value**	**odds ratio (95% CI)**	**P-value**	**odds ratio (95% CI)**	**P-value**	**odds ratio (95% CI)**	**P-value**
Men	Knee extensor strength in Nm (50/658)	1.00 (0.99,1.01)	0.79	1.01 (1.00,1.02)	0.19	1.01 (1.00,1.02)	0.07	1.01 (1.00,1.02)	0.05*
	Chair stand time in s. (73/882)	1.03(0.97,1.10)	0.285	1.01(0.93,1.09)	0.805	1.00(0.92,1.08)	0.926	1.00(0.92,1.09)	0.984
	PASE (75/926)	1.00(1.00,1.00)	0.52	1.00(1.00,1.00)	0.64	1.00(1.00,1.00)	0.48	1.00(1.00,1.00)	0.78
Women	Knee extensor strength in Nm (121/1,285)	0.98(0.97,0.99)	<.001*	0.98(0.97,0.99)	<.001*	0.99(0.98,1.00)	<.01*	0.99(0.98,1.00)	0.27
	Chair stand time in s. (149/1,621)	1.05(1.01,1.09)	<.01*	1.04(1.00,1.08)	0.03*	1.02(0.98,1.06)	0.27	1.03(0.98,1.07)	0.20
	PASE (174/1,787)	1.00(1.00,1.00)	0.91	1.00(1.00,1.00)	0.16	1.00(1.00,1.00)	0.11	1.00(1.00,1.00)	0.26

[1] The number of knees with incident knee replacement in men was less than the required number by rule of thumb (10 outcome events per predictor variable). The number of knee visits in the table corresponds to the number of knees evaluated at 30 or 84 months. KR=Knee replacement; PASE= Physical Activity Scale for the Elderly

[2] Adjusted for: [1] Age, BMI, race, site, education, occupation, knee injury, surgery; [2] Age, BMI, race, site, education, occupation, knee injury, surgery, WOMAC knee pain; [3] Age, BMI, race, site, education, occupation, knee injury, surgery, WOMAC knee pain, KL grade.

Significant ($p < 0.05$) associations are indicated by *.