Published in final edited form as:

Ann Intern Med. 2010 March 2; 152(5): 287–295. doi:10.1059/0003-4819-152-5-201003020-00006.

ASSOCIATIONS OF LEG LENGTH INEQUALITY WITH PREVALENT, INCIDENT, AND PROGRESSIVE KNEE OSTEOARTHRITIS: A COHORT STUDY

WF Harvey^{1,6}, M Yang¹, TDV Cooke², N Segal³, N Lane⁴, CE Lewis⁵, and DT Felson¹

¹Boston University School of Medicine, Boston, MA

²Queen's University, Canada

³University of Iowa, IA

⁴University of California at Davis, Davis, CA

⁵University of Alabama, Birmingham

⁶Tufts Medical Center, Boston, MA

Abstract

Background—Leg length inequality is common in the general population and may accelerate development of knee osteoarthritis.

Objective—To determine if leg length inequality is associated with prevalent, incident and progressive knee osteoarthritis,

Design—Prospective observational cohort study.

Setting—Subjects recruited from the community in Birmingham, AL and Iowa City, IA

Patients—3026 subjects, age 50-79, with or at high risk for knee osteoarthritis.

For reprints, contact: William F. Harvey, MD, MSc, Tufts Medical Center, 800 Washington Street Box #406, Boston, MA 02111, wharvey@tuftsmedicalcenter.org.

Availability of Data

The protocols for the Multicenter Osteoarthritis Study and the measurements of leg length inequality and the statistical code used for analysis are available to interested parties by contacting Dr. Harvey at wharvey@tuftsmedicalcenter.org. Some of the data used in this project will be released to the public in early 2010 as a documented analytic data set.

Publisher's Disclaimer: "This is the prepublication, author-produced version of a manuscript accepted for publication in Annals of Internal Medicine. This version does not include post-acceptance editing and formatting. The American College of Physicians, the publisher of Annals of Internal Medicine, is not responsible for the content or presentation of the author-produced accepted version of the manuscript or any version that a third party derives from it. Readers who wish to access the definitive published version of this manuscript and any ancillary material related to this manuscript (e.g., correspondence, corrections, editorials, linked articles) should go to www.annals.org or to the print issue in which the article appears. Those who cite this manuscript should cite the published version, as it is the official version of record."

Author current address information

William F Harvey, As above

Mei Yang, David Felson, Boston University Clinical Epidemiology and Training Unit, 650 Albany Street, Suite 200, Boston, MA 02118

TDV Cooke, T. Derek V. Cooke, Queen's University, 797 Princess St. Suite 404, Kingston, ON. K7L 1G1 Canada

Neil Segal, Department of Orthopedics & Rehabilitation, University of Iowa, 200 Hawkins Drive, 0728 JPP, Iowa City, IA 52242-1088

Nancy E. Lane, Director and Endowed Professor, Aging Center, Medicine and Rheumatology, University of California at Davis Medical Center, 4800 2nd Avenue, Suite 2600, Sacramento, California 95817

C Elizabeth Lewis, University of Alabama-Birmingham, 1717 11th Avenue South, Ste 614 Birmingham AL 35205

Measurements—The exposure was leg length inequality measured from full limb radiographs. The outcomes were prevalent, incident, and progressive knee osteoarthritis. Radiographic osteoarthritis was defined as Kellgren and Lawrence grade ≥ 2 and symptomatic osteoarthritis was defined as radiographic disease in a consistently painful knee.

Results—Leg length inequality ≥ 1 cm was associated with prevalent radiographic (53% vs. 36%, OR 1.9, 95%CI 1.5-2.4) and symptomatic (30% vs. 17%, OR 2.0, 95%CI 1.6-2.6) osteoarthritis in the shorter limb. Inequality ≥ 1 cm was associated with incident symptomatic osteoarthritis in the shorter (15% vs. 9%, OR 1.7, 95%CI 1.2-2.4) and longer (13% vs. 9%, OR 1.5, 95%CI 1.0-2.1) limb. Inequality ≥ 1 cm was associated with increased odds (29% vs. 24%, OR 1.3, 95%CI 1.0-1.7) of progressive osteoarthritis in the shorter limb.

Limitations—The duration of follow-up may not be long enough to adequately identify cases of incidence and progression. Measurements of leg length, including radiographic, have measurement error which could result in misclassification.

Conclusions—Radiographic leg length inequality was associated with prevalent, incident symptomatic and progressive knee osteoarthritis. These results point to leg length inequality as a potentially modifiable risk factor for knee osteoarthritis.

Primary Funding Source—National Institute on Aging

Keywords

knee osteoarthritis; leg length inequality; epidemiology

INTRODUCTION

Leg length inequality, defined as the difference in lengths of the two limbs, is very common, occurring in up to 70% of the population (1). Leg length inequality may be from trauma or mild developmental abnormalities with onset in birth or childhood. It has been implicated as a cause of a variety of medical conditions, including low back pain, trochanteric bursitis, osteoarthritis of the hip and knee, knee pain, and running injuries such as Achilles rupture. (2-10)

Various imaging techniques have been used to measure leg length inequality. Radiography has been considered the gold standard for measurement, with accepted methods including full limb radiographs, scanogram (three separate exposures of the hip, knee, and ankle), and computerized digital radiographs (11). In addition, magnetic resonance imaging and computed tomography can be used but are costly. Although it is subject to parallax error, the full limb radiograph method, with measurement from the femoral head to the ankle is the most commonly used (12).

Studies of leg length inequality to date have predominantly been of small size, uncontrolled, cross-sectional, and in some instances used artificially-induced leg length inequality (shoe inserts) to study the effects of leg length inequality on biomechanical asymmetry during motion. Bhavé *et al* reported that leg length inequality causes increased ground reaction forces in the longer limb (13). Since a shorter limb has to come from a higher level to reach the ground during walking, it is likely that a shorter limb would also incur an increased ground reaction force compared with a situation without leg length inequality. Therefore, compared to limbs equal in length, both shorter and longer limbs may subject the knee to increased biomechanical loading and increase the risk of osteoarthritis of the knee. However, we are not aware of any longitudinal study assessing risk.

Few studies have looked directly at the association of leg length inequality with knee osteoarthritis. Since there is loss of articular cartilage with the development of knee osteoarthritis, leg length inequality can develop as a consequence of disease and a longitudinal study is needed to evaluate causal effects. Any study of leg length inequality and knee osteoarthritis should control for alignment, as severe angular deformity from malalignment increases risk for knee osteoarthritis and, if present in only one limb, could cause leg length inequality. In studies of leg length inequality as a risk factor for other musculoskeletal disorders such as low back pain or trochanteric bursitis, no definitive effect of leg length inequality has been noted, nor has any specific threshold been determined (3;4;7;9;10;14).

We studied the relationship between leg length inequality and knee osteoarthritis within the Multi-center Osteoarthritis Study (MOST). The goals of the MOST study are to characterize risk factors for knee osteoarthritis progression and incidence.

Our study had two objectives. First we sought to describe the cross sectional relationship between leg length inequality by radiographic measurement and prevalent knee osteoarthritis. Second, we sought to examine the relationship of leg length inequality and both incident and progressive knee osteoarthritis. While clinical intervention is generally targeted when the leg length inequality is ≥ 2 cm, this value is either arbitrary or based on small case control studies (6). Therefore within the two goals outlined above, we wished to explore multiple definitions of leg length inequality to determine if there is a more appropriate clinical cutoff.

METHODS

The MOST study is a multi-center longitudinal community-based study of 3026 subjects age 50-79 years with knee osteoarthritis or at high risk for knee osteoarthritis due to knee pain, obesity, knee injury or prior knee surgery. At baseline, the parent study collected demographic information (age, gender, height, weight, and body mass index), full-limb radiographs, and standard knee radiographs. Subjects were reassessed at a 30-month follow-up visit. Written informed consent was obtained prior to participation at each visit as approved by the Institutional Review Boards at each participating institution (15).

Leg length was measured on full-limb radiographs by trained technologists. Leg length was defined as the distance from the femoral head center to the tibial mid-Plafond point (Figure 1a). The mid-Plafond point is the most distal portion of the tibia directly over the talar dome and does not include the ankle joint. Reliability of leg length measurement was determined using intra- and inter-rater test-retest measurements performed on 10% of the films which were re-read with readers blinded to initial results. Full-limb films were also read for alignment using the mechanical axis which was measured in degrees from the intersection of lines drawn from the above two points through the tibial spines, as shown in Figure 1b. Standard fixed-flexion and lateral weight-bearing knee radiographs were scored for osteophytes and joint space narrowing using the OARSI atlas and for Kellgren and Lawrence grade (16;17). Participation in the 30-month follow-up clinical visits occurred in 89.6% of subjects studied at baseline. While knee radiographs were reacquired at the 30-month follow-up visit permitting the assessment of change in radiographic features of osteoarthritis, full-limb films were not.

Definition of variables

The primary exposure variable was **leg length inequality** calculated from the measurements taken on the baseline full-limb radiographs. We maintained a leg specific definition, allowing a knee-based analysis to determine if the shorter or longer limb was at higher risk

(see statistical analysis for details). Initially we defined clinically significant leg length inequality as ≥ 1 cm difference between limbs, creating a dichotomous variable (presence or absence of leg length inequality). We conducted additional analyses using a leg length inequality cutoff of ≥ 2 cm. We conducted exploratory analyses to determine if there was an important threshold value of leg length inequality above which knee osteoarthritis was more likely by stratifying leg length inequality into 4 categorical groups of <0.5 cm (referent group), ≥ 0.5 cm to <1 cm, ≥ 1 cm to <2 cm and ≥ 2 cm.

Radiographic definitions of knee osteoarthritis

Prevalent radiographic knee osteoarthritis was defined based on the standard radiographic definition of Kellgren and Lawrence grade ≥ 2 (18). Incident knee osteoarthritis was defined among knees with Kellgren and Lawrence grade < 2 at baseline as presence at the 30 month visit of Kellgren and Lawrence ≥ 2 or new total knee replacement. Radiographic knee osteoarthritis progression was defined as an increase in joint space narrowing score from baseline to the 30-month follow-up, or the presence of a new total knee replacement not present at the baseline visit. This definition was chosen because progression measured by Kellgren and Lawrence score is insensitive to some obvious examples of progression (19).

Symptomatic definitions of knee osteoarthritis

Symptomatic osteoarthritis was defined in accordance with the convention used in MOST analyses (20;21). A knee was defined as having symptomatic osteoarthritis if it had knee radiographic osteoarthritis in either of both of the tibiofemoral or patellofemoral compartments (22) in a knee that was consistently painful. We defined consistently painful as when the subjects answered yes to the question, "Do you have knee pain in or around the knee on most days in the past 30 days?" at both telephone call and clinical visit conducted less than 30 days apart. We identified prevalent symptomatic osteoarthritis in participants who met this definition at baseline. We identified incident symptomatic osteoarthritis in participants who at baseline did not have the combination of consistent knee pain and radiographic osteoarthritis who developed that combination at 30 months.

Statistical analysis

The mean and standard deviations were calculated for study subject characteristics. We determined the association of leg length inequality with prevalent, incident and progressive knee osteoarthritis using logistic regression models with generalized estimating equations (23) to account for correlation between knees within a subject. All analyses were adjusted for the following potential confounders: age, gender, body height, body mass index, and alignment using baseline visit data. Alignment is particularly important since as a potential confounder, it has been associated with progression of knee osteoarthritis in previous studies (24). Alignment was measured in degrees as a continuous variable in this study. In our statistical models we explored the relationship between alignment and our outcomes. Based on the shape of the distribution for the alignment variable we used a categorical definition of alignment with the strata: varus ($\leq 178^\circ$), neutral (179° - 181°) and valgus ($\geq 182^\circ$). We ran models controlling for alignment difference (defined as the difference in degrees between the two limbs); however, it did not significantly change the results.

We also examined whether leg length inequality affected the risk of incident or progressive radiographic disease in one or both knees. For categorical analyses, varying definitions of leg length inequality were used to explore gradient-response relationships. In order to maintain knee specific analyses, this was done using a seven level ordinal variable (3 categories for shorter limbs, 3 categories for longer limbs, and one category for equal limbs). We calculated a p-value for trend for longer limb analyses (shorter limbs were excluded and the lowest exposure category was equal limbs) and a similar one for shorter limbs. In

addition, we examined loss to follow-up rates by leg length inequality to examine the possibility that participation was biased by leg length inequality group; however, there was no significant differential loss to follow-up.

All analyses were conducted using SAS, version 9.1 (SAS Institute, Inc., Cary, North Carolina, PROC GENMOD routine), software. All p values were two sided. We show a representative model: prevalent radiographic knee osteoarthritis = inequality (seven-level variable, <0.5cm as the reference group) + age (continuous variable) + sex (male as the reference group) + body mass index (continuous variable) + body height (continuous variable) + malalignment (three-level categorical variable with neutral as the reference group). Goodness of fit was tested using the Hosmer-Lemeshow goodness-of-fit test.

Role of the Funding Source

The MOST study is supported by NIH grants from the National Institute on Aging to Drs. Lewis (U01-AG-18947), Torner (U01-AG-18832), Nevitt (U01-AG-19069), and Felson (U01-AG-18820). Funding for this project was also provided to Dr. Harvey by the American College of Rheumatology Research and Education Foundation's Clinical Investigator Fellowship Award. Dr. Nancy Lane's work on this manuscript was supported in part by NIH/NIAMS grants K24-AR-048841. The study sponsor was not involved in study design; collection, analysis, or interpretation of data; writing of the report; or the decision to submit the paper for publication.

RESULTS

There were 3026 subjects enrolled in the MOST study at baseline, 2964 of whom had no missing data for the measure of leg length inequality. The most common reason for missing data for leg length inequality was poor quality of full-limb radiograph.

The characteristics of the study participants are shown in Table 1. Using a definition of leg length inequality ≥ 1 cm, the group with leg length inequality was slightly older, taller, had a higher body mass index and had a smaller percentage of female subjects. The mean alignment, a knee-based variable, was the same in both groups; however, the standard deviation was higher in the group with leg length inequality ≥ 1 cm. 14.5% of the study population (n=429) had leg length inequality ≥ 1 cm and 0.9% (n=27) had leg length inequality ≥ 2 cm.

For leg length inequality, repeated measurement showed an intra-rater and inter-rater intraclass correlation coefficients of 0.96 and 0.97 respectively (both $p < .001$). The p-value from the Hosmer-Lemeshow goodness-of-fit test was >0.05 for each statistical model, indicating no evidence for lack of fit (data not shown).

Prevalent Knee Osteoarthritis

At baseline, there was an association between leg length inequality and prevalent radiographic and symptomatic knee osteoarthritis after controlling for age, sex, height, body mass index and alignment. Leg length inequality of ≥ 1 cm was associated with increased odds of having knee radiographic osteoarthritis in the shorter limb (53% vs. 36%, OR 1.9 (95%CI 1.5-2.4) but not in the longer limb (38% vs. 36%, OR 1.0, 95%CI 0.8-1.3) compared to those with leg length inequality <1 cm. Further, a leg length inequality of ≥ 2 cm, was associated with even greater odds of having radiographic knee osteoarthritis in the shorter limb (68% vs. 37%, OR 4.4, 95%CI 1.9-10.1) but did not significantly change the odds of having knee osteoarthritis in the longer limb (42% vs. 37%, OR 1.4 95%CI 0.7-3.0) compared to those with leg length inequality <2 cm. Similar associations were found in the shorter limb for prevalent symptomatic knee osteoarthritis (Table 2a).

Leg length inequality of ≥ 1 cm is associated with an increased risk of prevalent radiographic (OR 1.5, 95% CI 1.1-1.9) and symptomatic (OR 1.6, 95% CI 1.2-2.1) osteoarthritis in at least one knee. There was a gradient-response relationship between increasing amounts of leg length inequality and presence of radiographic knee osteoarthritis as demonstrated by the categorical analyses (Table 2b). These results demonstrate that leg length inequality as small as 0.5 to 1 cm increased the risk of prevalent knee osteoarthritis, primarily in the shorter limb (shorter limb $p_{\text{trend}} < 0.0001$, longer limb $p_{\text{trend}} = 0.21$). The trend for symptomatic knee osteoarthritis was significant for both the shorter ($p_{\text{trend}} < 0.0001$) and longer ($p_{\text{trend}} = 0.03$) limbs.

Incident Knee osteoarthritis

Individuals with leg length inequality of ≥ 1 cm did not have increased odds of developing radiographic knee osteoarthritis in either limb over 30-months compared to those with leg length inequality < 1 cm. In individuals with leg length inequality ≥ 2 cm, there were no increased odds of incident radiographic osteoarthritis in either limb (Table 2a).

Individuals with leg length inequality ≥ 1 cm had increased odds of incident symptomatic knee osteoarthritis in the shorter limb (15% vs. 9%, OR 1.7, (95% CI 1.2-2.4) and in the longer limb (13% vs. 9%, OR 1.5, (95% CI 1.0-2.1) compared to those with inequality < 1 cm. The risk in at least one knee was also increased (OR 1.7, 95% CI 1.2-2.3). The categorical analyses showed no significant gradient response relationship for incident radiographic disease in either limb (shorter limb $p_{\text{trend}} = 0.71$, longer limb $p = 0.54$). There was a gradient response relationship increasing leg length inequality and increased odds of developing symptomatic knee osteoarthritis in the shorter limb only (shorter limb $p_{\text{trend}} = 0.04$, longer limb $p_{\text{trend}} = 0.09$) over 30-months of follow-up (Table 2b).

Progressive Radiographic Knee Osteoarthritis

Leg length inequality of ≥ 1 cm was associated with 1.3 (95% CI 1.0-1.7, 29% vs. 24%) times the odds of having progression in the shorter limb over 30-months of follow-up compared to those with leg length inequality < 1 cm. The association in the longer limb (28% vs. 24%, OR 1.2, 95% CI 0.9-1.5) between leg length inequality and progression of knee osteoarthritis did not reach significance. Leg length inequality of ≥ 2 cm resulted in no significant increase in odds of knee osteoarthritis progression in the shorter limb (29% vs. 24%, OR 1.4, 95% CI 0.5-3.7) or in the longer limb (24% vs. 23%, OR 1.0 95% CI 0.4-2.5), however only 6 of the 26 knees with leg length inequality ≥ 2 cm exhibited progression (Table 2a).

Greater leg length inequality was not associated with increased odds of having progressive knee osteoarthritis in the shorter limb ($p_{\text{trend}} = 0.19$) or the longer limb ($p_{\text{trend}} = 0.21$) (See Table 2b),

The odds of progression in at least one knee were not significantly increased (data not shown).

DISCUSSION

This study provides the first longitudinal evaluation of leg length inequality and radiographic knee osteoarthritis in a large cohort. We observed leg length inequality ≥ 1 cm in 14.5% of the study subjects at baseline, and this was significantly associated with prevalent radiographic and symptomatic osteoarthritis at baseline and predicted incident symptomatic knee osteoarthritis 30-months later. Further, in knees with radiographic osteoarthritis at baseline, shorter limbs were at high risk of x-ray progression. These results suggest that leg length inequality may be an important risk factor for knee osteoarthritis.

The results for prevalent knee osteoarthritis suggest that the risk is primarily in the shorter limb. The pathogenesis of increased risk in the shorter limb likely depends primarily on the biomechanical mechanisms an individual employs to adapt to their leg length inequality. One explanation is that the shorter limb has to travel a greater (albeit minimally so) distance to reach the ground and has a higher impact velocity as a result. The shorter limb may be, in effect, going 'downhill' with every stride. In addition, leg length inequality may induce inter-limb differences in hip muscle lengths, and thus length-tension muscle properties may differ between the two limbs for a given hip angle. This could result in a unilateral functional hip weakness which, in turn, could alter mechanical forces across the knee, as suggested by Souza and Powers (25). Our results are not consistent with a previous biomechanical study which indicated that the longer limb exhibited increased ground reaction forces (13) and therefore should be at greater risk for osteoarthritis.

We searched for related literature by searching Medline (English language) from inception until December 31, 2008 using the MeSH terms "leg length inequality" AND "knee osteoarthritis". Our finding that leg length inequality was associated with prevalent knee osteoarthritis is consistent with the recently published study by Golightly et al (5). Compared with that study which was physical examination based, ours used a radiographic measurement of leg length inequality. The increased precision and accuracy of the radiographic measure adds validity to the conclusion and also allowed for analysis using a smaller cutoff for leg length inequality. In addition, controlling for alignment added to the validity of our results because malalignment that is greater in one limb can create leg length inequality.. We were also able to control for knee specific alignment by using a knee based analysis. Lastly, our knee based analysis suggests that the shorter limb is at greater risk. Our analyses of the risk posed by longer limbs were inconsistent. We conducted an additional analysis using conditional logistic regression, but it lacked enough power to confirm that the shorter limb is at greater risk.

The longitudinal results suggest that leg length inequality is an important risk factor for both incident and progressive knee osteoarthritis. Previous studies investigating leg length inequality and knee osteoarthritis have only been cross-sectional. Joint space narrowing is well known to be a feature of knee osteoarthritis. If this happens more in one knee compared to the other (a common scenario), then the disease itself can cause leg length inequality (reverse causation). We eliminated potential reverse causation by looking at subjects with and without leg length inequality and no radiographic joint space narrowing at baseline, and we showed that those with leg length inequality ≥ 1 cm were approximately 1.5 times more likely to develop symptomatic osteoarthritis over 30-months of follow-up.

The results for progressive knee osteoarthritis are less clear. The potential modest increase in risk (as opposed to the higher odds ratio for incident symptomatic disease) may be due to the fact that the knee osteoarthritis group within our study population has many other risk factors for progression. After controlling for additional variables, identifying leg length inequality as an additional risk factor is difficult. This has been previously found to be the case in the MOST population for potent risk factors such as obesity (26). Even so, the data suggest a small but significant risk of progressive knee osteoarthritis in the shorter limb.

Our results indicate that leg length inequality as small as 0.5cm may be associated with increased odds of prevalent symptomatic osteoarthritis. This is the first prospective study to our knowledge to demonstrate the importance of leg length inequality of this small a magnitude as a risk factor for knee osteoarthritis. Nearly half of our study population exhibited this amount of leg length inequality. Possibly, our study was able to observe this significant finding due to the large sample size as well as the radiographic measurement technique. Physical examination may not provide sufficiently accurate or reproducible

measurement of leg length inequality of 0.5cm. Although the risk associated with such a small degree of inequality may be minor, it is potentially correctible at low cost and with virtually no adverse effects.

Although this study has several important strengths including a large study population, longitudinal outcomes data and consideration of important confounders such as alignment, several potential limitations should be considered. The numbers of incident radiographic cases were too small to definitively evaluate effects of leg length inequality and we were, for similar reasons, unable to clearly define the risk associated with longer limbs and whether shorter limbs conferred more risk than longer ones. Further biomechanical studies of leg length inequality may help to clarify this. A second limitation is the unknown duration of exposure. Due to design of the study, we have the opportunity to look at follow-up times as long as 30-months, however this still may not be enough time to detect new cases of progression of knee osteoarthritis. Lastly, the measurements of leg length, even radiographically is imperfect. In particular, it is susceptible to variation in knee flexion angle which occurs perpendicular to the plane of the image and therefore can not be measured. Despite excellent measurement reliability, the possibility remains for some misclassification of exposure resulting in bias. As the radiographic measurements were made blinded to the other variables, the misclassification is likely to be non-differential, thus biasing the results toward the null. Therefore the positive results in this analysis are likely to be true effects, with the caveat that the possibility always exists for residual confounding.

Leg length inequality may be under-recognized and undertreated in subjects with knee osteoarthritis. Leg length inequality is easily corrected using shoe modifications, which brings up the intriguing possibility that correction of leg length inequality represents a potentially simple and cost effective method of treatment and prevention of knee osteoarthritis. There is not sufficient evidence however to recommend routine radiographic measurement of leg length using full limb radiographs. Studies investigation the impact of correcting leg length inequality are warranted to determine if correction of this risk factor results in reduced incidence and progression of knee osteoarthritis.

Acknowledgments

We would like to thank the participants and staff of MOST. We would also like to thank the staff of the Boston University Clinical Epidemiology Research and Training Unit who assisted in coordinating the radiograph readings.

REFERENCE LIST

- (1). Woerman AL, Binder-Macleod SA. Leg length discrepancy assessment: accuracy and precision in five clinical methods of evaluation. *J Orthop Sports Phys Ther* 1984;5:230–238. [PubMed: 18806409]
- (2). Carlson M, Wilkerson J. Are differences in leg length predictive of lateral patello-femoral pain? *Physiother Res Int* 2007;12:29–38. [PubMed: 17432392]
- (3). Friberg O. Clinical symptoms and biomechanics of lumbar spine and hip joint in leg length inequality. *Spine* 1983;8:643–51. [PubMed: 6228021]
- (4). Giles LG, Taylor JR. Low-back pain associated with leg length inequality. *Spine* 1981;6:510–521. [PubMed: 6458101]
- (5). Golightly YM, Allen KD, Renner JB, Helmick CG, Salazar A, Jordan JM. Relationship of limb length inequality with radiographic knee and hip osteoarthritis. *Osteoarthritis Cartilage* 2007;15:824–29. [PubMed: 17321169]
- (6). Gurney B. Leg length discrepancy. *Gait Posture* 2002;15:195–206. [PubMed: 11869914]
- (7). Hellsing AL. Leg length inequality. A prospective study of young men during their military service. *Ups J Med Sci* 1988;93:245–53. [PubMed: 2977001]

- (8). Kujala UM, Friberg O, Aalto T, Kvist M, Osterman K. Lower limb asymmetry and patellofemoral joint incongruence in the etiology of knee exertion injuries in athletes. *Int J Sports Med* 1987;8:214–20. [PubMed: 3623784]
- (9). Soukka A, Alaranta H, Tallroth K, Heliovaara M. Leg-length inequality in people of working age. The association between mild inequality and low-back pain is questionable. *Spine* 1991;16:429–31. [PubMed: 1828627]
- (10). Swezey RL. Pseudo-radiculopathy in subacute trochanteric bursitis of the subgluteus maximus bursa. *Arch Phys Med Rehabil* 1976;57:387–90. [PubMed: 133652]
- (11). Moseley CF. Assessment and prediction in leg-length discrepancy. *Instr Course Lect* 1989;38:325–30. [PubMed: 2703719]
- (12). Stevens PM. Radiographic distortion of bones: a marker study. *Orthopedics* 1989;12:1457–63. [PubMed: 2587449]
- (13). Bhavé A, Paley D, Herzenberg JE. Improvement in gait parameters after lengthening for the treatment of limb-length discrepancy. *J Bone Joint Surg Am* 1999;81:529–34. [PubMed: 10225798]
- (14). Vink P, Huson A. Lumbar back muscle activity during walking with a leg inequality. *Acta Morphol Neerl Scand* 1987;25:261–71. [PubMed: 3506381]
- (15). Felson DT, Nevitt MC. Epidemiologic studies for osteoarthritis: new versus conventional study design approaches. *Rheum Dis Clin North Am* 2004;30:783–97. vii. [PubMed: 15488693]
- (16). Altman RD, Hochberg M, Murphy WA Jr, Wolfe F, Lequesne M. Atlas of individual radiographic features in osteoarthritis. *Osteoarthritis Cartilage* 1995;3(Suppl A):3–70. [PubMed: 8581752]
- (17). Kellgren, JH.; Lawrence, JS. *Atlas of Standard Radiographs*. Oxford: 1963.
- (18). KELLGREN JH, LAWRENCE JS. Radiological assessment of osteo-arthritis. *Ann Rheum Dis* 1957;16:494–502. [PubMed: 13498604]
- (19). Felson DT, Nevitt MC, Yang M, Clancy M, Niu J, Torner JC, et al. A new approach yields high rates of radiographic progression in knee osteoarthritis. *J Rheumatol* 2008;35:2047–54. [PubMed: 18793000]
- (20). Felson DT, Niu J, Guermazi A, Roemer F, Aliabadi P, Clancy M, et al. Correlation of the development of knee pain with enlarging bone marrow lesions on magnetic resonance imaging. *Arthritis Rheum* 2007;56:2986–92. [PubMed: 17763427]
- (21). Segal NA, Harvey W, Felson DT, Yang M, Torner JC, Curtis JR, et al. Leg-length inequality is not associated with greater trochanteric pain syndrome. *Arthritis Res Ther* 2008;10:R62. [PubMed: 18510741]
- (22). Felson DT, McAlindon TE, Anderson JJ, Naimark A, Weissman BW, Aliabadi P, et al. Defining radiographic osteoarthritis for the whole knee. *Osteoarthritis Cartilage* 1997;5:241–50. [PubMed: 9404469]
- (23). Zhang Y, Glynn RJ, Felson DT. Musculoskeletal disease research: should we analyze the joint or the person? *J Rheumatol* 1996;23:1130–1134. [PubMed: 8823682]
- (24). Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA* 2001;286:188–95. [PubMed: 11448282]
- (25). Souza RB, Powers CM. Differences in hip kinematics, muscle strength, and muscle activation between subjects with and without patellofemoral pain. *J Orthop Sports Phys Ther* 2009;39:12–19. [PubMed: 19131677]
- (26). Niu J, Zhang YQ, Torner J, Nevitt M, Lewis CE, Aliabadi P, et al. Is obesity a risk factor for progressive radiographic knee osteoarthritis? *Arthritis Rheum* 2009;61:329–35. [PubMed: 19248122]

Figure 1.
Diagram of a bilateral standing full limb radiograph depicting the measurements of leg length inequality (A), Mechanical axis alignment (B).

Figure 2.
Graphical depiction of selected results (from Table 2a) showing the associations of leg length inequality (LLI) and Knee Osteoarthritis (OA).

Table 1

Characteristics of the Subjects

	LLI < 1 cm N=2535	LLI ≥ 1cm N=429
Age (yrs) at baseline (SD)	62.4 (8.1)	63.1 (8.0)
Body Mass Index (kg/m ²) at baseline (SD)	30.4 (5.7)	31.0 (5.7)
Height (cm) at baseline (SD)	168.7 (9.3)	170.2 (9.9)
Gender (% female)	61.6%	53.4 %
Alignment ^{*†} (SD)	178.5° (3.6)	178.2° (4.7)

LLI = Leg length inequality

* Values ≤178° represent varus alignment and values ≥182° represent valgus alignment (see methods)

[†] Knee based variable, N_{LLI} = 858, N_{no LLI} = 5070

Table 2a

Odds of knee osteoarthritis using dichotomous definitions of exposure

LLI Category	< 1 cm	≥ 1 cm	< 2 cm	≥ 2 cm
Prevalent radiographic knee OA using K/L ≥ 2 as outcome				
Shorter leg:				
(n/N (%)) [§]	1810/4998 (36%)	224/424 (53%)	2158/5774 (37%)	21/31 (68%)
Adj OR* (95%CI)	1.0 (Ref)	1.9 (1.5-2.4)	1.0 (Ref)	4.4 (1.9-10.1)
Longer leg:				
(n/N (%)) [§]	1810/4998 (36%)	158/414 (38%)	2158/5774 (37%)	13/31 (42%)
Adj OR* (95%CI)	1.0 (Ref)	1.0 (0.8-1.3)	1.0 (Ref)	1.4 (0.7-3.0)
Prevalent symptomatic knee OA				
Shorter leg:				
(n/N (%)) [§]	794/4705 (17%)	121/297 (30%)	978/5425 (18%)	6/30 (20%)
Adj OR* (95%CI)	1.0 (Ref)	2.0 (1.6-2.6)	1.0 (Ref)	1.2 (0.5-2.8)
Longer leg:				
(n/N (%)) [§]	794/4705 (17%)	74/382 (19%)	978/5425 (18%)	5/29 (17%)
Adj OR* (95%CI)	1.0 (Ref)	1.1 (0.9-1.5)	1.0 (Ref)	1.0 (0.4-2.8)
Incident radiographic knee OA using K/L > 2 or new TKR as outcome				
Shorter leg:				
(n/N (%)) [§]	176/2881 (6%)	12/173 (7%)	206/3248 (6%)	0/10 (0%)
Adj OR* (95%CI)	1.0 (Ref)	1.2 (0.7-2.1)	1.0 (Ref)	
Longer leg:				
(n/N (%)) [§]	176/2881 (6%)	19/220 (9%)	206/3248 (6%)	1/16 (7%)
Adj OR* (95%CI)	1.0 (Ref)	1.4 (0.8-2.3)	1.0 (Ref)	
Incident symptomatic knee OA				
Shorter leg:				
(n/N (%)) [§]	358/3793 (9%)	41/265 (15%)	428/4305 (10%)	7/22 (32%)
Adj OR* (95%CI)	1.0 (Ref)	1.7 (1.2-2.4)	1.0 (Ref)	4.1 (1.5-11.4)
Longer leg:				
(n/N (%)) [§]	358/3793 (9%)	39/292 (13%)	428/4305 (10%)	3/23 (13%)
Adj OR* (95%CI)	1.0 (Ref)	1.5 (1.0-2.1)	1.0 (Ref)	1.6 (0.5-5.6)
Progressive knee OA using any increase in JSN score or new TKR as outcome				
Shorter leg:				

LLI Category	< 1 cm	≥ 1 cm	< 2 cm	≥ 2 cm
(n/N (%)) [§]	986/4168 (24%)	90/304 (29%)	1157/4757 (24%)	6/21 (29%)
Adj OR * (95%CI)	1.0 (Ref)	1.3 (1.0-1.7)	1.0 (Ref)	1.4 (0.5-3.7)
Longer leg:				
(n/N (%)) [§]	986/4168 (24%)	93/332 (28%)	1157/4757 (24%)	6/26 (23%)
Adj OR * (95%CI)	1.0 (Ref)	1.2 (0.9-1.5)	1.0 (Ref)	1.0 (0.4-2.5)

LLI = Leg Length Inequality, OA = Osteoarthritis, K/L = Kellgren and Lawrence grade, JSN = joint space narrowing, TKR = Total Knee Replacement, Ref = referent group for odds ratios

[§] n knees with outcome / N knees in LLD category – varies due to missing data

* adjusted for age, sex, body mass index, body height and alignment

Table 2b

Odds of knee osteoarthritis using categories of exposure

LLI Category	<0.5 cm	≥ 0.5 cm – 1 cm	≥ 1 cm – 2 cm	≥ 2 cm
Prevalent radiographic knee osteoarthritis at baseline using K/L ≥ 2 as outcome				
Shorter leg:	P_{trend} <0.001			
(n/N (%)) [§]	1026/3022 (34%)	416/993 (42%)	203/393 (52%)	21/31 (68%)
Adj OR* (95%CI)	1.0 (Ref)	1.4 (1.2-1.6)	2.0 (1.6-2.5)	5.1 (2.2-11.7)
Longer leg:	P_{trend} = 0.21			
(n/N (%)) [§]	1026/3022 (34%)	368/983 (37%)	145/383 (38%)	13/31 (42%)
Adj OR* (95%CI)	1.0 (Ref)	1.1 (1.0-1.4)	1.1 (0.8-1.4)	1.6 (0.8-3.4)
Prevalent symptomatic knee OA at baseline using K/L ≥ 2 as outcome				
Shorter leg:	P_{trend} <0.001			
(n/N (%)) [§]	420/2862 (15%)	214/927 (23%)	115/367 (31%)	6/30 (20%)
Adj OR* (95%CI)	1.0 (Ref)	1.7 (1.4-2.1)	2.5 (1.9-3.2)	1.5 (0.6-3.6)
Longer leg:	P_{trend} = 0.03			
(n/N (%)) [§]	420/2862 (15%)	160/916 (17%)	69/353 (20%)	5/29 (17%)
Adj OR* (95%CI)	1.0 (Ref)	1.2 (1.0-1.5)	1.3 (1.0-1.8)	1.3 (0.5-3.6)
Incident radiographic knee OA at 30-months using K/L ≥ 2 or new TKR as outcome				
Shorter leg:	P_{trend} = 0.71			
(n/N (%)) [§]	112/1824 (6%)	26/512 (5%)	12/173 (7%)	
Adj OR* (95%CI)	1.0 (Ref)	0.8 (0.5-1.3)	1.2 (0.7-2.1)	
Longer leg:	P_{trend} = 0.54			
(n/N (%)) [§]	112/1824 (6%)	38/545 (7%)	19/220(9%)	
Adj OR* (95%CI)	1.0 (Ref)	1.1 (0.8-1.7)	1.4 (0.8-2.3)	
Incident symptomatic knee OA at 30-months using K/L ≥ 2 or new TKR as outcome				
Shorter leg:	P_{trend} = 0.04			
(n/N (%)) [§]	214/2377(9%)	60/690 (9%)	41/265 (15%)	
Adj OR* (95%CI)	1.0 (Ref)	1.0 (0.7-1.4)	1.8 (1.3-2.6)	
Longer leg:	P_{trend} = 0.09			
(n/N (%)) [§]	214/2377(9%)	84/726 (12%)	39/292 (13%)	
Adj OR* (95%CI)	1.0 (Ref)	1.4 (1.0-1.8)	1.6 (1.1-2.3)	
Progressive knee OA at 30-months using any increase in JSN score or new TKR as outcome				

LLI Category	<0.5 cm	≥ 0.5 cm – 1 cm	≥ 1 cm – 2 cm	≥ 2 cm
Shorter leg:	$P_{\text{trend}} = 0.19$			
(n/N (%)) [§]	599/2594 (23%)	187/774 (24%)	84/283 (30%)	6/21 (29%)
Adj OR* (95%CI)	1.0 (Ref)	1.1 (0.9-1.3)	1.3 (1.0-1.7)	1.4 (0.5-4.0)
Longer leg:	$P_{\text{trend}} = 0.21$			
(n/N (%)) [§]	599/2594 (23%)	200/800 (25%)	87/306 (28%)	6/26 (23%)
Adj OR* (95%CI)	1.0 (Ref)	1.1 (0.9-1.3)	1.3 (0.9-1.7)	1.0 (0.4-2.7)

LLI = Leg Length Inequality, OA = Osteoarthritis, K/L = Kellgren and Lawrence grade, JSN = joint space narrowing, TKR = Total Knee Replacement, Ref = referent group for odds ratios

[§] n knees with outcome / N knees in inequality category – varies due to missing data

* adjusted for age, sex, body mass index, body height and alignment