

Published in final edited form as:

*Osteoarthritis Cartilage*. 2014 July ; 22(7): 912–917. doi:10.1016/j.joca.2014.05.013.

## Influences of Alignment and Obesity on Knee Joint Loading in Osteoarthritic Gait

**Stephen P. Messier<sup>1,2</sup>, Mackenzie Pater<sup>1</sup>, Daniel P. Beavers<sup>3</sup>, Claudine Legault<sup>3</sup>, Richard F. Loeser<sup>4</sup>, David J. Hunter<sup>5</sup>, and Paul DeVita<sup>6</sup>**

Stephen P. Messier: messier@wfu.edu; Mackenzie Pater: mhooops2@uic.edu; Claudine Legault: clegault@wfubmc.edu; Richard F. Loeser: rloeser@wfubmc.edu; David J. Hunter: david.hunter@sydney.edu.au; Paul DeVita: devitap@ecu.edu

<sup>1</sup>Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA

<sup>2</sup>Section on Gerontology and Geriatric Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA

<sup>3</sup>Department of Public Health Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA

<sup>4</sup>Section of Molecular Medicine, Wake Forest School of Medicine, Winston-Salem, NC, USA

<sup>5</sup>Rheumatology Department, Northern Clinical School, University of Sydney, Sydney, Australia

© 2014 OsteoArthritis Society International. Published by Elsevier Ltd. All rights reserved.

Address for correspondence: Stephen P. Messier, J.B. Snow Biomechanics Laboratory, Department of Health & Exercise Science, Wake Forest University, Winston-Salem, NC 27109, P: 336-758-5849, F: 336-758-4680.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

### Suppliers

Agfa-Gevaert N.V. Septestraat 27 B-2640 Mortsel Belgium

Lafayette photoelectric control system Model 63501-IR, Lafayette Instruments Co., Lafayette, IN

Motion Analysis Corporation, Santa Rosa, CA.

AMTI (Advanced Medical Technologies, Inc.) Newton, MA

SAS Institute, Cary, NC

### Author Contributions

Dr. Messier had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis.

Conception and design: *Messier, Pater, Beavers, Legault, Loeser, Hunter, DeVita*

• Analysis and interpretation of the data: *Messier, Pater, Beavers, Legault, Loeser, Hunter, DeVita*

• Drafting of the article: *Messier, Pater, Beavers, Legault, Loeser, Hunter, DeVita*

• Critical revision of the article for important intellectual content: *Messier, Pater, Beavers, Legault, Loeser, Hunter, DeVita*

• Final approval of the article: *Messier, Pater, Beavers, Legault, Loeser, Hunter, DeVita*

• Provision of study materials or patients: *Messier*

• Statistical expertise: *Beavers, Legault*

• Obtaining of funding: *Messier, Legault, Loeser, Hunter, DeVita*

• Administrative, technical, or logistic support: *Messier*

• Collection and assembly of data: *Messier, Beavers, Legault, Loeser*

**Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Messier reported receiving grants from the US Army, giving expert testimony for Anspach Meeks Ellenberger, receiving payments for lectures from the Michigan Arthritis Collaboration and Boston University and receiving travel expenses from the Hospital for Special Surgery. Dr. Beavers reported receiving grants from the NIH. Dr. Legault reported receiving payments for lectures from Charité University in Berlin. Dr. DeVita reported consulting with Wake Forest personnel. Dr. Hunter reported serving on the board of the Osteoarthritis Research Society International; receiving grants from the national Health and Medical research Council, Australian Research Council, and the NIH; and receiving royalties from DonJoy. No other disclosures were reported.

<sup>6</sup>Department of Kinesiology, East Carolina University, Greenville, NC, USA

## Abstract

**Objective**—To determine the influences of frontal plane knee alignment and obesity on knee joint loads in older, overweight and obese adults with knee osteoarthritis.

**Methods**—Cross-sectional investigation of alignment and obesity on knee joint loads using community dwelling older adults (age 55 yrs.; 27 kg·m<sup>-2</sup> BMI 41 kg·m<sup>-2</sup>; 69% female) with radiographic knee osteoarthritis that were a subset of participants (157 out of 454) enrolled in the Intensive Diet and Exercise for Arthritis (IDEA) clinical trial.

**Results**—A higher BMI was associated with greater ( $p = 0.0006$ ) peak knee compressive forces [overweight, 2411 N (2182, 2639), class 1 obesity, 2772 N (2602, 2943), class 2+ obesity, 2993 N (2796, 3190)] and greater ( $p = 0.004$ ) shear forces [overweight, 369 N (322, 415), class 1 obesity, 418 N (384, 453), class 2+ obesity, 472 N (432, 513)], independent of alignment, and varus alignment was associated ( $p < 0.0001$ ) with greater peak external knee adduction moments, independent of BMI [valgus, 18.7 Nm (15.1, 22.4), neutral, 27.7 Nm (24.0, 31.4), varus, 37.0 Nm (34.4, 39.7)].

**Conclusion**—BMI and alignment were associated with different joint loading measures; alignment was more closely associated with the asymmetry or imbalance of loads across the medial and lateral knee compartments as reflected by the frontal plane external adduction moment, while BMI was associated with the magnitude of total tibio-femoral force. These data may be useful in selecting treatment options for knee osteoarthritis patients (e.g., diet to reduce compressive loads or bracing to change alignment).

---

Knee osteoarthritis (OA) is the leading cause of chronic disability, affecting 15% of the United States population over 65 years of age (1;2). Knee malalignment and obesity are both important biomechanical risk factors for incident knee OA, primarily due to their tendency to increase knee joint loading (3–8). Joint stress across the articular surfaces from excessive body mass and malalignment promote cartilage breakdown, osteophyte formation, subchondral bone hypertrophy, and lead to progression of knee joint destruction (4;9). However, the relationship between these risk factors and knee joint loading may not be straightforward because they may interact with one another (10).

Several studies suggest that alignment may mediate the effect that body mass or body mass index (BMI) have on disease progression (4;5;8;11). Moyer et al. (11) found that alignment and body mass produced an interaction effect: that the association between alignment and the external knee adduction moment was strongest in patients with the greatest body mass such that a one degree increase in varus alignment produced a 3.2 Nm (6% of mean value) increase in the external adduction moment in the tertile with the highest mass. While alignment accounted for 32–45% of the variance in the external knee adduction moment, body mass only accounted for 6–10%, signifying that the external knee adduction moment is more affected by differences in alignment. Additionally, only 10% of the participants had valgus alignment, hinting that joint loads were concentrated in the medial compartment of the tibiofemoral joint, thereby driving the presence of the interaction with the external knee adduction moment.

The external knee adduction moment is an important surrogate measure of medial compartment knee joint loading (11;12), primarily due to its association with disease severity and progression (5;7;13). However, no studies have examined the effect of alignment and obesity on more direct measures of knee joint loading. Studies with knee OA patients found that bone-on-bone joint forces derived from musculoskeletal models were attenuated in obese patients with knee OA after reductions in body mass (14;15) and actually increased consequent to pain medication (16). Hence, these bone-on-bone estimates of joint loads appear sensitive to both mechanical and clinical changes.

There is a great need to improve our understanding of the relationship between alignment and obesity so that interventions targeting both are better understood, thereby improving clinicians' ability to select the best treatment options. The purpose of this cross-sectional study was to investigate the interaction between alignment and BMI with knee joint loading in overweight and obese sedentary adults with knee OA. We hypothesized that there would be a significant interaction between alignment and BMI, expressed by a stronger relationship with measures of knee joint loading in people with higher BMIs.

## Methods

### Participants

The Intensive Diet and Exercise for Arthritis (IDEA) trial was a weight loss and exercise trial of overweight and obese sedentary older adults with grade II-III radiographic knee OA. A detailed description of the study design and resulting outcomes can be found elsewhere (15;17). Briefly, participants were ambulatory, community-dwelling persons age  $\geq 55$  yrs. with  $27 \text{ kg}\cdot\text{m}^{-2} \leq \text{BMI} \leq 41 \text{ kg}\cdot\text{m}^{-2}$ . A stratified random sample of 157 (out of 454) IDEA participants, with equal numbers from each group (Exercise, Diet, Diet+Exercise) received a full length anteroposterior (AP) x-ray at baseline to measure lower extremity alignment. Exclusion criteria included: (1) significant co-morbid disease; (2) the inability to walk; (3) previous acute knee injury; (4) knee OA other than tibiofemoral or tibiofemoral plus patellofemoral; (5) unwillingness to change eating or physical activity habits; and (5) knee injection (i.e. cortisone, hyaluronic acid, etc) or knee surgery within the past 6 months. Descriptive characteristics of the cohort are presented in Table 1.

### Radiographic Analysis

Bilateral posteroanterior (PA) weight-bearing knee radiographs were used to identify tibiofemoral OA and sunrise views to identify those with patellofemoral OA. PA radiographs were obtained with the participants' knees flexed at a  $15^\circ$  angle using a positioning device and the x-ray beam was centered on the joint space. Tibiofemoral disease severity was determined using the Kellgren and Lawrence (K-L) grading scale that includes the formation of osteophytes, narrowing of joint cartilage, sclerosis of subchondral bone, and altered shape of bone ends with 0 = no disease; 1 = questionable; 2 = definite; 3 = moderate; and 4 = severe (18).

A full-length A-P radiograph for alignment was obtained using the Agfa ADC system (Quantum Q-Rad based imaging) approach. Participants were positioned using the methods

of Sharma et al. (5) such that both lower extremities were imaged simultaneously. Both tibial tubercles were faced directly forward and the participants' feet were positioned 15 cm apart. Participants stood upright with weight equally distributed to both feet. Alignment (mechanical axis) was defined as the measure of the angle formed by the intersection of the lines connecting the centers of the femoral head and the intercondylar notch and the centers of the ankle talus and tibial spines. Alignment was categorized into three groups: a varus knee was an angle  $>2^\circ$  in the varus direction (or a bowlegged appearance); valgus was an angle  $<0^\circ$  in the valgus direction (or a knock-kneed appearance); and a neutral knee was defined as an angle between  $0-2^\circ$  in the varus direction (19). All of the measurements were made by two physicians using the NIH ImageJ program. The intra-rater reliability of the two readers was 0.99 and the inter-rater reliability was 0.98.

### Gait Analysis

Prior to testing, participants walked at their freely chosen walking speed on a 22.5 m walkway. Freely chosen walking speed was assessed using a Lafayette photoelectric control system (Model 63501-IR) with integrated digital timers and was calculated as the average time for six trials.

Participants were prepped with a 37-reflective marker set arranged in the Cleveland Clinic full-body configuration and wore a pair of laboratory running shoes (type: cushioned) to control for footwear. Successful trials were defined as placing the entire foot on the force platform during a normal walking stride while maintaining walking speed within the established range ( $\pm 3.5\%$ ). Three successful trials were collected and corresponding outcomes averaged to provide representative values for each participant. Data from the most affected side (i.e., the knee with the most pain or the dominant side if the pain was equal in both knees) were used for subsequent analysis. 3-D videography (60 Hz) was accomplished using a 6-camera motion analysis system (Motion Analysis Corporation). An AMTI (Advanced Medical Technologies, Inc.) model OR-6-5-1 force-plate (480 Hz) interfaced with a 6 channel amplifier (model SGA6-4) was integrated with the motion capture system to allow simultaneous kinetic and kinematic data collection. Kinematic data were collected, tracked, edited, and smoothed using EVaRT 4.6 software (Motion Analysis Co.) and raw coordinate data were smoothed using a 4<sup>th</sup> order low-pass Butterworth filter set at a cut-off frequency of 6 Hz. Processed data were compiled using Orthotrak 6.0  $\beta$ 4 clinical gait analysis software (Motion Analysis Co.) to generate lower extremity kinetic and kinematic data, and calculate joint moments and joint reaction forces. Kinematic and kinetic data were synchronized to calculate external joint moments and forces using standard inverse dynamics. The variables of interest included the peak external knee flexion and adduction moments during the first 50% of stance, knee joint forces, and ground reaction forces on the most affected side. Test-retest reliability of our gait measures ranged from intra-class correlation coefficients of 0.86 to 0.98(20).

A musculoskeletal model developed by DeVita and Hortobagyi (21) was used to calculate knee joint (tibiofemoral) compressive and AP shear forces, the compressive force between the femur and the patella, and quadriceps, hamstrings and gastrocnemius muscle forces. Our musculoskeletal torque-driven model has two basic components. The first involves

calculating joint moments and joint-reaction forces from kinematic, physiological, and force-plate data. The second uses joint moments and joint-reaction forces to calculate individual muscle forces and compressive and shear forces in three steps: (1) determining the forces in the quadriceps, hamstrings and gastrocnemius muscles and lateral support tissues in the knee; (2) applying them along with joint-reaction forces onto the tibia; and (3) determining knee-joint forces. Our estimates for knee muscle and joint forces compare favorably to those of other predictive models (22–26) and are highly similar to measured forces from instrumented knee joint prostheses (27;28). Our model also incorporates the procedures of Schipplein et al. (23) to directly assess the contributions of the lateral ligaments, other supporting structures, and the quadriceps muscle to frontal plane loads. The model and its limitations are comprehensively discussed elsewhere (29).

### Statistical Analysis

Initial analyses included descriptive statistics of participant demographic and clinical characteristics consisting of frequency tables and percentages for categorical variables and means and 95% confidence intervals (95% CI) for continuous variables. Statistical comparisons to compare the baseline characteristics of the x-ray subsample to the remaining IDEA participants utilized t-tests for continuous characteristics and chi-square tests for categorical characteristics. Alignment data were summarized showing the frequencies and relative frequencies of the three alignment categories as well as summary characteristics of the alignment angles within categories. Similarly, gait analysis data including forces and moments were summarized using unadjusted means and 95% CI, and the extremes within the sample. For each of the measures of knee joint loading a multivariable ANCOVA model was created using SAS v9.3 software to determine the effects that BMI and alignment had on joint loading. Three BMI groups were created: overweight (27–29.9 kg·m<sup>-2</sup>), class 1 obesity (30–34.9 kg·m<sup>-2</sup>), and class 2+ obesity (35–41.3 kg·m<sup>-2</sup>) to go along with the three alignment categories [valgus (<0.0 deg), neutral (0–2.0 deg) and varus (>2.0 deg)]. The model included both BMI and alignment categories, the interaction between the two, and adjustment variables gender and walking speed. For each model, regression assumptions were checked by analyzing residuals using univariate statistics testing for normality and visually using quantile-quantile plots and histograms. The significance level was set at a P value = 0.05, and pairwise comparisons within the 3-category BMI and alignment groupings were performed using Tukey's method. The outcome estimates and comparisons are generated from an ANCOVA model that simultaneously fits BMI category and alignment category, their interaction, gender, and gait speed. No interactions were significant (p>0.05) hence; the main effects for BMI and alignment categories are presented.

### Results

There were no statistically significant differences in BMI (p=0.38), gender (p=0.34), age (p=0.95), self-reported function (p = 0.07), and walking speed (p=0.33) between the 157 individuals included in this study and the other 297 IDEA participants.

Mean alignment data measured from the full length radiographs are summarized in Table 2. The outcomes of interest from the biomechanical gait analysis are presented in Table 3.

Mean peak compressive force was 2.9 times mean body weight (BW), shear force was 0.45 BW, and patellofemoral compressive force was 0.47 BW.

Measures of alignment and BMI were included in the ANCOVA models to estimate knee joint loads (both bone-on-bone knee joint forces and joint moments) after adjusting for gender and walking speed. The BMI-alignment interaction was not statistically significant for all models; thus Table 4 presents the least squares means of the main model effects. Participants in the highest BMI category had the greatest compressive ( $p = 0.0006$ ) and shear forces ( $p = 0.004$ ), independent of alignment.

After adjusting for gender and walking speed, the association of alignment with the knee adduction moment was statistically significant ( $p < 0.0001$ ) such that individuals with varus alignment had higher mean adduction moments than those with a neutral alignment, independent of BMI category (Table 4). Those with valgus alignment, on average had adduction moments that were 10 Nm less than those with a neutral alignment ( $p < 0.0001$ ). In contrast, knee force variables and the external flexion moment were not significantly related to alignment.

## Discussion

Alignment and BMI were associated with different measures of joint loads in older adults with knee OA; *i*) alignment with the external knee adduction moment and *ii*) BMI with knee compressive and shear forces. However, there was no significant interaction effect after controlling for gender and walking speed; alignment did not influence the relationship between BMI and joint loads, and BMI did not influence the association between alignment and joint loads. These results may prove useful in determining the appropriate outcome measures to use in randomized clinical trials. For example, the external adduction moment would be more appropriate for a study on bracing, which seeks to alter alignment, whereas the bone-on-bone knee compressive force would be the outcome of choice for a weight loss study.

Although the results of previous studies are mixed, knee malalignment and obesity are suggested risk factors for the incidence and progression of knee OA, principally by increasing joint loading beyond normal healthy values, but with a metabolic role for obesity likely serving as a contributing factor (3–8;11). Previous work suggests that varus malalignment may mediate the effect that obesity has on OA disease progression. Moyer et al. (11) found a significant interaction of body mass with alignment on the external knee adduction moment such that people with a high body mass and varus malalignment exhibited a greater external adduction moment, a surrogate measure of medial knee joint loading. In addition to the external adduction moment used in the Moyer et al. study, we analyzed the bone-on-bone joint forces derived from musculoskeletal modeling. Furthermore, we used BMI instead of body mass because our interest was in the association of alignment with obesity. Analysis of the data using body mass instead of BMI, however, resulted in similar significant results (data not shown).

Moyer et al. (11) suggested that when evaluating the effects of an intervention that attempts to alter alignment, controlling for body mass is important because it moderates the relationship between alignment and the external knee adduction moment. In contrast, within our cohort of knee OA patients that had a wide range of frontal plane knee alignment angles, there was no significant interaction between alignment and BMI indicating that they influence different measures of joint loading; alignment is more closely associated with the symmetry or balance of loads across medial and lateral knee compartments (i.e., the external adduction moment), while BMI is associated with the magnitude of total tibio-femoral force (i.e., bone-on-bone joint forces). Both studies agree, however, that weight loss interventions do not need to control for alignment because weight has little effect on the external adduction moment.

Higher BMI was associated with greater knee joint forces. Participants in the class 2+ obesity group (BMI between 35–41 kg·m<sup>-2</sup>) had significantly greater compressive and shear forces, with a clear dose response effect (Table 4). Specifically, the class 2+ obese group exerted a peak knee compressive force per step that was 8% greater than the class 1 obesity group [(2993 N–2772 N)/2772 N × 100 = 8%] and 24% greater (582 N) than participants in the overweight group. For peak shear forces, these differences were 13% (54 N) and 28% (103 N) between class 2+ and class 1 obesity, and class 2+ and overweight, respectively. An adult takes approximately 2,000–2,500 steps per mile walked; based on our data the difference in peak compressive loads could exceed 1.2 million N and the difference in peak shear loads could exceed 206,000 N per mile walked between class 2+ obesity and overweight. Importantly, the difference in compressive loads between class 2+ and overweight (mean difference = 582 N, see Table 4) is approximately 2.5 times the group differences in body weight (difference in body weight = 230 N, see Table 2), accentuating both the detrimental mechanical effect of increased obesity on joint loads and the therapeutic benefits possible with weight loss.

The external knee adduction moment is a valuable surrogate measure of medial compartment joint loading because it is predictive of OA progression (30). Schipplein and Andriacchi (23) proposed that it is the primary determinant of medial compartment loading. Our results also indicate that malalignment influences the adduction moment, such that varus malalignment resulted in a 33% greater peak adduction moment than neutral alignment and twice the value in valgus aligned knees. Unfortunately, efforts to alter varus alignment and unload the medial compartment by reducing the length of the frontal plane knee moment arm with lateral wedges have only met with modest success (31–33).

### Study Limitations

Musculoskeletal modeling provides a non-invasive prediction of the bone-on-bone forces using lower extremity joint forces and moments calculated with inverse dynamics, lower extremity kinematics from gait analysis, and anatomical and physiologic characteristics of the participants (29). Each musculoskeletal model used to estimate knee joint loads has limitations; however, they provide useful insight into factors influencing forces at the knee (24). The absence of several knee ligaments, the assumption of no co-contraction by the hip flexors, and the use of a lumped muscle model are limitations of our model. However, our

estimated forces and muscle force curves are similar to those of other biomechanical models and produce acceptable and accurate data relative to these models (22;24;26;34). Our results also compare favorably with studies using instrumented prostheses that provide direct measurement of joint forces (25;27;35). Other limitations included the inability to infer causality from the results, and a hypothesis generating rather than a hypothesis driven study design.

## Conclusions

Our results suggest that BMI and alignment influence different joint loading measures each linked to disease progression; alignment is more closely associated with the external knee adduction moment, an indication of the asymmetry or imbalance of loads across the medial and lateral compartments (36;37), while BMI is associated with the magnitude of total tibio-femoral force.

Although limited by the cross sectional study design, these data may be useful in selecting treatment options or interventions for knee OA patients and help determine the appropriate outcome measures. For example, bracing or lateral wedges will not likely affect total knee joint compressive loads, but may be an effective treatment to reduce the external knee adduction moment in knee OA patients whereas weight reduction, a common non-pharmacologic intervention in an obese knee OA population, may have a greater effect on knee compressive loads (29).

## Acknowledgments

Support for this study was provided by grants from the National Institutes of Health-R01 AR052528-01 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases, P30 AG21332 from the National Institute on Aging, M01-RR00211 from the National Center for Research Resources-and by General Nutrition Centers.

The sponsors had no role in the design and conduct of the study; collection, analysis, and interpretation of data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

## Reference List

1. Felson DT, Chaisson CE, Hill CL, Totterman SM, Gale ME, Skinner KM, Kazis L, Gale DR. The association of bone marrow lesions with pain in knee osteoarthritis. *Ann Intern Med.* 2001 Apr 3; 134(7):541–549. [PubMed: 11281736]
2. Cheng Y, Macera CA, Davis DR, Ainsworth BE, Troped PJ, Blair SN. Physical activity and self-reported, physician-diagnosed osteoarthritis: is physical activity a risk factor? *J. Clin. Epidemiol.* 2000 Mar 1; 53(3):315–322. [PubMed: 10760643]
3. Brouwer GM, van Tol AW, Bergink AP, Belo JN, Bernsen RM, Reijman M, Pols HA, Bierma-Zeinstra SM. Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis Rheum.* 2007 Apr; 56(4):1204–1211. [PubMed: 17393449]
4. Niu J, Zhang YQ, Torner J, Nevitt M, Lewis CE, Aliabadi P, Sack B, Clancy M, Sharma L, Felson DT. Is obesity a risk factor for progressive radiographic knee osteoarthritis? *Arthritis Rheum.* 2009 Mar 15; 61(3):329–335. [PubMed: 19248122]
5. Sharma L, Lou C, Cahue S, Dunlop DD. The mechanism of the effect of obesity in knee osteoarthritis: the mediating role of malalignment. *Arthritis Rheum.* 2000 Mar; 43(3):568–575. [PubMed: 10728750]



6. Reijman M, Pols HA, Bergink AP, Hazes JM, Belo JN, Lievense AM, Bierma-Zeinstra SM. Body mass index associated with onset and progression of osteoarthritis of the knee but not of the hip: the Rotterdam Study. *Ann. Rheum. Dis.* 2007 Feb; 66(2):158–162. [PubMed: 16837490]
7. 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 Jul 11; 286(2):188–195. [PubMed: 11448282]
8. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. *Arthritis Rheum.* 2004 Dec; 50(12):3904–3909. [PubMed: 15593215]
9. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann. Intern. Med.* 1988 Jul 1; 109(1):18–24. [PubMed: 3377350]
10. Wilson DR, McWalter EJ, Johnston JD. The measurement of joint mechanics and their role in osteoarthritis genesis and progression. *Rheum. Dis. Clin. North. Am.* 2008 Aug; 34(3):605–622. [PubMed: 18687275]
11. Moyer RF, Birmingham TB, Chesworth BM, Kean CO, Giffin JR. Alignment, body mass and their interaction on dynamic knee joint load in patients with knee osteoarthritis. *Osteoarthritis Cartilage.* 2010 Jul; 18(7):888–893. [PubMed: 20417288]
12. Andriacchi TP, Mundermann A. The role of ambulatory mechanics in the initiation and progression of knee osteoarthritis. *Curr. Opin. Rheumatol.* 2006 Sep; 18(5):514–518. [PubMed: 16896293]
13. Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD, Schnitzer TJ, Kirwan-Mellis G, Andriacchi TP. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis Rheum.* 1998 Jul; 41(7):1233–1240. [PubMed: 9663481]
14. Messier SP, Gutekunst DJ, Davis C, Devita P. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. *Arthritis Rheum.* 2005 Jul; 52(7):2026–2032. [PubMed: 15986358]
15. Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, Devita P, Beavers DP, Hunter DJ, Lyles MF, Eckstein F, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA.* 2013 Sep 25; 310(12):1263–1273. [PubMed: 24065013]
16. Henriksen M, Simonsen EB, Alkjaer T, Lund H, Graven-Nielsen T, Danneskiold-Samsøe B, Bliddal H. Increased joint loads during walking--a consequence of pain relief in knee osteoarthritis. *Knee.* 2006 Dec; 13(6):445–450. [PubMed: 17011194]
17. Messier SP, Legault C, Mihalko S, Miller GD, Loeser RF, Devita P, Lyles M, Eckstein F, Hunter DJ, Williamson JD, et al. The Intensive Diet and Exercise for Arthritis (IDEA) trial: design and rationale. *BMC. Musculoskelet. Disord.* 2009; 10:93. [PubMed: 19638215]
18. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann. Rheum. Dis.* 1957 Dec; 16(4):494–502. [PubMed: 13498604]
19. Hunter DJ, Sharma L, Skaife T. Alignment and osteoarthritis of the knee. *J. Bone Joint Surg. Am.* 2009 Feb; 91(Suppl 1):85–89. [PubMed: 19182031]
20. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, Devita P, Carr JJ, Hunter DJ, Williamson JD, Bennell KL, Guermazi A, et al. Strength Training for Arthritis Trial (START): design and rationale. *BMC. Musculoskelet. Disord.* 2013 Jul 15. 14(1):208. [PubMed: 23855596]
21. Devita P, Hortobagyi T. Functional knee brace alters predicted muscle and joint forces in people with ACL reconstruction during walking. *J. Appl. Biomech.* 2001; 17:297–311.
22. Winby CR, Lloyd DG, Besier TF, Kirk TB. Muscle and external load contribution to knee joint contact loads during normal gait. *J Biomech.* 2009 Oct 16; 42(14):2294–2300. [PubMed: 19647257]
23. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. *J. Orthop. Res.* 1991 Jan; 9(1):113–119. [PubMed: 1984041]

24. Lin YC, Walter JP, Banks SA, Pandy MG, Fregly BJ. Simultaneous prediction of muscle and contact forces in the knee during gait. *J. Biomech.* 2010 Mar 22; 43(5):945–952. [PubMed: 19962703]
25. D'Lima DD, Steklov N, Patil S, Colwell CW Jr. The Mark Coventry Award: in vivo knee forces during recreation and exercise after knee arthroplasty. *Clin. Orthop. Relat Res.* 2008 Nov; 466(11):2605–2611. [PubMed: 18563502]
26. Wu JZ, Chiou SS, Pan CS. Analysis of musculoskeletal loadings in lower limbs during stilts walking in occupational activity. *Ann. Biomed. Eng.* 2009 Jun; 37(6):1177–1189. [PubMed: 19296222]
27. Fregly BJ, Besier TF, Lloyd DG, Delp SL, Banks SA, Pandy MG, D'Lima DD. Grand challenge competition to predict in vivo knee loads. *J. Orthop. Res.* 2012 Apr; 30(4):503–513. [PubMed: 22161745]
28. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, Devita P, Carr JJ, Hunter DJ, Williamson JD, Lyles M, Bennell KL, et al. Strength training for arthritis trial (START): Design and rationale. *BMC. Musculoskelet. Disord.* Forthcoming.
29. Messier SP, Legault C, Loeser RF, VanArsdale SJ, Davis C, Ettinger WH, Devita P. Does high weight loss in older adults with knee osteoarthritis affect bone-on-bone joint loads and muscle forces during walking? *Osteoarthritis and Cartilage.* 2011; 19:272–280. [PubMed: 21134477]
30. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann. Rheum. Dis.* 2002 Jul; 61(7):617–622. [PubMed: 12079903]
31. Malvankar S, Khan WS, Mahapatra A, Dowd GS. How Effective are Lateral Wedge Orthotics in Treating Medial Compartment Osteoarthritis of the Knee? A Systematic Review of the Recent Literature. *Open. Orthop. J.* 2012; 6:544–547. [PubMed: 23248725]
32. Hinman RS, Payne C, Metcalf BR, Wrigley TV, Bennell KL. Lateral wedges in knee osteoarthritis: what are their immediate clinical and biomechanical effects and can these predict a three-month clinical outcome? *Arthritis Rheum.* 2008 Mar 15; 59(3):408–415. [PubMed: 18311763]
33. Bennell KL, Bowles KA, Payne C, Cicuttini F, Williamson E, Forbes A, Hanna F, Davies-Tuck M, Harris A, Hinman RS. Lateral wedge insoles for medial knee osteoarthritis: 12 month randomised controlled trial. *BMJ.* 2011; 342:d2912. [PubMed: 21593096]
34. Taylor WR, Heller MO, Bergmann G, Duda GN. Tibio-femoral loading during human gait and stair climbing. *J. Orthop. Res.* 2004 May; 22(3):625–632. [PubMed: 15099644]
35. Kutzner I, Heinlein B, Graichen F, Bender A, Rohlmann A, Halder A, Beier A, Bergmann G. Loading of the knee joint during activities of daily living measured in vivo in five subjects. *J. Biomech.* 2010 Aug 10; 43(11):2164–2173. [PubMed: 20537336]
36. Hurwitz DE, Ryals AB, Case JP, Block JA, Andriacchi TP. The knee adduction moment during gait in subjects with knee osteoarthritis is more closely correlated with static alignment than radiographic disease severity, toe out angle and pain. *J. Orthop. Res.* 2002 Jan; 20(1):101–107. [PubMed: 11853076]
37. Baliunas AJ, Hurwitz DE, Ryals AB, Karrar A, Case JP, Block JA, Andriacchi TP. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis. Cartilage.* 2002 Jul; 10(7):573–579. [PubMed: 12127838]

Descriptive baseline characteristics of the population (n = 157) and comparison to the other IDEA participants (n = 297) not included in this analysis.

**Table 1**

Variable	Alignment Cohort N = 157		Others N = 297		P-value
	N (%)	N (%)	N (%)	N (%)	
Gender					
Female, n (%)	108 (69)		325 (72)		0.34
Race					
White, n (%)	129 (82)		377 (83)		
	Mean (SD)	Range	Mean (SD)		
BMI (kg • m <sup>-2</sup> )	33.4 (3.7)	27.0 – 41.3	33.6 (3.7)		0.38
Body mass (kg)	92.6 (13.9)	66.9 – 145.6	92.9 (14.7)		0.78
Age (years)	66 (6)	55 – 84	66 (6)		0.95
WOMAC function	22.9 (10.8)	0 – 48	24.2 (10.9)		0.07
Walking speed (m•s <sup>-1</sup> )	1.2 (0.2)	0.7 – 1.9	1.2 (0.2)		0.33

**Table 2**

Baseline alignment and body weight data per classification.

Alignment Classification	N (%)	Alignment Angle		
		Mean (SD)	Minimum	Maximum
Varus	76 (48)	5.6 (3.4)	2.1	20.9
Neutral	42 (27)	1.2 (0.6)	0.0	2.0
Valgus	39 (25)	-2.7 (2.3)	-11.4	-0.1
BMI Classification	N (%)	Body Weight		
		Mean (SD)	Minimum	Maximum
Overweight	36 (23)	78.9 (8.7)	66.9	110.2
Class 1 Obese	67 (43)	82.2 (11.8)	69.9	113.5
Class 2+ Obese	54 (34)	102.3 (11.1)	84.0	145.6

**Table 3**

Mean (SD) bone-on-bone knee forces, and peak knee external moments during walking. Mean body weight = 912 N (93 kg). PF = patellofemoral.

<b>Forces and Moments</b>	<b>Mean (SD)</b>	<b>Minimum</b>	<b>Maximum</b>
Knee Compressive force (N)	2645 (873)	1241	6337
Knee Shear force (N)	408 (156)	88	894
PF Compressive Force (N)	430 (345)	1.3	2300
Knee Adduction Moment (Nm)	30 (13)	2.2	69
Knee Flexion Moment (Nm)	36 (22)	-12	122

Least square means (Tukey-adjusted 95% CI) bone-on-bone forces and knee external moments during walking for BMI and alignment, controlling for gender and walking speed. The interaction between BMI and alignment was not statistically significant hence; the main effects of BMI and alignment are reported. Mean body weight = 912 N (93 kg).

**Table 4**

Knee Joint Load	BMI (kg·m <sup>-2</sup> )					Alignment			P-value Alignment
	27 – 29.9 Overweight	30 – 34.9 Class 1 Obese	35 – 41.3 Class 2+ Obese	P-value BMI category	<0° Valgus	0°–2° Neutral	>2° Varus		
Compressive Force (N)	2411 (2182, 2639)	2772 (2602, 2943)	2993 (2796, 3190)	0.0006	2734 (2520, 2949)	2651 (2430, 2871)	2791 (2634, 2948)	0.58	
Shear Force (N)	369 (322, 415)	418 (384, 453)	472 (432, 513)	0.004	394 (351, 438)	435 (390, 480)	429 (397, 461)	0.33	
PF Force (N)	402 (292, 511)	459 (378, 540)	492 (398, 586)	0.45	452 (348, 555)	410 (305, 515)	491 (416, 565)	0.44	
Knee Adduction Moment (Nm)	26.4 (22.6, 30.3)	30.4 (27.5, 33.3)	26.6 (23.3, 29.9)	0.12	18.7 (15.1, 22.4)	27.7 (24.0, 31.4)	37.0 (34.4, 39.7)	<0.0001	
Knee Flexion Moment (Nm)	33.5 (26.6, 40.4)	36.7 (31.6, 41.9)	41.7 (35.8, 47.7)	0.17	35.6 (29.2, 42.1)	37.1 (30.4, 43.7)	39.2 (34.5, 43.9)	0.65	

Pairwise significant differences:

Compressive force: Overweight vs Class 1, Overweight vs. Class 2+

Shear force: Overweight vs. Class 2+, Class 1 vs. Class 2+

Knee Adduction: All alignment categories were significantly different at a Tukey adjusted 0.05 level.