MR. ALESSIO BRICCA (Orcid ID : 0000-0001-9717-918X)

PROF. DAVID J HUNTER (Orcid ID : 0000-0003-3197-752X)

Article type : Original Article

Moderate physical activity may prevent cartilage loss in women with knee osteoarthritis: data from the Osteoarthritis Initiative

[1,2]Alessio Bricca (PhD), [3,4]Wolfgang Wirth (PhD), [1,5]Carsten B Juhl (PhD, PT), [3]Jana Kemnitz (MSc), [6]David J Hunter (PhD), [7]C Kent Kwoh (MD), [3,4]Felix Eckstein (MD), [3,8]Adam G Culvenor (PhD, PT)

[1]University of Southern Denmark, Odense, Denmark; [2]Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, United Kingdom. [3]Institute of Anatomy, Paracelsus Medical University Salzburg & Nuremberg, Salzburg, Austria; [4]Chondrometrics GmbH, Ainring, Germany; [5]University of Copenhagen, Herlev and Gentofte Hospital, Copenhagen, Denmark; [6]Rheumatology Department, Royal North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Royal North Shore Hospital, Pacific Hwy, Australia; [7]Division of Rheumatology, University of Arizona Arthritis Center, University of Arizona, USA; [8]La Trobe Sport and Exercise Medicine Research Centre, School of Allied Health, La Trobe University, Bundoora, Australia.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/acr.23791

Corresponding author:

Alessio Bricca,

Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sport Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55,

DK-5230 Odense M, Denmark. Email abricca@health.sdu.dk

Word count manuscript: 2,781

Keywords: physical activity, cartilage, load, thickness, osteoarthritis

ABSTRACT

Objective. To examine the impact of physical activity (PA) on cartilage thickness loss in knee osteoarthritis (KOA).

Methods. 689 participants with radiographic KOA (Kellgren/Lawrence grade ≥2) at baseline, from the Osteoarthritis Initiative completed the Physical Activity Scale for the Elderly (PASE) questionnaires at annual intervals over four years. Magnetic resonance imaging-based cartilage thickness change in the medial femorotibial compartment (MFTC) over four years was the main outcome. The impact of PASE tertiles (low, moderate, high) on changes in MFTC cartilage thickness was estimated using a mixed effect model adjusted for baseline characteristics. Furthermore, straficiation by sex was performed for secondary analyses.

Results. Structural progression of MFTC cartilage loss of -0.20 mm (95% confidence interval: -0.22 to -0.17mm) was observed in the entire cohort, with no statistically significant difference between PA levels after adjustment for baseline characteristics. A sex-by-physical activity interaction was observed in the adjusted analysis (p=0.02). Stratification by sex showed that women with low PA had a statistically greater cartilage loss than women with moderate PA level (adjusted between group difference -0.09 mm [-0.16 to -0.02 mm]), whereas no significant differences were observed in men.

Conclusion. While physical activity was not associated with cartilage thickness loss in the whole cohort, this relationship significantly differed between sexes. In women, but not in men, moderate PA may slow down structural disease progression compared to low PA levels. For both men and women, high PA does not appear to be more detrimental than lower PA levels for cartilage thickness loss.

Significance and innovation

- Physical activity was not associated with cartilage thickness loss in the whole cohort.
- Sex modifies the relationship between physical activity and cartilage thickness loss.
- In women, moderate physical activity appears to be protective of structural progression of knee osteoarthritis compared to low physical activity.
- In men and women, high PA does not appear to be more harmful than lower PA levels for cartilage thickness loss.

Physical activity (PA) is commonly recommended as a first line treatment for knee osteoarthritis (KOA), as it has been suggested to reduce pain and improve physical function (1). While having positive effects on knee symptoms and activities of daily living, PA may have detrimental effects on structural progression through excessive mechanical loading (2). However, systematic reviews have reported large inconsistencies regarding the influence of PA on the incidence and progression of radiographic KOA (3, 4). The time between the detrimental PA exposure and development and progression of structural radiographic disease can be decades and hence, the true relationship can be difficult to capture. Assessment of articular cartilage with magnetic resonance imaging (MRI) may provide an ability to detect structural progression during a shorter window of disease.

Several studies have previously investigated the impact of PA on knee cartilage (5-10). Some of these studies reported high (or very low) levels of PA to have detrimental effects on cartilage lesion scores or cartilage composition (10) in particular in knees with preexisting structural pathology (5). However, other studies did not observe an association between PA and knee cartilage morphology or composition (6, 7). These inconsistent results may be attributed to the diversity of PA assessments (pedometer, accelerometer, self-reported), outcome measures (cartilage volume/thickness, semi-quantitative lesion scores, or compositional measures), and cohort composition (with/without symptomatic/radiographic KOA). None of these studies, however, reported the relationship between PA and knee cartilage stratified by sex, despite men and women clearly having a different risk profile for OA development and structural progression (11-13). Further, only a single study that analyzed the association between PA and cartilage thickness loss in 100 Osteoarthritis Initiative (OAI) participants with full-thickness femoral cartilage defects (6) focused on participants with definite radiographic KOA. Considering that PA is promoted worldwide for many health conditions, including OA, and that people with OA avoid being physically active due to the belief that exercise damage their joints (14) it is important to investigate whether PA is related to cartilage thickness changes in men and women with established radiographic KOA.

The objective of this study was, therefore, to examine the impact of PA levels on the robust imaging biomarker longitudinal cartilage loss, as observed over four years by MRI in participants with radiographic KOA. We additionally examined this relationship stratified by sex.

MATERIALS AND METHODS

Participants

This study used data from the Osteartoarthritis Initiative (OAI), an ongoing prospective observational cohort study of 4,976 participants designed to identify risk factors for the development and progression of radiographic KOA (http://www.oai.ucsf.edu/, clinicaltrials.gov identifier: NCT00080171). As part of the OAI, participants were recruited from four centres in the US and completed annual evaluations over a four-year period, including image acquisition, clinical assessments, and questionnaires assessing PA levels. The OAI was approved by the local institutional review board at each of the four clinical centers, and all participants gave informed consent. Inclusion criteria for the current study were: i) presence of baseline radiographic KOA (Kellgren/Lawrence [KL] grade ≥2 based on central readings); ii) PA recorded at baseline and every annual follow-up assessments up to year four; and iii) availability of MRI-based cartilage thickness assessed at baseline and at year four assessment. If both knees were eligible, the one with less lateral joint space narrowing (JSN) or the lower KL grade was selected, and if these were identical, then the right knee was included (Figure 1).

Analysis of cartilage thickness

Cartilage thickness measurements were performed from 3T sagittal DESS MRIs based on a manual, quality-controlled segmentation of cartilage surfaces (15). The baseline and four-year follow-up visit were processed by the same reader using custom software (Chondrometrics GmbH, Ainring, Germany), with blinding to image acquisition order. The mean cartilage thickness in the medial femorotibial compartment (MFTC) and the combined central MFTC subregions (cMFTC) was computed for each visit individually, and change was calculated by subtracting the cartilage thickness at baseline from cartilage thickness at follow-up. We focussed on longitudinal change in the medial femorotibial compartment (MFTC and cMFTC), because the sensitivity to change of cartilage thickness measures depends on the radiographic disease stage and the predominantly affected compartment (16) and because radiographic OA in the medial compartment is more prevalent than radiographic OA in the lateral compartment (17). Additionally, based on longitudinal changes in the 16 femorotibial subregions, location-independent cartilage thinning and thickening scores (Thinning/Thickening) were also computed for the change between the baseline and year-four follow-up visit by summing all negative (thinning)/positive (thicknening) changes across the 16 subregions within each knee (18). Location-independent measures have been suggested to be more sensitive to differences in change between groups than location-based measures, because these measures only depend on the magnitude of change (18-20). Precision errors for MFTC in people with mild to moderate OA using similar techniques were found to be 1.4% (21).

Physical Activity Assessment

Self-reported PA was assessed with the PASE questionnaire at baseline, 1-, 2-, 3- and 4-year follow-up. The PASE is a valid and reliable questionnaire consisting of a numerical score assessing self-reported occupational, household and leisure PA over a one-week period (22) that has been previously used in KOA studies (6, 9, 10, 23). The overall score, ranging from 0 (completely sedentary) to 793 (extremely active), is calculated from weights and frequency values for each of the 12 components listed in the questionnaire (i.e., walking, sports (light/moderate/strenuous), muscular strength/endurance, job – standing/walking, housework (light/heavy), home repair, lawn work, outdoor gardening, caring for another person). Participants in the current study were categorized into PA tertiles based on the PASE score averaged over all five visits (low, moderate, and high PA).

Statistical analysis

The relationship between the four-year (average) PA level (low, moderate, high) and four-year cartilage thickness change was investigated in STATA (Version 14.2, StataCorp, College Station, Texas) using mixed-effect models (restricted maximum likelihood) to calculate mean differences and 95% confidence intervals (CIs), adjusted for baseline age, sex, BMI (kg/m^2), knee pain using the WOMAC Likert pain scale ranging from 0; no pain to 20; worse pain (24) in the following activities: (1) walking on flat ground; (2) going up or down stairs; (3) at night while in bed; (4) sitting or lying; and (5) standing upright, KL grade, knee alignment (assessed as frontal plane mechanical axis from full-limb X-rays), and comorbidities using the Charlson index (25). In the primary analysis, the association between PA level and change in cartilage thickness was analyzed for the entire sample. Following evaluation of the interaction term for PA and sex, the primary analytical approach was repeated in secondary analyses stratified by sex (using sex-specific PA tertiles). Finally, we explored if baseline radiographic disease stage (early radiographic OA [KL grade 2] vs. advanced radiographic OA [KL grade 3/4]), baseline PA level or percent changes in MFTC and cMFTC modified the relationship between PA and cartilage thickness loss.

The primary outcome measure was defined as cartilage thickness change in the MFTC, as this is the region that is strongly associated with KOA progression (26, 27). Changes in the cMFTC and location-independent thinning and thickening scores were considered exploratory.

RESULTS

Participants characteristics

Of the 4,976 OAI participants aged 45-79 years at baseline, 689 knees from 689 participants (404 women) met the inclusion criteria. Demographic data are shown in Table 1.

Relationship between physical activity and cartilage thickness change

A cartilage thickness change in MFTC of -0.20 mm (95%CI: -0.22 to -0.17 mm) was observed in the entire cohort. Cartilage thickness loss (MFTC, cMFTC) was greater in participants with low PA, although it did not differ significantly from cartilage thickness loss in participants with high PA (adjusted between group difference MFTC (-0.03 mm [-0.10 to 0.03mm]); cMFTC (-0.06 mm [-0.16 to 0.04 mm]), or participants with moderate PA (adjusted between group difference MFTC (-0.04 mm [-0.10 to 0.02 mm]); cMFTC (-0.04 mm [-0.13 to 0.06 mm]) (Table 2).

Change in cartilage thinning scores were also observed to be greater in the low PA compared to moderate (adjusted between group difference (-0.19 mm [-0.46 to 0.09 mm]) and high PA groups (adjusted between group difference (-0.20 mm [-0.50 to 0.95 mm]), but the differences did not reach statistical significance. Thickening scores did not differ significantly between PA tertiles (Table 2).

A statistically significant sex-by-physical activity interaction was observed in the adjusted analysis (p=0.02) indicating a different effect of physical activity in men and women. The analysis stratified by sex showed that women with low PA had a statistically significantly larger MFTC and cMFTC cartilage thickness loss and cartilage thinning compared with women with moderate PA (adjusted between group difference MFTC (-0.09 mm [-0.16 to -0.02 mm]); cMFTC (-0.14 mm [-0.26 to -0.02 mm])/ thinning ((-0.42 mm [-0.80 to -0.05 mm]) (Table 2). Interestingly, cartilage thickness loss in the MFTC and cMFTC of women with high PA tended to be slightly larger than the observed loss in women with moderate PA (adjusted between group difference MFTC (-0.06 mm [-0.13 to 0.02 mm]); cMFTC (-0.07 mm [-0.19 to 0.05 mm]). On the contrary, men with moderate PA had a statistically significantly larger cMFTC thickness loss compared with high PA (adjusted between group difference cMFTC (-0.18 mm [-0.35 to -0.02 mm]) (Table 2). Exploratory analyses showed that the relationship between PA and cartilage thickness loss did not differ between KL grades (Supplementary Table 1) and the results for the MFTC and cMFTC percent changes (Supplementary table 3) are in line with the primary analysis. Finally, the baseline PASE score did not influence cartilage thickness loss over 4-year follow-up (Supplementary table 2).

DISCUSSION

In this evaluation of the relationship between physical activity and cartilage MRI-assessed structural changes in people with knee osteoarthritis over a four-year period, we observed that sex modifies the relationship between physical activity and cartilage thickness loss. Although no association was observed between PA and cartilage loss in the whole cohort, in women moderate PA may slow down structural disease progression compared to low PA activity levels. Furthermore, high PA seems not to be more harmful than lower PA levels for structural changes either in women or men.

Our findings that PA levels did not influence cartilage thickness loss in the overall cohort extends data from a systematic review on randomized controlled trials, showing that exercise does not harm articular cartilage (28) and two previous studies that observed no association between PA and cartilage loss or cartilage composition in people with cartilage defects or at risk of OA, respectively (6, 7). Importantly, evaluation of sex-specific relationships revealed that PA levels, particularly in women, influenced cartilage thickness loss, which has not previously been reported. More precisely, the observation that moderate PA may be structurally protective in women with radiographic KOA, extends previous findings from the OAI suggesting that moderate PA may slow cartilage compositional change (specifically cartilage MRI transverse relaxation time T2) in those without radiographic KOA (10). Although the greatest amount of cartilage thickness loss was observed in men and women with low PA, the differences in structural progression between PA tertiles were more pronounced in women than in men. The typical annual rate of cartilage loss in the MFTC of knees with radiographic KOA is 0.06 mm (26), suggesting that the moderate (and high) PA observed in the current study may be protective against cartilage loss (annualized loss 0.04 mm and 0.05mm, respectively), whereas low PA appears to be associated with structural progression (annualized cartilage loss 0.06 mm). Although only displaying small annualised differences over 4 years, high PA does not appear to be as detrimental as low PA for structural progression of knee OA.

The specific type of PA preferably selected by women or men may partly explain the sex-specific association we observed in the current study. Men had higher absolute PASE scores than women and the differences between men and women were most pronounced in the subscale related to sports activities, indicating that also the type of activity might have an impact on cartilage thickness loss. Yet, a higher PA level may be related to a higher frequency of trauma and injury (32) (and hence to a greater loss of cartilage) however, we adjusted for knee injury in our analyses. Muscle weakness may have also influenced the sex-specific relationship between PA and cartilage thickness. Quadriceps weakness in particular is closely related to PA (29) and has been shown to be a risk factor for developing radiographic KOA (13), worsening of joint space narrowing (13, 30), and for undergoing knee replacement surgery (31) in women, but did not display such relationships in men. The influence of quadriceps weakness on the relationship between PA levels in women and cartilage thickness should be considered in future analyses.

The results we observed for the location-independent cartilage thinning score were similar but not superior to the results obtained for the primary, location-based outcome measures. Importantly, the location-independent analysis showed that the differences between PASE groups were driven by differences in cartilage thinning (i.e. cartilage loss) and not by differences in cartilage thickening, which could be caused by swelling or hypertrophy (33).

An important consideration in interpreting the results of this study is the use of self-reported PASE scores for defining PA tertiles. The PASE questionnaire covers only a limited period of time before each assessment (i.e. seven days) and in hip OA, it has been claimed not to be sufficiently sensitive to detect differences that may be important to structural progression (34). Also, patients with KOA tend to overestimate their activity level when self-reporting (35) and the aggregate PASE data reported in the OAI limited our ability to analyse individuals based on specific types of activities within each PASE component. It is perhaps not surprising that such a limited window of PA assessment was not associated with cartilage loss over time, (Supplementary Table 2) and was an important reason for our use of the mean PASE score over the 4-year study window.. In addition, the mean PASE score in the moderate PA tertile was in the range previously suggested to be associated with a favorable waist circumference (36) which reassures that the level of moderate PA observed in the current study is clinically important. Furthermore, although participant selection was based on the availability of cartilage thickness measurements performed as part of previous studies (26, 37, 38) we adjusted for potential covariates to minimize their impact on results. The phenomenon of index event (collider) bias, while influencing risk factor studies for disease progression, is less likely to have influenced the current study because both underload and overload are risk factors for incident radiographic disease (39). Also a limitation of the current study is the relatively modest sample size compared to the total OAI population, which may have limited the power in detecting significant differences. However, we included all eligible participants from the OAI, and to maximise power we focussed our primary analysis on the whole cohort (men and women combined) (n=689). Finally, the study sample was not randomly selected from the general population. Indeed participants were from the OAI progression cohort and by definition had more severe disease than the average OAI participant (which included those without KOA), limiting the generalizability of our findings to other samples.

Implications for clinicians, patients and researchers

Patients with KOA should be counselled and reassured that high PA levels do not appear to be more harmful than lower PA levels for structural progression of the disease. In the context of current clinical practice guidelines, this is important, as exercise-therapy, which is a first line treatment for KOA, is clinically effective regardless of the PA level (40). Although we cannot be sure whether the moderate PA level in our study, assessed by tertiles, reflects the actual PA guidelines of moderate PA, in a non-OA population the PASE has been shown to discriminate between participants' PA level and PA guidelines, where participants who met the PA guidelines had a higher PASE score than sedentary participants (41). Although it was outside the scope of the current study (only 66, 16 and 70 participants maintained low, moderate and high PA, respectively), future studies should focus on the influence of PA changes over time, since, for example, a sudden increase in PA and the consequent increased load may have a different effect on cartilage that is unaccustomed to such a spike in load.

CONCLUSION

Physical activity was not associated with cartilage thickness loss in the whole cohort, however, this relationship significantly differed between men and women. Particularly in women, moderate physical activity may slow down cartilage thickness loss compared to low PA activity levels. For both men and women, high PA does not appear to be detrimental for cartilage thickness loss. People with knee osteoarthritis can be informed that higher activity levels do not further damage their knee joints.

Ethics approval

The OAI study and public use of clinical and imaging data was approved by the local ethic committees at the four clinical OAI centres.

Contributorship statement

Contributors: All authors have contributed in writing this manuscript and gave their final approval of the submitted version. AB is the guarantor. All authors had full access to the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interest and fundings

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: data acquisition in this study was funded by the Osteoarthritis Initiative, a public–private partner-ship comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259;N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the Osteoarthritis Initiative study Investigators. Private funding partners of the OAI include Merck Research Laboratories, Novartis Pharmaceuticals Corporation, GlaxoSmithKline, and Pfizer, Inc. Private sector funding for the Osteoarthritis Initiative is managed by the Foundation for the National Institutes of Health. The image analysis in this study was partly funded by the FNIH OA Biomarkers Consortium, with grants, direct and in-kind contributions, provided by: AbbVie; Amgen Inc.; Arthritis Foundation; Bioiberica S.A.; DePuy Mitek, Inc.; Flexion Therapeutics, Inc.; GlaxoSmithKline; Merck KGaA; Rottapharm | Madaus; Sanofi; and Stryker. Other parts of funding were provided by a direct grant from Merck KGaA, by a contract with the University of Pittsburgh (Pivotal OAI MRI Analyses [POMA]: NIH/NHLBI Contract No. HHSN2682010000 21C), by a vendor contract from the OAI coordinating center at University of California, San Francisco (N01-AR-2-2258), and by an ancillary study to the OAI held by the Division of Rheumatology, Feinberg School of Medicine, Northwestern University (R01 AR52918). This research has also received funding from the European Union Seventh Framework Programme (FP7-PEOPLE-2013-ITN; KNEEMO) under grant agreement number 607510. AGC is supported by a National Health and Medical Research Council (NHMRC) of Australia Early Career Fellowship (Neil Hamilton Fairley Clinical Fellowship No.1121173). The sponsors were not involved in the design and conduct of this particular study, in the analysis and interpretation of the data, and in the preparation, review, or approval of the manuscript.

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TABLES

Table 1. **Demographic characteristics of the participants included in the analysis.**

			Four-year physical activity level		
		Whole cohort (n=689)	**Low (n=231)**	**Moderate (n=230)**	**High (n=228)**
Baseline age (years) (mean ± SD)		61.6 (8.9)	65.0 (8.7)	62.8 (8.6)	57.1 (7.5)
Sex, male		285 (41%)	95 (41%)	96 (42%)	94 (41%)
Baseline BMI (kg/m^2) (mean ± SD) [a]		30.0 (4.8)	29.9 (4.4)	30.2 (5.4)	29.9 (4.7)
Baseline knee injury [b]		264 (38%)	82 (35%)	85 (37%)	95 (42%)
Baseline knee pain (WOMAC Likert pain scale)		3.3 (3.5)	3.6 (3.7)	3.3 (3.5)	3.1 (3.2)
Charlson comorbidity index score [c]	0	514 (75%)	162 (70%)	164 (72%)	188 (83%)
	≥1	171 (25%)	68 (30%)	65 (28%)	38 (17%)
Baseline KOA severity	KL grade 2	387 (56%)	126 (55%)	121 (52%)	140 (61%)
	KL grade 3	277 (40%)	98 (42%)	96 (42%)	83 (36%)
	KL grade 4	25 (4%)	7 (3%)	12 (5%)	6 (3%)
Baseline knee alignment [d] **(degrees)*** (mean ± SD)	M&F	-1.7 (3.8)	-2.1 (3.7)	-1.3 (3.6)	-1.7 (4.0)
	M	-2.9 (3.7)	-3.6 (3.6)	-2.1 (3.8)	-3.0 (3.7)
	F	-0.8 (3.5)	-1.0 (3.3)	-0.6 (3.4)	-0.7 (3.8)
Baseline MFTC cartilage thickness (mm) (mean ± SD)	M&F	3.3 (0.7)	3.2 (0.7)	3.3 (0.7)	3.5 (0.7)
	M	3.6 (0.8)	3.5 (0.7)	3.6 (0.8)	3.8 (0.8)
	F	3.2 (0.6)	3.1 (0.6)	3.2 (0.6)	3.2 (0.6)
Four-year PASE	M&F	153 (65)	87 (23)	145 (19)	227 (45)
	M	164 (69)	91 (26)	156 (19)	244 (42)

overall score (mean ± SD)	F	145 (61)	84 (19)	137 (16)	215 (43)
	M&F	83 (31)	60 (21)	90 (27)	99 (29)
Four-year PASE household activity (mean ± SD)	M	87 (31)	63 (23)	93 (28)	103 (27)
	F	81 (30)	59 (58)	87 (26)	96 (30)
	M&F	44 (50)	8 (14)	29 (31)	94 (49)
Four-year PASE work-related (mean ± SD)	M	46 (52)	6 (11)	31 (32)	102 (46)
	F	42 (49)	10 (15)	28 (30)	89 (51)
Four-year PASE sport /recreational (mean ± SD)	M&F	25 (19)	18 (13)	25 (18)	33 (24)
	M	30 (21)	21 (14)	31 (19)	38 (27)
	F	22 (17)	15 (11)	21 (15)	28 (21)

* Negative values represent varus alignment. KOA = knee osteoarthritis; KL = Kellgren–Lawrence grade; MFTC = medial femorotibial compartment; SD = standard deviation; PASE = Physical Activity Scale for the Elderly; KOA = Knee Osteoarthritis; BMI = Body mass index. Low = PASE first tertile; Moderate = PASE second tertile; High = PASE third tertile. Values are N and %, unless otherwise stated; M = Male; F = Female. [a] = one missing value in men ; [b] = 107 missing values (38 men and 69 women); [c] = 4 missing values (1 men and 3 women); [d] = 3 missing values (1 men and 2 women).

Table 2: Four-year change in cartilage thickness (in mm) in OAI participants with established radiographic OA stratified by physical activity (PA)

		Low PA	**Moderate PA**	**High PA**	**Low vs. Moderate** P-value		**High vs. Moderate** P-value		**Low vs. High** P-value	
Overall		Mean 95% CI	Mean 95% CI	Mean 95% CI	Non-adjusted	**Adjusted§**	Non-adjusted	**Adjusted§**	Non-adjusted	**Adjusted§**
(n=689)	MFTC (mm)	-0.23(-0.28 to -0.19)	-0.17 (-0.21 to -0.13)	-0.18 (-0.22 to -0.14)	0.04	**0.27**	0.80	**0.66**	0.07	**0.55**
	cMFTC (mm)	-0.41 (-0.48 to -0.34)	-0.33 (-0.39 to -0.26)	-0.33 (-0.39 to -0.26)	0.10	**0.55**	0.97	**0.87**	0.09	**0.48**
	Thinning (mm)	-1.81 (-2.02 to -1.62)	-1.63 (-1.80 to -1.45)	-1.61 (-1.79 to -1.44)	0.15	**0.27**	0.93	**0.93**	0.13	**0.35**
	Thickening (mm)	0.45 (0.40 to 0.50)	0.51 (0.46 to 0.57)	0.53 (0.47 to 0.58)	0.10	**0.14**	0.77	**0.22**	0.05	**0.80**
Men										
(n=285)	MFTC (mm)	-0.27 (-0.34 to -0.19)	-0.25 (-0.32 to 0.18)	-0.21 -(0.28 to -0.14)	0.77	**0.31**	0.40	**0.07**	0.26	**0.43**
	cMFTC (mm)	-0.45 (-0.57 to -0.32)	-0.47 (-0.58 to -0.35)	-0.37 (-0.48 to -0.27)	0.82	**0.13**	0.25	**0.03**	0.36	**0.52**
	Thinning (mm)	-1.85 (-2.15 to -1.55)	-1.90 (-2.20 to -1.59)	-1.76 (-2.03 to -1.50)	0.81	**0.16**	0.51	**0.19**	0.68	**0.88**
	Thickening (mm)	0.40 (0.32 to 0.48)	0.43 (0.36 to 0.50)	0.43 (0.37 to 0.50)	0.56	**0.52**	0.90	**0.86**	0.48	**0.67**
Female										
(n=404)	MFTC (mm)	-0.21 (-0.27 to -0.16)	-0.12 (-0.16 to - 0.07)	-0.16 (-0.21 to -0.11)	0.01	**0.01**	0.21	**0.06**	0.14	**0.50**
	cMFTC (mm)	-0.38 (-0.47 to -0.29)	-0.23 (-0.30 to -0.15)	-0.29 (-0.37 to -0.21)	0.01	**0.02**	0.28	**0.16**	0.13	**0.34**
	Thinning (mm)	-1.79 (-2.08 to -1.51)	-1.43 (-1.63 to -1.24)	-1.51 (-1.74 to -1.29)	0.03	**0.02**	0.65	**0.38**	0.10	**0.17**
	Thickening (mm)	0.49 (0.42 to 0.56)	0.58 (0.50 to 0.66)	0.59 (0.51 to 0.67)	0.10	**0.20**	0.80	**0.18**	0.06	**0.96**

Non-adjusted mean cartilage thickness changes and 95% confidence intervals reported stratified by physical activity tertiles for the whole cohort and separately for men and women. Negative values represent cartilage thickness loss. MFTC= medial tibiofemoral compartment; cMFTC= central medial femorotibial compartment; PA= physical activity. § Adjusted for age, sex, body mass index, knee injury, Kellgren-Lawrence grade, knee alignment, comorbidity index and WOMAC pain. 113 participants (41 men and 72 women) were not included in the adjusted analysis due to missing data on knee alignment, comorbidities index, previous knee injury and BMI.

Figure Legends

Figure 1: Flow chart of participants included in the study and reasons for exclusion. KL= Kellgren–Lawrence grade; JSN= Joint space narrowing.

Figure 2. Cartilage thickness changes and 95% confidence interval between baseline and year-4 stratified by sex and physical activity tertiles. a) MFTC= medial tibiofemoral compartment; b) cMFTC= central medial femorotibial compartment; c) location-independent cartilage thinning score; d) location-independent cartilage thickening score.

Figure 1

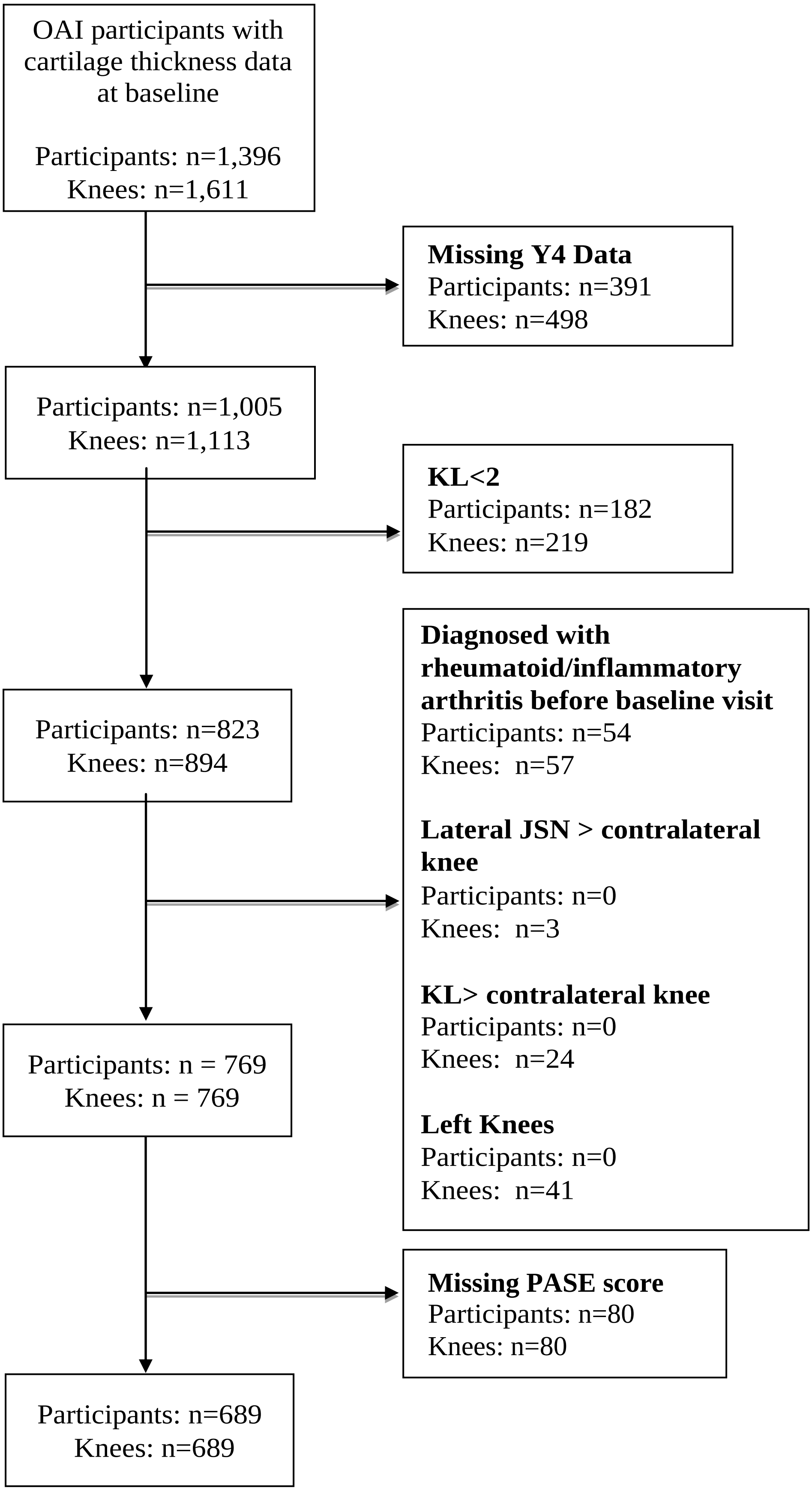
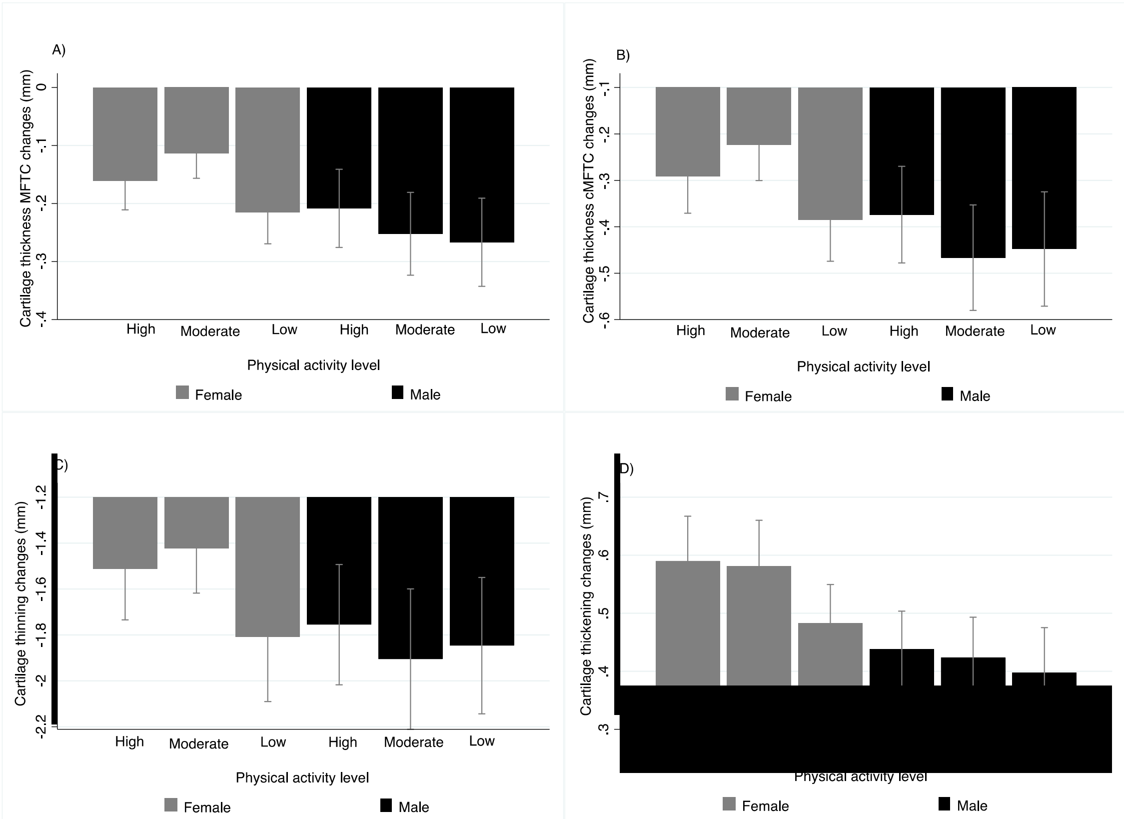

OAI participants with cartilage thickness data at baseline
Participants: n=1,396
Knees: n=1,611
Missing Y4 Data
Participants: n=391
Knees: n=498
Participants: n=1,005
Knees: n=1,113
KL<2
Participants: n=182
Knees: n=219
Participants: n=823
Knees: n=894
Diagnosed with rheumatoid/inflammatory arthritis before baseline visit
Participants: n=54
Knees: n=57
Lateral JSN > contralateral knee
Participants: n=0
Knees: n=3
KL> contralateral knee
Participants: n=0
Knees: n=24
Left Knees
Participants: n=0
Knees: n=41
Participants: n = 769
Knees: n = 769
Missing PASE score
Participants: n=80
Knees: n=80
Participants: n=689
Knees: n=689

Figure 2


A)
Cartilage thickness MFTC changes (mm)
0
-.1
-.2
-.3
-.4
High
Moderate
Low
High
Moderate
Low
Physical activity level
Female
Male
B)
Cartilage thickness cMFTC changes (mm)
-.1
-.2
-.3
-.4
-.5
-.6
High
Moderate
Low
High
Moderate
Low
Physical activity level
Female
Male
C)
Cartilage thinning changes (mm)
-1.2
-1.4
-1.6
-1.8
-2
-2.2
High
Moderate
Low
High
Moderate
Low
Physical activity level
Female
Male
D)
Cartilage thickening changes (mm)
.7
.6
.5
.4
.3
[redacted]
Female
Male