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nosis (Figure 1). Both knee and hip OA persons have increased risk of diabetes, however only for knee OA the 95% confidence interval excluded 1 (HR 1.19 [95%CI 1.12, 1.25]). In addition, only knee OA patients have an increased risk of fracture to the forearm. For the rest of the diagnoses, we found either no increased risk for knee or hip OA persons (i.e. HR estimates close to 1.00), or estimates with wide confidence intervals, excluding any clear interpretations of the direction or size of the effects.

Conclusions: Incident doctor-diagnosed knee and hip OA are associated with increased risk of consultation for depression, cardiovascular diseases, back pain, osteoporosis, and diabetes. Results confirm previous findings regarding cardiovascular diseases and diabetes, however suggest, that the risk of diabetes is mainly associated with knee OA, whereas hip OA in general, has more impact on the risk of other conditions than knee OA has. Part of the found associations might be driven by BMI, which could not be adjusted for in the present study.

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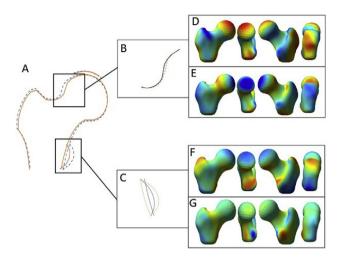
IS LESSER TROCHANTER SIZE A NOVEL RISK FACTOR FOR HIP **OSTEOARTHRITIS? FINDINGS FROM THE MROS STUDY**

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Purpose: Previously, we used statistical shape modelling (SSM) of hip dual x-ray absorptiometry (DXA) scans to examine associations between two-dimensional (2D) whole hip shape and radiographic hip osteoarthritis (rHOA). A limitation in this approach is that it is difficult to know precisely which aspects of shape underlie the relationships we observed. We aimed to define which shape characteristics are related to rHOA in more detail, by examining individual subregions of the hip, and utilising three-dimensional (3D) hip shape derived from quantitative computed tomography (QCT) scans to validate our findings.

Methods: Within the Osteoporotic Fractures in Men Study (MrOS), hip DXAs taken at baseline were used for SSM, and pelvic radiographs taken at visit 2 (~5 years later) were graded for rHOA (Croft score). A composite 2D model of whole hip shape at risk for rHOA was obtained, based on associations between hip shape modes (HSMs; derived from principal components analysis of the whole hip by SSM) and rHOA. Following inspection of the at-risk whole shape model, sub-regional models were subsequently built to describe particular aspects of hip shape suggested to be associated with rHOA. Sub-regional hip shapes were then derived, and relationships with rHOA examined by logistic regression. The sub-regional HSMs were further analysed for associations with 3D-HSMs derived from concurrent hip quantitative computed tomography (QCT) scans using linear regression. Bonferroni correction was used to adjust for multiple testing.

Results: 4098 participants were identified with hip DXAs and radiographs. Inspection of the composite whole hip shape associated with rHOA [reflecting associations with HSMs 2,3,4 & 9 (OR 0.82,0.76,0.71 & 1.2; $P < 5 \times 10^{-3}$ respectively)], suggested that a pistol-grip femoral head and larger lesser trochanter are related to rHOA (Fig 1A). Sub-regional models were built for these subregions termed cam-type modes (CTM) and lesser trochanter modes (LTM). CTM3 [OR 1.27; 95% CI 1.13,1.42; P 7.89 x 10 ⁻⁰⁵], representing a classic pistol-grip deformity (Fig 1B), and LTM1 [OR 0.74; 0.63,0.87; P 2.26 x 10⁻⁰⁴], representing a larger lesser trochanter (Fig 1C), were found to be associated with rHOA. 515 participants also had available data from hip QCT scans, from which 3D-HSMs were derived. CTM3 was associated with 3D-HSM3 [beta -0.16; 95% CI -0.25,-0.07; P 2.9x10⁻⁴], such that a larger 2D lateral pistol-grip bulge was inversely associated with a smaller 3D lateral femoral head (Fig 1D). CTM 3 was also associated with 3D-HSM6 [β 0.19; 95% CI 0.10,0.28; P 2.0x10⁻⁵] with a larger 2D lateral pistol-grip bulge associated with a larger 3D lateral femoral head (Fig 1E). LTM1 was associated with 3D-HSM7 [beta -0.23; 95% CI -0.33,-0.14; P 3.1x10⁻⁶], such that a larger 2D lesser trochanter was associated with a larger 3D lesser trochanter (Fig 1F). LTM1 was also associated with 3D-HSM9 [β 0.36; 95% CI 0.27,0.45; *P* 3.0x10⁻¹³], with a smaller 2D lesser trochanter associated with a smaller 3D lesser trochanter (Fig 1G). Figure 1: Pictorial representation of our analysis and the hip shapes found to be associated with radiographic hip osteoarthritis A) The dotted line represents the composite whole hip shape at risk for rHOA and the solid



line represents the mean hip shape for this population B) CTM3; the solid line represents +2 SD and the dashed line represents -2 SD C) LTM1; the solid line represents +1 SD and the dashed line represents -1 SD D)-G) 3D-HSM3, 3D-HSM6, 3D-HSM7 & 3D-HSM9 respectively. These pictures represent 1 SD change, colour coded dark red +6mm to dark blue -6mm

Conclusions: Sub-regional SSM of hip DXA scans suggested a larger lesser trochanter and pistol-grip femoral head deformity underlie associations between overall hip shape and rHOA. 3D hip shape modelling confirmed our sub-regional HSMs represent true anatomical variations in hip shape rather than 2D image artefact, for example resulting from altered rotation of the hip during image acquisition. A pistol grip femoral head is well known to be associated with rHOA, but the association between a larger lesser trochanter and rHOA represents a novel finding. The iliopsoas muscle, a powerful hip flexor and stabiliser inserts at the lesser trochanter, suggesting possible mechanisms whereby lesser trochanter size relates to aspects of biomechanics involved in the development of hip OA.

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THE RELATION OF PHYSICAL ACTIVITY WITH FATIGUE IN PERSONS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS AND ITS POTENTIAL **MEDIATION BY PHYSICAL FUNCTION OR DEPRESSIVE SYMPTOMS:** THE MOST STUDY

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Purpose: Depressive symptoms and impaired physical function are determinants of fatigue in symptomatic knee osteoarthritis (OA) and these factors are related to physical activity. However, potential causal pathways underlying the relationship between physical activity and fatigue are poorly understood in persons with symptomatic knee OA. We examined the association of physical activity with fatigue and quantified the extent to which the association of physical activity and fatigue could be mediated by physical function or depressive symptoms. We hypothesised that depressive symptoms or physical function would mediate the association between baseline physical activity and fatigue at follow-up in the overall population. We also hypothesised that in people with high levels of baseline fatigue, increased physical activity would be associated with decreased fatigue at follow-up.

Methods: This longitudinal study included physical activity at baseline (60-month exam), fatigue at 2-year follow-up (84-month exam), depressive symptoms and physical function at baseline and follow-up from the Multicenter Osteoarthritis Study (MOST) cohort. MOST participants were classified as having symptomatic knee OA based on both the presence of radiographic whole knee OA evidence (either in tibiofemoral or patellofemoral joints) and frequent knee pain at either of the two interviews at baseline for this analysis. Exposure was defined as