FROM A 2-YEAR MULTICENTRE CLINICAL TRIAL IN HIP SHAPE PREDICTS KNEE OSTEOARTHRITIS, A METABOLOCIC ANALYSIS REVEALS THAT OVER ACTIVATION OF THE CONVERSION PATHWAY OF PHOSPHATIDYLCHOLINE TO LYSOPHOSPHATIDYLCHOLINE IS ASSOCIATED WITH KNEE CARTILAGE VOLUME LOSS OVER TIME

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Background: While progression of osteoarthritis (OA) is variable, no tools yet exist to predict disease course.

Objectives: To identify, using a metabolomic approach, serum marker(s) for predicting knee cartilage volume loss over time measured by magnetic resonance imaging (MRI) in a 24 month Phase III clinical trial in patients with symptomatic knee OA.

Methods: 139 knee OA patients who completed the clinical trial according to protocol were selected from a 24 month DMOAD trial studying the effect of licofelone versus naproxen. MRI was performed at baseline and 24 months. Targeted metabolomic profiling was performed on serum collected at baseline. Metabolite ratios as proxies for enzymatic reaction were calculated and used in the analysis. The levels of 186 metabolites were measured and 152 met the quality control requirements. The metabolite concentrations were standardised using the z-score. 21952 pair wise metabolite ratios were analysed. A metabolite-wide significance level of $p<2.3 \times 10^{-5}$ was defined after correcting multiple testing with the Bonferroni method. Univariable and multivariable analyses adjusted for sex, BMI and treatment were performed. Gene expression analysis of human OA articular cartilage (n=32) and subchondral bone (n=39) tissues from total joint replacement, and controls (non-OA) from individuals having a fracture (n=21; n=9, respectively) was done to further explore the potential metabolic pathway(s).

Results: Data revealed that the baseline ratio of the metabolite lysophosphatidylcholine 18:2 (lysoPC 18:2) to phosphatidylcholine 44:3 (PC 44:3) was associated with the cartilage volume loss in the lateral compartment (univariable, $b=-0.21 \pm 0.04$, $p=8.53 \times 10^{-2}$; multivariable, $b=0.18 \pm 0.04$, $p=9.50 \times 10^{-4}$). Further experiments demonstrated that the lysoPC 18:2:PC 44:3 ratio was also significantly ($p=0.0002$) correlated with an articular degeneration marker, COMP. The data demonstrated that in both human cartilage and subchondral bone tissues, a PLAG2, PLAG2 group 5 (PLAG2G5), was markedly overexpressed in OA cartilage and subchondral bone compared to these non-OA tissues (445% and 158% increase, respectively, all $p<0.02$). Interestingly, in these tissues TNF-$
alpha$-a was also upregulated ($p=0.007$, $p=0.08$, respectively), and positively correlated with PLAG2G5 ($r=0.71$, $p=0.02$).

Conclusions: Our data suggest that the ratio of lysoPC 18:2:PC 44:3 is predictive of greater risk of cartilage loss in OA. We speculate that this specific conversion pathway may produce a bioactive molecule like oleoylthanolamide (OEA), which has been demonstrated to bind to a novel cannabinoid receptor, GPR119, thus could be a novel therapeutic target for OA treatment.

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SAT0562

HIP SHAPE PREDICTS KNEE OSTEOARTHRITIS OUTCOMES OVER A DECADE IN OLDER-ADULTS

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Background: Various hip shapes may be important as a risk factor for development and progression of knee osteoarthritis, due to the biomechanical link between the two joints.

Objectives: This study aims to identify the relationship between hip morphology and structural and clinical osteoarthritis outcomes in the knee over 10.7 years, in older-adults.

Methods: 377 community-dwelling older-adults aged 50-80 years were studied. At baseline, dual-energy X-ray absorptiometry images of the left hip were obtained and hip shapes were described using mode scores from an 85-point statistical shape model. MRI scans were conducted at baseline and a mean follow-up of 10.7 (SD:0.67) years later, to assess right knee tibial cartilage volume and bone marrow lesions (BMLs). Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Knee replacement (KR) data were obtained by data linkage to the Australian Orthopaedic Association National Joint Replacement Registry. Linear mixed-effects, log-binomial models
and survival analysis, were used to investigate associations between hip shape modes and change in cartilage volume, incident BMLs, worsening knee pain and left KR respectively. All models were adjusted for baseline age, sex, BMI, knee injury or surgery and hip radiographic osteoarthritis (ROA), while the KR model was additionally adjusted for WOMAC pain and knee ROA.

**Results:** Ten hip shape modes were identified, describing 78% of the total shape variance in descending order from mode 01 (31% variance) to mode 10 (1.82% variance). Hip shapes with a larger greater trochanter (mode 07) were associated with higher knee cartilage volume loss (Beta=2.14, 95% CI 0.74,2.14), while a shorter and narrower femoral neck shape (mode 09) was related to increased volume loss (Beta=–3.86, 95% CI:–6.16,–1.56). Increasingly non-spherical femoral head (mode 04) was associated with an increased risk of incident BMLs (RR=1.19, 95% CI 1.07,1.34). Those with a longer, wider femoral neck and a larger femoral head (mode 01) had an increased risk of worsening knee pain (RR=1.33, 95% CI 1.01,1.76), whereas those with a smooth curving upper femoral neck (mode 09) had a lower risk of worsening knee pain (RR=0.78, 95% CI 0.67,0.90). A larger greater trochanter and wider femoral neck shape (mode 08) was associated with an increased risk of KR (RR=1.73, 95% CI 1.18,2.52), while increasing acetabular coverage (mode 10) was associated with a lower risk of KR (RR=0.54, 95% CI 0.36,0.8).

**Conclusions:** Hip shape variations were associated with significant MRI-based and clinical outcomes in knee over 10.7 years, possibly due to biomechanical, life-style or other factors related to both joints. These results suggest that hip shape may play an important role in the onset and progression of knee osteoarthritis over time.

**Disclosure of Interest:** None declared

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### SAT0564

**EFFECTS OF EDUCATION AND INCOME ON PREVALENCE, INCIDENCE, AND PROGRESSION OF RADIOGRAPHIC KNEE OSTEOARTHRITIS: AN ANALYSIS OF THE OSTEARTHRITIS INITIATIVE DATA**

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**Background:** Low socioeconomic status (SES) is one of the strongest predictors of morbidity and mortality from many chronic diseases including cardiovascular diseases, obesity, and diabetes. There is insufficient data regarding impact of SES on knee osteoarthritis (OA).

**Objectives:** To evaluate the associations between education, income levels and prevalence, incidence, and progression of radiographic knee OA

**Methods:** For the current analysis we used data from the publically available Osteoarthritis Initiative (OAI) database. The education status of the participants was dichotomized into either low/moderate or high educational attainment. The income status was dichotomized using 50 K US threshold. A baseline sample was used to analyse the impact of SES on knee OA prevalence (prevalence sample). To evaluate the effects of SES on knee OA incidence and progression we analysed the samples of OAI participants with KL <2 at baseline (incidence sample) and OAI participants with JSN <3 at baseline (progression sample), respectively. We used logistic regression models to assess the association between SES and prevalence and incidence of radiographic knee OA (defined as KL2 and JSN or joint replacement), and disease progression (defined as increase in semiquantitative JSN or a new knee replacement). Generalised estimating equations (GEE) were used to adjust for the correlation between knees. The models were adjusted for multiple covariates including age, race, and body mass index.

**Results:** Prevalence, incidence, and progression samples consisted of 4371 participants (8741 knees), 2268 participants (4535 knees), and 3950 participants (4013 knees), respectively.

Higher education attainment and higher income were associated with decreased prevalence of the knee OA in the crude analyses. After adjustment for confounders these associations became insignificant (Table). There was no effect of SES on incidence and progression of the knee OA.

**Table**

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<th>Unadjusted</th>
<th>Adjusted</th>
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<tr>
<td>Unadjusted</td>
<td>Adjusted</td>
<td>OR (95% CI)</td>
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<tr>
<td>Education</td>
<td>0.8 (0.7–0.9)</td>
<td>&lt;0.001</td>
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<tr>
<td>Income</td>
<td>0.71 (0.64–0.79)</td>
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| OR = odds ratio; CI = confidence interval

**Conclusions:** Higher levels of education and income are linked with decreased prevalence of radiographic knee OA. Lack of this association after adjustment suggests confounding or mediating effects of other risk factors. Future studies are needed to delineate the precise mechanisms of how SES impact knee OA.

**REFERENCE:**


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### SAT0565

**ADJUSTING FOR THE INTRA-ARTICULAR PLACEBO EFFECT IN KNEE OSTEOARTHRITIS THERAPIES**

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**Background:** Currently, there is a large debate regarding the appropriateness of intra-articular (IA) saline injection as a “placebo” comparator in knee osteoarthritis (OA) trials and meta-analyses. There is substantial evidence to suggest that the injection of saline into the joint is not without treatment effect.

**Objectives:** This study aimed to assess the current literature’s estimates of the IA-saline treatment effect against a range of appropriate minimal clinically important difference (MCID) values to identify if IA-saline provides a therapeutic effect that is not indicative of a null-effect.

**Methods:** The treatment effect estimates of IA-saline and topical placebo for knee OA pain, relative to oral placebo, were derived from a published network meta-analysis Bannuru et al, 2015 and compared across a range of plausible...