calculated, and individual trajectories in change in pain from baseline were plotted to visualise patterns of change. A minimal clinically important difference of 2 was used to classify participants as not changed, improved, or worse at 3 months, using average and worst pain severity.

Results: 99 participants were included in this analysis (71 [72%] women, mean [SD] age 60.5 [7.5] years, BMI 29.3 [6.3] kg/m^2, knee pain duration 6 [6.7] years). On average, participants reported no change in knee pain severity over the 3-month period (average pain: baseline mean 5.3 [SD 2.5], 6 weeks 5.1 [2.1], 3 months 5.2 [2.1]; worst pain: baseline 6.4 [2.5], 6 weeks 6.9 [2], 3 months 6.8 [2.1]). However, individual trajectories for average and worst pain severity demonstrated substantial variation over 3 months (Figure). From baseline to 3 months, 61 (62%) participants were unchanged, 22 (22%) improved, and 16 (16%) were worse, on the measure of average knee pain severity. For worst knee pain severity, data were available for 84 participants. 56 (67%) participants were unchanged, 9 (11%) improved, and 19 (22%) were worse at 3 months compared to baseline.

Conclusions: Knee pain severity tends to remain stable in individuals with PFOA over a 3-month period without intervention. The majority of participants did not report clinically meaningful changes in their knee pain over this period. This contrasts with previous studies in knee pain and other musculoskeletal pain conditions, where pain severity tends to decrease over time. However, our findings highlight that a proportion of individuals do experience meaningful changes in their knee pain symptoms within a 3-month period. This highlights the need for future studies to identify factors that predict symptom change in this population. This may help to identify individuals with PFOA who may improve with time or who are at risk of worsening symptoms, as well as potential treatment targets to modify the natural history of the condition.

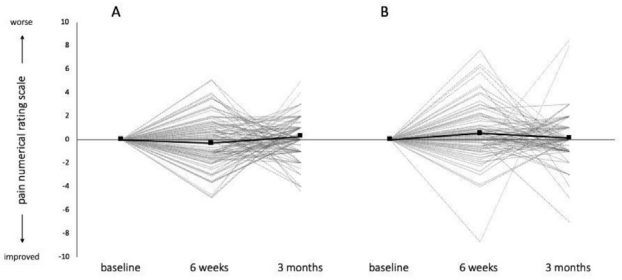

Figure. Change scores for average (A) and worst (B) pain severity NRS during participants' most aggravating activity, at 6 weeks and 3 months. Black solid lines represent group means, and grey dashed lines represent individual participant data.

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PAIN DISTANT FROM THE INDEX SITE AND SENSITIZATION IN PEOPLE WITH KNEE PAIN AND LOW BACK PAIN

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Purpose: Knee pain and low back pain, each associated with osteoarthritis, are leading causes of disability worldwide. Pain is attributed to pathology at the index site, but is only weakly associated with objective joint pathology. Peripheral and central neuronal sensitization contribute importantly to pain severity, and may cause pain and sensitivity to spread beyond the index site. American College of Rheumatology (ACR) classification of Widespread Pain is associated with reduced Pressure Pain detection Thresholds (PPTs) in people with fibromyalgia. However, it is unknown which pattern of self-reported pain distribution best indicates sensitization in people with a `localised' (knee or low back) index pain.

This study aims to measure associations between self-reported pain distribution and PPT distant from the index site in people with knee pain or low back pain, and to define an optimal manikin-derived classification of spreading pain sensitivity in these `localised' chronic pain conditions.

Methods: Baseline data from the Knee Pain and related health In the Community (KPIC)(knee pain n=322, no pain n=98), and Pain Experience in Individuals with Chronic Low Back Pain (back pain n=98) studies were used for analysis. PPT was measured at the proximal tibia (knee pain), or at the forearm (brachioradialis, back pain). Using shaded areas on a manikin, painful sites other than the index site were coded according to 7 mutually exclusive regions, and derived binary classifications including ACR Widespread Pain and other distributions. Logarithmically transformed PPT values were used in correlation and regression analyses. `Spreading sensitization', defined as a binary outcome, was identified as the lower 25% of PPTs in the back pain group, and as Z-scores >1.28 for anterior tibia PPT in the knee pain group - indicating the 80% confidence limit of the pain free group. T-tests compared between-group differences in PPTs as a function of a priori, or ROC-derived binary manikin classifications.

Results: PPTs showed significant but weak correlations with number of painful sites both in knee- ($r < -0.2$, $p<0.01$) and in back- ($r = -0.3$, $p=0.03$) pain groups. For both pain groups, at least 5 out of 7 other painful sites ([knee pain group: AUC = 0.58; sensitivity = 0.3; specificity = 0.8]; [back pain group: AUC = 0.62; sensitivity = 0.3; specificity = 0.9]) optimally distinguished those with low PPTs. PPTs were significantly lower in individuals who met the ROC-derived cut-offs of '$\geq$5/7- other painful sites.

In the knee pain group, individuals reporting 'pain other than knee pain below the waist' associated with PPTs ($\beta = -0.14$; $p< 0.02$) more strongly than did other binary classifications. Other pain below the waist did not significantly associate with PPTs in the low back pain group. ACR Widespread Pain criteria did not significantly associate with PPTs either in knee pain or in back pain groups. None of the other binary classifications showed significant associations with PPTs in the back pain group.

Conclusions: Increased number of self-reported painful sites was associated with reduced PPTs at sites away from the index joint, both in people with knee pain, and in those with low back pain. Number of painful sites additional to the index site might be more closely associated with spreading pain sensitivity than is the ACR Widespread Pain criterion. Multiple mechanisms might underlie the spreading of pain and pressure sensitivity beyond the index joint, and differences between people with knee or low back pain might reflect different mechanisms of spreading pain that can respond differently to treatments. Pain distribution explains only a small proportion of reduced PPTs distant from the index site, and composite measures which include other characteristics, such as psychological distress and neuropathic-like pain, in addition to pain distribution, may better explain widespread sensitivity than can any single trait.

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EFFECT OF METFORMIN USE ON RISK OF TOTAL KNEE ARTHROPLASTY IN PATIENTS WITH KNEE OSTEOARTHRITIS COMBINED WITH DIABETES AND/OR OBESITY

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Purpose: Metformin (MET) is a first-line drug for type 2 diabetes, and metabolic mechanisms including reduced hepatic gluconeogenesis and insulin production are thought to underlie this effect. In recent years, epidemiological studies have found that in addition to lowering blood glucose, MET can reduce the incidence and mortality of cancer, improve intestinal microbiota, reverse the effects of aging and has anti-inflammatory effects. These effects make MET a popular investigational drug in obesity and age-related diseases. Studies have found that the pathogenesis of obesity-related osteoarthritis (OA) is not only related to mechanical loading, but also mediated by inflammatory and metabolic mechanisms. Recent studies have suggested that the imbalance of intestinal flora in obesity and metabolic syndrome is related to the onset of OA. It was also found that gut microbiota produces the intermediate agmatine which is a regulator of MET effect on host lipid metabolism and longevity. Theoretically, MET may play a potential therapeutic role targeting obese OA by regulating inflammatory factors, metabolic factors and intestinal flora. However, clinical studies