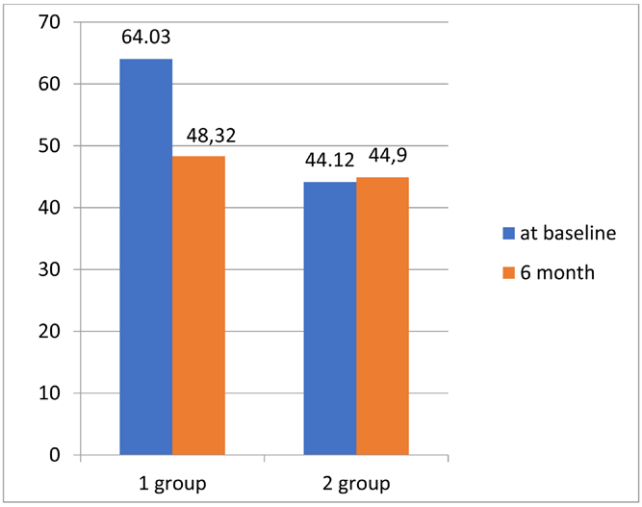
Patients from group 1 (n=25) took orlistat 120mg 3 times a day in combination with a hypocaloric diet and exercise for 6 months. Patients from group 2 (n=25) were on a hypocaloric diet in combination with exercise for 6 months. The groups were comparable in clinical parameters. The clinical course of OA was determined by the WOMAC and VAS. Anthropometric data (height, weight) were determined. All patients underwent a laboratory examination at 2 points (initially and after 6 months): a biochemical blood test, leptin was determined by PCR in peripheral blood.

Results: 8% of patients had 1 MS component, 34% - 2 MS components, 34% - 3 MS components, 22% - 4 MS components, and 2% - 5 MS components at the beginning of the study. High leptin levels (p=0.001) were determined in patients with more than 3 MS components. The correlation analysis showed direct correlations of high leptin levels with the severity of knee WOMAC pain (r=0.36, p=0.02) and VAS pain (r=0.51, p=0.01). A positive correlation was determined between high leptin levels and body weight (r=0.56, p<0.01) and waist circumference (r=0.38, p<0.01). Patients from group 1 had a significant decrease of body weight by 10.07% (p<0.05), the indicators of the WOMAC index improved: pain decreased by 52.5% (p<0.05), stiffness by 47.98% (p<0.05), joint functional failure by 51.55% (p<0.05) after 6 months of drug therapy for obesity. Patients of group 2 had a not significant decrease of body weight by 0.84% (p>0.05), and they were worse indicators of clinical manifestations of OA according to WOMAC compared to group 1 (p<0.05). 24% of patients from group 1 showed a decrease in the number of MS components. 12% of patients from group 2 had a decrease in the number of MS components and 12% patients increase in MS components. Patients from 1 group with a significant decrease in body weight, there was a decrease in the level of leptin (p = 0.05) (graphic 1), in contrast to patients without weight loss on the background of non-drug therapy (p = 0.64). We found direct correlations between a decrease in leptin levels and a decrease in the WOMAC index (pain, stiffness, joint functional failure, total WOMAC) (r=0.5, p=0.01; r=0.4, p=0.04; r=0.4, p=0.03; r=0.5, p=0.01, respectively). Patients with a decrease in the number of MS components had a significantly lower leptin levels (p=0.01).



Graphic 1. Dynamic of leptin.

Conclusion: Leptin is a predictor of a worse course of the metabolic phenotype of OA associated with MS and obesity. High levels of leptin were observed with more MS components, and were associated with the severity of knee pain and body weight. We observed a decrease in the level of leptin, a decrease in the number of MS components, and an improvement in the clinical manifestations of OA against the background of a significant decrease in body weight. Thus, the treatment of obesity in patients with the metabolic phenotype of OA and other interventions aimed at reducing the level of leptin may contribute to reducing the progression of knee OA.

Disclosure of Interests: None declared

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Monitoring and restoring health: Should we have a core set for multidisciplinary care in rheumatology_

OP0198-HPR

A STRUCTURED MODEL FOR OA CARE IN PRIMARY HEALTHCARE IS A COST-EFFECTIVE ALTERNATIVE COMPARED TO USUAL CARE FOR PEOPLE WITH HIP AND KNEE OA

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Background: To improve quality of care for patients with hip and knee osteoarthritis (OA), a structured model for integrated OA care was developed based on international treatment recommendations. A previous analysis of a cluster RCT (cRCT) showed that compared to usual care, the intervention group reported higher quality of care and greater satisfaction with care. Also, more patients were treated according to international guidelines and fulfilled recommendations for physical activity at the 6-month follow-up.

Objectives: To assess the cost-utility of a structured model for hip or knee OA care.

Methods: A cRCT with stepped-wedge cohort design was conducted in 6 Norwegian municipalities (clusters) in 2015-17. The OA care model was implemented in one cluster at the time by switching from "usual care" to the structured model. The implementation of the model was facilitated by interactive workshops for general practitioners (GPs) and physiotherapists (PTs) with an update on OA treatment recommendations. The GPs explained the OA diagnosis and treatment alternatives, provided pharmacological treatment when appropriate, and suggested referral to physiotherapy. The PT-led patient OA education programme was group-based and lasted 3 hours followed by an 8–12-week individually tailored resistance exercise programme with twice weekly 1-hour supervised group sessions (5–10 patients per PT). An optional 10-hours Healthy Eating Program was available. Participants were ≥45 years with symptomatic hip or knee OA.
Costs were measured from the healthcare perspective and collected from several sources. Patients self-reported visits in primary healthcare at 3, 6, 9 and 12 months. Secondary healthcare visits and joint surgery data were extracted from the Norwegian Patient Register. The health outcome, quality-adjusted life-year (QALY), was estimated based on the EQ-5D-5L scores at baseline, 3, 6, 9 and 12 months. The result of the cost-utility analysis was reported using the incremental cost-effectiveness ratio (ICER), defined as the incremental costs relative to incremental QALYs (QALYs gained). Based on Norwegian guidelines, the threshold is €27500. Sensitivity analyses were performed using bootstrapping to assess the robustness of reported results and presented in a cost-effectiveness plane (Figure 1).

Results: The 393 patients' mean age was 63 years (SD 9.6) and 74% were women. 109 patients were recruited during control periods (control group), and 284 patients were recruited during interventions periods (intervention group). Only the intervention group had a significant increase in EQ-5D-5L utility scores from baseline to 12 months follow-up (mean change 0.03; 95% CI 0.01, 0.05) with QALYs gained: 0.02 (95% CI -0.08, 0.12). The structured OA model cost approx. €301 p.p. with an additional €50 for the Healthy Eating Program. Total 12 months healthcare cost p.p. was €1281 in the intervention and €3147 in the control group, resulting in an incremental cost of -€1866 (95% CI -3147, -584) p.p. Costs related to surgical procedures had the largest impact on total healthcare costs in both groups. During the 12-months follow-up period, 5% (n=14) in the intervention compared to 12% (n=13) in the control group underwent joint surgery; resulting in a mean surgical procedure cost of €553 p.p. in the intervention as compared to €1624 p.p. in the control group. The ICER was -€93300, indicating that the OA care model resulted in QALYs gained and cost-savings. At a threshold of €27500, it is 99% likely that the OA care model is a cost-effective alternative.

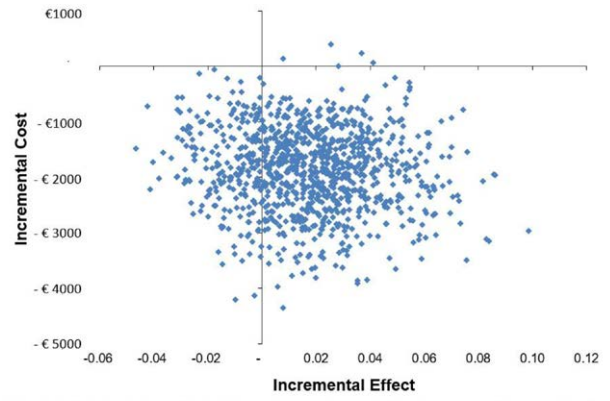

Figure 1 Cost-effectiveness plane for the comparison of implementation of a structured model for OA care (intervention group) and usual care (control group)

Conclusion: The results of the cost-utility analysis show that implementing a structured model for OA care in primary healthcare based on international guidelines is highly likely a cost-effective alternative compared to usual care for people with hip and knee OA. More studies are needed to confirm this finding, but this study results indicate that implementing structured OA care models in primary healthcare may be beneficial for the individual as well as for the society.

Disclosure of Interests: None declared

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Emerging molecular targets in OA

OP0199 EX VIVO BIOMARKER PROFILING IDENTIFIES ONCOSTATIN-M AS SPINE OSTEOARTHRITIS-SPECIFIC OSTEOIMMUNOLOGICAL TARGET

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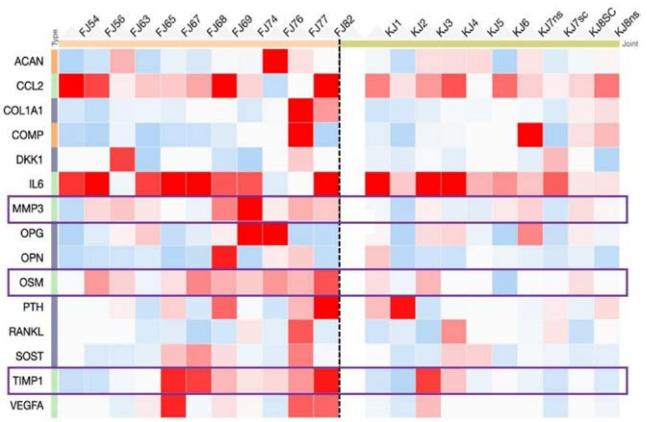
Background: Disease heterogeneity, both clinically and molecularly, has been a major hurdle in the development of efficacious disease-modifying osteoarthritis drugs (DMOADs). Biomechanical, inflammatory, osteoporotic and metabolic OA have been proposed as clinically relevant subtypes for stratification of knee OA patients, yet this remains to be included in clinical trial design. Disease heterogeneity does not only occur within, but also between joint types. However, robust data on joint-specific pathomechanisms of OA are still lacking.

Objectives: In this study, we performed ex vivo biomarker profiling of human osteochondral tissue of knee and spine OA to identify joint-specific pathomechanisms and DMOAD treatment responses.

Methods: Facet joint and tibial plateaus were obtained from patients undergoing lumbar spinal fusion (n=11, mean age 72.8) and total joint arthroplasty (n=8, mean age 73.0) respectively. Osteochondral specimens were cut in equal-sized samples (100-300 mg wet weight) and randomly assigned to treatment groups: control (DMSO), inflammation (1 µg/mL LPS) or inflammation + DMOAD (TGF-beta type I receptor inhibitor,10 µM SB-505124). Explant culture was conducted for one week and biomarkers of bone metabolism (Pro-Col-Ia, SOST, OPG, SPP1), inflammation (MCP-1, IL-6, MMP3, OSM, TIMP1, VEGFA) and cartilage metabolism (ACAN, COMP) were determined by ELISA. Normalized biomarker secretion was analysed using clusteranalyses and ANOVA. Cartilage proteoglycans were assessed by whole mount Alcian blue staining. Expression of Oncostatin-M (OSM) and its receptors OSMR and LIFR in joint tissues was assessed by RT-PCR and immunohistochemistry.

Results: Clusteranalyses revealed that LPS stimulation increased IL-6 and MCP-1 secretion by both facet joint (FJ) and knee joint (KJ) tissues. Interestingly, Oncostatin-M (OSM) and its downstream mediators MMP3 and TIMP1 were increased in the majority of FJ, but not KJ specimens. Statistical analyses corroborated increased OSM, MMP3 and TIMP1 levels in a spine-specific fashion (Figure).



Whole mount Alcian blue staining revealed heterogeneous effects of LPS treatment on cartilage proteoglycans, which was negatively correlated with OSM (r=-0.54) and TIMP1 levels (r=-0.45) – yet poorly associated with ACAN (r=0.19). Inhibition of TGF-beta type I receptor signalling in osteochondral tissues led to a drastic reduction of Pro-Collagen-Ia and IL-6 secretion in both spine and knee OA specimens. Interestingly, DMOAD treatment significantly reduced OSM, TIMP1 and MMP3 levels in FJ specimens only. Vice versa, KJ tissues revealed a specific upregulation of monocyte chemoattractant protein-1 (MCP-1) and osteopontin (SPP1) upon inhibition of TGF-beta signalling. OSM was exclusively expressed in subchondral bone marrow macrophages. Isolated chondrocytes and osteoblasts expressed both LIFR and OSMR, yet intact cartilage only showed OSMR expression, while OSMR and LIFR was expressed in marrow tissue

Conclusion: Oncostatin-M expression and signalling was uncovered as specific pathomechanism of spine OA. DMOAD treatment effects suggested interplay of OSM and TGF-beta signalling pathways in facet joint osteoarthritis. Known to be predominantly expressed by macrophages and immune cells, OSM may be an important osteoimmunological mediator of tissue damage and remodelling in spine, but not knee OA. This study also highlights the value of *ex vivo* human tissue models for OA phenotyping and preclinical evaluation of DMOADs.

Disclosure of Interests: None declared

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OP0200 BLOCKING ROR2 IMPROVES CARTILAGE INTEGRITY AND PROVIDES PAIN RELIEF IN OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is the leading cause of chronic disability worldwide, affecting 12% of the population, and yet we still do not have a disease-modifying treatment. Cartilage breakdown is the hallmark of OA, and patients suffer from pain and loss of joint function/independence, severely affecting quality of life. Therefore, there is a huge unmet clinical need.

Receptor tyrosine kinase–like orphan receptor 2 (ROR2) is a non-canonical WNT receptor that regulates the planar cell polarity pathway, controlling limb outgrowth during development. During skeletal development, chondrocytes require ROR2 to undergo hypertrophy throughout the process of endochondral bone formation[1]. Loss of function mutations in humans causes Recessive Robinow Syndrome, leading to limb shortening and brachydactyly[2,3].