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Purpose: Osteoarthritis (OA) is the most common joint disease with a great impact on the quality of life. Obesity and the related metabolic disease are main risk factors, in which low-grade systemic inflammation is an important regulator. In this regard, the infrapatellar fat pad (IPFP) also came forward as a local OA joint tissue, contributing to and influenced by inflammatory responses in the OA knee.
Our study aims to investigate the association between obesity and local inflammatory, fibrotic responses in the IPFP of obese end-stage knee OA patients.
Methods: After ethical approval by the Central Denmark Region Committees on Health Research Ethics, human IPFPs were obtained as waste material during total knee replacement in 48 patients with increased body mass index (BMI) (mean 35.44kg/m2). The fat pads were frozen at -80°C maximum 1 hour after being removed. We performed gene expression analyses for the following primers: PLOD2 (involved in the regulation of hydroxyallysine collagen crosslinks), aSMA (corresponding with the myofibroblast phenotype), COL1 (encoding for alfa-1 type collagen), and IL6, TNFa, Il1b as markers of inflammation. Blood samples (non-fasting) were collected to assess glucose, lipid status (total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride). In addition, serum leptin concentration was measured as a biomarker of adiposity. Total body composition (fat mass, lean mass, and bone mass) was measured using dual-energy X-ray absorptiometry.
Results: Univariate analysis of BMI and gene expression in IPFP explants resulted in a positive correlation between BMI and PLOD2 expression with 13.15% of the variance explained by this variable (r2=0.1315). No correlation was found for BMI and other determinants of fibrosis such as aSMA (α-smooth muscle actin) or COL1 (type I collagen α1 chain gene), nor inflammatory markers such as TNFα, IL1ß or IL6. To explore the correlation between BMI and PLOD2, metabolic factors associated with BMI were also analyzed for correlation with PLOD2. In the univariate analysis, significant correlations with PLOD2 expression were found for lean and fat mass (r2=0,1988), serum cholesterol (r2 =0,1669), serum triglycerides (r2 =0.1861), and serum leptin (r2 =0.1040). A collinearity plot was performed to investigate the correlation between all different independent variables and PLOD2 before performing a multivariate analysis. We withheld age, sex, glucose, fat mass, total cholesterol as independent variables. The multivariate analysis with PLOD2 indicated a strong correlation between fat mass and PLOD2 with a P-value of 0.0025. No other significant correlations were withheld within this multivariate analysis.
Conclusions: Taken together, our study is the first to demonstrate the positive association between fat-mass and PLOD2 expression in the IPFP of end stage knee OA patients. This may indicate that the fibrotic process in the IPFP in obese end-stage knee OA patients is influenced by systemic adipose tissue , next to local inflammatory processes in the knee joint, that may alter this proces.Further research is necessary to confirm these findings and its role in the knee OA disease process.

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INVESTIGATING OUTCOME INEQUALITIES IN OSTEOARTHRITIS MANAGEMENT PROGRAMMES: AN ANALYSIS OF REGISTRY DATA FROM THE GOOD LIFE WITH OSTEOARTHRITIS IN DENMARK (GLA:D®) PROGRAMME USING TAPERED BALANCING

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Purpose: The burden of osteoarthritis (OA) is often greater among disadvantaged people and communities, prompting calls for more attention to equity-focussed research and policy. A specific concern is whether healthcare interventions may inadvertently widen health inequalities. OA management programmes (OAMP) have emerged in the past decade in a major international effort to improve provision of core non-surgical care for people with OA. Recent studies have focussed on equity of access. We address a complementary issue: having gained access, do people from socially disadvantaged groups have poorer outcomes than their advantaged counterparts, and if so, what might determine this?
Methods: The study population was consecutive adults with knee OA attending the 8-week GLA:D® supervised exercise and education programme in Denmark between Oct 2014-Feb 2018. We defined a 'multiple social disadvantage' group based on primary/secondary school education and being either born outside Denmark or not having Danish citizenship. Their outcomes were compared with those of native Danish citizens with higher education. Outcomes of interest were pain intensity (0-100 VAS), KOOS Quality of Life subscale (QOL 0-100), EQ-5D-5L health utility (-0.624-1.0) at 3 and 12 months. Missing data were imputed using multiple imputation with chained equations. We used Coarsened Exact Matching (CEM) to restrict group comparisons to areas of common support, i.e. sufficient overlap on key prognostic factors (age, sex, body mass index, baseline value of the outcome measure of interest). We then used Entropy Balancing to sequentially control for differences between disadvantaged and advantaged groups in: (1) baseline value of the outcomes of interest (2) type of treatment centre, enrollment year (3) age, sex (4) BMI, previous knee injury, previous knee surgery (5) no. of selected comorbidities, no. of other non-knee pain sites (6) self-efficacy score, self-reported presence of depression (7) previous/current tailored exercise advice, weight loss counselling, analgesia/natural remedies (8) attendance at GLA:D® education and exercise sessions. Mean differences in outcomes between disadvantaged and advantaged groups were then estimated by weighted linear regression without balancing and then with entropy balancing weights from steps 1-8.
Results: Of 18,448 eligible participants, 250 (1.4%) were classed as disadvantaged. Compared with advantaged participants, they were younger, less likely to have attended GLA:D® in a private physiotherapy clinic, reported more comorbidity, pain sites, depression, lower self-efficacy, and lower attendance on GLA:D® sessions. Both groups showed overall improvements over baseline in mean pain VAS, KOOS QOL and EQ5D scores at 3 months, typically maintained at 12 months. Before covariate balancing, disadvantaged participants had substantially worse scores than advantaged participants on each measure at both follow-up points (e.g. crude between-group mean differences (95%CI) in pain VAS at 12 months: 8.6 (4.5, 12.6) respectively: Table 1). Balancing for differences on baseline score, comorbidity, self-efficacy, and depression had the greatest effect on reducing differences in outcomes.
Conclusions: Both disadvantaged and advantaged adults with knee OA reported improvements in key outcomes up to 12 months after OAMP attendance. However, compared with more advantaged adults, disadvantaged adults typically began the OAMP with more severe pain and poorer quality of life. This gap in outcomes was not reduced following OAMP attendance: for generic health-related quality of life in particular the gap widened slightly. Low self-efficacy, depression and other comorbidities may be potential determinants. Our analysis is of observed outcomes in a relatively small group with multiple disadvantage attending one OAMP. We encourage further work in other settings and groups. If confirmed, our findings suggest that while improving access to OAMPs for socially disadvantaged people with OA is important, additional actions may be needed to reduce outcome inequalities.

Mean difference in outcomes following GLA:D for 'disadvantaged' versus 'advantaged' participants using tapered balancing of covariates

Outcome	Pain VAS (0 - 100)[a]		KOOS QOL (0 - 100)[b]		EQ5D (-0.624 – 1)[c]	
Timepoint	3 months	12 months	3 months	12 months	3 months	12 months
Crude	6.0 (2.4, 9.4)	8.6 (4.5, 12.6)	-2.7 (-4.9, -0.5)	-5.3 (-8.2, -2.3)	-0.06 (-0.07, -0.04)	-0.06 (-0.08, -0.04)
1	3.8 (0.0, 7.5)	6.8 (2.4, 11.1)	-0.2 (-2.8, 2.4)	-3.1 (-6.3, 0.1)	-0.03 (-0.05, -0.01)	-0.04 (-0.06, -0.02)
2	3.4 (-0.5, 7.2)	6.0 (1.6, 10.4)	0.1 (-2.6, 2.7)	-2.8 (-6.0, 0.4)	-0.03 (-0.05, -0.01)	-0.04 (-0.06, -0.02)
3	3.4 (-0.5, 7.3)	6.2 (1.7, 10.7)	0.3 (-2.4, 3.0)	-2.7 (-6.0, 0.6)	-0.03 (-0.05, -0.01)	-0.04 (-0.06, -0.01)
4	3.6 (-0.4, 7.6)	6.2 (1.6, 10.7)	-0.1 (-2.9, 2.6)	-3.0 (-6.4, 0.4)	-0.03 (-0.05, -0.01)	-0.04 (-0.05, -0.01)
5	2.3 (-1.8, 6.4)	4.9 (0.2, 9.6)	0.5 (-2.3, 3.2)	-2.0 (-5.4, 1.4)	-0.03 (-0.05, -0.01)	-0.03 (-0.05, -0.01)
6	0.7 (-3.6, 4.9)	3.4 (-1.3, 8.2)	1.3 (-1.7, 4.3)	-1.3 (-4.9, 3.2)	-0.02 (-0.04, 0.00)	-0.02 (-0.05, 0.00)
7	0.7 (-3.6, 5.0)	3.5 (-1.3, 8.2)	1.3 (-1.7, 4.2)	-1.3 (-4.9, 2.3)	-0.02 (-0.04, -0.00)	-0.02 (-0.05, 0.00)
8	0.7 (-3.6, 4.9)	3.5 (-1.2, 8.3)	1.2 (-1.8, 4.2)	-1.4 (-5.0, 2.2)	-0.02 (-0.04, -0.00)	-0.03 (-0.05, 0.00)

Figures are between-group mean differences (95%CI) for disadvantaged – advantaged groups.

[a] Based on 228 disadvantaged and 3118 advantaged participants; positive values for between-group mean differences on pain VAS represent worse outcome for disadvantaged group
[b] Based on 236 disadvantaged and 4715 advantaged participants; negative values for between-group mean differences on KOOS QOL represent worse outcome for disadvantaged group
[c] Based on 225 disadvantaged and 5969 advantaged participants; negative values for between-group mean differences on KOOS QOL represent worse outcome for disadvantaged group

Entropy balancing algorithm, continuous covariates balanced for mean, variance, and skewness
1=Balanced for baseline measure of outcome
2=Balanced for 1 AND calendar year and treatment centre type
3= Balanced for 1-2 AND age and sex
4=Balanced for 1-3 AND body mass index and previous injury and previous surgery
5=Balanced for 1-4 AND number of comorbidities and non-knee pain sites
6=Balanced for 1-5 AND Arthritis self-efficacy pain subscale score and self-reported depression
7=Balanced for 1-6 AND previous non-surgical management
8=Balanced for 1-7 AND attendance at GLA:D education and exercise sessions