Results: The proteomic analysis resulted in the identification of 558 proteins (10,466 peptides) in the serum samples. A label-free quantification algorithm was employed to quantify 468 proteins in the samples. Hierarchical clustering of the data showed the differences in protein abundance were more relevant longitudinally (BL to 24M) than in cross-sectional comparisons between the three groups under study (N, P or S). Sixty-three proteins were significantly altered (fold change >=1.5, p<0.05) when comparing BL to 24M in the N group (15 increased and 48 decreased), 53 in the P group (20 increased and 33 decreased) and 93 in the S group (19 increased and 74 decreased). Interestingly, two different endotypes were detected at baseline in the N and S groups, based on these protein modulations.

The overlapping of these proteomic profiles was analyzed between groups and is shown in the Figure 1. Proteins modulated specifically in the N group may be associated with mechanisms related with joint repair. On the other hand, six proteins (including two apolipoproteins) were increased at 24M only in the P group. Finally, 30 proteins were modulated only in the S group: five of them increased and 25 decreased. Remarkably, this latter group includes lubricin, chaperones and proteins related with proteoglycan binding, such as COMP, fibronectin or histidine-rich glycoprotein.

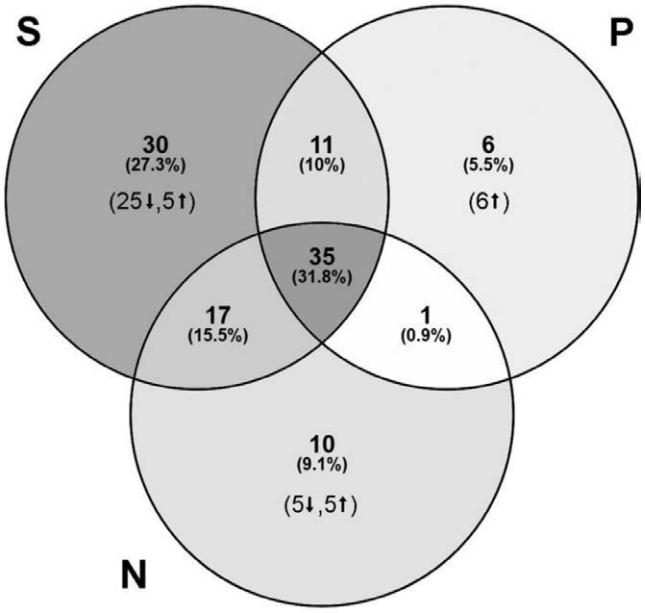

Figure 1. Circulating proteins identified as modulated after 24M follow-up in 45 patients from the APPROACH cohort that progressed in structure (S group; n=15), pain (P group; n=15) or did not progressed (N group; n=15). The numbers with arrows indicate those proteins that decrease (arrow pointing down) or increase (arrow pointing up) compared to baseline.

Conclusion: The modulation of specific protein profiles in serum were identified as associated with the progression in structure, pain or non-progression in patients from the APPROACH cohort. Proteomic changes found specifically in the S group may be interesting circulating markers of the structural affectation occurring in the joint.

REFERENCES:

[1] van Helvoort EM, et al., BMJ Open. 2020 Jul 28;10(7):e035101. doi: 10.1136/bmjopen-2019-035101.

Disclosure of Interests: Cristina Ruiz-Romero: None declared, Patrik Önnerfjord: None declared, Valentina Calamia: None declared, Patricia Fernández Puente: None declared, Lucía Lourido: None declared, Rocío Paz González: None declared, Pawel Widera: None declared, Jaume Bacardit: None declared, Anne-Christine Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Francis Berenbaum Consultant of: AstraZeneca, Boehringer, Bone Therapeutics, CellProthera, Expanscience, Galapagos, Gilead, Grunenthal, GSK, Eli Lilly, Merck Sereno, MSD, Nordic, Nordic Bioscience, Novartis, Pfizer, Roche, Sandoz, Sanofi, Servier, UCB, Peptinov, 4P Pharma, 4Moving Biotech, Grant/research support from: TRB Chemedica, Ida K. Haugen Consultant of: Abbvie and Novartis, Grant/research support from: Pfizer, Margreet Kloppenburg Consultant of: Abbvie, Pfizer, Levicept, GlaxoSmithKline, Merck-Serono, Kiniksa, Flexion, Galapagos, Jansen, CHDR, Novartis, UCB, Simon Mastbergen: None declared, Jonathan Larkin Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, Ali Mobasheri Consultant of: Merck KGaA, Kolon TissueGene, Pfizer Inc., Galapagos-Servier, Image Analysis Group (IAG), Artialis SA, Aché Laboratórios Farmacêuticos, AbbVie, Guidepoint Global, Alphasights, Science Branding Communications, GSK, Flexion Therapeutics, Pacira Biosciences, Sterifarma, Bioiberica, SANOFI, Genacol, Kolon Life Science, BRASIT/BRASOS, GEOS, MCI Group, Alcimed, Abbot, Laboratoires Expansciences, SPRIM Communications, Frontiers Media and University Health Network (UHN) Toronto, Grant/research support from: Merck KGaA, Kolon TissueGene, Pfizer Inc., Galapagos-Servier, Image Analysis Group (IAG), Artialis SA, Aché Laboratórios Farmacêuticos, AbbVie, Guidepoint Global, Alphasights, Science Branding Communications, GSK, Flexion Therapeutics, Pacira Biosciences, Sterifarma, Bioiberica, SANOFI, Genacol, Kolon Life Science, BRASIT/BRASOS, GEOS, MCI Group, Alcimed, Abbot, Laboratoires Expansciences, SPRIM Communications, Frontiers Media and University Health Network (UHN) Toronto, Francisco J. Blanco Consultant of: Gedeon Richter Plc., Bristol-Myers Squibb International Corporation (BMSIC), Sun Pharma Global FZE, Celgene Corporation, Janssen Cilag International N.V, Janssen Research & Development, Viela Bio, Inc., Astrazeneca AB, UCB BIOSCIENCES GMBH, UCB BIOPHARMA SPRL, AbbVie Deutschland GmbH & Co.KG, Merck KGaA, Amgen, Inc., Novartis Farmacéutica, S.A., Boehringer Ingelheim España, S.A, CSL Behring, LLC, Glaxosmithkline Research & Development Limited, Pfizer Inc, Lilly S.A., Corbus Pharmaceuticals Inc., Biohope Scientific Solutions for Human Health S.L., Centrexion Therapeutics Corp., Sanofi, TEDEC-MEIJI FARMA S.A., Kiniksa Pharmaceuticals, Ltd., Fundación para la Investigación Biomédica Del Hospital Clínico San Carlos, Grünenthal and Galapagos, Grant/research support from: Pfizer
DOI: 10.1136/annrheumdis-2022-eular.1091

OP0225

RISK OF COMORBIDITY FOLLOWING OSTEOARTHRITIS DIAGNOSIS: A COHORT STUDY IN THE NETHERLANDS FROM THE FOREUM* INITIATIVE

A. Kamps[1], J. Runhaar[1], M. de Wilde[2], M. de Ridder[2], J. van der Lei[2], S. Swain[3,4], W. Zhang[3], D. Prieto-Alhambra[4], M. Englund[5], E. de Schepper[1], S. M. A. Bierma-Zeinstra[1,6]on behalf of FOREUM Comorbiditis in Osteoarthritis.
[1]Erasmus Universty Medical Center, Department of General Practice, Rotterdam, Netherlands; *[2]Erasmus Universty Medical Center, Department of Medical Informatics, Rotterdam, Netherlands*; *[3]University of Nottingham, School of Medicine, Nottingham, United Kingdom*; *[4]University of Oxford, Nuffield Department of Primary Care Health Sciences, Oxford, United Kingdom*; *[5]Lund University, Clinical Epidemiology Unit, Lund, Sweden*; *[6]Erasmus Universty Medical Center, Department of Orthopedics & Sports Medicine, Rotterdam, Netherlands*

Background: Osteoarthritis (OA) is a common and disabling disease that places a significant burden on both patients and health care systems. Previous studies have already shown that patients with OA have a higher risk of developing comorbidities. However, many focused on one or a few conditions only, or did not consider the chronology of the disease onset relative to OA.

Objectives: To determine the risk of physician-diagnosed comorbidity following the diagnosis of knee or hip OA, using electronic health records in the Netherlands.

Methods: A cohort study was conducted using the Integrated Primary Care Information (IPCI) database, an electronic health record database with medical records of 2.5 million patients from Dutch general practice. The study population consisted of patients aged 18 years or older, that were at risk for incident OA and comorbidity. Diagnosis of knee or hip OA (i.e. exposure) was defined as the first registration of the corresponding diagnostic code from the International Classification of Primary Care (ICPC) coding system in the medical record. Fifty-eight long-term comorbidities (i.e. outcome) were selected and defined by their corresponding ICPC codes.

Patients' follow-up started after registration in the database, and ended at the diagnosis date of the comorbidity (i.e. event), or at deregistration, death or at December 31st, 2019 (i.e. censoring), whichever came first. Exposure to knee or hip OA was a time-varying exposure: time between the start of follow-up and diagnosis of OA was defined as unexposed time, and between diagnosis of OA and the end of follow-up as exposed time. Patients' age was used as time axis to correct for age non-linearly. Sex-adjusted hazard ratios (HRs) comparing exposed and unexposed patient status were estimated with 99.9% confidence intervals (CI).

Results: The study population consisted of 1,890,712 patients. For 11 of the 58 studied comorbidities exposure to knee OA showed a statistically significant HR larger than 1, indicating an increased risk of being diagnosed with these comorbidities after a diagnosis of knee OA. For none of the comorbidities there was a statistically significant negative association (HR<1) with exposure to knee OA. For 7 comorbidities exposure to hip OA showed a statistically significant HR larger than 1. Again, for all other comorbidities the HR of hip OA was non-significant. For an overview of the statistically significant positive associations see Table 1.

Table 1. ***Comorbidities with significant HRs of exposure to knee or hip OA***

Knee OA				Hip OA			
Comorbidity	**HR**	**99.9% CI**		**Comorbidity**	**HR**	**99.9% CI**	
Anemia	1.33	1.09	1.64	**Anemia**	1.29	1.02	1.63
Back pain	1.28	1.04	1.57	**Atrial fibrillation**	1.46	1.14	1.88
Cataract	1.27	1.02	1.59	**Fibromyalgia**	6.09	1.25	29.53
Chronic kidney disease	1.30	1.06	1.59	**Peripheral vascular disease**	1.64	1.09	2.49
Coronary heart disease	1.34	1.03	1.75	**Sleeping disorder**	1.44	1.10	1.87
Gout	1.43	1.01	2.03	**Solid malignancy**	1.32	1.11	1.55
Hearing loss	1.34	1.00	1.79	**Spinal disc herniation**	2.03	1.46	2.83
Neck pain	1.58	1.16	2.16				
Obesity	2.02	1.06	3.83				
Sleeping disorder	1.33	1.04	1.69				
Thromboembolic disease	1.40	1.01	1.94				

Conclusion: This study showed that certain comorbidities were diagnosed more often in patients exposed to knee or hip OA, and none were less frequently diagnosed in patients exposed OA. This suggests that the management of OA should consider the risk of other long-term-conditions and that further research on causality between OA and comorbidity is needed.

REFERENCES:

[1] **https://www.foreum.org/projects.cfm?projectid=159*

Acknowledgements: We thank the Patient Research Participants members Jenny Cockshull, Stevie Vanhegan, and Irene Pitsillidou for their involvement in the project. We would like to thank the FOREUM for financially supporting the research.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.836

OP0226 TRAJECTORIES OF BODY MASS INDEX FROM EARLY ADULTHOOD TO LATE MIDLIFE AND INCIDENCE OF TOTAL KNEE ARTHROPLASTY FOR OSTEOARTHRITIS: FINDINGS FROM A PROSPECTIVE COHORT STUDY

S. M. Hussain[1], I. Ackerman[1], Y. Wang[1], D. English[2], A. Wluka[1], G. Giles[3], S. Graves[4], F. Cicuttini[1]. [1]*Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Australia*; [2]*The University of Melbourne, Melbourne School of Population and Global Health, Melbourne, Australia*; [3]*Cancer Council Victoria, Cancer Epidemiology Division, Melbourne, Australia*; [4]*Australian Orthopaedic Association National Joint Replacement Registry, South Australian Health and Medical Research Institute, Adelaide, Australia*

Background: There is limited evidence regarding the association between trajectories of body mass index (BMI) across adulthood and knee osteoarthritis.

Objectives: We examined the association between body mass index (BMI) trajectories across early adulthood to midlife and risk of total knee arthroplasty (TKA) for osteoarthritis.

Methods: This study examined 24,368 participants (40-70 years at recruitment) in the Melbourne Collaborative Cohort Study who had weight collected at 1990–1994, 1995–1998, and 2003–2007 and recalled weight at age 18–21 years. BMI trajectories were derived using weight data at the four timepoints. Incidence of TKA after 2003–2007 until December 2018 was determined by linking cohort records to the National Joint Replacement Registry.

Results: Using group-based trajectory modelling, six distinct trajectories (TR) of BMI from early adulthood to late midlife were identified: lower normal to normal BMI (TR1: BMI at age 18-21 years to BMI at approximately 62 years (kg/m2), 20.0±1.9 to 22.1±1.7; 19.7%); normal BMI to borderline overweight (TR2: 21.5±2.3 to 25.8±1.7; 36.7%), normal BMI to overweight (TR3: 22.0±2.2 to 29.5±1.9; 26.8%), overweight to borderline obese (TR4: 28.5±2.7 to 30.5±2.3; 3.5%), normal BMI to class 1 obesity (TR5: 22.8±2.5 to 34.3±2.3; 10.1%), and overweight to class 2 obesity (TR6: 25.6±3.9 to 39.2±2.9; 3.2%). Over 12.4 years, 1,328 (5.4%) participants had TKA. The hazard ratios for TKA increased in all TR compared with TR1: TR2 2.03 (95% CI 1.64-2.52), TR3 4.00 (3.19-4.91), TR4 5.17 (3.77-7.10), TR5 7.00 (5.54-8.80), and TR6 8.59 (6.44-11.46). It is estimated that 28.4% TKA would be reduced if individuals followed the trajectory that was one lower, a national health system savings of $AUD 373 million. Most of this reduction would occur in TR2 (population attributable fraction 37.9% (26.7%-47.3%) and TR3 PAF 26.8% (20.0%, 31.2%) (Table 1).

Conclusion: Our study suggests that prevention of weight gain from young adulthood to midlife in order to reduce overweight and obesity could have a major impact on reducing the burden of severe knee osteoarthritis and associated healthcare costs.

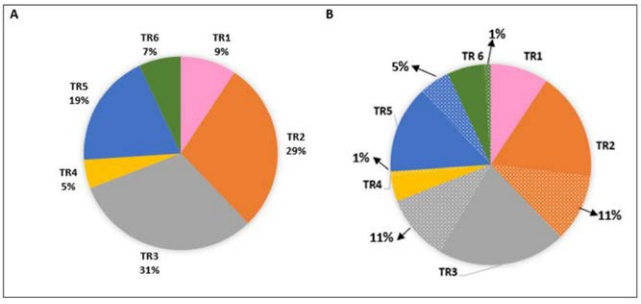

Figure 1. A. Proportion of Total Knee Arthroplasties in each trajectory category B. Speculated patters and associated percentages represents the proportion of Total Knee Arthroplasties that could be avoided in each trajectory category if the participants followed the lower trajectory category i.e. TR2 followed TR1

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2022-eular.3619

OP0227 WEIGHT LOSS IS ASSOCIATED WITH REDUCED INCIDENCE AND PROGRESSION OF STRUCTURAL DEFECTS IN KNEE OSTEOARTHRITIS, AS ASSESSED BY RADIOGRAPHY OVER 4 TO 5 YEARS: A PROSPECTIVE MULTI-COHORT STUDY

Z. Salis[1], H. Keen[2], B. Gallego[1], T. V. Nguyen[3,4], A. Sainsbury-Salis[5]. [1]*The University of New South Wales, Centre for Big Data Research in Health, Kensington, Australia*; [2]*The University of Western Australia, Medical School, Crawley, WA, Australia*; [3]*University of Technology Sydney, Centre for Big Data Research in Health, Sydney, Australia*; [4]*The University of*

Table 1. Reduction in TKA if individuals followed the trajectory that was one lower

Population counterfactuals	Population at risk, n (%)	TKA under the original scenario, n (%)	TKA under the new scenario*, n (%)	Difference in risk, n (%)	PAF** (95% CI), %
TR1	4811 (19.7)	124 (2.6%)	No change 124 (2.6%)	0	-
If TR2 followed TR1 trajectory and rate of TKA*	8943 (36.7)	378 (4.2%)	2.6% of 8943 = 233	145 (10.9)	37.9 (26.7, 47.3)
If TR3 followed TR2 trajectory and rate of TKA*	6526 (26.8)	416 (6.4%)	4.2% of 6526 = 274	142 (10.7)	26.8 (20.0, 31.2)
If TR4 followed TR3 trajectory and rate of TKA*	845 (3.5)	64 (7.6%)	6.4% of 845 = 54	10 (0.8)	3.1 (0, 6.0)
If TR5 followed TR4 trajectory and rate of TKA*	2466 (10.1)	253 (10.3%)	7.6% of 2466 =187	66 (5.0)	20.2 (0, 36.3)
If TR6 followed TR5 trajectory and rate of TKA*	777 (3.2)	93 (12.0%)	10.3% of 777 = 80	13 (1.0)	0.4 (0.0, 10.0)
Total population	24368	1328	952	376 (28.4)	-

*if the trajectory is changed, ** PAFs and related 95%CIs were calculated using the Stata punafcc package using the formula $\sum pKR_i[(HR_i - 1)/HR_i]$, where pKR_i is the proportion of total knee replacements observed in the ith obesity trajectory and HR_i is the hazard ratio (HR) associated with that category. PAFs were calculated using pKR_i and HR_i estimated from the entire sample. All HR_i values were generated from Cox proportional hazards regression models adjusted for covariates (age at baseline, sex, country of birth, physical activity, smoking history, and comorbidity) and postestimation analyses.