

Table 1: Mean T-scores, and prevalence of osteoporosis (T-score <-2.5) and osteopenia (T-score >-2.5 & <-1) in all those aged over 50 years

Study (n)	Country	Men			Women		
		Mean T-score (SD)	% (n) Osteoporosis	% (n) Osteopenia	Mean T-score (SD)	% (n) Osteoporosis	% (n) Osteopenia
GambAS (678 (314 men))	Gambia	-0.17 (1.19)	1.6 (5)	22.6 (71)	-1.72 (1.19)	28.3 (103)	47.3 (172)
HCS (2116 (1067 men))	UK	0.55 (1.23)	0.7 (7)	9.7 (104)	-0.74 (1.16)	5.3 (56)	38.1 (400)
HealthABC Black (4195 (1738 men))	US	0.30 (1.37)	1.7 (30)	13.7 (238)	-1.07 (1.38)	14.6 (359)	38.9 (955)
HealthABC White (6813 (3509 men))	US	-0.32 (1.30)	3.9 (137)	27.4 (961)	-1.83 (1.12)	27.1 (896)	50.1 (1656)
Agincourt (642 (224 men))	South Africa	-0.13 (1.30)	3.6 (3)	22.9 (19)	-0.32 (1.22)	4.2 (7)	23.5 (39)
Menopause study (200 women)	Zimbabwe	-	-	-	0.23 (1.22)	0	17.0 (17)

OC19**GENETIC BIOMARKERS, SNP GENES AND MTDNA HAPLOGROUPS, PREDICT OSTEOARTHRITIS STRUCTURAL PROGRESSORS THROUGH THE USE OF SUPERVISED MACHINE LEARNING**

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Objective: Current treatments of osteoarthritis (OA) are only symptomatic, and the conventional diagnosis and prognosis of the disease are not very effective in the early identification of patients who will progress rapidly. Biomarkers enabling early stratification would assist in a better therapeutic strategy for individuals, thus precision medicine, as well as in the development of disease-modifying OA drugs. Some genetic markers have been linked to knee OA and could be used as biomarkers in such phenotyping. We investigated, using machine learning (ML), whether some single nucleotide polymorphism (SNP) genes and mtDNA haplogroups/clusters, alone or combined, could predict early knee OA structural progression.

Methods: Participants (901) from the Osteoarthritis Initiative cohort were classified for the probability of being structural progressors using applied imaging-based prediction, as described¹. Two major OA risk factors (age and body mass index [BMI]), SNP genes (*TP63*, *FTO*, *GNL3*, *DUS4L*, *GDF5*, *SUPT3H*, *MCF2L*, *TGFA*), and mtDNA haplogroups (H, J, T, Uk, others) and clusters (HV, TJ, KU, C-others) were considered for prediction. Seven supervised ML methods were evaluated; the support vector machine was used to build the models. The models were developed as gender-based and validation assessed under tenfold cross-validation experiments.

Results: Models (277) were generated, and sensitivity and synergy analyses led to the development of two gender-based models to predict structural progressors. Both used age and BMI and, for the first model, the SNP genes *TP63*, *DUS4L*, *GDF5*, *FTO* with an accuracy of 87.5%. The second model had one less variable with the

same accuracy (87.5%) and profits from the association of haplogroups and the SNP genes *FTO* and *SUPT3H*. For the latter, the highest impact was associated with haplogroup H, the presence of CC alleles at *FTO*, and the absence of AA at *SUPT3H*. The excellent validation accuracy (mean: 82.3%) reinforces the robustness and generalizability of the developed models.

Conclusion: This study introduces a novel source of decision support in precision medicine in which, for the first time, two gender-based models using SNP genes, mtDNA haplogroups, and supervised ML were developed for early detection of at-risk knee OA structural progressors.

Reference: 1. Jamshidi A et al. *Ther Adv Musculoskelet Dis*. 2020;12:1-12.

OC20**EROSIVE OSTEOARTHRITIS OF THE HAND: EFFICACY OF PRESCRIPTION-GRADE CRYSTALLINE GLUCOSAMINE SULFATE AS AN ADD-ON THERAPY TO CONVENTIONAL TREATMENTS**

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Objective: To evaluate the efficacy of prescription-grade Crystalline Glucosamine Sulfate (pCGS), as an add-on treatment to conventional therapy, compared to usual therapy alone, in patients with erosive osteoarthritis of the hand (EHOA).

Material and Methods: This is a 6-months retrospective study including patients with concomitant gonarthrosis and EHOA, defined as the presence of central erosion in at least two interphalangeal joints. Eligibility criteria were symptoms duration for at least 3 months, with a global hand pain score ≥ 40 mm on a 0–100 Visual Analogue Scale (VAS) and a Functional Index for Hand Osteoarthritis (FIHOA) score ≥ 6 . The participants were stratified into two groups based on whether or not pCGS, at the daily dose of 1500 mg, was added to the conventional therapy for hand osteoarthritis (HOA). The latter consisted in education and training in ergonomic principles, exercise and the use on-demand of acetaminophen or oral non-steroidal anti-inflammatory drugs. Patients were evaluated at baseline, after 3 and 6 months. Primary outcome measures were the change from baseline to month 6 in VAS and in FIHOA score. Secondary outcomes were duration of morning stiffness, health assessment questionnaire (HAQ), medical outcomes study 36-item short form (SF-36), symptomatic drugs consumption and percentage of treatment responders, according to the OMERACT/OARSI criteria.

Results: 123 patients were included: 67 treated with pCGS in addition to conventional therapy (pCGS Group) and 56 with conventional therapy alone (Control Group). After 6 months a significant difference in VAS pain and in FIHOA score ($p < 0.01$ and $p < 0.001$, respectively) was observed between groups in favor of pCGS Group. Furthermore, similar results were found for morning stiffness duration ($p < 0.05$), HAQ ($p < 0.01$) and for physical and mental component score of SF-36 ($p < 0.05$ and $p < 0.001$, respectively) at 6 months. A significant reduction of symptomatic drug consumption at 3 and 6 months was reported in the pCGS Group ($p < 0.001$). The rate of responders was greater in pCGS Group than Controls at all time points ($p \leq 0.001$ between groups). No serious adverse event was recorded in both groups.

Conclusions: This study suggests the potential symptomatic effectiveness of pCGS, when used in combination with conventional therapy in EHOA.

OC21

HEALTH ECONOMICS EVALUATION OF A HIGH AND LOW MOLECULAR WEIGHT HYALURONIC ACID FORMULATION IN PATIENTS WITH KNEE OSTEOARTHRITIS. ANALYSES FROM A RANDOMIZED CLINICAL TRIAL

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Introduction: In a recent randomized placebo controlled trial, a single intra-articular injection of a high and low molecular weight hyaluronic acid formulation (HA-HL) has been shown to be effective in providing a clinically relevant reduction in pain and functional limitation up to 24 weeks in subjects with painful knee osteoarthritis (OA). The objective of the current study is to assess the cost-effectiveness of HA-HL compared with placebo using individual patient data from this clinical trial in a Swiss health care perspective.

Methods: A total of 692 patients fulfilling the criteria to enter the trial were randomly allocated to HA-HL or placebo. Each patient received one intra-articular injection of HA-HL or placebo at baseline and was then followed-up for a total duration of 24 weeks with 5 follow-up visits (i.e. week 1, 6, 12, 18 and 24). The EQ-5D-5L 5-point verbal Likert scale was used to calculate the Health Utility Index and the related quality-adjusted life-years (QALY) using the area-under-the-curve (AUC) method. For the costs, price of HA-HL in Switzerland was used. The primary threshold for the incremental cost/effectiveness ratio (ICER) below which HA-HL was considered as cost effective was 91,540 Swiss franc (CHF) per QALY (i.e. 100,000 USD).

Results: No significant difference between the baseline characteristics of the HA-HL group and placebo group was observed. With a mean ICER of 27,212 CHF per QALY (95% CI 20,135 – 34,289), HA-HL was considered as cost-effective compared to placebo. Sensitivity analyses (e.g. using lower or upper limit prices or using other threshold values) gave similar results, i.e. ICER far below the threshold values of cost-effectiveness.

Conclusion: These results confirm the role of HA-HL as an efficient pharmacological modality in the management of OA.

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LOWER LIMB MUSCLE STRENGTH AND MUSCLE MASS ARE ASSOCIATED WITH INCIDENT SYMPTOMATIC KNEE OSTEOARTHRITIS: A LONGITUDINAL COHORT STUDY

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Objective: Recent literature suggests that sarcopenia, often represented by low lower limbs muscle mass and strength, can be considered a potential risk factor for knee osteoarthritis (OA), but the

available literature is still limited. We therefore aimed to investigate whether sarcopenia is associated with a higher risk of radiographic (ROA) and symptomatic knee OA (SxOA) in a large cohort of North American people in the context of the OA initiative.

Material and Methods: Sarcopenia at baseline was diagnosed in case of low skeletal muscle mass (i.e., lower skeletal mass index) and poor performance in the chair stands test. The outcomes of interest for this study included ROA (radiographical osteoarthritis) if a knee developed a Kellgren and Lawrence (KL) grade ≥ 2 at follow-up, and SxOA (symptomatic osteoarthritis) defined as new onset of a combination of painful knee OA.

Results: Altogether, 2,492 older participants (mean age: 68.4 years, 61.4% females) were included. At baseline, sarcopenia was present in 6.1% of the population. No significant difference in ROA prevalence was observed between those with and without sarcopenia ($p = 0.76$), whilst people with sarcopenia reported a significant higher prevalence of SxOA ($p < 0.0001$). Using a logistic regression analysis, adjusting for potential confounders at baseline and the diagnosis of sarcopenia during follow-up, sarcopenia was associated with a higher incidence of knee SxOA (odds ratio, OR = 2.29; 95%CI [confidence interval]: 1.42-3.71; $p = 0.001$), but not knee ROA (OR = 1.48; 95%CI: 0.53-4.10; $p = 0.45$).

Conclusion: Sarcopenia could be associated with a higher risk of negative knee OA outcomes, in particular symptomatic forms

OC23

DOES LOW MUSCLE STRENGTH MODIFY RELATIONSHIPS BETWEEN INDIVIDUAL COMORBIDITIES AND MORTALITY? FINDINGS FROM THE HERTFORDSHIRE COHORT STUDY

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Objective: Ischemic heart disease (IHD), diabetes and chronic obstructive pulmonary disease (COPD) have been individually related to increased mortality; here we report how mortality risks for these conditions differ when coexisting with low muscle strength in a population-based UK cohort study.

Material and Methods: Men ($n = 1502$) and women ($n = 1330$) from the Hertfordshire Cohort Study, aged 59-73 years at baseline, were analysed. Muscle strength was ascertained by grip dynamometry; COPD was defined as a forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio of < 0.7 ; diabetes was ascertained through self-report and via a 2-h fasted oral glucose tolerance test; and previous diagnosis of IHD was ascertained by self-report. Low grip strength was defined according to the Sarcopenia Definitions and Outcomes Consortium thresholds (< 35.5 kg [men], < 20 kg [women]). Deaths were recorded from baseline (1998-2004) until 31st December 2018. Associations between combinations of conditions and mortality were examined using Cox regression with adjustment for sex and age.

Results: Low grip strength, COPD, diabetes and IHD were each related to increased mortality risk ($p < 0.001$). Having both low grip strength and COPD was related to greater mortality risk than having COPD only (hazard ratio (95% CI): 1.47 (1.11, 1.95), $p = 0.006$); the same was the case for having low grip strength and IHD compared to IHD only (1.57 (1.05, 2.34), $p = 0.027$). In contrast, mortality risk was not significantly greater for those with low grip strength and diabetes in comparison to having diabetes alone ($p = 0.127$).

Conclusion: Weaker muscle strength in combination with COPD or IHD was related to greater mortality risk than simply having the individual conditions. However, differential results with individual comorbidities suggest that individual comorbidities impact mortality