questionnaire was sent to the 19 academic sites across Canada participating in the FH Canada network. We previously identified 79 cases across the country, and have captured 46 of these cases. Here we describe their medical history, lipid levels, treatments and clinical outcomes. At the time of entry in the Registry, the mean age was 44 +/- 19 years, with a majority of females (54.4%), representing cases across 5 provinces. The average age of diagnosis was 16 4 years. with 67.4% having untreated LDL > 10 mmol/L. Presence of physical markers, such as xanthomas or corneal arcus, were also found in 80.4% and 26.1% of patients, respectively. For lipid-lowering therapy, 52.2% were undergoing LDL-apheresis, 91% were on statins and 41% on PCSK9 inhibitors. 54.3% displayed ASCVD, with 43.5% having aortic stenosis, 15.2% having experienced a myocardial infarction, and 36.9% having undergone one or more coronary artery bypass graft procedures.

CONCLUSION: We plan to use this data at provincial and national levels, helped by the Canadian Organization for Rare Diseases (CORD) and the Réseau Québecois des maladies orphelines (RQMO), to provide HoFH patients access to care, including orphan drugs such as evinacumab, and treatment techniques such as LDL apheresis. This work will provide important new health-related knowledge about the determinants of ASCVD risk and phenotypic manifestations of HoFH in Canada, and examine the quality of life and burden to the healthcare system.

P037
INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-7 AS A MARKER OF CARDIAC REVERSE REMODELING WITH EMPAGLIFLOZIN: A SECONDARY ANALYSIS OF THE EMPA-HEART CARDIOLINK-6 RANDOMIZED CONTROLLED TRIAL

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BACKGROUND: Reverse cardiac remodeling is believed to contribute to the cardiovascular benefits offered by sodium-glucose transport protein 2 inhibitors (SGLT2i). Given the association between insulin-like growth factor binding protein 7 (IGFBP7) levels and cardiac remodeling, it has been postulated that IGFBP7 may serve as a predictor for individuals who may derive greater benefit from SGLT2i therapy. This exploratory sub-analysis of the EMPA-HEART CardioLink-6 trial examined the association between serum IGFBP7 levels and reverse cardiac remodeling in patients treated with empagliflozin.

METHODS AND RESULTS: The EMPA-HEART CardioLink-6 trial randomized 97 patients with type 2 diabetes and coronary artery disease to either empagliflozin (10 mg/d) or matching placebo for 6 months. The primary outcome was change in left ventricular mass indexed to body surface area (LVMi) from baseline to 6 months as measured by cardiac magnetic resonance imaging. Serum samples collected from patients at baseline were processed for detection of IGFBP7. A linear model adjusted for baseline characteristics was used to evaluate the relationship between baseline IGFBP7, 6-month change in LVMi, and treatment arm. An adjusted multivariable linear regression model was used to evaluate the association between baseline IGFBP7 and baseline LVMi. Patients with missing covariate data were excluded which resulted in a final analysis set of 74 patients. We observed no association between baseline IGFBP7 levels and change in LVMi, nor was there any significant difference in treatment effect between empagliflozin versus placebo patients (empagliflozin 6-month change in LVMi: 0.25g/m2 (95% CI: -0.17 g/m2 to 0.67 g/m2) per 1 ng/mL higher IGFBP7 vs. placebo 6-month change in LVMi: 0.07 g/m2 (95% CI: -0.21 g/m2 to 0.35 g/m2) per 1 ng/mL higher IGFBP7; Pinteraction = 0.49). We also did not detect any association between baseline IGFBP7 and baseline LVMi (P = 0.52). Additional sensitivity analysis assessing the association between IGFBP7 as a categorical variable and 6-month change in LVMi did not reveal any significant interaction (Pinteraction=0.86).

CONCLUSION: Our results suggest that empagliflozin-mediated cardiac reverse remodeling in patients with type 2 diabetes and coronary artery disease is independent of serum IGFBP7 levels. However, given the sample size and short study duration of the EMPA-HEART CardioLink-6 trial, further investigations evaluating whether IGFBP7 levels influence the clinical efficacy of SGLT2i are warranted.

P038
LEFT VENTRICULAR MASS PREDICTS CARDIAC REVERSE REMODELING IN PATIENTS TREATED WITH EMPAGLIFLOZIN: AN EXPLORATORY SUB-ANALYSIS OF THE EMPA-HEART CARDIOLINK-6 RANDOMIZED CONTROLLED TRIAL

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BACKGROUND: Left ventricular (LV) hypertrophy is associated with an elevated risk for cardiovascular (CV) disease events and all-cause mortality. The CV benefits of sodium-glucose transport protein 2 inhibitors (SGLT2i) have been attributed, in part, to cardiac reverse remodeling. The EMPA-HEART CardioLink-6 study reported that SGLT2 inhibition with empagliflozin was associated with a significant reduction in LV mass indexed to body surface area (LVMi) after 6 months. In this exploratory sub-analysis of the same trial, we evaluated how baseline LVMi may influence cardiac reverse remodeling with empagliflozin.

METHODS AND RESULTS: A total of 97 patients with type 2 diabetes and coronary artery disease were randomized to empagliflozin (10 mg/d) or matching placebo for 6 months. To determine if the impact of empagliflozin on the 6-month change in LVMi was dependent on baseline LVMi, the EMPA-HEART CardioLink-6 cohort was stratified into two groups − baseline LVMi ≥60 g/m2 and < 60 g/m2. Between-group comparisons were conducted using a linear regression model adjusted for

baseline differences in LVMi (ANCOVA) that included an interaction term between baseline LVMi sub-group and treatment. The effect of empagliflozin on 6-month change in LVMi was significantly different between patients with a baseline LVMi $\geq$60 g/m2 and those whose LVMi was $<$ 60 g/m2 (Pinteraction=0.0064). The adjusted difference between those randomized to empagliflozin and those assigned placebo was -0.46 g/m2 (95% CI: -3.44 g/m2, 2.52 g/m2, P=0.76) and -7.26 g/m2 (95% CI: -11.40 g/m2, -3.12 g/m2, P=0.0011) in the LVMi $<$ 60 g/m2 and LVMi $\geq$60 g/m2 subgroups, respectively. These associations persisted following multivariate adjustment for baseline characteristics with adjusted differences of 0.59 g/m2 (95% CI: -3.01 g/m2, 4.19 g/m2, P=0.74) in the LVMi $<$ 60 g/m2 group and -7.03 g/m2 (95% CI: -11.06 g/m2, -2.99 g/m2, P=0.001) in the LVMi $\geq$60 g/m2 group (Pinteraction=0.0054). No significant associations were found between baseline LVMi and 6-month change in LV end systolic volume-indexed (Pinteraction=0.086), LV end diastolic volume-indexed (Pinteraction=0.34), or LV ejection fraction (Pinteraction=0.15).

CONCLUSION: Patients with larger LVMi at baseline experienced substantially greater cardiac reverse remodeling benefits with empagliflozin. The effect baseline LV mass has on the benefits derivable from SGLT2i therapies warrants further investigation.

P039
ROLE OF SEX AND GENDER IN DEVELOPMENT OF METABOLIC SYNDROME: A PROSPECTIVE COHORT STUDY

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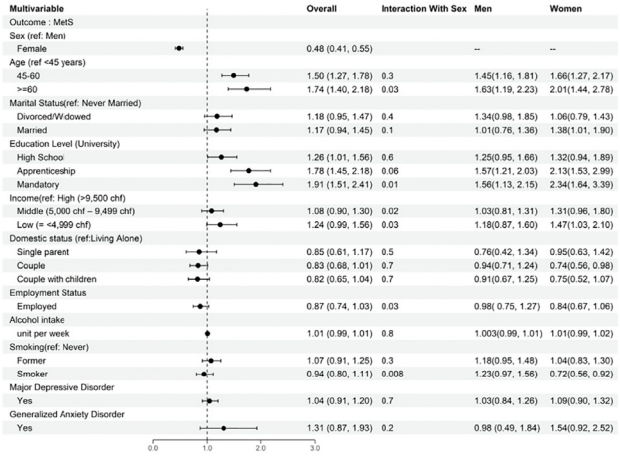
BACKGROUND: The burden of metabolic syndrome (MetS) and its components has been increasing mainly amongst male individuals. Nevertheless, clinical outcomes related to MetS (i.e., cardiovascular diseases), are worse among females. Whether these sex differences in the components and sequalae of MetS are influenced by psycho-socio-cultural factors (gender) is a matter of debate. Therefore, the purpose of this study was to determine the association between gender-related factors and the development of MetS, and to assess if the magnitude of the associations vary by sex.

METHODS AND RESULTS: Data from the Colaus/PsyColaus study, a prospective population-based cohort of 6,734 middle-aged participants in Lausanne (Switzerland) (2003-2006) were used. The primary endpoint was the development of MetS as defined by the Adult Treatment Panel III of the National Cholesterol Education Program. Multivariable models were estimated using logistic regression to assess the association between gender-related factors and the development of MetS. Two-way interactions between sex and age and gender-related factors were also tested. Among 5,195 participants without MetS (mean age=51.3±10.6, 56.1% females), 27.9% developed MetS during a mean follow-up of 10.9 years. Female sex (OR:0.48, 95%CI:0.41- 0.55) was associated with decreased risk of developing MetS. Conversely, older age, educational attainment less than university, and low income were associated with an increased risk of developing MetS. Statistically significant interaction between sex and strata of age, education, income, smoking, and employment were identified. The reduced risk of MetS in females was attenuated in the lowest education, income, and advanced age strata. However, females who smoke and reported being employed demonstrated increased risk of METS. Conversely smoking and unemployment were significant risk factors for MetS development among male adults.

CONCLUSION: Gender-related factors such as income level and educational attainment play a greater role in the development of MetS in females. These factors represent novel modifiable targets for implementation of sex & gender specific strategies to realize health equity for all people.

Association between Gender-related Factors and risk of developing MetS



P040
TEMPORAL TRENDS OF THE PREVALENCE OF ISCHEMIA WITH NON-OBSTRUCTIVE CORONARY ARTERY DISEASE (INOCA) IN ALBERTA, CANADA

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BACKGROUND: Ischemia with non-obstructive coronary artery disease (INOCA) is a common heart condition often overlooked in cardiology practice. There is still under-recognition of this condition, but it is unclear if the referral patterns for invasive testing have changed. We aimed to determine if the prevalence of patients diagnosed with INOCA through invasive testing has changed over time.

METHODS AND RESULTS: A population-based cohort of patients who had their first cardiac angiography for a chest pain syndrome in Alberta between 1999 and 2019 was extracted retrospectively from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH©) database. A temporal trend analysis was performed to compare patients with INOCA to obstructive coronary artery disease (CAD) and investigate the ratios of these two populations