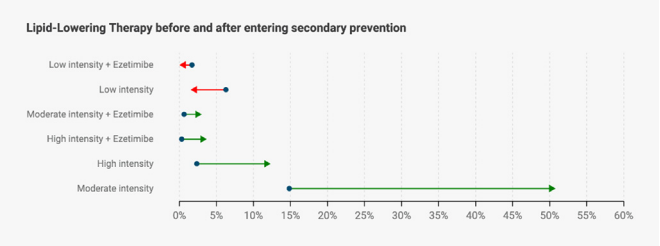

Conclusions: A worrisome gap between guidelines on dyslipidemia management and clinical implementation persists even in those at very high-risk or with established ASCVD.

SS182 / #59, SAAG SESSION 28: CUTTING-EDGE NEW BIOMARKERS, 23-05-2023 2:05 PM - 3:05 PM.
SYSTEMIC OXIDATIVE STRESS AND CIRCULATING LONG NON-CODING RNAS AS POTENTIAL NOVEL CARDIOVASCULAR RISK FACTORS IN THE GENERAL POPULATION

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Background and Aims: A significant proportion of the general population escape CVR lowering approaches basing on the currently used CVR estimators, which mostly rely on traditional CVR factors. We studied systemic oxidative stress and circulating long non-coding RNAs (lncRNAs) as potential novel CVR factors.

Methods: Systemic oxidative stress was assessed by OxyScore and AntioxyScore in 896 adults (17-65 years old) considering <30 years old as controls. Standardized values of carbonyl groups, 8-hydroxy-2'-deoxyguanosine, and oxidized LDL were included in OxyScore, and total antioxidant capacity, catalase activity, and superoxide dismutase activity in AntioxyScore. lncRNAs CoroMarker, KCNQOT1, UCA1, LeXis, MALAT-1, MIAT and Wisper were measured in plasma of a subset of 142 patients. CVR was determined by QRisk-lifetime.

Results: OxyScore and AntioxyScore were associated with CVR independently of sex and age ($p<0.05$), traditional CVR factors (smoking, SBP, cholesterol, LDL, blood glucose, BMI, eGFR, family history; $p<0.01$), and antihypertensive ($p<0.001$) and statin ($p<0.01$) treatments. Circulating KCNQ1OT1 correlated with age and blood glucose ($p<0.05$ and $p<0.01$), UCA1 with LDL ($p<0.05$), and CoroMarker, UCA1, and LeXis with cholesterol ($p<0.05$). Interestingly, Wisper was associated with OxyScore ($p<0.01$) independently of traditional CVR factors.

Conclusions: The association between systemic oxidative stress and CVR suggests that integrating multimarker scores such as OxyScore and AntioxyScore into CVR estimators might improve CVR assessment. Moreover, we show for the first time the associations between a panel of lncRNAs and traditional CVR factors, pointing to their potential as clinical biomarkers. Finally, we describe Wisper as a novel lncRNA associated with oxidative stress, and which specific role deserves further investigation.

SS183 / #572, SAAG SESSION 28: CUTTING-EDGE NEW BIOMARKERS, 23-05-2023 2:05 PM - 3:05 PM.
DIFFERENTIALLY METHYLATED DNA LOCI BETWEEN EASTERN AND WESTERN FINNS ASSOCIATE WITH CHD RISK FACTORS

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Background and Aims: The coronary heart disease (CHD) mortality rate is unequally distributed in Finland, with a higher risk in the East than in the West. Although differences in genetics and lifestyle choices partly explain the increased risk of CHD in Eastern Finns, the molecular mechanisms mediating the discrepancy between the sub-populations are still largely unknown. This study aims to investigate whether there is a difference in DNA methylation levels between Eastern and Western Finns and whether this might mediate the discrepancy in CHD risk.

Methods: 'The Cardiovascular Risk in Young Finns Study' ($n=1529$), a longitudinal population cohort which includes genome-wide DNA methylation and cardiometabolic data, was utilized for this study. An Epigenome-Wide Association Study (EWAS) was performed on individuals originating from East and West Finland, followed by linear regression to determine association with cardiometabolic phenotypes.

Results: The EWAS identified 82 differentially methylated CpG sites (FDR <0.05) between Eastern and Western Finns. Of these, 21 CpG sites had a difference in median methylation levels of $\geq$2.5% and 10 of these 21 sites are regulated by genetic variation according to the GoDMC database. Linear regression analysis revealed an association between the methylation levels at some non-genetically regulated CpG sites with triglyceride and HDL cholesterol levels as well as blood pressure.

Conclusions: The difference in DNA methylation levels between East and West Finns at certain CpG locations is associated with risk factors for CHD. These results indicate that DNA methylation may play a role in the increased rate of CHD mortality in Eastern Finns.

SS184 / #1454, SAAG SESSION 28: CUTTING-EDGE NEW BIOMARKERS, 23-05-2023 2:05 PM - 3:05 PM.
GENETIC RISK SCORE FOR HUMAN SERUM LIPIDOME AND ITS ASSOCIATION WITH ANGIOGRAPHIC CORONARY ARTERY DISEASE

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Background and Aims: The modest added predictive value of the existing genetic risk scores (GRSs) over the traditional risk factors for cardiovascular disease (CVD) could be partly due to missing genetic components in the current GRSs. We aimed to test association of GRS for human serum lipidome with coronary artery disease (CAD).

Methods: We calculated GRS for human serum lipidome ($GRS_{Lipidome}$) using genetic data from the Ludwigshafen Risk and Cardiovascular Health (LURIC) study participants. The GRS was constructed using genetic summary data from the most comprehensive genome-wide association study of human serum lipidome to date. We then investigated the association of GRSs with CAD in the LURIC study participants. The association test of the $GRS_{Lipidome}$ with CAD was performed using logistic regression adjusted for the risk factors used in Framingham risk score (FRS), that are age, sex, systolic blood pressure, total cholesterol, HDL cholesterol, smoking habit and medication for hypertension. In addition to the association study of the GRS with CAD, we also assessed added predictive value of the $GRS_{Lipidome}$ on the top of the FRS related risk factors.

Results: The $GRS_{Lipidome}$ was associated with CAD risk in the LURIC participants with p-value of 0.01. However, there was no statistically significant added predictive value of the $GRS_{Lipidome}$ over the used traditional FRS related risk factors

Conclusions: This study showed that $GRS_{Lipidome}$ is a new risk factor for CAD in an European cohort, however with no added predictive value over the traditional risk factors used in FRS.