

***Atherosclerosis* newsletter**

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International guidelines have recommended methods for risk assessment as well as risk-dependent treatment goals for LDL-cholesterol. This issue of *Atherosclerosis* contains several articles that investigated the quality of these strategies or their implementation. In addition, strategies towards improving the prognostic values of risk algorithms or the identification of individuals at risk are investigated.

Comparative performance of the two pooled cohort equations for predicting atherosclerotic cardiovascular disease

Atherosclerotic cardiovascular disease (ASCVD) is one of the leading causes of death worldwide. Since ASCVD is a predominantly asymptomatic condition, multivariable algorithms have been developed to accurately predict ASCVD absolute risk to assist clinicians in identifying patients at higher risk. Shortly after the introduction of the the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations (PCE), a systematic overestimation of risk was identified. As such, a revised PCE was proposed to more accurately assess ASCVD risk. Campos-Staffico et al. aimed to compare the accuracy of both PCE in predicting 10-year ASCVD risk within a large, real-world patient sample in the USA.

20,843 patients with primary hypercholesterolemia aged between 40 and 75 years with no previous ASCVD were identified. Model fit, calibration, and discrimination were compared between PCE using Bayesian Information Criterion (BIC), Hosmer-Lemeshow test, area under the ROC curves (AUC), Brier score, and precision-recall analysis. In addition, race and sex subgroups for effect modification were examined.

Both PCE showed poor calibration and discrimination. The lack of improvement in discrimination of the revised PCE was confirmed with the AUC precision-recall curves. In contrast, the AHA/ACC PCE showed a strong positive risk prediction compared to the revised PCE, although calibration curves had overlapped.

Both PCE had poor calibration and discrimination of ASCVD risk in a large, real-world patient sample followed up for over 2 years. There was no evidence of improvement in the accuracy of the revised PCE in assessing the risk of ASCVD in relation to the AHA/ACC PCE.

Implications of the 2019 American College of Cardiology/American Heart Association Primary Prevention Guidelines and potential value of the coronary artery calcium score among South Asians in the US: The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study

South Asian (SA) ethnicity is associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD) compared to most other racial/ethnic groups. However, the implications of considering SA ethnicity as a “risk-enhancing factor” per the recent American College of Cardiology/American Heart Association guidelines are not fully understood. Haque et al. assessed the implications of implementing the 2018/2019 ACC/AHA recommendations for ASCVD risk assessment in SAs and of considering SA ethnicity as a risk-enhancing feature. They also described the burden of cardiovascular risk factors with special attention to characteristics associated with increased risk of incident diabetes, such as pre-diabetes and abdominal obesity.

Data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study, a community-based cohort study of individuals of SA ancestry living in the USA, were used for the analysis. The Pooled Cohort Equations were used to estimate 10-year ASCVD risk. Metabolic risk factors and coronary artery calcium (CAC) scores were assessed.

Among 1114 MASALA participants included, 28% were already using a statin at baseline, 25% had prevalent diabetes, and 59% qualified for 10-year ASCVD risk assessment for statin allocation purposes. The prevalence of low, borderline, intermediate, and high estimated ASCVD risk was 65%, 11%, 20% and 5%, respectively. Among participants at intermediate risk, 30% had CAC = 0 and 37% had CAC > 100, while among participants at borderline risk, 54% had CAC = 0 and 13% had CAC > 100. Systematic consideration of intermediate and, particularly, of borderline risk individuals as statin candidates would enrich the statin-consideration group with CAC = 0 participants up to 35%. Prediabetes and abdominal obesity were highly prevalent across all estimated risk strata, including among those with CAC = 0.

These findings suggest that systematic consideration of borderline risk SAs as statin candidates might result in considerable overtreatment, and further risk assessment with CAC may help better personalize statin allocation in these individuals. Early, aggressive lifestyle interventions aimed at reducing the risk of incident diabetes should be strongly recommended in USA SAs, particularly among those considered candidates for statin therapy for primary prevention. Longitudinal studies are needed to confirm the favorable prognosis of CAC = 0 in SAs.

Impact of a coronary artery calcium-guided statin treatment protocol on cardiovascular risk at 12 months: Results from a pragmatic, randomised controlled trial

Coronary artery calcium score (CAC) is an established cardiovascular disease (CVD) risk re-classification tool of value in low-intermediate CVD risk patients. In those with family history of

coronary artery disease, CAC can help address mis-calibration from global risk tools, identify those with subclinical disease and target therapy to those who are likely to benefit. Recent evidence has showed improvements in cardiovascular risk profile in those who visualised carotid atherosclerosis and commenced on statins compared to those blinded to their imaging results. However, the relative contribution of pharmacological therapy and lifestyle risk factor modification to improvement in risk is unknown. Venkataraman et al. sought to evaluate the benefit of a CAC-guided risk-management protocol in those with a family history of premature coronary artery disease (FHCAD).

In this Australian multi-centre, randomized controlled trial (Coronary Artery Calcium score: Use to Guide management of Hereditary Coronary Artery Disease, CAUGHT-CAD), asymptomatic, statin-naïve participants at low-intermediate cardiovascular risk with FHCAD underwent CAC assessment. Those with CAC between 1 and 400 were randomized (1:1) to disclosing the CAC result to both patient and physician and commencing atorvastatin (intervention) or blinding the CAC result with risk factor education only (control). The primary endpoint of this sub-study was change in Pooled Cohort Equation (PCE) at 12 months.

Of 1088 participants who were scanned, 450 were randomised and 214 in both groups completed 1-year follow-up. At 1 year, PCE-risk decreased by 1.0% in the CAC-disclosed group and increased by 0.43% in the CAC-blinded group. LDL-C decreased in the CAC-disclosed group in both those who continued and discontinued statins but was unchanged in the CAC-blinded group.

Participants unblinded to their CAC showed reductions in low-density lipoprotein irrespective of statin continuation when compared to controls at 12 months. Improvements in individual risk factors and PCE risk were also noted. CAC assessment may positively influence patients and physicians to improve risk factor control.

Lipid-lowering therapy use in primary and secondary care in Central and Eastern Europe: DA VINCI observational study

Cardiovascular disease (CVD) remains the most common cause of mortality in Europe, resulting in more than 4 million deaths per year, and accounting for 45% of all mortality in this region. Although Europe is commonly regarded as a single entity, it is comprised of different countries with diverse populations. Central and Eastern Europe (CEE) is a largely understudied region, despite having the highest cardiovascular disease mortality in Europe. Vrablik et al. aimed to assess the proportion of patients in CEE who achieved their low-density lipoprotein cholesterol (LDL-C) goals based on individual cardiovascular risk recommended by the 2016 and 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines.

The DA VINCI study was a cross-sectional observational study of primary and secondary prevention patients receiving lipid-lowering therapy across Europe between June 2017 and November 2018.

In total, 2154 patients were enrolled from the Czech Republic, Hungary, Poland, Romania, Slovakia and Ukraine. At LDL-C measurement, most patients were on either moderate- or high-intensity statin monotherapy. Despite this, only 44% of patients achieved risk-based LDL-C goals recommended by the 2016 ESC/EAS guidelines, ranging from 21% in Ukraine to 50% in Hungary and Romania. Only 24% of patients overall achieved the risk-based LDL-C goals recommended by the 2019 ESC/EAS guidelines, ranging from 11% in Ukraine to 32% in Poland.

Among patients receiving lipid-lowering therapy, more than half did not achieve their 2016 LDL-C goals. In one of the first comparative analyses evaluating 2019 risk-based goal attainment among countries in CEE, three-quarters of patients did not meet their 2019 LDL-C goals, highlighting a significant gap between guidelines and clinical practice for lipid management in CEE.

Spousal similarities in cardiometabolic risk factors: A cross-sectional comparison between Dutch and Japanese data from two large biobank studies

Observational studies have explored spousal similarities in cardiometabolic risk factors, such as blood pressure, cholesterol level, triglycerides level, abnormal glucose tolerance, and smoking. Further, a meta-analysis showed statistically significant positive spousal concordances for the main coronary risk factors, such as hypertension and diabetes. However, relatively small sample sizes in many previous studies may have led to insufficient statistical power in identifying moderate spousal similarities for some risk factors. Although some studies had large sample sizes, they assessed single populations, and none of them compared European and Asian populations. Nakaya et al. aimed to quantify and compare spousal similarities in cardiometabolic risk factors and diseases between Dutch and Japanese populations.

This cross-sectional study included 28,265 Dutch Lifelines Cohort Study spouse pairs and 5,391 Japanese Tohoku Medical Megabank Organization (ToMMo) Cohort Study pairs. Spousal similarities in cardiometabolic risk factors were evaluated using Pearson's correlation or logistic regression analyses adjusted for spousal age.

The husbands' and wives' average ages in the Lifelines and ToMMo cohorts were 50.0 and 47.7 years and 63.2 and 60.4 years, respectively. Significant spousal similarities occurred with all cardiometabolic risk factors and diseases of interest in both cohorts. The age-adjusted correlation coefficients ranged from 0.032 to 0.263, with the strongest correlations observed in anthropometric traits. Spousal odds ratios for the Lifelines vs. ToMMo cohort ranged from 1.45 vs. 1.20 for hypertension to 6.86 vs. 4.60 for current smoking. An increasing trend in spousal concordance with

age was observed for sufficient physical activity in both cohorts. For current smoking, those aged 20–39 years showed the strongest concordance between pairs in both cohorts. The Dutch pairs showed stronger similarities in anthropometric traits and lifestyle habits (smoking and drinking) than their Japanese counterparts.

Spouses showed similarities in several cardiometabolic risk factors among Dutch and Japanese populations, with regional and cultural factors influencing such similarities. Interventions targeting spouses, rather than individuals, may be more effective.