[1] *Warden BA, Miles JR, Oleaga C et al.* **Unusual responses to PCSK9 inhibitors in a clinical cohort utilizing a structured follow-up protocol**. Am J Prev Cardiol 2020; 1:100012.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327453

***ABSTRACT***

OBJECTIVE: To characterize unusual responses to PCSK9 inhibitor (PCSK9i) therapy in a real-world setting, given their extremely low prevalence in clinical trials. METHODS: A retrospective study of patients seen in a structured academic PCSK9i clinic who had LDL-C measurements before and after initiation of PCSK9i (up to 12 months). Unusual response was defined as: (1) no response: no changes in LDL-C level at all time points; (2) delayed response: <30% LDL-C reduction by the third dose, but achieving this threshold at a later time; (3) reduced response: <30% LDL-C reduction at all time points; and (4) lost response: ≥30% LDL-C reduction by the third dose, but displaying <30% reduction at a later time. RESULTS: Of the 411 patients meeting inclusion criteria, 54 were initially classified as unusual responders. After excluding those not adherent to prescribed interventions, 31 patients (7.5%) were classified as true unusual responders. These included: 2 with no response, 12 with delayed response, 3 with reduced response, 6 with delayed or reduced response, 4 with lost response, and 4 with delayed and lost response. Response to PCSK9i therapy at all time points revealed higher on-treatment LDL-C values (94-100 vs. 47-51 mg/dL, $p < 0.001$) and lower degree of percent reduction in LDL-C (23.3-34% vs. 61.1-64.5%, $p < 0.001$) in the unusual versus usual responders. Lipoprotein (a) (Lp[a]) values were consistently higher in the unusual responders (81-92.5 vs. 28.5-52 mg/dL, $p < 0.01$). Fold change in post-versus pre-treatment PCSK9 plasma results was similar between the two cohorts ($p > 0.05$), suggesting that unusual responses were not due to insufficient plasma PCSK9 blockade. Multiple logistic regression analysis identified clinical FH (OR 2.9, 95% CI 1.27-7.24) and no ezetimibe therapy (OR 0.334, 95% CI 0.150-0.728) as factors related to true unusual response. CONCLUSIONS: Unusual responses to PCSK9i in a clinical cohort are more common than reported in clinical trials. Of the suspected unusual responders, nearly half were the result of adherence issues, and thus careful medication reconciliation should be the first step in diagnosing an unusual response.

[2] *Tung H, Lin HJ, Chen PL et al.* **Characterization of familial hypercholesterolemia in Taiwanese ischemic stroke patients**. Aging 2021; 13:19339-19351.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34314377

***ABSTRACT***

Familial hypercholesterolemia (FH) is a common genetic disorder characterized by a lifelong elevated low-density lipoprotein cholesterol (LDL-C) level. The relationship between FH and ischemic stroke is still controversial. We enrolled ischemic stroke patients prospectively in our neurological ward, and divided them into two groups according to LDL-C levels with a threshold of 130 mg/dl. Targeted sequencing was performed in all stroke patients for LDLR, APOB, and PCSK9 genes. The fifty-eight high-LDL subjects were older, prevalence of previous myocardial infarction/stroke history was lower, and the first stroke age was older compared with values in the sixty-three low-LDL cases. The prevalence of FH in Han-Chinese stroke patients was 5.0%, and was 10.3% in those with a higher LDL-C level. We identified six carriers, who had higher percentages of large vessel stroke subtype (66.7% vs. 15.4%) and transient ischemic attack (33.3% vs. 3.8%), previous myocardial infarction/stroke history (50.0% vs. 11.5%), statin use (50.0% vs. 11.5%), and increased carotid intima-media thickness (IMT) (0.9-1.2mm vs.0.7-9.0mm) compared with the other

hypercholesterolemic patients without pathogenic variants. Ischemic stroke patients carrying FH pathogenic variants seemed to have a higher risk for large artery stroke and transient ischemic attack. The IMT exam could be useful to screen for FH in hypercholesterolemic stroke patients.

[3] *Tuleta I, Frangogiannis NG*. **Fibrosis of the diabetic heart: Clinical significance, molecular mechanisms, and therapeutic opportunities**. Adv Drug Deliv Rev 2021:113904.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34331987

***ABSTRACT***

In patients with diabetes, myocardial fibrosis may contribute to the pathogenesis of heart failure and arrhythmogenesis, increasing ventricular stiffness and delaying conduction. Diabetic myocardial fibrosis involves effects of hyperglycemia, lipotoxicity and insulin resistance on cardiac fibroblasts, directly resulting in increased matrix secretion, and activation of paracrine signaling in cardiomyocytes, immune and vascular cells, that release fibroblast-activating mediators. Neurohumoral pathways, cytokines, growth factors, oxidative stress, advanced glycation end-products (AGEs), and matricellular proteins have been implicated in diabetic fibrosis; however, the molecular links between the metabolic perturbations and activation of a fibrogenic program remain poorly understood. Although existing therapies using glucose- and lipid-lowering agents and neurohumoral inhibition may act in part by attenuating myocardial collagen deposition, specific therapies targeting the fibrotic response are lacking. This review manuscript discusses the clinical significance, molecular mechanisms and cell biology of diabetic cardiac fibrosis and proposes therapeutic targets that may attenuate the fibrotic response, preventing heart failure progression.

[4] *Rafiee S, Bagherniya M, Askari G et al.* **The Effect of Curcumin in Improving Lipid Profile in Patients with Cardiovascular Risk Factors: A Systematic Review of Clinical Trials**. Advances in experimental medicine and biology 2021; 1291:165-177.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34331690

***ABSTRACT***

Cardiovascular disease (CVD) is a major cause of death worldwide. Lipid abnormalities are one of the major risk factors for CVD. Curcumin is a natural polyphenol with lipid-lowering properties. Therefore, we carried out a systematic review to summarize the randomized controlled trials (RCTs) investigating the effect of curcumin on lipid profile in patients at risk of CVD. A comprehensive systematic search was conducted in PubMed, Scopus, Web of Science, and Google Scholar up to March 1, 2020, to identify controlled clinical trials assessing the effects of curcumin on lipid profile in patients at risk of CVD. From 1051 initially identified studies, 22 met the eligibility criteria. Curcumin supplementation significantly reduced at least one of the lipid profile indices (triglycerides, total cholesterol, low-density lipoprotein-cholesterol, and high-density lipoprotein-cholesterol) in 15 studies and improved more than one index in five studies. However, curcumin had no effect on any of lipid profile indices in seven studies. Overall, studies using a bioavailable formulation of curcumin had a better impact on the lipid profile. The findings of this systematic review showed that curcumin supplementation significantly reduced at least one of the lipid profile indices in more than two-thirds of the included studies. Curcumin might be used as an accessible, inexpensive, and safe agent to reduce risk of CVD. More randomized, clinical controlled trials are needed to verify these results.

[5] *Kovanen PT, Raal F, Vuorio A*. **Patients with familial hypercholesterolemia and COVID-19: Efficient and ongoing cholesterol lowering is paramount for the prevention of acute myocardial infarction**. Am J Prev Cardiol 2021; 7:100224.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34312613
***ABSTRACT***

[6] *Klimchak AC, Patel MY, Iorga Ş R et al.* **Lipid treatment and goal attainment characteristics among persons with atherosclerotic cardiovascular disease in the United States**. Am J Prev Cardiol 2020; 1:100010.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327452
***ABSTRACT***
OBJECTIVE: National estimates of atherosclerotic cardiovascular disease (ASCVD) in the United States (US) are scarce, especially for patients grouped by cardiovascular risk, lipid-lowering therapy use, and low-density lipoprotein cholesterol (LDL-C) levels. The objective of this study was to estimate the size of the ASCVD population, including the subgroup at very high risk for recurrent events as defined by the 2018 Multi-Society Cholesterol Guidelines. METHODS: Patient-level data from the Truven MarketScan Research Database were used and extrapolated to approximate national figures based on known national demographic and ASCVD prevalence numbers. Demographic and clinical characteristics, including LDL-C levels and lipid-lowering therapy use, were captured. RESULTS: The extrapolated prevalence of ASCVD in 2014 was 18.3 million, of whom 690,524 had an acute coronary syndrome event in the past year. An estimated 41.4% of patients with ASCVD had diabetes, 44.9% had polyvascular disease, and 23.8% had multiple cardiovascular events. A third of those with ASCVD were estimated to be at very high risk for subsequent events per the 2018 Multi-Society Cholesterol Guidelines. Of those with ASCVD, 74.2% were estimated to have an LDL-C level of ≥70 md/dL, and more than half of these patients were neither on statins nor ezetimibe. Only 9.2% of patients with ASCVD and LDL-C ≥70 mg/dL were on a high-intensity statin. CONCLUSIONS: The underutilization of lipid-lowering therapies in general, and in particular the relatively low usage of high-intensity statins among patients with uncontrolled LDL-C (including those at very high risk), suggests that eligible patients for proprotein convertase subtilisin/kexin type 9 inhibitor therapy may not be as numerous as previously estimated.

[7] *Hagström E, Sorio Vilela F, Svensson MK et al.* **Cardiovascular Event Rates After Myocardial Infarction or Ischaemic Stroke in Patients with Additional Risk Factors: A Retrospective Population-Based Cohort Study**. Adv Ther 2021; 38:4695-4708.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34312813
***ABSTRACT***
INTRODUCTION: The impact of additional risk factors on major cardiovascular event (MACE) rates in patients with a history of myocardial infarction (MI) or ischaemic stroke (IS) treated with statins is not well defined. METHODS: In this retrospective population-based cohort study, patients with a history of MI or IS treated with moderate- or high-intensity statins were identified using Swedish national register data. Patients were incident (index event between July 2006 and December 2014 and followed from diagnosis) or prevalent (MI or IS before July 2006 and followed thereafter). Four subgroups were defined on the basis of additional risk factors associated with increased cardiovascular risk: diabetes mellitus with target organ damage; chronic kidney disease stages 3-4;

index event within 2 years after prior MI or IS; and polyvascular disease. First and total MACE rates (i.e. MI, IS, or cardiovascular death) were calculated, and first MACE 10-year risks (prevalent cohort only) were predicted. RESULTS: Numerically, MACE rates in subgroups were 1.5-3 times higher than in overall populations, and were highest in the 2 years after the index event. First MACE rates in the additional risk factor subgroups were 17.2-33.5 per 100 person-years for the incident cohorts and 9.9-13.2 per 100 person-years for the prevalent cohorts. Total MACE rates per 100 person-years were 20.1-39.8 per 100 person-years and 12.4-17.6 per 100 person-years, respectively. CONCLUSION: Despite previous use of moderate- or high-intensity statins, patients with a history of MI or IS, and additional risk factors remain at very high cardiovascular risk.

[8] *Watts GF, Sullivan DR, Hare DL et al.* **Synopsis of an integrated guidance for enhancing the care of familial hypercholesterolaemia: an Australian perspective**. Am J Prev Cardiol 2021; 6:100151.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327493
***ABSTRACT***
INTRODUCTION: Familial hypercholesterolaemia (FH) is a common, heritable and preventable cause of premature coronary artery disease, with significant potential for positive impact on public health and healthcare savings. New clinical practice recommendations are presented in an abridged guidance to assist practitioners in enhancing the care of all patients with FH. MAIN RECOMMENDATIONS: Core recommendations are made on the detection, diagnosis, assessment and management of adults, children and adolescents with FH. There is a key role for general practitioners (GPs) working in collaboration with specialists with expertise in lipidology. Advice is given on genetic and cholesterol testing and risk notification of biological relatives undergoing cascade testing for FH; all healthcare professionals should develop skills in genomic medicine. Management is under-pinned by the precepts of risk stratification, adherence to healthy lifestyles, treatment of non-cholesterol risk factors, and appropriate use of low-density lipoprotein (LDL)-cholesterol lowering therapies, including statins, ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Recommendations on service design are provided in the full guidance. POTENTIAL IMPACT ON CARE OF FH: These recommendations need to be utilised using judicious clinical judgement and shared decision making with patients and families. Models of care need to be adapted to both local and regional needs and resources. In Australia new government funded schemes for genetic testing and use of PCSK9 inhibitors, as well as the National Health Genomics Policy Framework, will enable adoption of these recommendations. A broad implementation science strategy is, however, required to ensure that the guidance translates into benefit for all families with FH.

[9] *Vikulova DN, Skorniakov IS, Bitoiu B et al.* **Lipid-lowering therapy for primary prevention of premature atherosclerotic coronary artery disease: Eligibility, utilization, target achievement, and predictors of initiation**. Am J Prev Cardiol 2020; 2:100036.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327459
***ABSTRACT***
OBJECTIVES: Despite advances in screening and prevention, rates of premature coronary artery disease (CAD) have been stagnant. The goals of this study were to investigate the barriers to early risk detection and preventive treatment in patients with premature CAD. In particular, we: 1) assessed

the performance of the latest versions of major international guidelines in detection of risk of premature CAD and eligibility for preventive treatment; and, 2) investigated real-life utilization of primary prevention with lipid-lowering therapies in these patients. METHODS: We included patients in the Study to Avoid cardioVascular Events in British Columbia (SAVE BC), an observational study of patients with premature (males ≤ 50 years, females ≤ 55 years) angiographically confirmed CAD. Eligibility for primary prevention and treatment received were assessed retrospectively based on information recorded prior to or at the index presentation with CAD. RESULTS: Of 417 patients (28.1% females) who met the criteria, 94.3% had at least one major cardiovascular risk factor. In the retrospective risk assessment, 41.7%, 61.4%, and 34.3% ($p < 0.001$) of patients met criteria for initiation of statin therapy, and an additional 13.9%, 8.4%, and 46.8% may be considered for treatment using the American College of Cardiology/American Heart Association, Canadian Cardiovascular Society, and European Society of Cardiology guidelines, respectively. Only 17.1% of patients received statins and 11.0% achieved guideline-recommended lipid goals before presentation. Diabetes and elevated plasma lipid levels were positively associated with treatment initiation, while smoking was associated with non-treatment. CONCLUSIONS: The current versions of major guidelines fail to recognize many patients who develop premature CAD as being at risk. The vast majority of these patients, including patients who have guideline-directed indications, do not receive lipid-lowering therapy before presenting with CAD. Our findings highlight the need for more effective screening and prevention strategies for premature CAD.

[10] *Sikand G, Severson T*. **Top 10 dietary strategies for atherosclerotic cardiovascular risk reduction**. Am J Prev Cardiol 2020; 4:100106.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327475

***ABSTRACT***

Poor dietary quality has surpassed all other mortality risk factors, accounting for 11 million deaths and half of CVD deaths globally. Implementation of current nutrition recommendations from the American Heart Association (AHA), American College of Cardiology (ACC) and the National Lipid Association (NLA) can markedly benefit the primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD). These include: 1) incorporate nutrition screening into medical visits; 2) refer patients to a registered dietitian nutritionist (RDN) for medical nutrition therapy, when appropriate, for prevention of ASCVD; 3) follow ACC/AHA Nutrition and Diet Recommendations for ASCVD prevention and management of overweight/obesity, type 2 diabetes and hypertension; 4) include NLA nutrition goals for optimizing low-density lipoprotein cholesterol (LDL-C) and non-high-density lipoprotein cholesterol (non-HDL-C) and reducing ASCVD risk; 5) utilize evidence-based heart-healthy eating patterns for improving cardiometabolic risk factors, dyslipidemia and ASCVD risk; 6) implement ACC/AHA/NLA nutrition and lifestyle recommendations for optimizing triglyceride levels; 7) understand the impact of saturated fats, trans fats, omega-3 and omega-6 polyunsaturated fats and monounsaturated fats on ASCVD risk; 8) limit excessive intake of dietary cholesterol for those with dyslipidemia, diabetes and at risk for heart failure; 9) include dietary adjuncts such as viscous fiber, plant sterols/stanols and probiotics; and 10) implement AHA/ACC and NLA physical activity recommendations for the optimization of lipids and prevention of ASCVD. Evidence on controversies pertaining to saturated fat, processed meat, red meat, intermittent fasting, low-carbohydrate/very-low-carbohydrate diets and caffeine are discussed.

[11] *Nelson AJ, Puri R, Brennan DM et al.* **C-reactive protein levels and plaque regression with evolocumab: Insights from GLAGOV**. Am J Prev Cardiol 2020; 3:100091.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327467

***ABSTRACT***

OBJECTIVE: On-treatment levels of high sensitivity C-reactive protein (hsCRP) in statin-treated patients predict plaque progression and the prospective risk of atherosclerotic cardiovascular events. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors produce additional LDL-C lowering, reduce plaque burden and improve cardiovascular outcomes in statin-treated patients. It is unknown whether residual systemic inflammation attenuates their favorable effects on plaque burden. METHODS: GLAGOV compared the effects of treatment for 78 weeks with evolocumab or placebo on progression of coronary atherosclerosis in statin-treated patients with coronary artery disease.Clinical demographics, biochemistry and changes in both the burden (percentage atheroma volume (PAV), total atheroma volume (TAV), n = 413) and composition (n = 162) of coronary plaque were evaluated in evolocumab-treated patients according to baseline hsCRP strata (<1, 1-3, >3 mg/L). RESULTS: The study cohort comprised 413 evolocumab-treated patients (32% low [<1 mg/L], 41% intermediate [1-3 mg/L] and 27% high [>3 mg/L] baseline hsCRP levels). Patients in the highest hsCRP stratum were more likely to be female and had a higher prevalence of diabetes, hypertension, and the metabolic syndrome. LDL-C levels were similar across the groups, however participants with higher hsCRP levels had higher triglyceride and lower HDL-C levels at baseline. At follow-up, the change in PAV from baseline (-0.87% [low] vs. -0.84% [intermediate] vs. -1.22% [high], p = 0.46) and the proportion of patients experiencing any degree of regression (65.9% vs. 63.5% vs. 63.1%, p = 0.88) was similar across hsCRP strata and when evaluated by levels of achieved LDL-C. There were no serial differences in plaque composition by hsCRP strata. CONCLUSION: The ability of evolocumab to induce regression in statin-treated patients is not attenuated by the presence of enhanced systemic inflammation. This underscores the potential benefits of intensive lipid lowering, even in the presence of heightened inflammatory states.

[12] *Langslet G, Johansen AK, Bogsrud MP et al.* **Thirty percent of children and young adults with familial hypercholesterolemia treated with statins have adherence issues**. Am J Prev Cardiol 2021; 6:100180.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327501

***ABSTRACT***

OBJECTIVE: To assess adherence to lipid lowering therapy (LLT), reasons for poor adherence, and achievement of LDL-C treatment goals in children and young adults with familial hypercholesterolemia (FH). METHODS: Retrospective review of the medical records of 438 children that started follow-up at the Lipid Clinic, Oslo University hospital, between 1990 and 2010, and followed-up to the end of July 2019. Based on information on adherence to the LLT at the latest visit, patients were assigned to "good adherence" or "poor adherence" groups. Reasons for poor adherence were categorized as: "lack of motivation", "ran out of drugs", or "side effects". RESULTS: Three hundred and seventy-one patients were included. Mean (SD) age and follow-up time at the latest visit was 24.0 (7.1) and 12.9 (6.7) years; 260 patients (70%, 95% CI: 65-74%) had "good adherence" and 111 (30%, 95% CI: 25-35%) had "poor adherence". "Lack of motivation" was the most common reason for poor adherence (n = 85, 23%). In patients with good adherence, compared to patients with poor adherence, age at latest visit (24.6 versus 22.0 years; p = 0.001), years of

follow-up (13.5 versus 11.4 years; p = 0.003), and number of visits (8.1 versus 6.5 visits; p<0.001) were significantly higher, whereas LDL-C at the latest visit was lower, (3.1 (0.8) versus 5.3 (1.6) mmol/L; p<0.001) and percentage of patients reaching LDL-C treatment goal was higher, (34.5% versus 2.7%; p<0.001). Gender, BMI, age at first visit and premature cardiovascular disease in first degree relatives were not significantly associated with adherence. CONCLUSION: Thirty percent of young patients with FH had poor adherence to LLT, with lack of motivation as the main reason. Higher age, more visits and more years of follow-up were associated with good adherence.

[13] *Khan SU, Michos ED*. **Cardiovascular mortality after intensive LDL-Cholesterol lowering: Does baseline LDL-Cholesterol really matter?** Am J Prev Cardiol 2020; 1:100013.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327454
***ABSTRACT***
It remains controversial whether reductions in cardiovascular mortality after intensive lowering of low density lipoprotein cholesterol (LDL-C) depend on baseline LDL-C levels. To reassess these findings, in this brief report, we performed an updated literature search through February 2020 and selected randomized controlled trials which reported cardiovascular mortality and major adverse cardiovascular events (MACE) as outcomes. We included 53 randomized controlled trials (329,897 patients) of LDL-C lowering therapies (statin, ezetimibe and PCSK9 inhibitors) and stratified the meta-analysis according to the baseline LDL-C thresholds. Our meta-analysis found that each 38.7 mg/dL (1 mmol/L) lowering in LDL-C reduced the risk of cardiovascular mortality (RR, 0.85; 95% CI, 0.81-0.89), but this varied by baseline LDL-C of those in the trials (P = 0.04 for interaction). The risk reduction in cardiovascular mortality was limited to trials with baseline LDL-C of >100 mg/dL. In contrast, the reduction in MACE was independent of baseline LDL-C levels. These findings were consistent in primary and secondary prevention settings for both outcomes and by sex for MACE. Our results support the professional cholesterol guidelines which recommend achieving a ≥50% reduction in LDL-C from baseline for high-risk patients.

[14] *Jackson CL, Zordok M, Kullo IJ*. **Familial hypercholesterolemia in Southeast and East Asia**. Am J Prev Cardiol 2021; 6:100157.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327494
***ABSTRACT***
Familial hypercholesterolemia (FH) is a relatively common autosomal dominant disorder associated with a significantly increased risk of coronary heart disease (CHD). Most (~85-90%) cases are due to pathogenic variants in the LDL-receptor gene (LDLR), while the remaining are due to pathogenic variants in the apolipoprotein B (APOB) and proprotein convertase subtilisin/kexin type 9 (PCSK9) genes, though the proportion may vary depending on geographic location. Even though at least a quarter of the world's FH population lives in Southeast and East Asia, there are substantial gaps in knowledge regarding the epidemiology of FH due to low awareness, the absence of national screening programs, and limited availability of genetic testing. In this review, we discuss the most recent and relevant information available related to diagnostic criteria, prevalence, awareness, clinical characteristics, genetic epidemiology, and treatment in the FH population of Southeast and East Asia. Increasing awareness and improving the diagnosis and management of FH will reduce the burden of premature CHD in these regions of the world.

[15] *Feldman DI, Wu KC, Hays AG et al.* **The Johns Hopkins Ciccarone Center's expanded 'ABC's approach to highlight 2020 updates in cardiovascular disease prevention**. Am J Prev Cardiol 2021; 6:100181.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327502

***ABSTRACT***
In recent years, improvement in outcomes related to cardiovascular disease is in part due to the prioritization and progress of primary and secondary prevention efforts. The Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease expanded 'ABC's approach is used to highlight key findings in Preventive Cardiology from 2020 and further emphasize the importance of cardiovascular prevention. This simplified approach helps clinicians focus on the most relevant and up to date recommendations for optimizing cardiovascular disease risk through accurate risk assessment and appropriate implementation of lifestyle, behavioral and pharmacologic interventions. While 2020 not only provided practice changing updates by way of clinical guidelines and randomized controlled trials on topics related to antithrombotic and lipid lowering therapy, diabetes management and risk assessment, it also provided promising data on how to improve dietary and exercise adherence and manage genetic risk. By providing clinicians with a systematic approach to cardiovascular prevention and key highlights from the prior year, the goal of significantly reducing the burden of cardiovascular disease worldwide can be achieved.

[16] *Feldman DI, Michos ED, Stone NJ et al.* **Same evidence, varying viewpoints: Three questions illustrating important differences between United States and European cholesterol guideline recommendations**. Am J Prev Cardiol 2020; 4:100117.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327477

***ABSTRACT***
In 2018, the AHA/ACC Multisociety Guideline on the Management of Blood Cholesterol was released. Less than one year later, the 2019 ESC/EAS Dyslipidemia Guideline was published. While both provide important recommendations for managing atherosclerotic cardiovascular disease (ASCVD) risk through lipid management, differences exist. Prior to the publication of both guidelines, important randomized clinical trial data emerged on non-statin lipid lowering therapy and ASCVD risk reduction. To illustrate important differences in guideline recommendations, we use this data to help answer three key questions: 1) Are ASCVD event rates similar in high-risk primary and stable secondary prevention? 2) Does imaging evidence of subclinical atherosclerosis justify aggressive use of statin and non-statin therapy (if needed) to reduce LDL-C levels below 55 mg/dL as recommended in the European Guideline? 3) Do LDL-C levels below 70 mg/dL achieve a large absolute risk reduction in secondary ASCVD prevention? The US guideline prioritizes both the added efficacy and cost implications of non-statin therapy, which limits intensive therapy to individuals with the highest risk of ASCVD. The European approach broadens the eligibility criteria by incorporating goals of therapy in both primary and secondary prevention. The current cost and access constraints of healthcare worldwide, especially amidst a COVID-19 pandemic, makes the European recommendations more challenging to implement. By restricting non-statin therapy to a subgroup of high- and, in particular, very high-risk individuals, the US guideline provides primary and secondary ASCVD prevention recommendations that are more affordable and attainable. Ultimately, finding a common ground for both guidelines rests on our ability to design trials that assess cost-effectiveness in addition to efficacy and safety.

[17] *Baum SJ, Rane PB, Nunna S et al.* **Geographic variations in lipid-lowering therapy utilization, LDL-C levels, and proportion retrospectively meeting the ACC/AHA very high-risk criteria in a real-world population of patients with major atherosclerotic cardiovascular disease events in the United States**. Am J Prev Cardiol 2021; 6:100177.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327500

***ABSTRACT***

OBJECTIVE: We assessed national- and state-level geographic variations among patients with a history of ≥1 major atherosclerotic cardiovascular disease (ASCVD) event in: (1) the proportion of patients with retrospectively identified 2018 American College of Cardiology/American Heart Association guideline very high-risk (VHR) ASCVD criteria; (2) utilization of guideline-directed lipid-lowering therapy (LLT); and (3) the proportion of patients with persistent low-density lipoprotein cholesterol (LDL-C) elevations despite statin and/or ezetimibe use. METHODS: A retrospective cohort study using the Prognos LDL-C database linked to IQVIA longitudinal medical and prescription claims databases. The study period was from January 01, 2011, to November 30, 2019 and the index period was from January 01, 2016, to November 30, 2019; the index date was defined as the most recent LDL-C test during the index period. The study included patients aged ≥18 years at index who had a measured LDL-C level during the index period and had ≥1 inpatient/outpatient claim for ASCVD during the 5-year pre-index period. RESULTS: Of patients with any ASCVD (N=4652,468), 1537,514 (33.1%) patients had ≥1 major ASCVD event. Among patients with ≥1 major ASCVD event, the VHR ASCVD criteria were retrospectively identified in 1139,018 (74.1%) patients; Hawaii had the highest (81.7%) and Colorado the lowest (65.0%) proportion of these patients. Nationally, 48.8% and 50.2% of patients with ≥1 major ASCVD event and retrospectively identified VHR ASCVD criteria, respectively, had current LLT use; Massachusetts and Colorado had the highest and lowest proportions, respectively. After standardizing for age and sex, 57.3% and 58.8% of patients with ≥1 major ASCVD event and retrospectively identified VHR ASCVD criteria, respectively, had LDL-C ≥70 mg/dL (≥1.8 mmol/L) despite statin and/or ezetimibe use, with substantial state-level variations observed. CONCLUSIONS: The study highlights high rates of elevated LDL-C and pervasive underuse of LLT in health-insured patients with a history of major ASCVD events treated in the United States, with state-level geographic variations observed.

[18] *Wang M, Zhou Y, He X et al.* **Two novel mutations of the LPL gene in two Chinese family cases with familial chylomicronemia syndrome**. Clinica chimica acta; international journal of clinical chemistry 2021; 521:264-271.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34324844

***ABSTRACT***

The aim of this study was to investigate the clinical features and genetic causes of two family cases with familial chylomicronemia syndrome (FCS). Clinical manifestations of proband 1 and her families, and also proband 2 showed severe hypertriglyceridemia, especially the triglycerides levels of two probands were extremely high. Gene sequencing results showed that the LPL genes in each of the two probands had a new mutation site. For the proband 1, a compound heterozygous mutation at c.429 (c.429 + 1G > T) was detected in the LPL gene, which was splicing mutation and inherited from her mother. Homozygous mutation was detected in the LPL gene of proband 2, the nucleotide mutation at c.802 (c.802C > T) exhibited missense mutation, his parents and brother had a

heterozygous mutation at the same site. It was confirmed that the conservative lipoprotein lipase superfamily domain changed an amino acid from histidine to tyrosine at p. 268 (p. His268Tyr). Flow cytometry confirmed the deficient expression of LPL protein in two families. These results indicated that the mutation in LPL gene might be the cause of familial chylomicronemia syndrome.

[19] *Toth PP*. **Low-Density Lipoprotein Cholesterol Treatment Rates in High Risk Patients: More Disappointment Despite Ever More Refined Evidence-Based Guidelines**. Am J Prev Cardiol 2021; 6:100186.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327506
***ABSTRACT***

[20] *Lu M, Fang F, Wang Z et al.* **Association Between OSA and Quantitative Atherosclerotic Plaque Burden: A Coronary CT Angiography Study**. Chest 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34331905
***ABSTRACT***
BACKGROUND: Limited evidence is available regarding the association between OSA and coronary plaque assessed by using quantitative coronary CT angiography. RESEARCH QUESTION: Are there any associations between OSA severity-related indexes and the presence and burden of coronary plaque? STUDY DESIGN AND METHODS: Cross-sectional data from 692 patients who underwent sleep monitoring and coronary CT angiography were used for this study. Of these patients, 120 (17.3%) underwent polysomnography, and 572 (82.7%) underwent respiratory polygraphy. Multivariable logistic and linear regression analyses were used to investigate the associations of OSA severity-related indexes with the presence, volume, and composition of plaque. RESULTS: In multivariable analyses, patients with moderate to severe OSA were more likely to have coronary plaques (P = .037), and plaques were more likely to contain a noncalcified plaque (NCP) component (P = .032) and a low-density NCP (LD NCP) component (P = .030). Furthermore, the apnea-hypopnea index and oxygen desaturation index as continuous variables were both associated with the presence of plaque, NCP, and LD NCP (all, P < .05). Multivariable linear regression models showed that moderate to severe OSA was associated with NCP volume (β = 50.328; P = .042) and LD NCP volume (β = 15.707; P = .011). Moreover, the apnea-hypopnea index (P = .015), oxygen desaturation index (P = .005), and percentage of nighttime with oxygen saturation < 90% (P = .017) were all significant predictors of LD NCP volume. Compared with those with no or mild OSA, patients with severe OSA had a significantly higher total plaque volume (P = .036), NCP volume (P = .036), and LD NCP volume (P = .013). INTERPRETATION: OSA was independently associated with the presence and burden of coronary plaque, which suggests an increased risk of coronary events. CLINICAL TRIAL REGISTRATION: Chinese Clinical Trial Registry; No. ChiCTR-ROC-17011027; http://chictr.org.cn.

[21] *Kudinov VA, Torkhovskaya TI, Zakharova TS et al.* **High-density lipoprotein remodeling by phospholipid nanoparticles improves cholesterol efflux capacity and protects from atherosclerosis**. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2021; 141:111900.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34328100
***ABSTRACT***

The efficiency of cholesterol efflux from cells promoted by high-density lipoproteins (HDLs) depends on HDL concentration and functional properties. The term "dysfunctional HDL" describes HDLs with impaired protective properties. Cholesterol efflux capacity (CEC) of HDL is reduced in patients with atherosclerosis, but the exact mechanisms underlying this impairment are not well characterized. Enriching HDLs with phospholipids (PLs) improves CEC. Herein, we assessed the potential of PL nanoparticles in improving HDL functionality. We lipidated HDL subfractions by incubating with PL nanoparticles containing soybean polyunsaturated phosphatidylcholine. Incubating blood plasma with PL nanoparticles resulted in the dose-dependent lipidation of all HDL subfractions. Changes in apolipoprotein A1 (apoA-1) and PL concentrations were the most prominent in the HDL(2) fraction. Concentrations of PL in the HDL(3) fraction and the fraction with a density > 1.21 g/mL increased by 30-50%, whereas apoA-1 levels decreased. We hypothesized that PL nanoparticles may cause HDL remodeling that can improve their functions. The CECs of lipidated HDLs were analyzed by incubating apolipoprotein B (apoB)-depleted plasma with (3)H-cholesterol-labeled THP-1 macrophages. The findings revealed a two-fold increase in cholesterol efflux compared with native apoB-depleted plasma. Moreover, intravenous administration of PL nanoparticles restored lipid profiles and effectively protected blood vessels from atherosclerosis progression in cholesterol-fed rabbits compared with that of fenofibrate and atorvastatin. PL nanoparticles also protected against atherosclerosis and decreased the atherogenic index. Altogether, these results indicate that PL nanoparticles can be used to correct the lipid composition and CEC of HDLs. DATA AVAILABILITY: Additional data can be provided upon reasonable request from the date of publication of this article within 5 years. The request should be sent to the author-correspondent at the address cd95@mail.ru.

[22] *He Y, Qin MZ, Chen YW*. **Liver injury caused by fenofibrate within 48 h after first administration: a case report**. BMC gastroenterology 2021; 21:298.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34325660
***ABSTRACT***
BACKGROUND: Fenofibrate is commonly used in the treatment of dyslipidemia. Fenofibrate is related to mild aminotransferase elevations and in some cases severe chronic injury such as fibrosis or cirrhosis, resulting in liver transplantation or death. The latency of disease has been reported to range between weeks to years. CASE PRESENTATION: A 63 years old male with hypertriglyceridemia developed symptoms of fatigue and anorexia 48 h after taking fenofibrate for the first time. The patient's aminotransferase level was more than 10 times ULN. Immediately, fenofibrate was discontinued and aminotransferase level returned to normal 23 days later. To assess causality between the drug and liver damage, the standardized Roussel Uclaf Causality Assessment Method (RUCAM) was used. The patient's RUCAM score was 7, which fell in the group of "probable". Eight months later, follow-up examination suggested the liver function was normal. CONCLUSIONS: Weakness, fatigue and abnormal liver function during fenofibrate therapy should be closely monitored and trigger prompt withdrawal if these symptoms occur.

[23] *Fang Y, Gu Y, Zhao C et al.* **Impact of supervised beego, a traditional Chinese water-only fasting, on thrombosis and haemostasis**. BMJ Nutr Prev Health 2021; 4:4-17.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34308107
***ABSTRACT***

Beego is a traditional Chinese complete water-only fasting practice initially developed for spiritual purposes, later extending to physical fitness purposes. Beego notably includes a psychological induction component that includes meditation and abdominal breathing, light body exercise and ends with a specific gradual refeeding program before returning to a normal diet. Beego has regained its popularity in recent decades in China as a strategy for helping people in subhealthy conditions or with metabolic syndrome, but we are unaware of any studies examining the biological effects of this practice. To address this, we here performed a longitudinal study of beego comprising fasting (7 and 14 day cohorts) and a 7-day programmed refeeding phase. In addition to detecting improvements in cardiovascular physiology and selective reduction of blood pressure in hypertensive subjects, we observed that beego decreased blood triacylglycerol (TG) selectively in TG-high subjects and increased cholesterol in all subjects during fasting; however, the cholesterol levels were normalised after completion of the refeeding program. Strikingly, beego reduced platelet formation, activation, aggregation and degranulation, resulting in an alleviated thrombosis risk, yet maintained haemostasis by sustaining levels of coagulation factors and other haemostatic proteins. Mechanistically, we speculate that downregulation of G6B and MYL9 may influence the observed beego-mediated reduction in platelets. Fundamentally, our study supports that supervised beego reduces thrombosis risk without compromising haemostasis capacity. Moreover, our results support that beego under medical supervision can be implemented as non-invasive intervention for reducing thrombosis risk, and suggest several lines of intriguing inquiry for future studies about this fasting practice (http://www.chictr.org.cn/index.aspx, number, ChiCTR1900027451).

[24] *Duarte JA, de Barros ALB, Leite EA*. **The potential use of simvastatin for cancer treatment: A review**. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2021; 141:111858.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34323700

***ABSTRACT***

Statins, typically used to reduce lipid levels, have been rediscovered for exhibiting anticancer activities. Among them, especially simvastatin may influence the proliferation, migration, and survival of cancer cells. The concept of using statins to treat cancer has been adopted since the 1990s In vitro and in vivo experiments and cohort studies using statins have been carried out to demonstrate their antitumor effects (such as proliferation and migration impairment) by influencing inflammatory and oxidative stress-related tumorigenesis. Nevertheless, the biological mechanisms for these actions are not fully elucidated. In this review, we present an overview of the most important studies conducted from 2015 to date on the use of simvastatin in cancer therapy. This review brings the most recent perspectives and targets in epidemiological, in vitro, and in vivo studies, regarding the use of simvastatin alone or in combination with other drugs for the treatment of various types of cancer.

[25] *Castro BBA, Foresto-Neto O, Saraiva-Camara NO, Sanders-Pinheiro H*. **Renal lipotoxicity: insights from experimental models**. Clinical and experimental pharmacology & physiology 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34314523

***ABSTRACT***

In recent decades, there has been a progressive increase in the prevalence of obesity and chronic kidney disease. Renal lipotoxicity has been associated with obesity. Although lipids play fundamental physiological roles, the accumulation of lipids in kidney cells may cause dysfunction and/or renal fibrosis. Adipose tissue that exceed their lipid storage capacity begins to release triglycerides into the

bloodstream that can get stored in several organs, including the kidneys. The mechanisms underlying renal lipotoxicity involve intracellular lipid accumulation and organelle dysfunction, which trigger oxidative stress and inflammation that consequently result in insulin resistance and albuminuria. However, the specific pathways involved in renal lipotoxicity have not yet been fully understood. We aimed to summarize the current knowledge on the mechanisms by which lipotoxicity affects the renal morphology and function in experimental models of obesity. The accumulation of fatty acids in tubular cells has been described as the main mechanism of lipotoxicity; however, lipids and their metabolism also affect the function and the survival of podocytes. In this review, we presented indication of mitochondrial, lysosomal, and endoplasmic reticulum alterations involved in kidney damage caused by obesity. The kidney is vulnerable to lipotoxicity, and studies of the mechanisms underlying renal injury caused by obesity can help identify therapeutic targets to control renal dysfunction.

[26] *Cai C, Wen Z, Li L*. **The relationship between ApoE gene polymorphism and the efficacy of statins controlling hyperlipidemia**. American journal of translational research 2021; 13:6772-6777.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34306425

***ABSTRACT***

OBJECTIVE: To explore the relationship between ApoE gene polymorphism and clinical efficacy of statins on lipidemia. METHODS: Peripheral venous blood was obtained from 220 patients with hyperlipidemia who were admitted to the outpatient department of our hospital. The potential relationship between ApoE gene polymorphism and clinical effect of statins was analyzed. RESULTS: In the three isomers (E2, E3, E4) of ApoE, expression level of ApoE protein in ApoE4 gene carriers was significantly different from that in E2 or E3 gene carriers (both $P<0.05$). At the same time, both the decrease rate of total cholesterol (TC) in blood lipid and low density lipoprotein cholesterol (LDL-C) and the rise rate of high density lipoprotein cholesterol (HDL-C) in ApoE4 carriers after taking statins were much lower than those in non-ApoE4 patients ($P<0.05$). CONCLUSION: ApoE gene polymorphism is associated with hyperlipidemia and has certain influence on the clinical efficacy of statins in treatment of hyperlipidemia.

[27] *Blanchard V, Chemello K, Hollstein T et al.* **The size of apolipoprotein (a) is an independent determinant of the reduction in lipoprotein (a) induced by PCSK9 inhibitors**. Cardiovascular research 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34314498

***ABSTRACT***

AIMS: Lipoprotein (a) [Lp(a)] is a lipoprotein species causatively associated with atherosclerosis. Unlike statins, PCSK9 inhibitors (PCSK9i) reduce Lp(a), but this reduction is highly variable. Levels of Lp(a) are chiefly governed by the size of its signature protein, apolipoprotein (a) [apo(a)]. Whether this parameter determines some of the reduction in Lp(a) induced by PCSK9i remains unknown. We aimed to investigate if the Lp(a) lowering efficacy of PCSK9i is modulated by the size of apo(a), which is genetically determined by the variable number of KIV domains present on that protein. METHODS AND RESULTS: The levels of Lp(a) and the size of apo(a) were assessed in plasma samples from 268 patients before and after treatment with PCSK9i. Patients were recruited at the Outpatient Lipid Clinic of the Charité Hospital (Berlin) between 2015 and 2020. They were hypercholesterolemic at very high CVD risk with LDL-cholesterol levels above therapeutic targets despite maximally tolerated lipid-lowering therapy. Patients received either Alirocumab (75 or 150 mg) or Evolocumab (140 mg)

every 2 weeks. Apo(a), apoB100, and apoE concentrations as well as apoE major isoforms were determined by liquid chromatography high-resolution mass spectrometry. Apo(a) isoforms sizes were determined by Western Blot. PCSK9i sharply reduced LDL-cholesterol (-57%), apoB100 (-47%) and Lp(a) (-36%). There was a positive correlation between the size of apo(a) and the relative reduction in Lp(a) induced by PCSK9i ($r = 0.363$, $p = 0.0001$). The strength of this association remained unaltered after adjustment for baseline Lp(a) levels and all other potential confounding factors. In patients with two detectable apo(a) isoforms, there was also a positive correlation between the size of apo(a) and the reduction in Lp(a), separately for the smaller ($r = 0.350$, $p = 0.0001$) and larger ($r = 0.324$, $p = 0.0003$) isoforms. The relative contribution of the larger isoform to the total concentration of apo(a) was reduced from 29% to 15% ($p < 0.0001$). CONCLUSIONS: The size of apo(a) is an independent determinant of the response to PCSK9i. Each additional kringle domain is associated with a 3% additional reduction in Lp(a). This explains in part the variable efficacy of PCSK9i and allows to identify patients who will benefit most from these therapies in terms of Lp(a) lowering. TRANSLATIONAL PERSPECTIVE: Unlike statins, PCSK9 inhibitors reduce the circulating levels of the highly atherogenic Lipoprotein (a). The underlying mechanism remains a matter of considerable debate. The size of apo(a), the signature protein of Lp(a), is extremely variable (300 to more than 800 kDa) and depends on its number of kringle domains. We now show that each increase in apo(a) size by one kringle domain is associated with a 3% additional reduction in Lp(a) following PCSK9i treatment and that apo(a) size polymorphism is an independent predictor of the reduction in Lp(a) induced by these drugs. In an era of personalized medicine, this allows to identify patients who will benefit most from PCSK9i in terms of Lp(a) lowering.

[28] *Woo JS, Hong SJ, Cha DH et al.* **Comparison of the Efficacy and Safety of Atorvastatin 40 mg/ω-3 fatty acids 4 g Fixed-Dose Combination and Atorvastatin 40 mg Monotherapy in Hypertriglyceridemic Patients Who Poorly Respond to Atorvastatin 40 mg Monotherapy: An 8-Week, Multicenter, Randomized, Double-Blind Phase III Study**. Clinical therapeutics 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34332788

***ABSTRACT***

PURPOSE: Residual cardiovascular risk in patients with hypertriglyceridemia, despite optimal low-density lipoprotein cholesterol levels being achieved with intensive statin treatment, is a global health issue. The purpose of this study was to investigate the efficacy and tolerability of treatment with a combination of high-dose atorvastatin/Ω-3 fatty acid compared to atorvastatin + placebo in patients with hypertriglyceridemia who did not respond to statin treatment. METHODS: In this multicenter, randomized, double-blind, placebo-controlled study, patients who had residual hypertriglyceridemia after a 4-week run-in period of atorvastatin treatment were randomly assigned to receive UI-018 (fixed-dose combination atorvastatin/Ω-3 fatty acid 40 mg/4 g) or atorvastatin 40 mg + placebo (control). The primary efficacy end points were the percentage change from baseline in non-high density lipoprotein cholesterol (non-HDL-C) level at the end of treatment and the adverse events recorded during treatment. A secondary end point was the percentage change from baseline in triglyceride level. FINDINGS: After 8 weeks of treatment, the percentage changes from baseline in non-HDL-C (-4.4% vs +0.6%; p = 0.02) and triglycerides (-18.5% vs +0.9%; p < 0.01) were significantly greater in the UI-018 group (n = 101) than in the control group (n = 99). These changes were present in subgroups of advanced age (≥65 years), status (body mass index ≥25 kg/m(2)), or without diabetes. The prevalences of adverse events did not differ between the 2 treatment groups.

IMPLICATIONS: In patients with residual hypertriglyceridemia despite receiving statin treatment, a combination of high-dose atorvastatin/Ω-3 fatty acid was associated with a greater reduction of triglyceride and non-HDL-C compared with atorvastatin + placebo, without significant adverse events.

[29] *van Solingen C, Oldebeken SR, Salerno AG et al.* **High-Throughput Screening Identifies MicroRNAs Regulating Human PCSK9 and Hepatic Low-Density Lipoprotein Receptor Expression**. Frontiers in cardiovascular medicine 2021; 8:667298.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34322524

***ABSTRACT***

Investigations into the regulatory mechanisms controlling cholesterol homeostasis have proven fruitful in identifying low-density lipoprotein (LDL)-lowering therapies to reduce the risk of atherosclerotic cardiovascular disease. A major advance was the discovery of proprotein convertase subtilisin/kexin type 9 (PCSK9), a secreted protein that binds the LDL receptor (LDLR) on the cell surface and internalizes it for degradation, thereby blunting its ability to take up circulating LDL. The discovery that loss-of-function mutations in PCSK9 lead to lower plasma levels of LDL cholesterol and protection from cardiovascular disease led to the therapeutic development of PCSK9 inhibitors at an unprecedented pace. However, there remain many gaps in our understanding of PCSK9 regulation and biology, including its posttranscriptional control by microRNAs. Using a high-throughput region(3'-UTR) of human microRNA library screen, we identified microRNAs targeting the 3' untranslated region of human PCSK9. The top 35 hits were confirmed by large-format PCSK9 3'-UTR luciferase assays, and 10 microRNAs were then selected for further validation in hepatic cells, including effects on PCSK9 secretion and LDLR cell surface expression. These studies identified seven novel microRNAs that reduce PCSK9 expression, including miR-221-5p, miR-342-5p, miR-363-5p, miR-609, miR-765, and miR-3165. Interestingly, several of these microRNAs were also found to target other genes involved in LDLR regulation and potently upregulate LDLR cell surface expression in hepatic cells. Together, these data enhance our understanding of post-transcriptional regulators of PCSK9 and their potential for therapeutic manipulation of hepatic LDLR expression.

[30] *Li Z, Zhang J, Xue Y et al.* **Pitavastatin stimulates retinal angiogenesis via HMG-CoA reductase-independent activation of RhoA-mediated pathways and focal adhesion**. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie 2021; 259:2707-2716.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34328550

***ABSTRACT***

BACKGROUND: Excessive angiogenesis of the retina is a key component of irreversible causes of blindness in many ocular diseases. Pitavastatin is a cholesterol-lowering drug used to reduce the risk of cardiovascular diseases. Various studies have shown the effects of pitavastatin on angiogenesis but the conclusions are contradictory. The effects of pitavastatin on retinal angiogenesis have not been revealed. This study investigated the effects of pitavastatin at clinically relevant concentrations on retinal angiogenesis and its underlying mechanisms using retinal microvascular endothelial cells (RMECs). METHODS: The effects of pitavastatin on retinal angiogenesis were determined using in vitro model of retinal angiogenesis, endothelial cell migration, adhesion, proliferation, and apoptosis assays. The mechanism studies were conducted using immunoblotting and stress fiber staining. RESULTS: Pitavastatin stimulated capillary network formation of RMECs in a similar manner as

vascular endothelial growth factor (VEGF) and lipopolysaccharide (LPS). Pitavastatin also increased RMEC migration, adhesion to Matrigel, growth, and survival. The combination of pitavastatin with VEGF or LPS was more effective than VEGF or LPS alone in stimulating biological activities of RMECs, suggesting that pitavastatin can enhance the stimulatory effects of VEGF and LPS on retinal angiogenesis. Pitavastatin acted on RMECs in a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase-independent manner. In contrast, pitavastatin activated pro-angiogenic microenvironment via promoting the secretion of VEGF and stimulated retinal angiogenesis via multiple mechanisms including activation of RhoA-mediated pathways, induction of focal adhesion complex formation, and activation of ERK pathway. CONCLUSION: Our work provides a preclinical evidence on the pro-angiogenic effect of pitavastatin in retina via multiple mechanisms that are irrelevant to mevalonate pathway.

[31] *Israel A, Schäffer AA, Cicurel A et al.* **Identification of drugs associated with reduced severity of COVID-19 - a case-control study in a large population**. eLife 2021; 10.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34313216
***ABSTRACT***
BACKGROUND: Until coronavirus disease 2019 (COVID-19) drugs specifically developed to treat COVID-19 become more widely accessible, it is crucial to identify whether existing medications have a protective effect against severe disease. Toward this objective, we conducted a large population study in Clalit Health Services (CHS), the largest healthcare provider in Israel, insuring over 4.7 million members. METHODS: Two case-control matched cohorts were assembled to assess which medications, acquired in the last month, decreased the risk of COVID-19 hospitalization. Case patients were adults aged 18 to 95 hospitalized for COVID-19. In the first cohort, five control patients, from the general population, were matched to each case (n=6202); in the second cohort, two non-hospitalized SARS-CoV-2 positive control patients were matched to each case (n=6919). The outcome measures for a medication were: odds ratio (OR) for hospitalization, 95% confidence interval (CI), and the p-value, using Fisher's exact test. False discovery rate was used to adjust for multiple testing. RESULTS: Medications associated with most significantly reduced odds for COVID-19 hospitalization include: ubiquinone (OR=0.185, 95% CI [0.058 to 0.458], p<0.001), ezetimibe (OR=0.488, 95% CI [0.377 to 0.622], p<0.001), rosuvastatin (OR=0.673, 95% CI [0.596 to 0.758], p<0.001), flecainide (OR=0.301, 95% CI [0.118 to 0.641], p<0.001), and vitamin D (OR=0.869, 95% CI [0.792 to 0.954], p<0.003). Remarkably, acquisition of artificial tears, eye care wipes, and several ophthalmological products were also associated with decreased risk for hospitalization. CONCLUSIONS: Ubiquinone, ezetimibe, and rosuvastatin, all related to the cholesterol synthesis pathway were associated with reduced hospitalization risk. These findings point to a promising protective effect which should be further investigated in controlled, prospective studies. FUNDING: This research was supported in part by the Intramural Research Program of the National Institutes of Health, NCI.

[32] *Hsu JJ, Tintut Y, Demer LL*. **Lipids and cardiovascular calcification: contributions to plaque vulnerability**. Current opinion in lipidology 2021; 32:308-314.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34320564
***ABSTRACT***

PURPOSE OF REVIEW: Cardiovascular calcification, a common feature of atherosclerotic lesions, has long been known to associate with cardiovascular risk. The roles of lipoproteins in atherosclerosis are also established, and lipid-modifying therapies have shown capacity for plaque regression. However, the association of lipid-modifying therapies with calcification is more complex, and currently no medical therapies have been found to reverse or attenuate calcification in patients. In this review, we summarize recent developments in our understanding of the interplay between lipids and cardiovascular calcification, as well as new imaging modalities for assessing calcified atherosclerotic plaque vulnerability. RECENT FINDINGS: Recent clinical studies have highlighted the associations of lipoprotein subtypes, such as low-density and high-density lipoprotein particles, as well as lipoprotein (a) [Lp(a)], with coronary calcification and calcific aortic valve disease. Further, evidence continues to emerge for the utility of fused 18F-sodium fluoride positron-emission tomographic and computed tomographic (18F-NaF PET/CT) imaging in characterizing the microarchitecture and vulnerability of atherosclerotic plaque, in both humans and animal models. SUMMARY: The relationship between lipids and cardiovascular calcification is complex, and new imaging techniques, such as 18F-NaF PET/CT imaging, may allow for better identification of disease-modifying therapies and prediction of calcified plaque progression and stability to help guide clinical management.

[33] *Gialeli C, Shami A, Gonçalves I*. **Extracellular matrix: paving the way to the newest trends in atherosclerosis**. Current opinion in lipidology 2021; 32:277-285.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34320563
***ABSTRACT***
PURPOSE OF REVIEW: The extracellular matrix (ECM) is critical for all aspects of vascular pathobiology. In vascular disease the balance of its structural components is shifted. In atherosclerotic plaques there is in fact a dynamic battle between stabilizing and proinflammatory responses. This review explores the most recent strides that have been made to detail the active role of the ECM - and its main binding partners - in driving atherosclerotic plaque development and destabilization. RECENT FINDINGS: Proteoglycans-glycosaminoglycans (PGs-GAGs) synthesis and remodelling, as well as elastin synthesis, cross-linking, degradation and its elastokines potentially affect disease progression, providing multiple steps for potential therapeutic intervention and diagnostic targeted imaging. Of note, GAGs biosynthetic enzymes modulate the phenotype of vascular resident and infiltrating cells. In addition, while plaque collagen structure exerts very palpable effects on its immediate surroundings, a new role for collagen is also emerging on a more systemic level as a biomarker for cardiovascular disease as well as a target for selective drug-delivery. SUMMARY: The importance of studying the ECM in atherosclerosis is more and more acknowledged and various systems are being developed to visualize, target and mimic it.

[34] *Dardano A, Daniele G, Penno G et al.* **Breaking Therapeutic Inertia With Alirocumab in an 80-Year-Old Patient With Severe Hypercholesterolemia: A Case Report**. Frontiers in medicine 2021; 8:699477.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34307425
***ABSTRACT***
Background: Therapeutic inertia, defined as the failure to initiate or intensify therapy in a timely manner as per evidence-based clinical guidelines, is an important barrier limiting optimal care in the elderly. Therefore, overcoming therapeutic inertia is the core challenge when dealing with geriatric

patients. Case Description: The patient was an 80-year-old man that attended our Outpatient Lipid Clinic (Pisa University Hospital) because of persistent high LDL cholesterol (LDLc) levels in a setting of a statin contraindication. He underwent five percutaneous coronary angioplasties with drug-eluting stents. In 2014, upon starting treatment with rosuvastatin for LDLc level of 7.59 mmol/L, the patient was admitted to the Emergency Room for a presumptive diagnosis of rhabdomyolysis (creatine kinase 6685 U/L) secondary to statin. Patient developed acute kidney injury treated with dialysis. After resolution, he was discharged with ezetimibe (10 mg daily). This treatment however failed to effectively reduce LDLc levels that ranged between 5.9 and 6.6 mmol/L for the ensuing 4-years. In 2018, at the time of our evaluation, in consideration of the age, we performed a comprehensive geriatric assessment that showed good functional and mental status supporting a reliable treatment with a proprotein convertase subtilisin-kexin type 9 inhibitor. Therefore, alirocumab was prescribed as add-on to ezetimibe. At 24-month follow-up, the geriatric assessment showed no significant changes, and alirocumab was well-tolerated. LDLc was 82% lower as compared to baseline values (from 6.6 to 1.2 mmol/L). Conclusions: This report describes a case of therapeutic inertia despite a very high-risk profile. It is also instrumental in highlightening that appropriate intensification of therapy in an elderly patient at high cardiovascular risk, by means of a patient-centered approach, may allow reaching therapeutic targets and overcoming the condition of therapeutic inertia.

[35] *Chemello K, Jaafar AK, Lambert G*. **Heart to heart with PCSK9**. European heart journal 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34324660
***ABSTRACT***

[36] *Barrios V, Escobar C, Arrarte V et al.* **Analysis of the prescription process of PCSK9 inhibitors in the cardiology departments of Spanish hospitals and optimization proposal. The IKIGAI study**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34315626
***ABSTRACT***
AIMS: To ascertain the formalities and procedures required for the prescription of PCSK9 inhibitors in the cardiology departments of Spanish hospitals, making proposals for improvement to optimize the prescription process. METHODS: A first phase of collecting information about the variables and administrative procedures required for the prescription of PCK9 inhibitors and the elaboration of a specific questionnaire and a second phase of collecting data with an online self-administered questionnaire. RESULTS: A total of 88 hospitals participated in the study (mean number of beds 625; mean number of cardiologists 18 ± 10; 78% university hospitals). There was underuse of PCSK9 inhibitors (real prescription of 30 treatments/year; potential prescription of 80), mainly because of not fulfilling the therapeutic positioning report (52%) and application refusal (31%). Beyond the requirements of the therapeutic positioning report, 1.2 ± 0.4 applications are required with 8.5 ± 4.2 variables. Only 21% of hospitals did not require a previous authorization process and in the remaining hospitals, approval from a committee was necessary. The accumulated time of the prescription process was 6 weeks. Discontinuation rates during follow-up were 9% ± 12%. CONCLUSIONS: Treatment with PCSK9 inhibitors is clearly underused in Spain. This is mainly due to both inappropriate identification of patients, and complex administrative procedures that could

inhibit/discourage prescription by cardiologists and consequently, limit their use. In addition, there is a substantial delay from drug approval tadministration.

[37] *Alcántara-Alonso E, Molinar-Ramos F, González-López JA et al.* **High triglyceride to HDL-cholesterol ratio as a biochemical marker of severe outcomes in COVID-19 patients**. Clinical nutrition ESPEN 2021; 44:437-444.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34330502

***ABSTRACT***

BACKGROUND & AIMS: Coronavirus disease 2019 (COVID-19) patients with severe complications have shown comorbidities with cardiovascular-disease, hypertension and type 2 diabetes mellitus; clinical disorders that share the common metabolic alterations of insulin resistance and dyslipidaemia. A high triglyceride to high density lipoprotein cholesterol (Tg/HDL c) ratio has been associated with reduced insulin sensitivity, metabolic syndrome and adverse cardiovascular events. Our aim in this study was to determine the association between different components of the lipid profile and particularly the Tg/HDL c ratio with severe complications like the requirement of invasive mechanical ventilation in COVID-19 patients. METHODS: We collected demographic, clinical and biochemical data to conduct a cohort study in 43 adult patients with confirmed COVID-19 diagnosis by quantitative polymerase chain reaction (qPCR) at baseline and in the subsequent 15 days. Patients were subjected to a very similar treatment scheme with the JAK1/2 inhibitor ruxolitinib. Descriptive statistics, variable association and logistic regression were applied to identify predictors of disease severity among elements and calculations from the lipid profile. RESULTS: Patients were aged 57 ± 14 years; 55.8% were male from which 75% required hospitalization and 44.2% were female who 58% were hospitalized. The most common comorbidities were type 2 diabetes mellitus (58%) and hypertension (40%). Hospitalized and critical care patients showed lower HDL c blood levels and increased Tg/HDL c ratio than those with outpatient management and mild/asymptomatic COVID-19. Tg/HDL c ratio correlated with variables of disease severity such as lactate dehydrogenase (LDH) levels ($r = 0.356$; $p < 0.05$); National Early Warning Score 2 (NEWS 2) ($r = 0.495$; $p < 0.01$); quick sequential organ failure assessment (qSOFA) ($r = 0.538$; $p < 0.001$); increased need of oxygen support ($r = 0.447$; $p < 0.01$) and requirement of mechanical ventilation ($r = 0.378$; $p < 0.05$). Tg/HDL c ratio had a negative correlation with partial oxygen saturation/fraction of inspired oxygen (SaO 2/FiO2) ratio ($r = -0.332$;$p < 0.05$). Linear regression analysis showed that Tg/HDL c ratio can predict increases in inflammatory factors like LDH ($p < 0.01$); ferritin ($p < 0.01$) and D-dimer ($p < 0.001$). Logistic regression model indicated that ≥7.45 Tg/HDL c ratio predicts requirement of invasive mechanical ventilation (OR 11.815, CI 1.832-76.186, $p < 0.01$). CONCLUSIONS: The Tg/HDLc ratio can be used as an early biochemical marker of COVID-19 severe prognosis with requirement of invasive mechanical ventilation.

[38] *Williams MC, Earls JP, Hecht H.* **Quantitative assessment of atherosclerotic plaque, recent progress and current limitations**. Journal of cardiovascular computed tomography 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34326003

***ABSTRACT***

An important advantage of computed tomography coronary angiography (CCTA) is its ability to visualize the presence and severity of atherosclerotic plaque, rather than just assessing coronary artery stenoses. Until recently, assessment of plaque subtypes on CCTA relied on visual assessment

of the extent of calcified/non-calcified plaque, or visually identifying high-risk plaque characteristics. Recent software developments facilitate the quantitative assessment of plaque volume or burden on CCTA, and the identification of subtypes of plaque based on their attenuation density. These techniques have shown promise in single and multicenter studies, demonstrating that the amount and type of plaque are associated with subsequent cardiac events. However, there are a number of limitations to the application of these techniques, including the limitations imposed by the spatial resolution of current CT scanners, challenges from variations between reconstruction algorithms, and the additional time to perform these assessments. At present, these are a valuable research technique, but not yet part of routine clinical practice. Future advances that improve CT resolution, standardize acquisition techniques and reconstruction algorithms and automate image analysis will improve the clinical utility of these techniques. This review will discuss the technical aspects of quantitative plaque analysis and present pro and con arguments for the routine use of quantitative plaque analysis on CCTA.

[39] *Van der Heiden K, Barrett HE, Meester EJ et al.* **SPECT/CT imaging of inflammation and calcification in human carotid atherosclerosis to identify the plaque at risk of rupture**. Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34318395

***ABSTRACT***

BACKGROUND: Calcification and inflammation are atherosclerotic plaque compositional biomarkers that have both been linked to stroke risk. The aim of this study was to evaluate their co-existing prevalence in human carotid plaques with respect to plaque phenotype to determine the value of hybrid imaging for the detection of these biomarkers. METHODS: Human carotid plaque segments, obtained from endarterectomy, were incubated in [111In]In-DOTA-butylamino-NorBIRT ([111In]In-Danbirt), targeting Leukocyte Function-associated Antigen-1 (LFA-1) on leukocytes. By performing SPECT/CT, both inflammation from DANBIRT uptake and calcification from CT imaging were assessed. Plaque phenotype was classified using histology. RESULTS: On a total plaque level, comparable levels of calcification volume existed with different degrees of inflammation and vice versa. On a segment level, an inverse relationship between calcification volume and inflammation was evident in highly calcified segments, which classify as fibrocalcific, stable plaque segments. In contrast, segments with little or no calcification presented with a moderate to high degree of inflammation, often coinciding with the more dangerous fibrous cap atheroma phenotype. CONCLUSION: Calcification imaging alone can only accurately identify highly calcified, stable, fibrocalcific plaques. To identify high-risk plaques, with little or no calcification, hybrid imaging of calcification and inflammation could provide diagnostic benefit.

[40] *Schwartz GG, Szarek M, Bittner VA et al.* **Lipoprotein(a) and Benefit of PCSK9 Inhibition in Patients With Nominally Controlled LDL Cholesterol**. Journal of the American College of Cardiology 2021; 78:421-433.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34325831

***ABSTRACT***

BACKGROUND: Guidelines recommend nonstatin lipid-lowering agents in patients at very high risk for major adverse cardiovascular events (MACE) if low-density lipoprotein cholesterol (LDL-C) remains ≥70 mg/dL on maximum tolerated statin treatment. It is uncertain if this approach benefits

patients with LDL-C near 70 mg/dL. Lipoprotein(a) levels may influence residual risk. OBJECTIVES: In a post hoc analysis of the ODYSSEY Outcomes (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) trial, the authors evaluated the benefit of adding the proprotein subtilisin/kexin type 9 inhibitor alirocumab to optimized statin treatment in patients with LDL-C levels near 70 mg/dL. Effects were evaluated according to concurrent lipoprotein(a) levels. METHODS: ODYSSEY Outcomes compared alirocumab with placebo in 18,924 patients with recent acute coronary syndromes receiving optimized statin treatment. In 4,351 patients (23.0%), screening or randomization LDL-C was <70 mg/dL (median 69.4 mg/dL; interquartile range: 64.3-74.0 mg/dL); in 14,573 patients (77.0%), both determinations were ≥70 mg/dL (median 94.0 mg/dL; interquartile range: 83.2-111.0 mg/dL). RESULTS: In the lower LDL-C subgroup, MACE rates were 4.2 and 3.1 per 100 patient-years among placebo-treated patients with baseline lipoprotein(a) greater than or less than or equal to the median (13.7 mg/dL). Corresponding adjusted treatment hazard ratios were 0.68 (95% confidence interval [CI]: 0.52-0.90) and 1.11 (95% CI: 0.83-1.49), with treatment-lipoprotein(a) interaction on MACE (P(interaction) = 0.017). In the higher LDL-C subgroup, MACE rates were 4.7 and 3.8 per 100 patient-years among placebo-treated patients with lipoprotein(a) >13.7 mg/dL or ≤13.7 mg/dL; corresponding adjusted treatment hazard ratios were 0.82 (95% CI: 0.72-0.92) and 0.89 (95% CI: 0.75-1.06), with P(interaction) = 0.43. CONCLUSIONS: In patients with recent acute coronary syndromes and LDL-C near 70 mg/dL on optimized statin therapy, proprotein subtilisin/kexin type 9 inhibition provides incremental clinical benefit only when lipoprotein(a) concentration is at least mildly elevated. (ODYSSEY Outcomes: Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab; NCT01663402).

[41] *Rosenson RS, Goonewardena SN*. **The Residual Risk Odyssey: From LDL to Lp(a)**. Journal of the American College of Cardiology 2021; 78:434-436.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34325832
***ABSTRACT***

[42] *Reiff T, Eckstein HH, Mansmann U et al.* **Contralateral Stenosis and Echolucent Plaque Morphology are Associated with Elevated Stroke Risk in Patients Treated with Asymptomatic Carotid Artery Stenosis within a Controlled Clinical Trial (SPACE-2)**. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association 2021; 30:105940.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34311420
***ABSTRACT***
BACKGROUND: Asymptomatic carotid artery stenosis (ACS) has a low risk of stroke. To achieve an advantage over noninterventional best medical treatment (BMT), carotid endarterectomy (CEA) or carotid artery stenting (CAS) must be performed with the lowest possible risk of stroke. Therefore, an analysis of risk-elevating factors is essential. Grade of ipsilateral and contralateral stenosis as well as plaque morphology are known risk factors in ACS. METHODS: The randomized, controlled, multicenter SPACE-2 trial had to be stopped prematurely after recruiting 513 patients. 203 patients were randomized to CEA, 197 to CAS, and 113 to BMT. Within one year, risk factors such as grade of stenosis and plaque morphology were analyzed. RESULTS: Grade of contralateral stenosis (GCS) was higher in patients with any stroke (50%(ECST) vs. 20%(ECST); p=0.012). Echolucent plaque morphology was associated with any stroke on the day of intervention (OR 5.23; p=0.041). In the

periprocedural period, any stroke was correlated with GCS in the CEA group (70%(ECST) vs. 20%(ECST); p=0.026) and with echolucent plaque morphology in the CAS group (6% vs. 1%; p=0.048). In multivariate analysis, occlusion of the contralateral carotid artery (CCO) was associated with risk of any stroke (OR 7.00; p=0.006), without heterogeneity between CEA and CAS. CONCLUSION: In patients with asymptomatic carotid artery stenosis, GCS, CCO, as well as echolucent plaque morphology were associated with a higher risk of cerebrovascular events. The risk of stroke in the periprocedural period was increased by GCS in CEA and by echolucent plaque in CAS. Due to small sample size, results must be interpreted carefully.

[43] *Lo S, Leiter LA, Langer A et al.* **Cardiovascular risk factor management in patients with diabetes: Does management differ with disease duration?** Journal of diabetes and its complications 2021:107997.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34332851
***ABSTRACT***
AIMS: Our objective was to examine risk factor modification targets and treatment in relation to duration of diabetes. METHODS: The Diabetes Mellitus Status in Canada (DM-SCAN) study collected data on 5109 patients with type 2 diabetes mellitus (T2DM) in 2012 in primary care. We compared the prevalence of vascular complications, treatment targets, and interventions between patients with diagnosed diabetes duration ≤10 and > 10 years. RESULTS: Physicians more frequently assigned HbA1c (glycated hemoglobin) targets of 7.1-8.5% (54-69 mmol/mol) to patients with longer duration of diabetes (n = 1647) (19.8% vs 9.5%, p < 0.001). Patients with longer duration of diabetes were less likely to achieve HbA1c targets of ≤7.0% (53 mmol/mol) (39% vs. 55%, p < 0.001), had similar likelihood of achieving blood pressure targets of ≤130/80 mmHg (38% vs. 36%, p = 0.26) and were more likely to achieve LDL-C targets of ≤2.0 mmol/L (≤77.3 mg/dL) (63% vs. 53%, p < 0.001) compared to patients with shorter duration of diabetes (n = 3462). Achievement of all three targets between both groups were similar (13% vs. 13%, p = 0.82). Overall, patients with longer duration of diabetes were more likely to be prescribed anti-hyperglycemic, anti-hypertensive, lipid-lowering medications and referred for diabetes education. CONCLUSIONS: Only 13% of patients achieved glycemic, blood pressure, and LDL-C targets irrespective of duration of diabetes. Despite being managed with more medications, patients with longer duration of diabetes were less likely to achieve glycemic targets. More focus is needed on developing methods to bridge best care and real-world practice.

[44] *Liu Q, Wu H, Yu Z et al.* **APOE gene ε4 allele (388C-526C) effects on serum lipids and risk of coronary artery disease in southern Chinese Hakka population**. Journal of clinical laboratory analysis 2021; 35:e23925.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34313350
***ABSTRACT***
OBJECTIVE: To analyze the relationship of Apolipoprotein E (APOE) and solute carrier organic anion transporter family member 1B1 (SLCO1B1) gene polymorphisms with coronary artery disease (CAD). METHODS: 1,129 CAD patients and 1,014 non-CAD controls were included in the study, and relevant information and medical records were collected. The single-nucleotide polymorphisms (SNPs) were analyzed, including rs429358, rs7412 in APOE gene and rs2306283, rs4149056 in SLCO1B1 gene. RESULTS: The CAD patients' average age was 66.3 ± 10.7 years, while

65.5 ± 12.0 years in controls. The frequencies of APOE allele ε3, ε4, and ε2 were 83.01%, 10.08%, and 6.91% respectively. There were statistically significant differences in genotype ε3/ε4 ($\chi(2) = 8.077$, $p = 0.005$) in CAD patients compared with the controls. The SLCO1B1 genotype *1b/*1b and haplotype *1b showed the highest frequency in the study sample. Moreover, ε4 carriers had significantly lower HDL-C, Apo-A1 levels than ε3 carriers among CAD patients, while ε2 carriers showed lower LDL-C, Apo-B level, and higher Apo-A1/Apo-B level than ε3 and ε4 carriers. In controls, ε2 carriers showed lower LDL-C and Apo-B level, higher Apo-A1, and Apo-A1/Apo-B level than ε4 carriers. Logistic regression analysis showed that high LDL-C and Apo-B level, low HDL-C level, smoking, and the ε4 allele were risks for the presence of CAD. CONCLUSIONS: APOE ε4 allele may be associated with susceptibility to CAD in southern Chinese Hakka population. It indicated that the APOE SNPs rs429358 and rs7412 are associated with CAD, but not SNPs rs2306283 and rs4149056 of SLCO1B1 gene.

[45] *Kaya Z, Sal E, Yorulmaz A et al.* **Genetic basis and hematologic manifestations of sitosterolemia in a group of Turkish patients**. Journal of clinical lipidology 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34304999
***ABSTRACT***
BACKGROUND: Sitosterolemia is a rare lipid disorder caused by mutations in adenosine triphosphate-binding cassette genes (ABCG) 5 and 8. OBJECTIVE: To evaluate the phenotypic/genotypic features of sitosterolemia in a group of Turkish patients. METHODS: Seven probands with unexplained hematologic abnormalities and their 13 relatives were enrolled. Sterol levels were measured by gas chromatography and genetic studies were performed using Sanger sequencing. Individuals were diagnosed with sitosterolemia if they were found to have frankly elevated sitosterol level >15 μg/mL and/or pathogenic variants of the ABCG5/ABCG8. RESULTS: The seven probands and their six relatives were diagnosed with frank sitosterolemia, and all these patients had hematologic abnormalities. The remaining seven relatives were asymptomatic heterozygous carriers. Three novel variants in the ABCG5 gene (c.161G>A, c.1375C>T, IVS10-1G>T), one novel variant in the ABCG8 gene (c.1762G>C) and one known variant in the ABCG5 gene (c.1336 C>T) were identified. No variant was identified in one case. The mean sitosterol level was significantly higher and mean platelet count was significantly lower in patients with homozygous variants compared to heterozygous variants ($p<0.05$, for all). Diets low in plant sterols were recommended for 13 symptomatic cases. Four homozygotes received ezetimibe, and their splenomegaly, anemia, and thrombocytopenia completely resolved except one. CONCLUSION: The five pathogenic variants identified in this study indicate the genetic heterogeneity of sitosterolemia in Turkish population. Patients with unexplained hematologic abnormalities (specifically macrothrombocytopenia) should have their sterol level measured as initial testing. Ezetimibe can be a good choice for sitosterolemia.

[46] *Goncalves I, Sun J, Tengryd C et al.* **Plaque Vulnerability Index Predicts Cardiovascular Events: A Histological Study of an Endarterectomy Cohort**. Journal of the American Heart Association 2021; 10:e021038.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34325529
***ABSTRACT***

Background The balance between stabilizing and destabilizing atherosclerotic plaque components is used in experimental studies and in imaging studies to identify rupture prone plaques. However, we lack the evidence that this balance predicts future cardiovascular events. Here we explore whether a calculated histological ratio, referred to as vulnerability index (VI), can predict patients at higher risk to suffer from future cardiovascular events. Methods and Results Carotid plaques and clinical information from 194 patients were studied. Tissue sections were used for histological analysis to calculate the VI (CD68 [cluster of differentiation 68], alpha-actin, Oil red O, Movat pentachrome, and glycophorin A). Postoperative cardiovascular events were identified through the Swedish National Inpatient Health Register (2005-2013). During the follow-up (60 months) 45 postoperative cardiovascular events were registered. Patients with a plaque VI in the fourth quartile compared with the first to third quartiles had significantly higher risk to suffer from a future cardiovascular event (P=0.0002). The VI was an independent predictor and none of the 5 histological variables analyzed separately predicted events. In the 13 patients who underwent bilateral carotid endarterectomy, the VI of the right plaque correlated with the VI of the left plaque and vice versa (r=0.7, P=0.01). Conclusions Our findings demonstrate that subjects with a high plaque VI have an increased risk of future cardiovascular events, independently of symptoms and other known cardiovascular risk factors . This strongly supports that techniques which image such plaques can facilitate risk stratification for subjects in need of more intense treatment.

[47] *Derenbecker R, Kapoor K, Brown E et al.* **Novel Presentation of Homozygous Familial Hypercholesterolemia With Homozygous Variants in Both LDLR and APOB Genes**. JACC Case Rep 2019; 1:346-349.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34316823
***ABSTRACT***
This case report describes a 50-year-old-woman from Southeast Asia with extensive atherosclerotic cardiovascular disease, found to have homozygous familial hypercholesterolemia caused by variants of uncertain significance in both the APOB and LDLR genes. Medications were insufficient, and thus LDL apheresis was initiated to further decrease LDL-C. (Level of Difficulty: Beginner.).

[48] *Warden BA, Kaufman T, Minnier J et al.* **Use of PCSK9 Inhibitors in Solid Organ Transplantation Recipients**. JACC Case Rep 2020; 2:396-399.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34317250
***ABSTRACT***
Standard lipid-lowering therapies in solid organ transplantations pose challenges due to interactions with immunosuppressants. Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) represent a new class of lipid-lowering therapies with potential promise in this population. We describe PCSK9i as an efficacious and safe option for management of hypercholesterolemia in solid organ transplantations. (Level of Difficulty: Advanced.).

[49] *Susekov AV*. **[Omega-3 Polyunsaturated Fatty Acids in Patients with Hypertriglyceridemias and Atherosclerosis]**. Kardiologiia 2021; 61:88-96.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34311692
***ABSTRACT***

Along with increased levels of low-density cholesterol, lipid factors of the risk of cardiovascular complications (CVC) include hypertriglyceridemia, particularly increased plasma levels of remnant particles. Omega-3 polyunsaturated fatty acids (ω-3 PUFA) are essential for normal functioning of cell membranes, retina, nerve tissue, skeletal muscles, etc. Among the large family of fatty acids (FA), eicosapentaenoic (EPC) and docosahexaenoic (DHX) FA are most studied. The beneficial effect of ω-3 PUFA consumption on the cardiovascular system is related with improvement of blood rheology, antiarrhythmic and anti-inflammatory effects, and a decrease in triglycerides. Large randomized studies of ω-3 PUFA (mixed EPC and DHX or only EPC) have demonstrated their efficiency and safety and a capability for reducing the incidence of CVC and sudden death as well as improvement of the prognosis in various patient populations. In the STRENGTH study (combination of omega-3 and statins), no significant decrease in the risk of CVC was achieved in patients with high triglycerides and low high-density lipoproteins. The ω-3 PUFA treatment is regulated by current international Guidelines and Consensuses as a part of combination therapy with statins for reduction of the risk of CVC and correction of pronounced hypertriglyceridemia.

[50] *Pickett JK, Shah M, Gillette M et al.* **Acute Tubular Injury in a Patient on a Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor**. JACC Case Rep 2020; 2:1042-1045.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34317411

***ABSTRACT***

A 72-year-old man with coronary artery disease, statin intolerance, and chronic kidney disease stage IIIa was initiated on alirocumab, a proprotein convertase subtilisin/kexin type 9 inhibitor, and developed acute kidney injury. A kidney biopsy was performed and suggested acute tubular injury. The serum creatinine returned to baseline after discontinuation of alirocumab. (Level of Difficulty: Intermediate.).

[51] *Orlova NV, Gololobova TV, Suranova TG et al.* **[Analysis of the development of acute coronary syndrome during the COVID-19 pandemic]**. Probl Sotsialnoi Gig Zdravookhranenniiai Istor Med 2021; 29:603-606.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34327930

***ABSTRACT***

The study compares two groups of patients with acute coronary syndrome, depending on the presence of COVID-19 in the anamnesis. The comparison groups analyzed the risk factors for cardiovascular diseases, including smoking, heredity, gender differences, age, diabetes, and obesity. The results of biochemical blood tests were analyzed. It was found that patients with acute coronary syndrome who underwent COVID-19 were less likely to have risk factors for cardiovascular diseases. Patients with acute coronary syndrome who underwent COVID-19 were found to have lower blood glucose, cholesterol, very-low-density lipoprotein, and triglycerides. As a result of the study, it was revealed that COVID-19 is an independent risk factor for the development of acute coronary syndrome.

[52] *Laird J, Falk RH, Coyle M, Cuddy SAM*. **Rhabdomyolysis in the Setting of Concomitant Use of Tafamidis, Atorvastatin, and Amiodarone**. JACC Case Rep 2020; 2:2372-2375.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34317174

***ABSTRACT***

An 85-year-old women with transthyretin cardiac amyloidosis presented with generalized weakness, elevated liver function test levels, and creatinine kinase consistent with rhabdomyolysis 1 week after starting tafamidis. She was already taking atorvastatin and amiodarone, raising the possibility of a drug-drug interaction inhibiting the breakdown and excretion of atorvastatin, causing drug-induced rhabdomyolysis. (Level of Difficulty: Intermediate.).

[53] *La Sala L, Pontiroli AE*. **Coffee, LDL-cholesterol and cardiovascular risk**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2021; 31:2735-2736.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34332863
***ABSTRACT***

[54] *Kolovou G, Tsoutsinos A, Mastorakou I et al.* **Xanthomas Regression in an 8-Year-Old Boy Treated With Lomitapide**. JACC Case Rep 2019; 1:414-416.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34316840
***ABSTRACT***
This case reports on an 8-year-old boy with homozygous familial hypercholesterolemia with large tuberous xanthomas over his hands, elbows, buttocks, knees, and feet. Lomitapide 40 mg daily (steadily increased) was added to his classical lipid-lowering therapy. A 50% reduction in the thickness, hardness, size, and color intensity of xanthomas was reported after 2 years of treatment. (Level of Difficulty: Intermediate.).

[55] *Genkel VV, Kuznetsova AS, Lebedev EV, Shaposhnik, II*. **Factors associated with atherosclerotic plaque echogenicity in patients aged 40-64 with carotid atherosclerosis**. Kardiologiia 2021; 61:35-40.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34311686
***ABSTRACT***
Aim To identify clinical and laboratory indexes related with the atherosclerotic plaque (ASP) echogenicity based on results of the analysis of grey-scale median (GSM) in patients aged 40-64 years.Material and methods The study included patients aged 40-64 years with carotid atherosclerosis. The carotid duplex scanning was performed for all patients. The GSM analysis of obtained images was performed with the Adobe Photoshop CS6 software.Results Atherosclerotic cardiovascular diseases were found in 31 (21.4%) patients. Correlation analysis determined inverse interrelationships between GSM and the body weight index (BWI) (r=-0.359; p<0.0001), waist circumference (r=-0.357; p<0.0001), and levels of uric acid (r=-0.244; p=0.021) and glucose (r=-0.205; p=0.032). According to the regression, statistically significant correlations remained between GSM and BWI as well as the waist circumference after the adjustment for sex and age.Conclusion In patients with carotid atherosclerosis aged 40-64 years, the decrease in ASP GSM was associated with increases in BWI and waist circumference.

[56] *Fu Q, Hu L, Xu Y et al.* **High lipoprotein(a) concentrations are associated with lower type 2 diabetes risk in the Chinese Han population: a large retrospective cohort study**. Lipids in health and disease 2021; 20:76.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34315495
***ABSTRACT***

BACKGROUND: Lipoprotein (a) [Lp(a)] is a proven independent risk factor for coronary heart disease. It is also associated with type 2 diabetes mellitus (T2DM). However, the correlation between Lp(a) and T2DM has not been clearly elucidated. METHODS: This was a retrospective cohort study involving 9248 T2DM patients and 18,496 control individuals (1:2 matched). Patients were randomly selected from among inpatients in the Second Affiliated Hospital of Nanchang University between 2006 and 2017. Clinical characteristics were compared between the two groups. Spearman rank-order correlation coefficients were used to evaluate the strength and direction of monotonic associations of serum Lp(a) with other metabolic risk factors. Binary logistic regression analysis was used to establish the correlation between Lp(a) levels and T2DM risk. RESULTS: The median Lp(a) concentration was lower in T2DM patients than in controls (16.42 vs. 16.88 mg/dL). Based on four quartiles of Lp(a) levels, there was a decrease in T2DM risk from 33.7% (Q1) to 31.96% (Q4) (P for trend <0.0001). Then, Lp(a) levels >28.72 mg/dL (Q4) were associated with a significantly lower T2DM risk in the unadjusted model [0.924 (0.861, 0.992), P = 0.030]. Similar results were obtained in adjusted models 1 [Q4, 0.925 (0.862, 0.993), P = 0.031] and 2 [Q4, 0.919 (0.854, 0.990), P = 0.026]. Furthermore, in the stratified analysis, Q4 of Lp(a) was associated with a significantly lower T2DM risk among men [0.813 (0.734, 0.900), P < 0.001] and those age > 60 years [0.819 (0.737, 0.910), P < 0.001]. In contrast, the low-density lipoprotein cholesterol (LDL-C) levels and coronary heart disease (CHD) did not impact these correlations between Lp(a) and diabetes. CONCLUSIONS: There is an inverse association between Lp(a) levels and T2DM risk in the Chinese population. Male patients, especially those aged more than 60 years with Lp(a) > 28.72 mg/dL, are low-risk T2DM individuals, regardless of LDL-C levels and CHD status.

[57] *Bjornstad P, Drews KL, Caprio S et al.* **Long-Term Complications in Youth-Onset Type 2 Diabetes**. The New England journal of medicine 2021; 385:416-426.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34320286

***ABSTRACT***

BACKGROUND: The prevalence of type 2 diabetes in youth is increasing, but little is known regarding the occurrence of related complications as these youths transition to adulthood. METHODS: We previously conducted a multicenter clinical trial (from 2004 to 2011) to evaluate the effects of one of three treatments (metformin, metformin plus rosiglitazone, or metformin plus an intensive lifestyle intervention) on the time to loss of glycemic control in participants who had onset of type 2 diabetes in youth. After completion of the trial, participants were transitioned to metformin with or without insulin and were enrolled in an observational follow-up study (performed from 2011 to 2020), which was conducted in two phases; the results of this follow-up study are reported here. Assessments for diabetic kidney disease, hypertension, dyslipidemia, and nerve disease were performed annually, and assessments for retinal disease were performed twice. Complications related to diabetes identified outside the study were confirmed and adjudicated. RESULTS: At the end of the second phase of the follow-up study (January 2020), the mean (±SD) age of the 500 participants who were included in the analyses was 26.4±2.8 years, and the mean time since the diagnosis of diabetes was 13.3±1.8 years. The cumulative incidence of hypertension was 67.5%, the incidence of dyslipidemia was 51.6%, the incidence of diabetic kidney disease was 54.8%, and the incidence of nerve disease was 32.4%. The prevalence of retinal disease, including more advanced stages, was 13.7% in the period from 2010 to 2011 and 51.0% in the period from 2017 to 2018. At least one complication occurred in 60.1% of the participants, and at least two complications occurred

in 28.4%. Risk factors for the development of complications included minority race or ethnic group, hyperglycemia, hypertension, and dyslipidemia. No adverse events were recorded during follow-up. CONCLUSIONS: Among participants who had onset of type 2 diabetes in youth, the risk of complications, including microvascular complications, increased steadily over time and affected most participants by the time of young adulthood. Complications were more common among participants of minority race and ethnic group and among those with hyperglycemia, hypertension, and dyslipidemia. (Funded by the National Institute of Diabetes and Digestive and Kidney Diseases and others; ClinicalTrials.gov numbers, NCT01364350 and NCT02310724.).

[58] *Zhang Y, Zhang Q, Thomas R et al.* **Association of Hypertriglyceridemia and Incident Glaucoma in a Rural Chinese Population: The Handan Eye Study**. Transl Vis Sci Technol 2021; 10:25.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34319388
***ABSTRACT***
PURPOSE: The purpose of this paper was to investigate the association between baseline metabolic risk factors and incident glaucoma over a 5-year period in rural Chinese adults. METHODS: Population-based prospective cohort study. Participants aged 30 years and older without glaucoma at baseline who underwent comprehensive examinations at baseline and after a 5-year interval in the Handan Eye Study were enrolled. Incident glaucoma was defined as people without glaucoma in either eye at baseline that had developed glaucoma in at least one eye in the 5-year follow-up. Five metabolic syndrome components, mean blood pressure, fasting plasma glucose, total cholesterol, triglycerides (TGs), low density lipoprotein cholesterol, high-density lipoprotein cholesterol, and obesity, determined as body mass index ≥30 kg/m2 at baseline were considered as potential metabolic risk factors for incident glaucoma. Univariate and multivariate logistic regression analyses were carried out to determine baseline metabolic risk factors associated with incident glaucoma. RESULTS: A total of 5184 participants were included in our study. During the 5-year follow-up, incident glaucoma developed in 82 subjects. Age (odds ratio [OR] = 1.060, 95% confidence interval [CI] = 1.034, 1.086, $P < 0.001$) and TGs level (OR = 1.213, 95% CI = 1.030, 1.429, $P = 0.021$) were independently and positively associated with incident glaucoma. CONCLUSIONS: Our study revealed that increased age and high TGs level, one of the baseline metabolic features, were independent risk factors for incident glaucoma. The data implied that the metabolic features be involved in the pathogenesis of glaucoma. TRANSLATIONAL RELEVANCE: This study shed the light on that the TGs level was involved in the pathogenesis of glaucoma.

[59] *Yang R, Wang L, Cao S et al.* **Sex difference in lipid levels in first-diagnosed drug-naïve depression patients: A case-control and 12-weeks follow-up study**. World J Biol Psychiatry 2021:1-9.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34320901
***ABSTRACT***
AIM: Patients with depression have a high prevalence of developing dyslipidemia. In this study, we aim to investigate the difference of serum lipids, including total cholesterol (TCH), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), between the depressed patients and healthy controls. Sex differences in lipids and their psychological correlations were also included. METHODS: The study included 56 healthy controls (males/females =

26/30) and 110 first-diagnosed drug-naïve outpatients (males/females = 35/75). A total of 42 patients (males/females = 14/28) were followed for 3 months. RESULTS: A significant difference was found in TCH and LDL-C among healthy control and patients. Interestingly, female patients with first-diagnosed, drug-naïve depression had lower atherogenic indices than male patients. After 3 months of antidepressants therapy, female patients exhibited detrimental changes in serum lipids, namely increased TG and atherogenic index. Moreover, correlation analysis showed significant correlations between changes of depression inventory (HAMD and BDI) score and serum lipids (TCH, HDL-C) in depressed patients. CONCLUSION: We found that dyslipidemia was more common in female patients with depression during therapy with antidepressants. Moreover, the altered serum lipids and atherogenic index might be a hallmark of female patients. Further investigation of sex differences in lipid metabolism of depression is warranted.

[60] *Thompson GR*. **The scientific basis and future of lipoprotein apheresis**. Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34331508
***ABSTRACT***
Lipoprotein apheresis plays a vital role in the management of the severe hyperlipidemias that predispose to atherosclerosis. Determinants of efficacy are the acute reduction in lipoproteins achieved by each apheresis procedure, their frequency, and the fractional catabolic rates and hence pool sizes of low-density lipoprotein (LDL) or lipoprotein (a) (Lp(a)) of the patient being treated. A useful criterion of the efficacy of apheresis plus lipid-lowering drug therapy is the decrease in the interval (time-averaged) mean of serum total or LDL cholesterol or Lp(a) between procedures, expressed as the percent decrease in the interval means below the maximal levels of these lipoproteins when off all treatment. Recent advances in lipid-lowering drug therapy may diminish the use of lipoprotein apheresis but will not abolish its unique role as a therapeutic "last chance saloon," especially for children and pregnant women with homozygous familial hypercholesterolemia.

[61] *Steinmeyer J, Flechtenmacher J*. **Drug-induced Myopathies**. Z Orthop Unfall 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34320661
***ABSTRACT***
Differential diagnosis of muscle pain and weakness is extensive, including neurological, vertebral, arthrogenic, vascular, traumatic, immunological, endocrine, genetic and infectious aetiologies, as well as medication or toxin-related causes. Muscles are highly sensitive to a large number of drugs, especially with high doses. Although many drug classes can cause toxic myopathy, a significant number of cases are caused by lipid-lowering drugs, long-term use of corticosteroids, and, most often, alcohol misuse. Some drug interactions, e.g. those that are metabolised via the enzyme CYP3A4, can increase the serum levels of the drugs and drug-induced toxicity. A careful history of patient's drug and alcohol consumption is therefore vital. Clinical symptoms depend on the drug, dosage and patient's sensitivity. They can vary from asymptomatic increase in serum levels of creatine kinase, mild myalgia and cramps to muscle weakness, rhabdomyolysis, kidney failure and even death. The pathogenesis is often only partially known and multifactorial. Toxic myopathy is often reversible once the drug is discontinued, alternative drug therapy is started or a different dosage

regimen is chosen. Complications such as acute kidney failure must be avoided, and analgesic therapy may be indicated.

[62] *Nativel B, Ramin-Mangata S, Couret D et al.* **PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) Inhibition in Hyperglycemic Mice Increases the Risk of Hemorrhagic Transformation of Ischemic Stroke**. Stroke 2021; 52:e545-e547.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34315254
***ABSTRACT***
[Figure: see text].

[63] *Liu Y, Pan Y, Yin Y et al.* **Association of dyslipidemia with the severity and mortality of coronavirus disease 2019 (COVID-19): a meta-analysis**. Virol J 2021; 18:157.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34315474
***ABSTRACT***
BACKGROUND: The numbers of confirmed cases of coronavirus disease 2019 (COVID-19) and COVID-19 related deaths are still increasing, so it is very important to determine the risk factors of COVID-19. Dyslipidemia is a common complication in patients with COVID-19, but the association of dyslipidemia with the severity and mortality of COVID-19 is still unclear. The aim of this study is to analyze the potential association of dyslipidemia with the severity and mortality of COVID-19. METHODS: We searched the PubMed, Embase, MEDLINE, and Cochrane Library databases for all relevant studies up to August 24, 2020. All the articles published were retrieved without language restriction. All analysis was performed using Stata 13.1 software and Mantel-Haenszel formula with fixed effects models was used to compare the differences between studies. The Newcastle Ottawa scale was used to assess the quality of the included studies. RESULTS: Twenty-eight studies involving 12,995 COVID-19 patients were included in the meta-analysis, which was consisted of 26 cohort studies and 2 case-control studies. Dyslipidemia was associated with the severity of COVID-19 (odds ratio [OR] = 1.27, 95% confidence interval [CI] 1.11-1.44, P = 0.038, I(2) = 39.8%). Further, patients with dyslipidemia had a 2.13-fold increased risk of death compared to patients without dyslipidemia (95% CI 1.84-2.47, P = 0.001, I(2) = 66.4%). CONCLUSIONS: The results proved that dyslipidemia is associated with increased severity and mortality of COVID-19. Therefore, we should monitor blood lipids and administer active treatments in COVID-19 patients with dyslipidemia to reduce the severity and mortality.

[64] *Chahine J, Kreykes S, Van't Hof JR et al.* **Variable and Severe Phenotypic Expression of the "Lebanese Allele" in Two Sisters with Familial Hypercholesterolemia**. Vascular health and risk management 2021; 17:415-419.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=34321884
***ABSTRACT***
The "Lebanese allele" {LDLR c.2043 C>A (p.cys681X)} is a nonsense mutation in the low-density lipoprotein receptor (LDLR) gene that results in a truncated non-functioning LDLR protein. We report two sisters of Lebanese descent who presented with familial hypercholesterolemia (FH) and were both heterozygous for the Lebanese allele, but had very distinct LDL-C levels and clinical phenotypes. Whereas one of the sisters had LDL-C in the expected range of Heterozygous FH (HeFH) with the Lebanese allele (LDL-C of 292 mg/dl), the other sister had a more severe LDL-C

phenotype in the Homozygous FH (HoFH) range (LDL-C of 520 mg/dl) along with manifest atherosclerosis. Surprisingly, she did not demonstrate a compound heterozygote or double heterozygote status. We discuss different mechanisms that are purported to play a role in modifying the phenotype of FH, including different variants and polygenic modifiers. HeFH patients with the Lebanese allele can have a wide spectrum of LDL-C levels that range from the typical heterozygous to homozygous phenotypes.