[1] *Leuti A, Fazio D, Fava M et al.* **Bioactive lipids, inflammation and chronic diseases**. Adv Drug Deliv Rev 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32628989
ABSTRACT
Endogenous bioactive lipids are part of a complex network that modulates a plethora of cellular and molecular processes involved in health and disease, of which inflammation represents one of the most prominent examples. Inflammation serves as a well-conserved defence mechanism, triggered in the event of chemical, mechanical or microbial damage, that is meant to eradicate the source of damage and restore tissue function. However, excessive inflammatory signals, or impairment of pro-resolving/anti-inflammatory pathways leads to chronic inflammation, which is a hallmark of chronic pathologies. All main classes of endogenous bioactive lipids - namely eicosanoids, specialized pro-resolving lipid mediators, lysoglycerophopsholipids and endocannabinoids - have been consistently involved in the chronic inflammation that characterises pathologies such as cancer, diabetes, atherosclerosis, asthma, as well as autoimmune and neurodegenerative disorders and inflammatory bowel diseases. This review gathers the current knowledge concerning the involvement of endogenous bioactive lipids in the pathogenic processes of chronic inflammatory pathologies.

[2] *Hilleman DE, Wiggins BS, Bottorff MB*. **A Response to: Letter to the Editor Regarding "Critical Differences Between Dietary Supplement and Prescription Omega-3 Fatty Acids: a Narrative Review"**. Adv Ther 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32647913
ABSTRACT

[3] *Volis I, Saliba W, Jaffe R et al.* **Effect of Cerebrovascular and/or Peripheral Artery Disease With or Without Attainment of Lipid Goals on Long-Term Outcomes in Patients With Coronary Artery Disease**. The American journal of cardiology 2020; 128:28-34.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32650921
ABSTRACT
Involvement of atherosclerosis in extracardiac vascular territories may identify coronary artery disease (CAD) patients at higher risk for adverse events. We investigated the long-term prognostic implications of polyvascular disease in patients with CAD, and further analyzed lipid goal attainment and its relation to patient outcomes. The study was a retrospective analysis of 10,297 patients who underwent coronary revascularization, categorized as having CAD alone (83.1%) or with multisite artery disease (MSAD) (16.9%) including cerebrovascular disease (CBVD) and/or peripheral artery disease (PAD). Incidence rates and hazard ratios (HR) for major adverse cardiovascular events (MACE) (myocardial infarction, ischemic stroke, or all-cause death) according to vascular territories involved, and in relation to most-recent lipid levels attained, were analyzed. Patients with MSAD were older with higher burden of co-morbidities. The rate of MACE (myocardial infarction, ischemic stroke, or all-cause death) and its individual components increased with the number of affected vascular beds. Adjusted HR (95% confidence interval) for MACE was 1.41 (1.24 to 1.59) in patients with CAD and CBVD, 1.46 (1.33 to 1.62) in CAD and PAD, and 1.69 (1.49 to 1.92) in those with CAD and CBVD and PAD, compared with CAD alone. Most-recent low-density lipoprotein cholesterol (LDL-C) levels <55 mg/dl and <70 mg/dl were attained by 21.8% and 44.6% of patients with CAD alone, in comparison to 22.7% and 43.3% in MSAD. Compared with patients with most-recent

LDL-C > 100 mg/dl, attaining LDL-C < 70 mg/dl had an adjusted HR for MACE of 0.52 (0.47 to 0.57) in CAD only patients and 0.66 (0.57 to 0.78) in MSAD patients. In conclusion, the presence of CBVD and/or PAD in patients with CAD is associated with higher burden of co-morbidities and progressive increase in long-term MACE. More than half of CAD patients with or without MSAD do not achieve lipid goals, which are associated with a significantly lower risk for adverse events.

[4] *Ye Q, Svatikova A, Meeusen JW et al.* **Effect of Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors on Plasma Ceramide Levels**. The American journal of cardiology 2020; 128:163-167.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32650914
ABSTRACT
Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are novel drugs that provide striking lowering of low-density lipoprotein cholesterol (LDL-C) when added to maximum tolerated therapy in patients with hypercholesterolemia. Ceramides, novel cardiac risk markers, have been associated with increased cardiovascular mortality, independent of traditional cardiovascular risk factors. The Ceramide Risk Score (CRS) predicts the likelihood of adverse cardiovascular events within 1 to 3 years in patients with coronary artery disease. The effect of PCSK9 inhibition on plasma ceramides is not well known. The study examines the effect of PCSK9 inhibitors on plasma ceramides and CRS in patients with clinical indication for this therapy. Retrospective chart review of consecutive patients with hypercholesterolemia on PCSK9 inhibitors was conducted (n = 24; Mayo Clinic 2015 to 2018). Plasma ceramides were measured before the initiation of PCSK9 inhibitors and 2 to 12 months after treatment. CRS was calculated before and after therapy based on individual plasma concentrations of 4 ceramides. Treatment with PCSK9 inhibitors was associated with significant reduction in mean CRS and individual ceramides levels ($p < 0.0001$). CRS significantly improved with PCSK9 therapy. PCSK9 inhibitors significantly decreased LDL-C levels by 63% ($p < 0.0001$). The absolute reduction in CRS did not correlate with the absolute reduction in LDL-C ($r = 0.31$; confidence interval -0.10 to 0.64), indicating that CRS may evaluate a different pathway for risk reduction beyond LDL-C lowering. In conclusion, treatment with PCSK9 inhibitors is associated with significant reduction in CRS and distinct ceramide levels.

[5] *Lamb YN*. **Rosuvastatin/Ezetimibe: A Review in Hypercholesterolemia**. American journal of cardiovascular drugs : drugs, devices, and other interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32648167
ABSTRACT
Rosuvastatin/ezetimibe combines two lipid-lowering agents: rosuvastatin, an HMG-CoA reductase inhibitor (i.e. statin) with particularly strong inhibitory effects on hepatic cholesterol synthesis, and ezetimibe, which inhibits the intestinal absorption of cholesterol. A fixed-dose combination (FDC) of rosuvastatin/ezetimibe is indicated as an adjunctive therapy to diet for the management of primary hypercholesterolemia in adults in numerous countries worldwide. In well-designed clinical trials evaluating the therapeutic efficacy of rosuvastatin/ezetimibe administered as either separate agents or as an FDC, rosuvastatin/ezetimibe was significantly more effective than rosuvastatin monotherapy (including at double the dose of rosuvastatin) or simvastatin/ezetimibe in reducing low-density lipoprotein cholesterol (LDL-C) and total cholesterol in adults with hypercholesterolemia. Furthermore, rosuvastatin/ezetimibe enabled

significantly higher proportions of patients to achieve recommended LDL-C levels than rosuvastatin monotherapy or simvastatin/ezetimibe. Rosuvastatin/ezetimibe did not significantly differ from rosuvastatin monotherapy with respect to incidences of treatment-related or serious adverse events in these short-term trials and displayed a similar safety profile to simvastatin/ezetimibe. While additional cardiovascular outcomes data and head-to-head comparisons with atorvastatin/ezetimibe would be of interest, rosuvastatin/ezetimibe is a potent and generally well-tolerated drug combination that extends the range of options available for the pharmacological management of primary hypercholesterolemia in adults.

[6] *Danial JSH, Murad F, Saez AG et al.* **Computed Histological Quantification of Atherosclerotic Plaque Microcalcifications**. Angiology 2020:3319720939466.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32633543
ABSTRACT
Inflammation has a central role in atherosclerotic plaque formation and rupture. Intense macrophage inflammatory activity results in microcalcifications which are strongly associated with plaque vulnerability. Microcalcifications with specific critical size between 5 and 65 μ, located in the fibrous cap producing local mechanical stress on the plaque surface and may directly contribute to plaque rupture. Hence, accurate assessment of microcalcifications size and dimension has significant clinical importance. Current invasive and noninvasive plaque imaging has limited spatial resolution which limits accurate definition of microcalcifications in the atherosclerotic plaques. We describe a new imaging technique with high spatial resolution, based on confocal microscopic analysis, using a dedicated software which allows automatic characterization of microcalcifications and quantitative assessment of their extent and localization.

[7] *Xu Q, Li H, Zhou W et al.* **Age-Related Changes in Serum Lipid Levels, Hepatic Morphology, Antioxidant Status, Lipid Metabolism Related Gene Expression and Enzyme Activities of Domestic Pigeon Squabs (Columba livia)**. Animals (Basel) 2020; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32630261
ABSTRACT
The objective of this study was to evaluate the age-related changes in antioxidant status and the lipid metabolism of pigeon squabs (Columba livia), by determining the BW, antioxidant indices, serum lipid levels, lipid metabolism-related enzyme activities, lipid metabolism-related gene expression, and liver morphology in squabs. Ten squabs were randomly selected and sampled on the day of hatching (DOH), days 7 (D7), 14 (D14) and 21 (D21) post-hatch, respectively. The results showed that BW of squabs increased linearly from DOH to D21. The minimum fold of BW gain was observed in the phase from D14 to D21. Serum triglyceride and free fatty acid levels displayed linear and quadratic trends as age increased, with these maximum responses in D14. Serum low-density lipoprotein cholesterol level responded to age linearly and quadratically with the minimum in D14. Serum high-density lipoprotein cholesterol level and the ratio of high-density lipoprotein cholesterol to low-density lipoprotein cholesterol increased linearly with age, whereas the very low-density lipoprotein cholesterol level decreased linearly. The activities of glutathione peroxidase, catalase, and superoxide dismutase in liver displayed linear and quadratic trends as age increased, with these minimum responses in D14. Hepatic malondialdehyde concentration responded to age linearly and quadratically, with the maximum in D14. Activities of lipoprotein lipase, hepatic lipase, and 3-

hydroxy-3-methyl glutaryl coenzyme A reductase in liver responded to age linearly and quadratically, with these minimum responses in D14. Hepatic hormone-sensitive lipase activity displayed linear and quadratic trends as age increased with the maximum in D14. Hepatic acetyl CoA carboxylase activity on D14 was significantly lower than squabs on DOH and D7. Hepatic carnitine palmitoyltransferase 1 mRNA expression responded to age linearly and quadratically, with minimum response in D14. Hepatic mRNA expression of acetyl CoA carboxylase and fatty acid synthetase increased linearly with age. Hepatic Oil-Red-O staining area displayed a quadratic trend as age increased, with the maximum response in D14. In conclusion, the phase from DOH to D14 was a crucial development stage for growth, antioxidant status and lipid metabolism in pigeon squabs. The results suggest it is better to take nutritional manipulation in squabs before D14.

[8] *Choi HS, Kim CS, Ma SK et al.* **Treatment of hyperlipidemia with proprotein convertase subtilisin/kexin type 9 inhibitor in a patient with nephrotic syndrome: a case report**. Ann Palliat Med 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32648458
ABSTRACT
We report the case of a patient with nephrotic syndrome and toxic epidermal necrolysis (TEN) caused by statin use. The associated hyperlipidemia was controlled using proprotein convertase subtilisin/ kexin type 9 (PCSK9) inhibitors. This is a unique case of treating hyperlipidemia with PCSK9 inhibitor in patient with nephrotic syndrome with TEN. A 54-year-old woman was admitted owing to generalized edema. She had massive proteinuria and was diagnosed with minimal change disease through kidney biopsy. Statins were used for treatment of hyperlipidemia associated with nephrotic syndrome; however, she developed a skin rash, which progressed to TEN. After discontinuation of statins, her skin symptoms improved; however, hyperlipidemia persisted. Because statins could not be administered, we injected evolocumab, a PCSK9 inhibitor, every 2 weeks. Since then, hyperlipidemia has been well controlled without any side effects. Thus, PCSK9 inhibitors may be a good alternative to control hyperlipidemia in patients with statin intolerance or serious side effects.

[9] *Bulut M, Nisli K, Dindar A*. **The effect of DALI lipid apheresis in the prognosis of homozygous familial hypercholesterolemia: Seven patients' experience at a DALI apheresis center**. Annals of pediatric cardiology 2020; 13:111-116.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641881
ABSTRACT
INTRODUCTION: Familial hypercholesterolemia (FH) is characterized by severe hypercholesterolemia that can result in coronary artery disease occurring at an early age. If patients are not cured with lipid-lowering drugs and diets, lipid apheresis may be an effective treatment option in these cases. Here, we evaluate the efficacy, selectivity and safety of the DALI apheresis technique. MATERIALS AND METHODS: Seven pediatric patients (2 girls; 5 boys) with ages between 7 and 14 years (mean age: 6.5±2.1 years) with HFH were included in this study. We restrospectively evaluated clinical and laboratory findings. We used the DALI system for lipid apheresis concomitant with medical treatment and diet for hyperlipidemia. RESULTS: The cohort's mean T.cholesterol level prior to apheresis was 700.57±136.36 mg/dl,the mean LDL-C value was 526.86±131.56 mg and the mean HDL-C level was 36.57±4.58 mg/dl.The mean cholesterol levels after apheresis were consecutively

317.57±93.70 /257.29±90.38 / 33.36±4.78 mg/dl.We noted a 51.1% reduction in LDL-C level and an 8.7% reduction in HDL-C level in our apheresis sessions.The reduction in LDL-C was statistically significant (p<0.05). During 1025 apheresis therapy, the most frequent mild and moderate adverse events were deviceaccess problems and hypotension (in all patients);severe adverse events were mainly due to cardiac problems(myocardial infarct and arrhythmia) and hypotension. CONCLUSION: Lipid apheresis is an inevitable alternative treatment for HFH. Despite all of its application problems, DALI system is an effective therapy for decreasing atherogenic lipids from circulation.

[10] *Gianazza E, Brioschi M, Martinez Fernandez A et al.* **LIPID PEROXIDATION IN ATHEROSCLEROTIC CARDIOVASCULAR DISEASES**. Antioxidants & redox signaling 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32640910
ABSTRACT
SIGNIFICANCE: Atherosclerotic cardiovascular diseases (ACVDs) continue to be a primary cause of mortality worldwide in adults aged 35-70 years, occurring more often in countries with lower economic development, and is an ever-growing global burden that has a considerable socio-economic impact on society. ACVDs encompass diverse pathologies such as coronary artery disease and heart failure among others. Recent Advances: It is known that oxidative stress plays a relevant role in ACVDs and some of its effects are mediated by lipid oxidation. In particular, lipid peroxidation is a process under which oxidants such as reactive oxygen species attack unsaturated lipids generating a wide array of oxidation products. These molecules can interact with circulating lipoproteins, to diffuse inside the cell and even to cross biological membranes, modifying target nucleophilic sites within biomolecules such as DNA, lipids and proteins, and resulting in a plethora of biological effects. CRITICAL ISSUES: This review summarizes the evidence of the effect of lipid peroxidation in the development and progression of atherosclerosis-based diseases, heart failure and other CVDs, highlighting the role of protein adduct formation. Moreover, potential therapeutic strategies targeted on lipoxidation in ACVDs are also discussed. FUTURE DIRECTIONS: The identification of valid biomarkers for the detection of lipoxidation products and adducts may provide insights into the improvement of the cardiovascular risk stratification of patients and the development of therapeutic strategies against the oxidative effects which can then be applied within a clinical setting.

[11] *Zelber-Sagi S, Ivancovsky-Wajcman D, Fliss-Isakov N et al.* **Serum Malondialdehyde is Associated with Non-Alcoholic Fatty Liver and Related Liver Damage Differentially in Men and Women**. Antioxidants (Basel, Switzerland) 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32630732
ABSTRACT
BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) and steatohepatitis (NASH) are associated with increased oxidative stress and lipid peroxidation, but large studies are lacking. The aim was to test the association of malondialdehyde (MDA), as a marker of oxidative damage of lipids, with NAFLD and liver damage markers, and to test the association between dietary vitamins E and C intake and MDA levels. METHODS: A cross-sectional study was carried out among subjects who underwent blood tests including FibroMax for non-invasive assessment of NASH and fibrosis. MDA was evaluated by reaction with Thiobarbituric acid and HPLC-fluorescence detection method. NAFLD was diagnosed by abdominal ultrasound.

FINDINGS: MDA measurements were available for 394 subjects. In multivariate analysis, the odds for NAFLD were higher with the rise of MDA levels in a dose-response manner, adjusting for age, gender, BMI, and lifestyle factors. Only among men, higher serum MDA was associated of higher odds for NAFLD and NASH and/or fibrosis (OR = 2.59, 95% CI 1.33-5.07, P = 0.005; OR = 2.04, 1.02-4.06, P = 0.043, respectively). Higher vitamin E intake was associated with lower odds of high serum MDA level (OR = 0.28 95% CI 0.13-0.62, P = 0.002). In conclusion, serum MDA is associated with NAFLD and markers of NASH or fibrosis among men. Dietary vitamin E may be protective among women.

[12] *Ozalp L, Danış Ö, Yuce-Dursun B et al.* **Investigation of HMG-CoA reductase inhibitory and antioxidant effects of various hydroxycoumarin derivatives**. Arch Pharm (Weinheim) 2020:e1900378.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32648617
ABSTRACT
Cardiovascular diseases are one of the primary causes of deaths worldwide, and the development of atherosclerosis is closely related to hypercholesterolemia. As the reduction of the low-density lipoprotein cholesterol level is critical for treating these diseases, the inhibition of 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase, which is essentially responsible for cholesterol biosynthesis, stands out as a key solution to lower plasma cholesterol levels. In this study, we synthesized several dihydroxycoumarins and investigated their antioxidant and in vitro HMG-CoA reductase inhibitory effects. Furthermore, we carried out in silico studies and examined the quantum-chemical properties of the coumarin derivatives. We also performed molecular docking experiments and analyzed the binding strength of each coumarin derivative. Our results revealed that compound IV displayed the highest HMG-CoA reductase inhibitory activity (IC(50) = 42.0 μM) in vitro. Cupric-reducing antioxidant capacity and ferric-reducing antioxidant power assays demonstrated that coumarin derivatives exhibit potent antioxidant activities. Additionally, a close relationship was found between the lowest unoccupied molecular orbital energy levels and the antioxidant activities.

[13] *Nezhadebrahimi A, Sepehri H, Jahanshahi M et al.* **The effect of simvastatin on gene expression of low-density lipoprotein receptor, sterol regulatory element-binding proteins, stearoyl-CoA desaturase 1 mRNA in rat hepatic tissues**. Archives of physiology and biochemistry 2020:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32643419
ABSTRACT
The study aimed to assess the effect of simvastatin on gene expression of LDLR, SREBPs, and SCD1 in rat hepatic tissues fed with high-fat diets (HFD) and its association with some biochemical parameters. Thirty-two male Wister albino rats were divided into four equal groups (three test and one control groups). The biochemical parameters were determined by using spectrophotometer techniques and the Elisa method. Low-density lipoprotein receptor, sterol regulatory element-binding proteins, stearoyl-CoA desaturase1, Beta-actin were analysed by real-time quantitative polymerase chain reaction (RT-PCR) method. At the end of study, the livers of the rats were separated and changes of hepatic tissue were determined. LDLR, SREBP2, and SCD1 expression increased significantly when compared G1 versus G4 and G2 versus G4. The expression of LDLR, SREBP2, and SCD1 also increased significantly when compared G2 versus G3, G1versus G3 and G1 versus G3 and G2 versus G3. The serum level

of cholesterol, triglyceride, glucose, LDL, and HDL increased significantly when compared G1 versus G3. LDL showed significantly decreased when compared G1 versus G2. Cholesterol, glucose and HDL and triglyceride levels were increased significantly when compared G1 versus G4 and G2. Treatment of rats with HFD and simvastatin 20 mg/kg, triglyceride and LDL were almost the same as a control group and LDLR expression increased 98% in liver tissue. Gene expressions may be up-regulated in liver tissue and they showed different effects on biochemical parameters.

[14] *Vitturi BK, Gagliardi RJ*. **Effects of statin therapy on outcomes of ischemic stroke: a real-world experience in Brazil**. Arquivos de neuro-psiquiatria 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32627806
ABSTRACT
BACKGROUND: Statin therapy has become one of the most important advances in stroke secondary prevention. OBJECTIVE: To provide evidence from real-world data for evaluating detailed associations between secondary prevention of stroke and statin use in Brazil. METHODS: We conducted a prospective cohort study including consecutive patients diagnosed with an ischemic stroke. Subjects were classified into non-statin, simvastatin 20 mg, simvastatin 40 mg, and high-potency statin groups. We also registered the onset of statin therapy, previous use of statins, the adherence to medication, and if there was discontinuation of the therapy. After two years, the functional outcome, stroke recurrence, major cardiovascular events, and mortality were assessed. RESULTS: Among the 513 patients included in our cohort, there were 96 (18.7%) patients without statins, 169 (32.9%) with simvastatin 20 mg, 202 (39.3%) with simvastatin 40 mg, and 46 (9.0%) with high-potency statins. Patients without statins were at increased risk of stroke recurrence and worse functional outcomes. Concerning etiology, evidence of beneficial use of statins was observed in cases of large-artery atherosclerosis, small-vessel occlusion, and stroke of undetermined cause. Those who presented poor adherence to statins or discontinuation of the treatment had worse prognosis after stroke whereas the early onset of statins use was associated with better outcomes. Patients with simvastatin 40 mg and high-potency statins presented the best functional recovery throughout the follow-up. CONCLUSIONS: Statins play an important role in the treatment of ischemic stroke, preventing stroke recurrence and cardiovascular events, and improving functional performance.

[15] *Mahdieh N, Heshmatzad K, Rabbani B*. **A systematic review of LDLR, PCSK9, and APOB variants in Asia**. Atherosclerosis 2020; 305:50-57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32629184
ABSTRACT
BACKGROUND AND AIMS: Genetic identification is a public health care concern for management of familial hypercholesterolemia (FH) associated cardiovascular morbidity and mortality. This study presents the spectrum and distribution of LDLR, APOB, PCSK9 gene mutations in Asia. METHODS: Databases were searched for English papers from 1950 to 2019. The spectrum of the variants was investigated in 8994 FH families in 48 Asian countries. We determined the frequency of variants, zygosity, and clinical features. RESULTS: Twenty countries have studied LDLR variants. A total of 629 mutations were reported and twenty variants were accounted as common variants in different populations. China, Japan, India and Taiwan constituted 68% of published articles. The most frequent mutation was reported in

Japan but was not common in other countries. Other missense variants accounted for 50% of the mutations, frameshifts 19%, and nonsense 11%. The pooled frequency of variation was estimated in 1867 individuals. Approximately 67% of Iranian families were homozygous.,The common variant was p.Ser130Ter. p.Arg3527Trp in APOB was common among 184 heterozygous patients; the common variant of PCSK9 was p.Glu32Lys. CONCLUSIONS: This is the first systematic review of LDLR, APOB, PCSK9 mutations in FH patients in Asia. These findings underscore the need to fill in the gap of studies on different populations in Asia. It also underlies the importance of early detection and management to decrease atherosclerosis and cardiovascular risk in different ethnicities.

[16] *Bai X, Feng Y, Li L et al.* **Treatment strategies for asymptomatic carotid artery stenosis in the era of lipid-lowering drugs: protocol for a systematic review and network meta-analysis**. BMJ open 2020; 10:e035094.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32624471
ABSTRACT
INTRODUCTION: Carotid endarterectomy (CEA), carotid artery stenting (CAS) and best medical therapy (BMT) are the major treatments used for significant asymptomatic carotid artery stenosis (ACAS, ≥50%). However, the widespread use of lipid-lowering drugs in this century has improved BMT outcomes. This study aims to compare the treatment efficacy of current BMT, CEA+BMT and CAS+BMT in patients with significant ACAS. METHODS AND ANALYSIS: This protocol was designed based on the guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols. Publication time for studies will be set from 1 January 2000 to 1 June 2020. We will search three databases: PubMed, EMBASE and The Cochrane Library. Suitable randomised controlled studies will be screened. The primary outcomes will include short-term and long-term mortality, stroke and myocardial infarction. OR and HR for dichotomous data and time-to-event data with 95% CIs will be calculated. Treatment effects among different therapies will be ranked according to the surface under the cumulative ranking curve and mean rank. A comprehensive evaluation of the risk of bias, heterogeneity and transitivity will be performed before data synthesis. Consistency and evidence quality will also be assessed. ETHICS AND DISSEMINATION: There will be no need for ethics approval as this systematic review is a summary and analysis of existing literature. Final results may be presented in international conferences or a peer-reviewed journal. PROSPERO REGISTRATION NUMBER: CRD42019138942.

[17] *Takaeko Y, Matsui S, Kajikawa M et al.* **Relationship between high-density lipoprotein cholesterol levels and endothelial function in women: a cross-sectional study**. BMJ open 2020; 10:e038121.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641366
ABSTRACT
OBJECTIVES: The purpose of this study was to evaluate the relationship between high-density lipoprotein cholesterol (HDL-C) levels and endothelial function in women. DESIGN: Cross-sectional study. SETTING: 22 university hospitals and affiliated clinics in Japan. PARTICIPANTS: 1719 Japanese women aged 17-90 years who were not receiving lipid-lowering therapy. MEASURES: We evaluated flow-mediated vasodilation (FMD) and serum levels of HDL-C. All participants were divided into four groups by HDL-C level: low HDL-C (<40 mg/dL), moderate HDL-C (40-59 mg/dL), high HDL-C (60-79 md/dL) and extremely high

HDL-C (≥80 mg/dL). RESULTS: Univariate regression analysis revealed a significant relationship between FMD and HDL-C (r=0.12, p<0.001). FMD values were significantly smaller in the low HDL-C group (5.2%±3.8%) and moderate HDL-C group (5.2%±3.8%) than in the extremely high HDL-C group (6.7%±3.4%) (p=0.024 and p=0.003, respectively), while there was no significant difference in FMD between the high HDL-C group and the extremely high HDL-C group. Multiple logistic regression analysis did not show a significant association between HDL-C levels and FMD. CONCLUSIONS: Endothelial function increased in relation to HDL-C levels. However, there was no association of HDL-C levels with endothelial function after adjustment of traditional cardiovascular risk factors in women. TRIAL REGISTRATION NUMBER: UMIN000012950; Results.

[18] *Teramoto T, Sawa T, Iimuro S et al.* **The Prevalence and Diagnostic Ratio of Familial Hypercholesterolemia (FH) and Proportion of Acute Coronary Syndrome in Japanese FH Patients in a Healthcare Record Database Study**. Cardiovascular therapeutics 2020; 2020:5936748.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32636924
ABSTRACT
BACKGROUND: Familial hypercholesterolemia (FH) is a genetic disorder characterized by high levels of low-density lipoprotein cholesterol (LDL-C). Because of underdiagnosis, acute coronary syndrome (ACS) is often the first clinical manifestation of FH. In Japan, there are few reports on the prevalence and diagnostic ratios of FH and the proportion of ACS among FH patients in clinical settings. METHODS: This retrospective, observational study used anonymized data from electronic healthcare databases between April 2001 and March 2015 of patients who had ≥2 LDL-C measurements recorded after April 2009. The index date was defined as the date of the first LDL-C measurement after April 2009. The primary endpoint was the prevalence of definite or suspected FH; secondary endpoints included the proportion of FH patients hospitalized for ACS, the proportion of patients using lipid-lowering drugs (LLDs), and LDL-C levels. RESULTS: Of the 187,781 patients screened, 1547 had definite or suspected FH (0.8%) based on data from the entire period; 832 patients with definite (n = 299, 0.16%) or suspected FH (n = 533, 0.28%) before the index date were identified in the main analysis cohort. LLDs were used in 214 definite FH patients (71.6%) and 137 suspected FH patients (25.7%). Among definite or suspected FH patients with ACS (n = 84) and without ACS (n = 748), 32.1% and 30.1% with definite FH and 3.2% and 2.4% with suspected FH had LDL-C levels < 2.6 mmol/L (<100 mg/dL), respectively. Sixty patients (7.2%) were hospitalized due to ACS at the index date. CONCLUSIONS: The prevalence of FH in this Japanese cohort of patients with ≥2 LDL-C measurements at hospitals was 0.8%, which is higher than that currently reported in epidemiological studies (0.2-0.5%). Patients with suspected FH, with or without ACS, had poorly controlled LDL-C levels and were undertreated. The proportion of FH patients who were hospitalized due to ACS was 7.2%.

[19] *Xu J, Duan X*. **Association between periodontitis and hyperlipidaemia: A systematic review and meta-analysis**. Clinical and experimental pharmacology & physiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32623762
ABSTRACT
To date, it has been reported that periodontitis (PD) may be associated with hyperlipidaemia in clinical practice. However, data on this issue are inconsistent and controversial. The purpose

of this meta-analysis was to identify the association between PD and hyperlipidaemia. Here, 21 case-control and eight cross-sectional studies on PD and hyperlipidaemia were included in the random-effects meta-analysis, involving 2060 patients with PD and 2776 healthy controls (HC). Meta-analysis showed that serum triglyceride (TG) and total cholesterol (TC) levels in the PD group were significantly higher than those in the HC group [TG, weighted mean difference (WMD) = 19.4 mg/dL, 95% confidence interval (CI) 13.3-25.5 mg/dL, P = .000; TC, WMD = 15.4 mg/dL, 95%CI 10.2-20.6 mg/dL, P = .000]. Subgroup analysis stratified by study design validated that PD was associated with higher serum TG and TC levels. In addition, compared with the HC group, serum low-density lipoprotein (LDL) in patients with PD showed a markedly higher level (WMD = 11.7 mg/dL, 95% CI 8.3-15.0 mg/dL, P = .000), whereas serum high-density lipoprotein (HDL) in PD group exhibited a significantly lower level (WMD = -4.5 mg/dL, 95%CI -6.4 - -2.7 mg/dL, P = .000). Finally, no significant publication bias was observed and sensitivity analysis also confirmed the stability of our meta-analyses. In conclusion, the accumulated evidence suggests that PD is indeed associated with hyperlipidaemia in humans. More interventions for lowering lipids or increasing HDL may benefit the patients with PD, which need be further investigated in prospective clinical trials.

[20] *Gurha N, Rehan HS, Yadav M, Gupta LK*. **Association of statin induced reduction in serum coenzyme Q10 level and conduction deficits in motor and sensory nerves: An observational cross-sectional study**. Clinical neurology and neurosurgery 2020; 196:106046.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32634700

ABSTRACT

OBJECTIVE: The reduction of Coenzyme Q10 (CoQ10) levels following statin use has been linked to cause peripheral neuropathy. Hence, this study was planned to explore the effect of statin on the serum HMGCR (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase), serum CoQ10 levels and nerve conduction and their correlation. PATIENTS AND METHODS: In an open labelled, cross-sectional, observational study, estimation of serum HMGCR and CoQ10 levels was performed in 50 atorvastatin/rosuvastatin users and 50 normal healthy volunteers (NHV). Statin users were also subjected to nerve conduction studies (NCS). RESULTS: Mean serum HMGCR level in NHV was higher (73.58 ± 7.64 ng/ml; p = 0.003) than that in statin users (49.11 ± 1.98 ng/ml). Similarly, mean serum CoQ10 levels was also lower (30.54 ± 2.03 ng/ml, p < 0.0001) in statin users than in NHV (49.43 ± 3.23 ng/ml). Amongst the 50 statin users, 29 had impaired NCS in sural, tibial and common peroneal nerve with lower mean serum CoQ10 levels (24.05 ± 1.96 ng/ml; p < 0.0001). Significant negative correlation was observed between onset time of action potential (AP) of the sural nerve and serum CoQ10 (r=-0.32) and HMGCR (r=-0.43) levels. There was significant positive correlation of conduction velocity of sural (r = 0.38) and tibial (r = 0.31) nerves with serum CoQ10 level. While conduction velocity in sural (r = 0.37) and common peroneal (r = 0.34) nerves positively correlated with serum HMGCR levels. The amplitude of the AP of the common peroneal nerve positively correlated with both serum CoQ10 (r = 0.52) and HMGCR (r = 0.46) levels. CONCLUSION: Statin users had lower serum CoQ10 and HMGCR levels associated with nerve conduction deficits suggesting a role of CoQ10 in the occurrence of the neurological adverse effects.

[21] *Kuo WC, Stevens JM, Ersig AL et al.* **Correction to: Does 24-h Activity Cycle Influence Plasma PCSK9 Concentration? A Systematic Review and Meta-Analysis**. Current atherosclerosis reports 2020; 22:40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32632660
ABSTRACT
Due to typesetting mistake, an unknown image was accidentally captured as graphical abstract. This should be removed.

[22] *de Souza Groia Veloso RC, Cruzeiro MGM, Dias BM, Reis AMM*. **Profile of use and access to statins in patients with coronary arterial disease in an outpatient clinic of a teaching hospital**. Current medical research and opinion 2020:1-5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32634034
ABSTRACT
OBJECTIVE: The aim of the study is to describe statin use pattern and access among individuals with coronary artery disease of a secondary care service of the Brazilian Unified Health System. METHODS: This is a cross-sectional study carried out in a multi-professional outpatient cardiology clinic at a public, university, and general hospital in the state of Minas Gerais, Brazil. The level of adherence to the recommendations of intensity of the statin therapy of Brazilian and American dyslipidemia guidelines was established. The prescribed statin, adherence to treatment, access, and clinically relevant drug interactions with statins were identified. Access to statin was analyzed through the availability and acquisition capacity realms. RESULTS: The sample consisted of 148 patients who were selected from April 2018 to February 2019. Approximately 90% of patients were under 75 years old. The most prevalent cardiovascular diagnoses were acute myocardial infarction with ST-segment elevation and without ST-segment elevation. All patients had a very high cardiovascular risk. Polypharmacy and cardiovascular polypharmacy were identified in 91.2% and 74.3% of patients, respectively. We identified that 90.6% of the patients used a moderate-intensity statin, and simvastatin was the most common stain used. The level of adherence to the recommendations of Brazilian and American dyslipidemia guidelines for statin use was 9.4% and 21.6%, respectively. Total free access to statins by the Unified Health System was 44.6%, with 52.1% of respondents reporting that they received statins at the health center, 25.7% through the popular pharmacy program via copayment, and 33.8% from a private pharmacy. CONCLUSION: The level of adherence to the recommendations of U.S. and Brazilian guidelines of dyslipidemia for statin use was low. Most patients used a moderate intensity statin, despite having a high cardiovascular risk. Simvastatin was the most prescribed statin.

[23] *Patel KV, Vaduganathan M*. **Targeting multiple domains of residual cardiovascular disease risk in patients with diabetes**. Current opinion in cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32649348
ABSTRACT
PURPOSE OF REVIEW: There has been a recent resurgence of diabetes-related cardiovascular complications after years of steady improvement. This review highlights established and emerging contemporary secondary prevention approaches that lower the risk of atherosclerotic and nonatherosclerotic cardiovascular disease events among patients with diabetes. RECENT FINDINGS: Secondary prevention therapies modify residual risk targets, including cardiometabolic pathways, lipoproteins, thrombosis, and inflammation. Large-scale

clinical trials of sodium-glucose cotransporter-2 inhibitors have demonstrated significant reductions in hospitalization for heart failure. Glucagon-like peptide-1 receptor agonists have reduced the risk of major adverse cardiovascular events. Recent clinical trials provide evidence supporting the use of nonstatin lipid-lowering therapies, novel antiplatelet and anticoagulant strategies, and antiinflammatory strategies in select cases. SUMMARY: Therapeutic approaches targeting multiple distinct pathways have been shown to improve cardiometabolic risk in diabetes. Individual patient characteristics and consideration of residual risk targets may help guide selection of comprehensive secondary prevention approaches.

[24] *Elserafy AS, Farag NM, El Desoky AI, Eletriby KA*. **Effect of high-intensity statin preloading on TIMI flow in patients presenting with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention**. The Egyptian heart journal : (EHJ) : official bulletin of the Egyptian Society of Cardiology 2020; 72:40.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32651772
ABSTRACT
BACKGROUND: Acute ST-elevation myocardial infarction (STEMI) is a major cause of morbidity and mortality worldwide. Primary percutaneous coronary intervention (PCI) has improved the outcomes from STEMI and improved myocardial perfusion. However, there is still room for medical therapy to help perfuse the myocardium. The aim of this study was to assess the impact of high-intensity statins used prior to primary PCI in patients presenting with acute STEMI on myocardial perfusion. The study included 170 patients who presented with acute STEMI to Ain Shams University Hospitals and underwent primary percutaneous coronary intervention (PCI). They were divided into two groups where the first group received high-intensity statins (80 mg of atorvastatin or 20 mg of rosuvastatin) besides guideline-recommended therapy before primary PCI and the second group served as a control group and received guideline-recommended therapy, and high-intensity statins were given as usual after going back to the coronary care unit after primary PCI. Post-interventional thrombolysis in myocardial infarction (TIMI) flow grade and myocardial blush grade (MBG) were recorded, and ST-segment resolution was measured. RESULTS: The LAD was the culprit vessel for the majority of patients in both groups. In the control group, there were 4 patients with TIMI I flow and MBG I, 13 with TIMI II flow and MBG II, and 68 with TIMI III flow and MBG III. Meanwhile, in the cases group, there was 1 patient with TIMI I flow and MBG I, 3 with TIMI II flow and MBG II, and 81 with TIMI III flow and MBG III. This difference was statistically significant with a P value of 0.010. There were 34 patients in the cases group who showed complete ST-segment resolution (40%) vs. 19 patients (22.4%) in the control group which was statistically significant with a P value of 0.013. In addition, ejection fraction had values of mean ± SD of 45.91 ± 5.49 in the cases group vs. 43.01 ± 8.80 in the control group which was statistically significant with a P value of 0.011. CONCLUSION: High-intensity statin loading before primary PCI resulted in improved post-procedural TIMI flow, MBG, complete ST-segment resolution, and ejection fraction.

[25] *Nakano Y, Komiya C, Shimizu H et al.* **A case of ezetimibe-effective hypercholesterolemia with a novel heterozygous variant in ABCG5**. Endocrine journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641618
ABSTRACT

Sitosterolemia is caused by homozygous or compound heterozygous gene mutations in either ATP-binding cassette subfamily G member 5 (ABCG5) or 8 (ABCG8). Since ABCG5 and ABCG8 play pivotal roles in the excretion of neutral sterols into feces and bile, patients with sitosterolemia present elevated levels of serum plant sterols and in some cases also hypercholesterolemia. A 48-year-old woman was referred to our hospital for hypercholesterolemia. She had been misdiagnosed with familial hypercholesterolemia at the age of 20 and her serum low-density lipoprotein cholesterol (LDL-C) levels had remained about 200-300 mg/dL at the former clinic. Although the treatment of hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors was ineffective, her serum LDL-C levels were normalized by ezetimibe, a cholesterol transporter inhibitor. We noticed that her serum sitosterol and campesterol levels were relatively high. Targeted analysis sequencing identified a novel heterozygous ABCG5 variant (c.203A>T; p.Ile68Asn) in the patient, whereas no mutations were found in low-density lipoprotein receptor (LDLR), proprotein convertase subtilisin/kexin type 9 (PCSK9), or Niemann-Pick C1-like intracellular cholesterol transporter 1 (NPC1L1). While sitosterolemia is a rare disease, a recent study has reported that the incidence of loss-of-function mutation in the ABCG5 or ABCG8 gene is higher than we thought at 1 in 220 individuals. The present case suggests that serum plant sterol levels should be examined and ezetimibe treatment should be considered in patients with hypercholesterolemia who are resistant to HMG-CoA reductase inhibitors.

[26] *Jabr R, Gharaibeh M, Zayed AA, Zihlif M*. **The Association between Apolipoprotein E Polymorphism and Response to Statins in Group of Hyperlipidemic Patients**. Endocrine, metabolic & immune disorders drug targets 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32628603

ABSTRACT

BACKGROUND AND OBJECTIVES: APOE has an important role in lipids metabolism, and in the variability in low density lipoprotein (LDL) response to statins treatment between individuals. In this study we aim to investigate the association between APOE polymorphism and response to statins in Jordanian hyperlipidemic patients at the diabetic clinic of Jordan University Hospital. METHODS: One hundred and fifty two Jordanian Hyperlipidemic patients (52 males and 100 females) aged between 35-75 years were enrolled in this study. This study was approved by the Institutional Review Board (IRB) of Jordan University Hospital. The genotypes of the patients were identified by polymerase chain reaction followed by restriction fragment length polymorphism assay method (PCR-RFLP). RESULTS AND CONCLUSIONS: The study showed that there is an association between APOE polymorphism and response to statin therapy. Patients who were APOE ε4 carriers had lower response to statins compared to ε3 and ε2 carriers (p=0.002). In addition we found that there were no significant association between APOE polymorphism and LDL baseline (p=0.214). No significant differences in APOE genotypes distribution between males and females (p=0.06).No significant association was found between age and APOE genotypes (p=0.347). A genotype screening test for dyslipidemic Jordanian patients is recommended to choose the appropriate treatment decisions, dosage, and to recognize the potential side effects of the statin therapy.

[27] *Muscas M, Seo SS, Louros SR, Osterweil EK*. **A differential effect of lovastatin versus simvastatin in neurodevelopmental disorders**. eNeuro 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32651266

ABSTRACT

Significance statement The statin drug lovastatin normalizes excessive protein synthesis and thereby ameliorates pathological changes in animal models of Fragile X Syndrome (FX), the most commonly identified genetic cause of autism. Recently, we compared the efficacy of lovastatin to the more potent and brain-penetrant drug simvastatin for correcting phenotypes in the Fmr1(-/y) mouse (Muscas et al., 2019). Surprisingly, we find simvastatin worsens excessive protein synthesis and has no impact on audiogenic seizures (AGS) in Fmr1(-/y) mice, suggesting it does not work in a similar fashion to lovastatin. A recent commentary by Ottenhoff et al. suggests that differences in dose and/or study design might account for our results. Here we discuss the points raised by Ottenhoff et al., as well as the evidence supporting a therapeutic role for lovastatin versus simvastatin. We conclude that differences between lovastatin and simvastatin warrant careful consideration with respect to the treatment of neurodevelopmental disorders.

[28] **Corrigendum: ESC position paper on statins adherence and implementation of new lipid-lowering medications: barriers to be overcome**. European heart journal. Cardiovascular pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32633751
ABSTRACT

[29] *Zeitouni M, Sabouret P, Kerneis M et al.* **2019 ESC/EAS Guidelines for management of dyslipidaemia: strengths and limitations**. European heart journal. Cardiovascular pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32652000
ABSTRACT

In 2019, the European Society of Cardiology and European Atherosclerosis Society released a new guideline document with substantial changes regarding the assessment of cardiovascular risk and treatments. The update of high-risk criteria and categories led to a better detection and primary prevention of patients at risk of a first cardiovascular event. Nonetheless, additional efforts are needed for a better inclusion of risk modifiers, especially specific to women, to improve risk stratification and direct primary prevention. Eventually, we discuss how these new guidelines implement PCSK9 inhibitors for very-high risk individuals and the evidence supporting new LDL-C goals below such as 55 mg/dL and 40 mg/dL.

[30] *Rioja J, Ariza MJ, García-Casares N et al.* **Evaluation of the Chylomicron-TG to VLDL-TG ratio for Type I Hyperlipoproteinemia diagnostic**. European journal of clinical investigation 2020:e13345.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32649781
ABSTRACT

BACKGROUND: The aim of this study is to confirm the diagnostic performance of the Chylomicron to Very Low Density Lipoproteins Triglycerides (CM/VLDL-TG) ratio, the Triglycerides to Cholesterol ratio (TG/TC) and a dichotomic rule including the Tryglicerides to Apolipoprotein B (TG/APOB) ratio for the presence of Type I Hyperlipoproteinemia (HPLI) in patients with severe hypertriglyceridemia (sHTG) that were at high risk for Familial Chylomicronemia Syndrome (FCS). METHODS: Two cohorts (Derivation and Validation) of patients with sHTG were included in the study. Anthropometric, clinical, biochemical and

genetic data were obtained. The CM/VLDL-TG, TG/TC and TG/APOB ratios were calculated. Finally, a diagnostic performance study was developed to establish Sensitivity, Specificity and cut-offs by a ROC curve analysis in the Derivation Cohort as well as Agreement and Predictive Values in the Validation Cohort. RESULTS: Patients with FCS in both cohorts showed an earlier presence in pancreatitis, greater number of acute pancreatitis episodes and lower BMI. FCS patients also showed higher ratios of CM/VLDL-TG, TG/TC and TG/APOB ratios, whereas their HDL-C, LDL-C and APOB levels were lower than in non-FCS patients. Sensitivity and Agreement were low for both the TG/TC and TG/APOB ratios, although Predictive Values were good. The CM/VLDL-TG ratio showed greatest sensitivity, specificity, Agreement and Predicitve Values for cut-off of 3.8 and 4.5. CONCLUSIONS: Our results suggest that in subjects at high risk of FCS a total serum TG/TC ratio or TG/APOB ratio are feasible to initially screen for HLPI; however, a CM/VLDL-TG ratio ≥ 4.5 is a better diagnostic criterion for HPLI.

[31] *Amput P, Palee S, Arunsak B et al.* **PCSK9 inhibitor effectively attenuates cardiometabolic impairment in obese-insulin resistant rats**. European journal of pharmacology 2020; 883:173347.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32650007
ABSTRACT
Long-term high-fat diet consumption causes obese-insulin resistance and cardiac mitochondrial dysfunction, leading to impaired left ventricular (LV) function. Atorvastatin effectively improved lipid profiles in obese patients. However, inadequate reduction in low density lipoprotein cholesterol (LDL-C) level was found. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor effectively reduced LDL-C levels. We hypothesized that this PCSK9 inhibitor has a greater efficacy in attenuating cardiometabolic impairments than atorvastatin in obese-insulin resistant rats. Female rats were fed with either a high fat or normal diet for 12 weeks. High fat diet fed rats (HFD) were then divided into 3 groups and were given vehicle, atorvastatin (40 mg/kg/day; s.c.), or PCSK9 inhibitor (4 mg/kg/day; s.c.) for additional 3 weeks. The metabolic parameters, cardiac and mitochondrial function and [Ca(2+)](i) transients were determined. HFD rats developed obese-insulin resistance as indicated by increased plasma insulin and HOMA index. Although high-fat diet fed rats treated with vehicle (HFV) rats had markedly impaired LV function as indicated by reduced %LVFS, impaired cardiac mitochondrial function, and [Ca(2+)](i) transient regulation, these impairments were attenuated in high-fat diet fed rats treated with atorvastatin (HFA) and high-fat diet fed rats treated with PCSK9 inhibitor (HFP) rats. However, these improvements were greater in HFP rats than HFA rats. Our findings indicated that the PCSK9 inhibitor exerted greater cardioprotection than atorvastatin through improved mitochondrial function in obese-insulin resistant rats.

[32] *Huang CQ, Jin WX, Yu GF*. **Correlation between carotid atherosclerotic plaque properties and serum levels of lncRNA CCAT2 and miRNA-216b**. European review for medical and pharmacological sciences 2020; 24:7033-7038.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32633397
ABSTRACT
OBJECTIVE: The purpose of this study was to uncover the clinical values of serum long non-coding RNA (lncRNA) CCAT2 and miRNA-216b in the properties of carotid atherosclerotic plaques. PATIENTS AND METHODS: Patients with carotid atherosclerotic plaques were

assigned into stable plaque group (n=60) and unstable plaque (n=75) group based on their examination results of cervical contrast-enhanced CT examination. Maximal plaque thickness (MAPT) and intima-media thickness (IMT) in each group were determined. Serum levels of lncRNA CCAT2 and miRNA-216b in patients with carotid atherosclerotic plaques were detected by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Moreover, the correlation between serum levels of CCAT2 and miRNA-216b was analyzed by Pearson's correlation analysis. Besides, potential correlations of serum levels of CCAT2 and miRNA-216b with MAPT and IMT in patients with carotid atherosclerotic plaques were assessed as well. RESULTS: Results revealed that MAPT and IMT were markedly higher in unstable plaque group than those in stable plaque group. Serum level of CCAT2 was higher in unstable plaque group, while miRNA-216b was lower than those in stable group. A negative correlation was identified between serum levels of CCAT2 and miRNA-216b. In addition, CCAT2 level was positively correlated with IMT and MAPT in patients with carotid atherosclerotic plaques, while miRNA-216b level was negatively correlated with them. CONCLUSIONS: Detection of serum levels of CCAT2 and miRNA-216b could be applied for predicting the rupture of carotid atherosclerotic plaques. They may be potential biomarkers predicting ischemic stroke.

[33] *Sun FR, Wang SL, Wang M, Sun LM*. **Simvastatin induces apoptosis of nasopharyngeal carcinoma cells through NF-κB signaling pathway**. European review for medical and pharmacological sciences 2020; 24:6726-6734.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32633363

ABSTRACT

OBJECTIVE: The aim of this study was to investigate the mechanism of simvastatin-induced apoptosis in nasopharyngeal carcinoma (NPC) cells. MATERIALS AND METHODS: CNE1 and HK1 cell lines were treated with different concentrations of simvastatin for different time course. Subsequently, Cell Counting Kit-8 (CCK-8), colony formation assay, and flow cytometry were conducted to evaluate cell activity, colony formation ability, as well as cell cycle of NPC cells, respectively. The mRNA expressions of p21, Bim, and cyclin D1 were examined by qPCR. Meanwhile, the protein expression levels of apoptosis-related proteins (including caspase-3, Bax, Bcl-2) were detected by Western blot. Caspase-3 activity was determined to estimate cell apoptosis. An NPC xenotransplantation model was constructed to further determine the role of simvastatin in vivo. In addition, NF-κB activity was assessed through Luciferase reporter gene assay and Western blot. RESULTS: Simvastatin treatment lead to significantly reduced viability of NPC cells and the number of cell colonies dose-dependently and time-dependently. Meanwhile, simvastatin treatment caused cell cycle arrest in G0/G1 phase, remarkably downregulated expression of cyclin D1, and upregulated expressions of p21 and Bim. In addition, simvastatin induced apoptosis of NPC cells and enhanced the Luciferase activity of caspase-3. Western blot results indicated that simvastatin promoted the protein level of Bax and caspase-3, whereas suppressed the protein expression of Bcl-2. In vivo experiments showed that simvastatin was able to suppress the growth of NPC cells. Further studies demonstrated that simvastatin remarkably attenuated the Luciferase activity of pNF-κB-Luc, thereby specifically inhibiting the NF-κB signaling pathway. CONCLUSIONS: Simvastatin inhibits proliferation and promotes apoptosis of NPC cells by inhibiting the NF-κB pathway.

[34] *Di Bello E, Zwergel C, Mai A, Valente S*. **The Innovative Potential of Statins in Cancer: New Targets for New Therapies**. Front Chem 2020; 8:516.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32626692
ABSTRACT
Numerous and different types of cancers possess the dysregulation of the mevalonate pathway as a common feature. Statins, traditionally applied in cardiovascular diseases to reduce lipid levels, subsequently have been discovered to exhibit anti-cancer activities also. Indeed, statins influence proliferation, migration, and survival of cancer cells by regulating crucial signaling proteins, such as Rho, Ras, and Rac. Recently, several studies have demonstrated that simvastatin, fluvastatin, and lovastatin are implicated in different pathways that enhance the survival time of patients with cancer under treatment in combination with antineoplastic agents. In this minireview, we present an overview of the most important studies conducted regarding the use of statins in cancer therapy up to date.

[35] *Haufe S, Kahl KG, Kerling A et al.* **Employers With Metabolic Syndrome and Increased Depression/Anxiety Severity Profit Most From Structured Exercise Intervention for Work Ability and Quality of Life**. Frontiers in psychiatry 2020; 11:562.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32625123
ABSTRACT
BACKGROUND: Major depressive disorder and anxiety disorders are associated with less productivity, earlier retirement, and more sick-days at the workplace. These associations also exist for patients with metabolic syndrome. For both, exercise is a generally recommended part of multimodal treatments. However, for individuals with metabolic syndrome, in which depression and anxiety is more prevalent and severe, evidence for the efficacy of exercise interventions is limited. METHODS: Company employees with diagnosed metabolic syndrome (n=314, age: 48 ± 8 yrs) were randomized to a 6-month exercise intervention (150 min per week) or wait-list control. Participants received individual recommendations for exercise activities by personal meetings, telephone, or via a smartphone app. Physical activities were supervised and adapted using activity monitor data transferred to a central database. Work ability (work ability index), depression severity and anxiety severity [hospital anxiety and depression scale (HADS)], and health-related quality of live [short form 36 (SF-36)] were assessed. RESULTS: We included 314 subjects from which 287 finished the intervention. Total work ability, depression- and anxiety severity, and the mental component score of the SF-36 improved after 6 months exercise compared to controls. After baseline stratification for normal (HADS scores 0-7) and increased depression- and anxiety scores (HADS scores 8-21) individuals with increased severity scores had similar age, body composition, blood lipids, and cardiorespiratory fitness compared to those with normal scores, but lower total work ability and component sum scores of health-related quality of life. After 6 months total work ability increased in the exercise group compared to controls with the magnitude of the observed increase being significantly greater for subjects with increased depression- and anxiety severity at baseline compared to those with normal severity scores. CONCLUSIONS: A 6-month exercise intervention for company employees with metabolic syndrome showed strongest effects on self-perceived work ability in individuals with mild to severe depression- and anxiety severity. This suggests exercise programs offered to workers with metabolic syndrome not only reduces individual disease risk but may also reduce healthcare and

employers costs arising from metabolic syndrome and mental disease conditions. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, identifier NCT03293264.

[36] *Koganti S, Karanasos A, Regar E, Rakhit RD*. **Association of systemic inflammatory biomarkers with morphological characteristics of coronary atherosclerotic plaque by intravascular optical coherence tomography**. Hellenic journal of cardiology : HJC = Hellenike kardiologike epitheorese 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32628997
ABSTRACT
Despite significant advances in preventive, medical, and interventional management, coronary artery disease remains the leading cause of death worldwide. We now know that in the majority of acute coronary syndromes, a thrombotic event is triggered either by the rupture or erosion of the so-called high-risk or 'vulnerable' plaque. However, accurately identifying the individual who is at significant risk of acute event remains the holy grail of preventive cardiology. To better stratify an individual's risk of developing and suffering a cardiovascular event, biomarkers are needed that can accurately predict coronary events and, if possible, monitor disease activity in response to medical or interventional therapies. In order to be able to understand the association of these biomarkers with the morphological substrate of high-risk plaques, intravascular imaging modalities can provide invaluable assistance. Novel imaging tools such as optical coherence tomography (OCT) have not only helped in identifying atherosclerotic plaque characteristics that are unstable but also in estimating global plaque burden. In this study, we provide an overview of our current knowledge of association of various inflammatory markers with atherosclerotic plaque characteristics seen on OCT.

[37] *Davis LE, Pogge EK*. **A Retrospective Chart Review Evaluating Efficacy, Tolerability, and Cost of Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitors (PCSK9i) in Older Adults**. High blood pressure & cardiovascular prevention : the official journal of the Italian Society of Hypertension 2020; 27:331-338.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32651891
ABSTRACT
INTRODUCTION: Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) are proven to have profound lowering of low-density lipoprotein cholesterol (LDL-C) in patients with clinical atherosclerotic cardiovascular disease or familial hypercholesterolemia. AIM: The primary purpose of this study was to evaluate PCSK9i utilization in older adults, with a focus on efficacy outcomes within 6 months of initiation. Secondary outcomes included tolerability, out-of-pocket expenses (OPE), and barriers to initiation of therapy. METHODS: We conducted a retrospective chart review of patients ≥ 65 years prescribed PCSK9i therapy by a pharmacist-run lipid clinic within a cardiology practice. RESULTS: A total of 136 older adults were prescribed PCSK9i therapy for a Food and Drug Administration-approved indication between September 2015 and March 2019 with 98 patients included in the analyses. In terms of efficacy, 51 patients who took ≥ 3 doses of PCSK9i with baseline and follow-up lipid panels were assessed. On average, LDL-C reduced by 60% (169-67 mg/dL, $p < 0.001$). For tolerability, 15 patients reported treatment-emergent side effects, resulting in 10 therapy discontinuations. For the cost analysis, 72 patients reported anticipated OPE for 1 month of therapy. Ultimately 17 patients were approved for manufacturer patient assistance with $0 OPE and 31 patients utilized insurance coverage to obtain therapy reporting a median OPE of

$9 United States Dollars ($0-$450). The main barrier to initiation was high OPE. CONCLUSIONS: PCSK9i are effective at lowering LDL-C in older adults. Tolerability was high among patients without a history of statin intolerance. PCSK9i remain high-cost medications to both insurance companies and patients in terms of cost-sharing responsibilities.

[38] *Su W, Wang M, Zhu J et al.* **Underweight Predicts Greater Risk of Cardiac Mortality Post Acute Myocardial Infarction**. Int Heart J 2020; 61:658-664.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641636
ABSTRACT
Increased body mass index (BMI) is a well-established risk factor for cardiovascular disease; however, patients with elevated BMI, in comparison to those with low BMI, seem to have better survival, a phenomenon reported as "obesity paradox," which remains controversial. We investigated the effect of BMI on cardiac mortality post acute myocardial infarction (AMI).In this analysis, 3562 AMI patients were included and classified into four groups based on BMI values. The primary endpoint was cardiac death. Compared to normoweight group, overweight and obese group subjects were younger, mostly men, and more likely to receive percutaneous coronary intervention (PCI) and had higher levels of glucose and lipids, but lower level of NTproBNP. Subjects in the underweight group were older, were mostly women, had lower Barthel index (BI), were less likely to receive PCI, and had lower levels of glucose and lipids, but higher level of N-terminal pro-brain natriuretic peptide (NTproBNP) and higher rates of left ventricular ejection fraction (LVEF) < 50%. During a median follow-up period of 1.9 years, cardiac death occurred significantly more in the underweight group (30.0%, 10.6%, 7.0%, and 5.0% among the four groups from underweight to obese; P < 0.001 for trend). The Cox analysis revealed that underweight was an independent predictor of subsequent cardiac death (odds ratio (OR), 1.86; 95% confidence interval (CI), 1.07-3.25) and identified that older age, BI < 60, higher levels of cardiac troponin I (cTnI), LVEF < 50%, and not receiving PCI were independently associated with increased risk of cardiac death.Patients who were underweight were at greater risk of cardiac death post AMI. In addition, older age, frail, higher levels of cTnI, LVEF < 50%, and not receiving PCI also independently predicted cardiac mortality post AMI.

[39] *Athyros VG, Stavropoulos K, Imprialos KP, Doumas M*. **Suboptimal management of dyslipidemia in everyday clinical practice: Alarming signals from real-world data**. International journal of cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32634493
ABSTRACT

[40] *Wun CH, Zhang MJ, Ho BH et al.* **Efficacy of a Six-Week Dispersed Wingate-Cycle Training Protocol on Peak Aerobic Power, Leg Strength, Insulin Sensitivity, Blood Lipids and Quality of Life in Healthy Adults**. International journal of environmental research and public health 2020; 17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32640602
ABSTRACT
The aim of this study was to evaluate the efficacy of a six-week dispersed Wingate Anaerobic test (WAnT) cycle exercise training protocol on peak aerobic power (VO(2peak)), isokinetic leg strength, insulin sensitivity, lipid profile and quality of life, in healthy adults. Methods: We

conducted a match-controlled cohort trial and participants were assigned to either the training (intervention, INT, N = 16) or non-training (control, CON, N = 17) group. INT performed 30-s WAnT bouts three times a day in the morning, afternoon and evening with each bout separated by ~4 h of rest, performed for 3 days a week for 6 weeks. Criterion measures of peak oxygen uptake (VO(2peak)), leg strength, insulin markers such as homeostatic model assessment (HOMA) and quantitative insulin-sensitivity check index (QUICKI), blood lipids profile and health-related quality of life (HRQL) survey were assessed before and after 6 weeks in both groups. Results: Absolute VO(2peak) increased by 8.3 ± 7.0% ($p < 0.001$) after INT vs. 0.9 ± 6.1% in CON ($p = 0.41$) group. Maximal voluntary contraction at 30°·s(-1) of the dominant lower-limb flexors in INT increased significantly post-training ($p = 0.03$). There were no changes in the INT individuals' other cardiorespiratory markers, HOMA, QUICKI, blood lipids, and HRQL measures (all $p > 0.05$) between pre- and post-training; but importantly, no differences were observed between INT and CON groups (all $p > 0.05$). Conclusions: The results indicate that 6 weeks of dispersed sprint cycle training increased cardiorespiratory fitness and dynamic leg strength but had minimal impact on insulin sensitivity, blood lipids and quality of life in the exercising individuals.

[41] *Stancioiu F, Papadakis GZ, Kteniadakis S et al.* **A dissection of SARS-CoV2 with clinical implications (Review)**. International journal of molecular medicine 2020; 46:489-508.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32626922
ABSTRACT
We are being confronted with the most consequential pandemic since the Spanish flu of 1918-1920 to the extent that never before have 4 billion people quarantined simultaneously; to address this global challenge we bring to the forefront the options for medical treatment and summarize SARS-CoV2 structure and functions, immune responses and known treatments. Based on literature and our own experience we propose new interventions, including the use of amiodarone, simvastatin, pioglitazone and curcumin. In mild infections (sore throat, cough) we advocate prompt local treatment for the naso-pharynx (inhalations; aerosols; nebulizers); for moderate to severe infections we propose a tried-and-true treatment: the combination of arginine and ascorbate, administered orally or intravenously. The material is organized in three sections: i) Clinical aspects of COVID-19; acute respiratory distress syndrome (ARDS); known treatments; ii) Structure and functions of SARS-CoV2 and proposed antiviral drugs; iii) The combination of arginine-ascorbate.

[42] *Korostovtseva L, Alieva A, Rotar O et al.* **Sleep Duration, Lipid Profile and Insulin Resistance: Potential Role of Lipoprotein(a)**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32630105
ABSTRACT
Lipoprotein (a) (Lp(a)) is considered a genetic factor for cardiovascular disease playing an important role in atherogenesis and thrombosis, but the evidence about its association with sleep duration is controversial. We evaluated the relation between self-reported sleep duration and Lp(a). Among 1600 participants of the population-based sample, we selected 1427 subjects without previously known cardiovascular events, who answered the questions about their sleep duration; had valid lipid profile results (total cholesterol, low- and high-density lipoproteins, Lp(a), apolipoprotein AI (ApoAI), ApoB, and ApoB/ApoAI); and did not take lipid-

lowering drugs (mean age 46 ± 12 years). We performed a structured interview, which included questions about lifestyle, medical history, complaints, and sleep duration (How long have you been sleeping per night during the last month?). Sleep duration was classified as follows: <6 h/night-short, 6-9 h/night-normal, and ≥10 h/night-long. Overall, 73 respondents (5.2%) were short-sleepers and 69 (4.8%) long-sleepers. Males were slightly more prevalent among short-sleepers. The groups matched by age, body mass index, blood pressure, diabetes mellitus, and hypertension rate. Short-sleepers had lower rates of high total cholesterol (≥5.0 mmol/L), lower Lp(a) levels and lower rates of increased Lp(a) ≥0.5 g/L, and higher insulin and insulin resistance (assessed by the homeostatic model assessment for insulin resistance (HOMA-IR)). ApoAI, ApoB, their ratio, and other lab tests were similar in the groups. The multinomial logistic regression demonstrated that only the short sleep duration was independently (odds ratio (OR) 0.29, 95% confidence interval (CI) (0.09-0.91), p = 0.033) associated with Lp(a) ($\chi(2) = 41.58$, p = 0.003). Other influencing factors were smoking and HOMA-IR. Such an association was not found for long-sleepers. In conclusion, a short-sleep duration is associated with Lp(a). The latter might mediate the higher insulin resistance and higher cardiometabolic risks in short-sleepers.

[43] *St Paul A, Corbett CB, Okune R, Autieri MV*. **Angiotensin II, Hypercholesterolemia, and Vascular Smooth Muscle Cells: A Perfect Trio for Vascular Pathology**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32630530
ABSTRACT
Cardiovascular disease is the leading cause of morbidity and mortality in the Western and developing world, and the incidence of cardiovascular disease is increasing with the longer lifespan afforded by our modern lifestyle. Vascular diseases including coronary heart disease, high blood pressure, and stroke comprise the majority of cardiovascular diseases, and therefore represent a significant medical and socioeconomic burden on our society. It may not be surprising that these conditions overlap and potentiate each other when we consider the many cellular and molecular similarities between them. These intersecting points are manifested in clinical studies in which lipid lowering therapies reduce blood pressure, and anti-hypertensive medications reduce atherosclerotic plaque. At the molecular level, the vascular smooth muscle cell (VSMC) is the target, integrator, and effector cell of both atherogenic and the major effector protein of the hypertensive signal Angiotensin II (Ang II). Together, these signals can potentiate each other and prime the artery and exacerbate hypertension and atherosclerosis. Therefore, VSMCs are the fulcrum in progression of these diseases and, therefore, understanding the effects of atherogenic stimuli and Ang II on the VSMC is key to understanding and treating atherosclerosis and hypertension. In this review, we will examine studies in which hypertension and atherosclerosis intersect on the VSMC, and illustrate common pathways between these two diseases and vascular aging.

[44] *Pekkala T, Hall A, Mangialasche F et al.* **Association of Peripheral Insulin Resistance and Other Markers of Type 2 Diabetes Mellitus with Brain Amyloid Deposition in Healthy Individuals at Risk of Dementia**. Journal of Alzheimer's disease : JAD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32623394
ABSTRACT

We explored the association of type 2 diabetes related blood markers with brain amyloid accumulation on PiB-PET scans in 41 participants from the FINGER PET sub-study. We built logistic regression models for brain amyloid status with12 plasma markers of glucose and lipid metabolism, controlled for diabetes and APOEε4 carrier status. Lower levels of insulin, insulin resistance index (HOMA-IR), C-peptide, and plasminogen activator (PAI-1) were associated with amyloid positive status, although the results were not significant after adjusting for multiple testing. None of the models found evidence for associations between amyloid status and fasting glucose or HbA1c.

[45] *Blom DJ, Harada-Shiba M, Rubba P et al.* **Efficacy and Safety of Alirocumab in Adults With Homozygous Familial Hypercholesterolemia: The ODYSSEY HoFH Trial**. Journal of the American College of Cardiology 2020; 76:131-142.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32646561
ABSTRACT
BACKGROUND: Homozygous familial hypercholesterolemia (HoFH) is characterized by extremely elevated low-density lipoprotein-cholesterol (LDL-C) levels and early onset atherosclerotic cardiovascular disease despite treatment with conventional lipid-lowering treatment. OBJECTIVES: This study was designed to assess LDL-C reduction with the proprotein convertase subtilisin/kexin type 9 inhibitor alirocumab in adult patients with HoFH. METHODS: This randomized, double-blind, placebo-controlled, parallel-group, phase 3 study evaluated efficacy and safety of alirocumab 150 mg every 2 weeks. The primary endpoint was percent reduction from baseline in LDL-C versus placebo after 12 weeks of treatment. RESULTS: Patients (N = 69) were randomized 2:1 to alirocumab or placebo. At baseline, background lipid-lowering treatment included 67 patients receiving statin (59 patients on high-intensity statin); 50 patients on ezetimibe; 10 patients on lomitapide; and 10 patients undergoing apheresis. Mean baseline LDL-C was 259.6 mg/dl in the placebo group and 295.0 mg/dl in the alirocumab group. At week 12, the least squares mean difference in LDL-C percent change from baseline was -35.6% (alirocumab [-26.9%] vs. placebo [8.6%]; $p < 0.0001$). Reductions (least squares mean difference) in other atherogenic lipids at week 12 were: apolipoprotein B, -29.8%; non-high-density lipoprotein cholesterol, -32.9%; total cholesterol, -26.5%; and lipoprotein(a), -28.4% (all $p < 0.0001$). No serious adverse events, permanent treatment discontinuations, or deaths due to treatment-emergent adverse events were reported during the double-blind treatment period. CONCLUSIONS: In the largest randomized controlled interventional trial in HoFH patients to date, alirocumab resulted in significant and clinically meaningful reductions in LDL-C at week 12. Alirocumab was generally well tolerated, with a safety profile comparable to that of placebo. (Study in Participants With Homozygous Familial Hypercholesterolemia [HoFH] [ODYSSEY HoFH] NCT03156621.).

[46] *Thompson GR*. **PCSK9 Inhibitors for Homozygous Familial Hypercholesterolemia: Useful But Seldom Sufficient**. Journal of the American College of Cardiology 2020; 76:143-145.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32646562
ABSTRACT

[47] *Hamamura H, Adachi H, Enomoto M et al.* **Serum Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) is Independently Associated with Insulin Resistance,**

Triglycerides, Lipoprotein(a) Levels but not Low-Density Lipoprotein Cholesterol Levels in a General Population. Journal of atherosclerosis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32624555
ABSTRACT
AIM: Proprotein convertase subtilisin/kexin type 9 (PCSK9) has been identified as an important regulator of low-density lipoprotein (LDL) receptor processing. Evolocumab and alirocumab are PCSK9 inhibitors; however, little is known about the association between PCSK9 levels and lipid profiles in a general population. Because PCSK9 inhibitors have LDL-C lowering effects, we investigated whether there is a positive correlation between serum PCSK9 levels and LDL-C or lipoprotein(a) [Lp(a)]. METHODS: In Uku town, 674 residents (mean age; 69.2±8.3 years) received health check-ups. The participants underwent a physical examination and blood tests, including PCSK9 and Lp(a). Serum PCSK9 and Lp(a) were measured by ELISA and Latex methods, respectively. HOMA-IR was calculated by fasting plasma glucose×insulin levels/405. RESULTS: The mean (range) of PCSK9 and Lp(a) were 211.2 (49-601) ng/mL and 60 (1-107) mg/dL, respectively. Because of a skewed distribution, the log-transformed values were used. With univariate linear regression analysis, PCSK9 levels were associated with Lp(a) ($p=0.028$), triglycerides ($p<0.001$), and HOMA-IR ($p<0.001$), but not with LDL-C ($p=0.138$) levels. Multiple stepwise regression analysis revealed that serum PCSK9 levels were independently associated with triglycerides ($p<0.001$), Lp(a) ($p=0.033$) and HOMA-IR ($p=0.041$). CONCLUSIONS: PCSK-9 is independently associated with triglycerides, Lp(a) levels, and HOMA-IR, but not LDL-C, in a relatively large general population sample.

[48] *Derosa G, Colletti A, Maffioli P et al.* **Lipid-lowering nutraceuticals update on scientific evidence**. Journal of cardiovascular medicine (Hagerstown, Md.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32639326
ABSTRACT
: Cardiovascular diseases (CVDs) are the main cause of mortality worldwide. Risk factors of CVD can be classified into modifiable (smoking, hypertension, diabetes, hypercholesterolemia) through lifestyle changes or taking drug therapy and not modifiable (age, ethnicity, sex and family history). Elevated total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C) levels have a lead role in the development of coronary heart disease (CHD), while high levels of high-density lipoprotein-cholesterol (HDL-C) seem to have a protective role.The current treatment for dyslipidemia consists of lifestyle modification or drug therapy even if not pharmacological treatment should be always considered in addition to lipid-lowering medications.The use of lipid-lowering nutraceuticals alone or in association with drug therapy may be considered when the atherogenic cholesterol goal was not achieved.These substances can be classified according to their mechanisms of action into natural inhibitors of intestinal cholesterol absorption, inhibitors of hepatic cholesterol synthesis and enhancers of the excretion of LDL-C. Nevertheless, many of them are characterized by mixed or unclear mechanisms of action.The use of these nutraceuticals is suggested in individuals with borderline lipid profile levels or with drug intolerance, but cannot replace standard lipid-lowering treatment in patients at high, or very high CVD risk.Nutraceuticals can also have vascular effects, including improvement in endothelial dysfunction and arterial stiffness, as well as antioxidative properties. Moreover, epidemiological and clinical studies reported that in

patients intolerant of statins, many nutraceuticals with demonstrated hypolipidemic effect are well tolerated.

[49] *Amput P, Palee S, Arunsak B et al.* **PCSK9 inhibitor and atorvastatin reduce cardiac impairment in ovariectomized prediabetic rats via improved mitochondrial function and Ca(2+) regulation**. Journal of cellular and molecular medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32628813
ABSTRACT
Post-menopausal women have a higher risk of developing cardiometabolic dysfunction. Atorvastatin attenuates dyslipidaemia and cardiac dysfunction but it can have undesirable effects including increased risk of diabetes and myalgia. Currently, the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor efficiently reduces low-density lipoprotein cholesterol (LDL-C) levels more effectively than atorvastatin. We have been suggested that PCSK9 inhibitor attenuated cardiometabolic impairment more effectively than atorvastatin in ovariectomized prediabetic rats. Female Wistar rats (n = 48) were fed a normal diet (ND) or high-fat diet (HFD) for 12 weeks. Then, HFD rats were assigned to a sham-operated (Sham) or ovariectomized (OVX) group. Six weeks after surgery, the OVX group was subdivided into 4 treatment groups: vehicle (HFOV), atorvastatin (HFOA) (40 mg/kg/day; s.c.), PCSK9 inhibitor (HFOP) (4 mg/kg/day; s.c.) and oestrogen (HFOE(2)) (50 μg/kg/day; s.c.) for an additional 3 weeks. Metabolic parameters, cardiac and mitochondrial function, and [Ca(2+)](i) transients were evaluated. All HFD rats became obese-insulin resistant. HFS rats had significantly impaired left ventricular (LV) function, cardiac mitochondrial function and [Ca(2+)](i) transient dysregulation. Oestrogen deprivation (HFOV) aggravated all of these impairments. Our findings indicated that the atorvastatin, PCSK9 inhibitor and oestrogen shared similar efficacy in the attenuation in cardiometabolic impairment in ovariectomized prediabetic rats.

[50] *Gan ES, Tan HC, Duyen HLT et al.* **Dengue virus induces PCSK9 expression to alter antiviral responses and disease outcomes**. J Clin Invest 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32644974
ABSTRACT
Dengue virus (DENV) infection requires cholesterol as a pro-viral factor although statin treatment did not show antiviral efficacy in dengue patients. Here, we show that DENV infection manipulates cholesterol metabolism in cells residing in low oxygen microenvironments (hypoxia) such as the liver, spleen and lymph nodes. DENV infection induced proprotein convertase subtilisin/kexin type 9 (PCSK9), which reduces low-density lipoprotein receptor (LDLR) recycling and hence cholesterol uptake. We found that, whereas LDLR uptake would have distributed cholesterol throughout the various cell compartments, de novo cholesterol synthesis enriched this lipid in the endoplasmic reticulum (ER). With cholesterol enrichment in the ER, ER-resident STING and type-I interferon (IFN) activation were repressed during DENV infection. Our in vitro findings were further supported by the finding of elevated plasma PCSK9 levels in dengue patients with high viremia and increased severity of plasma leakage. Our findings thus suggest PCSK9 plays a hitherto unrecognized role in dengue pathogenesis and therefore PCSK9 inhibitors could be a suitable host-directed treatment for dengue patients.

[51] *Martinsen MH, Klausen IC, Tybjaerg-Hansen A, Hedegaard BS*. **Autosomal recessive hypercholesterolemia in a kindred of Syrian ancestry**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32636080

ABSTRACT

Autosomal recessive hypercholesterolemia is a rare genetic disorder due to homozygosity or compound heterozygosity for mutations in the low-density lipoprotein receptor adapter protein 1 gene (LDLRAP1), resulting in elevated low-density lipoprotein cholesterol (LDL-C) levels, large xanthomas, and increased cardiovascular risk. Here, we describe a Danish family of Syrian ancestry carrying a frameshift mutation in LDLRAP1, previously only described in Sardinia and Sicily in Italy and in Spain. In 2 children homozygous for this mutation, we evaluate the effect of long-term lipid-lowering treatment with atorvastatin as monotherapy or in combination with ezetimibe. At referral to the lipid clinic at Viborg Regional Hospital, 3 of 4 children had LDL-C levels of 468, 538, and 371 mg/dL, respectively, with 1 child already showing cutaneous xanthomas at 10 years of age. For comparison, the fourth child and the parents had LDL-C levels of 85, 116, and 124 mg/dL. Genetic testing revealed that all 3 children with severely elevated LDL-C were homozygous for a rare frameshift mutation in LDLRAP1, p.His144GlnfsTer27 (c.431dupA), whereas the fourth child and both parents were heterozygous for this mutation. Lipid-lowering treatment was started in the 2 oldest children (at 10 and 7 years of age). Atorvastatin (40 mg/d) combined with ezetimibe (10 mg/d) reduced LDL-C by 75% in the first child and resulted in near-complete regression of xanthomas. In the second child, atorvastatin (40 mg/d) as monotherapy reduced LDL-C by 61%. Both regimens were superior to treatment with pravastatin as monotherapy (20 mg/d) and to pravastatin in combination with cholestyramine (2 g twice daily). High-intensity statin therapy alone or in combination with ezetimibe resulted in marked reductions in LDL-C in 2 children homozygous for a rare frameshift mutation in LDLRAP1 and lead to regression of large xanthomas.

[52] *Greco MF, Sirtori CR, Corsini A et al.* **Lipoprotein(a) Lowering-From Lipoprotein Apheresis to Antisense Oligonucleotide Approach**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32635396

ABSTRACT

It is well-known that elevated lipoprotein(a)-Lp(a)-levels are associated with a higher risk of cardiovascular (CV) mortality and all-cause mortality, although a standard pharmacotherapeutic approach is still undefined for patients with high CV risk dependent on hyperlipoproteinemia(a). Combined with high Lp(a) levels, familial hypercholesterolemia (FH) leads to a greater CVD risk. In suspected FH patients, the proportion of cases explained by a rise of Lp(a) levels ranges between 5% and 20%. In the absence of a specific pharmacological approach able to lower Lp(a) to the extent required to achieve CV benefits, the most effective strategy today is lipoprotein apheresis (LA). Although limited, a clear effect on Lp(a) is exerted by PCSK9 antagonists, with apparently different mechanisms when given with statins (raised catabolism) or as monotherapy (reduced production). In the era of RNA-based therapies, a new dawn is represented by the use of antisense oligonucleotides APO(a)L(rx), able to reduce Lp(a) from 35% to over 80%, with generally modest injection site reactions. The improved knowledge of Lp(a) atherogenicity and possible prevention will be of benefit for patients with residual CV risk remaining after the most effective available lipid-lowering agents.

[53] *Meier R, Rachamin Y, Rosemann T, Markun S*. **The Impact of the 2019 European Guideline for Cardiovascular Risk Management: A Cross-Sectional Study in General Practice**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32645925

ABSTRACT
The aim of this study was to assess the impact of the 2019 published European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guideline on cardiovascular (CV) risk management compared with its predecessor from 2016 in a cohort in general practice. We performed a cross-sectional retrospective study with data from electronic medical records. The study cohort included 103,351 patients with known CV risk. We assessed changes in CV risk classification and low-density lipoprotein cholesterol (LDL-C) target values, the impact on LDL-C achievement rates, and the current lipid-lowering treatments. Under the 2019 ESC guideline, CV risk categories changed in 27.5% of patients, LDL-C target levels decreased in 71.4% of patients, and LDL-C target achievement rate dropped from 31.1% to 16.5%. Among non-achievers according to the 2019 guideline, 52.2% lacked lipid-lowering drugs entirely, and 41.5% had conventional drugs at a submaximal intensity. Of patients in the high-risk and very high-risk categories, at least 5% failed to achieve the LDL-C target level despite treatment at maximal intensity with conventional lipid-lowering drugs, making them eligible for PCSK-9 inhibitors. In conclusion, the 2019 ESC/EAS guideline lowered LDL-C target values for the majority of patients in general practice and halved LDL-C target achievement rates. There is still a large undeveloped potential to lower CV risk by introducing conventional lipid-lowering drugs, particularly in patients at high or very high CV risk. A substantial proportion of the patients can only achieve their LDL-C targets using PCSK-9 inhibitors, which would currently require an at least 10-fold increase in prescribing of these drugs.

[54] *Tu L, Wu X, Wang X, Shi W*. **Effects of fish oil replacement by blending vegetable oils in fattening diets on nonvolatile taste substances of swimming crab (Portunus trituberculatus)**. J Food Biochem 2020:e13345.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32627848

ABSTRACT
A 45-day fattening trial was conducted using iso-nitrogenous and iso-fatty fattening diets, among which 0%, 25%, 50%, 75%, and 100% of fish oil were, respectively, replaced by blending vegetable oils (canola oil: soybean oil = 1:1), recorded as Diet 1 ~ Diet 5, respectively. The results showed that the meat of crabs (150 ± 25 g) cultured by five fattening feed were distinguished effectively with the electronic tongue. The total free amino acids and taste nucleotides in the meat of crab cultured by Diet 1 were higher than others. The contents of betaine (taste activity value <1) and umami amino acids in the meat of Diet 3 were highest. The contents of sweet amino acids in the meat of crab cultured by Diet 5 was the highest among the different diet. The equivalent umami concentration of Diet 1 was the highest, suggesting that the umami taste is better. In conclusion, 50% of fish oil could be replaced by vegetable oil in fattening feeds. PRACTICAL APPLICATIONS: This paper provided technical support for blending vegetable oils instead of fish oil in fattening feed for swimming crab by using electronic tongue, automatic amino acid analysis, and high performance liquid chromatography to research the changes in the contents of free amino acids, nucleotides, and betaine in female meat of swimming crab, and the taste impacts were evaluated by taste activity values and equivalent umami concentration methods.

[55] *Carmena R, Ascaso JF, Redon J*. **Chronic kidney disease as a cardiovascular risk factor**. Journal of hypertension 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32649622
ABSTRACT
: Chronic kidney disease (CKD) is a public health threat with impact in cardiovascular risk. All forms of cardiovascular disease and mortality are more common in CKD. Treatment of cardiovascular risk factors, hypertension, dyslipidemia and diabetes is essential for cardiovascular and kidney protection. CKD is a marker of high or very high cardiovascular risk and its presence require early treatment and specific goals. Lifestyle is a pivotal factor, stopping smoking, reducing weight in the overweight or obese, starting regular physical exercise and healthy dietary pattern are recommended. Office BP should be lowered towards 130/80 mmHg or even lower if tolerated with sodium restriction and single pill combination, including angiotensin system blocker. Out-of-office BP monitoring, mainly 24-h assessment, is recommended. Diabetes requires treatment from the moment of diagnosis, but prediabetes benefits with lifestyle changes and metformin in patients stage 2 and 3a. iSGLT2 and GLP-1RA are initially recommended in T2D patients with high or very high cardiovascular risk. Concerning dyslipidemia, for patients in stage 4, LDL-C 55 mg/dl or less (1.4 mmol/l) and an LDL-C reduction of 50% or less from baseline is recommended. In stage 3, LDL-C goal is 70 mg/dl or less (1.8 mmol/l) and an LDL-C. reduction of at least 50% from baseline. Statins are the lipid-lowering therapy of choice with or without ezetimibe. Higher doses of statins are required as GFR declines. Available evidence suggests that combined PCSK9 inhibitors with maximally tolerated dose of statins may have an emerging role in treatment of dyslipidemia in CKD patients.

[56] *Overton ET, Kantor A, Fitch KV et al.* **An Evaluation of Baseline Kidney Function in the REPRIEVE Trial of Pitavastatin in Human Immunodeficiency Virus**. The Journal of infectious diseases 2020; 222:S41-s51.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32645164
ABSTRACT
BACKGROUND: Chronic kidney disease is a common comorbid condition among persons living with human immunodeficiency virus (PWH). We characterized baseline kidney function in the REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV) trial cohort. METHODS: REPRIEVE enrolled PWH with low to moderate cardiovascular risk based on traditional risk factors to evaluate the effect of statin therapy on cardiovascular events. We determined baseline estimated glomerular filtration rate (eGFR) with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), Modification of Diet in Renal Disease, and Cockcroft-Gault equations, and we evaluated baseline factors associated with eGFR <90 mL/min/1.73 m2 by logistic regression. We performed Bland-Altman plots and scatterplots to assess agreement between equations. RESULTS: Among 7770 participants enrolled, the median age was 50 years, 31% were female (natal sex), 43% black or African American and 15% Asian, the median body mass index (calculated as calculated as weight in kilograms divided by height in meters squared) was 25.8, and the median CD4 cell count 620/μL. The median CKD-EPI eGFR was 97 mL/min/1.73 m2, and 38% had an eGFR <90 mL/min/1.73 m2. In the adjusted model, factors associated with eGFR <90 mL/min/1.73 m2 included white race, older age, higher body mass index, high-income region of enrollment, hypertension, and tenofovir

disoproxil fumarate. The CKD-EPI and Modification of Diet in Renal Disease equations demonstrated strong agreement, particularly at lower eGFR values. Overall, there was 56% concordance between the 3 equations (categories <60, 60 to <90, ≥90 mL/min), improving to 73% after accounting for individual body surface area. CONCLUSIONS: REPRIEVE enrolled a diverse cohort including a substantial number of PWH with reduced kidney function. Factors associated with reduced eGFR included traditional risk factors and tenofovir disoproxil fumarate exposure. Three commonly used equations have only fair agreement, with potential implications for both clinical care and epidemiologic studies. CLINICAL TRIALS REGISTRATION: NCT02344290.

[57] *Bai Y, Huang R, Wan L, Zhao R*. **Association between CYP2C19 gene polymorphisms and lipid metabolism in Chinese patients with ischemic stroke**. J Int Med Res 2020; 48:300060520934657.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32644829
ABSTRACT
OBJECTIVE: The CYP2C19 genetic variation may be involved in the development of atherosclerotic cardiovascular disease (ASCVD). Serum lipid levels are important risk factors for ASCVD, but the effect of the CYP2C19 gene on serum lipid metabolism remains unclear. This retrospective cohort study investigated the relationship between the CYP2C19 gene polymorphism and serum lipid levels in patients with ischemic stroke (IS). METHODS: IS patients (n = 230) and control subjects (n = 100) were enrolled. All patients were diagnosed with IS via clinical manifestations and brain magnetic resonance imaging. All patients were genotyped. RESULTS: Triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c), and apolipoprotein B (ApoB) levels were significantly higher and high-density lipoprotein-cholesterol (HDL-c) and apolipoprotein A(1) (ApoA(1)) levels were significantly lower in the IS group compared with the control group. Lower ApoA(1) levels and higher ApoB levels were significant predictive factors for IS. Patients with higher ApoB levels had a higher risk of IS recurrence. Compared with extensive metabolizers, intermediate and poor CYP2C19 metabolizers had a higher risk of IS recurrence. CONCLUSIONS: Our study indicates CYP2C19 gene polymorphisms are related to lipid metabolism in patients with IS. IS patients who are poor CYP2C19 metabolizers may have a higher risk of disease recurrence.

[58] *Sawalha K, Kunnumpurath A, Kamoga GR*. **The Efficacy of Intravenous Insulin Infusion in the Management of Hypertriglyceridemia-Induced Pancreatitis in a Rural Community Hospital**. Journal of investigative medicine high impact case reports 2020; 8:2324709620940492.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32643965
ABSTRACT
A 28-year-old female presented to the emergency room with epigastric pain, nausea, and vomiting; her lipase was elevated, and computed tomography of abdomen showed evidence of acute pancreatitis. Her past medical history was significant for poorly controlled insulin requiring type 2 diabetes mellitus and 2 previous admissions for hypertriglyceridemia-induced pancreatitis. Due to the severity of her pancreatitis presentation, she was admitted to the intensive care unit. She received aggressive intravenous fluid hydration and was started on an insulin drip. Apheresis was strongly considered given the degree of her hypertriglyceridemia (11 602 mg/dL), but there was no timely access to this treatment option. She, however,

significantly improved with insulin therapy alone. Her triglyceride levels decreased rather quickly to 4783 mg/dL within 24 hours and by the fourth day of admission were comfortably <1000 mg/dL with insulin infusion along with clinical improvement. She was discharged on niacin and insulin therapy along with her home medications of statin and fenofibrate.

[59] *Adam RC, Mintah IJ, Alexa-Braun CA et al.* **Angiopoietin-like protein 3 (ANGPTL3) governs LDL-cholesterol levels through endothelial lipase-dependent VLDL clearance**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32646941
ABSTRACT
Angiopoietin-like protein 3 (ANGPTL3) regulates plasma lipids by inhibiting lipoprotein lipase (LPL) and endothelial lipase (EL). ANGPTL3 inactivation lowers LDL-cholesterol (LDL-C) independently of the classical LDL-receptor (LDLR)-mediated pathway and represents a promising therapeutic approach for individuals with homozygous familial hypercholesterolemia due to LDLR mutations. Yet, how ANGPTL3 regulates LDL-C levels is unknown. Here, we demonstrate in hyperlipidemic humans and mice that ANGPTL3 controls VLDL catabolism upstream of LDL. Using kinetic, lipidomic and biophysical studies, we show that ANGPTL3 inhibition reduces VLDL-lipid content and size, generating remnant particles that are efficiently removed from the circulation. This suggests that ANGPTL3 inhibition lowers LDL-C by limiting LDL particle production. Mechanistically, we discovered that EL is a key mediator of ANGPTL3's novel pathway. Our experiments revealed that, although dispensable in the presence of LDLR, EL-mediated processing of VLDL becomes critical for LDLR-independent particle clearance. In the absence of EL and LDLR, ANGPTL3 inhibition perturbed VLDL catabolism, promoted accumulation of atypical remnants, and failed to reduce LDL-C. Taken together, we uncover ANGPTL3 at the helm of a novel EL-dependent pathway that lowers LDL-C in the absence of LDLR.

[60] *Thompson GR*. **FH through the Retrospectoscope**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32651185
ABSTRACT
AbstractAfter training as a gastroenterologist in the UK the author became interested in lipidology while he was a research fellow in the USA and switched careers after returning home. Together with Nick Myant he introduced the use of plasma exchange to treat FH homozygotes and undertook non-steady state studies of LDL kinetics, which showed that the fractional catabolic rate of LDL remained constant irrespective of pool size. Subsequent steady-state turnover studies showed that FH homozygotes had an almost complete lack of receptor-mediated LDL catabolism, providing in vivo confirmation of the Nobel Prize-winning discovery by Goldstein and Brown that LDL receptor dysfunction was the cause of FH. Further investigation of metabolic defects in FH revealed that a significant proportion of LDL in homozygotes and heterozygotes was produced directly via a VLDL-independent pathway.Management of heterozygous FH has been greatly facilitated by statins and PCSK9 inhibitors but remains dependent upon lipoprotein apheresis in homozygotes. In a recent analysis of a large cohort treated with a combination of lipid-lowering measures survival was markedly enhanced in homozygotes in the lowest quartile of on-treatment serum cholesterol. Emerging therapies could further improve the prognosis of homozygous FH whereas in heterozygotes the current need is better detection.

[61] *Chowdhury MH, Ghosh S, Kabir MR et al.* **Effect of supplementary omega-3 fatty acids on pregnant women with complications and pregnancy outcomes: review from literature**. The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet 2020:1-17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32643471
ABSTRACT
Numerous benefits have been associated with omega-3 fatty acid consumption during pregnancy and the postpartum period, whether it is consumed in the diet with seafood or via supplements such as fish oil. This review primarily aimed to assess the current situation of the impact of omega-3 long-chain Poly Unsaturated Fatty Acid (PUFA) supplementation on the outcomes of pregnancy. The electronic search of Medline, PubMed, Public Library of Science (PLOS) and Google Scholar databases was carried out for papers from 01 February 1995 to 01 March 2017 using keywords such as "pregnancy," "supplement," "long-chain polyunsaturated fatty acids," "omega 3 fatty acids," and "clinical trials." Out of twenty-six studies, both observational and interventional, fourteen studies found the influence of omega 3 fatty acids during pregnancy or the early postpartum period on the duration of gestation and infant size at birth, preeclampsia, depression, and infant visual function and neurodevelopment have been reported. Omega 3 fatty acid intakes (both in terms of absolute amounts of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) and the ratio of these 2 fatty acids) varied widely in these studies, however, and no clear consensus exists regarding the effects of omega 3 fatty acids on any of these outcomes. Because of the potential importance of these fatty acids for pregnant or lactating women, fetus, and newborn infants and the limited data from clinical trials assessing the effect of these fatty acids on pregnancy and infant outcomes, additional research is required to better define optimal intakes of specific omega 3 fatty acids during these critical periods.

[62] *Okosun IS, Nkemjika S, Okosun B et al.* **Lifestyle Modification Practices and Drug Prescription Use in Elderly Americans with Metabolic Syndrome: A Nationwide Population-Based Study**. Journal of the National Medical Association 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641256
ABSTRACT
AIM: To determine differences in lifestyle modification practices and use of prescription drugs in a representative sample of Mexican American (MA), non-Hispanic White (NHW), and non-Hispanic Black (NHB) elderly Americans with metabolic syndrome (MetS). METHODS: Data from the United States National Health and Nutritional Examination Surveys were used in this study. Lifestyle modification practices include ongoing physical activity, weight control, and ongoing diet modifications. Prescription drugs include anti-diabetic, anti-obesity, lipid-lowering, insulin sensitizers, renin-angiotensin system (RAS) blockers, fibrates, and cilostazol. Race/ethnic-specific prevalence odds ratios from the multivariate logistic regression analyses were used to determine associations between selected independent variables and MetS control (defined as the use of lifestyle modification practices or prescription drugs), adjusting for covariates. RESULTS: The rates of ongoing weight control (73.4% versus 68.1% in MA and 66.3% in NHW) and diet modification practices (78.1% versus 77.4% in MA and 66.7% in NHW) were higher among NHB, and rate of ongoing physical activity (61.8% versus 52.8% in

NHW and 56.4% in NHB) was higher among MA participants compared to their other racial/ethnic elderly counterparts (P < 0.001). Lipid-lowering and insulin-sensitizing drugs were the most commonly used prescription drugs in the last 30 days. The prevalence of nonuse of lifestyle modification practices or prescription drugs for MetS management was 15.1%, 21.3%, and 12.7% in MA, NHW, and NHB participants, respectively. MA, NHB race/ethnicity, a higher level of education, and increased BMI were significantly associated with increased odds of MetS control. Lack of drug prescription insurance and increased age were associated with decreased odds of MetS control. CONCLUSIONS: Given the clinical importance of MetS, improving knowledge-based health decisions relative to lifestyle modification practices is very important. Moreover, sources of low-cost medications that links elderly patients with drug prescription coverage programs may help to improve the management of MetS.

[63] *Orkaby AR, Driver JA, Ho YL et al.* **Association of Statin Use With All-Cause and Cardiovascular Mortality in US Veterans 75 Years and Older**. Jama 2020; 324:68-78.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32633800

ABSTRACT

IMPORTANCE: Data are limited regarding statin therapy for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in adults 75 years and older. OBJECTIVE: To evaluate the role of statin use for mortality and primary prevention of ASCVD in veterans 75 years and older. DESIGN, SETTING, AND PARTICIPANTS: Retrospective cohort study that used Veterans Health Administration (VHA) data on adults 75 years and older, free of ASCVD, and with a clinical visit in 2002-2012. Follow-up continued through December 31, 2016. All data were linked to Medicare and Medicaid claims and pharmaceutical data. A new-user design was used, excluding those with any prior statin use. Cox proportional hazards models were fit to evaluate the association of statin use with outcomes. Analyses were conducted using propensity score overlap weighting to balance baseline characteristics. EXPOSURES: Any new statin prescription. MAIN OUTCOMES AND MEASURES: The primary outcomes were all-cause and cardiovascular mortality. Secondary outcomes included a composite of ASCVD events (myocardial infarction, ischemic stroke, and revascularization with coronary artery bypass graft surgery or percutaneous coronary intervention). RESULTS: Of 326 981 eligible veterans (mean [SD] age, 81.1 [4.1] years; 97% men; 91% white), 57 178 (17.5%) newly initiated statins during the study period. During a mean follow-up of 6.8 (SD, 3.9) years, a total 206 902 deaths occurred including 53 296 cardiovascular deaths, with 78.7 and 98.2 total deaths/1000 person-years among statin users and nonusers, respectively (weighted incidence rate difference [IRD]/1000 person-years, -19.5 [95% CI, -20.4 to -18.5]). There were 22.6 and 25.7 cardiovascular deaths per 1000 person-years among statin users and nonusers, respectively (weighted IRD/1000 person-years, -3.1 [95 CI, -3.6 to -2.6]). For the composite ASCVD outcome there were 123 379 events, with 66.3 and 70.4 events/1000 person-years among statin users and nonusers, respectively (weighted IRD/1000 person-years, -4.1 [95% CI, -5.1 to -3.0]). After propensity score overlap weighting was applied, the hazard ratio was 0.75 (95% CI, 0.74-0.76) for all-cause mortality, 0.80 (95% CI, 0.78-0.81) for cardiovascular mortality, and 0.92 (95% CI, 0.91-0.94) for a composite of ASCVD events when comparing statin users with nonusers. CONCLUSIONS AND RELEVANCE: Among US veterans 75 years and older and free of ASCVD at baseline, new statin use was significantly associated with a lower risk of all-cause and cardiovascular mortality. Further research, including from

randomized clinical trials, is needed to more definitively determine the role of statin therapy in older adults for primary prevention of ASCVD.

[64] *Puri R, Nissen SE, Arsenault BJ et al.* **Effect of C-Reactive Protein on Lipoprotein(a)-Associated Cardiovascular Risk in Optimally Treated Patients With High-Risk Vascular Disease: A Prespecified Secondary Analysis of the ACCELERATE Trial**. JAMA cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32639518

ABSTRACT
IMPORTANCE: Although lipoprotein(a) (Lp[a]) is a causal genetic risk factor for atherosclerotic cardiovascular disease, it remains unclear which patients with established atherosclerotic cardiovascular disease stand to benefit the most from Lp(a) lowering. Whether inflammation can modulate Lp(a)-associated cardiovascular (CV) risk during secondary prevention is unknown. OBJECTIVE: To examine whether Lp(a)-associated CV risk is modulated by systemic inflammation in optimally treated patients at high risk of CV disease. DESIGN, SETTING, AND PARTICIPANTS: A prespecified secondary post hoc analysis of the double-blind, multicenter randomized clinical Assessment of Clinical Effects of Cholesteryl Ester Transfer Protein Inhibition With Evacetrapib in Patients at a High Risk for Vascular Outcomes (ACCELERATE) trial was conducted between October 1, 2012, and December 31, 2013; the study was terminated October 12, 2015. The study was conducted at 543 academic and community hospitals in 36 countries among 12 092 patients at high risk of CV disease (acute coronary syndrome, stroke, peripheral arterial disease, or type 2 diabetes with coronary artery disease) with measurable Lp(a) and high-sensitivity C-reactive protein (hsCRP) levels during treatment. Statistical analysis for this post hoc analysis was performed from September 26, 2018, to March 28, 2020. INTERVENTIONS: Participants received evacetrapib, 130 mg/d, or matching placebo. MAIN OUTCOMES AND MEASURES: The ACCELERATE trial found no significant benefit or harm of evacetrapib on 30-month major adverse cardiovascular events (CV death, myocardial infarction [MI], stroke, coronary revascularization, or hospitalization for unstable angina). This secondary analysis evaluated rates of CV death, MI, and stroke across levels of Lp(a). RESULTS: High-sensitivity C-reactive protein and Lp(a) levels were measured in 10 503 patients (8135 men; 8561 white; 10 134 received concurrent statins; mean [SD] age, 64.6 [9.4] years). In fully adjusted analyses, in patients with hsCRP of 2 mg/L or more but not less than 2 mg/L, increasing quintiles of Lp(a) were significantly associated with greater rates of death, MI, and stroke (P = .006 for interaction). Each unit increase in log Lp(a) levels was associated with a 13% increased risk of CV death, nonfatal MI, or stroke only in those with hsCRP levels of 2 mg/L or more (P = .008 for interaction). There was also a significant stepwise relationship between increasing Lp(a) quintiles and time to first CV death, MI, or stroke (log-rank P < .001) when hsCRP levels were 2 mg/L or more but not less than 2 mg/L. Sensitivity analyses in the ACCELERATE placebo-treated group yielded similar significant associations exclusively in the group with hsCRP of 2 mg/L or more. CONCLUSIONS AND RELEVANCE: Elevated Lp(a) levels during treatment are related to CV death, MI, and stroke when hsCRP levels are 2 mg/L or more but not less than 2mg/L. This finding suggests a potential benefit of lowering Lp(a) in patients with residual systemic inflammation despite receipt of optimal medical therapy. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT01687998.

[65] *Senatus L, López-Díez R, Egaña-Gorroño L et al.* **RAGE impairs murine diabetic atherosclerosis regression and implicates IRF7 in macrophage inflammation and cholesterol metabolism**. JCI insight 2020; 5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641587
ABSTRACT
Despite advances in lipid-lowering therapies, people with diabetes continue to experience more limited cardiovascular benefits. In diabetes, hyperglycemia sustains inflammation and preempts vascular repair. We tested the hypothesis that the receptor for advanced glycation end-products (RAGE) contributes to these maladaptive processes. We report that transplantation of aortic arches from diabetic, Western diet-fed Ldlr-/- mice into diabetic Ager-/- (Ager, the gene encoding RAGE) versus WT diabetic recipient mice accelerated regression of atherosclerosis. RNA-sequencing experiments traced RAGE-dependent mechanisms principally to the recipient macrophages and linked RAGE to interferon signaling. Specifically, deletion of Ager in the regressing diabetic plaques downregulated interferon regulatory factor 7 (Irf7) in macrophages. Immunohistochemistry studies colocalized IRF7 and macrophages in both murine and human atherosclerotic plaques. In bone marrow-derived macrophages (BMDMs), RAGE ligands upregulated expression of Irf7, and in BMDMs immersed in a cholesterol-rich environment, knockdown of Irf7 triggered a switch from pro- to antiinflammatory gene expression and regulated a host of genes linked to cholesterol efflux and homeostasis. Collectively, this work adds a new dimension to the immunometabolic sphere of perturbations that impair regression of established diabetic atherosclerosis and suggests that targeting RAGE and IRF7 may facilitate vascular repair in diabetes.

[66] *Cho JM, Chae J, Jeong SR et al.* **The cholesterol-lowering effect of unripe Rubus coreanus is associated with decreased oxidized LDL and apolipoprotein B levels in subjects with borderline-high cholesterol levels: a randomized controlled trial**. Lipids in health and disease 2020; 19:166.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32646501
ABSTRACT
BACKGROUND: Rubus coreanus (R. coreanus) possesses properties that may decrease cholesterol levels. METHODS: The effects of unripe R. coreanus (uRC) consumption on low-density lipoprotein (LDL) and total cholesterol levels related to decreased circulating apolipoprotein (Apo) B and oxidized LDL levels were evaluated. This randomized, double-blind, placebo-controlled study included subjects with borderline-high cholesterol levels (between 200 and 239 mg/dL) who consumed one capsule daily containing 600 mg of freeze-dried uRC extract (n = 39) or the placebo (n = 38). RESULTS: After 12 weeks, the uRC group showed reductions of 21.23 ± 4.36 mg/dL in total cholesterol levels (P = 0.007) and 15.61 ± 4.16 mg/dL in LDL cholesterol levels (P = 0.032). In addition, significantly greater reductions in Apo B levels were observed in the uRC group (- 3.48 ± 3.40 mg/dL), but Apo B levels were increased in the placebo group (6.21 ± 2.84 mg/dL; P = 0.032). Furthermore, a remarkably lower oxidized LDL level was detected in the uRC group (57.76 ± 2.07 U/L) than in the placebo group (66.09 ± 3.47 U/L) after 12 weeks of consumption (P = 0.044). CONCLUSIONS: Because of its cholesterol-lowering effect, uRC shows great promise as a therapeutic agent for subjects with borderline-high total blood cholesterol levels. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03649620 (8/28/2018, retrospectively registered).

[67] *Li Y, Yun K, Mu R*. **A review on the biology and properties of adipose tissue macrophages involved in adipose tissue physiological and pathophysiological processes**. Lipids in health and disease 2020; 19:164.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32646451
ABSTRACT
Obesity exhibits a correlation with metabolic inflammation and endoplasmic reticulum stress, promoting the progression of metabolic disease such as diabetes, hyperlipidemia, hyperuricemia and so on. Adipose tissue macrophages (ATMs) are central players in obesity-associated inflammation and metabolic diseases. Macrophages are involved in lipid and energy metabolism and mitochondrial function in adipocytes. Macrophage polarization is accompanied by metabolic shifting between glycolysis and mitochondrial oxidative phosphorylation. Here, this review focuses on macrophage metabolism linked to functional phenotypes with an emphasis on macrophage polarization in adipose tissue physiological and pathophysiological processes. In particular, the interplay between ATMs and adipocytes in energy metabolism, glycolysis, OXPHOS, iron handing and even interactions with the nervous system have been reviewed. Overall, the understanding of protective and pathogenic roles of ATMs in adipose tissue can potentially provide strategies to prevent and treat obesity-related metabolic disorders.

[68] *Qiu W, Chen J, Huang X, Guo J*. **The analysis of the lipid levels in patients with coronary artery disease after percutaneous coronary intervention: a one-year follow-up observational study**. Lipids in health and disease 2020; 19:163.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32631347
ABSTRACT
BACKGROUND: Coronary heart disease (CHD) is one of the leading causes of death worldwide. Percutaneous coronary intervention (PCI) has been an important technology for the treatment of CHD. Blood lipid management is critical for PCI patients because not only should local vascular pathological changes be considered but the whole atherosclerotic process should be considered as well. METHODS: A total of 522 patients diagnosed with CHD (including acute myocardial infarction and unstable angina) successfully underwent stent implantation in acute or elective PCI in the cardiology department of one general hospital in Guangzhou from June 2015 to December 2017. The 2016 Chinese Guideline for the Management of dyslipidaemia in Adults and the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report (NCEP-ATP III) were used to classify total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) levels. RESULTS: A total of 522 patients were recruited for the study. The mean values of TC, TG, LDL-C, and HDL-C at baseline were 4.76, 1.80, 2.93 and 1.03 mmol/L, respectively. After 1 year of follow-up, the mean values of TC, TG, LDL-C, and HDL-C were 3.94, 1.62, 2.26 and 1.01 mmol/L, respectively. The prevalence of high TC, high TG, high LDL-C and low HDL-C at baseline was 12.05, 21.80, 10.90 and 56.79%, respectively, and the prevalence at follow-up was 4.59, 15.68, 3.25 and 59.85%, respectively. Logistic regression revealed that gender was risk factor for high TC (≥ 6.22 mmol/L), low HDL-C (< 1.04 mmol/L) and high LDL-C (≥ 4.14 mmol/L) at follow-up. Age was the factor associated with high TG (≥ 2.26 mmol/L) and low HDL-C (< 1.04 mmol/L) at follow-up. Besides, smoking

and diet control were risk factors for low HDL-C (< 1.04 mmol/L) and high LDL-C (≥ 4.14 mmol/L) at follow-up, respectively. CONCLUSION: The patients with PCI at follow-up experienced lower mean values of lipids and prevalence of dyslipidaemia than those at baseline. Gender, age, smoking and diet control were the risk factors associated with elevated lipids. Improvement in lipid management at follow up demonstrated that such intervention can be effective.

[69] *Yagin NL, Hajjarzadeh S, Aliasgharzadeh S et al.* **The association of dietary patterns with endocannabinoids levels in overweight and obese women**. Lipids in health and disease 2020; 19:161.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32631352
ABSTRACT
BACKGROUND: Higher levels of anandamide (AEA) and 2-arachidonoylglycerol (2-AG), the main arachidonic acid-derived endocannabinoids, are frequently reported in overweight and obese individuals. Recently, endocannabinoids have become a research interest in obesity area regarding their role in food intake. The relationship between dietary patterns and endocannabinoids is poorly understood; therefore, this study evaluated the association of the dietary patterns with AEA and 2-AG levels in overweight and obese women. METHODS: In this cross sectional study, 183 overweight and obese females from Tabriz, Iran who aged between 19 and 50 years old and with mean BMI = 32.44 ± 3.79 kg/m(2) were interviewed. The AEA and 2-AG levels were measured, and the dietary patterns were assessed using food frequency questionnaire. To extract the dietary patterns, factor analysis was applied. The association between AEA and 2-AG levels and dietary patterns was analyzed by linear regression. RESULTS: Three major dietary patterns including "Western", "healthy", and "traditional" were extracted. After adjusting for age, physical activity, BMI, waist circumference, and fat mass, higher levels of AEA and 2-AG were observed in participants who were in the highest quintile of the Western pattern (P < 0.05). Also, in both unadjusted and adjusted models, significantly lower levels of AEA and 2-AG were detected in the women of the highest quintile of the healthy pattern (P < 0.01). Moreover, there was no significant association between "traditional" pattern and AEA and 2- AG levels in both unadjusted and adjusted models (P > 0.05). CONCLUSION: In regard with the lower levels of endocannabinoids in healthy dietary pattern, adherence to healthy pattern might have promising results in regulating endocannabinoids levels.

[70] *Masyuko SJ, Page ST, Kinuthia J et al.* **Metabolic syndrome and 10-year cardiovascular risk among HIV-positive and HIV-negative adults: A cross-sectional study**. Medicine (Baltimore) 2020; 99:e20845.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32629671
ABSTRACT
To determine the prevalence and correlates of metabolic syndrome (MetS) and compare 10-year cardiovascular disease (CVD) risk among Kenyan adults with and without HIV infection.We conducted a cross-sectional study among adults ≥30 years of age with and without HIV infection seeking care at Kisumu County Hospital. Participants completed a health questionnaire and vital signs, anthropomorphic measurements, and fasting blood were obtained. MetS was defined using 2009 Consensus Criteria and 10-year Atherosclerotic CVD (ASCVD) risk score was calculated. Chi-square, independent t tests, Wilcoxon ranksum test

and multivariable logistic regression were used to determine differences and associations between HIV and MetS, CVD risk factors and ASCVD risk score.A total of 300 people living with HIV (PLWHIV) and 298 HIV-negative participants with median age 44 years enrolled, 50% of whom were female. The prevalence of MetS was 8.9% overall, but lower among PLWHIV than HIV-negative participants (6.3% vs 11.6%, respectively; P=.001). The most prevalent MetS components were elevated blood pressure, decreased high density lipoprotein, and abdominal obesity. Adjusting for covariates, PLWHIV were 66% less likely to have MetS compared to HIV-negative participants (adjusted odds ratio [aOR] 0.34; 95% confidence interval [95%CI] 0.18, 0.65; P=.005). Median ASCVD risk score was also lower among PLWHIV compared to HIV-negative participants (1.7% vs 3.0%, P=.002).MetS was more common among HIV-negative than HIV-positive adults, and HIV-negative adults were at greater risk for CVD compared to PLWHIV. These data support integration of routine CVD screening and management into health programs in resource-limited settings, regardless of HIV status.

[71] *Yui K, Imataka G, Sasaki H, Shiroki R*. **The role of lipid peroxidation in individuals with autism spectrum disorders**. Metabolic brain disease 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32643093
ABSTRACT
The role of malondialdehyde-modified low-density lipoprotein (MDA-LDL), an oxidized LDL, in the pathophysiology of autism spectrum disorder (ASD) is unclear. We studied association between MDA-LDL and behavioral symptoms in 11 individuals with ASD and 7 age -matched normal controls. Behavioral symptoms were assessed using the Aberrant Behavior Checklists (ABC). Because small sample size in this study, three measures were conducted: first, employment of adaptive Lasso for enhancing the accuracy of prediction and interpretability; second, calculation of coefficient of variation for an appropriate selection of plasma variables; and third, selection of good candidates of plasma variables. Plasma levels of MDA-LDL, eicosapentaenoic acid, docosahexaenoic acid (DHA) and DHA/arachidonic acid ratios were significantly higher, while plasma superoxide dismutase (SOD) levels were significantly lower in the ASD group than in the control group. The total ABC scores were significantly higher in the ASD group than in the control group. Multiple linear regression analysis and the adaptive Lasso revealed association of increased plasma DHA levels with the ABC total scores and increased plasma MDA-LDL levels. Such association between DHA and plasma MDA-LDL levels may contribute to behavior in individuals with ASD.

[72] *Evans RJ, Lavin B, Phinikaridou A et al.* **Targeted Molecular Iron Oxide Contrast Agents for Imaging Atherosclerotic Plaque**. Nanotheranostics 2020; 4:184-194.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32637296
ABSTRACT
Overview: Cardiovascular disease remains a leading cause of death worldwide, with vulnerable plaque rupture the underlying cause of many heart attacks and strokes. Much research is focused on identifying an imaging biomarker to differentiate stable and vulnerable plaque. Magnetic Resonance Imaging (MRI) is a non-ionising and non-invasive imaging modality with excellent soft tissue contrast. However, MRI has relatively low sensitivity (micromolar) for contrast agent detection compared to nuclear imaging techniques. There is also an increasing emphasis on developing MRI probes that are not based on gadolinium

chelates because of increasing concerns over associated systemic toxicity and deposits(1). To address the sensitivity and safety concerns of gadolinium this project focused on the development of a high relaxivity probe based on superparamagnetic iron oxide nanoparticles for the imaging of atherosclerotic plaque with MRI. With development, this may facilitate differentiating stable and vulnerable plaque in vivo. Aim: To develop a range of MRI contrast agents based on superparamagnetic iron oxide nanoparticles (SPIONs), and test them in a murine model of advanced atherosclerosis. Methods: Nanoparticles of four core sizes were synthesised by thermal decomposition and coated with poly(maleicanhydride-alt-1-octadecene) (PMAO), poly(ethyleneimine) (PEI) or alendronate, then characterised for core size, hydrodynamic size, surface potential and relaxivity. On the basis of these results, one candidate was selected for further studies. In vivo studies using 10 nm PMAO-coated SPIONs were performed in ApoE (-/-) mice fed a western diet and instrumented with a perivascular cuff on the left carotid artery. Control ApoE (-/-) mice were fed a normal chow diet and were not instrumented. Mice were scanned on a 3T MR scanner (Philips Achieva) with the novel SPION contrast agent, and an elastin-targeted gadolinium agent that was shown previously to enable visualisation of plaque burden. Histological analysis was undertaken to confirm imaging findings through staining for macrophages, CX3CL1, elastin, tropoelastin, and iron. Results: The lead SPION agent consisted of a 10 nm iron oxide core with poly(maleicanhydride-alt-1-octadecene), (-36.21 mV, r(2) 18.806 mmol(-1)/s(-1)). The irregular faceting of the iron oxide core resulted in high relaxivity and the PMAO provided a foundation for further functionalisation on surface -COOH groups. The properties of the contrast agent, including the negative surface charge and hydrodynamic size, were designed to maximise circulation time and evade rapid clearance through the renal system or phagocytosis. In vitro testing showed that the SPION agent was non-toxic. In vivo results show that the novel contrast agent accumulates in similar vascular regions to a gadolinium-based contrast agent (Gd-ESMA) targeted to elastin, which accumulates in plaque. There was a significant difference in SPION signal between the instrumented and the contralateral non-instrumented vessels in diseased mice ($p = 0.0411$, student's t-test), and between the instrumented diseased vessel and control vessels ($p = 0.0043$, 0.0022, student's t-test). There was no significant difference between the uptake of either contrast agent between stable and vulnerable plaques ($p = 0.3225$, student's t-test). Histological verification was used to identify plaques, and Berlin Blue staining confirmed the presence of nanoparticle deposits within vulnerable plaques and co-localisation with macrophages. Conclusion: This work presents a new MRI contrast agent for atherosclerosis which uses an under-explored surface ligand, demonstrating promising properties for in vivo behaviour, is still in circulation 24 hours post-injection with limited liver uptake, and shows good accumulation in a murine plaque model.

[73] *Zhong YH, Zheng BE, He RH et al.* **Serum Levels of HDL Cholesterol are Associated with Diffuse Axonal Injury in Patients with Traumatic Brain Injury**. Neurocritical care 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32642967

ABSTRACT

BACKGROUND: It is well known that lipids are vital for axonal myelin repair. Diffuse axonal injury (DAI) is characterized by widespread axonal injury. The association between serum lipids and DAI is not well known. The purpose of this study was to investigate the associations of serum lipid profile variables (triglycerides, high- and low-density lipoproteins, and total cholesterol) with DAI detected by magnetic resonance imaging (MRI) and with clinical outcome

for patients suffering from traumatic brain injury (TBI). METHODS: This study included 176 patients with a history of TBI who had undergone initial serum lipid measurements within 1 week and brain MRIs within 30 days. Based on MRI findings, patients were divided into negative and positive DAI groups. RESULTS: Of the 176 patients, 70 (39.8%) were assigned to DAI group and 106 (60.2%) patients to non-DAI group. Compared with the non-DAI group, patients with DAI had significantly lower levels of high-density lipoprotein cholesterol (HDL-C) in serum during the first week following TBI. Multivariate analysis identified HDL-C as an independent predictor of DAI. Patients with lower serum HDL-C levels were less likely to regain consciousness within 6 months in TBI patients with DAI lesions identified by MRI. CONCLUSIONS: Plasma levels of HDL-C may be a viable addition to biomarker panels for predicting the presence and prognosis of DAI on subsequent MRI following TBI.

[74] *Akhavan NS, Pourafshar S, Johnson SA et al.* **The Relationship between Protein Intake and Source on Factors Associated with Glycemic Control in Individuals with Prediabetes and Type 2 Diabetes**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32650580
ABSTRACT
Type 2 diabetes (T2D) is a major contributor to morbidity and mortality largely due to increased cardiovascular disease risk. This study examined the relationships among protein consumption and sources on glycemic control and cardiovascular health in individuals with prediabetes and T2D. Sixty-two overweight or obese participants with prediabetes or T2D, aged 45-75 years were stratified into the following three groups based on protein intake: <0.8 g (gram)/kg (kilogram) body weight (bw), ≥0.8 but <1.0 g/kg bw, and ≥1.0 g/kg bw as below, meeting, and above the recommended levels of protein intake, respectively. Body mass, body mass index (BMI), hip circumference (HC), waist circumference (WC), lean mass, and fat mass (FM) were significantly higher in participants who consumed below the recommended level of protein intake as compared with other groups. Higher animal protein intake was associated with greater insulin secretion and lower triglycerides (TG). Total, low-density, and high-density cholesterol were significantly higher in participants who met the recommended protein intake as compared with the other groups. These data suggest that high protein consumption is associated with lower BMI, HC, WC, and FM, and can improve insulin resistance without affecting lipid profiles in this population. Furthermore, higher intake of animal protein can improve β-cell function and lower plasma TG.

[75] *Basora J, Villalobos F, Pallejà-Millán M et al.* **Association between the Potential Influence of a Lifestyle Intervention in Older Individuals with Excess Weight and Metabolic Syndrome on Untreated Household Cohabitants and Their Family Support: The PREDIMED-Plus Study**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32635152
ABSTRACT
This cross-sectional study aims to evaluate the association between the PREDIMED-Plus study lifestyle intervention and (i) adherence to the Mediterranean diet (MedDiet) and (ii) physical activity of cohabiting study participants, and to define the related social characteristics of the household members. Participants were a subsample of 541 cohabitants of the PREDIMED-Plus study. Adherence to the MedDiet, physical activity, anthropometric measurements, family function, and social support were assessed. Multiple linear regressions

were applied to the data. Partners of the PREDIMED-Plus participants had higher adherence to the MedDiet compared to their sons/daughters (9.0 vs. 6.9 points). In comparison to partners with low adherence to the MedDiet, partners with high adherence were older, practiced more physical activity, ate more frequently with the PREDIMED-Plus participants, and had better family function (adaptability item). Compared to physically active partners, very active ones were older, more likely to be women, and had lower BMI and higher adherence to the MedDiet. In addition, they ate more frequently with the PREDIMED-Plus participants and had better family function. Using multiple lineal regressions, an increase in the adherence to the MedDiet of the PREDIMED-Plus participant, and better family function, were positively associated with their partner's adherence to the MedDiet. The PREDIMED-Plus intervention showed a positive association with adherence to the MedDiet of the study participants' partners. In addition, this association was influenced by the social characteristics of the household members.

[76] *Choi YJ, Jeon SM, Shin S*. **Impact of a Ketogenic Diet on Metabolic Parameters in Patients with Obesity or Overweight and with or without Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32640608
ABSTRACT
The aim of this meta-analysis was to explore the efficacy of a ketogenic diet in metabolic control in patients with overweight or obesity and with or without type 2 diabetes. Embase, PubMed, and Cochrane Library were searched for randomized controlled trials that enrolled patients with overweight or obesity on a ketogenic diet for metabolic control. Fourteen studies were included in meta-analysis. The effects of ketogenic diets on glycemic control were greater for diabetic patients relative to those of low-fat diets, indicated by lower glycated hemoglobin (SMD, -0.62; $p < 0.001$) and homeostatic model assessment index (SMD, -0.29; $p = 0.02$), while comparable effects were observed for nondiabetic patients. Ketogenic diets led to substantial weight reduction (SMD, -0.46; $p = 0.04$) irrespective of patients' diabetes status at baseline and improved lipid profiles in terms of lower triglyceride (SMD, -0.45; $p = 0.01$) and greater high-density lipoprotein (SMD, 0.31; $p = 0.005$) for diabetic patients. Other risk markers showed no substantial between-group difference post intervention. Our study findings confirmed that ketogenic diets were more effective in improving metabolic parameters associated with glycemic, weight, and lipid controls in patients with overweight or obesity, especially those with preexisting diabetes, as compared to low-fat diets. This effect may contribute to improvements in metabolic dysfunction-related morbidity and mortality in these patient populations.

[77] *Sánchez-García A, Simental-Mendía M, Millán-Alanís JM, Simental-Mendía LE*. **Effect of sodium-glucose co-transporter 2 inhibitors on lipid profile: A systematic review and meta-analysis of 48 randomized controlled trials**. Pharmacological research : the official journal of the Italian Pharmacological Society 2020; 160:105068.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32652200
ABSTRACT
Previous studies have suggested additional beneficial effects of sodium-glucose co-transporter-2 (SGLT2) inhibitors including the lipid-lowering effect; however, results on lipid profile are controversial. Thus, this meta-analysis aimed to determine the effect of SGLT2

inhibitors treatment on lipid levels in patients with type 2 diabetes. Randomized controlled trials assessing the impact of SGLT2 inhibitors on lipid parameters were searched in PubMed-MEDLINE, SCOPUS, Web of Science, and Google Scholar databases. Meta-analysis was conducted using a random-effects model and generic inverse variance method. Meta-analysis of 48 randomized controlled trials revealed that SGLT2 inhibitors therapy had a significant increase on total cholesterol (WMD: 0.09 mmol/L, 95 % CI: 0.05, 0.13, I(2) = 79 %, p < 0.0001), LDL-cholesterol (WMD: 0.10 mmol/L, 95 % CI: 0.07, 0.12, I(2) = 94 %, p < 0.00001), HDL-cholesterol (WMD: 0.06 mmol/L, 95 % CI: 0.05, 0.08, I(2) = 99 %, p < 0.00001), and non-HDL-cholesterol (WMD: 0.09 mmol/L, 95 % CI: 0.06, 0.12, I(2) = 96 %, p < 0.00001). Additionally, SGLT2 inhibitors administration showed a significant decrease in triglyceride levels (WMD: -0.10 mmol/L, 95 % CI: -0.13, -0.07, I(2) = 96 %, p < 0.00001). Finally, no significant alteration was found on LDL/HDL ratio after SGLT2 inhibitors treatment (WMD: -0.01 mmol/L, 95 % CI: -0.05, 0.03, I(2) = 99 %, p = 0.65). In conclusion, SGLT2 inhibitors significantly increase total cholesterol, LDL-cholesterol, non-HDL-cholesterol, and HDL-cholesterol, and decrease triglyceride levels.

[78] *Köhler-Forsberg O, Otte C, Gold SM, Østergaard SD*. **Statins in the treatment of depression: Hype or hope?** Pharmacology & therapeutics 2020:107625.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32652185
ABSTRACT
Many patients with depression do not respond sufficiently to antidepressant treatment, necessitating other treatment approaches. HMG-CoA reductase inhibitors (i.e. statins), which are frequently used for their cardioprotective properties, have also been studied regarding potential antidepressant effects. Possible mechanisms underlying an antidepressant effect of statins may include the anti-inflammatory, antioxidant and lipid lowering properties of this class of drugs. This review provides an overview of this field by reviewing the following aspects: 1) Candidate mechanisms that could mediate putative antidepressant effects of statins; 2) The evidence for and against antidepressant effects of statins in patients with major depressive disorder and among individuals with a medical disease and depressive symptoms; and 3) The safety of statin treatment. Three small placebo-controlled trials conducted in Iran (total N=172) have found that statins as add-on to selective serotonin reuptake inhibitors (SSRIs) have antidepressant effects in patients with major depressive disorder (MDD). Statin treatment in individuals without MDD do not seem to affect mood or protect against development of depression. Treatment with statins - including the combination with SSRIs - is generally considered to be safe. While the initial evidence for the antidepressant effect of the combination of an SSRI and a statin is promising, larger clinical trials, appropriately powered, and with depression as a pre-defined primary endpoint are needed.

[79] *Velz J, Esposito G, Wegener S et al.* **[Diagnostic and Therapeutic Management of Carotid Artery Disease]**. Praxis 2020; 109:705-723.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32635848
ABSTRACT
Diagnostic and Therapeutic Management of Carotid Artery Disease Abstract. A quarter of all ischemic strokes is caused by atherosclerotic obliterations of the extra- and intracranial brain-supplying vessels. The prevalence of atherosclerotic extracranial carotid stenosis rises up to 6-15 % from the age of 65. The risk of stroke in symptomatic carotid stenosis, i.e. after stroke or

transient ischemic attack (TIA), is very high at 25 % within 14 days. Conservative therapy is the cornerstone of treatment by controlling the risk factors, treatment with platelet aggregation inhibitors and antihypertensive and lipid-lowering medication. Carotid endarterectomy (CEA) is the first line treatment for symptomatic patients with a >50 % and asymptomatic patients with a >60 % carotid stenosis. In order to ensure the best possible treatment of patients with asymptomatic and symptomatic carotid stenosis, interdisciplinary cooperation in diagnostics, therapy and aftercare in a neuromedical centre of maximum care is necessary.

[80] *Palma Sobrinho ND, Campos JF, Silva RCD*. **Drug scheduling by nurses and drug interactions in patients with cardiovascular diseases**. Rev Bras Enferm 2020; 73:e20190307.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32638928
ABSTRACT
OBJECTIVES: to identify and characterize the potential serious drug interactions in patients hospitalized with cardiovascular diseases, relating them to the schedules established for drug administration by nurses. METHODS: a documentary, quantitative and sectional research. Ninety-nine prescriptions from patients admitted to the cardiology ward of a hospital in Rio de Janeiro for more than 48 hours were analyzed. Drug interaction was assessed using the Micromedex® software. The data were analyzed using descriptive and inferential statistics. RESULTS: serious interactions were evidenced in 22 drug pairs, most frequently at 6 p.m. and 6 a.m., times with higher dose scheduling performed by nurses. The most recurrent drug pairs involved in serious interactions were simvastatin + amlodipine and enoxaparin + clopidogrel. CONCLUSIONS: drug scheduling by nurses requires a review of the criteria for proposing schedules for drugs in order to ensure patient safety.

[81] *Ding Z, Wang X, Liu S et al.* **NLRP3 inflammasome via IL-1β regulates PCSK9 secretion**. Theranostics 2020; 10:7100-7110.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32641981
ABSTRACT
Background: Both PCSK9 and NLRP3 inflammasome play important roles in atherogenesis. This study was designed to test the hypothesis that NLRP3 inflammasome via IL-1β induces PCSK9 secretion. The inter-twined relationship between NLRP3 inflammasome, IL-1β and PCSK9 may be relevant in atherogenesis. Methods: We studied NLRP3 inflammasome-mediated PCSK9 secretion in mouse peritoneal macrophages and in a variety of tissues, such as liver, kidney and small intestine. Macrophages were derived from wild-type (WT) and a variety of gene deletion mice to define the mechanistic basis of NLRP3 inflammasome - mediated PCSK9 secretion. Additional studies were performed in high-fat diet fed mice. Results: We observed that NLRP3 and its downstream signals ASC, Caspase-1, IL-18, and IL-1β all participate in PCSK9 secretion. IL-1β seems to be more important than IL-18 in the induction of PCSK9 secretion. Further, there appears to be significant involvement of MAPKs in this process. Lastly, we observed that mice fed high fat diet have high expression of NLRP3 and a greater secretion of PCSK9 than mice fed a standard diet, and this increased secretion of PCSK9 in high fat diet-fed mice was attenuated in IL-1β(-/-) mice. Conclusions: This study based on extensive in vitro and in vivo data provides evidence that NLRP3 inflammasome via IL-1β plays an important role in determining PCSK9 secretion, particularly in the presence of high-fat diet.

[82] *Capoulade R, Cariou B*. **Lp(a) and calcific aortic valve stenosis: Direct LPA targeting or PCSK9-Lowering therapy?** Trends in cardiovascular medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32623063
ABSTRACT

[83] *Bonfigli AR, Protic O, Olivieri F et al.* **Effects of a novel nutraceutical combination (BruMeChol™) in subjects with mild hypercholesterolemia: study protocol of a randomized, double-blind, controlled trial**. Trials 2020; 21:616.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32631422
ABSTRACT
BACKGROUND: Elevated cholesterol levels and systemic inflammation are considered relevant risk factors for cardiovascular disease (CVD) development and progression. Increasing evidence suggests that cholesterol-lowering and inflammation-lowering nutraceuticals are useful in the management of moderate hypercholesterolemia. Here, we describe the study protocol of a clinical trial aimed to evaluate the cholesterol and inflammatory lowering effect of an innovative dietary supplement (BruMeChol™, Mivell S.r.l., Italy), composed of a mixture of extracts of bergamot and olive fruits in association with vitamin K2 in subjects with mild hypercholesterolemia. METHODS: The study was planned as a randomized, double-blind, placebo-controlled, parallel group clinical trial for 12 weeks at the Cardiology Unit of the IRCCS INRCA of Ancona, Italy. A total of 125 subjects (age ≥ 40 years) with mild hypercholesterolemia (total serum cholesterol levels ≥ 200 and ≤ 250 mg/dl) will be recruited. Intervention arm participants will take one capsule of dietary supplement two times a day, 15 min before the main meal. Control arm participants will receive one capsule of placebo in the same way. The dietary supplement capsule contains the following ingredients: phytosterols, flavonoid-rich extract of bergamot fruit (Citrus bergamia), flavonoid-rich extract of olive fruit (Olea europaea), and vitamin K2. Participants will undergo a medical evaluation and chemical-clinical examinations, which include lipid profile, glycemia, biomarkers of renal, liver and cardiac/muscular functions, interleukins (IL 6, IL-32, IL-37, and IL-38), and innovative mediators of inflammation such as inflamma-miRs (miR-21 and miR-146a), at baseline, and after 6 and 12 weeks of treatment. The decrease in total cholesterol levels and inflammatory biomarkers will be the primary and secondary endpoints of the study. DISCUSSION: This protocol study, planned to verify the effects of BruMeChol™ dietary supplementation in subjects with mild hypercholesterolemia, could also contribute to new study designs for next large-scale multicenter clinical trials. TRIAL REGISTRATION: Australian New Zealand Clinical Trials Registry: ACTRN12619000170123 . Retrospectively registered on 5 February 2019.