[1] *Nguyen NT, Nath PV, Mai VQ et al.* **Treatment of Severe Hypertriglyceridemia During Pregnancy With High Doses of Omega-3 Fatty Acid and Plasmapheresis**. AACE clinical case reports 2021; 7:211-215.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34095491

ABSTRACT
OBJECTIVE: Severe hypertriglyceridemia carries increased health risks, including the development of pancreatitis. The objective of this study was to report on management of 2 cases with severe gestational hypertriglyceridemia. CASES: In case 1, a 33-year-old pregnant woman presented with serum triglyceride level of 14 000 mg/dL after discontinuing hypolipidemic medications. She was treated with Lovaza 12 g/day, and serum triglyceride remained near normal at level of less than 800 mg mg/dL until delivery. In case 2, a 28-year-old patient (29(th) week gestation) presented with acute pancreatitis and triglycerides >4000 mg/dL. She was treated with Gemfibrozil, Lovaza, insulin infusion, subcutaneous heparin, and escalated to plasmapheresis. She successfully delivered a baby at the week of 36(th) and her triglyceride level was 304 mg/dL after that. DISCUSSION: Case 1 was treated with high-dose Lovaza and case 2 was treated with plasmapheresis successfully. Triglyceride levels were reduced to less than 500 mg/dL until delivery of healthy babies in both cases. CONCLUSION: Omega-3 fatty acids and plasmapheresis may be effective and safe to treat pregnant women with severe hypertriglyceridemia and pancreatitis.

[2] *Chen H, Chen W, Li H et al.* **Pharmacokinetics, Safety and Tolerability of Anacetrapib, a Novel Cholesteryl Ester Transfer Protein (CETP) Inhibitor, After Single and Multiple Doses in Healthy Chinese Subjects**. Adv Ther 2021; 38:3973-3985.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34101144

ABSTRACT
INTRODUCTION: Anacetrapib is a novel, powerful cholesteryl ester transfer protein (CETP) inhibitor with bidirectional lipid regulation, which was developed for dyslipidemia. The aim of this study is to evaluate the single- and multiple-dose pharmacokinetics (PK), safety and tolerability of anacetrapib in healthy Chinese subjects and assess the PK difference between Chinese and other populations. METHODS: Forty subjects were enrolled in an open-label study consisting of three panels (50 mg single dose; 100 mg single dose followed by 100 mg once-daily multiple doses for 10 days; a 200 mg single dose). Safety and tolerability were evaluated by monitoring adverse events, laboratory safety tests, ECGs, vital signs and physical examination. PK were evaluated and compared with historical data in black and white subjects. RESULTS: Anacetrapib was absorbed after administration of a single oral dose, with a median T(max) of 3.0-5.0 h and elimination half-life of 105.3-122.3 h. The AUC and C(max) of anacetrapib increased in a slightly less than dose-proportional manner over a dose range of 50-200 mg. Once-daily administration of 100 mg of anacetrapib for 10 days resulted in a median T(max) of 5.0 h with an apparent half-life of 193.7 h on Day 10 of multiple dosing. Anacetrapib accumulation ratios (Day 10 of multiple dosing/Day 1) were 1.39 (AUC(0-24 h)), 1.11 (C(max)) and 2.57 (C(24 h)). CONCLUSION: The PK properties of anacetrapib in Chinese subjects are comparable to those observed in the black population and in white subjects. Single and once-daily administration of anacetrapib was generally well tolerated in healthy Chinese subjects observed in this study. TRIAL REGISTRATION: chinadrugtrials.org.cn identifier number CTR20130983.

[3] *Lamprea-Montealegre JA, Katz R, Scharnagl H et al.* **Triglyceride-Rich Lipoproteins, Apolipoproteins, and Atherosclerotic Cardiovascular Events Among Patients with Diabetes Mellitus and End-Stage Renal Disease on Hemodialysis**. The American journal of cardiology 2021; 152:63-68.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34108090

ABSTRACT

Hypertriglyceridemia may be implicated in the high atherosclerotic cardiovascular disease (ASCVD) risk experienced by patients with end-stage renal disease (ESRD). In this post-hoc analysis of the "Die Deutsche Diabetes Dialyse Studie (4D)" clinical trial, we examined incident ASCVD events, defined as myocardial infarction, ischemic stroke, or a coronary revascularization procedure, among 1255 participants with type 2 diabetes and ESRD treated with hemodialysis. Cox-regression methods were used to evaluate the association of triglycerides, very-low density lipoprotein cholesterol (VLDL-C), and apolipoproteins B (Apo B) and C-III (Apo C-III) with ASCVD. During a median follow-up time of 2.3 years, 340 (27%) participants experienced an ASCVD event. Higher concentrations of triglycerides were not associated with ASCVD risk: Hazard ratio (HR) 0.95; 95% CI (0.83, 1.10) per doubling concentration. Similarly, VLDL-C HR 1.01; 95% CI (0.90, 1.13); Apo B HR 1.04; 95% CI (0.93, 1.16); and Apo C-III HR 0.97; 95% CI (0.86, 1.09) (per one standard deviation higher concentrations), were not associated with ASCVD events. These associations did not differ by allocation to treatment to atorvastatin or by concentrations of markers of inflammation or malnutrition. In conclusion, we found no evidence that triglycerides, triglyceride-rich lipoproteins, or apolipoproteins B or C-III were associated with risk of ASCVD events among patients with type 2 diabetes and ESRD on hemodialysis. These results suggest that lowering triglycerides may not decrease atherosclerotic cardiovascular risk in this population.

[4] *Chan SL, Rajesh R, Tang TY*. **Evidence-based medical treatment of peripheral arterial disease: A rapid review**. Ann Acad Med Singap 2021; 50:411-424.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34100518

ABSTRACT

INTRODUCTION: Peripheral arterial disease (PAD) treatment guidelines recommend the use of statins and antiplatelets in all PAD patients to reduce adverse cardiovascular and limb-related outcomes. In addition, hypertension and diabetes should be treated to reach recommended targets. The aim of this rapid review was to evaluate the level of adherence to evidence-based medical therapy (EBMT) recommended by PAD treatment guidelines in the real-world setting. METHODS: We searched PubMed and Embase using keywords, MeSH and Emtree terms related to the population, exposure and outcomes from their inception to 22 September 2020. We included randomised controlled trials, non-randomised studies, and observational studies reporting adherence to at least 1 of these 4 drug classes: (1) statins, (2) antiplatelets, (3) antihypertensives and (4) antidiabetic drugs. Non-English articles, abstracts, dissertations, animal studies and case reports or series were excluded. A narrative summary of the results was performed. RESULTS: A total of 42 articles were included in the review. The adherence to lipid-lowering drugs/statins ranged from 23.5 to 92.0% and antiplatelets from 27.5 to 96.3%. Only 7 and 5 studies reported use of "any anti-hypertensive" and "any anti-diabetic" medications, respectively, and the proportion of the cohort treated were generally close to the proportion with hypertension and/or diabetes. Adherence in studies published in 2016-2020 ranged from 52.4-89.6% for lipid-lowering drugs and 66.2-96.3% for antiplatelets.

CONCLUSION: EBMT adherence in PAD patients was highly variable and a substantial proportion in many settings were undertreated. There was also a notable lack of studies in Asian populations.

[5] *Guan J, Wu L, Xiao Q, Pan L*. **Levels and clinical significance of serum homocysteine (Hcy), high-density lipoprotein cholesterol (HDL-C), vaspin, and visfatin in elderly patients with different types of coronary heart disease**. Ann Palliat Med 2021; 10:5679-5686.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34107717

ABSTRACT

BACKGROUND: To investigate the levels and clinical significance of serum homocysteine (Hcy), high-density lipoprotein cholesterol (HDL-C), visceral adipose tissue-derived serine protease inhibitor (vaspin), and visceral fat-specific adipokine (visfatin) in elderly patients with different types of coronary heart disease (CHD). METHODS: A total of 208 elderly patients with CHD admitted to our hospital were selected as the observation group, and 57 healthy volunteers who received physical examinations during the same period were selected as the healthy control group. The patients in the observation group were divided into a stable angina pectoris (SAP) group, an unstable angina pectoris (UAP) group, and an acute myocardial infarction (AMI) group according to their clinical diagnosis. The levels of serum Hcy, HDL-C, vaspin, visfatin, and coronary angiography Gensini scores were compared among the CHD subgroups and the healthy control group. Pearson linear correlation analysis was used to analyze the correlation between levels of serum Hcy, HDL-C, vaspin, and visfatin with Gensini scores in elderly patients with different types of CHD. RESULTS: The levels of serum Hcy and visfatin in the observation group were significantly higher than those in the healthy control group ($P<0.05$), while the levels of serum HDL-C and vaspin were significantly lower than those in the healthy control group ($P<0.05$). There were statistically significant differences in the levels of serum Hcy, vaspin, and visfatin among the CHD subgroups ($P<0.05$). There were statistically significant differences in the Gensini scores and number of stenotic coronary arteries among the CHD subgroups ($P<0.05$). Pearson linear correlation analysis showed that the levels of serum Hcy, HDL-C, vaspin, and visfatin in the SAP group were not significantly correlated with Gensini scores ($P>0.05$). However, the levels of serum Hcy and visfatin in the UAP and AMI groups were positively correlated with Gensini scores ($P<0.05$), the level of serum vaspin was negatively correlated with Gensini scores ($P<0.05$). CONCLUSIONS: The levels of serum Hcy, vaspin, and visfatin vary according to the different types of CHD and are correlated with the degree of coronary artery stenosis. As such, these serum levels can be used as sensitive indicators for early detection and disease evaluation.

[6] *Vuignier Y, Beaud F, Kosinski C et al.* **Exposure to alirocumab during the first trimester of pregnancy: A case report**. Birth Defects Res 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34105316

ABSTRACT

BACKGROUND: Familial hypercholesterolemia can be efficiently treated with combined lipid-lowering drugs. Lipid-lowering drugs are usually withdrawn for pregnancy and breastfeeding, ideally preconception, followed by lipid apheresis, however, careful plans can be precipitated due to unexpected pregnancy. CASE: A 28-year old woman with familial hypercholesterolemia due to heterozygous LDLR mutations had an LDL-cholesterol level at 14.6 mmol/L and Lp(a) at 1150 mg/L. She required a three-vessel coronary artery bypass graft, drug-eluting stents, rosuvastatin, ezetimibe,

and alirocumab at maximal dosage. Contraception was advised during the following 12 months, with a planned drug withdrawal to bridge with lipid apheresis, such as the direct adsorption of lipoproteins (DALI). However, an unplanned pregnancy required an abrupt stop of all oral medications at six gestational weeks, except for aspirin. Lipid apheresis controlled LDL-cholesterol in the range of 4.9-7.9 mmol/L (before DALI session) to 1.2-3.2 mmol/L (after DALI session). Later, the regular pregnancy ultrasounds highlighted an isolated agenesis of the corpus callosum later confirmed by magnetic resonance imaging. CONCLUSIONS: A causal link between the early pregnancy exposure to PCSK9 inhibitors (or statins and ezetimibe taken concomitantly) and the observed complete agenesis of the corpus callosum seems unlikely in this case. Guidelines do not specifically recommend preconception measures to lower fetal and/or maternal risks of patients with severe FH considering pregnancy. We argue that lipid apheresis and other measures should be discussed with women with FH and maternity project on an individual basis, until pharmacoepidemiology studies assessing the safety of PCSK9 inhibitors in pregnancy are available.

[7] *Xie Q, Shang D, Wang Y et al.* **The Association between Baseline Serum Lipids and Mortality in Peritoneal Dialysis Patients**. Blood purification 2021:1-10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34120111
ABSTRACT
INTRODUCTION: Lipid disturbances are common in ESRD patients. In peritoneal dialysis (PD) patients, dyslipidemia is even more common. This study aimed to examine whether serum lipids were associated with prognosis of PD patients. METHODS: Patients from a multicenter retrospective cohort were used for the present study. The primary endpoint was all-cause mortality. Cox regression was used to analyze the association between serum lipids including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein, and triglycerides and the prognosis. RESULTS: The results showed that lower total cholesterol and LDL levels at the initiation of PD predicted higher all-cause mortality in PD patients. Multivariate analysis reveal that the association disappeared after adjusting for age, gender, albumin, prealbumin, protein catabolic rate normalized to body weight, C-reactive protein, and residual renal function. Further analysis showed that patients with lower total cholesterol/LDL had a higher mortality only during the first 24 months of follow-up. In the patients who survived >2 years after PD, lower total cholesterol/LDL was not associated with higher long-term all-cause mortality any more. CONCLUSION: Lower total cholesterol/LDL levels at the initiation of PD were associated with overall mortality in PD patients. The association could be potentially modified by malnutrition, inflammation, and residual renal function or disappeared after 24 months.

[8] *Chew BH, Hussain H, Supian ZA*. **Is therapeutic inertia present in hyperglycaemia, hypertension and hypercholesterolaemia management among adults with type 2 diabetes in three health clinics in Malaysia? a retrospective cohort study**. BMC family practice 2021; 22:111.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34116645
ABSTRACT
BACKGROUND: Good-quality evidence has shown that early glycaemic, blood pressure and LDL-cholesterol control in people with type 2 diabetes (T2D) leads to better outcomes. In spite of that, diseases control have been inadequate globally, and therapeutic inertia could be one of the main cause. Evidence on therapeutic inertia has been lacking at primary care setting. This retrospective cohort study aimed to determine the proportions of therapeutic inertia when treatment targets of

HbA1c, blood pressure and LDL-cholesterol were not achieved in adults with T2D at three public health clinics in Malaysia. METHODS: The index prescriptions were those that when the annual blood tests were reviewed. Prescriptions of medication were verified, compared to the preceding prescriptions and classified as 1) no change, 2) stepping up and 3) stepping down. The treatment targets were HbA1c<7.0% (53 mmol/mol), blood pressure (BP)<140/90 mmHg and LDL-cholesterol<2.6 mmol/L. Therapeutic inertia was defined as no change in the medication use in the present of not reaching the treatment targets. Descriptive, univariable, multivariable logistic regression and sensitive analyses were conducted. RESULTS: A total of 552 cohorts were available for the assessment of therapeutic inertia (78.9% completion rate). The mean (SD) age and diabetes duration were 60.0 (9.9) years and 5.0 (6.0) years, respectively. High therapeutic inertia were observed in oral anti-diabetic (61-72%), anti-hypertensive (34-65%) and lipid-lowering therapies (56-77%), and lesser in insulin (34-52%). Insulin therapeutic inertia was more likely among those with shorter diabetes duration (adjusted OR 0.9, 95% CI 0.87, 0.98). Those who did not achieve treatment targets were less likely to experience therapeutic inertia: HbA1c≥7.0%: adjusted OR 0.10 (0.04, 0.24); BP≥140/90 mmHg: 0.28 (0.16, 0.50); LDL-cholesterol≥2.6 mmol/L: 0.37 (0.22, 0.64). CONCLUSIONS: Although therapeutic intensifications were more likely in the presence of non-achieved treatment targets but the proportions of therapeutic inertia were high. Possible causes of therapeutic inertia were less of the physician behaviours but might be more of patient-related non-adherence or non-availability of the oral medications. These observations require urgent identification and rectification to improve disease control, avoiding detrimental health implications and costly consequences. TRIAL REGISTRATION: Number NCT02730754 , April 6, 2016.

[9] *Lee S, Zhou J, Leung KSK et al.* **Development of a predictive risk model for all-cause mortality in patients with diabetes in Hong Kong**. BMJ open diabetes research & care 2021; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34117050

ABSTRACT

INTRODUCTION: Patients with diabetes mellitus are risk of premature death. In this study, we developed a machine learning-driven predictive risk model for all-cause mortality among patients with type 2 diabetes mellitus using multiparametric approach with data from different domains. RESEARCH DESIGN AND METHODS: This study used territory-wide data of patients with type 2 diabetes attending public hospitals or their associated ambulatory/outpatient facilities in Hong Kong between January 1, 2009 and December 31, 2009. The primary outcome is all-cause mortality. The association of risk variables and all-cause mortality was assessed using Cox proportional hazards models. Machine and deep learning approaches were used to improve overall survival prediction and were evaluated with fivefold cross validation method. RESULTS: A total of 273 678 patients (mean age: 65.4±12.7 years, male: 48.2%, median follow-up: 142 (IQR=106-142) months) were included, with 91 155 deaths occurring on follow-up (33.3%; annualized mortality rate: 3.4%/year; 2.7 million patient-years). Multivariate Cox regression found the following significant predictors of all-cause mortality: age, male gender, baseline comorbidities, anemia, mean values of neutrophil-to-lymphocyte ratio, high-density lipoprotein-cholesterol, total cholesterol, triglyceride, HbA1c and fasting blood glucose (FBG), measures of variability of both HbA1c and FBG. The above parameters were incorporated into a score-based predictive risk model that had a c-statistic of 0.73 (95% CI 0.66 to 0.77), which was improved to 0.86 (0.81 to 0.90) and 0.87 (0.84 to 0.91) using random survival forests and deep survival learning models, respectively. CONCLUSIONS: A multiparametric model

incorporating variables from different domains predicted all-cause mortality accurately in type 2 diabetes mellitus. The predictive and modeling capabilities of machine/deep learning survival analysis achieved more accurate predictions.

[10] *Talic S, Marquina C, Ofori-Asenso R et al.* **Switching, Persistence and Adherence to Statin Therapy: a Retrospective Cohort Study Using the Australian National Pharmacy Data**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34097194
ABSTRACT
BACKGROUND: Statins are widely prescribed for the primary and secondary prevention of cardiovascular disease (CVD), but their effectiveness is dependent on the level of adherence and persistence. OBJECTIVES: This study aimed to explore the patterns of switching, adherence and persistence among the Australian general population with newly dispensed statins. METHODS: A retrospective cohort study was conducted using a random sample of data from the Australian national prescription claims data. Switching, adherence to and persistence with statins were assessed for people starting statins from 1 January 2015 to 31 December 2019. Switching was defined as either switching to another intensity of statin, to another statin or to a non-statin agent. Non-persistence to treatment was defined as discontinuation (i.e. ≥90 days with no statin) of coverage. Adherence was measured using proportion of days covered (PDC), and patients with PDC<0.80 were considered non-adherent. Cox proportional hazard models were used to compare discontinuation, switching and reinitiation between different statins. RESULTS: A cohort of 141,062 people dispensed statins and followed over a median duration of 2.5 years were included. Of the cohort, 29.3% switched statin intensity, 28.4% switched statin type, 3.7% switched to ezetimibe and in 2.7%, ezetimibe was added as combination therapy during the study period. Overall, 58.8% discontinued statins based on the 90-day gap criteria, of whom 55.2% restarted. The proportion of people non-adherent was 24.0% at 6 months to 49.0% at 5 years. People on low and moderate intensity statins were more likely to discontinue compared to those on high-intensity statins (hazard ratio [HR] 1.20, 95% confidence interval [CI] 1.09-1.31), (HR 1.28, 95%CI 1.14-1.42), respectively. Compared to maintaining same statin type and intensity, switching statins, which includes up-titration (HR 0.77, 95%CI 0.70 to 0.86) was associated with less likelihood of discontinuation after reinitiation. CONCLUSIONS: Long-term persistence and adherence to statins remains generally poor among Australians, which limits the effectiveness of these medicines and the consequent health impact they may provide for individuals (and by extension, the population impact when poor persistence and adherence is considered in the statin-taking population). Switching between statins is prevalent in one third of statin users, although any clinical benefit of the observed switching trend is unknown. This, combined with the high volume of statin prescriptions, highlights the need for better strategies to address poor persistence and adherence.

[11] *Ishii T, Ogura M, Nakamori H et al.* **Switching from lipoprotein apheresis to evolocumab in FH siblings on hemodialysis: case reports and discussion**. CEN case reports 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34100221
ABSTRACT

Familial hypercholesterolemia (FH) and chronic kidney disease, especially end-stage renal disease (ESRD), are common and put patients at a high risk of developing atherosclerotic cardiovascular disease (ASCVD). ESRD concomitant with FH may further increase the risk of ASCVD. Achieving target levels of low-density lipoprotein cholesterol (LDL-C) is difficult owing to the limitations of statin administration due to its side effects in ESRD. Therefore, some FH patients with ESRD require lipoprotein apheresis for the prevention of secondary ASCVD events. Although proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors may offer a safe and effective option for lowering lipid levels in such patients, no guidelines are available for their use. Here, we report the case of two male siblings with FH in secondary prevention undergoing hemodialysis combined with PCSK9 inhibitor treatment. The siblings, who showed a heterozygous c.1846-1G>A mutation in the LDLR gene, underwent hemodialysis. In combination with the lipoprotein apheresis, siblings were administered evolocumab, a PCSK9 inhibitor. Both the siblings had coronary artery disease, diabetes, and ESRD, and received hemodialysis. Their LDL-C levels did not reach the target values despite administering statin, ezetimibe, and biweekly lipoprotein apheresis. On the introduction of evolocumab treatment, their LDL-C levels were significantly reduced without any adverse effects, resulting in successful withdrawal from lipoprotein apheresis therapy. Although the effects of switching from lipoprotein apheresis to PCSK9 inhibitors for cardiovascular protection remain unclear in FH patients with and without ESRD, our case report will be helpful in guiding future therapeutic decisions.

[12] *Bonaca MP, Hamburg NM, Creager MA*. **Contemporary Medical Management of Peripheral Artery Disease**. Circulation research 2021; 128:1868-1884.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34110910

ABSTRACT

Peripheral artery disease (PAD) is a manifestation of systemic atherosclerosis. Modifiable risk factors including cigarette smoking, dyslipidemia, diabetes, poor diet quality, obesity, and physical inactivity, along with underlying genetic factors contribute to lower extremity atherosclerosis. Patients with PAD often have coexistent coronary or cerebrovascular disease, and increased likelihood of major adverse cardiovascular events, including myocardial infarction, stroke and cardiovascular death. Patients with PAD often have reduced walking capacity and are at risk of acute and chronic critical limb ischemia leading to major adverse limb events, such as peripheral revascularization or amputation. The presence of polyvascular disease identifies the highest risk patient group for major adverse cardiovascular events, and patients with prior critical limb ischemia, prior lower extremity revascularization, or amputation have a heightened risk of major adverse limb events. Medical therapies have demonstrated efficacy in reducing the risk of major adverse cardiovascular events and major adverse limb events, and improving function in patients with PAD by modulating key disease determining pathways including inflammation, vascular dysfunction, and metabolic disturbances. Treatment with guideline-recommended therapies, including smoking cessation, lipid lowering drugs, optimal glucose control, and antithrombotic medications lowers the incidence of major adverse cardiovascular events and major adverse limb events. Exercise training and cilostazol improve walking capacity. The heterogeneity of risk profile in patients with PAD supports a personalized approach, with consideration of treatment intensification in those at high risk of adverse events. This review highlights the medical therapies currently available to improve outcomes in patients with PAD.

[13] *Rohatgi A, Westerterp M, von Eckardstein A et al.* **HDL in the 21st Century: A Multifunctional Roadmap for Future HDL Research**. Circulation 2021; 143:2293-2309.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34097448

ABSTRACT

Low high-density lipoprotein cholesterol (HDL-C) characterizes an atherogenic dyslipidemia that reflects adverse lifestyle choices, impaired metabolism, and increased cardiovascular risk. Low HDL-C is also associated with increased risk of inflammatory disorders, malignancy, diabetes, and other diseases. This epidemiologic evidence has not translated to raising HDL-C as a viable therapeutic target, partly because HDL-C does not reflect high-density lipoprotein (HDL) function. Mendelian randomization analyses that have found no evidence of a causal relationship between HDL-C levels and cardiovascular risk have decreased interest in increasing HDL-C levels as a therapeutic target. HDLs comprise distinct subpopulations of particles of varying size, charge, and composition that have several dynamic and context-dependent functions, especially with respect to acute and chronic inflammatory states. These functions include reverse cholesterol transport, inhibition of inflammation and oxidation, and antidiabetic properties. HDLs can be anti-inflammatory (which may protect against atherosclerosis and diabetes) and proinflammatory (which may help clear pathogens in sepsis). The molecular regulation of HDLs is complex, as evidenced by their association with multiple proteins, as well as bioactive lipids and noncoding RNAs. Clinical investigations of HDL biomarkers (HDL-C, HDL particle number, and apolipoprotein A through I) have revealed nonlinear relationships with cardiovascular outcomes, differential relationships by sex and ethnicity, and differential patterns with coronary versus noncoronary events. Novel HDL markers may also have relevance for heart failure, cancer, and diabetes. HDL function markers (namely, cholesterol efflux capacity) are associated with coronary disease, but they remain research tools. Therapeutics that manipulate aspects of HDL metabolism remain the holy grail. None has proven to be successful, but most have targeted HDL-C, not metrics of HDL function. Future therapeutic strategies should focus on optimizing HDL function in the right patients at the optimal time in their disease course. We provide a framework to help the research and clinical communities, as well as funding agencies and stakeholders, obtain insights into current thinking on these topics, and what we predict will be an exciting future for research and development on HDLs.

[14] *Kanonidou C*. **Small dense low-density lipoprotein: Analytical review**. Clinica chimica acta; international journal of clinical chemistry 2021; 520:172-178.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34118239

ABSTRACT

BACKGROUND: The causal relationship between low-density lipoprotein (LDL) and atherosclerotic cardiovascular disease (CVD) has been firmly substantiated. LDL consists of a heterogeneous group of particles with different physicochemical and metabolic properties. Among them, small dense LDL (sdLDL) particles are considered an emerging CVD risk factor and a promising CVD risk biomarker. This paper reviews published analytical and calculation-based methods for sdLDL determination in plasma, present their principles, strengths, and weaknesses, and examine the challenges arising from method comparison. METHODS: A literature survey was conducted using the PubMed database. Subject headings and keywords facilitated the search strategy. Titles and abstracts were initially assessed, and the full-text article of the pre-selected ones was reviewed. RESULTS: A range of methods is currently available for the analysis of LDL subfractions and the measurement of sdLDL

particle size, number, and cholesterol concentration. Ultracentrifugation (UC), vertical auto profile, gradient gel electrophoresis (GGE), nuclear magnetic resonance (NMR) spectroscopy, high-performance liquid chromatography, ion mobility analysis, and a homogeneous assay are the most prevalent. To date, there is no "gold standard". UC and GGE are the most established techniques, albeit significantly sophisticated. NMR and the homogeneous assay are options with potential clinical use as they yield results rapidly and can be high-throughput. None of the proposed equations for the calculated sdLDL determination has been sufficiently validated to serve as a clinical tool. CONCLUSIONS: Many analytical procedures have been developed for the study of sdLDL particles. Their use remains largely restricted to research laboratories since their analytical and clinical performance, along with the clinical- and cost-effectiveness of sdLDL determination have not been fully established.

[15] *Luo Y, Yu F, Feng X et al.* **Molecular Biomarkers Associated with Early-Onset Symptomatic Intracranial Atherosclerosis**. Clin Interv Aging 2021; 16:1013-1022.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34103904
ABSTRACT
PURPOSE: Previous studies have shown a rising incidence of early-onset symptomatic intracranial atherosclerosis (sICAS), which has brought a severe economic burden to social development. This study aimed to evaluate the molecular biomarkers associated with early-onset sICAS and to seek possible intervention strategies for early prevention. PATIENTS AND METHODS: We consecutively recruited patients with sICAS and divided them into two groups based on age: early-onset sICAS group as age ≤60 years old and late-onset sICAS group as age >60 years old. We collected and compared the demographic data and laboratory results of each group. A bivariate logistic regression model was applied to evaluate the independent molecular biomarkers of early-onset sICAS. RESULTS: A total of 1007 subjects with sICAS were enrolled in this study, comprising 519 patients in the early-onset sICAS group and 488 patients in the late-onset sICAS group. Bivariate logistic regression analysis demonstrated an increased level of white blood cell, platelet, albumin globulin ratio, free triiodothyronine, and a decreased level of total bile acid, urea nitrogen, high-density lipoprotein, homocysteine, and fibrinogen in the early-onset sICAS group when compared to the late-onset group. CONCLUSION: Our study showed the relevance between early sICAS and circulating levels of different molecular biomarkers. Detection of these related molecular biomarkers may provide a simple way for early sICAS preventions in the future.

[16] *Lu B, Sun L, Seraydarian M et al.* **Effect of SLCO1B1 T521C on Statin-Related Myotoxicity With Use of Lovastatin and Atorvastatin**. Clinical pharmacology and therapeutics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34114646
ABSTRACT
The association between the c.521T>C variant allele in SLCO1B1 (reference single nucleotide polymorphism (rs)4149056) and simvastatin-induced myotoxicity was discovered over a decade ago; however, whether this relationship represents a class effect is still not fully known. The aim of this study was to investigate the relationship between rs4149056 genotype and statin-induced myotoxicity in patients taking atorvastatin and lovastatin. Study participants were from the Genetic Epidemiology Research on Adult Health and Aging (GERA) cohort. A total of 233 statin-induced myopathy + rhabdomyolysis cases met the criteria for inclusion and were matched to 2,342 controls. To validate

the drug response phenotype, we replicated the previously established association between rs4149056 genotype and simvastatin-induced myotoxicity. In particular, compared with homozygous T allele carriers, there was a significantly increased risk of simvastatin-induced myopathy + rhabdomyolysis in homozygous carriers of the C allele (CC vs. TT, odds ratio [OR] 4.62, 95% confidence interval [CI] 1.58-11.90, P = 0.003). For lovastatin users, homozygous carriers of the C allele were also at increased risk of statin-induced myopathy + rhabdomyolysis (CC vs. TT, OR 4.49, 95% CI 1.68-10.80, P = 0.001). In atorvastatin users, homozygous carriers of the C allele were twice as likely to experience statin-induced myopathy, though this association did not achieve statistical significance (CC vs. TT, OR 2.00, 95% CI 0.44-6.59, P = 0.30). In summary, our findings suggest that the association of rs4149056 with simvastatin-related myotoxicity may also extend to lovastatin. More data is needed to determine the extent of the association in atorvastatin users. Altogether, these data expand the evidence base for informing guidelines of pharmacogenetic-based statin prescribing practices.

[17] *Jin S, Nie X, Li Y et al.* **Effect of More Intensive LDL-C-Lowering Therapy on Long-term Cardiovascular Outcomes in Early-Phase Acute Coronary Syndrome: A Systematic Review and Meta-analysis**. Clinical therapeutics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34092409

ABSTRACT

PURPOSE: The effect of more intensive LDL-C-lowering therapy (ILLT) on long-term cardiovascular outcomes during the early phase of acute coronary syndromes (ACSs) remains uncertain. We aimed to explore the influence of more intensive LDL-C-lowering therapyduring the early disease phase on long-term cardiovascular events among patients with ACSs. METHODS: Randomized controlled trials that focused on the effect of more ILLT during early-phase ACSs on long-term major adverse cardiac events (MACEs) were searched in electronic databases (MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases) from database inception until November 23, 2019. The end points included the incidence of MACEs, myocardial infarction, stroke, revascularization, heart failure, and death events. Study risk of bias was assessed using the Cochrane Collaboration tools. Fixed- or random-effects models and meta-regression were performed to evaluate the association between baseline/proportional reduction of LDL-C levels during early-phase disease and the risk of end points using risk ratios with 95% CIs. FINDINGS: A total of 53,199 participants were involved from 19 studies. The risk of MACEs decreased by 17% (95% CI, 0.76-0.90; P = 0.0012) for more intensive versus control therapy but varied by baseline and proportional reduction of LDL-C levels during early disease phase. The risk reduction of MACEs for more intensive versus control therapy among different subgroups was 26% (95% CI, 0.57-0.95; P = 0.06) with a baseline level >130 mg/dL, 23% (95% CI, 0.63-0.94; P = 0.02) with a baseline level of 100 to 130 mg/dL, and 10% (95% CI, 0.83-0.99; P = 0.07) with a baseline level <100 mg/dL. A significant difference of risk reduction for MACEs existed between patients treated with statin plus ezetimibe versus statin alone in the subgroup with a baseline level >130 mg/dL and proportional reduction >50%. Patients treated with more intensive therapy benefited from reduced risk of myocardial infarction, stroke, revascularization, and heart failure compared with control therapy. IMPLICATIONS: More ILLT during early disease phase could significantly reduce the risk of long-term cardiovascular outcome in patients with ACSs. This benefit was most pronounced in patients with higher baseline and larger reduction of LDL-C levels in MACEs.

[18] *Adam S, Ho JH, Bashir B et al.* **The impact of atherosclerotic cardiovascular disease, dyslipidaemia and lipid lowering therapy on Coronavirus disease 2019 outcomes: an examination of the available evidence**. Current opinion in lipidology 2021; 32:231-243.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34116544

ABSTRACT
PURPOSE OF REVIEW: Coronavirus Disease 2019 (COVID19) has caused significant global morbidity and mortality, especially in persons with underlying cardiovascular disease. There have been concerns that lipid-lowering therapy (LLT) increases angiotensin-converting enzyme 2 levels. Conversely, pleiotropic effects of statins can theoretically protect against severe COVID19 infection, supporting evidence from other respiratory illnesses in which statin use probably confers benefit. RECENT FINDINGS: There is an abundance of studies that show that statins are safe and potentially protect against severe COVID19 infection (critical illness and death), even when adjustment for potential confounders is undertaken. However, the evidence is limited to retrospective cohorts. The benefit for patients with diabetes is less clear. There is a paucity of evidence for other LLT agents. Available clinical guidelines recommend the ongoing use of LLT in patients with COVID19 (unless specifically contra-indicated) and the data from available studies support these. SUMMARY: In patients with COVID19 infection, LLT should be continued. However, the current findings need substantiating in larger prospective clinical studies with specific examination of the possible mechanisms by which LLT confers benefit from COVID19.

[19] *Iqbal Z, Bashir B, Ferdousi M et al.* **Lipids and peripheral neuropathy**. Current opinion in lipidology 2021; 32:249-257.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34101657

ABSTRACT
PURPOSE OF REVIEW: Hyperlipidaemia is associated with the development of neuropathy. Indeed, a mechanistic link between altered lipid metabolism and peripheral nerve dysfunction has been demonstrated in a number of experimental and clinical studies. Furthermore, post hoc analyses of clinical trials of cholesterol and triglyceride-lowering pharmacotherapy have shown reduced rates of progression of diabetic neuropathy. Given, there are currently no FDA approved disease-modifying therapies for diabetic neuropathy, modulation of lipids may represent a key therapeutic target for the treatment of diabetic nerve damage. This review summarizes the current evidence base on the role of hyperlipidaemia and lipid lowering therapy on the development and progression of peripheral neuropathy. RECENT FINDINGS: A body of literature supports a detrimental effect of dyslipidaemia on nerve fibres resulting in somatic and autonomic neuropathy. The case for an important modulating role of hypertriglyceridemia is stronger than for low-density lipoprotein cholesterol (LDL-C) in relation to peripheral neuropathy. This is reflected in the outcomes of clinical trials with the different therapeutic agents targeting hyperlipidaemia reporting beneficial or neutral effects with statins and fibrates. The potential concern with the association between proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor therapy and cognitive decline raised the possibility that extreme LDL-C lowering may result in neurodegeneration. However, studies in murine models and data from small observational studies indicate an association between increased circulating PCSK9 levels and small nerve fibre damage with a protective effect of PCSK9i therapy against small fibre neuropathy. Additionally, weight loss with bariatric surgery leads to an improvement in peripheral neuropathy and

regeneration of small nerve fibres measured with corneal confocal microscopy in people with obesity with or without type 2 diabetes. These improvements correlate inversely with changes in triglyceride levels. SUMMARY: Hyperlipidaemia, particularly hypertriglyceridemia, is associated with the development and progression of neuropathy. Lipid modifying agents may represent a potential therapeutic option for peripheral neuropathy. Post hoc analyses indicate that lipid-lowering therapies may halt the progression of neuropathy or even lead to regeneration of nerve fibres. Well designed randomized controlled trials are needed to establish if intensive targeted lipid lowering therapy as a part of holistic metabolic control leads to nerve fibre regeneration and improvement in neuropathy symptoms.

[20] *Talic S, Marquina Hernandez C, Ofori-Asenso R et al.* **Trends in the Utilization of Lipid-Lowering Medications in Australia: An Analysis of National Pharmacy Claims Data**. Current problems in cardiology 2021:100880.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34108083
ABSTRACT
Lipid-lowering medications comprise standard of care in the prevention of cardiovascular disease. This study examined the trends in the utilization of statin and non-statin medications in the Australian general population between 2013 and 2019. Pharmacoepidemiological analyses were performed using pharmacy dispensing data from Australian Pharmaceutical Benefits Scheme. One-year prevalence and incidence of statin and non-statin prescribing patterns were reported, and relative variations in prescribing examined via Poisson regression modelling. The one-year prevalence of statins' prescriptions decreased between 2013-2019 by 5.5% (from 25.0%-19.5%). Females were less likely than males to be prescribed statins (rate ratio [RR]=0.90, 95% confidence interval [CI] 0.89-0.91). The one-year prevalence of ezetimibe alone, and in combination with statins, increased consistently from 2013-2019 from 1.5%-3.6% (P<0.01) and 0.1%-1.1% (P<0.01), respectively. The prevalence was higher among those aged 61-80 years (RR=1.20, 95%CI 1.10-1.21) and those aged older than 80 years (RR=1.34, 95%CI 1.22-1.47), when compared to people aged <60 years. The incidence of ezetimibe prescriptions was highest in people aged 61-80 years (RR=1.36, 95%CI 1.31-1.41) compared to those aged <60 years. The one-year prevalence of proprotein convertase subtilisin/kexin type 9 inhibitor prescriptions was highest among those aged 46-60 years (RR=1.24, 95%CI 0.97-4.97) compared to people aged <46 and >60 years. Females were less likely than males to be prescribed a proprotein convertase subtilisin/kexin type 9 inhibitor (RR=0.87, 95%CI 0.75-0.98). Statins remain the most prevalent lipid-lowering medication prescribed in Australia. The prescribing of non-statin medications remains low, but is increasing.

[21] *Civeira F, Pedro-Botet J.* **Cost-effectiveness evaluation of the use of PCSK9 inhibitors**. Endocrinologia, diabetes y nutricion 2021; 68:369-371.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34103163
ABSTRACT

[22] *Liang Y, Tang Z, Jiang Y et al.* **Lipid metabolism disorders associated with dioxin exposure in a cohort of Chinese male workers revealed by a comprehensive lipidomics study**. Environ Int 2021; 155:106665.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34098336

ABSTRACT
Dioxins, environmentally stable and ubiquitous, have been found to induce metabolic changes especially in lipids and be related to multiple diseases. However, limited study is available on lipid alternations related to human exposure to dioxins. This study aims to explore the serum lipidomic characterization and to understand the underlying mechanisms of adverse health risks associated with dioxin exposure. A lipidomic study integrating nontargeted lipidomics, and targeted free fatty acid (FFA) and acyl-coenzyme A (acyl-CoA) analyses were conducted to investigate the 94 serum samples from two groups of male workers with remarkably different dioxin concentrations. The obtained results exhibited distinct lipidomic signatures between the high and low exposed groups. A total of 37 lipids were identified with the significant changes. The results revealed that dioxin exposure caused accumulations of triglyceride (TG), ceramide (Cer) and sphingoid (So), remodeling of glycerophospholipid (GP), imbalanced FFA metabolism, as well as upregulation of platelet-activating factor (PAF). These findings implied the associations between dioxin exposure and potential adverse health risks including inflammation, apoptosis, cardiovascular diseases (CVDs), and liver diseases. This study is the first to explain the associations between dioxin exposure and health effects at the level of lipid metabolism.

[23] *Arnold N, Lechner K, Waldeyer C et al.* **Inflammation and Cardiovascular Disease: The Future**. European cardiology 2021; 16:e20.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34093741

ABSTRACT
Despite considerable advances in reducing the global burden of atherosclerotic cardiovascular disease by targeting conventional risk factors, significant residual risk remains, with low-grade inflammation being one of the strongest risk modifiers. Inflammatory processes within the arterial wall or systemic circulation, which are driven in a large part by modified lipoproteins but subsequently trigger a hypercoagulable state, are a hallmark of atherosclerotic cardiovascular disease and, in particular, its clinical complications. Extending conventional guideline-based clinical risk stratification algorithms by adding biomarkers of inflammation may refine phenotypic screening, improve risk stratification and guide treatment eligibility in cardiovascular disease prevention. The integration of interventions aimed at lowering the inflammatory burden, alone or in combination with aggressive lipid-modifying or even antithrombotic agents, for those at high cardiovascular risk may hold the potential to reduce the still substantial burden of cardiometabolic disease. This review provides perspectives on future clinical research in atherosclerosis addressing the tight interplay between inflammation, lipid metabolism and thrombosis, and its translation into clinical practice.

[24] *Crea F*. **Dyslipidaemias in stroke, chronic kidney disease, and aortic stenosis: the new frontiers for cholesterol lowering**. European heart journal 2021; 42:2137-2140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34097728

ABSTRACT

[25] *Fanni D, Gerosa C, Nurchi VM et al.* **Trace elements and the carotid plaque: the GOOD (Mg, Zn, Se), the UGLY (Fe, Cu), and the BAD (P, Ca)?** European review for medical and pharmacological sciences 2021; 25:3772-3790.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34109586

ABSTRACT
Multiple epidemiological studies have suggested that industrialization and progressive urbanization should be considered one of the main factors responsible for the rising of atherosclerosis in the developing world. In this scenario, the role of trace metals in the insurgence and progression of atherosclerosis has not been clarified yet. In this paper, the specific role of selected trace elements (magnesium, zinc, selenium, iron, copper, phosphorus, and calcium) is described by focusing on the atherosclerotic prevention and pathogenesis plaque. For each element, the following data are reported: daily intake, serum levels, intra/extracellular distribution, major roles in physiology, main effects of high and low levels, specific roles in atherosclerosis, possible interactions with other trace elements, and possible influences on plaque development. For each trace element, the correlations between its levels and clinical severity and outcome of COVID-19 are discussed. Moreover, the role of matrix metalloproteinases, a family of zinc-dependent endopeptidases, as a new medical therapeutical approach to atherosclerosis is discussed. Data suggest that trace element status may influence both atherosclerosis insurgence and plaque evolution toward a stable or an unstable status. However, significant variability in the action of these traces is evident: some - including magnesium, zinc, and selenium - may have a protective role, whereas others, including iron and copper, probably have a multi-faceted and more complex role in the pathogenesis of the atherosclerotic plaque. Finally, calcium and phosphorus are implicated in the calcification of atherosclerotic plaques and in the progression of the plaque toward rupture and severe clinical complications. In particular, the role of calcium is debated. Focusing on the COVID-19 pandemia, optimized magnesium and zinc levels are indicated as important protective tools against a severe clinical course of the disease, often related to the ability of SARS-CoV-2 to cause a systemic inflammatory response, able to transform a stable plaque into an unstable one, with severe clinical complications.

[26] *Boutari C, Karagiannis A, Athyros VG*. **Rosuvastatin and ezetimibe for the treatment of dyslipidemia and hypercholesterolemia**. Expert review of cardiovascular therapy 2021:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34102931

ABSTRACT
Introduction: Statins are powerful lipid-lowering agents which reduce cardiovascular (CV)-related morbidity and mortality. However, a large proportion of patients cannot attain the target low-density lipoprotein cholesterol (LDL-C) levels, despite receiving maximally tolerated doses of high-intensity statins. Also, adherence to treatment may be reduced due to statin-induced myopathy or other side effects. For these reasons, guidelines recommend adding the cholesterol absorption inhibitor ezetimibe.Areas covered: Authors discuss the main pharmacological characteristics of rosuvastatin and ezetimibe, their lipid-lowering and pleiotropic effects, as well as the clinical effects of the fixed dose combination of these drugs when used to treat dyslipidemia.Expert opinion: The rosuvastatin/ezetimibe combination is safe and effective in patients with hypercholesterolemia or dyslipidemia with or without diabetes and with or without cardiovascular disease. This drug combination enabled higher proportions of patients to achieve recommended LDL-C goals than rosuvastatin monotherapy or the simvastatin/ezetimibe combination, without additional adverse events. Despite the lack of additional CV outcomes data and comparisons with atorvastatin/ezetimibe, rosuvastatin/ezetimibe appears as a potent and generally well-tolerated drug combination eligible for the management of hypercholesterolemia and dyslipidemia in adults.

Recently, the 40 mg rosuvastatin/10 mg ezetimibe fixed combination was approved and is also evaluated.

[27] *Climent E, Benaiges D, Pedro-Botet J.* **Hydrophilic or Lipophilic Statins?** Frontiers in cardiovascular medicine 2021; 8:687585.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34095267

ABSTRACT

Drugs can be classified as hydrophilic or lipophilic depending on their ability to dissolve in water or in lipid-containing media. The predominantly lipophilic statins (simvastatin, fluvastatin, pitavastatin, lovastatin and atorvastatin) can easily enter cells, whereas hydrophilic statins (rosuvastatin and pravastatin) present greater hepatoselectivity. Although the beneficial role of statins in primary and secondary cardiovascular prevention has been unequivocally confirmed, the possible superiority of one statin or other regarding their solubility profile is still not well-established. In this respect, although some previously published observational studies and clinical trials observed a superiority of lipophilic statins in cardiovascular outcomes, these results could also be explained by a greater low-density lipoprotein cholesterol reduction with this statin type. On the other hand, previous studies reported conflicting results as to the possible superiority of one statin type over the other regarding heart failure outcomes. Furthermore, adverse events with statin therapy may also be related to their solubility profile. Thus, the aim of the present review was to collect clinical evidence on possible differences in cardiovascular outcomes among statins when their solubility profile is considered, and how this may also be related to the occurrence of statin-related adverse effects.

[28] *Ubilla CG, Prado Y, Angulo J et al.* **MicroRNA-33b is a Potential Non-Invasive Biomarker for Response to Atorvastatin Treatment in Chilean Subjects With Hypercholesterolemia: A Pilot Study**. Frontiers in pharmacology 2021; 12:674252.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34093203

ABSTRACT

Evidence accumulated so far indicates that circulating levels of microRNAs (miRNAs) are associated with several pathologies. Therefore, differential expression of extracellular miRNAs exhibits promising potential for screening and diagnosis purposes. We evaluated plasma miRNAs in response to the lipid-lowering drug atorvastatin in patients with hypercholesterolemia (HC) and controls. METHODS: We selected miRNAs based on previous data reported by our group and also by employing bioinformatics tools to identify 10 miRNAs related to cholesterol metabolism and statin response genes. Following miRNA identification, we determined plasma levels of miRNA-17-5p, miRNA-30c-5p, miRNA-24-3p, miRNA-33a-5p, miRNA-33b-5p, miRNA-29a-3p, miRNA-29b-3p, miRNA-454-3p, miRNA-590-3p and miRNA-27a-3p in 20 HC patients before and after 1 month of 20 mg/day atorvastatin treatment, evaluating the same miRNA set in a group of 20 healthy subjects, and employing qRT-PCR to determine differential miRNAs expression. RESULTS: HC individuals showed significant overexpression of miRNA-30c-5p and miRNA-29b-3p vs. NL ($p = 0.0008$ and $p = 0.0001$, respectively). Once cholesterol-lowering treatment was concluded, HC individuals showed a substantial increase of three extracellular miRNAs (miRNA-24-3p, miRNA-590, and miRNA-33b-5p), the latter elevated more than 37-fold ($p = 0.0082$). CONCLUSION: Data suggest that circulating miRNA-30c-5p and miRNA-29b-3p are associated with hypercholesterolemia. Also, atorvastatin induces a strong elevation of miRNA-33b-5p levels in HC individuals, which could indicate an

important function that this miRNA may exert upon atorvastatin therapy. Additional studies are needed to clarify the role of this particular miRNA in statin treatment.

[29] *Lazashvili T, Silagadze T, Kapetivadze V et al.* **ACTION OF SIMVASTATIN IN IMPROVING COGNITIVE FUNCTIONS IN VASCULAR DEMENTIA**. Georgian medical news 2021:98-101.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34103439

ABSTRACT

The purpose of this study was to determine the efficacy and safety of statins in improving cognitive function in patients with vascular dementia. As the most important etiological factors of the disease are atherosclerotic vascular lesions, one of the important areas of treatment is lipid metabolism analysis and drug treatment for dyslipidemia. 31 patients were selected for the study, ages 65-65 years, 18 males, 13 females. Twenty patients were included in the study group, treated with Simvastatin (80 mg daily dose). 11 patients were included in the control group. They received placebo therapy. Patients were examined every 4 weeks for 12 weeks using a neuropsychological test with mini-mental scaling, and both groups had low-density lipoprotein and cholesterol levels before and after treatment. In the 12-week post-treatment group, low-density lipoprotein levels were reduced by 54% and cholesterol by 48%. Neuropsychological status examination revealed deterioration of cognitive functions and no difference was observed between study and control group data. Based on the data obtained from our study, it should be noted that correction of lipid metabolism by statins in patients with vascular dementia did not lead to a reduction in cognitive impairment and clinical improvement in patients with vascular dementia.

[30] *Tam J, Thankam F, Agrawal DK, Radwan MM*. **Critical Role of LOX-1-PCSK9 Axis in the Pathogenesis of Atheroma Formation and Its Instability**. Heart, lung & circulation 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34092505

ABSTRACT

Cardiovascular disease (CVD) is a major contributor to annual deaths globally. Atherosclerosis is a prominent risk factor for CVD. Although significant developments have been recently made in the prevention and treatment, the molecular pathology of atherosclerosis remains unknown. Interestingly, the recent discovery of proprotein convertase subtilisin/kexin type 9 (PCSK9) introduced a new avenue to explore the molecular pathogenesis and novel management strategies for atherosclerosis. Initial research focussed on the PCSK9-mediated degradation of low density lipoprotein receptor (LDLR) and subsequent activation of pro-inflammatory pathways by oxidised low density lipoprotein (ox-LDL). Recently, PCSK9 and lectin-like oxidised low-density lipoprotein receptor-1 (LOX-1) were shown to positively amplify each other pro-inflammatory activity and gene expression in endothelial cells, macrophages and vascular smooth muscle cells. In this literature review, we provide insight into the reciprocal relationship between PCSK9 and LOX-1 in the pathogenesis of atheroma formation and plaque instability in atherosclerosis. Further understanding of the LOX-1-PCSK9 axis possesses tremendous translational potential to design novel management approaches for atherosclerosis.

[31] *Xian H, Liu Y, Rundberg Nilsson A et al.* **Metformin inhibition of mitochondrial ATP and DNA synthesis abrogates NLRP3 inflammasome activation and pulmonary inflammation**. Immunity 2021; 54:1463-1477.e1411.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34115964

ABSTRACT
Acute respiratory distress syndrome (ARDS), an inflammatory condition with high mortality rates, is common in severe COVID-19, whose risk is reduced by metformin rather than other anti-diabetic medications. Detecting of inflammasome assembly in post-mortem COVID-19 lungs, we asked whether and how metformin inhibits inflammasome activation while exerting its anti-inflammatory effect. We show that metformin inhibited NLRP3 inflammasome activation and interleukin (IL)-1β production in cultured and alveolar macrophages along with inflammasome-independent IL-6 secretion, thus attenuating lipopolysaccharide (LPS)- and SARS-CoV-2-induced ARDS. By targeting electron transport chain complex 1 and independently of AMP-activated protein kinase (AMPK) or NF-κB, metformin blocked LPS-induced and ATP-dependent mitochondrial (mt) DNA synthesis and generation of oxidized mtDNA, an NLRP3 ligand. Myeloid-specific ablation of LPS-induced cytidine monophosphate kinase 2 (CMPK2), which is rate limiting for mtDNA synthesis, reduced ARDS severity without a direct effect on IL-6. Thus, inhibition of ATP and mtDNA synthesis is sufficient for ARDS amelioration.

[32] *Ferraro F, Martín M, Verona J et al.* **Increased Cholesteryl Ester Transfer Protein and Lipoprotein-Associated Phospholipase A2 Activities in Children and Adolescents Presenting High Triglyceride/High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio**. Indian journal of pediatrics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34097230
ABSTRACT
OBJECTIVE: To explore the association between Triglyceride/High-density lipoprotein cholesterol (TG/HDL-C) index and these enzymes and proteins in a pediatric population. METHODS: Children and adolescents (7-14 y old) were recruited (n = 150) and anthropometric data were registered. Glucose, TG, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), HDL-C plus cholesteryl ester transfer protein (CETP), lipoprotein-associated phospholipase A(2) (Lp-PLA(2)) and paraoxonase 1 (PON1) activities were determined. RESULTS: Twenty-five individuals presented TG/HDL-C ratio ≥ 3.0. These individuals exhibited higher TG [164 (126-186) vs. 65 (48-72) mg/dL; $p < 0.01$] CETP [250 (232-263) vs. 223 (193-237)% mL/min; $p < 0.01$] and Lp-PLA(2) (4.5 ± 1.9 vs. 3.5 ± 1.3; $p < 0.05$) plus lower HDL-C [41 (37-49) vs. 52 (48-62) mg/dL; $p < 0.01$] compared to an age-matched group with TG/HDL-C < 3.0. TG/HDL-C ratio was associated to CETP ($p < 0.01$) and Lp-PLA(2) ($p < 0.05$). Multiple lineal regression analyses showed TG/HDL-C index as an independent predictor of CETP ($r(2) = 0.29$; beta = 0.49; $p < 0.01$) and Lp-PLA(2) ($r(2) = 0.21$; beta = 0.32; $p < 0.05$) activities. CONCLUSION: Children and adolescents with TG/HDL-C ≥ 3.0 presented a more atherogenic lipid profile and higher CETP and Lp-PLA(2) activities, which would indicate alterations in lipoprotein metabolism and quality.

[33] *Karabulut U, Çakır Ü*. **Non-HDL cholesterol is an independent predictor of long-term cardiovascular events in patients with dyslipidemia after renal transplantation**. Int J Clin Pract 2021:e14465.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34107128
ABSTRACT
BACKGROUND: Posttransplant dyslipidemia is a common condition in renal transplantation recipients (RTR) and is related to poor cardiac outcomes. We aimed to demonstrate the value of non-

high-density lipoprotein cholesterol (non-HDL-C) in predicting long-term major cardiovascular and cerebrovascular events (MACCE) in RTR with dyslipidemia. METHODS: Patients who had undergone renal transplantation between 2011 and 2019 were retrospectively analysed and were classified as normal non-HDL-C and high non-HDL-C groups based on first year levels. Development of high non-HDL-C levels was used to predict the occurrence of MACCE (a combination of cardiac death, nonfatal myocardial infarction, unstable angina, and nonfatal stroke) and all-cause death during the long-term follow-up. RESULTS: Overall, 674 patients were included, of whom 470 (69.7%) were male; the mean age was 43.6 ± 13.2 years. The mean follow-up duration was 5.5 ± 2.29 years 1 year after the transplant. MACCE occurred during the follow-up in 102 (61.8%) patients in the high non-HDL-C group and 13 (2.6%) patients in the normal non-HDL-C group (P < .001). High non-HDL-C was a predictor of MACCE in the multivariate analysis (hazard ratio [HR] 1.02, 95% confidence interval [CI] 1.01-1.02, P < .001). Smoking (HR: 1.92, 95% CI 1.16-3.20, P < .001), cadaver graft (HR: 2.55, 95% CI 1.52-4.26, P < .001), and left ventricular ejection fraction (HR: 0.96, 95% CI 0.94-0.98, P < .001) were also predictors of MACCE. Kaplan-Meier analysis revealed that all MACCE components and all-cause mortality were significantly higher in the high non-HDL-C group (P < .001). CONCLUSION: Non-HDL-C was closely related to long-term cardiac outcomes in RTR with dyslipidemia. Non-HDL-C should be among the primary goals in lipid-lowering treatment in post-transplant dyslipidemia.

[34] *Ogura M, Harada-Shiba M, Masuda D et al.* **Factors Associated with Carotid Atherosclerosis and Achilles Tendon Thickness in Japanese Patients with Familial Hypercholesterolemia: A Subanalysis of the Familial Hypercholesterolemia Expert Forum (FAME) Study**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34108342
ABSTRACT
AIMS: Familial hypercholesterolemia (FH) is characterized by high low-density lipoprotein (LDL) cholesterol levels, xanthomas including Achilles tendon thickening, and premature coronary artery disease (CAD). Carotid intima-media thickness (IMT) is a well-established surrogate marker for CAD in FH and Achilles tendon thickening is a specific physical finding in patients with FH. The objective of the present study was to identify factors associated with carotid IMT and Achilles tendon thickness in FH heterozygotes on lipid-lowering therapy. This study also aimed to examine the follow-up changes in carotid IMT and Achilles tendon thickness among them in the current real-world FH practice. METHODS: The current study is a subanalysis of the Familial Hypercholesterolemia Expert Forum (FAME) Study. The severity of carotid atherosclerosis was assessed with the maximal and mean IMT using ultrasonography, and Achilles tendon thickness was measured using X-rays. The present study used 571 patients under medical treatment for heterozygous FH who had baseline measurements for maximal IMT (n=511), mean IMT (n=459), or Achilles tendon thickness (n=486). The IMT was measured annually, and Achilles tendon thickness was evaluated every two years. RESULTS: Higher LDL cholesterol (LDL-C) level and lower HDL cholesterol (HDL-C) level were associated with greater maximal and mean IMT as well as greater Achilles tendon thickness. Achilles tendon thickness tended to be greater in patients who had a smoking history than in never-smokers. Maximal IMT and Achilles tendon thickness were significantly greater in patients with CAD than in those without. Additionally, lower HDL-C level and hypertension were associated with higher values of maximal and mean IMT, suggesting the importance of comprehensive risk management including reduced HDL-C

and blood pressure control in FH care. In longitudinal observations, percentage changes in maximal IMT and mean IMT gradually increased during the observation period. In contrast, percentage changes in Achilles tendon thickness became progressively thinner throughout the observation period. CONCLUSIONS: We found a positive association between LDL-C levels and severity of carotid atherosclerosis in heterozygous FH patients on treatment. This observation suggests the insufficiency of lipid-lowering therapy and the presence of therapeutic inertia among clinicians in the real-world FH practice.

[35] *Kayikcioglu M, Tokgozoglu L, Tuncel OK et al.* **Collateral damage of the COVID-19 pandemic on the management of homozygous familial hypercholesterolemia**. Journal of clinical lipidology 2021; 15:381-382.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34099193
ABSTRACT

[36] *Vuorio A, Raal F, Klingel R, Kovanen PT*. **Why continued lipoprotein apheresis is vital for homozygous familial hypercholesterolemia patients with COVID-19**. Journal of clinical lipidology 2021; 15:379-380.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34099192
ABSTRACT

[37] *Özgür Y*. **Relationship between Vitamin D Deficiency, Albuminuria, Peripheral Artery Disease and 5-year Mortality in Chronic Kidney Disease**. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP 2021; 30:644-650.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34102774
ABSTRACT
OBJECTIVE: To investigate the effects of vitamin D deficiency, albuminuria and peripheral artery disease (PAD) relationships, on 5-year mortality in patients with chronic kidney disease (CKD) . METHODOLOGY: Observational study. PLACE AND DURATION OF STUDY: Department of Internal Medicine, Kartal Dr Lutfi Kırdar City Hospital, İstanbul, Turkey, from August 2015 to August 2020. METHODOLOGY: The study included patients with stage 2-4 CKD, who were not previously diagnosed with peripheral artery disease (PAD) and were not on hemodialysis. Each patient's ankle-brachial index (ABI) was measured at rest with a portable vascular hand doppler; and an ABI of <0.9 was considered to be PAD. The mortality status of the participants were confirmed by the national death reporting system. RESULTS: A total of 110 CKD patients, mean age of 62.1±9.7 years, 36.4% women, were included in the study. It was found that 17.3% of the patients had vitamin D deficiency, 15.4% had vitamin D insufficiency, 32.7% had asymptomatic PAD, 33.9% had microalbuminuria and 39.4% had macroalbuminuria. It was observed that as vitamin D levels decreased, the frequency of albuminuria, and the prevalence of PAD, was on an increasing trend. A significant correlation was found between 5-year mortality, gender, body mass index (BMI), glomerular filtration rate (eGFR), urine albumin creatinine ratio (UACR), hemoglobin A1c (A1c), calcium (Ca), phosphate (P), vitamin D, ankle brachial index (ABI), and the neutrophil lymphocyte ratio (NLR) as a result of univariate cox-regressionanalysis. In the multivariate cox-regression model, it was observed that vitamin D, ABI and UACR levels continued being significant, independent of age, gender, BMI and eGFR levels. Conclusion: Vitamin D deficiency, PAD and albuminuria, which are separate predictors of

mortality, were shown to be independent predictors of long-term mortality in CKD patients. Key Words: Chronic kidney disease, Mortality, Peripheral arterial disease, Vitamin D deficiency, Albuminuria, Ankle-brachial index.

[38] *Di Bartolo BA, Cartland SP, Genner S et al.* **HDL Improves Cholesterol and Glucose Homeostasis and Reduces Atherosclerosis in Diabetes-Associated Atherosclerosis**. Journal of diabetes research 2021; 2021:6668506.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34095317
ABSTRACT
BACKGROUND AND AIMS: Apolipoprotein A-I (ApoA-I), the main component of high-density lipoprotein (HDL), not only promotes reverse cholesterol transport (RCT) in atherosclerosis but also increases insulin secretion in pancreatic β-cells, suggesting that interventions which raise HDL levels may be beneficial in diabetes-associated cardiovascular disease (CVD). Previously, we showed that TNF-related apoptosis-inducing ligand (TRAIL) deletion in Apolipoprotein Eknockout (Apoe(-/-)) mice results in diabetes-accelerated atherosclerosis in response to a "Western" diet. Here, we sought to identify whether reconstituted HDL (rHDL) could improve features of diabetes-associated CVD in Trail(-/-)Apoe(-/-) mice. METHODS AND RESULTS: Trail(-/-)Apoe(-/-) and Apoe(-/-) mice on a "Western" diet for 12 weeks received 3 weekly infusions of either PBS (vehicle) or rHDL (containing ApoA-I (20 mg/kg) and 1-palmitoyl-2-linoleoyl phosphatidylcholine). Administration of rHDL reduced total plasma cholesterol, triglyceride, and glucose levels in Trail(-/-)Apoe(-/-) but not in Apoe(-/-) mice, with no change in weight gain observed. rHDL treatment also improved glucose clearance in response to insulin and glucose tolerance tests. Immunohistological analysis of pancreata revealed increased insulin expression/production and a reduction in macrophage infiltration in mice with TRAIL deletion. Furthermore, atherosclerotic plaque size in Trail(-/-)Apoe(-/-) mice was significantly reduced associating with increased expression of the M2 macrophage marker CD206, suggesting HDL's involvement in the polarization of macrophages. rHDL also increased vascular mRNA expression of RCT transporters, ABCA1 and ABCG1, in Trail(-/-)Apoe(-/-) but not in Apoe(-/-) mice. Conclusions. rHDL improves features of diabetes-associated atherosclerosis in mice. These findings support the therapeutic potential of rHDL in the treatment of atherosclerosis and associated diabetic complications. More studies are warranted to understand rHDL's mechanism of action.

[39] *Giovannucci EL, Rezende LFM, Lee DH.* **Muscle-strengthening activities and risk of cardiovascular disease, type 2 diabetes, cancer and mortality: A review of prospective cohort studies**. Journal of internal medicine 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34120373
ABSTRACT
The benefits of aerobic moderate-to-vigorous physical activity (MVPA) on major non-communicable diseases (NCDs) are well established. However, much less is known whether muscle-strengthening activities (i.e., resistance/weight/strength training) confer similar benefits. Herein, we conducted a narrative literature review and summarized the existing evidence from large prospective cohort studies on muscle strengthening activities and risk of major chronic diseases and mortality in adults generally free of major NCDs at baseline. Current epidemiologic evidence suggests that engagement in muscle-strengthening activities over 1-2 sessions (or approximately 60-150 min) per week was associated with reduced risk of cardiovascular disease (seven studies; approximately 20%-25%

reduction), type 2 diabetes (four studies; approximately 30% reduction), cancer mortality (four studies; approximately 15%-20% reduction) as well as all-cause mortality (six studies; approximately 20%-25% reduction). For diabetes, the risk appears to lower further with even higher levels of muscle-strengthening activities, but some studies for cardiovascular and all-cause mortality suggest a reversal whereby higher levels (≥2.5 h/week) have less benefit, or are even harmful, relative to lower levels of activity. The likely mechanisms contributing to a benefit include improvement in body composition, lipid profile, insulin resistance and inflammation. The evidence supports engaging in 1-2 sessions (up to 2.5 h) per week, preferably performed complementary to the recommended levels of aerobic MVPA. Although data are limited, caution is suggested for training exceeding 2.5 h per week. Further studies are required to better understand the influence of frequency, duration and intensity of muscle-strengthening activities on major NCDs and mortality in diverse populations.

[40] *Cho SMJ, Lee H, Lee HH et al.* **Dyslipidemia Fact Sheets in Korea 2020: an Analysis of Nationwide Population-based Data**. J Lipid Atheroscler 2021; 10:202-209.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34095012

ABSTRACT

OBJECTIVE: The Korean Society of Lipid and Atherosclerosis (KSoLA) has published the Dyslipidemia Fact Sheets in Korea 2020 to provide an overview of magnitude and management status of dyslipidemia and their recent trends therein. METHODS: The Fact Sheets were based on the analyses of Korean adults aged 20 years or older of the 2007-2018 Korea National Health and Nutrition Examination Survey (KNHANES) and the 2002-2018 National Health Insurance Big Data (NHI-BD). RESULTS: Between 2007 and 2018, the crude prevalence of hypercholesterolemia increased from 9.0% to 20.7%. During the same period, its management rate also improved yet remained unsatisfactory. In 2018, the prevalence of dyslipidemia was 45.6% in men and 31.3% in women, which increased with older age and presence of metabolic abnormalities. Indeed, the number of people diagnosed with dyslipidemia has increased nearly 8-fold from 1.5 million in 2002 to 11.6 million in 2018; alongside, the number of people receiving pharmacological treatment for dyslipidemia has also risen. Of the 7.7 million people treated for dyslipidemia in 2018, statin accounted for the majority (91.8%) of lipid-lowering drug prescriptions, followed by ezetimibe (14.6%), fibrate (8.5%), and omega-3 acid (5.9%). The most frequently used combination therapy was statin plus ezetimibe, accounting for 72% of dual therapy prescriptions. CONCLUSION: Dyslipidemia continues to impose a substantial disease burden in Korea. Both healthcare practitioners and patients need to actively adopt guideline-recommended lifestyle modification and pharmacological treatment for comprehensive, timely, and sustained management.

[41] *Massy ZA, Kolla E, Ferrières J et al.* **Is a treat-to-target approach to lipid-lowering therapy appropriate in patients with chronic kidney disease? A prospective French cohort study**. Journal of nephrology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34117621

ABSTRACT

BACKGROUND: Whereas European guidelines recommend adjusting lipid-lowering therapy (LLT) to meet prespecified targets ('treat-to-target') for low-density lipoprotein cholesterol (LDL-C), other guidelines do not ('fire and forget'). In a large observational prospective cohort, we sought to evaluate which strategy could be associated with better cardiovascular outcomes in chronic kidney disease

(CKD). METHODS: In CKD-REIN, patients (CKD stages 3 and 4) on LLT were categorized according to achievement of LDL-C targets for high and very high cardiovascular risk (<2.6 and <1.8 mmol/L, respectively) at baseline. Primary outcome was fatal/non-fatal atheromatous cardiovascular disease (CVD). Secondary outcomes were non-atheromatous CVD, atheromatous or non-atheromatous CVD, and major adverse cardiovascular events. RESULTS: The population comprised 1521 patients (68 ± 12 years, 31% women, mean estimated glomerular filtration rate [eGFR] 35 mL/min/1.73 m(2)). Overall, 523 (34%) met their LDL-C targets at baseline. Median follow-up was 2.9 years (interquartile range 2.2-3.0). Incidence rates per 100 patient-years were 6.2% (95% confidence interval [CI] 5.5-7.0) for atheromatous CVD, 9.2% (8.3-10.1) for non-atheromatous CVD, 15.2% (14.0-16.4) for atheromatous/non-atheromatous CVD, and 6.3% (5.5-7.1) for major adverse cardiovascular events. Corresponding rates in patients who achieved targets were 6.6%, 9.8%, 16.1%, and 6.3%, respectively. Target achievement was not associated with risk of fatal/non-fatal atheromatous CVD (adjusted hazard ratio 1.04, 95% CI 0.76-1.44, p = 0.77) or fatal/non-fatal atheromatous or non-atheromatous CVD (0.98, 0.78-1.23, p = 0.91). CONCLUSIONS: These findings do not appear to support a treat-to-target approach in CKD patients on LLT, and may favor the hypothesis of an advantage of fire-and-forget. Randomized trials are needed to confirm this theory.

[42] *Kotwal RS, Mazuchowski EL, Howard JT et al.* **Autopsy-Determined Atherosclerosis in Elite US Military Special Operations Forces**. J Spec Oper Med 2021; 21:19-24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34105116
ABSTRACT
BACKGROUND: Autopsy studies of trauma fatalities have provided evidence for the pervasiveness of atherosclerosis in young and middle-aged adults. The objective of this study was to determine the prevalence of atherosclerosis in elite US military forces. METHODS: We conducted a retrospective study of all US Special Operations Command (USSOCOM) fatalities from 2001 to 2020 who died from battle injuries. Autopsies were evaluated from Afghanistan- and Iraq-centric combat operations for evidence of coronary and/or aortic atherosclerosis and categorized as minimal (fatty streaking only), moderate (10-49% narrowing of ≥1 vessel), and severe (≥50% narrowing of ≥1 vessel). Prevalence of atherosclerosis was determined for the total population and by subgroup characteristics of age, sex, race/ethnicity, combat operation, service command, occupation, rank, cause of death, manner of death, and body mass index (BMI). RESULTS: From the total of 388 USSOCOM battle injury fatalities, 356 were included in the analysis. The mean age was 31 years (range, 19-57 years), and 98.6% were male. The overall prevalence of coronary and/or aortic atherosclerosis was 17.4%. The prevalence of coronary atherosclerosis alone was 13.8%. Coronary atherosclerosis was categorized as minimal in 1.1%, moderate in 7.6%, and severe in 5.1%. Of those with atherosclerosis, 24.2% were <30 years old, 88.7% were from enlisted ranks, and 95.2% had combatant occupations. When BMI could be calculated, 73.5% of fatalities with atherosclerosis had a BMI =25. CONCLUSIONS: Autopsy-determined atherosclerosis is prevalent in elite US military Special Operations Forces despite young age and positive lifestyle benefits of service in an elite military unit.

[43] *Kosendiak A, Felińczak A, Szymańska-Chabowska A*. **The role of physical training in the prevention of cardiovascular disease in a population of healthy people**. J Sports Med Phys Fitness 2021; 61:844-850.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34110121

ABSTRACT

BACKGROUND: Cardiovascular diseases (CVD) are still a leading cause of death worldwide. The modification of risk factors and lifestyle is more important than pharmacotherapy and it is the most effective way to combat cardiovascular diseases. Recommendations to undertake physical activity are vital to the prevention of cardiovascular diseases. The aim of the study was to analyze the impact of physical activity on the modifiable risk factors of cardiovascular diseases. METHODS: Seventy-six participants, including 38 men, with a mean age of 37±9 were enrolled into the study in 2012-2013. Six months of advanced personal training program "You can be a marathon runner too" (twice a week for 3-4 hours) was carried out. Advice on healthy eating and changes in lifestyle were given. The following parameters: body composition analysis, Body Mass Index, lipids profile, glucose and morphology were measured twice at the beginning and after 6 months of the study. The data were statistically analyzed. RESULTS: A positive trend in some parameters was observed in all the respondents. The BMI decreased from 25 kg/m(2) to 23 kg/m(2) and the percentage of body fat - from 25% to 21%. Furthermore, some blood parameters decreased: cholesterol from 217mg/dL to 196mg/dL, triglycerides from 128 mg/dL to 97 mg/dL, and glucose from 82 mg/dL to 79 mg/dL. However, HDL increased from 66 mg/dL to 75 mg/dL. CONCLUSIONS: Regular physical activity has a positive influence on lowering the risk factors of cardiovascular diseases. Encouraging the implementation of behavioral changes and greater everyday physical activity may contribute to maintaining health for a long time.

[44] *Kim JS*. **Role of Blood Lipid Levels and Lipid-Lowering Therapy in Stroke Patients with Different Levels of Cerebral Artery Diseases: Reconsidering Recent Stroke Guidelines**. J Stroke 2021; 23:149-161.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34102752

ABSTRACT

Hyperlipidemia is an important risk factor for ischemic stroke; the Stroke Prevention by Aggressive Reduction in Cholesterol Level and Treat Stroke to Target studies have shown that statins are beneficial for patients with stroke and that a low target for low-density lipoprotein cholesterol (LDL-C) concentration may maximize this benefit. Based on these results, recent guidelines have emphasized the application of "high-intensity statins" and "low LDL-C target" strategies in patients with stroke. However, it should be kept in mind that the role of blood lipids as a risk factor and benefit of lipid-lowering therapy are different among patients with different levels of cerebral arterial diseases. Studies have suggested that hypolipidemia, but not hyperlipidemia, is a risk factor for small vessel diseases (SVDs) such as intracerebral hemorrhages, microbleeds, white matter hyperintensities, and perhaps, lacunar infarction. Although lipid-lowering agents might benefit certain patients with SVD, high-intensity statin and low LDL-C target strategies cannot be applied. In contrast, these strategies are important in patients with extracranial atherosclerosis, such as internal carotid disease, considering ample evidence of the benefits of lipid-lowering agents. Imaging studies have shown that statins stabilize vulnerable plaques in these patients. Although lipid-lowering agents are likely to benefit patients with intracranial atherosclerosis, the degree of their benefit and appropriate target LDL-C level for these patients remain unclear. More studies are needed to elucidate the appropriate lipid-modifying strategies in patients with stroke with different levels of cerebral artery disease.

[45] *Hu EA, Scharen J, Nguyen V, Langheier J.* **Evaluating the Impact of a Digital Nutrition Platform on Cholesterol Levels in Users With Dyslipidemia: Longitudinal Study**. JMIR Cardio 2021; 5:e28392.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34110291
ABSTRACT
BACKGROUND: A strong association exists between consuming a healthy diet and lowering cholesterol levels among individuals with high cholesterol. However, implementing and sustaining a healthy diet in the real world is a major challenge. Digital technologies are at the forefront of changing dietary behavior on a massive scale, as they can reach broad populations. There is a lack of evidence that has examined the benefit of a digital nutrition intervention, especially one that incorporates nutrition education, meal planning, and food ordering, on cholesterol levels among individuals with dyslipidemia. OBJECTIVE: The aim of this observational longitudinal study was to examine the characteristics of people with dyslipidemia, determine how their status changed over time, and evaluate the changes in total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), non-HDL-C, and triglycerides among individuals with elevated lipids who used Foodsmart, a digital nutrition platform that integrates education, meal planning, and food ordering. METHODS: We included 653 adults who used Foodsmart between January 2015 and February 2021, and reported a lipid marker twice. Participants self-reported age, gender, weight, and usual dietary intake in a 53-item food frequency questionnaire, and lipid values could be provided at any time. Dyslipidemia was defined as total cholesterol ≥200 mg/dL, HDL-C ≤40 mg/dL, LDL-C ≥130 mg/dL, or triglycerides ≥150 mg/dL. We retrospectively analyzed distributions of user characteristics and their associations with the likelihood of returning to normal lipid levels. We calculated the mean changes and percent changes in lipid markers among users with elevated lipids. RESULTS: In our total sample, 54.1% (353/653) of participants had dyslipidemia at baseline. Participants with dyslipidemia at baseline were more likely to be older, be male, and have a higher weight and BMI compared with participants who had normal lipid levels. We found that 36.3% (128/353) of participants who had dyslipidemia at baseline improved their lipid levels to normal by the end of follow-up. Using multivariate logistic regression, we found that baseline obesity (odds ratio [OR] 2.57, 95% CI 1.25-5.29; P=.01) and Nutriscore (OR 1.04, 95% CI 1.00-1.09; P=.04) were directly associated with achieving normal lipid levels. Participants with elevated lipid levels saw improvements as follows: HDL-C increased by 38.5%, total cholesterol decreased by 6.8%, cholesterol ratio decreased by 20.9%, LDL-C decreased by 12.9%, non-HDL-C decreased by 7.8%, and triglycerides decreased by 10.8%. CONCLUSIONS: This study characterized users of the Foodsmart platform who had dyslipidemia and found that users with elevated lipid levels showed improvements in the levels over time.

[46] *Petelina TI, Musikhina NA, Avdeeva KS et al.* **Gender characteristics of lipid profile parameters and markers of vascular inflammation in patients with stable angina pectoris in groups with presence and absence of type 2 diabetes**. Klinicheskaia laboratornaia diagnostika 2021; 66:325-332.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34105907
ABSTRACT
The study of the parameters of the lipid profile and markers of the inflammatory reaction of the vascular wall in patients with stable angina pectoris in the presence or absence of type 2 diabetes

mellitus (T2DM) is of great importance for revealing the gender characteristics of the pathophysiological mechanisms of the development and course of diseases, developing secondary prevention of complications and determining the prognosis. 194 patients with stable angina pectoris (SA), single-vessel coronary artery disease, mean age 60.3 ± 7.8 years were examined. Patients were divided into two groups: group 1 - patients with SA without diabetes 2 (n = 152), group 2 - with SA and diabetes 2 (n = 42). In each group, subgroups of men and women are distinguished. The study of biomarkers was carried out upon admission to the hospital on the background of therapy, taken on an outpatient basis. The study included a complex of parameters of the lipid spectrum, markers of the inflammatory response, endothelial dysfunction, and carbohydrate metabolism parameters. A comparative analysis of biomarkers revealed an excess of reference values of atherogenic lipid fractions in both groups of patients, regardless of patient gender. Moreover, in the first group of patients, in the subgroup of women, a significant excess of the level of TC, PL (a), and ApoA-1 was registered compared with the subgroup of men. In the second group, there were no significant differences in parameters between the male and female subgroups. Evaluation of the parameters of the inflammatory reaction revealed in the subgroup of women with T2DM a steady tendency to exceed the level of hs-CRP, TNF-α, homocysteine compared with both men and women in the SA group without T2DM. The logistic regression revealed the main biochemical markers that affect the aggravation of the course of IHD in women with T2DM: this is a uric acid level of more than 380 mmol / l - OS 11.5 (95% CI 1.71-77.69), TNF-α more 8 pg / ml - OR 7.5 (95% CI 1.07-52.46) and an increase in TG - OR 3.33 (95% CI 1.073-10.335). Thus, women of the 2nd group with the presence of T2DM are characterized by the highest level of atherogenic fractions of lipids, markers of vascular inflammation, glucose and HbA1c, which may indicate the greatest potential for the development of atherothrombotic complications in this subgroup of patients.

[47] *Reijman MD, Kusters DM, Wiegman A*. **Advances in familial hypercholesterolaemia in children**. Lancet Child Adolesc Health 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34119028

ABSTRACT

Familial hypercholesterolaemia is a common, dominantly inherited disease that results in high concentrations of low-density lipoprotein cholesterol and in premature cardiovascular disease. To prevent cardiovascular disease and premature mortality, patients with the condition need to be identified and to start treatment early in life. In this Review, we discuss the treatment of heterozygous and homozygous familial hypercholesterolaemia in children, including lifestyle modifications, current pharmacological treatment options, and promising novel lipid-lowering treatments. In particular, these new therapies are expected to improve outcomes for patients with severe heterozygous familial hypercholesterolaemia or statin intolerance. For patients with homozygous familial hypercholesterolaemia, lipoprotein apheresis is currently the most valuable therapy available, but new approaches might reduce the need for this effective yet invasive, time-consuming, and expensive treatment.

[48] *El-Sawaf ES, Saleh S, Abdallah DM et al.* **Vitamin D and rosuvastatin obliterate peripheral neuropathy in a type-2 diabetes model through modulating Notch1, Wnt-10α, TGF-β and NRF-1 crosstalk**. Life sciences 2021; 279:119697.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34102194

ABSTRACT
AIMS: Vitamin D and rosuvastatin are well-known drugs that mediate beneficial effects in treating type-2 diabetes (T2D) complications; however, their anti-neuropathic potential is debatable. Hence, our study investigates their neurotherapeutic potential and the possible underlying mechanisms using a T2D-associated neuropathy rat model. MAIN METHODS: Diabetic peripheral neuropathy (DPN) was induced with 8 weeks of administration of a high fat fructose diet followed by a single i.p. injection of streptozotocin (35 mg/kg). Six weeks later, DPN developed and rats were divided into five groups; viz., control, untreated DPN, DPN treated with vitamin D (cholecalciferol, 3500 IU/kg/week), DPN treated with rosuvastatin (10 mg/kg/day), or DPN treated with combination vitamin D and rosuvastatin. We determined their anti-neuropathic effects on small nerves (tail flick test); large nerves (electrophysiological and histological examination); neuronal inflammation (TNF-α and IL-18); apoptosis (caspase-3 activity and Bcl-2); mitochondrial function (NRF-1, TFAM, mtDNA, and ATP); and NICD1, Wnt-10α/β-catenin, and TGF-β/Smad-7 pathways. KEY FINDINGS: Two-month treatment with vitamin D and/or rosuvastatin regenerated neuronal function and architecture and abated neuronal inflammation and apoptosis. This was verified by the inhibition of the neuronal content of TNF-α, IL-18, and caspase-3 activity, while augmenting Bcl-2 content in the sciatic nerve. These treatments inhibited the protein expressions of NICD1, Wnt-10α, β-catenin, and TGF-β; increased the sciatic nerve content of Smad-7; and enhanced mitochondrial biogenesis and function. SIGNIFICANCE: Vitamin D and/or rosuvastatin alleviated diabetes-induced neuropathy by suppressing Notch1 and Wnt-10α/β-catenin; modulating TGF-β/Smad-7 signaling pathways; and enhancing mitochondrial function, which lessened neuronal degeneration, demyelination, and fibrosis.

[49] *Roy P, Koetter P, Cunningham J et al.* **A rare case of diabetic ketoacidosis presenting with severe hypertriglyceridemia requiring plasmapheresis in an adult with type-2 diabetes mellitus: Case report**. Medicine (Baltimore) 2021; 100:e26237.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34115010
ABSTRACT
INTRODUCTION: Severe hypertriglyceridemia (HTG) is a rare complication of insulin resistance. Its presentation with diabetic ketoacidosis (DKA) has been reported in a few cases, where most patients have type-1 diabetes mellitus (DM). Our case represents a unique presentation of DKA associated with severe HTG above 10,000 mg/dL in an adult with type-2 DM. PATIENT CONCERNS AND DIAGNOSIS: Case Report: A 51-year-old man with no prior illnesses presented to the emergency department with abdominal pain and nausea. He was found to have DKA with a blood glucose level of 337 mg/dL, pH of 7.17, beta-hydroxybutyrate of 7.93 mmol/L, and anion gap of 20 mmol/L. His triglyceride levels were >10,000 mg/dL. His serum was found to be lipemic. Computerized tomography scan of the abdomen demonstrated mild acute pancreatitis. Negative GAD65 antibodies supported the diagnosis of type-2 DM. INTERVENTIONS AND OUTCOMES: Endocrinology was consulted and one cycle of albumin-bound plasmapheresis was administered. This therapy significantly improved his HTG. DKA gradually resolved with insulin therapy as well. He was discharged home with endocrinology follow-up. CONCLUSION: This unique case highlights an uncommon but critical consequence of uncontrolled DM. It brings forth the possibility of severe HTG presenting as a complication of uncontrolled type-2 DM. Severe HTG commonly presents with acute pancreatitis, which can be debilitating if not managed promptly. Most patients with this presentation are managed with insulin infusion. The use of plasmapheresis for management of severe HTG has

not been well studied. Our case supports the use of plasmapheresis as an effective and rapid treatment for severe HTG.

[50] *Fang M, Wang D, Coresh J, Selvin E*. **Trends in Diabetes Treatment and Control in U.S. Adults, 1999-2018**. The New England journal of medicine 2021; 384:2219-2228.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34107181

ABSTRACT

BACKGROUND: Documenting current trends in diabetes treatment and risk-factor control may inform public health policy and planning. METHODS: We conducted a cross-sectional analysis of data from adults with diabetes in the United States participating in the National Health and Nutrition Examination Survey (NHANES) to assess national trends in diabetes treatment and risk-factor control from 1999 through 2018. RESULTS: Diabetes control improved from 1999 to the early 2010s among the participants but subsequently stalled and declined. Between the 2007-2010 period and the 2015-2018 period, the percentage of adult NHANES participants with diabetes in whom glycemic control (glycated hemoglobin level, <7%) was achieved declined from 57.4% (95% confidence interval [CI], 52.9 to 61.8) to 50.5% (95% CI, 45.8 to 55.3). After major improvements in lipid control (non-high-density lipoprotein cholesterol level, <130 mg per deciliter) in the early 2000s, minimal improvement was seen from 2007-2010 (52.3%; 95% CI, 49.2 to 55.3) to 2015-2018 (55.7%; 95% CI, 50.8 to 60.5). From 2011-2014 to 2015-2018, the percentage of participants in whom blood-pressure control (<140/90 mm Hg) was achieved decreased from 74.2% (95% CI, 70.7 to 77.4) to 70.4% (95% CI, 66.7 to 73.8). The percentage of participants in whom all three targets were simultaneously achieved plateaued after 2010 and was 22.2% (95% CI, 17.9 to 27.3) in 2015-2018. The percentages of participants who used any glucose-lowering medication or any blood-pressure-lowering medication were unchanged after 2010, and the percentage who used statins plateaued after 2014. After 2010, the use of combination therapy declined in participants with uncontrolled blood pressure and plateaued for those with poor glycemic control. CONCLUSIONS: After more than a decade of progress from 1999 to the early 2010s, glycemic and blood-pressure control declined in adult NHANES participants with diabetes, while lipid control leveled off. (Funded by the National Heart, Lung, and Blood Institute.).

[51] *Fitz NF, Nam KN, Wolfe CM et al.* **Phospholipids of APOE lipoproteins activate microglia in an isoform-specific manner in preclinical models of Alzheimer's disease**. Nature communications 2021; 12:3416.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34099706

ABSTRACT

APOE and Trem2 are major genetic risk factors for Alzheimer's disease (AD), but how they affect microglia response to Aβ remains unclear. Here we report an APOE isoform-specific phospholipid signature with correlation between human APOEε3/3 and APOEε4/4 AD brain and lipoproteins from astrocyte conditioned media of APOE3 and APOE4 mice. Using preclinical AD mouse models, we show that APOE3 lipoproteins, unlike APOE4, induce faster microglial migration towards injected Aβ, facilitate Aβ uptake, and ameliorate Aβ effects on cognition. Bulk and single-cell RNA-seq demonstrate that, compared to APOE4, cortical infusion of APOE3 lipoproteins upregulates a higher proportion of genes linked to an activated microglia response, and this trend is augmented by TREM2 deficiency. In vitro, lack of TREM2 decreases Aβ uptake by APOE4-treated microglia only,

suggesting TREM2-APOE interaction. Our study elucidates phenotypic and transcriptional differences in microglial response to Aβ mediated by APOE3 or APOE4 lipoproteins in preclinical models of AD.

[52] *Luque Linero P, Castilla-Guerra L, Rojas Marcos Rodriguez I, Rico Corral MA*. **Hypercholesterolemia treatment in a patient with family hypercholesterolemia and myopathy due to carnitine palmitoyltransferase II deficiency with PCSK9 inhibitors**. Neurologia 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34112556
ABSTRACT

[53] *Morris G, Berk M, Walder K et al.* **The lipid paradox in neuroprogressive disorders: Causes and consequences**. Neuroscience and biobehavioral reviews 2021; 128:35-57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34118292
ABSTRACT
Chronic systemic inflammation is associated with an increased risk of cardiovascular disease in an environment of low low-density lipoprotein (LDL) and low total cholesterol and with the pathophysiology of neuroprogressive disorders. The causes and consequences of this lipid paradox are explored. Circulating activated neutrophils can release inflammatory molecules such as myeloperoxidase and the pro-inflammatory cytokines interleukin-1 beta, interleukin-6 and tumour necrosis factor-alpha. Since activated neutrophils are associated with atherosclerosis and cardiovascular disease and with major depressive disorder, bipolar disorder and schizophrenia, it seems reasonable to hypothesise that the inflammatory molecules released by them may act as mediators of the link between systemic inflammation and the development of atherosclerosis in neuroprogressive disorders. This hypothesis is tested by considering the association at a molecular level of systemic inflammation with increased LDL oxidation; increased small dense LDL levels; increased lipoprotein (a) concentration; secretory phospholipase A(2) activation; cytosolic phospholipase A(2) activation; increased platelet activation; decreased apolipoprotein A1 levels and function; decreased paroxonase-1 activity; hyperhomocysteinaemia; and metabolic endotoxaemia. These molecular mechanisms suggest potential therapeutic targets.

[54] *Busch C, Katzmann JL, Jochmann C et al.* **General health of patients with diabetic macular edema-The LIPSIA study**. PloS one 2021; 16:e0252321.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34115786
ABSTRACT
PURPOSE: Cardiovascular risk factors such as hypertension or dyslipidemia can influence the incidence and progression of diabetic retinopathy (DR) and diabetic macular edema (DME). The aim of this study is to describe the comorbidities in patients with DME. METHODS: Prospective, monocentric observational study. Patients presenting for the treatment of DME received laboratory and clinical examinations including 24-hour blood pressure measurement. RESULTS: Seventy-five consecutive patients were included in the study. The mean age was 61.0 ± 14.5 years, and 83% had type 2 diabetes. The mean body mass index (BMI) was 32.8 ± 6.0 kg/m2. Overweight (BMI ≥ 25 kg/m2) was present in 92% of all patients. HbA1c values were > 7.0% in 57%. Although 87% of the patients already received antihypertensive therapy, the blood pressure (BP) of 82% was still above the recommended target values of systolic < 140 mmHg and diastolic < 80 mmHg. An insufficient nocturnal fall of the systolic BP (< 10%, non-dipping or reverse dipping) was observed in 62%. In 83%

of the patients the glomerular filtration rate was ≤ 90 ml/min/1.73m2. Despite 65% of the cohort already receiving lipid-lowering therapy, LDL cholesterol was above the target value of 1.4 mmol/l in 93%. All patients had at least one cardiovascular risk factor in addition to diabetes (overweight, hypertension, insufficient nocturnal BP fall, dyslipidemia, or renal dysfunction) and 86% had ≥ 3 risk factors. CONCLUSION: DME patients are characterized by highly prevalent cardiovascular risk factors that are poorly controlled. These comorbidities reduce the prognosis and negatively influence existing DR and DME. The data reveal an important opportunity for improving patient care by interaction of the ophthalmologist with the general practitioner and internal specialists for the detection and treatment of these conditions.

[55] *Kayamori Y, Nakamura M, Kishi K et al.* **Comparison of the Japan Society of Clinical Chemistry reference method and CDC method for HDL and LDL cholesterol measurements using fresh sera**. Practical laboratory medicine 2021; 25:e00228.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34095414

ABSTRACT

OBJECTIVES: In 2009, the Japan Society of Clinical Chemistry (JSCC) recommended a reference method for the measurement of serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels. This automated method uses cholesterol esterase-cholesterol dehydrogenase to measure cholesterol levels in fractions obtained after ultracentrifugation and dextran sulfate/magnesium chloride precipitation. In the present study, using fresh samples, we compared the LDL-C and HDL-C levels measured using this method with those measured using the traditional Centers for Disease Control and Prevention (CDC)-beta-quantification (BQ) method. DESIGN: and methods: Using both the JSCC and CDC-BQ methods, LDL-C/HDL-C levels were measured in 47 non-diseased and 126 diseased subjects, whose triglyceride levels were lower than 11.29 mmol/L (1000 mg/dL). RESULTS: For LDL-C, the equation of the line representing the correlation between the two methods was y = 0.991x + 0.009 mmol/L; r = 0.999; and Sy/x = 0.025 mmol/L, where x is the mean LDL-C level measured using the CDC-BQ method. Similarly, for HDL-C, the equation of the line representing the correlation between the two methods was y = 0.988x + 0.041 mmol/L, r = 0.999, and Sy/x = 0.019 mmol/L, where x is the mean HDL-C level measured using the CDC-BQ method. CONCLUSIONS: The JSCC method agreed with the CDC-BQ method in cases of both non-diseased and diseased subjects, including those with dyslipidemia.

[56] *Şimşek B, İnan D, Çınar T et al.* **Evaluation of Low-density Lipoprotein Cholesterol Target Attainment Rates According to the 2016 and 2019 European Society of Cardiology/European Atherosclerosis Society Dyslipidemia Guidelines for Secondary Prevention in Patients with Acute Myocardial Infarction**. Revista de investigacion clinica; organo del Hospital de Enfermedades de la Nutricion 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34098569

ABSTRACT

BACKGROUND: High-intensity statin (HIS) therapy is widely recommended for secondary prevention after an acute myocardial infarction (AMI). The 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) dyslipidemia guidelines have lowered the target low-density lipoprotein cholesterol (LDL-C) level, which necessitates a more frequent use of nonstatin therapies. OBJECTIVES: The objectives of the study were to investigate the rate of LDL-C target

attainment for secondary prevention in AMI patients. METHODS: This retrospective investigation included 1360 patients diagnosed with AMI in a tertiary heart center. Lipid parameters were collected within 24 h of admission and within 1 year after discharge. The medications used were retrieved from medical records, and the lowest LDL-C levels after statin treatment were used to assess the effectiveness of the therapy. LDL-C target attainment was defined according to the 2016 ESC/EAS dyslipidemia guidelines as an LDL-C level of < 70 mg/dL and a ≥ 50% reduction from baseline. In addition, the rate of LDL-C target attainment according to the 2019 fromESC/EAS guidelines was defined as an LDL-C level of < 55 mg/dL and a ≥ 50% reduction baseline. RESULTS: In total, 502 (36.9%) and 247 (18.2%) patients reached the LDL-C targets according to the 2016 and 2019 ESC/EAS guidelines, respectively. The admission LDL-C levels were significantly lower and HIS treatment was used more frequently in patients who subsequently attained the LDL-C goal. Remarkably, 461 (34%) patients failed to reach the LDL-C goals despite HIS treatment. Only 27 (1.9%) patients were prescribed ezetimibe. CONCLUSION: The rate of LDL-C goal attainment in AMI patients was low, which indicates the need for combination statin and non-statin lipid-lowering therapies.

[57] *Araújo PM, Nunes A, Torres S et al.* **Temporal trends of lipid control in very high cardiovascular risk patients**. Revista portuguesa de cardiologia : orgao oficial da Sociedade Portuguesa de Cardiologia = Portuguese journal of cardiology : an official journal of the Portuguese Society of Cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34112555
ABSTRACT
INTRODUCTION: Since 2011, the European guidelines have included a specific low-density lipoprotein cholesterol (LDL-C) target, <70 mg/dl, for very high cardiovascular risk (CVR) patients. However, registries have shown unsatisfactory results in obtaining this level of adequate lipid control. OBJECTIVES: To assess temporal trends in the use of lipid-lowering therapy (LLT) and attainment of adequate control in very high CVR patients since 2011. METHODS: We performed a retrospective observational study including very high CVR patients admitted in two periods: the first two years since the 2011 guidelines (2011/2012) and five years later (2016/2017). Lipid values, LLT, clinical variables and adequate lipid control rates were analyzed. RESULTS: A total of 1314 patients were reviewed (2011/2012: 638; 2016/2017: 676). Overall, 443 patients (33.7%) were not under LLT and only a slight improvement in drug prescription was observed from 2011/2012 to 2016/2017. In LLT users, the proportion of high-intensity LLT increased significantly in the later years (6.4% vs. 24.0%; p<0.001), but this was not associated with adequate lipid control. Overall, mean LDL-C was 95.4±37.2 mg/dl and adequate control was achieved in 320 patients (24.4%), without significant differences between 2011/2012 and 2016/2017 (p=0.282). Independent predictors of adequate control were male gender, older age, diabetes, chronic kidney disease, prior acute coronary syndrome, prior stroke and LLT, while stable coronary artery disease was associated with higher risk of failure. CONCLUSION: Even after the introduction of specific LDL-C targets, these are still not reached in most patients. Over a five-year period, LLT prescription only improved slightly, while adequate lipid control rates remained unchanged.

[58] *Washirasaksiri C, Srivanichakorn W, Godsland IF et al.* **Increasing glycaemia is associated with a significant decline in HDL cholesterol in women with prediabetes in two national populations**. Scientific reports 2021; 11:12194.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34108497
ABSTRACT
Internationally, studies have shown associations between lipids and glycemia; however, whether the link varies by gender and population has been rarely examined. We investigated relationships between glycemia and HDL- and Non-HDL-cholesterol and their modification by gender. We undertook a cross-sectional analysis from the National Health Examination Survey for Thailand (NHES-Thailand) and the Health Survey for England (HS-England) in adults aged 18-75 year. Glycaemia was assessed by FPG in Thailand and by HbA1c in the UK. In population- and gender-stratified analyses, the relationships between glycemia and lipids were explored. A total of 15,145 Thai and 3484 UK adults with blood measurement were included. The prevalences of prediabetes were: in NHES-Thailand, 16% (SE = 0.004), based on FPG (5.6 to < 7.0 mmol/L) and in HS-England, 19% (0.007) based on HbA1c (39 to < 48 mmol/mol). Increasingly abnormal glucose homeostasis was associated with increasing age, adiposity, SBP, proportion of antihypertensive and lipid-lowering agent use and with decreasing HDL-cholesterol. Independent of age, adiposity, smoking, alcohol, physical activity, and lipid and BP lowering drug use, increasing glycemia was associated with decreasing HDL-cholesterol specifically in women with prediabetes (NHES-Thailand, beta-coefficient -0.07 (95% CI -0.15, -0.001) p = 0.04 and HS-England, -0.03 (-0.04, -0.006) p = 0.01). In both populations, among those with prediabetes, increasing glycaemia is associated with an adverse, significant decline in HDL cholesterol, specifically in women. These adverse effects are apparent in widely-differing international populations.

[59] *Rodríguez Escobedo R, González Martínez S, Díaz Naya L et al.* **[Real-life efficacy and safety of PCSK9 inhibitors treatment: Experience in three hospitals in Asturias]**. Semergen / Sociedad Espanola de Medicina Rural y Generalista 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34112592
ABSTRACT
BACKGROUND: Inhibitors of proprotein convertase subtilisin/kexin type9 (PCSK9 inhibitors) are a treatment option for those patients with familial hypercholesterolemia or in secondary prevention who do not reach the LDL-C target with other therapeutic measures. The aim of this study is to assess the effectiveness and safety of these drugs. METHODS: Retrospective, multicentric, descriptive study. We collected data from all patients that have started PCSK9 inhibitors treatment in three hospitals in Asturias since the beginning of its use in 2016. We analysed changes in lipid profile with PCSK9 inhibitors and its side effects. RESULTS: We registered 98 patients, 75 of them affected by familial hypercholesterolemia (FH) and 23 unaffected. Two months after the beginning of PCSK9 inhibitors treatment, a 61% reduction rate in LDL-C in patients with FH and 52% in those without this condition was observed. This statistically significant reduction remained stable during follow-up. A significant decrease in total cholesterol was observed, without significant changes in HDL-C and triglycerides. 96% of patients had no complications. CONCLUSIONS: PCSK9 inhibitors are safe drugs that rapidly achieve significant reductions in LDL-C after the beginning of treatment, which are maintained over time. Hence, the use of PCSK9 inhibitors is an alternative for the control of LDL-C in those patients in which the LDL-C target is not reached with other therapeutic measures.

[60] *Ganji M, Nardi V, Prasad M et al.* **Carotid Plaques From Symptomatic Patients Are Characterized by Local Increase in Xanthine Oxidase Expression**. Stroke 2021:Strokeaha120032964.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34107737
ABSTRACT
BACKGROUND AND PURPOSE: XO (xanthine oxidase) is a key enzyme of uric acid metabolism and is thought to contribute to oxidative pathways that promote atherosclerotic plaque progression, yet its role in plaque destabilization is not well elucidated. We hypothesized that XO is expressed in carotid plaque from symptomatic patients in association with cardiovascular risk factors. METHODS: Patients were stratified by symptoms, defined as presentation with an ipsilateral cerebral ischemic event. Carotid atherosclerotic plaques were obtained from 44 patients with symptomatic plaque and 44 patients without ischemic cerebral events. Protein expression of XO was evaluated by immunohistochemical staining and the percentage of cells expressing XO and CD68 (macrophage marker) compared between the groups. Biochemical and demographic cardiometabolic risk factors of study participants also were measured. RESULTS: Carotid atherosclerotic plaques from symptomatic patients were associated with significantly higher XO expression versus asymptomatic plaque (median [interquartile range]: 1.24 [2.09] versus 0.16 [0.34]; P<0.001) and with significantly higher circulating uric acid levels (mean±SD: 7.36±2.10 versus 5.37±1.79 mg/dL; P<0.001, respectively). In addition, XO expression in atherosclerotic carotid plaque was inversely associated with serum high-density lipoproteins cholesterol levels (P=0.010, r=-0.30) and directly with circulating uric acid levels (P<0.001, r=0.45). The average percentage of macrophages that expressed XO was significantly higher in symptomatic versus asymptomatic plaques (median [interquartile range]: 93.37% [25] versus 46.15% [21], respectively; P<0.001). CONCLUSIONS: XO overexpression in macrophages is associated with increased serum uric acid and low high-density lipoproteins cholesterol levels and may potentially have a mechanistic role in carotid plaque destabilization. The current study supports a potential role for uric acid synthesis pathway as a target for management of carotid atherosclerosis in humans.

[61] *Shen Y, Ni P, Men RT, Yang L*. **[A case report of rare cause of abnormal liver function: sitosterolemia]**. Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology 2021; 29:477-479.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34107589
ABSTRACT