[1] *Zhou T, Li H, Zhong H et al.* **Association of apoE gene polymorphisms with lipid metabolism in renal diseases**. African health sciences 2020; 20:1368-1381.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33402986

ABSTRACT

BACKGROUND AND OBJECTIVES: Apolipoprotein E (apoE) plays a central role in the metabolism and homeostasis of lipids. ApoE gene encodes three major isoforms: ε2, ε3 a nd ε4 forming six phenotypes: E2E2, E2E3, E2E4, E3E3, E3E3 and E4E4. Disorders of the lipid metabolism and the homeostasis are frequently coexist in renal diseases. The association between gene polymorphisms of apoE and lipid metabolism were not consistent. This meta-analysis was performed to assess the association between gene polymorphisms of apoE and lipid metabolism in renal diseases. METHODS: A pre-defined literatures search and selection of eligible relevant investigations were performed to extract and collect data from electronic databases. RESULTS: Sixteen articles were enrolled for the analysis of association between apoE gene polymorphisms and lipid metabolism. Subjects with E3E4 had a higher total cholesterol (TC) than those with E3E3, and subjects with E2E3 had a lower TC than those with E3E3. Subjects with ε2, had a lower TC than those with ε3 or ε4, and subjects with ε4 had a higher TC than those with, ε3. Subjects with E2E2, E2E3 or E4E4 had a higher triglyceride (TG) than those with E3E3. Subjects with ε4 had a higher TG than those with ε3. Subjects with ε2, had a higher level of TG than those with non-ε2. Subjects with E3E4 had a slightly lower high-density lipoprotein (HDL) than those with E3E3. E3E4 appeared to be associated with lower levels of HDL. Subjects with E2E2, E2E3 had a notably lower low-density lipoprotein (LDL) than those with E3E3. Subjects with ε2, had a lower LDL than those with ε3 or ε4 ApoE gene polymorphisms were not associated with very low-density lipoprotein, and lipoprotein (a) [Lp(a)]. Subjects with E2E3 or E2E4 had higher apoE levels than those with E3E3, and subjects with E4E4 had lower apoE levels than those with E3E3. CONCLUSION: ApoE gene polymorphisms are associated with the expression of TC, TG HDL, LDL, Lp(a) or apoE.

[2] *Tomasdottir MM, Held C Md P, Hadziosmanovic N et al.* **Risk markers of incident atrial fibrillation in patients with coronary heart disease**. American heart journal 2021; 233:92-101.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33400910

ABSTRACT

BACKGROUND: In patients with coronary heart disease (CHD), atrial fibrillation (AF) is associated with increased morbidity and mortality. We investigated the associations between clinical risk factors and biomarkers with incident AF in patients with CHD. METHODS AND RESULTS: Around 13,153 patients with optimally treated CHD included in the STabilization of Atherosclerotic plaque By Initiation of darapLadIb TherapY (STABILITY) trial with plasma samples obtained at randomization. Mean follow-up time was 3.5 years. The association between clinical risk factors and biomarkers with incident AF was estimated with Cox-regression models. Validation was performed in 1,894 patients with non-ST-elevation acute coronary syndrome included in the FRISC-II trial. The median (min-max) age was 64 years (range 26-92) and 2,514 (19.1%) were women. A total of 541 patients, annual incidence rate of 1.2%, developed AF during follow-up. In multivariable models, older age, higher levels of NT-proBNP, higher body mass index (BMI), male sex, geographic regions, low physical activity, and heart failure were independently associated with increased risk of incident AF with hazard ratios ranging from 1.04 to 1.79 ($P \leq .05$). NT-proBNP improved the C-index from 0.70 to 0.71. In the validation cohort, age, BMI, and NT-proBNP were associated with increased risk of incident AF

with similar hazard ratios. CONCLUSIONS: In patients with optimally treated CHD, the incidence of new AF was 1.2% per year. Age, NT-proBNP as a marker of impaired cardiac function, and BMI were the strongest factors, independently and consistently associated with incident AF. Male sex and low physical activity may also contribute to the risk of AF in patients with CHD.

[3] *Delevry D, Gupta EK*. **Bempedoic acid: Review of a novel therapy in lipid management**. American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists 2021; 78:95-104.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33399194
ABSTRACT
PURPOSE: An update on clinical development of a first-in-class oral medication for adjunctive cholesterol lowering in high-risk patients with persistent elevation of low-density lipoprotein cholesterol (LDL-C) despite statin therapy is reviewed. SUMMARY: Despite the proven efficacy of statin therapy, many patients cannot reach LDL-C goals with statins alone, largely due to inadequate response or intolerance. Nonstatin treatment options to reduce LDL-C include ezetimibe, bile acid sequestrants, and proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors; however their use has been limited by modest clinical benefit or high treatment costs. Novel nonstatin treatments are in development to further address the needs of this population. Bempedoic acid is a first-in-class oral adenosine triphosphate (ATP) citrate lyase inhibitor being evaluated as an additional treatment option for high-risk patients requiring further reduction in LDL-C. Bempedoic acid has been evaluated in multiple phase 2 and phase 3 trials as monotherapy or for use in combination with ezetimibe and/or statin therapy. Treatment with bempedoic acid has been demonstrated to result in significant reductions in LDL-C and several other cardiovascular risk markers without the myalgia associated with statin therapy. CONCLUSION: Bempedoic acid, used alone or with ezetimibe in a fixed-dose combination formulation, may be an effective alternative to current guideline-recommended nonstatin therapies in patients who do not attain adequate LDL-C lowering with maximally tolerated statin therapy and in statin-intolerant patients at risk for atherosclerotic cardiovascular disease.

[4] *Ferreira HB, Melo T, Paiva A, Domingues MDR*. **Insights in the Role of Lipids, Oxidative Stress and Inflammation in Rheumatoid Arthritis Unveiled by New Trends in Lipidomic Investigations**. Antioxidants (Basel, Switzerland) 2021; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33401700
ABSTRACT
Rheumatoid arthritis (RA) is a highly debilitating chronic inflammatory autoimmune disease most prevalent in women. The true etiology of this disease is complex, multifactorial, and is yet to be completely elucidated. However, oxidative stress and lipid peroxidation are associated with the development and pathogenesis of RA. In this case, oxidative damage biomarkers have been found to be significantly higher in RA patients, associated with the oxidation of biomolecules and the stimulation of inflammatory responses. Lipid peroxidation is one of the major consequences of oxidative stress, with the formation of deleterious lipid hydroperoxides and electrophilic reactive lipid species. Additionally, changes in the lipoprotein profile seem to be common in RA, contributing to cardiovascular diseases and a chronic inflammatory environment. Nevertheless, changes in the lipid profile at a molecular level in RA are still poorly understood. Therefore, the goal of this review was to gather all the information regarding lipid alterations in RA analyzed by mass spectrometry. Studies on

the variation of lipid profile in RA using lipidomics showed that fatty acid and phospholipid metabolisms, especially in phosphatidylcholine and phosphatidylethanolamine, are affected in this disease. These promising results could lead to the discovery of new diagnostic lipid biomarkers for early diagnosis of RA and targets for personalized medicine.

[5] *Werida R, Khairat I, Khedr NF*. **Effect of atorvastatin versus rosuvastatin on inflammatory biomarkers and LV function in type 2 diabetic patients with dyslipidemia**. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2021; 135:111179.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33401219

ABSTRACT

BACKGROUND: Statins are potential drugs for decreasing risk of atherosclerotic cardiovascular complications in type 2 diabetic (T2D) patients. PURPOSE: To examine the efficacy of both rosuvastatin (ROSUVA) and atorvastatin (ATORVA) on LV function and markers of inflammation in T2D patients with dyslipidemia. METHODS: One hundred-sixty T2D patients were assigned to receive either atorvastatin (ATORVA group, n = 80, 40 mg) or rosuvastatin (ROSUVA group, n = 80, 10 mg), daily for 6 months. Blood was collected for biochemical analysis. The prevalence of left ventricular abnormalities was determined by echocardiography and two-dimensional Speckle-Strain to assess Global Longitudinal Strain (GLS). RESULTS: ROSUVA vs. ATORVA resulted in significant ($p < 0.001$) reduction in HbA1c % (9.13 vs 2.35%), LDL-C (22.23% vs. 14.75%), triglycerides (13.56 % vs. 8.21 %), total cholesterol (16.10 % vs. 10.81 %), atherogenic index (18.08. % vs. 10.97%), hs-CRP (23.51 % vs.18.96%), sortilin (33.33 % % vs. 15.08 %), and leptin (31.81 % vs. 23.17 %) but increased adiponectin (97.99 % vs.76.47.1 %) and HDL-C (76.47 % vs. 0.21 %) compared with baseline, respectively. Negative correlations between adiponectin and each of hs-CRP, HbA1c%, total cholesterol, LDL-C, atherogenic index and leptin were found. Also, left ventricular functions were correlated with adiponectin, lipids, HbA1c% and hs-CRP. The areas under receiver operating characteristic curve (AUC) showed that hs-CRP, leptin, sortlin, leptin, and adiponectin were good predictors for cardiovascular events. CONCLUSION: ROSUVA is more efficacious in improving lipid profile, atherogenic index and modulation of inflammatory biomarkers in dyslipidemic T2D patients compared with ATROVA. However, both statins are equivalent as cardioprotective agents in dyslipidemic T2D patients.

[6] *Li T, Zhang Y, Cong H*. **Effect of PCSK9 inhibitor on lipoprotein particles in patients with acute coronary syndromes**. BMC cardiovascular disorders 2021; 21:19.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33413096

ABSTRACT

BACKGROUND: To assess the effects of proprotein convertase subtilisin/kexin type 9 inhibitor (evolocumab) on lipoprotein particles subfractions with Nuclear Magnetic Resonance spectroscopy in patients with acute coronary syndromes. METHODS: A total of 99 consecutive patients with ACS were enrolled and assigned to either the experimental group (n = 54) or the control group (n = 45). The combination therapy of PCSK9 inhibitor (Repatha®, 140 mg, q2w) and moderate statin (Rosuvastatin, 10 mg, qn) was administered in the experimental group, with statin monotherapy (Rosuvastatin, 10 mg, qn) in the control group. The therapeutic effects on lipoprotein particle subfractions were assessed with NMR spectroscopy after 8 weeks treatment, and the achievement of LDL-C therapeutic target in both groups were analyzed. RESULTS: In the experimental group, after 8 weeks

of evolocumab combination treatment, the concentrations of blood lipids (TC, LDL-C and its subfractions [LDL-1 to 6], VLDL-C and its subfractions [VLDL-1 to 5], IDL-C, and HDL-C), lipoprotein particles, and their subfractions [VLDL-P, IDL-P, LDL-P, and its subfractions [LDL-P1 to 6], apoB, and LP(a)] demonstrated therapeutic benefits with statistical significance ($P<0.05$). The decrease in total LDL-P concentrations was mainly due to a decreased concentration of small-sized LDL particles (LDL-P 5+6), which was significantly more prominent than the decrease in medium-sized LDL-P (LDL-P3+4) and large-sized LDL-P (LDL-P1+2) ($P<0.001$). According to lipid control target recommended by the latest China Cholesterol Education Program Expert Consensus in 2019, after 8 weeks treatment, 96.3% patients in the experimental group and 13.3% in the control group had achieved the LDL-C therapeutic target ($P<0.01$). CONCLUSIONS: Evolocumab combination treatment for 8 weeks significantly improves the plasma lipid profiles in ACS patients, and significantly decrease the concentration of lipoprotein particles which might contribute to the pathonesis of atherosclerosis.

[7] *Ikeda J, Scipione CA, Hyduk S et al.* **Radiation Impacts Early Atherosclerosis by Suppressing Intimal LDL Accumulation**. Circulation research 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33397122
ABSTRACT
Rationale: Bone marrow transplantation (BMT) is used frequently to study the role of hematopoietic cells in atherosclerosis, but aortic arch lesions are smaller in mice after BMT. Objective: To identify the earliest stage of atherosclerosis inhibited by BMT and elucidate potential mechanisms. Methods and Results: Ldlr(-/-) mice underwent total body γ-irradiation, bone marrow reconstitution and 6-week recovery. Atherosclerosis was studied in the ascending aortic arch and compared to mice without BMT. In BMT mice neutral lipid and myeloid cell topography were lower in lesions after feeding a cholesterol-rich diet (CRD) for 3, 6 and 12 weeks. Lesion coalescence and height were suppressed dramatically in mice post-BMT, whereas lateral growth was inhibited minimally. Targeted radiation to the upper thorax alone reproduced the BMT phenotype. Classical monocyte recruitment, intimal myeloid cell proliferation and apoptosis did not account for the post-BMT phenotype. Neutral lipid accumulation was reduced in 5-day lesions, thus we developed quantitative assays for LDL accumulation and paracellular leakage using DiI-labeled human LDL and rhodamine B-labeled 70kD dextran. LDL accumulation was dramatically higher in the intima of Ldlr(-/-) relative to Ldlr(+/+) mice, and was inhibited by injection of HDL mimics, suggesting a regulated process. LDL, but not dextran, accumulation was lower in mice post-BMT both at baseline and in 5-day lesions. Since the transcript abundance of molecules implicated in LDL transcytosis was not significantly different in the post-BMT intima, transcriptomics from whole aortic arch intima, and at single cell resolution, was performed to give insights into pathways modulated by BMT. Conclusions: Radiation exposure inhibits LDL entry into the aortic intima at baseline and the earliest stages of atherosclerosis. Single cell transcriptomic analysis suggests that LDL uptake by endothelial cells is diverted to lysosomal degradation and reverse cholesterol transport pathways. This reduces intimal accumulation of lipid and impacts lesion initiation and growth.

[8] *Nguyen S, Alexander SA, Apenteng S, Castiglione A*. **Statin-Associated Necrotizing Myopathy: A Feared Complication**. Cureus 2020; 12:e11689.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33391923

ABSTRACT
Statins are a group of frequently-prescribed drugs with proven cardiovascular risk-benefit. The most common adverse effects include weakness and myalgias. However, prescribers need to be aware of a less common complication, statin-associated necrotizing myopathy, which can occur at any time during the treatment course and has been found to be <0.1% of adverse effects. High suspicion is warranted when patients taking statins develop weakness and myalgia. Increased risk of muscle injury has been observed when using gemfibrozil in combination with statins and should be avoided. We present a case of an elderly male with chronic use of combination lipid-lowering agents who initially presented with proximal weakness. He was diagnosed with statin-associated necrotizing myopathy and subsequently developed rapid end-stage renal disease in the setting of severe rhabdomyolysis. The case report discusses the work-up of proximal muscle weakness with focus on the importance of early recognition and prompt management of rhabdomyolysis to avoid life-threatening complications.

[9] *Umrani S, Jamshed W, Rizwan A*. **Comparison of Atorvastatin and Rosuvastatin in Reduction of Inflammatory Markers in Acute Coronary Syndrome**. Cureus 2020; 12:e11760.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33409009

ABSTRACT
INTRODUCTION: Patients suffering from acute coronary syndrome (ACS) are found to have elevated levels of inflammatory markers such as high sensitivity C-reactive protein (hsCRP) and erythrocyte sedimentation rate (ESR) in their blood. These elevated inflammatory markers can lead to complications in ACS. Statins such as atorvastatin and rosuvastatin are known to reduce inflammatory markers. Our aim is to compare the efficacy of atorvastatin and rosuvastatin in reducing inflammatory markers. METHODS: This prospective, open-label, randomized trial was conducted in the cardiovascular department of tertiary care in a rural area of Pakistan. There were 128 patients diagnosed with ACS who were enrolled in the study. They were randomized into two groups, i.e. group A in which patients received 40 mg rosuvastatin daily and group B in which patients received 20 mg atorvastatin daily. hsCRP and ESR were recorded for all the patients at baseline (before starting therapy) and then again after four weeks. The results were compared between both groups. RESULT: Out of 128 patients, 113 (88.2%) patients completed the study. According to this study, at the end of four weeks, rosuvastatin reduced hsCRP (p value: < 0.0001) and ESR (p value: 0.015) values significantly more when compared with atorvastatin. CONCLUSION: In this study, rosuvastatin was significantly superior to atorvastatin in reducing inflammatory markers such as ESR and hsCRP in patients suffering from ACS. Cardiologists should consider using rosuvastatin rather than atorvastatin in management of patients suffering from ACS with elevated inflammatory biomarkers.

[10] *Fruchart JC, Hermans MP, Fruchart-Najib J, Kodama T*. **Selective Peroxisome Proliferator-Activated Receptor Alpha Modulators (SPPARMα) in the Metabolic Syndrome: Is Pemafibrate Light at the End of the Tunnel?** Current atherosclerosis reports 2021; 23:3.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33392801

ABSTRACT
PURPOSE OF REVIEW: Adoption of poor lifestyles (inactivity and energy-dense diets) has driven the worldwide increase in the metabolic syndrome, type 2 diabetes mellitus and non-alcoholic

steatohepatitis (NASH). Of the defining features of the metabolic syndrome, an atherogenic dyslipidaemia characterised by elevated triglycerides (TG) and low plasma concentration of high-density lipoprotein cholesterol is a major driver of risk for atherosclerotic cardiovascular disease. Beyond lifestyle intervention and statins, targeting the nuclear receptor peroxisome proliferator-activated receptor alpha (PPARα) is a therapeutic option. However, current PPARα agonists (fibrates) have limitations, including safety issues and the lack of definitive evidence for cardiovascular benefit. Modulating the ligand structure to enhance binding at the PPARα receptor, with the aim of maximising beneficial effects and minimising adverse effects, underlies the SPPARMα concept. RECENT FINDINGS: This review discusses the history of SPPARM development, latterly focusing on evidence for the first licensed SPPARMα, pemafibrate. Evidence from animal models of hypertriglyceridaemia or NASH, as well as clinical trials in patients with atherogenic dyslipidaemia, are overviewed. The available data set the scene for therapeutic application of SPPARMα in the metabolic syndrome, and possibly, NASH. The outstanding question, which has so far eluded fibrates in the setting of current evidence-based therapy including statins, is whether treatment with pemafibrate significantly reduces cardiovascular events in patients with atherogenic dyslipidaemia. The PROMINENT study in patients with type 2 diabetes mellitus and this dyslipidaemia is critical to evaluating this.

[11] *Tokgozoglu L, Kocyigit D*. **Should We Target Global Risk or Risk Factors?** Current atherosclerosis reports 2021; 23:2.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33392794
ABSTRACT
PURPOSE OF REVIEW: Recent evidence has shaped the new guidelines for the management of dyslipidemia. The importance of accurate risk estimation, subclinical disease detection, and contemporary dyslipidemia management approaches are discussed in this review. RECENT FINDINGS: Risk prediction helps determine the intensity of management strategies and identify high-risk patients. To overcome the pitfalls of the current risk prediction systems, incorporating genetic scores, biomarkers, and imaging is being explored. Key initiating event in atherogenesis is low-density lipoprotein cholesterol (LDL-C) retention in the arterial wall. Recent dyslipidemia guidelines agree that LDL-C is the primary target, but management approaches vary. Guidelines are shaped by new studies that show the benefits of high-intensity lipid lowering, especially for patients at very high-risk. Global risk assessment should be performed in all individuals for cardiovascular disease prevention. Main target should be the causal risk factors, particularly LDL-C which is one of the most important modifiable causal factors. Lower LDL-C goals will help prevent further events in very high-risk patients.

[12] *Ferrer MJ, Silva AF, Abruzzese GA et al.* **Lipid Metabolism and Relevant Disorders to Female Reproductive Health**. Curr Med Chem 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33413060
ABSTRACT
BACKGROUND: Lipids are essential components of cells that participate in metabolic and endocrine regulation and reproductive functions. The main organs where lipid regulation takes place are the liver and adipose tissue. Besides, when each tissue specific action cannot be exerted, it could lead to several endocrine-metabolic disorders closely related to PCOS, such as non-alcoholic fatty liver

disease (NAFLD) and obesity. OBJECTIVE: This work aims to discuss the impact of lipid alterations on metabolic and reproductive health. Therefore, this review focus on the importance of carrying out an integrated study of the molecular pathways affected in PCOS for developing target therapies. RESULTS: Lipids play a major role in PCOS pathogenesis. In this regard, failures in lipid regulation, synthesis, and/or homeostasis contribute to metabolic and reproductive abnormalities, such as those seen in PCOS. Several lipid pathways and regulators are altered in this pathology, leading to dysfunctions that worsen reproductive functions. Therefore, there are several treatments to manage dyslipidemias. Non-pharmacological therapies are considered a first line treatment being the pharmacological treatments a second line option. CONCLUSION: The best treatment to improve the lipid profile is a lifestyle intervention, a combination of hypocaloric diet and exercise. Regarding pharmacological therapies, a combination of fibrate and statins would be the most recommended drugs. Still, in PCOS women, treatment with metformin or TZDs not only modulates the lipid metabolism, but also improves the ovulation. Also, metformin with lifestyle interventions has positive effects on the metabolic and reproductive features of PCOS patients.

[13] *Pirillo A, Catapano AL, Norata GD*. **Recent insights into low-density lipoprotein metabolism and therapy**. Current opinion in clinical nutrition and metabolic care 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33394716
ABSTRACT
PURPOSE OF REVIEW: Elevated levels of low-density lipoprotein cholesterol (LDL-C) are causal to atherosclerosis and, thus, the reduction of LDL-C represents a major objective for the prevention of cardiovascular disease. Aim of this review is to provide an overview on novel strategies to lower LDL-C. RECENT FINDINGS: Although inhibiting liver cholesterol biosynthesis by statins is used as the main therapeutic approach to increase hepatic LDL-receptor expression and lower plasma cholesterol levels, novel insights into lipid and lipoprotein biology have led to the development of additional lipid-lowering therapies that can be used in combination with or as an alternative to statins in patients with statin-intolerance. New approaches include bempedoic acid, proprotein convertase subtilisin/kexin type 9 inhibitors, and angiopoietin-like protein 3 inhibitors. SUMMARY: In the last decade, several novel therapeutic approaches have been tested and some of them have been approved as lipid-lowering agents. Some drugs are already available in clinical practice, whereas others are at late stages of development.

[14] *Agha AM, Virani SS, Ballantyne CM*. **Transatlantic guidelines on dyslipidemia and cardiovascular risk: key differences across the pond**. Current opinion in endocrinology, diabetes, and obesity 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33395089
ABSTRACT
PURPOSE OF REVIEW: The purpose of this review is to compare and contrast the key messages from the 2018 American Heart Association (AHA)/American College of Cardiology (ACC) Multisociety Guideline on the Management of Blood Cholesterol and the 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) Guidelines for the Management of Dyslipidemias. We also review some of the evidence that served as the basis for these guidelines and share our opinion regarding these guidelines. RECENT FINDINGS: Patients with atherosclerotic cardiovascular disease (ASCVD), severe hypercholesterolemia, familial hypercholesterolemia, or diabetes should be treated

aggressively with lipid-lowering therapy. In addition to traditional risk factors included in risk scores, assessment of risk enhancers/modifiers may improve risk stratification. The addition of ezetimibe ± proprotein convertase subtilisin/kexin type 9 inhibitors plays an integral role in the management of very-high-risk ASCVD patients; the ESC/EAS guidelines support more aggressive use of these medications. SUMMARY: Both the AHA/ACC Multisociety and ESC/EAS guidelines provide an evidence-based approach to management of blood cholesterol. The greatest difference between these two guidelines is the classification and recommended management of very-high-risk patients. Implementation of either guideline will likely lead to improved ASCVD outcomes compared with current treatment practice. VIDEO ABSTRACT: http://links.lww.com/COE/A22.

[15] *Mullan B, Chan D, Charlesworth J et al.* **Novel behavioural approaches and implementation science for mitigating genetic risk of cardiovascular disease due to elevated lipoprotein(a)**. Current opinion in endocrinology, diabetes, and obesity 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33395090
ABSTRACT
PURPOSE OF REVIEW: Elevated lipoprotein(a) [Lp(a)] is a genetic trait that indicates higher risk of atherosclerotic cardiovascular disease (ASCVD). We review novel strategies to mitigate behavioural risk-factors in this genetic condition. RECENT FINDINGS: Pharmacological and biological interventions are available for lowering Lp(a). However, the acceptability and feasibility of these approaches are questionable due to cost and lack of clinical evidence for their efficacy. A number of low-cost, minimal patient contact interventions are available for modifying behavioural risk-factors that are associated with increased risk of ASCVD familial hypercholesterolaemia and diabetes. These include lifestyle interventions designed to improve diet and physical activity. These interventions may be particularly important among individuals with elevated Lp(a) to manage their higher risk of diabetes and ASCVD. The following article outlines recent research that has examined such low-cost, minimal patient contact interventions. SUMMARY: The current research indicated that such interventions, which are grounded in psychological theory, can assist individuals to improve their diet and physical activity. These findings have implications for developing and implementing similar interventions for individuals with elevated Lp(a), so as to assist in reducing behavioural risk-factors associated with ASCVD.

[16] *Fong V, Patel SB*. **Recent advances in ABCG5 and ABCG8 variants**. Current opinion in lipidology 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33395105
ABSTRACT
PURPOSE OF REVIEW: In this review, we summarize the genetics and mechanisms of sitosterolemia and sterol trafficking, and provide an update on the understanding of the prevalence of ABCG5 and ABCG8 variants and their role in human disease. RECENT FINDINGS: Defects in ABCG5/G8 result in the accumulation of xenosterols. It had been previously thought that near total LoF of one of the proteins was required to cause pathology. However, recently there was the first report of a patient with Sitosterolemia who was heterozygous for mutations in both genes. Moreover, large population studies have demonstrated the even simple heterozygous carriers are associated with altered lipid profiles and cardiovascular risk. Broader screening has added to the rapidly growing list of gene variants indicating that the prevalence of ABCG5/G8 variants is higher than previous

thought, especially in patients with hypercholesterolemia. SUMMARY: These findings support a strategy of measuring xenosterol levels in patients with hypercholesterolemia to screen for ABCG5/G8 variants, and then tailoring treatment with a sterol absorption inhibitor, like ezetimibe, where indicated. Xenosterol trafficking affects remnant clearance and maybe pathogenically linked to the increased risk of atherosclerosis.

[17] *Trinder M, Brunham LR*. **Polygenic scores for dyslipidemia: the emerging genomic model of plasma lipoprotein trait inheritance**. Current opinion in lipidology 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33395106
ABSTRACT
PURPOSE OF REVIEW: Contemporary polygenic scores, which summarize the cumulative contribution of millions of common single-nucleotide variants to a phenotypic trait, can have effects comparable to monogenic mutations. This review focuses on the emerging use of 'genome-wide' polygenic scores for plasma lipoproteins to define the etiology of clinical dyslipidemia, modify the severity of monogenic disease, and inform therapeutic options. RECENT FINDINGS: Polygenic scores for low-density lipoprotein cholesterol (LDL-C), triglycerides, and high-density lipoprotein cholesterol are associated with severe hypercholesterolemia, hypertriglyceridemia, or hypoalphalipoproteinemia, respectively. These polygenic scores for LDL-C or triglycerides associate with risk of incident coronary artery disease (CAD) independent of polygenic scores designed specifically for CAD and may identify individuals that benefit most from lipid-lowering medication. Additionally, the severity of hypercholesterolemia and CAD associated with familial hypercholesterolemia-a common monogenic disorder-is modified by these polygenic factors. The current focus of polygenic scores for dyslipidemia is to design predictive polygenic scores for diverse populations and determining how these polygenic scores could be implemented and standardized for use in the clinic. SUMMARY: Polygenic scores have shown early promise for the management of dyslipidemias, but several challenges need to be addressed before widespread clinical implementation to ensure that potential benefits are robust and reproducible, equitable, and cost-effective.

[18] *Fang M, Selvin E*. **Thirty-year Trends in Complications in U.S. Adults With Newly Diagnosed Type 2 Diabetes**. Diabetes Care 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33419932
ABSTRACT
OBJECTIVE: To assess the prevalence of and trends in complications among U.S. adults with newly diagnosed diabetes. RESEARCH DESIGN AND METHODS: We included 1,486 nonpregnant adults (aged ≥20 years) with newly diagnosed diabetes (diagnosed within the past 2 years) from the 1988-1994 and 1999-2018 National Health and Nutrition Examination Survey. We estimated trends in albuminuria (albumin-to-creatinine ratio ≥30 mg/g), reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m(2)), retinopathy (any retinal microaneurysms or blot hemorrhages), and self-reported cardiovascular disease (history of congestive heart failure, heart attack, or stroke). RESULTS: From 1988-1994 to 2011-2018, there was a significant decrease in the prevalence of albuminuria (38.9 to 18.7%, P for trend <0.001) but no change in the prevalence of reduced eGFR (7.5 to 9.9%, P for trend = 0.30), retinopathy (1988-1994 to 1999-2008 only; 13.2 to 12.1%, P for trend = 0.86), or self-reported cardiovascular disease (19.0 to 16.5%, P for trend = 0.64). There were

improvements in glycemic, blood pressure, and lipid control in the population, and these partially explained the decline in albuminuria. Complications were more common at the time of diabetes diagnosis for adults who were older, lower income, less educated, and obese. CONCLUSIONS: Over the past three decades, there have been encouraging reductions in albuminuria and risk factor control in adults with newly diagnosed diabetes. However, the overall burden of complications around the time of the diagnosis remains high.

[19] *Jin Q, Shi N, Aroke D et al.* **Insulinemic and Inflammatory Dietary Patterns Show Enhanced Predictive Potential for Type 2 Diabetes Risk in Postmenopausal Women**. Diabetes Care 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33419931

ABSTRACT

OBJECTIVE: The empirical dietary index for hyperinsulinemia (EDIH) and empirical dietary inflammatory pattern (EDIP) scores assess the insulinemic and inflammatory potentials of habitual dietary patterns, irrespective of the macronutrient content, and are based on plasma insulin response or inflammatory biomarkers, respectively. The glycemic index (GI) and glycemic load (GL) assess postprandial glycemic potential based on dietary carbohydrate content. We tested the hypothesis that dietary patterns promoting hyperinsulinemia, chronic inflammation, or hyperglycemia may influence type 2 diabetes risk. RESEARCH DESIGN AND METHODS: We calculated dietary scores from baseline (1993-1998) food frequency questionnaires among 73,495 postmenopausal women in the Women's Health Initiative, followed through March 2019. We used multivariable-adjusted Cox regression to estimate hazard ratios (HRs) and 95% CIs for type 2 diabetes risk. We also estimated multivariable-adjusted absolute risk of type 2 diabetes. RESULTS: During a median 13.3 years of follow-up, 11,009 case subjects with incident type 2 diabetes were diagnosed. Participants consuming the most hyperinsulinemic or proinflammatory dietary patterns experienced greater risk of type 2 diabetes; HRs (95% CI) comparing highest to lowest dietary index quintiles were: EDIH 1.49 (1.32-1.68; P (trend) < 0.0001) and EDIP 1.45 (1.29-1.63; P (trend) < 0.0001). The absolute excess incidence for the same comparison was 220 (EDIH) and 271 (EDIP) case subjects per 100,000 person-years. GI and GL were not associated with type 2 diabetes risk: GI 0.99 (0.88-1.12; P (trend) = 0.46) and GL 1.01 (0.89-1.16; P (trend) = 0.30). CONCLUSIONS: Our findings in this diverse cohort of postmenopausal women suggest that lowering the insulinemic and inflammatory potentials of the diet may be more effective in preventing type 2 diabetes than focusing on glycemic foods.

[20] *Bertrand C, Saulnier PJ, Potier L et al.* **Plasma concentrations of lipoproteins and risk of lower-limb peripheral artery disease in people with type 2 diabetes: the SURDIAGENE study**. Diabetologia 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33409569

ABSTRACT

AIMS/HYPOTHESIS: The lipid profile has not been fully investigated in individuals with peripheral artery disease (PAD). We aimed to evaluate the relationship between plasma concentrations of lipoproteins and the prevalence of lower-limb PAD at baseline and its incidence during follow-up in people with type 2 diabetes. METHODS: Plasma concentrations of total cholesterol, HDL-cholesterol, triacylglycerol and apolipoprotein (Apo) A-I, ApoA-II, ApoB-100 and Apo(a) were measured at baseline using colorimetric or MS methods in the SURDIAGENE cohort. Total cholesterol/HDL-cholesterol ratio, non-HDL-cholesterol and LDL-cholesterol were estimated using computation

formulas. Logistic and Cox proportional hazard regression models were fitted to estimate OR or HR, with related 95% CI, for baseline prevalence or incidence of major PAD (lower-limb amputation or requirement of revascularisation) during follow-up by increasing lipoprotein tertiles, after adjustment for key confounders. RESULTS: Among 1468 participants (women 42%, mean ± SD age 65 ± 11 years, duration of diabetes 14 ± 10 years at baseline), 129 (8.8%) had a baseline history of major PAD. Major PAD was less prevalent at baseline in the highest (vs lowest) tertile of HDL-cholesterol (OR 0.42 [95% CI 0.26, 0.71], p = 0.001) and ApoA-I (OR 0.39 [95% CI 0.23, 0.67], p = 0.0007), and more frequent in the highest tertile of total cholesterol/HDL-cholesterol ratio (OR 1.95 [95% CI 1.18, 3.24], p = 0.01). Among 1339 participants without a history of PAD at baseline, incident PAD occurred in 97 (7.2%) during a median (25th-75th percentile) duration of follow-up of 7.1 (4.4-10.7) years, corresponding to 9685 person-years and an incidence rate of 9.8 (95% CI 8.0, 12.0) per 1000 person-years. The risk of incident PAD was lower in the top (vs bottom) tertile of HDL-cholesterol (HR 0.54 [95% CI 0.30, 0.95], p = 0.03) or ApoA-I (HR 0.50 [95% CI 0.28, 0.86], p = 0.01) and higher in the top tertile of total cholesterol/HDL-cholesterol ratio (HR 2.81 [95% CI 1.61, 5.04], p = 0.0002) and non-HDL-cholesterol (HR 1.80 [95% CI 1.06, 3.12], p = 0.03). CONCLUSIONS/INTERPRETATION: We reported independent associations between HDL-cholesterol, ApoA-I, total cholesterol/HDL-cholesterol ratio or non-HDL-cholesterol and the prevalence or the incidence of major PAD in people with type 2 diabetes. Our findings provide a picture of lipoprotein profile in people with type 2 diabetes. Graphical abstract.

[21] *Al-Doaiss A, Jarrar Y, Shati A et al.* **Renal Alterations Induced by Chronic Exposure to Therapeutic Doses of Antihypercholestremic Atorvastatin**. Endocrine, metabolic & immune disorders drug targets 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33413070

ABSTRACT

BACKGROUND: Atorvastatin (ATOR) is widely used for the treatment and prevention of hypercholesterolemia and various diseases, such as cardiovascular complication, with little data about the histopathological and ultrastructural renal alterations that might be induced by this drug. OBJECTIVES: The present study was undertaken to investigate the potential toxicity of therapeutic doses of atorvastatin on the microanatomy and ultrastructure of renal tissues from Wistar albino rats. METHODS: Adult male Wistar albino rats received an oral daily dose of 5 mg/kg body weight for 90 consecutive days. Biopsies from both kidneys of each study rat were taken for histopathological and ultrastructural examination. RESULTS: ATOR-treated rats exhibited glomerular, tubular, and interstitial histological alterations, including degeneration, necrosis, hyaline droplets, edema, cortical hemorrhages, mesangial hypercellularity, and blood capillary dilation and congestion. In addition, ATOR exposure increased the activity of glucose-6-phosphate dehydrogenase and alkaline phosphatase with a concurrent reduction in proteins and neutral mucosubstances content of the glomeruli and renal cells. Moreover, ATOR-treated animals demonstrated glomerular ultrastructural alterations, consisting mainly of capillary tuft dilatation, glomerular basement membrane thickening, and mesangial cell proliferation. The renal cells of the proximal tubules demonstrated damaged mitochondria, degenerative cellular changes, endoplasmic reticulum dilatation, lysosomal and autophagosome activation, nuclear alteration, myelin figure formation, and microvilli disorganization. CONCLUSION: The findings of the present work may indicate that ATOR can induce renal

histological, histochemical, and ultrastructural alterations that may affect kidney and other vital organ function.

[22] *Adamstein NH, MacFadyen JG, Rose LM et al.* **The neutrophil-lymphocyte ratio and incident atherosclerotic events: analyses from five contemporary randomized trials**. European heart journal 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33417682
ABSTRACT
AIMS: The neutrophil-lymphocyte ratio (NLR) is a readily available inflammatory biomarker that may associate with atherosclerosis and predict cardiovascular (CV) events. The aims of this study are to determine whether the NLR predicts incident major adverse cardiovascular events (MACE) and is modified by anti-inflammatory therapy. METHODS AND RESULTS: Baseline and on-treatment NLRs were calculated from complete blood counts among 60 087 participants randomized in the CANTOS, JUPITER, SPIRE-1, SPIRE-2, and CIRT trials to receive placebo or canakinumab, rosuvastatin, bococizumab, or methotrexate, respectively, and followed up for MACE. All analyses were performed first in CANTOS, and then externally validated in the other four trials. For the five trials, hazard ratios for major CV events and mortality comparing NLR quartiles were computed using Cox proportional hazards models, and the effect of each randomized intervention on the NLR was evaluated in comparison to placebo. The NLR modestly correlated with interleukin-6, C-reactive protein, and fibrinogen levels but minimally with lipids. In all five randomized trials, baseline NLR predicted incident CV events and death; the per-quartile increase in risk of MACE was 20% in CANTOS [95% confidence interval (CI) 14-25%, P < 0.0001], 31% in SPIRE-1 (95% CI 14-49%, P = 0.00007), 27% in SPIRE-2 (95% CI 12-43%, P = 0.0002), 9% in CIRT (95% CI 0.2-20%, P = 0.045), and 11% in JUPITER (95% CI 1-22%, P = 0.03). While lipid-lowering agents had no significant impact on the NLR, anti-inflammatory therapy with canakinumab lowered the NLR (P < 0.0001). CONCLUSION: The NLR, an easily obtained inflammatory biomarker, independently predicts CV risk and all-cause mortality, and is reduced by interleukin-1β blockade with canakinumab.

[23] *Speer T, Ridker PM, von Eckardstein A et al.* **Lipoproteins in chronic kidney disease: from bench to bedside**. European heart journal 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33393990
ABSTRACT
Chronic kidney disease (CKD) is associated with high cardiovascular risk. CKD patients exhibit a specific lipoprotein pattern termed 'uraemic dyslipidaemia', which is characterized by rather normal low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol, and high triglyceride plasma levels. All three lipoprotein classes are involved in the pathogenesis of CKD-associated cardiovascular diseases (CVDs). Uraemia leads to several modifications of the structure of lipoproteins such as changes of the proteome and the lipidome, post-translational protein modifications (e.g. carbamylation) and accumulation of small-molecular substances within the lipoprotein moieties, which affect their functionality. Lipoproteins from CKD patients interfere with lipid transport and promote inflammation, oxidative stress, endothelial dysfunction as well as other features of atherogenesis, thus contributing to the development of CKD-associated CVD. While, lipid-modifying therapies play an important role in the management of CKD patients, their efficacy is modulated by kidney function. Novel therapeutic agents to prevent the adverse remodelling of

lipoproteins in CKD and to improve their functional properties are highly desirable and partially under development.

[24] *Sagris D, Ntaios G, Georgiopoulos G et al.* **Proprotein Convertase Subtilisin-Kexin Type 9 inhibitors and stroke prevention: A meta-analysis**. European journal of internal medicine 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33419661
ABSTRACT

[25] *Ravnskov U, Alabdulgader A, de Lorgeril M et al.* **The new European guidelines for prevention of cardiovascular disease are misleading**. Expert Rev Clin Pharmacol 2021:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33416003
ABSTRACT
Introduction: The European Society of Cardiology and European Atherosclerosis Society (ESC/EAS) have recently published three major revisions of their guidelines for the management of chronic heart disease, blood lipids, and diabetes. Areas covered: We have scrutinized these guidelines in detail and found that the authors have ignored many studies that are in conflict with their conclusions and recommendations. Expert commentary: The authors of the guidelines have ignored that LDL-cholesterol (LDL-C) of patients with acute myocardial infarction is lower than normal; that high cholesterol is not a risk factor for diabetics; that the degree of coronary artery calcification is not associated with LDL-C; and that 27 follow-up studies have shown that people with high total cholesterol or LDL-C live just as long or longer than people with low cholesterol. They have also ignored the lack of exposure-response in the statin trials; that several of these trials have been unable to lower CVD or total mortality; that no statin trial has succeeded with lowering mortality in women, elderly people, or diabetics; and that cholesterol-lowering with statins has been associated with many serious side effects.

[26] *Tankoska M, Jakimovski D, Stamatova A et al.* **Demographic, Clinical and Biochemical Characteristics of Pediatric Obesity: Interim Analysis of a Larger Prospective Study**. Folia medica 2020; 62:746-752.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33415908
ABSTRACT
Pediatric obesity is a common nutritional disorder that affects more than a third of the young population and predis-poses individuals to greater future morbidity and mortality. Materials and methods: Sixty-two children were recruited in the study. Demographic and clinical information regarding the pa-tients and their parents was collected. Data about the weight, height, systolic (SP) and diastolic (DP) blood pressure, lipid metabolic profile, thyroid hormone levels, glucose and insulin levels before and after oral glucose tolerance test (OGTT) of participants were also collected. Body mass index (BMI) was calculated and patients were classified into groups according to the International Obesity Task Force criteria. Descriptive, comparative parametric, non-parametric tests and Spearman's ranked correlations were used in the statistical analysis. Results: The study sample consisted of 34 males and 28 females aged 11.6 and 11.8 years, respectively (p=0.781). The mean BMI was 30.5 (SD 5.5): 8 of participant had normal weight (≤25 BMI), 22 were overweight (25-30 BMI), and 32 were obese (≥30 BMI). The chil-dren's BMIs were significantly associated with parental BMIs (r=0.395, p=0.004). Both SP and DP were significantly different between BMI subgroups

(p=0.005 and p=0.001, respectively) with the obese group having the highest values (post-hoc Benjamini, p=0.004). Obese children had lower average T4 levels when compared to the comparators (7.5 μg/dL vs. 9.9 μg/dL, p=0.021). Obese children had significantly lower baseline glucose levels and higher insulin levels when compared to the overweight/normal BMI children (73.8 mg/dL vs. 86.4 mg/dL, p.

[27] *Vasilyev V, Zakharova F, Bogoslovskay T, Mandelshtam M*. **Familial Hypercholesterolemia in Russia: Three Decades of Genetic Studies**. Frontiers in genetics 2020; 11:550591.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33391333

ABSTRACT

The first studies of familial hypercholesterolemia (FH) in Russia go back to late 1980-ies. For more than 10 years the research in this field was carried out in Saint-Petersburg, the megapolis in the North-West Russia. Studies were focused on the search for causative mutations in low-density lipoprotein receptor gene (LDLR). Gradually the research was spread to Petrozavodsk in Karelia and in the XXI century two more centers contributed in investigations of genetics of FH, i.e., in Moscow and Novosibirsk. The best studied is the spectrum of mutations in LDLR, though genetic abnormalities in APOB and PCSK9 genes were also considered. Despite that some 40% mutations in LDLR found in Saint-Petersburg and Moscow are referred to as specific for Russian population, and this proportion is even higher in Karelia (ca. 70%), rapid introduction of NGS and intensifying genetic research all over the world result in continuous decrease of these numbers as "Slavic" mutations become documented in other countries. The samplings of genetically characterized patients in Russia were relatively small, which makes difficult to specify major mutations reflecting the national specificity of FH. Moreover, the majority of studies accomplished so far did not explore possible associations of certain mutations with ethnic origin of patients. By now the only exception is the study of Karelian population showing the absence of typical Finnish mutations in the region that borders on Finland. It can be concluded that the important primary research partly characterizing the mutation spectrum in FH patients both in the European and Siberian parts of Russia has been done. However, it seems likely that the most interesting and comprehensive genetic studies of FH in Russia, concerning various mutations in different genes and the variety of ethnic groups in this multi-national country, are still to be undertaken.

[28] *Meshkov A, Ershova A, Kiseleva A et al.* **The LDLR, APOB, and PCSK9 Variants of Index Patients with Familial Hypercholesterolemia in Russia**. Genes 2021; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33418990

ABSTRACT

Familial hypercholesterolemia (FH) is a common autosomal codominant disorder, characterized by elevated low-density lipoprotein cholesterol levels causing premature atherosclerotic cardiovascular disease. About 2900 variants of LDLR, APOB, and PCSK9 genes potentially associated with FH have been described earlier. Nevertheless, the genetics of FH in a Russian population is poorly understood. The aim of this study is to present data on the spectrum of LDLR, APOB, and PCSK9 gene variants in a cohort of 595 index Russian patients with FH, as well as an additional systematic analysis of the literature for the period of 1995-2020 on LDLR, APOB and PCSK9 gene variants described in Russian patients with FH. We used targeted and whole genome sequencing to search for variants. Accordingly, when combining our novel data and the data of a systematic literature

review, we described 224 variants: 187 variants in LDLR, 14 variants in APOB, and 23 variants in PCSK9. A significant proportion of variants, 81 of 224 (36.1%), were not described earlier in FH patients in other populations and may be specific for Russia. Thus, this study significantly supplements knowledge about the spectrum of variants causing FH in Russia and may contribute to a wider implementation of genetic diagnostics in FH patients in Russia.

[29] *Liampas I, Mylonas KS, Brotis A et al.* **Serum lipid abnormalities in migraine: A meta-analysis of observational studies**. Headache 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33398889

ABSTRACT
BACKGROUND: The association of migraine with vascular comorbidities is long-established. The contribution of the "traditional" cardiovascular risk factors to this connection remains unclear. OBJECTIVE: To determine-quantify the differences in the serum lipid concentrations between lipid-lowering agents-naïve individuals with migraine and healthy controls (HC). METHODS: The study protocol was not preregistered with an online systematic review-protocol registry. A literature search involving MEDLINE, EMBASE, CENTRAL, Google Scholar, and the OpenGrey database was performed. Case-control, cross-sectional, or cohort studies involving HC and participants with migraine (with and without aura regardless of the use of prophylactic treatment) that quantitatively assessed serum low-density lipoprotein cholesterol (LDL-C) (primary index) and/or total cholesterol (TC) and/or high-density lipoprotein cholesterol (HDL-C) and/or triglycerides (TG) (secondary indices) were retrieved. Articles including participants with known dyslipidemia (or under lipid-lowering medications) or with secondary causes of dyslipidemia (aside from the subjectively assessed lifestyle parameters) were excluded. Studies with abstracts and full texts not published in English and articles reporting the implementation of other study designs (reviews, meta-analyses, commentaries, case reports, etc.) were excluded as well. Conference abstracts and English abstracts from studies with full texts not published in English were evaluated as part of the gray literature. Each step of the review process was performed by two investigators independently, and relevant data were abstracted based on standardized extraction forms. Any discrepancies were resolved by a third investigator. RESULTS: Seventeen studies (16 case-control and 1 cross-sectional) fulfilled the eligibility criteria. Retrieved articles involved adult participants, principally during the fourth decade of life. Results were compatible with higher LDL-C levels in migraine individuals (1370) than in HC (1215) [12 studies, mean difference (MD) = 10.4 mg/dl, 95% confidence interval (CI) = (1.6, 19.2)]. Similarly, higher TC levels were determined in migraine patients [14 studies, migraine = 1325, HC = 1213, MD = 10.6 mg/dl, 95% CI = (1.8, 19.3)], as were TG levels [15 studies, migraine = 1526, HC = 1262, MD = 11.8 mg/dl, 95% CI = (3.6, 20.0)]. HDL-C concentrations were not different between the two groups [14 studies, migraine = 1488, HC = 1328, MD = -0.4 mg/dl, 95% CI = (-2.2, 1.5)]. Prespecified sensitivity analysis following the exclusion of studies not presenting comparable body mass index values between the groups nullified the significant difference regarding LDL-C levels [MD = 5.3 mg/dl, 95% CI = (-0.1, 10.8)]. Subgroup analyses as well as the direct comparison of migraine with aura and migraine without aura individuals were compatible with no difference regarding lipid concentrations, but only a small fraction of the retrieved studies presented relevant figures. CONCLUSIONS: Although our results are of limited generalizability, since most retrieved studies were performed in Turkey (nine studies), TC abnormalities may provide part of the explanation for the unfavorable cardiovascular profile of migraine patients. Lifestyle may be partly or entirely accountable for the

determined increased serum TC. Additional studies that will completely address the effect that lifestyle parameters exert on lipid concentrations are required to better capture existing abnormalities.

[30] *Blanc JF, Khemissa F, Bronowicki JP et al.* **Phase 2 trial comparing sorafenib, pravastatin, their combination or supportive care in HCC with Child-Pugh B cirrhosis**. Hepatology international 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33420951

ABSTRACT

BACKGROUND AND AIMS: There is limited data regarding the role for systemic treatment in patients with Hepatocellular Carcinoma with Child-Pugh B cirrhosis. METHODS: PRODIGE 21 was a multicentric prospective non-comparative randomized trial. Patients were randomized to receive sorafenib (Arm A), pravastatin (Arm B), sorafenib-pravastatin (Arm C) combination, or best supportive care (Arm D). Primary endpoint was time to progression (TTP), secondary endpoints included safety and overall survival (OS). RESULTS: 160 patients were randomized and 157 patients were included in the final analysis. 86% of patients were BCLC C and 55% had macrovascular invasion. The safety profiles of the drugs were as expected. Median TTP was 3.5, 2.8, 2.0 and 2.2 months in arms A, B, C and D, respectively, but analysis was limited by the number of patients deceased without radiological progression (59%). Median OS was similar between the four arms: 3.8 [95% CI: 2.4-6.5], 3.1 [95% CI: 1.9-4.3], 4.0 [95% CI: 3.2-5.5] and 3.5 months [95% CI: 2.2-5.4] in arms A, B, C and D, respectively. Median OS was 4.0 months [95% CI: 3.3-5.5] for patients treated with sorafenib, vs 2.9 months [95% CI: 2.2-3.9] for patients not treated with sorafenib. In patients with ALBI grade 1/2, median OS was 6.1 months [95% CI: 3.8-8.3] in patients treated with sorafenib vs 3.1 months [95% CI: 1.9-4.8] for patients not treated with sorafenib. CONCLUSION: In the overall Child-Pugh B population, neither sorafenib nor pravastatin seemed to provide benefit. In the ALBI grade 1/2 sub-population, our trial suggests potential benefit of sorafenib. CLINICAL TRIAL REGISTRATION: The study was referenced in clinicaltrials.gov (NCT01357486).

[31] *Kashour T, Halwani R, Arabi YM et al.* **Statins as an adjunctive therapy for COVID-19: the biological and clinical plausibility**. Immunopharmacology and immunotoxicology 2021:1-14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33406943

ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes the coronavirus disease 2019 (COVID-19) has infected millions of individuals and has claimed hundreds of thousands of human lives worldwide. Patients with underlying cardiovascular conditions are at high risk for SARS-CoV-2 infection, and COVID-19 patients have high incidence of cardiovascular complications such as acute cardiac injury, arrhythmias, heart failure, and thromboembolism. The disease has no approved proven effective therapy and hence repurposing of existing approved drugs has been considered as the fastest treatment approach. Statins have been shown to exhibit lipid lowering dependent and independent cardiovascular protective effects as well as favorable effects in various other pathophysiological states. These beneficial properties of statins are a result of their multiple pleotropic effects that include, anti-inflammatory, immunomodulatory, antithrombotic and antimicrobial properties. In this review, we provide a comprehensive description of the mechanisms of the pleotropic effects of statins, the relevant pre-clinical and clinical data pertinent to their role in infections and acute lung injury, the possible cardiovascular benefits of statins in COVID-19, and the

implications of the therapeutic potential of statins in COVID-19 disease. We conclude with the rationale for conducting randomized controlled trials of statins in COVID-19 disease.

[32] *Voutyritsa E, Damaskos C, Farmaki P et al.* **PCSK9 Antibody-based Treatment Strategies for Patients With Statin Intolerance**. In Vivo 2021; 35:61-68.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33402450

ABSTRACT

BACKGROUND: Statin intolerance refers to the inability of a patient to tolerate statin therapy, presenting muscle aches, pains, weakness and muscle inflammation. Thus, numerous patients are not treated with suitable statin-based therapy or take only very low doses. As a result, the desired decrease in low-density lipoprotein cholesterol (LDL-C) is not achieved, resulting in patients at a high risk for cardiovascular events, requiring an alternative lipid-lowering treatment. Common treatments manage to reduce the LDL-C level by up to 20%. Recently, new alternative treatment options have been proved to lower the LDL-C level by up to 70%. These treatment strategies are based on human monoclonal antibodies against protein convertase subtilisin/kexin 9 (PCSK9). MATERIALS AND METHODS: Herein, we review the efficiency of anti-PCSK9 in treatment of hypercholesterolemic patients with statin intolerance. We focused on the use of PCSK9 inhibitors in statin-intolerant patients and we estimated the clinical results concerning the reduction of the mean LDL-C concentration and the side effects that were observed. RESULTS: In the majority of cases, treatment strategy based on PCSK9 was successful and achieved the end-points. CONCLUSION: PCSK9 inhibition can be considered as a treatment of option for lipid-lowering in statin-intolerant patients.

[33] *Saba L, Sanagala SS, Gupta SK et al.* **Ultrasound-based internal carotid artery plaque characterization using deep learning paradigm on a supercomputer: a cardiovascular disease/stroke risk assessment system**. The international journal of cardiovascular imaging 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33423132

ABSTRACT

Visual or manual characterization and classification of atherosclerotic plaque lesions are tedious, error-prone, and time-consuming. The purpose of this study is to develop and design an automated carotid plaque characterization and classification system into binary classes, namely symptomatic and asymptomatic types via the deep learning (DL) framework implemented on a supercomputer. We hypothesize that on ultrasound images, symptomatic carotid plaques have (a) a low grayscale median because of a histologically large lipid core and relatively little collagen and calcium, and (b) a higher chaotic (heterogeneous) grayscale distribution due to the composition. The methodology consisted of building a DL model of Artificial Intelligence (called Atheromatic 2.0, AtheroPoint, CA, USA) that used a classic convolution neural network consisting of 13 layers and implemented on a supercomputer. The DL model used a cross-validation protocol for estimating the classification accuracy (ACC) and area-under-the-curve (AUC). A sample of 346 carotid ultrasound-based delineated plaques were used (196 symptomatic and 150 asymptomatic, mean age 69.9 ± 7.8 years, with 39% females). This was augmented using geometric transformation yielding 2312 plaques (1191 symptomatic and 1120 asymptomatic plaques). K10 (90% training and 10% testing) cross-validation DL protocol was implemented and showed an (i) accuracy and (ii) AUC without and with augmentation of 86.17%, 0.86 (p-value < 0.0001), and 89.7%, 0.91 (p-value < 0.0001), respectively. The DL characterization system consisted of validation of the two hypotheses: (a) mean feature

strength (MFS) and (b) Mandelbrot's fractal dimension (FD) for measuring chaotic behavior. We demonstrated that both MFS and FD were higher in symptomatic plaques compared to asymptomatic plaques by 64.15 ± 0.73% (p-value < 0.0001) and 6 ± 0.13% (p-value < 0.0001), respectively. The benchmarking results show that DL with augmentation (ACC: 89.7%, AUC: 0.91 (p-value < 0.0001)) is superior to previously published machine learning (ACC: 83.7%) by 6.0%. The Atheromatic runs the test patient in < 2 s. Deep learning can be a useful tool for carotid ultrasound-based characterization and classification of symptomatic and asymptomatic plaques.

[34] *Sun J, Lepor NE, Cantón G et al.* **Serial magnetic resonance imaging detects a rapid reduction in plaque lipid content under PCSK9 inhibition with alirocumab**. The international journal of cardiovascular imaging 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33392875
ABSTRACT
PCSK9 inhibitors lower low-density lipoprotein cholesterol (LDL-C) and reduce cardiovascular events. The clinical benefits presumably result from favorable effects on atherosclerotic plaques. Lipid-core and plaque inflammation have been recognized as main determinants of risk for plaque rupture and cardiovascular events. Both can be noninvasively assessed with carotid MRI. We studied if PCSK9 inhibition with alirocumab induces regression in lipid-core or plaque inflammation within 6 months as measured by MRI. Patients with non-calcified carotid plaque(s) and baseline LDL-C ≥ 70 mg/dl, who were statin-intolerant or taking a low-dose statin (≤ 10 mg per day of atorvastatin or an equivalent), received subcutaneous alirocumab 150 mg every 2 weeks. Carotid MRI was performed at baseline and 6 months after treatment, including pre- and post-contrast images for measuring percent lipid-core volume (%LC) and dynamic contrast-enhanced images for measuring microvessel leakiness (K(trans)), a marker of inflammation. Twenty-eight patients completed the study (69 ± 9 years; 64% male). Alirocumab led to significant changes in LDL-C ($p < 0.001$) and high-density lipoprotein cholesterol (HDL-C) ($p = 0.003$). At 6 months, there was a significant reduction in %LC (mean: - 2.1% [- 3.5, - 0.7], $p = 0.005$; a 17% reduction from baseline of 9.9%) without significant changes in lumen/wall area or in the inflammatory index K(trans). Carotid plaque lipid content was reduced by 17% after 6 months of PCSK9 inhibition with alirocumab. This was seen before observable changes in lumen or wall areas, which supports pursing plaque lipid content as a more sensitive marker of therapeutic response compared to lumen or wall areas in future technical developments and serial studies.

[35] *Ravaut G, Légiot A, Bergeron KF, Mounier C*. **Monounsaturated Fatty Acids in Obesity-Related Inflammation**. International journal of molecular sciences 2020; 22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33396940
ABSTRACT
Obesity is an important aspect of the metabolic syndrome and is often associated with chronic inflammation. In this context, inflammation of organs participating in energy homeostasis (such as liver, adipose tissue, muscle and pancreas) leads to the recruitment and activation of macrophages, which secrete pro-inflammatory cytokines. Interleukin-1β secretion, sustained C-reactive protein plasma levels and activation of the NLRP3 inflammasome characterize this inflammation. The Stearoyl-CoA desaturase-1 (SCD1) enzyme is a central regulator of lipid metabolism and fat storage. This enzyme catalyzes the generation of monounsaturated fatty acids (MUFAs)-major components of

triglycerides stored in lipid droplets-from saturated fatty acid (SFA) substrates. In this review, we describe the molecular effects of specific classes of fatty acids (saturated and unsaturated) to better understand the impact of different diets (Western versus Mediterranean) on inflammation in a metabolic context. Given the beneficial effects of a MUFA-rich Mediterranean diet, we also present the most recent data on the role of SCD1 activity in the modulation of SFA-induced chronic inflammation.

[36] *Guirgis FW, Black LP, DeVos E et al.* **Lipid intensive drug therapy for sepsis pilot: A Bayesian phase I clinical trial**. J Am Coll Emerg Physicians Open 2020; 1:1332-1340.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33392541

ABSTRACT

OBJECTIVES: Cholesterol may be protective in sepsis. Patients with early sepsis may have critically low cholesterol levels that are associated with poor outcomes. The study objective was to test the safety of a fish oil-containing lipid injectable emulsion for stabilizing early cholesterol levels in sepsis. METHODS: Phase I Bayesian optimal interval design trial of adult patients with septic shock (Sequential Organ Failure Assessment score ≥4 or vasopressor dependence). Using sequential dose escalation, participants received 2 doses of 1.0 to 1.6 g/kg of lipid emulsion (Smoflipid 20% lipid emulsion) within 48 hours of enrollment. Cholesterol levels, function, and organ failure were assessed serially during the first 7 days of hospital admission. MEASUREMENTS AND MAIN RESULTS: A total of 10 patients with septic shock were enrolled. One patient withdrew for social reasons. Another patient had an unrelated medical complication and received 1 drug dose. Of 9 patients, mean age was 58 years (SD 16), median Sequential Organ Failure Assessment was 8, and 28-day mortality was 30%. No serious adverse events related to lipid infusion occurred. The six occurrences of non-serious adverse events possibly related to lipid infusion included hyperglycemia (1), elevated triglycerides (3), anemia (1), and vascular access redness/pain (1) for all doses. The mean change in total cholesterol levels from enrollment was -7 (SD 16.6) at 48 hours and 14 (SD 25.2) at 7 days. CONCLUSIONS: Fish oil-containing lipid emulsion administration during early septic shock was safe. Further studies are needed to assess effects on cholesterol levels, function, and organ failure. CLINICAL TRIAL REGISTRATION: NCT03405870.

[37] *Shirakawa T, Fujisue K, Nakamura S et al.* **Dose-Dependent Inhibitory Effect of Rosuvastatin in Japanese Patients with Acute Myocardial Infarction on Serum Concentration of Matrix Metalloproteinases-INVITATION Trial**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33408315

ABSTRACT

AIM: Matrix metalloproteinases (MMPs) play critical roles in acute myocardial infarction (AMI). This trial was conducted to determine the potential effects of higher-dose rosuvastatin on circulating MMP levels in patients with AMI. METHODS: This was a multicenter, open-label, 1:1 randomized, parallel-group study. Patients with AMI were randomly assigned to the appropriate-dose group (10 mg rosuvastatin once daily) or the low-dose group (2.5 mg rosuvastatin once daily) within 24 hours after percutaneous coronary intervention. MMP-2 and MMP-9 levels were measured on day 1 and at week 4, 12, and 24 after enrollment. The primary endpoint was the change in MMP levels at 24 weeks after enrollment. The secondary endpoints were change in MMP levels at day 1 and weeks 4 and 12 after enrollment. RESULTS: Between August 2017 and October 2018, 120 patients with AMI from 19

institutions were randomly assigned to either the appropriate-dose or the low-dose group. There were 109 patients who completed the 24-week follow-up. The primary endpoint for both MMP-2 and MMP-9 was not significantly different between the two groups. The change in the active/total ratio of MMP-9 at week 12 after baseline was significantly lower in the appropriate-dose group compared with the low-dose group (0.81 [-52.8-60.1]% vs. 70.1 [-14.5-214.2]%, P=0.004), while the changes in MMP-2 were not significantly different between the two groups during the study period. CONCLUSIONS: This study could not demonstrate the superiority of appropriate-dose of rosuvastatin in inhibiting serum MMPs levels in patients with AMI.

[38] *Tang B, Kang P, Zhu L et al.* **Simvastatin protects heart function and myocardial energy metabolism in pulmonary arterial hypertension induced right heart failure**. J Bioenerg Biomembr 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33394312
ABSTRACT
The favorable effect of simvastatin on pulmonary arterial hypertension (PAH) has been well defined despite the unknown etiology of PAH. However, whether simvastatin exerts similar effects on PAH induced right heart failure (RHF) remains to be determined. We aimed to investigate the function of simvastatin in PAH induced RHF. Rats in the RHF and simvastatin groups were injected intraperitoneally with monocrotaline to establish PAH-induced RHF model. The expression of miR-21-5p in rat myocardium was detected and miR-21-5p expression was inhibited using antagomiRNA. The effect of simvastatin on hemodynamic indexes, ventricular remodeling of myocardial tissues, myocardial energy metabolism, and calmodulin was explored. Dual-luciferase reporter system was used to verify the binding relationship between miR-21-5p and Smad7. In addition, the regulatory role of simvastatin in Smad7, TGFBR1 and Smad2/3 was investigated. Simvastatin treatment improved hemodynamic condition, myocardial tissue remodeling, and myocardial energy metabolism, as well as increasing calmodulin expression in rats with PAH-induced RHF. After simvastatin treatment, the expression of miR-21-5p in myocardium of rats was decreased significantly. miR-21-5p targeted Smad7 and inhibited the expression of Smad7. Compared with RHF rats, the expressions of TGFBR1 and Smad2/3 in myocardium of simvastatin-treated rats were decreased significantly. Collectively, we provided evidence that simvastatin can protect ATPase activity and maintain myocardial ATP energy reserve through the miR-21-5p/Smad/TGF-β axis, thus ameliorating PAH induced RHF.

[39] *Jackson CL, Deng Y, Yao X et al.* **Proprotein convertase subtilisin/kexin type 9 inhibitor utilization and low-density lipoprotein-cholesterol control in familial hypercholesterolemia**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33419720
ABSTRACT
BACKGROUND: Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were approved in August 2015 as an adjunct to maximally tolerated statin treatment in those with familial hypercholesterolemia (FH). OBJECTIVE: To assess PCSK9 inhibitor utilization patterns and cholesterol control in the high-risk FH population. METHODS: This study was a retrospective analysis of a large administrative database that includes privately insured and Medicare Advantage patients. Individuals with diagnosis codes for FH from October 2016-September 2019 were identified. Differences in PCSK9 inhibitor utilization between various groups were evaluated using multivariable

logistic regression. RESULTS: During the study period, 1:371 people enrolled in medical/pharmacy plans had a diagnosis of FH. While 62.5% (n = 33,649) had medication fills for statins (without PCSK9 inhibitors), only 2.0% (n = 1062) had medication fills for PCSK9 inhibitors (with or without other medications). Compared to men, women were more likely to be untreated (OR 1.23, 95% confidence interval (CI):1.18-1.28, p < 0.01) but more likely to be treated with PCSK9 inhibitors (OR 2.18, 95%CI:1.90-2.49, p < 0.01). Compared to those younger than 55 years of age, older individuals were more likely to be treated (OR 1.64, 95%CI:1.56-1.72, p < 0.01) but less likely to be treated with PCSK9 inhibitors (OR 0.40, 95%CI:0.34-0.47, p < 0.01). Lastly, those with household incomes ≥$40,000 were more likely to be treated with PCSK9 inhibitors than those with lower household incomes (OR 1.69, 95%CI:1.41-2.02, p < 0.01). CONCLUSION: PCSK9 inhibitor utilization in FH remains low. Significant differences exist based on demographic factors. Female sex, higher household incomes, and younger age were associated with increased PCSK9 inhibitor utilization.

[40] *Mehta R, Martagon AJ, Galan Ramirez GA et al.* **Familial hypercholesterolemia in Mexico: Initial insights from the national registry**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33422452
ABSTRACT
BACKGROUND: Familial hypercholesterolemia (FH) remains underdiagnosed and undertreated. OBJECTIVE: Report the results of the first years (2017-2019) of the Mexican FH registry. METHODS: There are 60 investigators, representing 28 federal states, participating in the registry. The variables included are in accordance with the European Atherosclerosis Society (EAS) FH recommendations. RESULTS: To date, 709 patients have been registered, only 336 patients with complete data fields are presented. The mean age is 50 (36-62) years and the average time since diagnosis is 4 (IQR: 2-16) years. Genetic testing is recorded in 26.9%. Tendon xanthomas are present in 43.2%. The prevalence of type 2 diabetes is 11.3% and that of premature CAD is 9.8%. Index cases, male gender, hypertension and smoking were associated with premature CAD. The median lipoprotein (a) level is 30.5 (IQR 10.8-80.7) mg/dl. Statins and co-administration with ezetimibe were recorded in 88.1% and 35.7% respectively. A combined treatment target (50% reduction in LDL-C and an LDL-C <100 mg/dl) was achieved by 13.7%. Associated factors were index case (OR 3.6, 95%CI 1.69-8.73, P = .002), combination therapy (OR 2.4, 95%CI 1.23-4.90, P = .011), type 2 diabetes (OR 2.8, 95%CI 1.03-7.59, P = .036) and age (OR 1.023, 95%CI 1.01-1.05, P = .033). CONCLUSION: The results confirm late diagnosis, a lower than expected prevalence and risk of ASCVD, a higher than expected prevalence of type 2 diabetes and undertreatment, with relatively few patients reaching goals. Recommendations include, the use of combination lipid lowering therapy, control of comorbid conditions and more frequent genetic testing in the future.

[41] *Cacciapaglia F, Perniola S, Venerito V et al.* **The Impact of Biologic Drugs on High-Density Lipoprotein Cholesterol Efflux Capacity in Rheumatoid Arthritis Patients**. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases 2020; Publish Ahead of Print.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33394831
ABSTRACT
BACKGROUND: One of the most intriguing conundrums in patients with rheumatoid arthritis (RA) is the lack of correlation between cholesterol levels and cardiovascular (CV) events, mining the

reliability of plasmatic lipid levels in estimating the CV risk. High-density lipoprotein cholesterol efflux capacity (HDLc-EC) directly indicates the functional ability of HDL to scavenge cholesterol from vascular wall and may provide better information on the atherogenic risk. The aim of this study was to examine the effects of different disease-modifying antirheumatic drugs on HDLc-EC in RA. METHODS: Consecutive RA patients treated with different biologic disease-modifying antirheumatic drugs or methotrexate monotherapy were longitudinally observed. Demographic and clinical features as well as lipid profile were recorded at baseline, 24-week, and 52-week follow-up. At the same time points, HDLc-EC was evaluated using J771 macrophages and a fluorometric assay. RESULTS: We analyzed 100 RA patients on methotrexate, infliximab, tocilizumab, abatacept, or rituximab. No significant changes in the lipoprotein levels were detected, whereas the mean HDLc-EC statistically increased from baseline (22.5% ± 4.8%) to 24 weeks (24.5% ± 5.7%; $p < 0.001$) and 52 weeks (25.1% ± 5.9%; $p < 0.001$). Patients on tocilizumab showed the highest increase in HDLc-EC, already at 24 weeks. Patients on treatment with infliximab or rituximab showed a significant increase in HDLc-EC at 52 weeks. No significant changes were detected in abatacept and methotrexate groups. CONCLUSIONS: Some treatments may impact cholesterol reverse transport in RA. The improved HDLc-EC, independently from lipid levels, may be one of the missing links between inflammation, lipids, and CV risk in RA.

[42] *Yu WY, Hill ST, Chan ER et al.* **Computational drug repositioning identifies statins as a modifier of prognostic genetic expression signatures and metastatic behavior in melanoma**. The Journal of investigative dermatology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33417917
ABSTRACT
Despite advances in melanoma treatment, more than 70% of patients with distant metastasis die within 5 years. Proactive treatment of early melanoma to prevent metastasis could save lives and reduce overall healthcare costs. Currently, there are no treatments specifically designed to prevent early melanoma from progressing to metastasis. We used the Connectivity Map (cMap) to conduct an in silico drug screen and identified HMGCR inhibitors (statins) as a drug class that might prevent melanoma metastasis. To confirm the in vitro effect of statins, RNA-sequencing was completed on A375 cells after treatment with fluvastatin to describe changes in the melanoma transcriptome. Statins induced differential expression in genes associated with metastasis and used in commercially available prognostic tests for melanoma metastasis. Finally, we completed a chart review of 475 melanoma patients. Patients taking statins were less likely to have metastasis at the time of melanoma diagnosis in both univariate and multivariate analysis (24.7% taking statins vs 37.6% not taking statins, ARR = 12.9%, p=0.038). These findings suggest that statins might be useful as a treatment to prevent melanoma metastasis. Prospective trials are required to verify our findings and to determine the mechanism of metastasis prevention.

[43] *Ajima H, Kai Y, Fujimaki J et al.* **Effects of fenofibrate and its combination with lovastatin on the expression of genes involved in skeletal muscle atrophy, including FoxO1 and its targets**. J Toxicol Sci 2021; 46:11-24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33408297
ABSTRACT

Fibrates and statins have been widely used to reduce triglyceride and cholesterol levels, respectively. Besides its lipid-lowering effect, the side effect of muscle atrophy after fibrate administration to humans has been demonstrated in some studies. Combination therapy with fibrates and statins also increases the risk of rhabdomyolysis. FoxO1, a member of the FoxO forkhead type transcription factor family, is markedly upregulated in skeletal muscle in energy-deprived states and induces muscle atrophy via the expression of E3-ubiquitine ligases. In this study, we investigated the changes in FoxO1 and its targets in murine skeletal muscle with fenofibrate treatment. High doses of fenofibrate (greater than 0.5% (wt/wt)) over one week increased the expression of FoxO1 and its targets in the skeletal muscles of mice and decreased skeletal muscle weight. These fenofibrate-induced changes were diminished in the PPARα knockout mice. When the effect of combination treatment with fenofibrate and lovastatin was investigated, a significant increase in FoxO1 protein levels was observed despite the lack of deterioration of muscle atrophy. Collectively, our findings suggest that a high dose of fenofibrate over one week causes skeletal muscle atrophy via enhancement of FoxO1, and combination treatment with fenofibrate and lovastatin may further increase FoxO1 protein level.

[44] *Johnsrud K, Seierstad T, Russell D, Revheim ME*. **Inter-reader agreement of (18)F-FDG PET/CT for the quantification of carotid artery plaque inflammation**. JRSM Cardiovasc Dis 2020; 9:2048004020980941.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33403110
ABSTRACT
INTRODUCTION: A significant proportion of ischemic strokes are caused by emboli from unstable atherosclerotic carotid artery plaques. Inflammation is a key feature of plaque instability. Positron emission tomography/computed tomography (PET/CT) with 2-deoxy-2-((18)F)-fluoro-D-glucose ((18)F-FDG) is a promising technique to quantify plaque inflammation, but a consensus on the methodology has not been established. High inter-reader agreement is essential if (18)F-FDG PET/CT is to be used as a clinical tool for the assessment of unstable plaques and stroke risk. METHODS: We assessed the inter-reader variability of different methods for quantification of (18)F-FDG uptake in 43 patients with carotid artery stenosis ≥70%. Two independent readers delineated the plaque and collected maximum standardized uptake value (SUV(max)) from all axial PET slices containing the atherosclerotic plaque. RESULTS: Uptake values with and without background correction were calculated and intraclass correlation coefficients were highest for uncorrected uptake values (0.97-0.98) followed by those background corrected by subtraction (0.89-0.94) and lowest for those background corrected by division (0.74-0.79). CONCLUSION: Quantification methods without background correction have the highest inter-reader agreement for (18)F-FDG PET of carotid artery plaque inflammation. The use of the single highest uptake value (max SUV(max)) from the plaque will facilitate the method's clinical utility in stroke prevention.

[45] *Fang HSA, Gao Q, Lee ML et al.* **LDL-cholesterol change and goal attainment following statin intensity titration among Asians in primary care: a retrospective cohort study**. Lipids in health and disease 2021; 20:2.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33407522
ABSTRACT

BACKGROUND: Clinical trials have demonstrated that either initiating or up-titrating a statin dose substantially reduce Low-Density Lipoprotein-Cholesterol (LDL-C) levels. However, statin adherence in actual practice tends to be suboptimal, leading to diminished effectiveness. This study aims to use real-world data to determine the effect on LDL-C levels and LDL-C goal attainment rates, when selected statins are titrated in Asian patients. METHODS: A retrospective cohort study over a 5-year period, from April 2014 to March 2019 was conducted on a cohort of multi-ethnic adult Asian patients with clinical diagnosis of Dyslipidaemia in a primary care clinic in Singapore. The statins were classified into low-intensity (LI), moderate-intensity (MI) and high-intensity (HI) groups according to the 2018 American College of Cardiology and American Heart Association (ACC/AHA) Blood Cholesterol Guidelines. Patients were grouped into "No statin", "Non-titrators" and "Titrators" cohorts based on prescribing patterns. For the "Titrators" cohort, the mean percentage change in LDL-C and absolute change in LDL-C goal attainment rates were computed for each permutation of statin intensity titration. RESULTS: Among the cohort of 11,499 patients, with a total of 266,762 visits, there were 1962 pairs of LDL-C values associated with a statin titration. Initiation of LI, MI and HI statin resulted in a lowering of LDL-C by 21.6% (95%CI = 18.9-24.3%), 28.9% (95%CI = 25.0-32.7%) and 25.2% (95%CI = 12.8-37.7%) respectively. These were comparatively lower than results from clinical trials (30 to 63%). The change of LDL-C levels due to up-titration, down-titration, and discontinuation were - 12.4% to - 28.9%, + 13.2% to + 24.6%, and + 18.1% to + 32.1% respectively. The improvement in LDL-C goal attainment ranged from 26.5% to 47.1% when statin intensity was up-titrated. CONCLUSION: In this study based on real-world data of Asian patients in primary care, it was shown that although statin titration substantially affected LDL-C levels and LDL-C goal attainment rates, the magnitude was lower than results reported from clinical trials. These results should be taken into consideration and provide further insight to clinicians when making statin adjustment recommendations in order to achieve LDL-C targets in clinical practice, particularly for Asian populations.

[46] *Kim SH, Son KY*. **Association between lipoprotein cholesterol and future cardiovascular disease and mortality in older adults: a Korean nationwide longitudinal study**. Lipids in health and disease 2021; 20:3.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33407561

ABSTRACT

BACKGROUND: Dyslipidemia is considered an independent health risk factor of cardiovascular disease (CVD), a leading cause of mortality in older adults. Despite its importance, there have been few reports on the association between lipoprotein cholesterol and future CVD and cardiovascular (CV) mortality among elderly Asians aged ≥ 65 years. This study investigated the association between lipoprotein cholesterol and future CVD and CV mortality in an elderly Korean population using a large nationwide sample. METHODS: From the cohort database of the Korean National Health Insurance Service, 62,604 adults aged ≥ 65 years (32,584 men and 30,020 women) were included. High-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were categorized by quartiles. Cox proportional hazard models and linear regression analyses were used to assess the association between the quartiles of lipoprotein cholesterol and future CV events or mortality. RESULTS: The mean follow-up period was 3.3 years. The incidence rates of ischemic heart disease and ischemic brain disease were 0.97 and 0.61 per 1,000 person-years, respectively, and the mortality rates from these diseases were 0.22 and 0.34 per 1,000 person-years, respectively. In a

completely adjusted model, high HDL-C and LDL-C levels were not associated with total CV events and CVD mortality. However, high LDL-C levels were significantly associated with a lower incidence of ischemic brain disease. Furthermore, diabetic patients with high LDL-C levels were more likely to have higher CV mortality, whereas non-smokers with high LDL-C levels were less likely to be at risk of CV events. CONCLUSIONS: Neither high LDL-C nor HDL-C levels were significantly associated with future CV mortality in older adults aged ≥65 years. High LDL-C levels do not seem to be a risk factor for CVD in elderly individuals, and further studies are required.

[47] *Fusar-Poli L, Amerio A, Cimpoesu P et al.* **Lipid and Glycemic Profiles in Patients with Bipolar Disorder: Cholesterol Levels Are Reduced in Mania**. Medicina (Kaunas, Lithuania) 2020; 57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33396922
ABSTRACT
Background and Objectives: Bipolar disorder (BD) is a severe mental condition with a lifetime prevalence estimated around 2% among the general population. Due to risk factors, etiological mechanisms, and the chronic use of psychotropic medications, people with BD are frequently affected by medical comorbidities, such as metabolic syndrome (MetS), associated with altered blood levels of glucose, cholesterol, and triglycerides. Moreover, the lipid concentration may be associated with the severity of psychiatric symptoms. Materials and Methods: Five hundred and forty-two in- and outpatients (418 affected by BD and 124 affected by schizophrenia) were recruited in two Italian university hospitals. A blood examination assessing the fasting glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides was performed. Results: No significant differences were found in the lipid and glycemic profiles between patients with BD and schizophrenia. When considering only the BD sample, we found that patients experiencing a manic episode had significantly lower total cholesterol, HDL, and LDL than euthymic patients. Moreover, the total and LDL cholesterol levels were significantly lower in (hypo)manic than depressed patients. Mood episodes did not influence the triglyceride and glucose levels in our sample. Conclusions: Clinicians should pay attention to blood cholesterol levels in patients with BD, as differences in concentrations may predispose them to severe medical conditions and can be associated with the onset of mood episodes.

[48] *Dai L, Zou L, Meng L et al.* **Cholesterol Metabolism in Neurodegenerative Diseases: Molecular Mechanisms and Therapeutic Targets**. Mol Neurobiol 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33411241
ABSTRACT
Cholesterol is an indispensable component of the cell membrane and plays vital roles in critical physiological processes. Brain cholesterol accounts for a large portion of total cholesterol in the human body, and its content must be tightly regulated to ensure normal brain function. Disorders of cholesterol metabolism in the brain are linked to neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and other atypical cognitive deficits that arise at old age. However, the specific role of cholesterol metabolism disorder in the pathogenesis of neurodegenerative diseases has not been fully elucidated. Statins that are a class of lipid-lowering drugs have been reported to have a positive effect on neurodegenerative diseases. Herein, we reviewed the physiological and pathological conditions of cholesterol metabolism and

discussed the possible mechanisms of cholesterol metabolism and statin therapy in neurodegenerative diseases.

[49] *Bhuiyan AS, Bari MA, Aditya G et al.* **Prevalence and Pattern of Dyslipidemia in Diabetes Mellitus Patients Admitted in the Department of Cardiology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh**. Mymensingh medical journal : MMJ 2021; 30:21-27.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33397846

ABSTRACT

Patients with Diabetes Mellitus are at high risk of cardiovascular events because of abnormal lipid metabolism. Dyslipidemia is common in patients with Diabetes Mellitus (DM). However; in Bangladesh this issue is not yet properly addressed. The aim of this study is to determine the prevalence and patterns of dyslipidaemia in patients with DM in a divisional city Mymensingh. This cross-sectional study was conducted in randomly selected eligible patients from the indoor registry of the Department of Cardiology, Mymensingh Medical College Hospital (MMCH), Bangladesh from April 2012 to March 2013. A well structured questionnaire and blood investigation for lipid profile and blood sugar were the tools of data collection from 120 randomly selected DM patients registered in the department of cardiology, MMCH. Out of 120 enrolled participants the prevalence of dyslipidemia in DM patients was 86.0%, prevalence of dyslipidemia in males was 88.0% while in females was 85.0% but the difference was not significant (p=0.42). Regarding age group, BMI and duration of DM, there is no significant association exists with dyslipidemia. About half of the studied DM patients have high serum total cholesterol level (50.83%), while 22.5% had low serum HDL-C levels and 35.0% had high serum LDC-C level, most of patients had serum triglyceride levels above normal range (67.5%) and so the common patterns of dyslipidemia in this study were serum triglyceride level followed by total cholesterol. High prevalence of dyslipidemia among diabetes mellitus in Mymensingh city were observed and so the common patterns of dyslipidemia is triglyceride followed by total cholesterol. This study emphasizes the importance of screening of lipid profile as these abnormalities may lead to development of cardiovascular diseases.

[50] *Mondal E, Khan MM, Hossain MI et al.* **The Pattern of Lipid Profile in Patients with Chronic Kidney Disease**. Mymensingh medical journal : MMJ 2021; 30:48-55.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33397850

ABSTRACT

Dyslipidemia is a common problem in chronic kidney disease patients. Dyslipidemia in chronic kidney disease patients has been known to be a major risk factor of their cardiovascular disease and may contribute to progressive renal dysfunction. The result of the study might be of interest in improving preventive strategies and in management of dyslipidemia in chronic kidney disease patients. This cross sectional study was conducted to evaluate changes in lipid profile in patients with chronic kidney disease stage-3 to stage-5 patients and to correlate the biochemical abnormalities with progression of the disease in Mymensingh Medical College Hospital, Bangladesh from October, 2016 to April, 2017. In this study 200 patients were including and subjected to do complete blood count, erythrocyte sedimentation rate, random blood sugar, routine examination of urine, serum creatinine and fasting lipid profile. Two hundred (200) patients (134 males, 66 females) with the mean age were 50.5±12.43 years. 44.5% patients were in CKD stage-5, 37.5% patients were in CKD stage-4, 18% patients were in CKD stage-3. Mean value of Triglyceride (TG) was 194±47.20. Eighty nine percent

(89%) patient had hyper-triglyceridemia and 11% had normal triglyceride level. It was statistically significant increased in triglyceride level (p<0.05). Mean value of High density lipoprotein cholesterol (HDL-C) was 34±6.10. Low HDL-C had in 87.5% patients, normal in 12.5% patients and was statistically significant reduction in HDL-C level (p<0.05). Low Density Lipoprotein cholesterol (LDL-C) mean was 113±35.6. High level of LDL-C had optimal/or near optimal in 47% patients, 39% patients had borderline high and 14% patients had that was not statistically significant (p>0.10). Total cholesterol (TC) mean was 212±45.3. In 38% patients had within desirable level, 62% patients had high level of Total cholesterol (TC). It was not statistically significant change (p>0.01).

[51] *Gaudet D, Ruzza A, Santos RD*. **Evolocumab in Pediatric Heterozygous Familial Hypercholesterolemia. Reply**. The New England journal of medicine 2021; 384:84-85.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33406339
ABSTRACT

[52] *Singh A, Mittal S, Kazimuddin M*. **Evolocumab in Pediatric Heterozygous Familial Hypercholesterolemia**. The New England journal of medicine 2021; 384:84.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33406338
ABSTRACT

[53] *Zhang LJ, Qin J, Zhang LH, Yu DL*. **Huge Free-Floating Thrombus in the Internal Carotid Artery Under Duplex Ultrasound Surveillance: A Case Report**. Neurologist 2020; 26:22-23.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33394908
ABSTRACT
INTRODUCTION: Carotid free-floating thrombus (FFT) is an unusual finding in acute ischemic stroke. Atherosclerosis is the most common etiology of FFT formation. CASE REPORT: Here we report a 42-year-old male patient admitted to our department with left temporal and parietal lobe ischemic stroke with normal magnetic resonance angiography. A huge FFT in the left internal carotid artery were found by duplex ultrasound. Acute thrombosis based on atherosclerotic plaque were considered as the reason of this embolization. The thrombus shrunk significantly under anticoagulation and antiplatelet treatment. CONCLUSIONS: Evaluation of the intracranial vessel in the emergency is not enough and early carotid duplex ultrasound can help find of the FFT in time, which help to choose the early intervene by neurosurgeon. Early antithrombotic treatment can be a safe treatment option for reducing huge thrombus based on the nature of thrombus formation. Computed tomography angiography and high-resolution magnetic resonance imaging to certify the character of the plaque are recommended for plaque evaluation.

[54] *Valsdottir TD, Øvrebø B, Falck TM et al.* **Low-Carbohydrate High-Fat Diet and Exercise: Effect of a 10-Week Intervention on Body Composition and CVD Risk Factors in Overweight and Obese Women-A Randomized Controlled Trial**. Nutrients 2020; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33396889
ABSTRACT
We assessed the effect of weight-loss induced with a low-carbohydrate-high-fat diet with and without exercise, on body-composition, cardiorespiratory fitness and cardiovascular risk factors. A total of 57 overweight and obese women (age 40 ± 3.5 years, body mass index 31.1 ± 2.6 kg · m(-2)) completed

a 10-week intervention using a low-carbohydrate-high-fat diet, with or without interval exercise. An equal deficit of 700 kcal · day(-1) was prescribed, restricting diet only, or moderately restricting diet and adding exercise, producing four groups; normal diet (NORM); low-carbohydrate-high-fat diet (LCHF); normal diet and exercise (NORM-EX); and low-carbohydrate-high-fat diet and exercise (LCHF-EX). Linear Mixed Models were used to assess between-group differences. The intervention resulted in an average 6.7 ± 2.5% weight-loss ($p < 0.001$). Post-intervention % fat was lower in NORM-EX than NORM (40.0 ± 4.2 vs. 43.5 ± 3.5%, $p = 0.024$). NORM-EX reached lower values in total cholesterol than NORM (3.9 ± 0.6 vs. 4.7 ± 0.7 mmol/L, $p = 0.003$), and LCHF-EX (3.9 ± 0.6 vs. 4.9 ± 1.1 mmol/L, $p = 0.004$). Post intervention triglycerides levels were lower in NORM-EX than NORM (0.87 ± 0.21 vs. 1.11 ± 0.34 mmol/L, $p = 0.030$). The low-carbohydrate-high-fat diet had no superior effect on body composition, V˙O(2peak) or cardiovascular risk factors compared to a normal diet, with or without exercise. In conclusion, the intervention decreased fat mass, but exercise improved body composition and caused the most favorable changes in total cholesterol and triglycerides in the NORM-EX. Exercise increased cardiorespiratory fitness, regardless of diet.

[55] *Li R, Yuan M, Yu S et al.* **Effect of statins on the risk of recurrent venous thromboembolism: A systematic review and meta-analysis**. Pharmacological research : the official journal of the Italian Pharmacological Society 2021:105413.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33412275
ABSTRACT
BACKGROUND: Recent studies have suggested that statins may be associated with a lower risk of recurrent venous thromboembolism (VTE). METHODS: We systematically searched PubMed, Web of Science and Cochrane Library from inception until May 2020 to identify any eligible studies that reported the association between statin use and the risk of recurrent VTE, and conducted a comprehensive systematic review and meta-analysis (PROSPERO registration number: CRD42020190169) on this matter. RESULTS: A total of 14 observational studies were included for qualitative review and 12 of them qualified for meta-analyses. The main meta-analysis found that statin use was associated with a lower risk of disease recurrence among patients with VTE (pooled adjusted HR: 0.76, 95% CI: 0.69-0.83), which was robust in sensitivity analyses and free of significant publication bias. Additionally, such association was present when restricting to periods after anticoagulation withdrawal (pooled adjusted HR: 0.78, 95% CI: 0.70-0.88) and when separately analyzing recurrent deep vein thrombosis (pooled adjusted HR: 0.71, 95% CI: 0.62-0.81) and recurrent pulmonary embolism (pooled adjusted HR: 0.80, 95% CI: 0.66-0.97; P = 0.027). Furthermore, statin use in patients with VTE was also found to be associated with a lower risk of all-cause mortality (adjusted HR: 0.65, 95% CI: 0.56-0.77), and possibly an even lower risk of bleeding (adjusted HR: 0.88, 95% CI: 0.73-1.07), albeit not statistically significant. CONCLUSION: Statins have the potential to reduce recurrent events among patient with VTE. Randomized clinical trials to better explore the effect of statins in secondary prevention of VTE are warranted.

[56] *Zhu T, Ren L, Zhang L et al.* **Comparison of plaque characteristics of small and large subcortical infarctions in the middle cerebral artery territory using high-resolution magnetic resonance vessel wall imaging**. Quant Imaging Med Surg 2021; 11:57-66.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33392011
ABSTRACT

BACKGROUND: The characteristics of plaque that ultimately lead to different subcortical infarctions remain unclear. We explored the differences in plaque characteristics between patients with small subcortical infarction (SSI) and large subcortical infarction (LSI) of the middle cerebral artery (MCA) using high-resolution magnetic resonance vessel wall imaging (HR-MRVWI). METHODS: The study group comprised 71 patients (mean age, 47.49±11.5 years; 55 male) with MCA territory ischemic stroke. Whole-brain HR-MRVWI was performed using a three-dimensional T1-weighted variable-flip-angle turbo spin echo (SPACE) sequence. Patients were divided into SSI and LSI groups based on routine MRI images. Plaque distribution was classified as the superior, inferior, ventral, or dorsal wall of the MCA. The number of quadrants with plaque formation, location of plaque, plaque burden (PB), arterial remodeling pattern (positive or negative), and degree of stenosis were analyzed and compared between groups. RESULTS: Of the 71 patients, 43 (60.6%) and 28 (39.4%) were identified as the SSI and LSI groups, respectively. The proportion of plaques involving only one quadrant was significantly higher in the SSI group, and these plaques were located in the superior or dorsal MCA vessel wall. There was no significant difference between groups in the proportion of plaques involving two or more quadrants, plaque distribution, or PB. Most plaques in both groups showed positive remodeling, and the percentage of remodeling pattern was similar. A significantly higher incidence of low-grade stenosis (<50%) was observed in the SSI group. CONCLUSIONS: Both SSI and LSI may be associated with major intracranial artery atherosclerosis, but patients with SSI showed relatively fewer quadrants with plaque formation and a lesser degree of stenosis.

[57] *Jure BC, Sapiain PL, González FS*. **[Refractory severe hypertriglyceridemia treated with apheresis. Report of one case]**. Revista medica de Chile 2020; 148:1362-1367.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33399714
ABSTRACT
Severe Hypertriglyceridemia (HTG) is associated with complications such as acute pancreatitis (AP) with high morbidity and mortality rates. We report a 42 years-old man with refractory HTG diagnosed at 19 years of age, and multiple episodes of AP, admitted with the suspicion of a new AP episode. Serum triglycerides were over 2000 mg/dl. His body mass index was 18 kg/m2, there was no evidence of xanthomas or xanthelasmas, but lipemia retinalis was found. Management included heparin and insulin, added to his usual treatment with fibrates, statins, omega-3 fatty acids, and orlistat. Due to lack of response, apheresis was started. After five sessions, triglycerides decreased to 588 mg/dl (82% reduction) and levels remained below 1000 mg/dl with daily apheresis. The patient continued with weekly sessions as outpatient with a sustained good response.

[58] *Jaca A, Durão S, Harbron J*. **Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease**. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 2020; 110:1158-1159.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33403957
ABSTRACT
BACKGROUND: Cardiovascular diseases (CVDs) are defined as conditions involving decreased blood flow to the heart that can lead to heart attacks, stroke or other disorders. CVDs are a common cause of death in low- and middle-income countries. In South Africa (SA) in particular, CVD is the leading cause of death after HIV/AIDS, responsible for 1 in 6 deaths. CVD risk factors include unhealthy diets, hypertension, obesity, high cholesterol levels and diabetes. Omega-3 fatty acids may

have a protective role in the risk of developing heart disease. OBJECTIVES: To evaluate the consequences of an increased intake of fish and plant-based omega-3 fatty acids on the risk of CVD mortality and events. METHODS: The inclusion criteria for this review were randomised controlled trials (RCTs) lasting at least 12 months, which investigated men and women aged ≥18 years. These participants had to be at any risk of CVD while receiving dietary supplements and an advised diet to promote the intake of omega-3. This diet included oily fish, fish oils and seeds rich in omega-3. Comparisons with the interventions included the participants' usual diet, no advice, no supplements, placebo or lower-dose omega-3. The review evaluated the effectiveness of these interventions on primary (e.g. CVD deaths and events), secondary (e.g. major adverse cerebrovascular or CVD events, body weight and other adiposity measures, and lipids) and tertiary (e.g. blood pressure and side-effects) outcomes. RESULTS: Evidence from this review indicates that increasing the intake of long-chain omega-3 fatty acids (LCn3) or alpha-linolenic acid (ALA) probably has little or no effect on all-cause CVD or coronary heart disease mortality. Evidence was of moderate certainty, except for all-cause mortality, where there was a high certainty. CONCLUSIONS: According to moderate- to high-certainty evidence, short-chain fatty acids and LCn3 have little or no effect on mortality or cardiovascular health. However, omega-3 ALA slightly reduces the risk of CVD events and arrhythmias.

[59] *Klug EQ, Raal FJ*. **New cholesterol targets for patients at high or very high cardiovascular risk and the indications for PCSK9 inhibitors**. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde 2020; 110:13126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33403972
ABSTRACT

[60] *Li B, Liu Y, Yuan Q et al.* **Apolipoprotein A1 and Low-Density Lipoprotein as Risk Factors for Intraocular Metastases in Postmenopausal Breast Cancer**. Technol Cancer Res Treat 2021; 20:1533033820984180.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33413027
ABSTRACT
BACKGROUND: The outcomes of patients with postmenopausal breast cancer(PBC) can be improved through the early detection of intraocular metastases(IOMs). In this study, we investigated patients with PBC, and compared those with IOMs with those with non-intraocular metastases(NIOMs) in terms of blood lipid levels, and then differentiated the risk factors associated with IOMs. METHODS: Student's t-test and a chi-square test were used to discriminate between the IOMs and NIOMs groups. After establishing a Poisson regression model to analyze risk factors, we plotted receiver operating characteristic curves(ROC) to assess the quality of risk factors predicting IOMs. RESULTS: The incidence of IOMs in PBC was 1.16%. There was no significant difference in terms of histopathology between the 2 groups. The levels of total cholesterol (TC), apolipoprotein A1(APOA1) and low-density lipoprotein(LDL) in IOMs were significantly lower than in NIOMs groups. Poisson regression suggested that low levels of APOA1 and LDL were risk factors for IOMs ($P = 0.002$ and $P < 0.001$, respectively). ROC curve analysis demonstrated that the cut-off values of APOA1 and LDL were 1.025 g/L and 2.415 mmol/L. The highest prediction accuracy for IOMs involved the combination of APOA1 and LDL (AUC = 0.881, $P < 0.001$). CONCLUSION: Our research

demonstrates that low levels of APOA1 and LDL efficiently predict IOMs in PBC as risk factors, and the combination of APOA1 and LDL was more predictive than single factors.

[61] *Sorial AK, Anjum SA, Cook MJ et al.* **Statins, bone biology and revision arthroplasty: review of clinical and experimental evidence**. Ther Adv Musculoskelet Dis 2020; 12:1759720x20966229.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33403020

ABSTRACT

Osteoarthritis is a painful, disabling condition which is increasing in prevalence as a result of an ageing population. With no recognized disease-limiting therapeutics, arthroplasty of the hip and knee is the most common and effective treatment for lower limb osteoarthritis, however lower limb arthroplasty has a finite life-span and a proportion of patients will require revision arthroplasty. With increasing life expectancy and an increasing proportion of younger (<65 years) patients undergoing arthroplasty, the demand for revision arthroplasty after implant failure is also set to increase. Statins are cholesterol-modulating drugs widely used for cardiovascular risk reduction which have been noted to have pleiotropic effects including potentially influencing arthroplasty survival. In vitro studies have demonstrated pleiotropic effects in human bone cells, including enhancement of osteoblastogenesis following simvastatin exposure, and in vivo studies have demonstrated that intraperitoneal simvastatin can increase peri-implant bone growth in rats following titanium tibial implant insertion. There is evidence that statins may also influence osseointegration, enhancing bone growth at the bone-implant interface, subsequently improving the functional survival of implants. Data from the Danish Hip Arthroplasty Registry and the Clinical Practice Research Datalink in the UK suggest a reduction in the risk of lower limb revision arthroplasty in statin ever-users versus never-users, and a time-dependent effect of statins in reducing the risk of revision. In this article we review the clinical and experimental evidence linking statins and risk of revision arthroplasty.

[62] *Toyoda M, Murata T, Saito N et al.* **The Assessment of the Accuracy of an Intermittent-scanning Continuous Glucose Monitoring Device in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis (AIDT2H) Study**. Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33403763

ABSTRACT

FreeStyle Libre has been approved for use in patients undergoing hemodialysis (HD) in Japan, unlike Europe and the United States; however, evidences regarding its accuracy in such patients is sparse. Forty-one participants with type 2 diabetes undergoing HD were recruited. The overall mean absolute relative difference (MARD) and mean absolute difference (MAD) were 23.4% and 33.9 mg/dl, respectively. Sensor glucose levels and capillary glucose levels were significantly correlated (r=0.858, P<0.01), although the sensor glucose levels were significantly lower than the capillary glucose levels. The accuracy of FreeStyle Libre in patients undergoing HD became deteriorated with the days of usage. The percentage of sensor results in Zones A and B in the Consensus error grid analysis and in the Clarke error grid analysis were 99.7% and 99.0%, respectively. Its insufficient accuracy necessitates adjunct usage of FreeStyle Libre with self-monitoring of blood glucose (SMBG) in patients undergoing HD. This article is protected by copyright. All rights reserved.

[63] *Yang Y, Yang LY, Salayandia VM et al.* **Treatment with Atorvastatin During Vascular Remodeling Promotes Pericyte-Mediated Blood-Brain Barrier Maturation Following Ischemic Stroke**. Translational stroke research 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33423214

ABSTRACT

We previously showed that newly formed vessels in ischemic rat brain have high blood-brain barrier (BBB) permeability at 3 weeks after stroke due to a lack of major endothelial tight junction proteins (TJPs), which may exacerbate edema in stroke patients. Atorvastatin was suggested a dose-dependent pro-angiogenic effect and ameliorating BBB permeability beyond its cholesterol-lowering effects. This study examined our hypothesis that, during vascular remodeling after stroke, treatment with atorvastatin could facilitate BBB maturation in remodeling vasculature in ischemic brain. Adult spontaneously hypertensive rats underwent middle cerebral artery occlusion with reperfusion (MCAO/RP). Atorvastatin, at dose of 3 mg/kg, was delivered daily starting at 14 days after MCAO/RP onset for 7 days. The rats were studied at multiple time points up to 8 weeks with multimodal-MRI, behavior tests, immunohistochemistry, and biochemistry. The delayed treatment of atorvastatin significantly reduced infarct size and BBB permeability, restored cerebral blood flow, and improved the neurological outcome at 8 weeks after MCAO/RP. Postmortem studies showed that atorvastatin promoted angiogenesis and stabilized the newly formed vessels in peri-infarct areas. Importantly, atorvastatin facilitated maturation of BBB properties in the new vessels by promoting endothelial tight junction (TJ) formation. Further in vivo and in vitro studies demonstrated that proliferating peri-vascular pericytes expressing neural-glial antigen 2 (NG2) mediated the role of atorvastatin on BBB maturation through regulating endothelial TJ strand formations. Our results suggested a therapeutic potential of atorvastatin in facilitating a full BBB integrity and functional stroke recovery, and an essential role for pericyte-mediated endothelial TJ formation in remodeling vasculature.