[1] *Kamperidis N, Kamperidis V, Zegkos T et al.* **Atherosclerosis and Inflammatory Bowel Disease-Shared Pathogenesis and Implications for Treatment**. Angiology 2021; 72:303-314.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33601945
ABSTRACT
Atherosclerosis and inflammatory bowel disease (IBD) are often regarded as 2 distinct entities. The commonest manifestation of atherosclerosis is ischemic heart disease (IHD), and an association between IHD and IBD has been reported. Atherosclerosis and IBD share common pathophysiological mechanisms in terms of their genetics, immunology, and contributing environmental factors. Factors associated with atherosclerosis are implicated in the development of IBD and vice versa. Therefore, treatments targeting the common pathophysiology pathways may be effective in both conditions. The current review considers the pathophysiological pathways that are shared between the 2 conditions and discusses the implications for treatment and research.

[2] *Tokgözoğlu L, Casula M, Pirillo A, Catapano AL*. **Similarities and differences between European and American guidelines on the management of blood lipids to reduce cardiovascular risk**. Atherosclerosis. Supplements 2020; 42:e1-e5.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589218
ABSTRACT
The 2018 American Heart Association/American College of Cardiology/Multi-Society (AHA/ACC/MS) Guideline on the Management of Blood Cholesterol and the 2019 European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines for the Management of Dyslipidemias: Lipid Modification to Reduce Cardiovascular Risk, that were recently released by the United States and Europe, provide new recommendations for the management of blood lipid levels based on the latest evidence. Despite many common points, there are several differences in the recommendations, including the definition of very-high-risk patient category, the recommendations for some categories of patients, such as those with diabetes, familial hypercholesterolemia, chronic kidney disease, and aged patients, and the use of ezetimibe and PCSK9 inhibitors. These differences suggest that multiple approaches can be used to manage lipid abnormalities in the context of cardiovascular risk reduction.

[3] *Spence JD*. **It's time to stop the nonsense of withholding lipid lowering therapy on account of age**. Atherosclerosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33583573
ABSTRACT

[4] *Landmesser U, Pirillo A, Farnier M et al.* **Lipid-lowering therapy and low-density lipoprotein cholesterol goal achievement in patients with acute coronary syndromes: The ACS patient pathway project**. Atherosclerosis. Supplements 2020; 42:e49-e58.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589224
ABSTRACT
BACKGROUND AND AIMS: Post-acute coronary syndrome (ACS) patients are at very high risk for recurrent events and mortality, despite the availability of effective pharmacological approaches. Aim of this survey was to evaluate the compliance to ESC/EAS guidelines during the management of ACS patients and the effectiveness of secondary prevention in seven European countries. METHODS: By

means of an online questionnaire, data on 2775 ACS patients (either acute case or follow-up patients) were collected, including data on lipid profile, medications, follow-up visit planning, screening for familial hypercholesterolemia. RESULTS: Lipid profiles were obtained for 91% of ACS patients in the acute phase, mostly within the first day of hospitalization (73%). During hospitalization, 93% of the patients received a lipid-lowering treatment; at discharge, only 66% of the patients received a high intensity statin therapy. At the first follow-up, most of the patients (77.6%) had LDL-C >70 mg/dL; among them, 41% had no change in their lipid-lowering therapies. Similar data were obtained during the second follow-up visit. The analysis of a subgroup of patients with at least 2 follow-up visits and known LDL-C levels showed that the percentage of patients at goal increased from 9% to 32%, and patients with LDL-C <100 mg/dL raised from 23% to 72%. Among acute cases, 44 were admitted with a diagnosis of familial hypercholesterolemia (FH); only 18% of the remaining patients were screened for FH. CONCLUSIONS: Contemporary lipid management of very high CV risk patients is sub-optimal despite available treatments. Greater efforts are warranted to optimize cardiovascular prevention.

[5] *Javaherian M, Dabbaghipour N, Mohammadpour Z, Attarbashi Moghadam B*. **The role of the characteristics of exercise-based cardiac rehabilitation program in the improvement of lipid profile level: A systematic review and meta-analysis**. ARYA atherosclerosis 2020; 16:192-207.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33598040

ABSTRACT

BACKGROUND: The current study aimed to update prior systematic review and meta-analyses (SRMA) in order to determine the effects of supervised exercise-based cardiac rehabilitation (EBCR) and introduce a suitable exercise protocol for management of lipid profile abnormalities in patients with cardiovascular disease (CVD). METHODS: PubMed, Scopus, and Web of Science databases were searched from 1980 to December 2018. All published, randomized controlled trials (RCTs) reporting the efficacy of supervised EBCR in patients with CVD and measuring at least 1 component of lipid profile were included. The quality of articles was assessed based on the Physiotherapy Evidence Database (PEDro) scale. Random effect model was used to calculate the effect size of post-intervention data. RESULTS: Initially 774 RCTs were reviewed, 14 of them were included in the study. In comparison with the control group, supervised EBCR was associated with higher serum levels of high-density lipoprotein (HDL) [weight mean difference (WMD): 1.297; 95% confidence interval (CI): -1.620, 4.214] and lower serum level of low-density lipoprotein (LDL) (WMD: -7.797; 95%CI: -14.005, -1.588), total cholesterol (TC) (WMD: -11.029; 95%CI: -20.716, -1.342), and triglyceride (TG) (WMD: -14.602; 95%CI: -28.992, -0.212). CONCLUSION: It seems that EBCR is correlated with an insignificant increase in HDL serum level and a significant decrease in LDL, TC, and TG serum levels. Considering subgroup analysis results, it is suggested that long duration, moderate exercise volume (EV), and combination of aerobic exercise (AE) and resistance exercise (RE) be used to improve HDL and TG serum levels. Short duration, high EV, and AE+RE seem to significantly reduce LDL serum level. Moreover, moderate EV is associated with a significant reduction in TC level.

[6] *Föger B, Jennings C, Pirillo A et al.* **Hypercholesterolemia and cardiovascular disease: What to do before initiating pharmacological therapy**. Atherosclerosis. Supplements 2020; 42:e25-e29.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589220

ABSTRACT
The availability of efficient lipid-lowering drugs has substantially reduced the incidence and mortality for cardiovascular disease (CVD). Despite that, CVD still represents a major cause of death and disability; efforts are thus required to prevent this disease, since reducing the established CV risk factors may slow or prevent the onset of cardiovascular events. Current guidelines recommend a healthier lifestyle for all CV risk categories, as it may have a beneficial impact on several risk factors; in individuals with a low-to-moderate hypercholesterolemia, which are not eligible for a pharmacological approach and are not far from the cholesterol target recommended for their risk category, functional foods or nutraceuticals may be considered as supplement to reduce their CV risk status. Of note, counseling and lifestyle intervention in people at moderate CV risk represents a major issue for both preventing a further risk increase and reducing the need for drugs. Studies on general populations have clearly indicated that lifestyle interventions translate into a clinical benefit, with reduction of the incidence of myocardial infarction and the risk of developing type 2 diabetes.

[7] *Teo KK, Rafiq T*. **Cardiovascular risk factors and prevention: a perspective from developing countries**. The Canadian journal of cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33610690

ABSTRACT
By the beginning of the 21st century, cardiovascular disease (CVD) had become the leading cause of premature mortality and morbidity worldwide, with 80% originating from less developed lower income countries in line with societal and economic developments. Extensive research on causes and risk factors have been carried out since the mid-20(th) century and have established individual factors such as smoking, hypertension, diabetes and dyslipidemia as CVD risk factors, followed by others. Two recent major case-control studies have summarized the role of common major CVD risk factors in determining the risk of myocardial infarction (INTERHEART Study) and stroke (INTERSTROKE Study). They showed that 9 and 10 common risk factors accounted for over 90% of the risk of myocardial infarction and stroke, respectively, and established the focus in prevention of these common CVD. The efficacy of lowering blood pressure, blood glucose and lipid lowering therapies has been shown to reduce subsequent morbidity and mortality. Leading international health organizations have published guidelines which are updated regularly to set the standards for providing guidance for implementation and management of risk factors. Interventions can also be costly and long-term adherence, essential to be effective in reducing risks, tends to decrease drastically with time. Dietary recommendations have been incorporated into national and professional guidelines for CVD prevention since the 1960's. Based on new research, some existing dietary recommendation may be outdated and should be reviewed, and revised, if necessary. A perspective of CVD prevention and treatment in developing countries is highlighted.

[8] *Suadoni MT*. **Benefits and harms of LDL-cholesterol-lowering therapy in older people must be established through valid and clinically relevant evidence**. Atherosclerosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589133

ABSTRACT

[9] *Reeskamp LF, Balvers M, Peter J et al.* **Intronic variant screening with targeted next-generation sequencing reveals first pseudoexon in LDLR in familial hypercholesterolemia**. Atherosclerosis 2021; 321:14-20.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33601267

ABSTRACT
BACKGROUND AND AIMS: Familial hypercholesterolemia (FH) is caused by pathogenic variants in LDLR, APOB, or PCSK9 genes (designated FH+). However, a significant number of clinical FH patients do not carry these variants (designated FH-). Here, we investigated whether variants in intronic regions of LDLR attribute to FH by affecting pre-mRNA splicing. METHODS: LDLR introns are partly covered in routine sequencing of clinical FH patients using next-generation sequencing. Deep intronic variants, >20 bp from intron-exon boundary, were considered of interest once (a) present in FH- patients (n = 909) with LDL-C >7 mmol/L (severe FH-) or after in silico analysis in patients with LDL-C >5 mmol/L (moderate FH-) and b) absent in FH + patients (control group). cDNA analysis and co-segregation analysis were performed to assess pathogenicity of the identified variants. RESULTS: Three unique variants were present in the severe FH- group. One of these was the previously described likely pathogenic variant c.2140+103G>T. Three additional variants were selected based on in silico analyses in the moderate FH- group. One of these variants, c.2141-218G>A, was found to result in a pseudo-exon inclusion, producing a premature stop codon. This variant co-segregated with the hypercholesterolemic phenotype. CONCLUSIONS: Through a screening approach, we identified a deep intronic variant causal for FH. This finding indicates that filtering intronic variants in FH- patients for the absence in FH + patients might enrich for true FH-causing variants and suggests that intronic regions of LDLR need to be considered for sequencing in FH- patients.

[10] *Jang SH, Kwon DH, Han MK et al.* **Impact of statin pretreatment on the complications of carotid stenting in asymptomatic patients: observational study**. BMC neurology 2021; 21:75.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33588788

ABSTRACT
BACKGROUND: Carotid stenosis is a known risk factor for ischemic stroke, and carotid artery stenting is an effective preventive procedure. However, the stroke risk reduction for asymptomatic patients is small. Therefore, it is important to reduce the risk of complications, particularly in asymptomatic carotid stenosis. Statins are known to reduce the overall risk of periprocedural complications, although there is a lack of data focusing on asymptomatic patients. We aimed to investigate whether different doses of statin pretreatment can reduce periprocedural complications of carotid artery stenting (CAS) in patients with asymptomatic carotid artery stenosis. METHODS: Between July 2003 and June 2013, 276 consecutive patients received CAS for asymptomatic carotid stenosis. Periprocedural complications included the outcome of stroke, myocardial infarction, or death within 30 days of CAS. Statin pretreatment was categorized as no-statin (n = 87, 31.5%), standard-dose (< 40 mg, n = 139, 50.4%), and high-dose statin (≥40 mg, n = 50, 18.1%) according to the atorvastatin equivalent dose. The Cochran-Armitage (CA) trend test was performed to investigate the association of periprocedural complications with statin dose. RESULTS: The overall periprocedural complication rate was 3.3%. There was no significant difference in the risk of periprocedural complications between the three groups (no statin: n = 3 [3.4%]; standard-dose: n = 4 [2.9%]; high-dose n = 2 [4.0%] p = 0.923). The CA trend test did not demonstrate a trend in the proportion of

periprocedural complications across increasing statin equivalent doses (p = 0.919). CONCLUSIONS: Statin pretreatment before CAS showed neither absolute nor dose-dependent effects against periprocedural complications in asymptomatic patients undergoing CAS.

[11] *Bouwens E, Schuurman AS, Akkerhuis KM et al.* **Associations of serially measured PCSK9, LDLR and MPO with clinical outcomes in heart failure**. Biomarkers in medicine 2021; 15:247-255.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33590771

ABSTRACT

Aim: To investigate the temporal evolution of plasma proprotein convertase subtilisin/kexin type 9 (PCSK9), low-density lipoprotein receptor (LDLR) and myeloperoxidase (MPO) in relation to clinical outcome in chronic heart failure (CHF). Methodology & results: Trimonthly blood sampling was performed during a median follow-up of 2.2 (IQR 1.4-2.5) years in 263 CHF patients. Seventy patients reached the primary end point (PE) (cardiovascular death, heart transplantation, left ventricular assist device implantation or HF-hospitalization). MPO level was independently associated with the PE; the adjusted (for clinical factors) hazard ratio (aHR) per standard deviation difference in MPO was 1.71 (95% CI: 1.23-2.43) at any time during follow-up. PCSK9 level (HR: 1.45 [1.04-2.06]) and LDLR (HR: 0.66 [0.49-0.87]) were statistical significantly associated with the PE but only in unadjusted analyses. Slope of temporal MPO evolution (aHR: 1.34 [1.12-1.76] per 0.1 standard deviation/year difference in slope) and LDLR (aHR: 0.78 [0.61-0.90]) however, were associated with PE. Conclusion: Temporal patterns of MPO and LDLR are independently associated with clinical outcome in CHF, which illustrates the importance of assessing temporal evolutions. Clinical trial registration information: registered in ClinicalTrials.gov, number NCT01851538. https://clinicaltrials.gov/ct2/show/NCT01851538.

[12] *Wang D, Wang H, Xu M et al.* **The effect of atorvastatin on recurrence of chronic subdural hematoma after novel YL-1 puncture needle surgery**. Clinical neurology and neurosurgery 2021; 202:106548.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33609954

ABSTRACT

OBJECTIVE: Chronic subdural hematoma (CSDH) is a common neurological disorder with a high recurrence rate. This study investigates the effect that atorvastatin has when used as a postoperative adjuvant therapy on the prevention of CSDH recurrence after YL-1 puncture needle surgery. PATIENTS AND METHODS: A retrospective analysis of 516 CSDH patients who underwent YL-1 puncture needle surgery was undertaken. Baseline characteristics including sex, age, history of injury, past medical histories (anticoagulation, liver dysfunction, heart diseases, malignant tumors, diabetes, hemodialysis, and chronic alcoholism), and computed tomography (CT) or magnetic resonance imaging (MRI) diagnostic indicators (bilateral, mixed density or signal, maximum hematoma width, and brain atrophy) were recorded. Differences in recurrence rates were compared between two groups: one with atorvastatin after surgery and one without. RESULTS: 516 patients (429 men and 87 women), aged 14-98 years (mean age, 67.09 ± 11.74 years) were included in the study. YL-1 puncture needle surgery was performed 610 times. 94 patients had bilateral surgery, totaling 184 procedures. 301 patients with 360 procedures were treated with atorvastatin after surgery, of which 25 had recurrent CSDH; recurrence rate: 7.0 % (25/360). 215 patients with 250 procedures had surgery without subsequent atorvastatin, of which 14 had recurrent CSDH;

recurrence rate: 5.6 % (14/250). Univariate analysis indicated no statistically significant difference in recurrence rates between groups (P > 0.05). Baseline characteristics of the two groups (age, sex, history of injury, past medical histories, CT or MRI diagnostic indicators) also showed no statistical difference (all P > 0.05). CONCLUSIONS: YL-1 puncture needle surgery with irrigation and closed-system drainage is an effective surgical treatment for CSDH. Atorvastatin has no statistically significant effect on the prevention of CSDH recurrence after surgery.

[13] *Petrilli WL, Adam GC, Erdmann RS et al.* **From Screening to Targeted Degradation: Strategies for the Discovery and Optimization of Small Molecule Ligands for PCSK9**. Cell chemical biology 2021; 28:243.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33607006
ABSTRACT

[14] *Gomes PM, Almeida BO, Marinelli Pedrini S et al.* **Morphology and phenotype characteristics of atherosclerotic plaque in patients with acute coronary syndrome: contemporary optical coherence tomography findings**. Coronary artery disease 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33587362
ABSTRACT
BACKGROUND: Contemporary optical coherence tomography (OCT) findings in patients with acute coronary syndromes (ACS) are still subject of controversy. We sought to use OCT to evaluate plaque morphology and phenotype classification in patients with ACS. METHODS: Using optical coherence tomography, culprit lesions were morphologically classified as plaque rupture, plaque erosion, calcified nodule, thin-cap fibroatheroma, thick-cap fibroatheroma (TCFA) or fibrotic, fibrocalcific or fibrolipidic plaque. Quantitative and qualitative analyses also included cholesterol crystals, neovascularization, spotty calcification and thrombus. RESULTS: Of the 110 lesions imaged from June 2012 to April 2016, 54 (49%) were in patients with unstable angina (UA), 31 (28%) were in non-ST-elevation myocardial infarction (STEMI) patients and 25 (23%) were in STEMI patients. Compared with STEMI patients, patients with UA/non-STEMI were older and had more hypertension, hypercholesterolemia, known coronary artery disease, prior myocardial infarction and higher use of antiplatelet therapy. More patients with STEMI had lipidic arc >90% (36.6 versus 70.8%, P = 0.003), red and mixed thrombus (12.9 versus 28.0% and 7.1 versus 44.0%, respectively, all P < 0.001), plaque rupture (29.4 versus 76.0%, P < 0.001) and TCFA (57.1 versus 84.0%; P = 0.01). Predictors of plaque rupture were STEMI at presentation (odds ratio: 9.35, 95% confidence interval: 1.66-52.61, P = 0.01) and diabetes mellitus (odds ratio: 6.16, 95% confidence interval: 1.33-28.58, P = 0.02). CONCLUSIONS: In this single-center study, the culprit lesion of patients with STEMI had more lipid, red and mixed thrombus, plaque rupture and TCFA versus patients with UA/non-STEMI. Clinical presentation may be driven by distinct pathophysiologic mechanisms in patients with ACS.

[15] *Glitscher M, Martín DH, Woytinek K et al.* **Targeting cholesterol metabolism as efficient antiviral strategy against the Hepatitis E virus**. Cellular and molecular gastroenterology and hepatology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33601063
ABSTRACT

BACKGROUND AND AIMS: The Hepatitis E virus hijacks the endosomal system for its release. These structures are highly dependent on cholesterol. Hence, this study investigates the impact of HEV on cholesterol-metabolism, the effect of intracellular cholesterol content on HEV-release and the potential of cholesterol-modulators to serve as antivirals. METHODS: Intracellular cholesterol-content of cells was modulated and impacts on HEV were monitored using qPCR, Western Blot, microscopy, virus-titration and density-gradient centrifugation. Blood-lipids and HEV-RNA were routinely quantified in chronically infected patients during follow-up visits. RESULTS: In HEV-infected cells, decreased levels of cholesterol are found. In patients, HEV-infection decreases serum-lipid concentrations. Importantly, statin-treatment herein increases viral titers. Similarly, reduction of intracellular cholesterol via Simvastatin-treatment increases viral release in vitro. On the contrary, elevating intracellular cholesterol via LDL or 25-hydroxycholesterol strongly reduces viral release due to enhanced lysosomal degradation of HEV. Drug-induced elevation of intracellular cholesterol via Fenofibrate or PSC833 impairs HEV release via the same mechanism. CONCLUSIONS: This study analyses the crosstalk between HEV and intracellular cholesterol. The results highlight the importance of an intact cholesterol-homeostasis for HEV-release and thereby identify a potential target for antiviral strategies. Especially Fenofibrate is considered a promising novel antiviral against HEV. Beyond this, the study may help clinicians evaluating co-treatments of HEV-infected patients with statins, as this may be counter indicated.

[16] *Crone B, Krause AM, Hornsby WE et al.* **Translating genetic association of lipid levels for biological and clinical application**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33604704
ABSTRACT
PURPOSE OF REVIEW: This review focuses on the foundational evidence from the last two decades of lipid genetics research and describes the current status of data-driven approaches for transethnic GWAS, fine-mapping, transcriptome informed fine-mapping, and disease prediction. RECENT FINDINGS: Current lipid genetics research aims to understand the association mechanisms and clinical relevance of lipid loci as well as to capture population specific associations found in global ancestries. Recent genome-wide trans-ethnic association meta-analyses have identified 118 novel lipid loci reaching genome-wide significance. Gene-based burden tests of whole exome sequencing data have identified three genes-PCSK9, LDLR, and APOB-with significant rare variant burden associated with familial dyslipidemia. Transcriptome-wide association studies discovered five previously unreported lipid-associated loci. Additionally, the predictive power of genome-wide genetic risk scores amalgamating the polygenic determinants of lipid levels can potentially be used to increase the accuracy of coronary artery disease prediction. CONCLUSIONS: Lipids are one of the most successful group of traits in the era of genome-wide genetic discovery for identification of novel loci and plausible drug targets. However, a substantial fraction of lipid trait heritability remains unexplained. Further analysis of diverse ancestries and state of the art methods for association locus refinement could potentially reveal some of this missing heritability and increase the clinical application of the genomic association results.

[17] *Macaulay TE, Sheridan E, Ward S*. **Reconsidering the Polypill for Management of Cardiovascular Risk Factors in Underserved Patients**. Current cardiology reports 2021; 23:19.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33598864

ABSTRACT

PURPOSE OF REVIEW: The recent publication of "Polypill for Cardiovascular Disease Prevention in an Underserved Population" study prompts a thoughtful review of known care disparities in cardiovascular disease management in underserved patients. A polypill approach as a population health solution to this complex problem should also be reviewed. RECENT FINDINGS: Muñoz and colleagues open-label, randomized controlled trial of polypill vs. usual care was undertaken in minority patients at a federally qualified health center. The polypill, containing atorvastatin, amlodipine, losartan, and hydrochlorothiazide resulted in statistically significant improvements in systolic blood pressure and low-density lipoprotein levels ($p = 0.003$ and $p < 0.001$, respectively). The significant results of this study demonstrate the ability of a polypill approach to safely lower blood pressure, lipids, and thus estimated 10-year risk of CVD and are consistent with findings observed in previous literature. Uniquely, findings in a largely non-Hispanic Black patient population, offer an opportunity to examine this approach to combat important disparities in care in an underserved U.S. community. Further outcomes-based studies are warranted to explore the validity of these results and long-term safety of polypill treatment and are likely necessary prior to FDA approval and availability of a polypill product.

[18] *Kayikcioglu M*. **LDL Apheresis and Lp (a) Apheresis: A Clinician's Perspective**. Current atherosclerosis reports 2021; 23:15.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33594522

ABSTRACT

PURPOSE OF REVIEW: Lipoprotein apheresis is the most effective means of lipid-lowering therapy. However, it's a semi-invasive, time consuming, and chronic therapy with variable adherence. There are still no specific guideline recommendations for the management of patients on lipid apheresis. The purpose of this review is to discuss the clinical indications and major drawbacks of lipid apheresis in the light of recent evidence. RECENT FINDINGS: Lipoprotein apheresis should be initiated at early ages and performed frequently to receive the expected cardiovascular benefits. However, in clinical practice, most patients experience ineffective apheresis and fail to reach lipid targets. This real-world failure is due to several factors including late diagnosis, delayed referral, and improper frequency of procedures. All these denote that awareness is still low among physicians. Another important factor is the semi-invasive, time consuming nature of the apheresis, leading to high refusal and low adherence rates. Moreover, apheresis decreases quality of life and increases the risk of depression. Mental status is also deteriorated in patients with familial hypercholesterolemia on lipid apheresis. New effective lipid lowering agents are underway with promising cardiovascular results. To overcome the drawbacks, a structured approach, including standardized protocols for lipoprotein apheresis with regular cardiovascular follow-up is warranted. New effective lipid lowering agents with documented cardiovascular benefit, should be integrated into the treatment algorithms of patients on lipoprotein apheresis.

[19] *Chora JR, Bourbon M*. **Pharmacogenomics of statins and familial hypercholesterolemia**. Current opinion in lipidology 2021; 32:96-102.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33591029

ABSTRACT

PURPOSE OF REVIEW: To collect evidence on statin pharmacogenomics, and review what is known in this field for familial hypercholesterolemia (FH) patients. RECENT FINDINGS: There are well-known associations between specific single nucleotide polymorphisms involved in statin transport and metabolism and either adverse effects or altered lipid-lowering efficacy. However, the applicability of this knowledge is uncertain, especially in high-risk populations. There are alternative approaches to study plasma concentrations of statins and new insights on why some association studies fail to be replicated. SUMMARY: Statin therapy recommendations are not always followed in primary and secondary prevention and, even when followed, patients often fail to reach therapeutic target values. Considering the stringent 2019 European Atherosclerosis Society and European Society of Cardiology recommended target lipid levels, as well as the persistently high cost for alternative lipid-lowering therapies such as PCSK9 inhibitors, the variability in low-density lipoprotein cholesterol reductions on statin therapy is still an important factor that needs to be addressed to ensure better cardiovascular disease risk management, especially for FH patients, who have not been well studied historically in this context.

[20] *Anagnostis P, Rizos CV, Skoumas I et al.* **Prevalence of non-coronary heart disease in patients with familial hypercholesterolemia: an analysis from the HELLAS-FH**. Current pharmaceutical design 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33593250
ABSTRACT
AIMS: Despite the established link between familial hypercholesterolemia (FH) and increased risk of coronary heart disease (CHD), its association with other common atherosclerotic and metabolic diseases has not been extensively studied. The aim of this study was to report the prevalence of peripheral arterial disease (PAD) [i.e. common carotid artery disease (CCAD) and lower extremity arterial disease (LEAD)], aortic valve stenosis, chronic kidney disease (CKD) and non-alcoholic fatty liver disease (NAFLD) in patients with FH. Materials& Methods: This was a cross-sectional study retrieving data from the Hellenic Familial Hypercholesterolemia Registry (HELLAS-FH). RESULTS: A total of 1,633 adult patients (850 males) with heterozygous FH (HeFH) were included (mean age 51.3±14.6 years at registration and 44.3±15.9 years at diagnosis). Any common carotid artery stenosis (CCAS) was diagnosed in 124 out of 569 patients with available related data (21.8%), while the prevalence of CCAD (defined as a CCAS ≥50%) was 4.2%. The median (interquartile range - IQR) CCAS was 30% (20-40), whereas the median (IQR) carotid intima media thickness (CIMT) was 0.7 (0.1-1.4) mm. LEAD was reported in 44 patients (prevalence 2.7%). The prevalence of aortic valve stenosis and CKD was 2.0% and 6.4%, respectively. NAFLD was present in 24% of study participants. CONCLUSIONS: HeFH is associated with a relatively high prevalence of any CCAS and CCAD. The prevalence of LEAD, CKD and aortic valve stenosis was relatively low, whereas the prevalence of NAFLD was similar to that of the general population.

[21] *Volpe M, Patrono C*. **PCSK9 inhibition: Not just LDL-Cholesterol knock down: A glimmer for cancer**. European heart journal 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33585891
ABSTRACT

[22] *Nishihira K, Kuriyama N, Shibata Y*. **Impact of 1 month of intensive lipid-lowering therapy on plaque composition evaluated using near-infrared spectroscopy**. European heart journal. Case reports 2021; 5:ytaa569.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33598629
ABSTRACT

[23] *Li H, Xu X, Lu L et al.* **The comparative impact among different intensive statins and combination therapies with niacin/ezetimibe on carotid intima-media thickness: a systematic review, traditional meta-analysis, and network meta-analysis of randomized controlled trials**. Eur J Clin Pharmacol 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33604752
ABSTRACT
PURPOSE: To compare the impact of different statins therapies on the reduction of carotid intima-media thickness (CIMT) may reflect their cardiovascular benefits which is useful in clinical decision. METHODS: PubMed, EMBASE, Cochrane Library, and Web of Science were searched, and 3539 articles published from 1992 to 2020 were retrieved. CIMT in randomized controlled trials for statins therapies were included for traditional and network meta-analyses analyzed by Stata 16. The quality of included studies was assessed by the Cochrane Collaboration's tool. RESULTS: Thirty-three randomized controlled trials (n=8762) were eligible for network meta-analysis, of which 18 randomized controlled trials (n=5252) were included for comparison between statins and no statins and 11 randomized controlled trials (n=1338) were included for comparison between high-intensity statins or combination with niacin/ezetimibe and moderate/low-intensity statins in 2 traditional meta-analyses. In the traditional meta-analyses, the statins groups significantly reduce CIMT compared to no statins (standard mean difference=-0.207, 95% confidence interval: -0.291 to -0.123, p<0.001), while high-intensity statins or combination with niacin/ezetimibe performed significant CIMT reduction compared to moderate/low-intensity statins (standard mean difference=-0.287, 95% confidence interval: -0.460 to -0.114, p=0.001). In the network meta-analysis, a relative rank for the ability to reduce CIMT was given as follows: combination therapy with niacin (mean rank: 1.7), high-intensity statins, combination therapy with ezetimibe, and moderate/low-intensity statins. CONCLUSION: Statins combined with niacin performed a greater CIMT reduction compared to high-intensity statins alone and combination therapies with ezetimibe. The advantage of niacin-combined statins therapies to improve cardiovascular endpoint needs further validation through randomized controlled trials. CLINICAL TRIAL REGISTRATION: PROSPERO, CRD42020175972.

[24] *Xu H, Shen Y, Liang C et al.* **Inhibition of the mevalonate pathway improves myocardial fibrosis**. Experimental and therapeutic medicine 2021; 21:224.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33603833
ABSTRACT
The mevalonate (MVA) pathway serves an important role in ventricular remodeling. Targeting the MVA pathway has protective effects against myocardial fibrosis. The present study aimed to investigate the mechanism behind these effects. Primary cultured cardiac fibroblasts from C57BL/6 mice were treated in vitro in 5 groups: i) negative control; ii) angiotensin II (Ang II) model (1x10(-5) mol/l); iii) Ang II + rosuvastatin (ROS); iv) Ang II + alendronate (ALE); and v) Ang II + fasudil (FAS). Collagen and crystal violet staining were used to assess morphological changes in cardiac

fibroblasts. Reverse transcription quantitative PCR and western blotting were used to analyze the expression of key signaling molecules involved in the MVA pathway. Collagen staining in the ALE, FAS, and ROS groups was weak compared with the Ang II group, while the rate of cell proliferation in the ROS, ALE, and FAS groups was slower compared with that in the Ang II group. In addition, the expression of key signaling molecules in the MVA pathway, including transforming growth factor-β1 (TGF-β1), heat shock protein 47 (HSP47), collagen type I α1 (COL1A1), vascular endothelial growth factor 2 (VEGF2) and fibroblast growth factor 2 (FGF2), was decreased in the FAS and ROS groups compared with the Ang II model. Compared with the Ang II group, 3-Hydroxy-3-Methylglutaryl-CoA reductase (HMGCR) gene expression was significantly lowered in the drug intervention groups, whereas farnesyl pyrophosphate synthase (FDPS) expression was downregulated in the ALE group, but elevated in the FAS and ROS groups. Compared with that in the Ang II group, ras homolog family member A (RhoA) expression was downregulated in the FAS and ROS groups, whilst mevalonate kinase expression was reduced in the ROS group. Protein expression of TGF-β1, COL1A1 and HSP47 were decreased following intervention with each of the three drugs compared with the Ang II group. Overall, rosuvastatin, aledronate and fasudil decreased the proliferation of myocardial fibroblasts and inhibited collagen synthesis. Rosuvastatin had the strongest protective effects against myocardial fibrosis compared with the other drugs tested, suggesting this to be a potential agent for the clinical treatment of cardiovascular disease.

[25] *Singh K, Thanassoulis G, Dufresne L et al.* **A Comparison of Lipids and apoB in Asian Indians and Americans**. Global heart 2021; 16:7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33598387

ABSTRACT

BACKGROUND AND AIMS: Apolipoprotein B (apoB) integrates and extends the information from the conventional measures of atherogenic cholesterol and triglyceride. To illustrate how apoB could simplify and improve the management of dyslipoproteinemia, we compared conventional lipid markers and apoB in a sample of Americans and Asian Indians. METHODS: Data from the US National Health and Nutrition Examination Survey (NHANES) (11,778 participants, 2009-2010, 2011-2012), and the Centre for Cardiometabolic Risk Reduction in South Asia (CARRS) cohort study in Delhi, India (4244 participants), 2011 were evaluated. We compared means and distributions of plasma lipids, and apo B using the Mann-Whitney U test and Fisher's exact test. A p value of < 0.05 was considered significant. RESULTS: The plasma lipid profile differed between Asian Indians and Americans. Plasma triglycerides were greater, but HDL-C lower in Asian Indians than in Americans. By contrast, total cholesterol, non-HDL-C, and LDL-C were all significantly higher in Americans than Asian Indians. However, apoB was significantly higher in Asian Indians than Americans. The LDL-C/apoB ratio and the non-HDL-C/apoB ratio were both significantly lower in Asian Indians than Americans. CONCLUSION: Whether Americans or Asian Indians are at higher risk from apoB lipoproteins cannot be determined based on their lipid levels because the information from lipids cannot be integrated. ApoB, however, integrates and extends the information from triglycerides and cholesterol. Replacing the conventional lipid panel with apoB for routine follow ups could simultaneously simplify and improve clinical care.

[26] *Lassenius MI, Toppila I, Bergius S et al.* **Cardiovascular event rates increase after each recurrence and associate with poor statin adherence**. European journal of preventive cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33611439
ABSTRACT
AIMS: The study evaluated the quality of cardiovascular prevention in real-world clinical practice. The recurrence of up to five cardiovascular events was assessed, as data on recurrence beyond the first event and interindividual variations in event rates past the second event have been sparse. Low-density lipoprotein cholesterol concentrations and lipid-lowering therapy use were investigated. METHODS: This retrospective register-based study included adult patients with an incident cardiovascular event between 2004 and 2016 treated in the hospital district of southwest Finland. Patients were followed for consecutive cardiovascular events or cardiovascular death, low-density lipoprotein cholesterol and statin purchases. The timing of event recurrence was evaluated, and predictive factors were assessed. RESULTS: A wide interindividual variation in cardiovascular event recurrence was observed, each additional event caused an increased risk, the median time of recurrence decreased from 7 to one year for the second and fifth event. Event rates increased correspondingly from 12 to 43/100 patient-years and were most pronounced in the first years following the previous event. The low-density lipoprotein cholesterol goal (<1.8 mmol/l) was reached by 18% in the year after the event and statin underuse was associated with an increased risk of recurrence. Six months after the index event high intensity statins were used by only 22% of the cohort. CONCLUSION: The study provides new perspectives on individual risk assessment showing that event rates are not stable for all patients but increase 1.2-1.9-fold per consecutive event. The underuse of statins and poor adherence support the identification of these patients for intensified multifactorial preventive measures.

[27] *Cortes-Canteli M, Gispert JD, Salvadó G et al.* **Subclinical Atherosclerosis and Brain Metabolism in Middle-Aged Individuals: The PESA Study**. Journal of the American College of Cardiology 2021; 77:888-898.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33602472
ABSTRACT
BACKGROUND: Atherosclerosis has been linked to cognitive decline in late life; however, the impact of cardiovascular risk factors (CVRFs) and subclinical atherosclerosis on brain metabolism at earlier stages remains unexplored. OBJECTIVES: This study sought to determine the association between brain metabolism, subclinical atherosclerosis, and CVRFs in middle-aged asymptomatic individuals. METHODS: This study included 547 asymptomatic middle-aged participants (50 ± 4 years, 82% men) from the PESA (Progression of Early Subclinical Atherosclerosis) study with evidence of subclinical atherosclerosis. Participants underwent (18)F-fluorodeoxyglucose (FDG)-positron emission tomography. Global brain FDG uptake and voxel-wise analyses were used to evaluate the associations of cerebral metabolism with CVRFs and atherosclerotic plaque burden in carotids and femorals assessed by 3-dimensional vascular ultrasound. RESULTS: Global FDG uptake showed an inverse correlation with 30-year Framingham Risk Score (FRS) ($\beta = -0.15$, $p < 0.001$). This association was mainly driven by the presence of hypertension ($d = 0.36$, $p < 0.001$). Carotid plaque burden was inversely associated with global brain FDG uptake ($\beta = -0.16$, $p < 0.001$), even after adjusting for 30-year FRS. Voxel-wise approaches revealed that the brain areas most strongly

affected by hypometabolism in association with 30-year FRS, hypertension, and carotid plaque burden were parietotemporal regions (angular, supramarginal, and inferior/middle temporal gyri) and the cingulate gyrus. CONCLUSIONS: In asymptomatic middle-aged individuals, cardiovascular risk is associated with brain hypometabolism, with hypertension being the modifiable CVRF showing the strongest association. Subclinical carotid plaque burden is also linked to reduced brain metabolism independently of CVRFs. Cerebral areas showing hypometabolism include those known to be affected in dementia. These data reinforce the need to control CVRFs early in life in order to potentially reduce the brain's midlife vulnerability to future cognitive dysfunction.

[28] *Bornfeldt KE, Linton MF, Fisher EA, Guyton JR*. **JCL roundtable: Lipids and inflammation in atherosclerosis**. Journal of clinical lipidology 2021; 15:3-17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589093
ABSTRACT
Clinical effort in lipidology focuses largely on mitigating effects of atherosclerosis, a pathologic process localized to the intimal layer of larger arteries. This JCL Roundtable brings together 3 leading researchers to discuss the current understanding of pathogenesis in atherosclerosis. We begin by recognizing that low density lipoprotein concentrations in arterial intima far exceed concentrations in other connective tissues, consistent with the response-to-retention hypothesis of atherogenesis. High density lipoproteins facilitate reverse cholesterol transport and also have antioxidant and anti-inflammatory roles. New evidence points to remnants of triglyceride-rich lipoproteins as promoters of atherogenesis, highlighted by deleterious effects of apolipoprotein C-III. The multifaceted role of inflammation is becoming clearer through discoveries related to leukocyte recruitment, efferocytosis, resolution of inflammation, and crystal formation. MicroRNAs represent a new, complex mode of gene regulation bearing on lipoprotein and inflammation biology. Progress in understanding atherosclerosis portends a future in which residual risk related to obesity, diabetes, and other factors will yield to new targeted therapies.

[29] *Birnbaum RA, Horton BH, Gidding SS et al.* **Closing the gap: Identification and management of familial hypercholesterolemia in an integrated healthcare delivery system**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33583725
ABSTRACT
BACKGROUND: Familial hypercholesterolemia (FH) is an autosomal dominant genetic disorder that causes markedly elevated risk for early onset coronary artery disease. Despite availability of effective therapy, only 5-10% of affected individuals worldwide are diagnosed. OBJECTIVE: To develop and evaluate a novel approach for identifying and managing patients with FH in a large integrated health system with a diverse patient population, using inexpensive methods. METHODS: Using Make Early Diagnosis/Prevent Early Death (MEDPED) criteria, we created a method for identifying patients at high risk for FH within the Kaiser Permanente Northern California electronic medical record. This led to a pragmatic workflow for contacting patients, establishing a diagnosis in a dedicated FH clinic, and initiating management. We prospectively collected data on the first 100 patients to assess implementation effectiveness. RESULTS: Ninety-three (93.0%, 95%CI: 86.1%-97.1%) of the first 100 evaluated patients were diagnosed with FH (median age = 38 years) of whom only 5% were previously recognized; 48% were taking no lipid-lowering therapy, and 7% had acute coronary

symptoms. 82 underwent successful genetic testing of whom 55 (67.1%; 95%CI: 55.8%-77.1%) had a pathogenic mutation. Following clinic evaluation, 83 of 85 (97.6%) medication-eligible patients were prescribed combination lipid-lowering therapy. 20 family members in the healthcare system were diagnosed with FH through cascade testing. CONCLUSIONS: This novel approach was effective for identifying and managing patients with undiagnosed FH. Care gaps in providing appropriate lipid-lowering therapy were successfully addressed. Further development and dissemination of integrated approaches to FH care are warranted.

[30] *Alkhalil M, Kuzemczak M, Whitehead N et al.* **Meta-Analysis of Intensive Lipid-Lowering Therapy in Patients With Polyvascular Disease**. Journal of the American Heart Association 2021; 10:e017948.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33586467
ABSTRACT
Background Polyvascular atherosclerotic disease is associated with an increased risk of future cardiovascular events. Intensive lipid-lowering therapy (ILT) may mitigate this risk. The aims of this study-level meta-analysis were to examine the effects of ILT in patients with polyvascular disease and whether baseline low-density lipoprotein cholesterol (LDL-C) may determine the level of benefit. Methods and Results Electronic databases were searched through January 2020 to identify randomized controlled trials of treatments targeting upregulation of LDL-C receptors (ie, statins, ezetimibe, and PCSK9 [proprotein convertase subtilisin-kexin type 9] inhibitors). The primary end point was major adverse vascular events as defined by the included studies. A total of 94 362 patients (14 821 [18.6%] with polyvascular disease) from 7 studies were included. In patients with monovascular disease, ILT was associated with a 13% reduction in the primary end point (rate ratio [RR] 0.87; 95% CI, 0.81-0.93 [P=0.0002]) (absolute RR, 1.8%) compared with less ILT, while patients with polyvascular disease had 15% relative RR (0.85; 95% CI, 0.80-0.90 [P<0.00001]) (absolute RR, 6.5%) (P=0.66 for interaction). When factoring LDL-C, unlike patients with monovascular disease, the relative benefits of ILT, compared with less ILT, in patients with polyvascular disease were comparable with LDL-C >100 mg/dL (RR, 0.85; 95% CI, 0.80-0.90 [P<0.00001]) and LDL-C <100 mg/dL (RR, 0.88; 95% CI, 0.81-0.96 [P=0.003]) (P=0.23 for interaction). Conclusions Patients with polyvascular disease experienced comparable benefits to those with monovascular disease in response to ILT. The benefits of ILT in patients with polyvascular disease were not dependent on baseline LDL-C, challenging the approach of using LDL-C as a prerequisite to commence ILT for this high-risk subgroup.

[31] *Shi Z, Li J, Zhao M et al.* **Progression of Plaque Burden of Intracranial Atherosclerotic Plaque Predicts Recurrent Stroke/Transient Ischemic Attack: A Pilot Follow-Up Study Using Higher-Resolution MRI**. Journal of magnetic resonance imaging : JMRI 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33600033
ABSTRACT
BACKGROUND: Patients with intracranial atherosclerotic disease (ICAD) have a high frequency of stroke recurrence. However, there has been little investigation into the prognostic value of higher-resolution magnetic resonance imaging (HR-MRI). PURPOSE: To investigate the use of intracranial atherosclerotic plaques features in predicting risk of recurrent cerebrovascular ischemic events using HR-MRI. STUDY TYPE: Prospective. POPULATION: Fifty-eight patients with acute/subacute stroke

(N = 46) or transient ischemic attack (N = 12). FIELD STRENGTH/SEQUENCE: A 3.0 T, 3D time-of-flight gradient echo sequence and T1- and T2-weighted fast spin echo sequences with 0.31 x 0.39 mm(2) in-plane resolution, twice (with >3 months between scans) following the initial event. ASSESSMENT: Patients were also followed clinically for recurrent ischemic events for up to 48 months or until a subsequent event occurred. The degree of stenosis, plaque burden (PB), minimal lumen area (MLA), and contrast enhancement ratio were assessed at each scanning session and the percentage change of each over time was calculated. STATISTICAL TESTS: Univariable and multivariable Cox regression analyses were used to calculate the hazard ratio (HR) and 95% confidence interval (CI) for predicting recurrent events. RESULTS: The mean time interval between baseline and follow-up MRI scans was 6.2 ± 4.1 months. After the second MRI scan, 20.7% of patients (N = 12) had experienced ipsilateral recurrent TIA/stroke within 10.9 ± 9.2 months. Univariable analyses showed that baseline triglyceride, percentage change of PB, and progression of PB were significantly associated with recurrent events (all $P < 0.05$). Multivariable Cox regression indicated that progression of PB (HR, 6.293; 95% CI, 1.620-24.444; $P < 0.05$) was a significant independent imaging feature for recurrent ischemic events. DATA CONCLUSION: Progression of PB was independently associated with recurrent ischemic cerebrovascular events. HR-MRI may help risk stratification of patients at risk of recurrent stroke. LEVEL OF EVIDENCE: 2 TECHNICAL EFFICACY: Stage 4.

[32] *Pećin I, Reiner Ž*. **Novel Experimental Agents for the Treatment of Hypercholesterolemia**. J Exp Pharmacol 2021; 13:91-100.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33603500

ABSTRACT

Atherosclerotic cardiovascular diseases (ASCVD) are still the leading cause of morbidity and mortality in most developed countries and even more in developing countries. Dyslipidemia is a well known main risk factor for ASCVD. Lipid-lowering treatment, particularly lowering LDL-cholesterol (LDL-C), can decrease the risk for ASCVD. New data and guidelines based upon them suggest that we should go with LDL-C levels as low as we can. Therefore, conventional lipid lowering agents (statins and statins+ezetimibe) are not enough mainly because of poor compliance and statin intolerance which is in the real world mostly pseudo-intolerance. PCSK9 inhibitors provided a new hope to further decrease LDL-C but are still expensive, they have to be injected subcutaneously twice a month and their long-lasting adverse effects are not known. Therefore, there is a constant need to develop novel, more potent, more safe, less expensive, more user friendly regimens of hypolipemic agents (bempedoic acid, selective PPAR alpha receptor modulators etc). One of the ways to overcome poor compliance and increase the potency of therapy with less adverse effects are fixed combinations of established drugs (statin+ezetimibe). The future of hypolipemic agents is based on antisense therapy, ie. the use of specific oligonucleotide sequences blocking the translation of the selected protein (targeting apolipoprotein CIII, lipoprotein (a), apolipoprotein B) or RNA silencing technique (PCSK9 mRNA) and are in various stages of clinical trials. Some of them are almost ready to use in everyday clinical practice. High risk and very high risk patients (eg. familial hypercholesterolemia, familial severe chylomicronemia syndrome) will benefit most. The aim of this review is to inform about novel hypolipemic agents - potent and safe drugs for dyslipidemia which should reduce the risk of ASCVD.

[33] *Mourouzis K, Siasos G, Oikonomou E et al.* **Lipoprotein-associated phospholipase A2 levels, endothelial dysfunction and arterial stiffness in patients with stable coronary artery disease**. Lipids in health and disease 2021; 20:12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33583415

ABSTRACT

BACKGROUND: Lipoprotein-associated Phospholipase A2 (Lp-PLA2), can exert proinflammatory as well as proatherogenic properties on the vascular wall. The current study sought to evaluate the influence of high Lp-PLA2 levels on indices of arterial wall properties in patients with stable coronary artery disease (CAD). METHODS: Three hundred seventy-four consecutive patients with stable CAD (mean age 61 ± 11 years, 89% males) were enrolled in this single-center cross-sectional study. Flow-mediated dilation (FMD) was used to assess endothelial function and augmentation index (AIx) of the central aortic pressure was used to assess reflected waves. ELISA was used to determine Lp-PLA2 serum levels. RESULTS: After dividing the participants in 3 equal groups based on the tertiles of circulating Lp-PLA2 values, no significant differences were demonstrated between those in the 3rd tertile with Lp-PLA2 values > 138 μg/L, in the 2nd tertile with Lp-PLA2 values between 101 and 138 μg/L and in the 1st tertile (Lp-PLA2 values < 101 μg/L) regarding age, male gender, smoking habits, family history of CAD or history of a previous myocardial infarction, diabetes mellitus, arterial hypertension, hyperlipidemia, duration of CAD and treatment with relevant medication. Importantly, subjects with Lp-PLA2 values in the highest tertile, had significantly reduced FMD values compared to the middle and lower tertile (4.43 ± 2.37% vs. 4.61 ± 1.97% vs. 5.20 ± 2.52% respectively, P = 0.03). Patients in the highest tertile of Lp-PLA2 values had significantly higher AIx values (24.65 ± 8.69% vs. 23.33 ± 9.65%, P = 0.03), in comparison to the lowest tertile, with Lp-PLA2 values < 101 μg/L. A linear regression analysis showed that Lp-PLA2 values > 138 μg/L negatively correlated to FMD [b = - 0.45 (95% CI: - 0.79 - -0.11), P = 0.01] and AIx values [b = 1.81 (95% CI: 0.57-3.05), P < 0.001] independently of cofounders like gender, age, diabetes mellitus, arterial hypertension, dyslipidemia, smoking habits, family history of CAD, history of previous myocardial infarction, serum glucose, circulating lipid levels, duration of CAD, antihypertensive medication, antidiabetic drugs, statin therapy and treatment with β-blockers. CONCLUSIONS: Elevated Lp-PLA2 levels relate to endothelial dysfunction and arterial stiffness in patients with stable CAD independently from classical risk factors for CAD, statin use, antihypertensive treatment, and duration of the disease.

[34] *Attipoe-Dorcoo S, Yang P, Sperling L et al.* **Characteristics and trends of PCSK9 inhibitor prescription fills in the United States**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589405

ABSTRACT

BACKGROUND: PCSK9 inhibitors were approved by the Food and Drug Administration in 2015 to lower low-density lipoprotein cholesterol (LDL-C) levels. In the years following, additional research findings, changes in national guideline recommendations, and price reductions have occurred. OBJECTIVE: The goal of the study is to describe the characteristics and trends in PCSK9 inhibitor prescription fills and price, from initial FDA approval in Quarter 3 2015 through Quarter 4 2019, at the national and state levels. METHODS: Cross-sectional study of fills obtained using the IQVIA National Prescription Audit®, Extended Insights, New to Brand, and Regional databases. Prescription fills included injections that provided cholesterol-lowering therapy from 14 to 90 days for the two PCSK9 inhibitors: alirocumab (75 mg/mL and 150 mg/mL) or evolocumab (140 mg/mL and 420 mg/3.5 mL).

Quarterly prescription fills obtained nationally for Quarter 3 2015 through Quarter 4 2019, by sex, age, and state during 2019. RESULTS: Over the time period examined, 2.75 million PCSK9 inhibitor prescriptions were filled nationally (alirocumab: 38%; evolocumab: 62%), and the average retail price per fill (unadjusted $US) from retail pharmacies decreased by 40% from $1502 to $896 per fill. Year-over-year percent change in new PCSK9 inhibitor users increased throughout the observation period, with 9611 new alirocumab users and 25,381 new evolocumab users in Q4 2019. PCSK9 inhibitor fill rates ranged from 5.6 per 1000 in the Northeast to 3.4 per 1000 in the West in 2019, with the highest rate per 1000 in Louisiana (9.1), and lowest in Wyoming (1.3). CONCLUSIONS: PCSK9 inhibitor prescriptions have increased nationally since 2015, coinciding with additional evidence supporting their use for LDL-C lowering and cardiovascular event reduction. Although the retail price has decreased since introduction, cost and delivery mode likely continue as barriers.

[35] *Anderson JLC, Bakker SJL, Tietge UJF*. **The triglyceride to HDL-cholesterol ratio and chronic graft failure in renal transplantation**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589404

ABSTRACT

BACKGROUND: Transplant vasculopathy (TV) is a major contributing factor to chronic graft failure in renal transplant recipients (RTR). TV lesions resemble atherosclerosis in several ways, and it is plausible to believe that some risk factors influence both atherosclerotic plaque formation and formation of TV. OBJECTIVE: The objective of this prospective longitudinal study was to determine if dyslipidemia reflected by the triglyceride (TG)/high-density lipoprotein cholesterol (HDL-C) ratio is prospectively associated with death censored chronic graft failure in RTR. METHOD: 454 prospectively included RTR with a functioning graft for at least one year, were followed for a median of 7 years. RTR were matched based on propensity scores to avoid potential confounding and subsequently the association of the TG/HDL-C ratio with the endpoint chronic graft failure, defined as return to dialysis or re-transplantation, was investigated. RESULTS: Linear regression analysis showed that concentration of insulin, male gender, BMI and number of antihypertensives predict the TG/HDL-C ratio. Cox regression showed that the TG/HDL-C ratio is associated with chronic graft failure (HR = 1.43, 95%CI = 1.12-1.84, p = 0.005) in competing risk analysis for mortality. Interaction testing indicated that the relationship of the TG/HDL-C ratio with graft failure is stronger in subjects with a higher insulin concentration. CONCLUSION: Our results demonstrate that the TG/HDL-C ratio has the potential to act as a predictive clinical biomarker. Furthermore, there is a need for closer attention to lipid management in RTR in clinical practice with a focus on triglyceride metabolism.

[36] *Mammen AL*. **Statin-Associated Myalgias and Muscle Injury-Recognizing and Managing Both While Still Lowering the Low-Density Lipoprotein**. Med Clin North Am 2021; 105:263-272.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589101

ABSTRACT

Although statins are generally safe and well tolerated, some patients experience muscle complaints that can be attributed to their use. Those with muscle discomfort but no demonstrable muscle weakness or creatine kinase (CK) elevations may have statin-associated muscle symptoms. Individuals with elevated CK levels, with or without muscle discomfort or weakness, may have statin-associated myotoxicity. Rare patients have statin-associated autoimmune myopathy, a disease characterized by proximal muscle weakness, elevated CK levels, and autoantibodies recognizing

hydroxy-methyl-glutaryl coenzyme A reductase. In this review, the author provides the clinician with a practical approach to diagnosing and managing patients with each of these statin side effects.

[37] *Komiya I, Yamamoto A, Sunakawa S, Wakugami T*. **Pemafibrate decreases triglycerides and small, dense LDL, but increases LDL-C depending on baseline triglycerides and LDL-C in type 2 diabetes patients with hypertriglyceridemia: an observational study**. Lipids in health and disease 2021; 20:17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33610176
ABSTRACT
BACKGROUND: Pemafibrate, a selective PPARα modulator, has the beneficial effects on serum triglycerides (TGs) and very low density lipoprotein (VLDL), especially in patients with diabetes mellitus or metabolic syndrome. However, its effect on the low density lipoprotein cholesterol (LDL-C) levels is still undefined. LDL-C increased in some cases together with a decrease in TGs, and the profile of lipids, especially LDL-C, during pemafibrate administration was evaluated. METHODS: Pemafibrate was administered to type 2 diabetes patients with hypertriglyceridemia. Fifty-one type 2 diabetes patients (mean age 62 ± 13 years) with a high rate of hypertension and no renal insufficiency were analyzed. Pemafibrate 0.2 mg (0.1 mg twice daily) was administered, and serum lipids were monitored every 4-8 weeks from 8 weeks before administration to 24 weeks after administration. LDL-C was measured by the direct method. Lipoprotein fractions were measured by electrophoresis (polyacrylamide gel, PAG), and LDL-migration index (LDL-MI) was calculated to estimate small, dense LDL. RESULTS: Pemafibrate reduced serum TGs, midband and VLDL fractions by PAG. Pemafibrate increased LDL-C levels from baseline by 5.3% (-3.8-19.1, IQR). Patients were divided into 2 groups: LDL-C increase of >5.3% (group I, n = 25) and < 5.3% (group NI, n = 26) after pemafibrate. Compared to group NI, group I had lower LDL-C (2.53 [1.96-3.26] vs. 3.36 [3.05-3.72] mmol/L, P = 0.0009), higher TGs (3.71 [2.62-6.69] vs. 3.25 [2.64-3.80] mmol/L), lower LDL by PAG (34.2 [14.5, SD] vs. 46.4% [6.5], P = 0.0011), higher VLDL by PAG (28.2 [10.8] vs. 22.0% [5.2], P = 0.0234), and higher LDL-MI (0.421 [0.391-0.450] vs. 0.354 [0.341-0.396], P < 0.0001) at baseline. Pemafibrate decreased LDL-MI in group I, and the differences between the groups disappeared. These results showed contradictory effects of pemafibrate on LDL-C levels, and these effects were dependent on the baseline levels of LDL-C and TGs. CONCLUSIONS: Pemafibrate significantly reduced TGs, VLDL, midband, and small, dense LDL, but increased LDL-C in diabetes patients with higher baseline TGs and lower baseline LDL-C. Even if pre-dose LDL-C remains in the normal range, pemafibrate improves LDL composition and may reduce cardiovascular disease risk.

[38] *Ferguson LD, Sattar N, McInnes IB*. **Managing Cardiovascular Risk in Patients with Rheumatic Disease**. Med Clin North Am 2021; 105:247-262.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33589100
ABSTRACT
Individuals with rheumatoid arthritis, systemic lupus erythematosus, or gout have increased risk of cardiovascular disease (CVD) compared with the general population. This risk relates to a combination of traditional cardiovascular risk factors and disease-specific factors. Screening for CVD is important because CVD contributes to significant morbidity and mortality. Management includes tight control of disease activity to reduce inflammation, but with care to minimize use of nonsteroidal anti-inflammatory drugs and prolonged courses of high-dose corticosteroids. Traditional

cardiovascular risk factors should be managed with a combination of lifestyle interventions and pharmacotherapy. The decision to start antihypertensive and lipid-lowering therapy should be based on individual CVD risk.

[39] *Cruz-Bautista I, Huerta-Chagoya A, Moreno-Macías H et al.* **Familial hypertriglyceridemia: an entity with distinguishable features from other causes of hypertriglyceridemia**. Lipids in health and disease 2021; 20:14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33588820
ABSTRACT
BACKGROUND: Familial hypertriglyceridemia (FHTG) is a partially characterized primary dyslipidemia which is frequently confused with other forms hypertriglyceridemia. The aim of this work is to search for specific features that can help physicians recognize this disease. METHODS: This study included 84 FHTG cases, 728 subjects with common mild-to-moderate hypertriglyceridemia (CHTG) and 609 normotriglyceridemic controls. All subjects underwent genetic, clinical and biochemical assessments. A set of 53 single nucleotide polymorphisms (SNPs) previously associated with triglycerides levels, as well as 37 rare variants within the five main genes associated with hypertriglyceridemia (i.e. LPL, APOC2, APOA5, LMF1 and GPIHBP1) were analyzed. A panel of endocrine regulatory proteins associated with triglycerides homeostasis were compared between the FHTG and CHTG groups. RESULTS: Apolipoprotein B, fibroblast growth factor 21(FGF-21), angiopoietin-like proteins 3 (ANGPTL3) and apolipoprotein A-II concentrations, were independent components of a model to detect FHTG compared with CHTG (AUC 0.948, 95%CI 0.901-0.970, 98.5% sensitivity, 92.2% specificity, $P<0.001$). The polygenic set of SNPs, accounted for 1.78% of the variance in triglyceride levels in FHTG and 6.73% in CHTG. CONCLUSIONS: The clinical and genetic differences observed between FHTG and CHTG supports the notion that FHTG is a unique entity, distinguishable from other causes of hypertriglyceridemia by the higher concentrations of insulin, FGF-21, ANGPTL3, apo A-II and lower levels of apo B. We propose the inclusion of these parameters as useful markers for differentiating FHTG from other causes of hypertriglyceridemia.

[40] *Cao H, Su S, Yang Q et al.* **Metabolic profiling reveals interleukin-17A monoclonal antibody treatment ameliorate lipids metabolism with the potentiality to reduce cardiovascular risk in psoriasis patients**. Lipids in health and disease 2021; 20:16.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33602246
ABSTRACT
BACKGROUND: Psoriasis is a common chronic inflammatory skin disease associated with overproduction of interleukin-17A (IL-17A). IL-17A monoclonal antibodies (mAbs) have shown clinical efficacy in psoriasis patients. Although a series of different overlapping mechanisms have been found to establish a link between psoriasis and cardiovascular diseases, the underlying mechanisms of the two types of diseases and the potential efficacy of IL-17A mAbs in amelioration of cardiovascular comorbidities remain unclear. METHODS: Serum samples from two study cohorts including 117 individuals were analyzed using a high-throughput UHPLC-MS platform. Non-targeted metabolic profiling analysis was first conducted with samples from 28 healthy individuals and from 28 psoriasis patients before and after 12-weeks of ixekizumab treatment in study cohort 1. Study cohort 2 was additionally recruited to validate the correlations of the identified metabolites with cardiovascular diseases. RESULTS: A total of 43 differential metabolites, including lysophospholipids, free fatty

acids, acylcarnitines and dicarboxylic acids, were accurately identified in study cohort 1, and the analysis showed that lipid metabolism was impaired in psoriasis patients. Compared with healthy individuals, psoriasis patients had higher levels of lysophosphatidylcholines, lysophosphatidylinositols, lysophosphatidic acids and free fatty acids, but lower levels of acylcarnitines and dicarboxylic acids. The identified dicarboxylic acid levels were inversely correlated with psoriasis area and severity index (PASI) scores ($P<0.05$). The results for study cohort 2 were largely consistent with the results for study cohort 1. Moreover, the levels of all identified lysophosphatidylcholines were higher in psoriasis patients with coronary heart diseases than in psoriasis without coronary heart disease. Notably, most of these lipidic changes were ameliorated by ixekizumab treatment. CONCLUSION: The results of this non-targeted metabolomic analysis indicate that treatment with IL-17A mAbs can not only ameliorate psoriasis lesions but also restore dysregulated lipid metabolism to normal levels in psoriasis patients. Considering that dysregulated lipid metabolism has been regarded as the critical factor in cardiovascular diseases, the recovery of lipid metabolites in psoriasis patients indicates that IL-17A mAbs might have the potential protective effects against cardiovascular comorbidities.

[41] *Zhang S, Huang F, Xu R et al.* **Association between body mass index and cardio-metabolic risk factors among subjects in Wuhan, China: A cross-sectional study**. Medicine (Baltimore) 2021; 100:e23371.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33592823

ABSTRACT

The aim of this study is to evaluate the association between body mass index (BMI) and cardio-metabolic risk factors and to determine the optimal BMI cut-off values in male and female subjects in Wuhan, China.We conducted a retrospective cross-sectional analysis of 20218 adult subjects (aged 18-85 years, 12717 men of them) who had health examinations at the health management center of Tongji Hospital of Wuhan in 2017. Multivariate logistic regression analysis was preformed to calculate the odds ratios (ORs) of cardio-metabolic risk factors. Receiver operating characteristic curve was used to determine the area under the receiver operating characteristic curve and optimal cut-off values for BMI predictive of cardio-metabolic risk factors.Of the 20218 participants, the percentage of males with overweight and obesity was as twice as that of females and the prevalence of hypertension, diabetes mellitus (DM), dyslipidemia, and hyperuricemia was significantly higher in males than females (27.18% vs 17.69%, 7.88% vs 4.16%, 41.97% vs 15.20%, and 34.50% vs 9.93%, respectively). Multivariate logistic regression analysis showed that higher BMI was a significant risk factor for hypertension (OR:1.27, 95% confidence intervals [CI]: 1.25-1.29), DM (OR:1.25, 95% CI:1.22-1.28), dyslipidemia (OR:1.26, 95% CI:1.25-1.28), and hyperuricemia (OR:1.25, 95% CI:1.23-1.27) after adjusting for age in both sexes. But in overweight or obesity status, females had higher ORs for hypertension and DM, and lower ORs for dyslipidemia than that in males. The optimal cut-off values of BMI for the presence of cardio-metabolic risk factors were among 24.25 to 25.35kg/m2 in males, which were higher than in females among 22.85 to 23.45kg/m2.The association between BMI and cardio-metabolic risk factors is different by gender. It is necessary to determine appropriate threshold for overweight status in men and women separately.

[42] *Wang L, Breton C, Warzecha CC et al.* **Long-term stable reduction of low-density lipoprotein in nonhuman primates following in vivo genome editing of PCSK9**. Molecular therapy : the journal of the American Society of Gene Therapy 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33609733
ABSTRACT
Gene disruption via programmable, sequence-specific nucleases represents a promising gene therapy strategy in which the reduction of specific protein levels provides a therapeutic benefit. Proprotein convertase subtilisin/kexin type 9 (PCSK9), an antagonist of the low-density lipoprotein (LDL) receptor, is a suitable target for nuclease-mediated gene disruption as an approach to treat hypercholesterolemia. We sought to determine the long-term durability and safety of PCSK9 knockdown in non-human primate (NHP) liver by adeno-associated virus (AAV)-delivered meganuclease following our initial report on the feasibility of this strategy. Six previously treated NHPs and additional NHPs administered AAV-meganuclease in combination with corticosteroid treatment or an alternative AAV serotype were monitored for a period of up to 3 years. The treated NHPs exhibited a sustained reduction in circulating PCSK9 and LDL cholesterol (LDL-c) through the course of the study concomitant with stable gene editing of the PCSK9 locus. Low-frequency off-target editing remained stable, and no obvious adverse changes in histopathology of the liver were detected. We demonstrate similar on-target nuclease activity in primary human hepatocytes using a chimeric liver-humanized mouse model. These studies demonstrate that targeted in vivo gene disruption exerts a lasting therapeutic effect and provide pivotal data for safety considerations, which support clinical translation.

[43] *Turongkaravee S, Jittikoon J, Lukkunaprasit T et al.* **A systematic review and meta-analysis of genotype-based and individualized data analysis of SLCO1B1 gene and statin-induced myopathy**. The pharmacogenomics journal 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33608664
ABSTRACT
This meta-analysis was conducted to determine the genotypic effects of rs4149056 and rs2306283 polymorphism in SLCO1B1 gene on myopathy in patients with statin. Studies were searched using multiple databases and selected following inclusion criteria. Two reviewers independently performed data extraction and assessments for risk of bias. Fixed-or-random-effect was applied to pool allele frequency/effects. Mixed-effect logit model was used to pool genotypic effects using individual patient data. Heterogeneity and publication bias were explored. Fourteen studies were pooled for rs4149056; the minor C allele frequency were 15% in Caucasians and 14% in Asians. Six studies were pooled for rs2306283; the minor G allele frequency was 34% in Caucasian and 75% in Asians. Genotypic effects of rs4149056 polymorphism in Caucasians indicated that statin users who carried CC and TC genotypes had a significantly higher risk of myopathy than those who carried TT genotype, with a pooled odds ratio (OR) of 2.9 (95% confidence interval, 1.59, 5.34) and 1.6 (1.20, 2.16), respectively. For subgroup analysis, CC and TC genotypes also suggested a higher risk of myopathy in simvastatin users [OR = 2.8 (1.17, 6.77) and OR = 1.8 (1.15, 2.77), respectively] and in atorvastatin users [OR = 4.0 (1.23, 12.63) and OR = 2.0 (1.11, 3.52), respectively] than those who carried TT genotype. There was no significant association between rs2306283 polymorphism and myopathy in Caucasians and Asians. There was no evidence of publication bias for both polymorphisms.

[44] *Saad EJ, Finello M, Tabares AH et al.* **[Performance of equations to predict cardiovascular risk in an Argentine population]**. Medicina 2021; 81:16-23.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33611240

ABSTRACT

The performance of available risk scores to predict cardiovascular risk (CVR) in the Argentinian population is unknown. Our aim was to compare the CVR predicted by several equations with the occurrence of cardiovascular events (CVE) in patients without known cardiovascular disease in an Argentinian hospital. Adults between 40 and 70 years were randomly selected, excluding those with prior history of major CVE, active cancer, lipid lowering treatment and absence of follow-up data. Framingham 2008, SCORE (low and high-risk populations), ATP III, World Health Organization-American B region (WHO-B) and Pooled Cohort equations (PC) risk scores were used to calculate 10-y CVR at time of enrollment. End of follow-up was 10 years ± 6 months, occurrence of fatal myocardial infarction or death from any cause. We used ROC curves to assess discrimination (AUC > 0.75 good discrimination), and Hosmer Lemeshow chi-square to evaluate calibration (Chi > 20 or p value < 0.05 poor calibration). We included 606 patients in our study, 336 women, average age 56.7 ± 8.4 year. Of those, 10 (1.7%) non-cardiovascular deaths, and 5 (0.8%) cardiovascular deaths were observed. 58 (9.8%) a non-fatal CVE were recorded. There was acceptable discrimination for Framingham, ATP-III, and both PC equations. The global calibration was only good with the ATP-III and PC equations. The observed frequency of CVE was low, and the CVR was overestimated by all equations. However, applying ATP-III or PC equations to assess CVR could be considered in our population.

[45] *Ripon MAR, Bhowmik DR, Amin MT, Hossain MS*. **Role of arachidonic cascade in COVID-19 infection: A review**. Prostaglandins Other Lipid Mediat 2021; 154:106539.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33592322

ABSTRACT

The World Health Organization has described the 2019 Coronavirus disease caused by an influenza-like virus called SARS-CoV-2 as a pandemic. Millions of people worldwide are already infected by this virus, and severe infection causes hyper inflammation, thus disrupting lung function, exacerbating breath difficulties, and death. Various inflammatory mediators bio-synthesized through the arachidonic acid pathway play roles in developing cytokine storms, injuring virus-infected cells. Since pro-inflammatory eicosanoids, including prostaglandins, and leukotrienes, are key brokers for physiological processes such as inflammation, fever, allergy, and pain but, their function in COVID-19 is not well defined. This study addresses eicosanoid's crucial role through the arachidonic pathway in inflammatory cascading and recommends using bioactive lipids, NSAIDs, steroids, cell phospholipase A2 (cPLA2) inhibitors, and specialized pro-resolving mediators (SPMs) to treat COVID-19 disease. The role of soluble epoxide hydrolase inhibitors (SEHIs) in promoting the activity of epoxyeicosatrienoic acids (EETs) and 17-hydroxide-docosahexaenoic acid (17-HDHA) is also discussed. Additional research that assesses the eicosanoid profile in COVID-19 patients or preclinical models generates novel insights into coronavirus-host interaction and inflammation regulation.

[46] *Razi O, Mohammadi M, Zamani N et al.* **Walking exercise and lower-body blood flow restriction: Effects on systemic inflammation, lipid profiles and hematological indices in overweight middle-aged males**. Res Sports Med 2021:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33593160
ABSTRACT
The objective of present study is to investigate the effects of walk training with and without blood flow restriction (BFR and no-BFR) on lipid profiles, inflammatory and haematological factors in over-weighed men. Participants were divided into BFR (n = 9) or no-BFR (n = 9) groups. Both groups were exposed to 8-week walk training on a treadmill: 3 sessions/week at a speed of 50 m/min, 5 sets × 2 min/session. There were differences in pre- to post-levels of (TG) and fibrinogen in the BFR group ($p \leq 0.05$) that were accompanied by changes in red blood cells (RBC), haemoglobin (HGB) and haematocrit (HCT) levels ($p \leq 0.05$). RBC levels were increased in the BFR group ($p \leq 0.05$). The groups differed in their mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC). These findings suggest the efficiency of BFR walk training in individuals exposed to chronic diseases associated with overweight, such as metabolic syndrome.

[47] *Kozieł P, Jankowski P, Surowiec S et al.* **Temporal changes in the secondary prevention of coronary artery disease in patients following myocardial revascularization**. Postepy w kardiologii interwencyjnej = Advances in interventional cardiology 2020; 16:422-428.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33598015
ABSTRACT
INTRODUCTION: Well-organized, effective secondary prevention of coronary artery disease (CAD) has a potential to improve the patients' prognosis following myocardial revascularization procedures. AIM: To evaluate overtime changes in the implementation of the ESC guidelines for secondary prevention by assessing control of the main risk factors and the rate of cardioprotective drug use in patients following myocardial revascularization procedures. MATERIAL AND METHODS: Patients aged < 81 years who had been hospitalized for a myocardial revascularization procedure in five hospitals serving Krakow and surrounding districts were recruited and interviewed 6-18 months following discharge. Their personal medical history, medication use and control of the main cardiovascular risk factors were evaluated using a standard questionnaire in 2006-2007, 2011-2013, and 2016-2017. The same five hospitals took part in surveys on each occasion. RESULTS: We examined 260 patients in 2006-2007, 200 in 2011-2013 and 190 in 2016-2017. We noted a significant difference in the management of surveys participants: 62% underwent percutaneous coronary intervention (PCI) and 38% coronary artery coronary artery bypass grafting (CABG) in 2006-2007 whereas the corresponding proportions in 2016-2017 were 90% and 10%. The proportion of patients who did not achieve target blood pressure (according to ESC guidelines valid at the time of each survey) in 2006-2007, 2011-2013 and 2016-2017 was 53.5%, 52.3%, and 38.9%, respectively, the proportion of those who did not achieve the LDL cholesterol target (according to ESC guidelines valid at the time of each survey) was 36.3%, 64.0%, and 61.7%, respectively, and the proportion of those with high fasting glucose was 12.6%, 14.6%, and 19.7%, respectively. The proportion of smokers was 16.2%, 19.5%, and 16.8%, whereas 30.5%, 28.6% and 40.5% of patients were obese in 2006-2007, 2011-2013 and 2016-2017, respectively. The proportion of patients taking antiplatelets (91.8% vs. 92.0% vs. 96.3%), β-blockers (90.3% vs. 87.5% vs. 92.6%), and lipid-lowering drugs (88.7% vs. 91.0% vs. 93.7%) did not change significantly.Conclusions: The analysis of three multicenter surveys

provides evidence of the considerable potential for a further reduction in cardiovascular risk in patients following elective myocardial revascularization in Poland.

[48] *Banach M, Penson PE, Vrablik M et al.* **OPTIMAL USE OF LIPID-LOWERING THERAPY AFTER ACUTE CORONARY SYNDROMES: A Position Paper endorsed by the International Lipid Expert Panel (ILEP)**. Pharmacological research : the official journal of the Italian Pharmacological Society 2021:105499.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33607265
ABSTRACT
Atherosclerotic cardiovascular disease (ASCVD) and consequent acute coronary syndromes (ACS) are substantial contributors to morbidity and mortality across Europe. Much of these diseases burden is modifiable, in particular by lipid-lowering therapy (LLT). Current guidelines are based on the sound premise that with respect to low density lipoprotein cholesterol (LDL-C), "lower is better for longer", and the recent data have strongly emphasized the need of also "the earlier the better". In addition to statins, which have been available for several decades, the availability of ezetimibe and inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK9) are additional very effective approach to LLT, especially for those at very high and extremely high cardiovascular risk. LLT is initiated as a response to an individual's calculated risk of future ASCVD and is intensified over time in order to meet treatment goals. However, in real-life clinical practice goals are not met in a substantial proportion of patients. This Position Paper complements existing guidelines on the management of lipids in patients following ACS. Bearing in mind the very high risk of further events in ACS, we propose practical solutions focusing on immediate combination therapy in strict clinical scenarios, to improve access and adherence to LLT in these patients. We also define an 'Extremely High Risk' group of individuals following ACS, completing the attempt made in the recent European guidelines, and suggest mechanisms to urgently address lipid-medicated cardiovascular risk in these patients.

[49] *Sommer IE, Gangadin SS, de Witte LD et al.* **Simvastatin Augmentation for Patients With Early-Phase Schizophrenia-Spectrum Disorders: A Double-Blind, Randomized Placebo-Controlled Trial**. Schizophrenia bulletin 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33608711
ABSTRACT
Schizophrenia-spectrum disorders (SSD) are associated with increased inflammatory markers, both in brain and periphery. Augmentation with drugs that lower this pro-inflammatory status may improve clinical presentation. Simvastatin crosses the blood-brain barrier, has anti- inflammatory and neuroprotective effects and reduces metabolic syndrome. In this study, we investigated if 12 months of simvastatin augmentation can improve symptoms and cognition in patients with early SSD. This double-blind placebo-controlled trial included 127 SSD patients across the Netherlands, <3 years after their diagnosis. From these, 119 were randomly assigned 1:1 to simvastatin 40 mg (n = 61) or placebo (n = 58), stratified for sex and study site. Primary outcomes were symptom severity and cognition after 12 months of treatment. Depression, symptom subscores, general functioning, metabolic syndrome, movement disorders, and safety were secondary outcomes. Intention to treat analyses were performed using linear mixed models and ANCOVA. No main effect of simvastatin treatment was found on total symptom severity after 12 months of treatment as compared to placebo ($X2(1) = 0.01$, $P = .90$). Group differences varied over time (treatment*time $X2(4) = 11.2$; $P = .025$),

with significantly lower symptom severity in the simvastatin group after 6 months (mean difference = -4.8; P = .021; 95% CI: -8.8 to -0.7) and at 24 months follow-up (mean difference = -4.7; P = .040; 95% CI: -9.3 to -0.2). No main treatment effect was found for cognition (F(1,0.1) = 0.37, P = .55) or secondary outcomes. SAEs occurred more frequently with placebo (19%) than with simvastatin (6.6%). This negative finding corroborates other large scale studies on aspirin, minocycline, and celecoxib that could not replicate positive findings of smaller studies, and suggests that anti-inflammatory augmentation does not improve the clinical presentation of SSD.

[50] *Shimizu K, Takahashi M, Sato S et al.* **Rapid Rise of Cardio-Ankle Vascular Index May Be a Trigger of Cerebro-Cardiovascular Events: Proposal of Smooth Muscle Cell Contraction Theory for Plaque Rupture**. Vascular health and risk management 2021; 17:37-47.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33603388
ABSTRACT
Cardiovascular diseases have been recognized as the main cause of death all over the world. Recently, the established cardio-ankle vascular index (CAVI) has become known as an index of arterial stiffness of the arterial tree from the origin of the aorta to the ankle. CAVI reflects the progress of arteriosclerosis, and a rapid rise in CAVI indicates arterial smooth muscle cell contraction. Considering the vasculature of the atheroma where vasa vasorum penetrates the smooth muscle cell layer and supplies blood to the intimal atheromatous lesion, a rapid rise of CAVI means "choked" atheroma. Thus, we proposed a "smooth muscle cell contraction" hypothesis of plaque rupture.

[51] *Hoogeveen RM, Verweij SL, Kaiser Y et al.* **Atorvastatin treatment does not abolish inflammatory mediated cardiovascular risk in subjects with chronic kidney disease**. Scientific reports 2021; 11:4126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33602971
ABSTRACT
Individuals with chronic kidney disease are at an increased risk for cardiovascular disease. This risk may partially be explained by a chronic inflammatory state in these patients, reflected by increased arterial wall and cellular inflammation. Statin treatment decreases cardiovascular risk and arterial inflammation in non-CKD subjects. In patients with declining kidney function, cardiovascular benefit resulting from statin therapy is attenuated, possibly due to persisting inflammation. In the current study, we assessed the effect of statin treatment on arterial wall and cellular inflammation. Fourteen patients with chronic kidney disease stage 3 or 4, defined by an estimated Glomerular Filtration Rate between 15 and 60 mL/min/1.73 m(2), without cardiovascular disease were included in a single center, open label study to assess the effect of atorvastatin 40 mg once daily for 12 weeks (NTR6896). At baseline and at 12 weeks of treatment, we assessed arterial wall inflammation by (18)F-fluoro-deoxyglucose positron-emission tomography computed tomography ((18)F-FDG PET/CT) and the phenotype of circulating monocytes were assessed. Treatment with atorvastatin resulted in a 46% reduction in LDL-cholesterol, but this was not accompanied by an attenuation in arterial wall inflammation in the aorta or carotid arteries, nor with changes in chemokine receptor expression of circulating monocytes. Statin treatment does not abolish arterial wall or cellular inflammation in subjects with mild to moderate chronic kidney disease. These results imply that CKD-associated inflammatory activity is mediated by factors beyond LDL-cholesterol and specific anti-

inflammatory interventions might be necessary to further dampen the inflammatory driven CV risk in these subjects.

[52] *Coronado Arroyo JC, Concepción Zavaleta MJ, García Villasante EJ et al.* **Familial Chylomicronemia Syndrome-Induced Acute Necrotizing Pancreatitis during Pregnancy**. Rev Bras Ginecol Obstet 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33601464
ABSTRACT
Acute pancreatitis is a rare condition in pregnancy, associated with a high mortality rate. Hypertriglyceridemia represents its second most common cause. We present the case of a 38-year-old woman in the 24(th) week of gestation with a history of hypertriglyceridemia and recurrent episodes of pancreatitis. She was admitted to our hospital with acute pancreatitis due to severe hypertriglyceridemia. She was stabilized and treated with fibrates. Despite her favorable clinical course, she developed a second episode of acute pancreatitis complicated by multi-organ dysfunction and pancreatic necrosis, requiring a necrosectomy. The pregnancy was ended by cesarean section, after which three plasmapheresis sessions were performed. She is currently asymptomatic with stable triglyceride levels. Acute pancreatitis due to hypertriglyceridemia represents a diagnostic and therapeutic challenge in pregnant women, associated with serious maternal and fetal complications. When primary hypertriglyceridemia is suspected, such as familial chylomicronemia syndrome, the most important objective is preventing the onset of pancreatitis.

[53] *Wu X, Liu XB, Liu T et al.* **Effects of different statins application methods on plaques in patients with coronary atherosclerosis**. World journal of clinical cases 2021; 9:812-821.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33585627
ABSTRACT
BACKGROUND: Discontinued application of statins may be related to adverse cardiovascular events. However, it is unclear whether different statins administration methods have effects on coronary artery plaques. AIM: To evaluate the effects of different statins application methods on plaques in patients with coronary atherosclerosis. METHODS: A total of 100 patients diagnosed with atherosclerotic plaque by coronary artery computed tomography were continuously selected and divided into three groups according to different statins administration methods (discontinued application group, n = 32; intermittent application group, n = 39; sustained application group, n = 29). The effects of the different statins application methods on coronary atherosclerotic plaque were assessed. RESULTS: The volume change and rate of change of the most severe plaques were significantly reduced in the sustained application group ($P \leq 0.001$). The volume change of the most severe plaques correlated positively with low-density lipoprotein (LDL-C) levels only in the sustained application group ($R = 0.362$, $P = 0.013$). There were no changes in plaques or LDL-C levels in the intermittent and discontinued application groups. CONCLUSION: Continuous application of statins is effective for controlling plaque progression, whereas discontinued or intermittent administration of statins is not conducive to controlling plaques. Only with continuous statins administration can a reduction in LDL-C levels result in plaque volume shrinkage.

[54] *Giannopoulos S, Armstrong EJ*. **Medical therapy for cardiovascular and limb-related risk reduction in critical limb ischemia**. Vascular medicine (London, England) 2021:1358863x20987612.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33587692

ABSTRACT
Critical limb ischemia (CLI) constitutes the most advanced form of peripheral artery disease (PAD) and is characterized by ischemic rest pain, tissue loss and/or gangrene. Optimized medical care and risk factor modification in addition to revascularization could reduce the incidence of cardiovascular events and major adverse limb events, improving patients' quality of life and promising higher survival rates. Adequate adherence to cardioprotective medications, including antithrombotic therapy (e.g. antiplatelets, anticoagulants), cholesterol-lowering agents (e.g. statins, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors), angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and smoking cessation should be strongly encouraged for patients with CLI. This review examines these guideline-recommended therapies in terms of cardiovascular and limb-related risk reduction in patients with CLI.