[1] *Darwitan A, Wong YS, Nguyen LTH et al.* **Liposomal Nanotherapy for Treatment of Atherosclerosis**. Advanced healthcare materials 2020; 9:e2000465.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32543010
ABSTRACT
Atherosclerosis is a chronic disease that can lead to life-threatening events such as myocardial infarction and stroke, is characterized by the build-up of lipids and immune cells within the arterial wall. It is understood that inflammation is a hallmark of atherosclerosis and can be a target for therapy. In support of this concept, an injectable nanoliposomal formulation encapsulating fluocinolone acetonide (FA), a corticosteroid, is developed that allows for drug delivery to atherosclerotic plaques while reducing the systemic exposure to off-target tissues. In this study, FA is successfully incorporated into liposomal nanocarriers of around 100 nm in size with loading efficiency of 90% and the formulation exhibits sustained release up to 25 d. The anti-inflammatory effect and cholesterol efflux capability of FA-liposomes are demonstrated in vitro. In vivo studies carried out with an apolipoprotein E-knockout (Apoe(-/-)) mouse model of atherosclerosis show accumulation of liposomes in atherosclerotic plaques, colocalization with plaque macrophages and anti-atherogenic effect over 3 weeks of treatment. This FA-liposomal-based nanocarrier represents a novel potent nanotherapeutic option for atherosclerosis.

[2] *Chan J, Rajalingam T, Fossella J et al.* **Vascular Quality of Care Assessment: Clinicians' Adherence to Lipid-Lowering Therapy for Patients with Atherosclerotic Cardiovascular Disease**. Annals of vascular surgery 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32554202
ABSTRACT
BACKGROUND: Lipid-lowering medication can considerably lessen the risk for cardiovascular events in patients with atherosclerotic cardiovascular disease (ASCVD). Despite well-publicized guidelines and the accessibility of effective therapies, many patients do not attain their lipid goals and remain at high cardiovascular risk. Guidelines recommend statins as first-line therapy to reduce cardiovascular morbidity and mortality in ASCVD. We aimed to analyze admission lipid levels in a broad contemporary population of patients with ASCVD attending a vascular clinic or admitted to an inpatient vascular unit. METHODS: Patients with known ASCVD, current cholesterol levels, and lipid-lowering medications were documented and compared with published current Canadian Cardiovascular Society Guidelines recommendations for achieving <2.0 mmol/L or >50% reduction in low-density lipoprotein cholesterol (LDL-C). Cholesterol levels (current and previous), demographic characteristics, cardiovascular risk factors, and medical therapy were assessed from available patient records. RESULTS: Two hundred eight adult patients were identified. The mean age of the patients was 72 (±10) years, and 76% were men. About half had peripheral arterial disease (n = 118, 56.7%), one-third had coronary artery disease (n = 78, 37.5%), and one-third had diabetes (n = 76, 36.5%). Most were hypertensive (n = 140, 67.3%) and half gave a history of dyslipidemia (n = 103, 49.5%). Most patients (n = 183, 88%) were taking a statin and the majority at a moderate-intensity dose (n = 79, 43.2%) or high-intensity dose (n = 101, 55.2%). However, 32.7% of patients (n = 68) did not reach target of LDL-C level of <2.0 mmol/L or had ≤50% reduction from the baseline level. Of the patients who did not reach goals, 7 (10.3%) did not fill their statin prescriptions in the last 3 months. Only 26 patients (12.5%) were also on ezetimibe, a guideline-recommended second-line therapy if targets are not reached with

maximally tolerated statin therapy. One patient, who was able to reach target LDL-C, was on evolocumab monotherapy, a PCSK9 inhibitor, a contemporary nonstatin therapy that could be considered in ASCVD in those not at LDL-C goal. Of the 16 patients who were not prescribed any lipid-lowering therapy and did not reach target, 8 (50%) did not have any identified or documented reasons. Of the remaining 8 patients, 7 (87.5%) reported intolerance or side effects to statins only, and could benefit from nonstatin LDL-lowering therapy. CONCLUSIONS: In this observational study, we established suboptimal adherence to guideline recommendations for statin therapy and hesitancy to use nonstatin LDL-lowering agents in high-risk patients with ASCVD. These treatment gaps have an enormous effect on achieving improved cardiovascular clinical outcomes and must be tackled.

[3] *Montesano M, Reed JL, Tulloch HE et al.* **Cardiac rehabilitation is associated with greater improvements in psychological health following coronary artery bypass graft surgery when compared to percutaneous coronary intervention**. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32544341
ABSTRACT
Following coronary revascularization, patients treated with coronary artery bypass graft surgery (CABG) have lower risk of major adverse cardiovascular events when compared to those treated with percutaneous coronary intervention (PCI). We compared changes in cardiovascular risk factors, such as psychological and cardiometabolic health indicators, among patients who completed cardiac rehabilitation (CR) following CABG and PCI. Longitudinal records of 278 patients who completed an outpatient CR program following CABG or PCI were analyzed. We compared changes in anxiety and depression assessed by the Hospital Anxiety and Depression Scale (HADS); health-related quality of life (HR-QoL) measured by the Medical Outcomes Study Short Form-36 (SF-36); and, indicators of cardiometabolic health (i.e., body mass, blood pressure, glucose and lipid profiles) between CABG and PCI groups using analysis of covariance (ANCOVA). At baseline, patients treated with PCI (n=191) had better physical function (i.e., physical functioning: 62.5±22.1 vs. 54.3±23.0 points, p=0.006; and role limitations due to physical health: 31.2±36.8 vs. 20.6±31.8 points, p=0.024) when compared to those treated with CABG (n=87). Following CR, patients treated with PCI showed significantly smaller improvements in depression (-0.4±3.1 vs. -1.3±2.7 points, p=0.036) and mental HR-QoL (mental component summary: 2.4±10.8 vs. 5.7±10.7 points, p=0.020) when compared to those treated with CABG. Novelty •Patients with coronary artery disease treated with PCI have smaller functional limitations but similar psychological health when compared to those treated with CABG at CR enrollment. •Patients participating in CR following PCI appear to achieve smaller psychological health benefits from CR when compared to those recovering from CABG.

[4] *Lee S, Lee HJ, Kim SC, Joo JK*. **Association between nutrients and metabolic syndrome in middle-aged Korean women**. Archives of endocrinology and metabolism 2020; 64:298-305.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32555997
ABSTRACT
OBJECTIVES: The aim of this study was to evaluate the association between nutritional intake and metabolic syndrome in otherwise healthy middle-aged Korean women. SUBJECTS AND

METHODS: Retrospectively, medical records were reviewed for nutritional intake of 2,182 Korean women who had undergone routine medical check-ups from 2010 to 2016 at Pusan National University Hospital. The patients who met diagnostic criteria for metabolic syndrome based on NCEP-ATPIII were included, and each of the patients was assessed through self-report questionnaires and individual interview with a health care provider. The recommended dietary allowance (RDA) for women in Republic of Korea was based on 2015 criteria discussed in Dietary Reference Intake for Koreans, organized by the Ministry of Health and Welfare. RESULTS: Through univariate analysis, daily calorie, protein, fat, and carbohydrate consumption were significantly higher and exceeded RDA in the patients with metabolic syndrome; other than major nutrients, iron, vitamin B2, and niacin were also consumed in excess of the RDA in these patients. Multivariate analysis showed that carbohydrate consumption, along with protein and vitamin B2, were significantly higher in the patients with metabolic syndrome. CONCLUSION: In middle-aged Korean women, high consumption of carbohydrates, along with protein and vitamin B2, was found to have a statistically significant association with the presence of metabolic syndrome. Arch Endocrinol Metab. 2020;64(3):298-305.

[5] *Ahmed MA, Kamel EO*. **Involvement of H(2) S, NO and BDNF-TrkB signalling pathway in the protective effects of simvastatin against pentylenetetrazole-induced kindling and cognitive impairments**. Basic & clinical pharmacology & toxicology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32562563
ABSTRACT
Cognitive dysfunction was observed in pentylentetrazole (PTZ)-kindled mice. The potential effectiveness of simvastatin (SIM) on PTZ-induced kindling and cognitive impairments in mice was evaluated. The influence of SIM on hydrogen sulfide (H(2) S), nitric oxide (NO), reactive aldehydes and brain-derived neurotrophic factor/tyrosine receptor kinase B (BDNF-TrkB) signalling was also investigated. Kindling and cognitive impairments in mice were induced by 12 i.p. injections of PTZ (35 mg/kg) once every alternate day. The levels of reactive aldehydes and nitrite were increased while H(2) S was decreased in PTZ-treated mice. These results were accompanied by a reduction in the gene expression of aldehyde dehydrogenase 2, cystathionine β-synthase, BDNF and TrkB. In PTZ-kindled mice, a rise in brain inducible nitric oxide synthase protein expression associated with histopathological changes was observed. SIM administration (1, 5 and 10 mg/kg, daily orally) along with alternate day of PTZ (35 mg/kg) resulted in a decrease in PTZ-induced kindling with a dose-dependent improvement in cognitive function. SIM (10 mg/kg) prevented, to variable extent, the disturbances associated with PTZ-kindled mice with cortical, cerebellar and hippocampal structural improvement. These results suggested that SIM triggers multiple mechanisms that improve cognitive function in PTZ-kindled mice through modulation of oxidative stress, H(2) S, NO and BDNF-TrkB signalling pathway.

[6] *Niedzielski M, Broncel M, Gorzelak-Pabiś P, Woźniak E*. **New possible pharmacological targets for statins and ezetimibe**. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 2020; 129:110388.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32559626
ABSTRACT

Statin therapy is the gold standard in the treatment of dyslipidemia. Understanding the mechanisms of action of these drugs provides an opportunity to define new therapeutic goals for pharmacotherapy in patients with atherosclerotic lesions. The present review indicates the existence of previously unknown therapeutic targets for statins, such as Krüppel-like Factor 2 (KLF-2), Cystathionine γ lyase (CSE) and the microRNA regulating eNOS activity and synthesis; nuclear PXR receptor and EB transcription factor regulating Inflammasome NLRP3 activity; the Dickkopf-related protein 1 (DKK-1), which inhibits the WNT signalling pathway; the peroxisome proliferator-activated receptor (PPAR-γ) in vascular smooth muscle cells (VSMCs), which regulates the cell cycle, and the ERK5-Nrf2 pathway, which reduces the level of harmful advanced glycation end-products (AGE) in VSMCs during diabetic vasculopathy. Importantly, our review includes a number of promising discoveries, specifically those related to the effects of miR-221, miR-222 and miR-27b on the structure, synthesis and activity of eNOS, such as microRNA-based therapies, which offer promise in future targeted therapies. In contrast to numerous experiments confirming the pleiotropic effect of statins, there is still insufficient evidence on the pleiotropic effect of ezetimibe, which goes beyond its basic inhibitory effect on intestinal cholesterol absorption. However, recent studies indicate that this effect is limited to inhibiting macrophage migration, decreasing VCAM-1 expression and reducing the levels of reactive oxygen species. Defining new therapeutic goals for pharmacotherapy in patients with atherosclerotic lesions and ensuring effective treatment of dyslipidemia and its associated cardiovascular complications requires a thorough understanding of both the mechanisms of action of these drugs and of atherosclerosis itself.

[7] *Solomon A, Stanwix AE, Castañeda S et al.* **Points to consider in cardiovascular disease risk management among patients with rheumatoid arthritis living in South Africa, an unequal middle income country**. BMC Rheumatol 2020; 4:42.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32550295

ABSTRACT

BACKGROUND: It is plausible that optimal cardiovascular disease (CVD) risk management differs in patients with rheumatoid arthritis (RA) from low or middle income compared to high income populations. This study aimed at producing evidence-based points to consider for CVD prevention in South African RA patients. METHODS: Five rheumatologists, one cardiologist and one epidemiologist with experience in CVD risk management in RA patients, as well as two patient representatives, two health professionals and one radiologist, one rheumatology fellow and 11 rheumatologists that treat RA patients regularly contributed. Systematic literature searches were performed and the level of evidence was determined according to standard guidelines. RESULTS: Eighteen points to consider were formulated. These were grouped into 6 categories that comprised overall CVD risk assessment and management (n = 4), and specific interventions aimed at reducing CVD risk including RA control with disease modifying anti-rheumatic drugs, glucocorticoids and non-steroidal anti-inflammatory drugs (n = 3), lipid lowering agents (n = 8), antihypertensive drugs (n = 1), low dose aspirin (n = 1) and lifestyle modification (n = 1). Each point to consider differs partially or completely from recommendations previously reported for CVD risk management in RA patients from high income populations. Currently recommended CVD risk calculators do not reliably identify South African black RA patients with very high-risk atherosclerosis as represented by carotid artery plaque presence on ultrasound. CONCLUSIONS: Our findings indicate that optimal cardiovascular risk management likely differs substantially in RA patients from low or middle

income compared to high income populations. There is an urgent need for future multicentre longitudinal studies on CVD risk in black African patients with RA.

[8] *Mathew RO, Rosenson RS, Lyubarova R et al.* **Concepts and Controversies: Lipid Management in Patients with Chronic Kidney Disease**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32556851
ABSTRACT
Atherosclerotic cardiovascular disease (ASCVD) remains an important contributor of morbidity and mortality in patients with chronic kidney disease (CKD). CKD is recognized as an important risk enhancer that identifies patients as candidates for more intensive low-density lipoprotein (LDL) cholesterol lowering. However, there is controversy regarding the efficacy of lipid-lowering therapy, especially in patients on dialysis. Among patients with CKD, not yet on dialysis, there is clinical trial evidence for the use of statins with or without ezetimibe to reduce ASCVD events. Newer cholesterol lowering agents have been introduced for the management of hyperlipidemia to reduce ASCVD, but these therapies have not been tested in the CKD population except in secondary analyses of patients with primarily CKD stage 3. This review summarizes the role of hyperlipidemia in ASCVD and treatment strategies for hyperlipidemia in the CKD population.

[9] *Kenny DJ, Plichta DR, Shungin D et al.* **Cholesterol Metabolism by Uncultured Human Gut Bacteria Influences Host Cholesterol Level**. Cell Host Microbe 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32544460
ABSTRACT
The human microbiome encodes extensive metabolic capabilities, but our understanding of the mechanisms linking gut microbes to human metabolism remains limited. Here, we focus on the conversion of cholesterol to the poorly absorbed sterol coprostanol by the gut microbiota to develop a framework for the identification of functional enzymes and microbes. By integrating paired metagenomics and metabolomics data from existing cohorts with biochemical knowledge and experimentation, we predict and validate a group of microbial cholesterol dehydrogenases that contribute to coprostanol formation. These enzymes are encoded by ismA genes in a clade of uncultured microorganisms, which are prevalent in geographically diverse human cohorts. Individuals harboring coprostanol-forming microbes have significantly lower fecal cholesterol levels and lower serum total cholesterol with effects comparable to those attributed to variations in lipid homeostasis genes. Thus, cholesterol metabolism by these microbes may play important roles in reducing intestinal and serum cholesterol concentrations, directly impacting human health.

[10] *Vodička M, Slanař O, Pisár M, Šálek T*. **Rosuvastatin-induced rhabdomyolysis due to medication errors**. Ceska a Slovenska farmacie : casopis Ceske farmaceuticke spolecnosti a Slovenske farmaceuticke spolecnosti 2020; 69:100-102.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32545989
ABSTRACT
Case (description): A 74 years old Caucasian suffering from chronic kidney disease presented with progressive asthenia and diffuse myalgia. It was revealed that the patient used three different rosuvastatin-containing preparations in a total daily dose of 120 mg for 76 days.

Laboratory investigations revealed a marked elevation of serum urea, creatinine, myoglobin, creatine kinase (CK) and transaminases. Two serious medication errors have been identified as possible major factors that synergistically contributed to the development of rosuvastatin-induced rhabdomyolysis. First, 40 mg of rosuvastatin dose was prescribed to the patient, although the estimation of glomerular filtration rate (eGFR) declined below 40 ml/min/1.73 m2. Moreover, the patient used 3 different rosuvastatin formulations simultaneously in a total dose of 120 mg/day. The heterozygous CYP2C9*1/*3 genotype and warfarin co-administration could further contribute to the development of rhabdomyolysis. A number of preventive measures, notably in drug policy, are suggested to overcome unintended intoxications. Conclusion: Rosuvastatin-induced myopathy is a rare, but serious adverse effect. This case report highlights the need for a proper treatment and dose adjustment during chronic medical therapy, the need for adequate patient education and application of adequate drug policy measures in the era of fragmented health care delivery and polypragmasia.

[11] *Sgrignani J, Fassi EMA, Lammi C et al.* **Exploring Proprotein Convertase Subtilisin/Kexin 9 (PCSK9) Autoproteolysis Process by Molecular Simulations: Hints for Drug Design**. ChemMedChem 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32558225
ABSTRACT
Proprotein convertase subtilisin/kexin 9 (PCSK9) is a notable target for the treatment of hypercholesterolemia because it regulates the population of the low-density lipoprotein receptor (LDLR) on liver cells. The PCSK9 zymogen is a serine protease that spontaneously undergoes a double self-cleavage step. Available X-ray structures depict the PCSK9 mature state, but the atomic details of the zymogen state of the enzyme are still unknown. Additionally, why the protease activity of PCSK9 is blocked after the second autoprocessing step remains unclear, as this deviates from other members of the PCSK family. By performing constant-pH molecular dynamics (MD) simulations, we investigated the protonation state of the catalytic triad of PCSK9 and found that it strongly influences the catalytic properties of the enzyme. Moreover, we determined the final step of the maturation process by classical and steered MD simulations. This study could facilitate the identification of ligands capable of interfering with the PCSK9 maturation process.

[12] *Asare Y, Campbell-James TA, Bokov Y et al.* **Histone Deacetylase 9 Activates IKK to Regulate Atherosclerotic Plaque Vulnerability**. Circulation research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546048
ABSTRACT
Rationale: Arterial inflammation manifested as atherosclerosis is the leading cause of mortality worldwide. Genome-wide association studies have identified a prominent role of histone deacetylase 9 (HDAC9) in atherosclerosis and its clinical complications including stroke and myocardial infarction. Objective: To determine the mechanisms linking HDAC9 to these vascular pathologies and explore its therapeutic potential for atheroprotection. Methods and Results: We studied the effects of Hdac9 on features of plaque vulnerability using bone marrow reconstitution experiments and pharmacological targeting with a small molecule inhibitor in hyperlipidemic mice. We further employed two-photon and intravital microscopy to study endothelial activation and leukocyte-endothelial interactions. We show that hematopoietic Hdac9 deficiency reduces lesional macrophage content whilst increasing fibrous

cap thickness thus conferring plaque stability. We demonstrate that HDAC9 binds to IKKα and β resulting in their deacetylation and subsequent activation, which drives inflammatory responses in both macrophages and endothelial cells. Pharmacological inhibition of HDAC9 with the class IIa HDAC inhibitor TMP195 attenuates lesion formation by reducing endothelial activation and leukocyte recruitment along with limiting pro-inflammatory responses in macrophages. Transcriptional profiling using RNA-Seq revealed that TMP195 downregulates key inflammatory pathways consistent with inhibitory effects on IKKβ. TMP195 mitigates the progression of established lesions and inhibits the infiltration of inflammatory cells. Moreover, TMP195 diminishes features of plaque vulnerability and thereby enhances plaque stability in advanced lesions. Ex vivo treatment of monocytes from patients with established atherosclerosis reduced the production of inflammatory cytokines including IL-1β and IL-6. Conclusions: Our findings identify HDAC9 as a regulator of atherosclerotic plaque stability and IKK activation thus providing a mechanistic explanation for the prominence of HDAC9 as a vascular risk locus in genome-wide association studies. Its therapeutic inhibition may provide a potent lever to alleviate vascular inflammation.

[13] *Ruiz-García A, Arranz-Martínez E, López-Uriarte B et al.* **Prevalence of hypertriglyceridemia in adults and related cardiometabolic factors. SIMETAP-HTG study**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32534728
ABSTRACT
AIM: To determine in the adult population the crude and the sex- and age-adjusted prevalence rates of hypertriglyceridaemia (HTG) and to assess its association with cardiovascular risk factors, chronic kidney disease, cardiovascular and cardiometabolic diseases. METHODS: Cross-sectional observational study conducted in Primary Care, with 6,588 adult study subjects, randomly selected on base-population. Patients had HTG if the triglyceride level was≥150mg/dL (≥1.7mmol/L), or were on lipid-lowering therapy to lower triglyceride. Associations were assessed by univariate and multivariate analysis, and crude and sex- and age-adjusted prevalence rates were determined. RESULTS: The arithmetic and geometric means of triglyceride levels were respectively 120.5 and 104.2mg/dL in global population, 135.7 and 116.0mg/dL in men, and 108.6 and 95.7mg/dL in women. The crude HTG prevalence rates were 29.6% in global population, 36.9% in men and 23.8% in women. The sex- and age-adjusted HTG prevalence rates were 27.0% in global population, 34.6% in men and 21.4% in women. The independent variables that were most associated with HTG were hypercholesterolemia (OR: 4.6), low HDL-C (OR: 4.1), hepatic steatosis (OR: 2.8), diabetes (OR: 2.0), and obesity (OR: 1.9). CONCLUSIONS: The means of triglyceride levels and HTG prevalence rates are intermediate between those of other national and international studies. A fifth of the female adult population and more than a third of the male population had HTG. The independent factors associated with HTG were hypercholesterolemia and low HDL-C, and the cardiometabolic variables diabetes, hepatic steatosis and obesity.

[14] *Zaragoza-García O, Guzmán-Guzmán IP, Moreno-Godínez ME et al.* **PON-1 haplotype (-108C>T, L55M, and Q192R) modulates the serum levels and activity PONase promoting an atherogenic lipid profile in rheumatoid arthritis patients**. Clinical rheumatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32556934

ABSTRACT
INTRODUCTION/OBJECTIVE: Paraoxonase 1 (PON1) promotes antioxidant and antiatherogenic activity related to the hydrolysis of oxidized lipids of low-density lipoproteins. In rheumatoid arthritis (RA) patients, it has been reported that low PON1 activity is related to an impaired lipid profile, increasing cardiovascular risk (CVR). The goal of this study was to analyze the effect of common PON1 polymorphisms and haplotypes on enzymatic activity, PON1 serum levels (PON1s), and lipid parameters related to atherogenic profile in RA patients. METHODS: A cross-sectional study was carried out on 250 Mexican patients with RA. The lipid profile was determined by colorimetric tests. The PON1 activity (CMPAase) was measured by spectrophotometry. The levels of PON1s were determined by ELISA, and the polymorphisms in the PON-1 gene (-108C>T, L55M, and Q192R) were genotyped by the PCR-RFLP method. The haplotypes were estimated and statistical analysis was performed. RESULTS: The median of the CMPAase activity and PON1 levels was 13.91 U/mL and 24.75 ng/mL, respectively. The CMPAase activity was significantly lower in carriers of -108TT and 192QQ genotypes ($\beta = -4.09$, $P = 0.001$ and $\beta = -3.73$, $P = 0.002$, respectively); moreover, the PON1 levels were lower in 192Q allele carriers ($P < 0.01$). The TLQ haplotype was associated with CMPAase activity < 13.91 U/mL (OR = 2.29, $P < 0.001$), as well as with levels of PON1s < 24.75 ng/mL (OR = 1.65, $P = 0.017$). In this study, the CMPAase activity (< 13.91 U/mL) showed a positive association with lower levels of high-density lipoprotein cholesterol (HDL-c; < 40/50 mg/dL), and with a triglycerides/HDL-c ratio > 3%, and a total cholesterol/HDL-c ratio > 4.5/5%, all representatives of an atherogenic risk lipid profile. CONCLUSIONS: PON1 polymorphisms modulate the CMPAase activity and PON1 levels in Mexican patients with RA. The CMPAase activity < 13.91 U/mL is associated with an atherogenic lipid profile, independently of inflammation markers and treatment with anti-rheumatic drugs.Key Points•The haplotype TLQ is a marker for low PONase activity in rheumatoid arthritis.•The haplotype TLQ is a marker for low PON1 serum levels in rheumatoid arthritis.•The enzymatic PON1 activity represents the best marker for an atherogenic lipid profile in rheumatoid arthritis, in comparison with PON1 levels.•The haplotype TLQ is a marker of low PON1 activity, levels of PON1s, and atherogenic lipid profile, independent of treatment therapy in rheumatoid arthritis.

[15] *Adams SP, Alaeiilkhchi N, Wright JM*. **Pitavastatin for lowering lipids**. The Cochrane database of systematic reviews 2020; 6:Cd012735.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32557581
ABSTRACT
BACKGROUND: Pitavastatin is the newest statin on the market, and the dose-related magnitude of effect of pitavastatin on blood lipids is not known. OBJECTIVES: Primary objective To quantify the effects of various doses of pitavastatin on the surrogate markers: LDL cholesterol, total cholesterol, HDL cholesterol and triglycerides in participants with and without cardiovascular disease. To compare the effect of pitavastatin on surrogate markers with other statins. Secondary objectives To quantify the effect of various doses of pitavastatin on withdrawals due to adverse effects. SEARCH METHODS: The Cochrane Hypertension Information Specialist searched the following databases for trials up to March 2019: the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 2, 2019), MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. We also contacted authors of relevant papers

regarding further published and unpublished work. The searches had no language restrictions. SELECTION CRITERIA: RCT and controlled before-and-after studies evaluating the dose response of different fixed doses of pitavastatin on blood lipids over a duration of three to 12 weeks in participants of any age with and without cardiovascular disease. DATA COLLECTION AND ANALYSIS: Two review authors independently assessed eligibility criteria for studies to be included, and extracted data. We entered data from RCT and controlled before-and-after studies into Review Manager 5 as continuous and generic inverse variance data, respectively. Withdrawals due to adverse effects (WDAE) information was collected from the RCTs. We assessed all included trials using the Cochrane 'Risk of bias' tool under the categories of allocation (selection bias), blinding (performance bias and detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other potential sources of bias. MAIN RESULTS: Forty-seven studies (five RCTs and 42 before-and-after studies) evaluated the dose-related efficacy of pitavastatin in 5436 participants. The participants were of any age with and without cardiovascular disease, and pitavastatin effects were studied within a treatment period of three to 12 weeks. Log dose-response data over doses of 1 mg to 16 mg revealed strong linear dose-related effects on blood total cholesterol and LDL cholesterol and triglycerides. There was no dose-related effect of pitavastatin on blood HDL cholesterol, which was increased by 4% on average by pitavastatin. Pitavastatin 1 mg/day to 16 mg/day reduced LDL cholesterol by 33.3% to 54.7%, total cholesterol by 23.3% to 39.0% and triglycerides by 13.0% to 28.1%. For every two-fold dose increase, there was a 5.35% (95% CI 3.32 to 7.38) decrease in blood LDL cholesterol, a 3.93% (95% CI 2.35 to 5.50) decrease in blood total cholesterol and a 3.76% (95% CI 1.03 to 6.48) decrease in blood triglycerides. The certainty of evidence for these effects was judged to be high. When compared to other statins for its effect to reduce LDL cholesterol, pitavastatin is about 6-fold more potent than atorvastatin, 1.7-fold more potent than rosuvastatin, 77-fold more potent than fluvastatin and 3.3-fold less potent than cerivastatin. For the placebo group, there were no participants who withdrew due to an adverse effect per 109 subjects and for all doses of pitavastatin, there were three participants who withdrew due to an adverse effect per 262 subjects. AUTHORS' CONCLUSIONS: Pitavastatin lowers blood total cholesterol, LDL cholesterol and triglyceride in a dose-dependent linear fashion. Based on the effect on LDL cholesterol, pitavastatin is about 6-fold more potent than atorvastatin, 1.7-fold more potent than rosuvastatin, 77-fold more potent than fluvastatin and 3.3-fold less potent than cerivastatin. There were not enough data to determine risk of withdrawal due to adverse effects due to pitavastatin.

[16] *Kuo WC, Stevens JM, Ersig AL et al.* **Does 24-h Activity Cycle Influence Plasma PCSK9 Concentration? A Systematic Review and Meta-Analysis**. Current atherosclerosis reports 2020; 22:30.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32542587
ABSTRACT
PURPOSE OF REVIEW: Higher plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) concentration has been associated with a higher risk of atherosclerotic cardiovascular disease (ASCVD). Animal and human studies have examined the relationship between 24-h activity cycles (24-HAC) and PCSK9, but conflicting results exist. Therefore, this review aimed to examine the relationship between 24-HAC and plasma PCSK9 concentration in animals and humans.Three databases (PubMed, CINAHL, and Web of Science) were searched for eligible

articles. Descriptive data were summarized using network meta-analysis. The effect size was estimated using pairwise meta-analysis. RECENT FINDINGS: The interventions designed to increase moderate to vigorous physical activities (MVPA) did not significantly change plasma PCSK9 concentration (Hedges' g = 0.137; p = 0.337). However, the effect was influenced by statin therapy and intervention delivery mode. Specifically, physical activity interventions in conjunction with statin therapy significantly increased plasma PCSK9 concentration (Hedges' g = 0.275; p = 0.007). Supervised exercise training significantly increased plasma PCSK9 concentration (Hedges' g = 0.630; p = 0.001), but physical activity counseling did not (p = 0.845). The effects of MVPA on plasma PCSK9 may be moderated by statin therapy, intervention delivery mode, or other potential unknown mechanistic factors. Thus, caution should be taken when using plasma PCSK9 as an outcome indicator for physical activity interventions aimed at decreasing the risk of ASCVD. Graphical abstract.

[17] *Stefanutti C*. **Lomitapide-a Microsomal Triglyceride Transfer Protein Inhibitor for Homozygous Familial Hypercholesterolemia**. Current atherosclerosis reports 2020; 22:38.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32557261
ABSTRACT
PURPOSE OF REVIEW: Homozygous familial hypercholesterolemia (HoFH) is a rare, genetic condition characterized by high levels of Low density lipoprotein cholesterol (LDL-C); overt, early-onset atherosclerotic cardiovascular disease (ASCVD); and premature cardiovascular events and mortality. Lomitapide is a first-in-class microsomal triglyceride transfer protein inhibitor for the treatment of HoFH. This review provides an update on data emerging from real-world studies of lomitapide following on from its pivotal phase 3 clinical trial in HoFH. RECENT FINDINGS: Recent registry data have confirmed that HoFH is characterized by delayed diagnosis, with many patients not receiving effective therapy until they are approaching the age when major adverse cardiovascular events may occur. Data from case series of varying sizes, and from a 163-patient registry of HoFH patients receiving lomitapide, have demonstrated that lomitapide doses are lower and adverse events less severe than in the phase 3 study. Lomitapide enables many patients to reach European Atherosclerosis Society LDL-C targets. Some patients are able to reduce frequency of lipoprotein apheresis or, in some cases, stop the procedure altogether-unless there is significant elevation of lipoprotein (a). Modelling analyses based on historical and clinical trial data indicate that lomitapide has the potential to improve cardiovascular outcomes and survival in HoFH. Real-world clinical experience with lomitapide has shown the drug to be effective with manageable, less marked adverse events than in formal clinical studies. Event modelling data suggest a survival benefit with lomitapide in HoFH.

[18] *Masana L, Ibarretxe D, Plana N*. **Reasons Why Combination Therapy Should Be the New Standard of Care to Achieve the LDL-Cholesterol Targets : Lipid-lowering combination therapy**. Current cardiology reports 2020; 22:66.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32562015
ABSTRACT
PURPOSE OF REVIEW: The aim of this report is to review the scientific evidence supporting that lipid lowering therapy (LLT), beyond statins, reduces cardiovascular risk; therefore, treatment strategies based on lipid-lowering drug combination should be implemented. RECENT FINDINGS: A strong scientific body of evidence supports the effect of statins on

cardiovascular risk reduction. Recent trials using non-statin LLT, ezetimibe, and PCSK9 inhibitors have provide scientific evidence about their impact on cardiovascular prevention. Current clinical guidelines still recommend using high-intensity statin monotherapy before considering combination therapy. The causal effect of LDL-C on atherosclerosis is well established. Moreover, new RCT, meta-analysis, and Mendelian randomization data, support that the main determinant of risk reduction is the absolute LDL reduction regardless of LLT. Accordingly, the "high-intensity statin therapy" concept should be substituted by "high-intensity lipid lowering therapy." Combination therapy must become the standard of care of hypercholesterolemia treatment.

[19] *Chow YL, Teh LK, Chih LH et al.* **Lipid metabolism genes in stroke pathogenesis: The Atherosclerosis**. Current pharmaceutical design 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32534558
ABSTRACT
Stroke is the second leading cause of death and a major cause of disability worldwide. Both modifiable and non-modifiable risk factors can affect the occurrence of ischemic stroke at varying degrees. Among them, atherosclerosis has been well recognized as one of the main culprits for the rising incidence of stroke-related mortality. Hence, the current review aimed to summarize the prominent role of lipid metabolism genes such as PCSK9, ApoB, ApoA5, ApoC3, ApoE and ABCA1 in mediating ischemic stroke occurrence.

[20] *Felekos I, Karamasis GV, Pavlidis AN*. **PCSK9 inhibitors for the management of dyslipidemia in people with Type 2 Diabetes: How low is too low?** Current pharmaceutical design 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32552640
ABSTRACT
Diabetic patients are considered as high risk for development of atherosclerotic disease. Cholesterol treatment is of paramount importance in order to optimise cardiovascular outcomes in this subset of patients. Although statins are regarded as the mainstay of treatment, these may not be tolerated or as efficacious as they should be. Recently the advent of PCSK-9 inhibitors has drawn attention in the management of dyslipidemias. In this review we discuss current trends in their use and we focus in their role in diabetic dyslipidemia management.

[21] *Xu X, Chai M, Cheng Y et al.* **Efficacy and Safety of Evolocumab in Reducing Low Density Lipoprotein Cholesterol Levels in Chinese Patients with Non-ST-segment Elevation Acute Coronary Syndrome**. Current vascular pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32543364
ABSTRACT
AIMS: To explore early intensive lipid-lowering therapy in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). BACKGROUND: Lowering low-density lipoprotein cholesterol (LDL-C) levels can reduce cardiovascular morbidity and mortality in patients with atherosclerotic cardiovascular disease. Due to many reasons, the need for early intensive lipid-lowering therapy is far from being met in Chinese NSTE-ACS patients at high-risk of recurrent ischaemic events. OBJECTIVE: To evaluate the feasibility, safety and efficacy of starting evolocumab in hospital to lower LDL-C levels in Chinese patients with NSTE-ACS.

METHODS: In this prospective cohort study initiated by researchers, 334 consecutive patients with NSTE-ACS who had sub-standard LDL-C levels (LDL-C ≥2.3 mmol/L after regular oral statin treatment for at least 4 weeks; or LDL-C ≥3.2 mmol/L without regular oral statin treatment) were included. Patients who agreed to treatment with evolocumab (140 mg subcutaneously every 2 weeks, initiated in hospital and used for 12 weeks after discharge) were enrolled in the evolocumab group (n=96) and others in the control group (n=238). All enrolled patients received regular statin treatment (atorvastatin 20 mg/day or rosuvastatin 10 mg/day; doses unchanged throughout the study).The primary endpoint was the change in LDL-C levels from baseline to week 12. RESULTS: Most patients (67.1%) had not received regular statin treatment before. In the evolocumab group, LDL-C levels decreased significantly at week 4 and remained stable at week 8 and 12 (all p<0.001). At week 12, the LDL-C percentage change from baseline in the evolocumab group was -79.2±12.7% (from an average of 3.7 to 0.7 mmol/L), while in the control group it was -37.4±15.4% (from an average of 3.3 to 2.0 mmol/L). The mean difference between these 2 groups was -41.8% (95% CI -45.0 to -38.5%; p<0.001). At week 12, the proportions of patients with LDL-C levels <1.8 mmol/L and 1.4 mmol/L in the evolocumab group were significantly higher than in the control group (96.8 vs 36.1%; 90.6 vs 7.1%; both p<0.001). The incidence of adverse events and cardiovascular events was similar in both groups. CONCLUSIONS: In this prospective cohort study we evaluated the early initiation of evolocumab in NSTE-ACS patients in China. Evolocumab combined with statins significantly lowered LDL-C levels and increased the probability of achieving recommended LDL-C levels, with satisfactory safety and well tolerance.

[22] *Jialal I*. **Management of diabetic dyslipidemia: Navigating the new American and European Guidelines**. Diabetes & metabolic syndrome 2020; 14:877-879.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32562865
ABSTRACT

[23] *Hwang JG, Yu KS, Lee S*. **Comparison of the Pharmacokinetics of Highly Variable Drugs in Healthy Subjects Using a Partial Replicated Crossover Study: A Fixed-Dose Combination of Fimasartan 120 mg and Atorvastatin 40 mg versus Separate Tablets**. Drug design, development and therapy 2020; 14:1953-1961.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546962
ABSTRACT
PURPOSE: A fixed-dose combination (FDC) of fimasartan and atorvastatin is used to treat hypertension and dyslipidemia. The peak plasma concentration (C(max)) of fimasartan and atorvastatin has a large intra-subject variability with a maximum coefficient of variation of 65% and 48%, respectively. Therefore, both drugs are classified as highly variable drugs. The purpose of this study was to compare the pharmacokinetics (PK) between a FDC of fimasartan 120 mg and atorvastatin 40 mg versus separate tablets in healthy male Korean subjects. SUBJECTS AND METHODS: A randomized, single-dose, two-treatment, three-sequence, three-period, partial replicated crossover study was conducted with a 7-day washout interval between periods. Blood samples for fimasartan and atorvastatin were collected until 48 hours after administration in each period. PK parameters were calculated using the non-compartmental method. Geometric mean ratios (GMRs) for PK parameters of FDC to loose combination and their 90% confidence intervals (90% CIs) were estimated. RESULTS: A total of 56 subjects completed the study. GMRs (90% CIs) of the C(max) for fimasartan and

atorvastatin were 1.08 (0.93-1.24) and 1.02 (0.92-1.13), respectively. The expanded 90% CIs of both drugs using the intra-subject variability was calculated range of 0.70-1.43 and 0.73-1.38, respectively. The corresponding values of area under the concentration-time curve from zero to the last measurable time point were 1.02 (0.97-1.08) and 1.02 (0.98-1.07), respectively. CONCLUSION: FDC of fimasartan 120 mg and atorvastatin 40 mg between their loose combination showed similar PK characteristics.

[24] *Aoki K, Kamiyama H, Takihata M et al.* **Effect of liraglutide on lipids in patients with type 2 diabetes: a pilot study**. Endocrine journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32554954
ABSTRACT
The mechanism for the cholesterol-lowering effect of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) remains unknown in patients with type 2 diabetes. We evaluated the effect of liraglutide on serum lipid profiles, including cholesterol synthesis and absorption markers, during daily clinical practice in Japanese patients with type 2 diabetes. We enrolled 38 patients with type 2 diabetes mellitus who were not treated with a GLP-1 RA (≥20 years of age, HbA1c ≥6.5%). Liraglutide, a GLP-1 RA, was administered subcutaneously once a day for three months to these patients. Blood samples and body weights were collected at 0, 1, and 3 months. Total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) at 1 month, and non-high-density lipoprotein cholesterol (non-HDL-C) and calculated TC at 1 and 3 months, were decreased, while the cholesterol synthesis and cholesterol absorption markers were unchanged by this treatment. In patients with LDL-C levels over 100 mg/dL, LDL-C, non-HDL-C, TC, and calculated TC levels were decreased significantly by the treatment at 1 and 3 months, and the cholesterol absorption marker, campesterol, was decreased at 3 months. The administration of liraglutide for 3 months decreased non-HDL-C and calculated TC significantly, while the cholesterol synthesis and absorption markers were not changed by this treatment.

[25] *Devasani K, Kaul R, Majumdar A*. **Supplementation of pyrroloquinoline quinone with atorvastatin augments mitochondrial biogenesis and attenuates low grade inflammation in obese rats**. European journal of pharmacology 2020; 881:173273.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32535101
ABSTRACT
Mitochondrial dysfunction and Inflammation play a significant role in the manifestation of the co-morbidities of obesity. The study deciphered the impact of Pyrroloquinoline quinone (PQQ) per se and with Atorvastatin (ATS) on high fat, 10% fructose diet (HFFD) induced obese rats expressing low-grade inflammation, dyslipidemia, and mitochondrial dysfunction. HFFD was fed for 10 weeks followed by treatment for 5 weeks with ATS 10 or 20 mg/kg, PQQ 10 or 20 mg/kg, p.o. per se or their combinations. The impact on blood glucose, lipid profile and serum insulin, TNF-α, IL-1β, IL-18, IL-6 was estimated. Gene and protein expression of peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC 1α), Sirtuin 1 (SIRT1), Mitochondrial transcriptional factor A (TFAM) and augmented mitochondrial DNA (mtDNA), NOD like receptor protein 3 (NLRP3) and Caspase 1 was assessed. Rats receiving PQQ and ATS revealed significant decrease in body weights, anthropometric parameter, and adipose tissue vis-à-vis positive control. PQQ alone and with ATS improved glucose tolerance, lipid profile, insulin indices and lowered serum levels of inflammatory cytokines IL-18, IL-1β,

TNF-α and IL-6 along with a rise in adiponectin. PQQ supplementation with ATS upregulated the mRNA expression of PGC 1α, SIRT1, TFAM and augmented mtDNA while downregulating inflammatory markers NLRP3 and Caspase 1. PQQ supplementation with atorvastatin holds therapeutic promise to effectively combat mitochondrial dysfunction and chronic low-grade inflammation in obesity.

[26] *Dai L, Zuo Y, You Q et al.* **Efficacy and safety of bempedoic acid in patients with hypercholesterolemia: A systematic review and meta-analysis of randomized controlled trials**. European journal of preventive cardiology 2020:2047487320930585.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32551969

ABSTRACT

AIM: Bempedoic acid is a novel oral drug, which has been increasingly researched to play an important role in the treatment of hypercholesterolemia recently. However, results from original studies were inconsistent and inconclusive. We aimed to conduct a meta-analysis to quantitatively appraise the efficacy and safety of bempedoic acid. METHODS: PubMed, Embase, Web of Science and Scopus were searched from inception to 30 January 2020. We included randomized controlled trials that compared the efficacy and safety of bempedoic acid with placebo in patients with hypercholesterolemia. Results from trials were presented as mean differences or odds ratios (ORs) with 95% confidence intervals (CIs) and were pooled by random or fixed effects model. The risk of bias and heterogeneity among trials were also assessed and analyzed. RESULTS: Pooled analysis of 10 eligible trials showed that bempedoic acid treatment resulted in greater lowering of the low-density lipoprotein cholesterol level than the placebo group (mean difference -23.16%, 95% CI -26.92% to -19.04%). We also found that improvements in lipid parameters and biomarkers were still maintained at weeks 24 and 52 from the long-term trials. As for safety, bempedoic acid did not increase the risk of overall adverse events (OR 1.02, 95% CI 0.88 to 1.18). However, the incidence of adverse events leading to discontinuation was higher in the bempedoic acid group (OR 1.44, 95% CI 1.14 to 1.82). CONCLUSIONS: Available evidence from randomized controlled trials suggests that bempedoic acid provides a well-tolerated and effective therapeutic option for lipid lowering in patients with hyperlipidemia.

[27] *Geng J, Xu H, Fu W et al.* **Rosuvastatin protects against endothelial cell apoptosis in vitro and alleviates atherosclerosis in ApoE(-/-) mice by suppressing endoplasmic reticulum stress**. Experimental and therapeutic medicine 2020; 20:550-560.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32537013

ABSTRACT

The development of abnormal lipid-induced atherosclerosis is initiated with endothelial cell apoptosis. Vascular endothelial cells possess highly developed endoplasmic reticulum (ER), which is involved in lipid metabolism, indicating that ER stress may contribute chiefly to the induction of endothelial cell apoptosis. Based on its ability to reduce cholesterol levels, rosuvastatin may play an endothelial and vascular protective role by regulating ER stress. In the present study, the involvement of the inhibition of the ER stress-induced endothelial injury was investigated in combination with the lipid lowering effects of rosuvastatin. This compound can be used to inhibit cholesterol synthesis in atherosclerosis. Rosuvastatin decreased the apoptotic rates of human umbilical vascular endothelial cells (HUVECs) that had been stimulated with ox-low density lipoprotein (LDL) in vitro and repressed the mRNA levels of

CHOP, sXBP1 and caspase-12, and decreased caspase-12 activity, as well as the content of glucose-regulated protein 78 (GRP78), phosphorylated (p)-protein kinase RNA-like ER kinase (PERK), p-inositol-requiring protein 1α (IRE1α) and p-eIF2α proteins. In addition, ApoE(-/-) mice were fed with atherogenic chow for 8 weeks for atherosclerosis induction and rosuvastatin was provided by intragastric administration for an additional 4 weeks. Subsequently, the atherosclerotic plaque formation in the aorta was evaluated by Oil Red O and hematoxylin and eosin staining, and the serum LDL, high-density lipoprotein, total cholesterol (TC) and triacylglycerol (TG) levels were measured. In addition, the induction of apoptosis of endothelial cells and the expression levels of GRP78, p-PERK, p-IRE1α and p-eIF2α were assessed in the aorta. Rosuvastatin repressed atherosclerotic plaque formation and endothelial apoptosis in the aorta and decreased LDL and TG levels in the serum, as determined by in vivo results. Furthermore, it downregulated the expression levels of protein chaperone GRP78, p-PERK, p-IRE1α and p-eIF2α in the aortic intima. The data indicated that rosuvastatin could protect HUVECs from ER stress-induced apoptosis triggered by oxidized LDL. It could also inhibit atherosclerosis formation in ApoE(-/-) mice aorta by regulating the PERK/eIF2α/C/EBPα-homologous protein and IRE1α/sXBP1 signaling pathways. Taken collectively, the present study demonstrated the preventive and therapeutic effects of rosuvastatin in protecting from the development of endothelial cell dysfunction diseases.

[28] *Essa H, Torella F, Lip GYH*. **Current and emerging drug treatment strategies for peripheral arterial disease**. Expert opinion on pharmacotherapy 2020:1-14.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32558590
ABSTRACT
INTRODUCTION: Peripheral artery disease (PAD) is a prevalent but underdiagnosed manifestation of atherosclerosis that has a worse prognosis than coronary artery disease. Patients with PAD are at heightened risk of both systemic cardiovascular adverse events and limb-related morbidity. There is insufficient awareness of its clinical manifestations, including intermittent claudication and critical limb ischemia and of its risk of adverse cardiovascular and limb outcomes. AREAS COVERED: The authors present the current knowledge concerning medications and their mechanism of action, landmark trials, and the evidence base behind the most commonly utilized pharmacological therapy including but not limited aspirin, clopidogrel, ticagrelor, warfarin, rivaroxaban, statins, angiotensin-converting enzyme inhibitors, Evolocumab and Ezetimibe. EXPERT OPINION: Relative to coronary artery disease, peripheral artery disease is an undertreated and under-investigated condition. The majority of the evidence base in the management of PAD is extrapolated from data subsets of large trials examining different conditions. This creates a paucity of management decisions based on trials powered for outcomes in PAD.

[29] *Zhou XH, Cai LY, Lai WH et al.* **Impact of Plasma Exposure of Statins and Their Metabolites With Major Adverse Cardiovascular Events in Chinese Patients With Coronary Artery Disease**. Frontiers in pharmacology 2020; 11:675.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32536863
ABSTRACT
The selection of optimum statin intensity is inconclusive, and the association of plasma exposure of statins and metabolites with major adverse cardiovascular events (MACEs) is unclear. This study sought to compare the effect of low (quartile 1), intermediate (quartiles 2

and 3), and high (quartile 4) plasma exposure of statins and metabolites on MACE, re-ischemia events and death in patients with coronary artery disease (CAD) at 5 years. A total of 1,644 patients in atorvastatin (AT) cohort and 804 patients in rosuvastatin (RST) cohort were included, and their plasma concentration of statins and metabolites was categorized as low-, mid-, or high-group. The association between the plasma levels of statins and metabolites and the incidence of primary endpoint in patients was assessed by Cox proportional hazard models. Intensive AT exposure (Q4 > 5.32 ng/ml) was significantly associated with increased risk of death compared with low (hazard ratio [HR]: 1.522; 95% confidence interval [CI]: 1.035-1.061; P = 0.0022) or moderate exposure (HR: 2.054; 95% CI: 1.348-3.130; P = 0.0008). This association was also found in AT's five metabolites (all P < 0.01). In patients with RST treatment, moderate RST concentration (0.53-4.29 ng/ml) versus low concentration had a significantly lower risk of MACE and re-ischemia events. (HR: 0.532, 95% CI: 0.347-0.815, P = 0.0061 and HR: 0.505, 95% CI: 0.310-0.823, P = 0.0061, respectively). A higher plasma exposure of AT and metabolites has a significantly higher risk of death, and moderate RST exposure has a significantly lower risk of MACE and re-ischemia events in Chinese patients with CAD. The harms of high plasma exposure should be considered when prescribing statins to patients because it may be a risk factor for having poor prognosis in patients with CAD.

[30] *Patti G, Lio V, Cavallari I et al.* **[Antithrombotic treatments in patients with SARS-CoV-2 infection: from current evidence to reasonable recommendations - A position paper from the Italian Working Group on Atherosclerosis, Thrombosis and Vascular Biology]**. Giornale italiano di cardiologia (2006) 2020; 21:489-501.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32555564
ABSTRACT
Given the high prevalence of preexisting cardiovascular diseases and the increased incidence of adverse cardiovascular events in patients hospitalized for SARS-CoV-2 infection, the identification of optimal antithrombotic approaches in terms of risk/benefit ratio and outcome improvement appears crucial in this setting. In the present position paper we collected current evidence from the literature to provide practical recommendations on the management of antithrombotic therapies (antiplatelet and anticoagulant) in various clinical contexts prevalent during the SARS-CoV-2 outbreak: in-home management of oral anticoagulant therapy; interactions between drugs used in the SARS-CoV-2 infection and antithrombotic agents; in-hospital management of antithrombotic therapies; diagnosis, risk stratification and treatment of in-hospital thrombotic complications.

[31] *Aguilar MT, Chascsa DM*. **Update on Emerging Treatment Options for Primary Biliary Cholangitis**. Hepat Med 2020; 12:69-77.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32547264
ABSTRACT
Primary biliary cholangitis (PBC) is a rare autoimmune cholestatic liver disease that may progress to fibrosis or cirrhosis. Treatment options are currently limited. Ursodeoxycholic acid (UDCA) remains first-line therapy and has been proven to normalize serum biochemistries, halt histologic disease progression, and lead to patient survival comparable to the general population. Obeticholic acid (OCA) was recently approved as adjunct therapy in PBC patients with inadequate response or intolerance to UDCA. However, OCA has been associated with worsening pruritus in clinical studies which may limit its use in this patient population. Several

studies are currently underway to address the lack of treatment options for PBC. Of these, fibrates, which have been used in Japan for over a decade, have produced promising results. Furthermore, as currently approved therapies for PBC do not address the potentially debilitating clinical symptoms of PBC such as pruritus and fatigue, supplemental therapy is often required for symptom control.

[32] *Hassanpour M, Rezaie J, Nouri M, Panahi Y*. **The role of extracellular vesicles in COVID-19 virus infection**. Infect Genet Evol 2020; 85:104422.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32544615
ABSTRACT
Extracellular vesicles releasing from various types of cells contribute to intercellular communication via delivering bio-molecules like nucleic acids, proteins, and lipids to recipient cells. Exosomes are 30-120 nm extracellular vesicles that participate in several pathological conditions. Virus-infected cells release exosomes that are implicated in infection through transferring viral components such as viral-derived miRNAs and proteins. As well, exosomes contain receptors for viruses that make recipient cells susceptible to virus entry. Since December 2019, SARS-CoV-2 (COVID-19) infection has become a worldwide urgent public health concern. There is currently no vaccine or specific antiviral treatment existing for COVID-19 virus infection. Hence, it is critical to find a safe and effective therapeutic tool to patients with severe COVID-19 virus infection. Extracellular vesicles may contribute to spread this virus as they transfer such receptors as CD9 and ACE2, which make recipient cells susceptible to virus docking. Upon entry, COVID-19 virus may be directed into the exosomal pathway, and its component is packaged into exosomes for secretion. Exosome-based strategies for the treatment of COVID-19 virus infection may include following items: inhibition of exosome biogenesis and uptake, exosome-therapy, exosome-based drug delivery system, and exosome-based vaccine. Mesenchymal stem cells can suppress nonproductive inflammation and improve/repair lung cells including endothelial and alveolar cells, which damaged by COVID-19 virus infection. Understanding molecular mechanisms behind extracellular vesicles related COVID-19 virus infection may provide us with an avenue to identify its entry, replication, spreading, and infection to overcome its adverse effects.

[33] *Kim G, DeSalvo D, Guffey D et al.* **Dyslipidemia in adolescents and young adults with type 1 and type 2 diabetes: a retrospective analysis**. Int J Pediatr Endocrinol 2020; 2020:11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32536946
ABSTRACT
BACKGROUND: Youth onset type 1 diabetes (T1D) and type 2 diabetes (T2D) is increasing and associated with earlier vascular complications and mortality. Dyslipidemia is an important modifiable cardiovascular (CVD) risk factor that is under-recognized and undertreated in youth with T1D and T2D. Given this, we evaluated the prevalence and associations between lipid concentrations and clinical CVD risk factors in youth with T1D compared to T2D at our large ethnically diverse diabetes center. METHODS: A retrospective chart review was performed, evaluating patients with T1D or T2D seen at least once in clinic from 2015 to 2017, age 10-22 years of age, duration of diabetes at least 6 months on the date of most recent LDL-cholesterol (LDL-C) concentration, and not on statin therapy. We performed independent and multivariable linear regressions of LDL-C and HDL-cholesterol (HDL-C) concentrations.

RESULTS: There were 32.7% with T1D (n = 1701) and 47.7% with T2D (n = 298) with LDL-C above recommend goal (> 100 mg/dL/2.6 mmol/L). Furthermore, there were 9% with T1D and 16.4% with T2D with LDL > 130 mg/dL (> 3.4 mmol/L), who likely met criteria for starting statin therapy. Higher LDL-C and/or lower HDL-C were associated with increased age, diabetes duration, higher HbA1C, female sex, Hispanic ethnicity, obesity, and T2D. After adjusting for these risk factors in a multivariable linear regression model, the association of higher LDL-C and lower HDL-C was higher with T2D than T1D. CONCLUSIONS: This highlights the need for more aggressive dyslipidemia screening and treatment in youth with diabetes, especially T2D. At our institution we have created and instituted quality improvement algorithms to try to address this need.

[34] *Dong S, Ji W, Zeng S et al.* **Admission Low-Density Lipoprotein Cholesterol Stratified by Circulating CD14++CD16+ Monocytes and Risk for Recurrent Cardiovascular Events Following ST Elevation Myocardial Infarction: Lipid Paradox Revised**. Journal of cardiovascular translational research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32557321
ABSTRACT
Lower level of low-density lipoprotein cholesterol (LDL-C) is paradoxically associated with increased mortality in ST elevation myocardial infarction (STEMI) patients. The underlying mechanism remains unclear. In a cohort of 220 de novo STEMI patients receiving timely primary percutaneous coronary intervention, admission LDL-C was negatively associated with circulating CD14++CD16+ monocyte counts. Moreover, admission LDL-C < 85 mg/dL was associated with increased risk for major adverse cardiovascular events (MACE) during a median follow-up of 2.7 years. After categorizing the patients according to the cutoff values of 85 mg/dL for LDL-C and the median for CD14++CD16+ monocytes, low LDL-C-associated MACE risk was only observed in those with high CD14++CD16+ monocyte counts (low LDL-C/high CD14++CD16+ monocytes vs. low LDL-C/low CD14++CD16+ monocytes: hazard ratio 5.38, 95% confidence interval 1.52 to 19.06, P = 0.009). This work provided the proof-of-principle evidence indicating a role of CD14++CD16+ monocytes in risk stratification of STEMI patients presenting with low LDL-C level. Graphical abstract.

[35] *Cichosz SL, Jensen MH, Hejlesen O*. **Associations between smoking, glucose metabolism and lipid levels: A cross-sectional study**. Journal of diabetes and its complications 2020:107649.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32534887
ABSTRACT
AIMS: The aim of this study was to investigate glucose profiles assessed by oral glucose tolerance tests (OGTT), fasting glucose, and lipid profiles among smokers, ex-smokers and never-smokers. MATERIALS AND METHODS: The study design used was a cross-sectional analysis of data from several years of the NHANES (National Health and Nutrition Examination Survey) from 2005 to 2014. A total of 12,460 participants with measures of OGTT, triglycerides, LDL-cholesterol and HDL-cholesterol were included for the data analysis. Outcomes were all assessed in an unadjusted and in an adjusted gender analysis. A GLM model was used to assess 2-hour OGTT, fasting plasma glucose, difference between fasting plasma glucose and OGTT, HbA1c, HDL-cholesterol, LDL-cholesterol, and triglyceride in relation to current smoking, ex-smoking and never smoking. The effects were adjusted with

covariates: gender, BMI, age, alcohol usage, educational level and ethnicity. RESULTS: The OGTT results was lower for the group smoking (-10.1 [-13.2; -7.1], p < 0.001), and no effect was observed from ex-smoking (-2.7 [-5.7; 0.8], p = 0.08). Fasting glucose was not different for smokers (-0.2 [-1.6; 1.2], p = 0.80) or ex-smokers (0.1 [-1.3; 1.5], p = 0.90). For smokers', triglycerides (1.2 [1.1; 1.3], p < 0.001), LDL-cholesterol (7.7 [6.0; 9.3], p < 0.001) were increased and HDL-cholesterol was decreased (-2.1 [-2.8; -1.5], p < 0.001). CONCLUSIONS: Although this study is cross-sectional and cannot, by the same nature of the design, prove a cause-effect relationship, the present results indicate that cigarette smoking may be associated with factors that are adversely related to the metabolic syndrome. But the evidence from our results are not unanimous pointing in the same direction as 2-hour OGTT measurements are considerably lower in participants smoking.

[36] *Foster C, Smith L, Alemzadeh R*. **Excess serum uric acid is associated with metabolic syndrome in obese adolescent patients**. Journal of diabetes and metabolic disorders 2020; 19:535-543.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32548073
ABSTRACT
PURPOSE: Obesity is a significant cause of morbidity in adolescents. Excess serum uric acid (SUA) has been associated with metabolic syndrome (MS) among adults. We evaluated the relationship among SUA and markers of insulin resistance (IR) and low-grade inflammation in obese adolescents with and without MS. METHODS: The study was a retrospective chart review of obese patients seen in the LeBonheur Endocrine clinic seen in clinic between September 2016 and December 2017. MS was defined as according to the International Diabetes Federation. Body mass index standard deviation score (BMI SDS), systolic blood pressure (SBP), diastolic blood pressure (DBP), body composition, fasting lipids, glucose, high sensitivity c-reactive protein (hs-CRP), serum uric acid (SUA), HbA1c, alanine transferase (ALT), aspartate transferase (AST), insulin and homeostatic model assessment for insulin resistance (HOMA-IR) were extracted from the charts of the 100 obese adolescents (57% female). RESULTS: Hyperuricemia (SUA >357 umol/L) was present in 41.8% of entire cohort without significant ethnic/racial and/or gender differences. Adolescents with HUA had higher FM, SBP, HbA1c, insulin and HOMA-IR (p < 0.05). While SUA was positively correlated with FM, SBP, HOMA-IR and HbA1c, and triglyceride:HDL-C ratio (TG:HDL-C) (p < 0.05). MS was identified in 32.8% of cohort. MS showed significantly higher FM, SBP, DBP, SUA, ALT, insulin, HOMA-IR, and TG:HDL-c ratio than non-MS subgroup (p < 0.05). FM was positively correlated with SUA, HOMA-IR and hsCRP (p < 0.01). CONCLUSIONS: In our study, those with hyperuricemia (HUA) showed elevated markers of metabolic syndrome including BP, serum glucoses, IR and triglycerides. In our cohort, SUA appears to correlate with MS comorbidities.

[37] *Tremblay K, Gaudet D, Khoury E, Brisson D*. **Dissection of Clinical and Gene Expression Signatures of Familial versus Multifactorial Chylomicronemia**. Journal of the Endocrine Society 2020; 4:bvaa056.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32537545
ABSTRACT
Familial chylomicronemia syndrome (FCS) is a rare disorder associated with chylomicronemia (CM) and an increased risk of pancreatitis. Most individuals with CM do not have FCS but

exhibit multifactorial CM (MCM), which differs from FCS in terms of risk and disease management. This study aimed to investigate clinical and gene expression profiles of FCS and MCM patients. Anthropometrics, clinical, and biochemical variables were analyzed in 57 FCS and 353 MCM patients. Gene expression analyses were performed in a subsample of 19 FCS, 28 MCM, and 15 normolipidemic controls. Receiver operating characteristic (ROC) curve analyses were performed to analyze the capacity of variables to discriminate FCS from MCM. Sustained fasting triglycerides ≥20 mmol/L (>15 mmol/L with eruptive xanthomas), history of pancreatitis, poor response to fibrates, diagnosis of CM at childhood, body mass index <22 kg/m(2), and delipidated apolipoprotein B or glycerol levels <0.9 g/L and <0.05 mmol/L, respectively, had an area under the ROC curve ≥0.7. Gene expression analyses identified 142 probes differentially expressed in FCS and 32 in MCM compared with controls. Among them, 13 probes are shared between FCS and MCM; 63 are specific to FCS and 2 to MCM. Most FCS-specific or shared biomarkers are involved in inflammatory, immune, circadian, postprandial metabolism, signaling, docking systems, or receptor-mediated clearance mechanisms. This study reveals differential signatures of FCS and MCM. It opens the door to the identification of key mechanisms of CM expression and potential targets for the development of new treatments.

[38] *Sharma T, Mandal CC*. **Omega-3 fatty acids in pathological calcification and bone health**. J Food Biochem 2020:e13333.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32548903
ABSTRACT
Omega-3 fatty acids (ω-3FAs) such as Docosahexaenoic acid (DHA) and Eicosapentanoic acid (EPA), are active ingredient of fish oil, which have larger health benefits against various diseases including cardiovascular, neurodegenerative, cancers and bone diseases. Substantial studies documented a preventive role of omega-3 fatty acids in pathological calcification like vascular calcification and microcalcification in cancer tissues. In parallel, these fatty acids improve bone quality probably by preventing bone decay and augmenting bone mineralization. This study also addresses that the functions of ω-3FAs not only depend on tissue types, but also work through different molecular mechanisms for preventing pathological calcification in various tissues and improving bone health. PRACTICAL APPLICATIONS: Practical applications of the current study are to improve the knowledge about the supplementation of omega-3 fatty acids. This study infers that supplementation of omega-3 fatty acids aids in bone preservation in elder females at the risk of osteoporosis and also, on the contrary, omega-3 fatty acids interfere with pathological calcification of vascular cells and cancer cells. Omega-3 supplementation should be given to the cardiac patients because of its cardio protective role. In line with this, omega-3 supplementation should be included with chemotherapy for cancer patients as it can prevent osteoblastic potential of breast cancer patients, responsible for pathological mineralization, and blocks off target toxicities. Administration of omega-3 fatty acid with chemotherapy will not only improve survival of cancer patients, but also improve the bone quality. Thus, this study allows a better understanding on omega-3 fatty acids in combating pathological complications such as osteoporosis, vascular calcification, and breast microcalcification.

[39] *Boettiger DC, Newall AT, Chattranukulchai P et al.* **Statins for atherosclerotic cardiovascular disease prevention in people living with HIV in Thailand: a cost-effectiveness analysis**. Journal of the International AIDS Society 2020; 23 Suppl 1:e25494.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32562359

ABSTRACT

INTRODUCTION: People living with HIV (PLHIV) have an elevated risk of atherosclerotic cardiovascular disease (CVD) compared to their HIV-negative peers. Expanding statin use may help alleviate this burden. However, the choice of statin in the context of antiretroviral therapy is challenging. Pravastatin and pitavastatin improve cholesterol levels in PLHIV without interacting substantially with antiretroviral therapy. They are also more expensive than most statins. We evaluated the cost-effectiveness of pravastatin and pitavastatin for the primary prevention of CVD among PLHIV in Thailand who are not currently using lipid-lowering therapy. METHODS: We developed a discrete-state microsimulation model that randomly selected (with replacement) individuals from the TREAT Asia HIV Observational Database cohort who were aged 40 to 75 years, receiving antiretroviral therapy in Thailand, and not using lipid-lowering therapy. The model simulated each individual's probability of experiencing CVD. We evaluated: (1) treating no one with statins; (2) treating everyone with pravastatin 20mg/day (drug cost 7568 Thai Baht ($US243)/year) and (3) treating everyone with pitavastatin 2 mg/day (drug cost 8182 Baht ($US263)/year). Direct medical costs and quality-adjusted life-years (QALYs) were assigned in annual cycles over a 20-year time horizon and discounted at 3% per year. We assumed the Thai healthcare sector perspective. RESULTS: Pravastatin was estimated to be less effective and less cost-effective than pitavastatin and was therefore dominated (extended) by pitavastatin. Patients receiving pitavastatin accumulated 0.042 additional QALYs compared with those not using a statin, at an extra cost of 96,442 Baht ($US3095), giving an incremental cost-effectiveness ratio of 2,300,000 Baht ($US73,812)/QALY gained. These findings were sensitive to statin costs and statin efficacy, pill burden, and targeting of PLHIV based on CVD risk. At a willingness-to-pay threshold of 160,000 Baht ($US5135)/QALY gained, we estimated that pravastatin would become cost-effective at an annual cost of 415 Baht ($US13.30)/year and pitavastatin would become cost-effective at an annual cost of 600 Baht ($US19.30)/year. CONCLUSIONS: Neither pravastatin nor pitavastatin were projected to be cost-effective for the primary prevention of CVD among PLHIV in Thailand who are not currently using lipid-lowering therapy. We do not recommend expanding current use of these drugs among PLHIV in Thailand without substantial price reduction.

[40] *Hashimoto K, Akagi M*. **The role of oxidation of low-density lipids in pathogenesis of osteoarthritis: A narrative review**. J Int Med Res 2020; 48:300060520931609.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32552129

ABSTRACT

Osteoarthritis (OA) is a chronic joint disorder that causes degeneration of cartilage, synovial inflammation, and formation of osteophytes. Aging, obesity, and sex are considered the main risk factors of OA. Recent studies have suggested that metabolic syndrome (MetS) disorders, such as hypertension, hyperlipidemia, diabetes mellitus, and obesity, may be involved in the pathogenesis and progression of OA. MetS disorders are common diseases that also result in atherosclerosis. Researchers believe that OA and atherosclerosis have underlying similar molecular mechanisms because the prevalence of both diseases increases with age.

Oxidation of low-density lipoprotein (ox-LDL) is believed to play a role in the pathogenesis of atherosclerosis. Recent reports have shown that ox-LDL and low-density lipoprotein receptor 1 (LOX-1) are involved in the pathogenesis of OA. The purpose of this narrative review is to summarize the current understanding of the role of the LOX-1/ox-LDL system in the pathogenesis of OA and to reveal common underlying molecular pathways that are shared by MetS in OA and the LOX-1/ox-LDL system.

[41] *Pannia E, Yang NV, Ho M et al.* **Folic acid content of diet during pregnancy determines post-birth re-set of metabolism in Wistar rat dams**. The Journal of nutritional biochemistry 2020; 83:108414.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32544644
ABSTRACT
Maternal metabolism begins to return to homeostasis (re-set) following birth and is accelerated by lactation. Delay in metabolic re-set may contribute to postpartum weight retention and later-life metabolic consequences. Folic acid (FA) is essential during pregnancy but inadequate intakes may alter 1-carbon metabolism, consequently affecting energy homeostatic systems. Our objectives were to examine the effects of FA content 1)below and 2)above requirements during pregnancy on the re-set of body weight, markers of hepatic 1-carbon metabolism and central and peripheral energy metabolic pathways in Wistar rat mothers early post-weaning (PW) compared to pregnant controls. Pregnant Wistar rats were fed an AIN-93G diet with FA at 0X, 1X (control, 2 mg FA/kg) or a range above requirements at 2.5X, 5X or 10X recommended levels then the control diet during lactation up to 1 week PW. Dams fed below (0X) or above (5X and 10X) FA requirements had delayed weight-loss from weaning up to 1 week PW, higher plasma insulin and HOMA-IR and changes in glucose and lipid metabolism-regulating genes in muscle, but not liver or adipose tissue compared to controls. Expression of folate-related genes in liver were lower in high FA fed dams. Central food intake neurons were not affected by FA diets. In conclusion, intakes of FA below (0X) or above (5X, 10X) requirements during pregnancy delayed weight-loss, dysregulated 1-carbon pathways in the liver and peripheral energy metabolic pathways in the Wistar rat mother up to 4 weeks after dietary exposure; potentially programming long-term negative metabolic effects and that of her future offspring.

[42] *Berkley A, Ferro A*. **Changes in C-reactive protein in response to anti-inflammatory therapy as a predictor of cardiovascular outcomes: A systematic review and meta-analysis**. JRSM Cardiovasc Dis 2020; 9:2048004020929235.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32547736
ABSTRACT
BACKGROUND: Despite the availability of aggressive lipid-lowering strategies, many patients remain at risk of cardiovascular events. C-reactive protein is a marker of inflammation elevated in patients at high risk of cardiovascular events. C-reactive protein has demonstrated value as a predictor of cardiovascular risk; however, it is unclear whether targeting C-reactive protein levels improves outcomes. This systematic review aimed to characterise the relationship between C-reactive protein and cardiovascular outcomes and to assess whether the magnitude of C-reactive protein reduction correlates to the extent of cardiovascular risk reduction. METHODS: A systematic review was conducted to identify randomised controlled trials that measured C-reactive protein before and after administration of therapies for

cardiovascular disease and measured incidence of cardiovascular events. A meta-analysis of placebo-controlled studies assessed the relationship between extent of C-reactive protein reduction and cardiovascular risk reduction. Placebo-controlled studies where low-density lipoprotein and triglyceride data were available were also included in a meta-regression to assess the influence of these established risk factors on the efficacy of treatment when compared to C-reactive protein. RESULTS: Fifteen studies met the criteria for inclusion in this review, of which six were active comparator studies and nine were placebo controlled. Six placebo-controlled studies had data available for meta-regression. Eight studies demonstrated a reduction in events that could be explained by changes in lipid levels, whereas the results of five studies suggested that the association between C-reactive protein reduction and event rates cannot be explained by changes in lipid levels alone. No correlation was found between magnitude of C-reactive protein reduction and cardiovascular risk reduction. A strong correlation was found between C-reactive protein and low-density lipoprotein reduction (adjusted r (2) = 0.8). CONCLUSIONS: Targeting C-reactive protein does not offer additional benefit over targeting low-density lipoprotein across the general population in terms of cardiovascular risk reduction. However, there is value in targeting C-reactive protein in patients at high residual inflammatory risk despite non-elevated lipid levels or use of lipid-lowering therapy.

[43] *Saleem MA, Yasir Siddique M, Nazar MF et al.* **Formation of Antihyperlipidemic Nano-Ezetimibe from Volatile Microemulsion Template for Enhanced Dissolution Profile**. Langmuir 2020; 36:7908-7915.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32551692
ABSTRACT
Nanostructures play an important role in targeting sparingly water-soluble drugs to specific sites. Because of the structural flexibility and stability, the use of template microemulsions (μEs) can produce functional nanopharmaceuticals of different sizes, shapes, and chemical properties. In this article, we report a new volatile oil-in-water (o/w) μE formulation comprising ethyl acetate/ethanol/brij-35/water to obtain the highly water-dispersible nanoparticles of an antihyperlipidemic agent, ezetimibe (EZM-NPs), to enhance its dissolution profile. A pseudoternary phase diagram was delineated in a specified brij-35/ethanol ratio (1:1) to describe the transparent, optically isotropic domain of the as-formulated μE. The water-dilutable μE formulation, comprising an optimum composition of ethyl acetate (18.0%), ethanol (25.0%), brij-35 (25.0%), and water (32.0%), showed a good dissolvability of EZM around 4.8 wt % at pH 5.2. Electron micrographs showed a fine monomodal collection of EZM-loaded μE droplets (∼45 nm) that did not coalesce even after lyophilization, forming small spherical EZM-NPs (∼60 nm). However, the maturity of nanodrug droplets observed through dynamic light scattering suggests the affinity of EZM to the nonpolar microenvironment, which was further supported through peak-to-peak correlation of infrared analysis and fluorescence measurements. Moreover, the release profile of the as-obtained EZM-nanopowder increased significantly >98% in 30 min, which indicates that a reduced drug concentration will be needed for capsules or tablets in the future and can be simply incorporated into the multidosage formulation of EZM.

[44] *Kaur R, Myrie SB*. **Association of Dietary Phytosterols with Cardiovascular Disease Biomarkers in Humans**. Lipids 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32557606

ABSTRACT

Cardiovascular disease (CVD) is a leading cause of death worldwide. Elevated concentrations of serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) are major lipid biomarkers that contribute to the risk of CVD. Phytosterols well known for their cholesterol-lowering ability, are non-nutritive compounds that are naturally found in plant-based foods and can be classified into plant sterols and plant stanols. Numerous clinical trials demonstrated that 2 g phytosterols per day have LDL-C lowering efficacy ranges of 8-10%. Some observational studies also showed an inverse association between phytosterols and LDL-C reduction. Beyond the cholesterol-lowering beneficial effects of phytosterols, the association of phytosterols with CVD risk events such as coronary artery disease and premature atherosclerosis in sitosterolemia patients have also been reported. Furthermore, there is an increasing demand to determine the association of circulating phytosterols with vascular health biomarkers such as arterial stiffness biomarkers. Therefore, this review aims to examine the ability of phytosterols for CVD risk prevention by reviewing the current data that looks at the association between dietary phytosterols intake and serum lipid biomarkers, and the impact of circulating phytosterols level on vascular health biomarkers. The clinical studies in which the impact of phytosterols on vascular function is investigated show minor but beneficial phytosterols effects over vascular health. The aforementioned vascular health biomarkers are pulse wave velocity, augmentation index, and arterial blood pressure. The current review will serve to begin to address the research gap that exists between the association of dietary phytosterols with CVD risk biomarkers.

[45] *Hou J, Deng Q, Guo X et al.* **Association between apolipoprotein E gene polymorphism and the risk of coronary artery disease in Hakka postmenopausal women in southern China**. Lipids in health and disease 2020; 19:139.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546237

ABSTRACT

BACKGROUND: Apolipoprotein E (APOE) is involved in the pathogenesis of atherosclerosis and conveys a higher risk of coronary artery disease (CAD). The aim of the present study was to investigate the possible association between APOE gene polymorphism and the risk of CAD in postmenopausal Hakka women in southern China. METHODS: The APOE genotypes of 653 CAD patients and 646 control participants were determined by the polymerase chain reaction (PCR) and hybridization to a Sinochip. RESULTS: The prevalence of each APOE genotype differed between CAD patients and control participants (P = 0.011). The E3/E3 genotype was the most common and the E2/E2 genotype was the least common in the study sample. Moreover, the presence of ε4 allele was associated with higher serum concentrations of triglycerides (TG), total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C), and lower concentration of high-density lipoprotein-cholesterol (HDL-C). Multiple logistic regression analysis revealed that participants with ε4 allele have a significantly higher risk of CAD after adjustment for the presence of diabetes mellitus and hypertension, and their serum uric acid, TC, and LDL-C concentrations (adjusted odds ratio (OR) 1.50, 95% confidence interval (CI) 1.10-2.05, P = 0.010). CONCLUSIONS: The present results suggest that APOE polymorphism is associated with a higher risk of CAD in postmenopausal Hakka women in southern China.

[46] *Pertiwi K, Küpers LK, Geleijnse JM et al.* **Associations of linoleic acid with markers of glucose metabolism and liver function in South African adults**. Lipids in health and disease 2020; 19:138.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546275
ABSTRACT
BACKGROUND: The relation between dietary and circulating linoleic acid (18:2 n-6, LA), glucose metabolism and liver function is not yet clear. Associations of dietary and circulating LA with glucose metabolism and liver function markers were investigated. METHODS: Cross-sectional analyses in 633 black South Africans (aged > 30 years, 62% female, 51% urban) without type 2 diabetes at baseline of the Prospective Urban Rural Epidemiology study. A cultural-sensitive 145-item food-frequency questionnaire was used to collect dietary data, including LA (percentage of energy; en%). Blood samples were collected to measure circulating LA (% total fatty acids (FA); plasma phospholipids), plasma glucose, glycosylated hemoglobin (HbA1c), serum gamma-glutamyl transferase (GGT), alanine (ALT) and aspartate aminotransferase (AST). Associations per 1 standard deviation (SD) and in tertiles were analyzed using multivariable regression. RESULTS: Mean (±SD) dietary and circulating LA was 6.8 (±3.1) en% and 16.0 (±3.5) % total FA, respectively. Dietary and circulating LA were not associated with plasma glucose or HbA1c (β per 1 SD: - 0.005 to 0.010, P > 0.20). Higher dietary LA was generally associated with lower serum liver enzymes levels. One SD higher circulating LA was associated with 22% lower serum GGT (β (95% confidence interval): - 0.25 (- 0.31, - 0.18), P < 0.001), but only ≤9% lower for ALT and AST. Circulating LA and serum GGT associations differed by alcohol use and locality. CONCLUSION: Dietary and circulating LA were inversely associated with markers of impaired liver function, but not with glucose metabolism. Alcohol use may play a role in the association between LA and liver function. TRIAL REGISTRATION: PURE North-West Province South Africa study described in this manuscript is part of the PURE study. The PURE study is registered in ClinicalTrials.gov (Identifier: NCT03225586; URL).

[47] *Zhou B, Ren H, Zhou X, Yuan G*. **Associations of iron status with apolipoproteins and lipid ratios: a cross-sectional study from the China Health and Nutrition Survey**. Lipids in health and disease 2020; 19:140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546165
ABSTRACT
BACKGROUND: Iron overload has been found to be related with various cardiometabolic disorders, like dyslipidemia, metabolic syndrome, and diabetes. The disturbance of the iron status and lipid metabolism can contribute to organ damage such as atherosclerotic plaque growth and instability. An assessment on the associations of iron status with apolipoproteins and lipid ratios would be informative for maintenance of metabolic homeostasis and hinderance of disease progression. Hence, this study aims to establish the relationships of iron status with apolipoproteins and lipid ratios. METHODS: A cross-sectional study of 7540 adult participants from the China Health and Nutrition Survey 2009 was conducted. Logistic regression analyses were used to investigate the relationships between indicators of iron status and the prevalence of unfavorable apolipoprotein profiles. Multivariate linear regression models were constructed to assess the dose-response correlations between serum ferritin and lipid parameters. RESULTS: After adjustment for confounding factors, in both sexes, the subjects in the top quartile of ferritin had the highest prevalence of an elevated apolipoprotein

B (men: odds ratio (OR) 1.97, 95% confidence interval (CI) 1.50-2.62; women: OR 2.13, 95% CI 1.53-2.97) and an elevated apolipoprotein B/apolipoprotein A1 ratio (men: OR 2.00, 95% CI 1.50-2.66; women: OR 1.41, 95% CI 1.04-1.92) when compared with individuals in the lowest quartile. Hemoglobin were also independently associated with unfavorable apolipoprotein B and apolipoprotein B/apolipoprotein A1 ratio both in men and women. However, transferrin (men: OR 0.74, 95% CI 0.56-0.99; women: OR 0.73, 95% CI 0.56-0.95) and soluble transferrin receptor (men: OR 0.75, 95% CI 0.57-0.99; women: OR 0.71, 95% CI 0.55-0.91) were found to be negatively associated with a decreased apolipoprotein A1. Moreover, after controlling for potential confounders, the ferritin concentrations were significantly associated with the levels of lipid ratios including TG/HDL-C, non-HDL-C/HDL-C, TC/HDL-C, apoB/apoA1, and LDL-C/HDL-C ratio in men (β coefficient = 0.147, 0.061, 0.043, 0.038, 0.032, respectively, all P values < 0.001) and in women (β coefficient = 0.074, 0.034, 0.025, 0.020, 0.018, respectively, all P values < 0.05). CONCLUSIONS: The indicators of iron status are significantly associated with unfavorable apolipoprotein profiles. Serum ferritin concentrations are positively correlated with the levels of lipid ratios. The management on the modifiable iron status and lipid metabolism has a clinical significance. The atherosclerotic lipid profiles of the patients with iron overload deserve special clinical concerns.

[48] *Gao M, Yang C, Wang X et al.* **ApoC2 deficiency elicits severe hypertriglyceridemia and spontaneous atherosclerosis: A rodent model rescued from neonatal death**. Metabolism 2020; 109:154296.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32562799

ABSTRACT

RATIONALE: ApoC2 is an important activator for lipoprotein lipase-mediated hydrolysis of triglyceride-rich plasma lipoproteins. ApoC2-deficient patients display severe hypertriglyceridemia (sHTG) and recurrent acute pancreatitis. However, due to embryonic lethality in ApoC2 deleted mouse extensive understanding of ApoC2 function is limited in mammalian species. OBJECTIVE: We sought to generate an animal model with ApoC2 deficiency in a rodent with some human-like features and then study the precise effects of ApoC2 on lipid and glucose homeostasis. METHODS AND RESULTS: Using CRISPR/Cas9, we deleted Apoc2 gene from golden Syrian hamster and the homozygous (-/-) pups can be born in matured term but exhibited neonatal lethality. By continuous iv administration of normal hamster serum the ApoC2(-/-) pups could survive till weaning and displayed severe HTG in adulthood on chow diet. A single iv injection of AAV-hApoC2 at birth can also rescue the neonatal death of ApoC2(-/-) pups. Adult ApoC2(-/-)hamsters exhibited a unique phenotype of sHTG with hypoglycemia, hypoinsulinemia and spontaneous atherosclerosis. The sHTG in ApoC2(-/-) adult hamsters could not be corrected by various lipid-lowering medications, but partially ameliorated by medium chain triglyceride diet and completely corrected by AAV-hApoC2. CONCLUSIONS: Our study provides a novel ApoC2-deleted mammalian model with severe hypertriglyceridemia that was fully characterized and highlights a potential therapeutic approach for the treatment of ApoC2 deficient patients.

[49] *Stoian AP, Sachinidis A, Stoica RA et al.* **The efficacy and safety of dipeptidyl peptidase-4 inhibitors compared to other oral glucose-lowering medications in the treatment of type 2 diabetes**. Metabolism 2020; 109:154295.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32553739

ABSTRACT
INTRODUCTION: The dipeptidyl peptidase-4 inhibitors (DPP-4is), which belong to the class of incretin-based medications, are recommended as second or third-line therapies in guidelines for the management of type 2 diabetes mellitus. They have a favorable drug tolerability and safety profile compared to other glucose-lowering agents. OBJECTIVE: This review discusses data concerning the use of DPP-4is and their cardiovascular profile, and gives an updated comparison with the other oral glucose-lowering medications with regards to safety and efficacy. Currently available original studies, abstracts, reviews articles, systematic reviews and meta-analyses were included in the review. DISCUSSION: DPP4is are moderately efficient in decreasing the HbA1c by an average of 0.5% as monotherapy, and 1.0% in combination therapy with other drugs. They have a good tolerability and safety profile compared to other glucose-lowering drugs. However, there are possible risks pertaining to acute pancreatitis and pancreatic cancer. CONCLUSION: Cardiovascular outcome trials thus far have proven the cardiovascular safety for ischemic events in patients treated with sitagliptin, saxagliptin, alogliptin, linagliptin and vildagliptin. Data showing increased rate of hospitalisation in the case of saxagliptin did not seem to be a class effect.

[50] *Trotta F, Avena P, Chimento A et al.* **Statins reduce intratumor cholesterol affecting adrenocortical cancer growth**. Molecular cancer therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32546662

ABSTRACT
Mitotane causes hypercholesterolemia in ACC patients. We suppose that cholesterol increases within the tumor and can be used to activate proliferative pathways. In this study, we used statins to decrease intratumor cholesterol and investigated the effects on ACC growth related to ERα action at the nuclear and mitochondrial levels. We first used microarray to investigate mitotane effect on genes involved in cholesterol homeostasis and evaluated their relationship with patients' survival in ACC TCGA. We then blocked cholesterol synthesis with simvastatin and determined the effects on H295R cell proliferation, estradiol production and ERα activity in vitro and in xenograft tumors. We found that mitotane increases intratumor cholesterol content and expression of genes involved in cholesterol homeostasis, among them INSIG, whose expression affects patients' survival. Treatment of H295R cells with simvastatin to block cholesterol synthesis decreased cellular cholesterol content and this affected cell viability. Simvastatin reduced estradiol production and decreased nuclear and mitochondrial ERα function. A mitochondrial target of ERα, the respiratory complex IV (COX IV) was reduced after simvastatin treatment, which profoundly affected mitochondrial respiration activating apoptosis. In vivo experiments confirmed the ability of simvastatin to reduce tumor volume and weight of grafted H295R cells, intratumor cholesterol content, Ki-67 and ERα, COX IV expression and activity and increase TUNEL positive cells. Collectively these data demonstrate that a reduction in intratumor cholesterol content prevents estradiol production, inhibits mitochondrial respiratory chain inducing apoptosis in ACC cells. Inhibition of mitochondrial respiration by simvastatin represents a novel strategy to counteract ACC growth.

[51] *Liu Q, Zhao W, Xing Y et al.* **Low Triglyceride Levels are Associated with Unfavorable Outcomes in Patients with Spontaneous Intracerebral Hemorrhage**. Neurocritical care 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32557109

ABSTRACT
BACKGROUND AND AIMS: The relationship between serum lipid level and clinical outcome after spontaneous intracerebral hemorrhage (ICH) remains controversial. We sought to evaluate the association of serum lipid levels with clinical outcomes in patients with ICH. METHODS: Data on consecutive patients hospitalized with spontaneous ICH were prospectively collected from May 2005 to May 2018 and retrospectively analyzed. Following clinical and demographic data, age and gender, risk factors, serum lipid levels [total cholesterol, triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol] and the outcomes were analyzed. RESULTS: A total of 1451 patients with ICH (mean age, 60.41 ± 12.3 years; 32.6% women) was evaluated. Although admission TG levels were associated with the outcomes at hospital discharge and 3 months in initial univariate analyses, the former association did not retain its statistical significance in multivariate logistic regression analyses adjusting for potential confounders. However, lower admission TG levels were independently associated ($p = 0.045$) with a higher likelihood of 12-month unfavorable outcomes (odds ratio 0.91, 95% confidence interval 0.83-0.99) in multivariate logistic regression models. CONCLUSIONS: Low TG levels at hospital admission were an independent predictor for unfavorable long-term outcomes in patients with spontaneous ICH. The exact mechanisms of the association need further investigations.

[52] *Al-Sari N, Suvitaival T, Mattila I et al.* **Lipidomics of human adipose tissue reveals diversity between body areas**. PloS one 2020; 15:e0228521.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32544198

ABSTRACT
BACKGROUND AND AIMS: Adipose tissue plays a pivotal role in storing excess fat and its composition reflects the history of person's lifestyle and metabolic health. Broad profiling of lipids with mass spectrometry has potential for uncovering new knowledge on the pathology of obesity, metabolic syndrome, diabetes and other related conditions. Here, we developed a lipidomic method for analyzing human subcutaneous adipose biopsies. We applied the method to four body areas to understand the differences in lipid composition between these areas. MATERIALS AND METHODS: Adipose tissue biopsies from 10 participants were analyzed using ultra-high-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry. The sample preparation optimization included the optimization of the lipid extraction, the sample amount and the sample dilution factor to detect lipids in an appropriate concentration range. Lipidomic analyses were performed for adipose tissue collected from the abdomen, breast, thigh and lower back. Differences in lipid levels between tissues were visualized with heatmaps. RESULTS: Lipidomic analysis on human adipose biopsies lead to the identification of 186lipids in 2 mg of sample. Technical variation of the lipid-class specific internal standards were below 5%, thus indicating acceptable repeatability. Triacylglycerols were highly represented in the adipose tissue samples, and lipids from 13 lipid classes were identified. Long polyunsaturated triacylglycerols in higher levels in thigh ($q<0.05$), when compared with the abdomen, breast and lower back, indicating that the lipidome was area-specific. CONCLUSION: The method presented here is suitable for the analysis of lipid profiles in 2 mg of adipose tissue. The amount of fat across the body is important for health but we argue that also the distribution and the particular profile of the lipidome may be relevant for metabolic outcomes. We suggest that the method presented in this paper could be useful for detecting such aberrations.

[53] *Lairez O, Hyafil F*. **A Clinical Role of PET in Atherosclerosis and Vulnerable Plaques?** Semin Nucl Med 2020; 50:311-318.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32540028
ABSTRACT
Atherosclerosis is a chronic and most often progressive disease with a long clinically apparently silent period, and can become unstable at any time, due to a plaque rupture or erosion, leading to an acute atherothrombotic event. Atherosclerosis has a progression rate that is highly variable among patients and in the same patient. The progression of atherosclerotic plaque from asymptomatic to symptomatic phase depends on its structure and composition in which inflammation plays an essential role. Prototype of the ruptured plaque contains a large, soft, lipid-rich necrotic core with intraplaque hemorrhage that accounts for more than half of the volume of the plaque covered by a thin and inflamed fibrous cap with few smooth muscle cells, and a heavy infiltrate of inflammatory cells. Noninvasive imaging modalities might provide an assessment of the atherosclerotic disease process through the exploration of these plaque features. Computed tomography angiography and magnetic resonance imaging can characterize plaque morphology, whereas molecular imaging, owing to the high sensitivity of nuclear medicine for the detection of radiopharmaceuticals in tissues, allows to explore plaque biology. During the last 2 decades, FDG-PET imaging has also emerged as a powerful tool to explore noninvasively inflammatory activities in atherosclerotic plaques providing new insights on the evolution of metabolic activities in the vascular wall over time. This review highlights the role of PET imaging for the exploration of metabolic activities in atherosclerotic plaques. It will resume the evidence that have been gathered from clinical studies using FDG-PET and will discuss the perspectives of new radiopharmaceuticals for vulnerable plaque imaging.

[54] *Mashaqi S, Gozal D*. **"Circadian misalignment and the gut microbiome. A bidirectional relationship triggering inflammation and metabolic disorders"- a literature review**. Sleep medicine 2020; 72:93-108.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32559717
ABSTRACT
Over the last decade, emerging studies have related the gut microbiome and gut dysbiosis to sleep and sleep disorders. For example, intermittent hypoxia associated with obstructive sleep apnea was shown to reproducibly alter the gut microbiome. Circadian rhythm disorders (CRD) (eg, shift work disorders, delayed sleep phase syndrome, and advanced sleep phase syndrome) constitute another group of conditions that might be influenced by gut dysbiosis. Indeed, both central and peripheral clocks can affect and be affected by gut microbiota and their metabolites. In addition, the tight rhythmic regulation of almost all metabolic pathways involved in the anabolism and catabolism of carbohydrates, protein, and lipids in addition to detoxification processes that take place in specific cells could be ultimately linked to changes in the microbiota. Since there are no studies to date examining the impact of gut dysbiosis on delayed sleep phase and advanced sleep phase syndrome, and considering the ever-increasing number of people engaging in shift work, more accurate and informed delineation of the association between gut dysbiosis and shift work can provide guidance and opportunities for new avenues of treating circadian rhythm disorders and preventing the metabolic complications of shiftwork via restoration of gut dysbiosis. In this review, the potential

bidirectional relationships between gut dysbiosis and circadian rhythm misalignment, their impact on different metabolic pathways, and the potential development of metabolic and systemic disorders, especially in shift work models are critically assessed.

[55] *Kim EJ, Wierzbicki AS*. **The history of proprotein convertase subtilisin kexin-9 inhibitors and their role in the treatment of cardiovascular disease**. Therapeutic advances in chronic disease 2020; 11:2040622320924569.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32537117
ABSTRACT
A consensus has formed based on epidemiological studies and clinical trials that intervention to reduce low density lipoprotein cholesterol (LDL-C) will reduce cardiovascular disease (CVD) events. This has progressively reduced the thresholds for intervention and targets for treatment. Whist statins are sufficient for many people in primary prevention, they only partially achieve the newer targets of secondary prevention for established CVD. Increasing use of statins has highlighted that 1-2% cannot tolerate these drugs. Other cholesterol-lowering drugs such as ezetimibe add to the benefits of statins but have limited efficacy. The discovery of activating mutations in proprotein convertase subtilisin kexin-9 (PCSK9) as a cause of familial hypercholesterolaemia while inactivating mutations lower LDL-C led to the idea to develop PCSK9 inhibitors as drugs. This article reviews the history of lipid-lowering therapies, the discovery of PCSK9 and the development of PCSK9 inhibitors. It reviews the key trials of the current antibody-based drugs and how these have influenced new guidelines. It also reviews the controversy caused by their cost and the increasing application of health economics to determine the optimum strategy for implementation of novel therapeutic pathways and surveys other options for targeting PCSK9 as well as other LDL-C lowering compounds in late development.

[56] *Mihaila SM, Faria J, Stefens MFJ et al.* **Drugs Commonly Applied to Kidney Patients May Compromise Renal Tubular Uremic Toxins Excretion**. Toxins 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32545617
ABSTRACT
In chronic kidney disease (CKD), the secretion of uremic toxins is compromised leading to their accumulation in blood, which contributes to uremic complications, in particular cardiovascular disease. Organic anion transporters (OATs) are involved in the tubular secretion of protein-bound uremic toxins (PBUTs). However, OATs also handle a wide range of drugs, including those used for treatment of cardiovascular complications and their interaction with PBUTs is unknown. The aim of this study was to investigate the interaction between commonly prescribed drugs in CKD and endogenous PBUTs with respect to OAT1-mediated uptake. We exposed a unique conditionally immortalized proximal tubule cell line (ciPTEC) equipped with OAT1 to a panel of selected drugs, including angiotensin-converting enzyme inhibitors (ACEIs: captopril, enalaprilate, lisinopril), angiotensin receptor blockers (ARBs: losartan and valsartan), furosemide and statins (pravastatin and simvastatin), and evaluated the drug-interactions using an OAT1-mediated fluorescein assay. We show that selected ARBs and furosemide significantly reduced fluorescein uptake, with the highest potency for ARBs. This was exaggerated in presence of some PBUTs. Selected ACEIs and statins had either no or a slight effect at supratherapeutic concentrations on OAT1-mediated fluorescein uptake. In conclusion, we demonstrate that PBUTs may compete with co-administrated drugs commonly used in

CKD management for renal OAT1 mediated secretion, thus potentially compromising the residual renal function.

[57] *Khezrian S, Salati AP, Agh N, Pasha-Zanoosi H*. **Effect of replacement of fish oil with different plant oils in Oncorhynchus mykiss broodstocks diets on egg and larval antioxidant defense development**. Veterinary research forum : an international quarterly journal 2020; 11:83-88.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32537111

ABSTRACT
This study was undertaken to investigate the effects of feeding rainbow trout (Oncorhynchus mykiss) broodstocks with different ratio of plant oils to evaluate the changes in antioxidant defense status in the progenies. In the experimental diets, fish oil was replaced with different combination of plant oils including corn oil, olive oil, sunflower oil, and coconut oil, to gain different levels of polyunsaturated fatty acids (PUFA) and highly unsaturated fatty acids (HUFA) in the experimental diets. Fish fed eight weeks with experimental diets before reproduction. After spawning, samples were taken on days 0, 5, 10, 15, 20, 25, 30 and 35 after fertilization. The samples were homogenized, centrifuged and the supernatant was removed for determination of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) activity and malondialdehyde (MDA) content. Results showed that SOD activity was significantly increased from the first sampling to day 35 in all treatment groups. The CAT activity showed a downward trend, as the highest CAT activity was observed in the eggs immediately after fertilization. The GPX activity declined until day five and then showed an increasing trend. The MDA content did not show significant changes in different groups and at different sampling times. The antioxidant enzymes activity was significantly influenced by the dietary PUFA level in the experimental groups but no change in MDA content was recorded, suggesting that the different percentages of fish oil replacement used in this study could not result in oxidative stress in early life stages of O. mykiss.