[1] *Jalili R, Somi MH, Hosseinifard H et al.* **The Evaluation of Effective Drugs for the Treatment of Non-Alcoholic Fatty Liver Disease: A Systematic Review and Network Meta-Analysis**. Advanced pharmaceutical bulletin 2020; 10:542-555.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33072533

ABSTRACT

Purpose: Non-alcoholic fatty liver disease (NAFLD) and steatohepatitis are two forms of fatty liver disease with benign and malignant nature, respectively. These two conditions can cause an increased risk of liver cirrhosis and hepatocellular carcinoma. Given the importance and high prevalence of NAFLD, it is necessary to investigate the results of different studies in related scope to provide a clarity guarantee of effectiveness. Therefore, this systematic review and meta-analysis aim to study the efficacy of various medications used in the treatment of NAFLD. Methods: A systematic search of medical databases identified 1963 articles. After exclusion of duplicated articles and those which did not meet our inclusion criteria, eta-analysis was performed on 84 articles. Serum levels of alanine aminotransferase (ALT), aspartate amino transferase (AST) were set as primary outcomes and body mass index (BMI), hepatic steatosis, and NAFLD activity score (NAS) were determined as secondary outcomes. Results: Based on the P-score of the therapeutic effects on the non-alcoholic steatohepatitis (NASH), we observed the highest efficacy for atorvastatin, tryptophan, orlistat, omega-3 and obeticholic acid for reduction of ALT, AST, BMI, steatosis and NAS respectively. Conclusion: This meta-analysis showed that atorvastatin. life-style modification, weight loss, and BMI reduction had a remarkable effect on NAFLD-patients by decreasing aminotransferases.

[2] *Singh C, Jain S, Dhawan V et al.* **Uric acid as a predictor of endothelial dysfunction in patients with metabolic syndrome**. Archives of endocrinology and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33085991

ABSTRACT

OBJECTIVE: We conducted a study to examine the association of endothelial dysfunction and oxidative stress with uric acid levels in patients of metabolic syndrome. METHODS: One hundred and two patients of Metabolic Syndrome (International Diabetes Federation definition) were included in the study. Anthropometric measurements, serum uric acid levels, fasting blood sugar levels and lipid levels, as well as malondialdehyde and reactive nitrogen intermediates were measured after an 8-hour fasting period. Flow mediated vasodilation (FMD) of the brachial artery was measured and endothelial dysfunction was defined as an increase in diameter < 10% post compression. RESULTS: A total of 102 patients were included in the study. Mean uric acid level was 5.49 ± 1.61 mg%. A total of 59 patients in the study had endothelial dysfunction, defined by an abnormal FMD. Patients with an abnormal FMD had higher levels of serum uric acid which was statistically significant (p value = 0.010). Serum RNI and MDA levels were negatively correlated with uric acid, but did not reach statistical significance. Patients with an abnormal FMD had a lower RNI level, but this did not reach statistical significance. Serum MDA levels were significantly higher in patients with an abnormal FMD (p value = 0.038). CONCLUSION: Uric acid was significantly associated with endothelial dysfunction in patients with metabolic syndrome in our study. It was inversely correlated with serum RNI and MDA levels, but this did not reach statistical significance.

[3] *Pimentel LL, Rodríguez-Alcalá LM*. **Cholesterol, inflammation, and phospholipids: COVID-19 share traits with cardiovascular disease**. Biochimica et biophysica acta. Molecular and cell biology of lipids 2020; 1866:158839.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33080357
ABSTRACT

[4] *Feng JL, Qin X*. **Does adherence to lipid-lowering medications improve cancer survival? A nationwide study of breast and colorectal cancer, and melanoma**. British journal of clinical pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33084072
ABSTRACT
AIMS: Inconclusive findings of lipid-lowering medications (LLMs) on cancer survival benefit require more evidence. We tested the hypothesis that adherence to this drug is associated with reduced cancer-specific mortality in a homogeneous population who had used this drug before cancer diagnosis. METHODS: The Australian Cancer Database was linked to the Pharmaceutical Benefits Scheme database, and to the National Death Index (up to 2015). Medication adherence was calculated by proportion of days covered. Cox regression models with time-varying covariates were used to derive multivariable-adjusted cause-specific hazard ratio (HR) and 95% confidence interval (CI) for the associations between adherence to LLMs, statins, lipophilic, and hydrophilic statins and cancer-specific mortality. RESULTS: From 2003 to 2013, 3 separate cohorts of 20 046, 11 719 and 6430 female patients with newly diagnosed breast, colorectal cancer, and melanoma respectively were identified. The 1-year adherence was similar at 1-year prediagnosis in the 3 cohorts, on average 82%. Each 10% increase in 1-year adherence to LLMs was inversely associated with cancer-specific mortality among women with breast cancer (fully adjusted HR = 0.92, 95% CI 0.91-0.93), colorectal cancer (fully adjusted HR = 0.92, 95% CI 0.91-0.93), or melanoma (fully adjusted HR = 0.97, 95% CI 0.94-1.00). The reductions in cancer-specific mortality were more pronounced for women who adhered to lipophilic than hydrophilic statins in all 3 cancers albeit not statistically significant for melanoma. CONCLUSION: Among LLM users, adherence to this drug is associated with a decrease in cancer-specific mortality. If confirmed, LLMs could be considered as an adjuvant cancer therapy to improve prognosis in cancer survivors.

[5] *Liang Z, Chen Q, Yang F et al.* **Cost-Effectiveness of Evolocumab Therapy for Myocardial Infarction: The Chinese Healthcare Perspective**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33090294
ABSTRACT
PURPOSE: Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are an indispensable lipid-lowering treatment option, but their cost-effectiveness has been questioned. This study aimed to perform a health economic evaluation of evolocumab versus placebo in patients with myocardial infarction (MI) in China. METHODS: A Markov cohort state-transition model was developed in decision analysis software to estimate the incremental cost-effectiveness ratio (ICER), defined as cost per quality-adjusted life-year (QALY) saved. The simulation subjects could undergo non-fatal MI and/or stroke, or vascular or non-vascular death event. We integrated the Chinese population-specific demographics and event rates with the risk reduction of evolocumab based on the FOURIER trial and/or lowering of low-density

lipoprotein cholesterol (LDL-C). Age-related change, event costs and utilities were included from published sources. RESULTS: At its current list price [33,748 Chinese yuan (CNY) annually per person], the ICER for evolocumab therapy was 927,713 CNY per QALY gained when integrating the FOURIER trial with absolute reduction of LDL-C. The probability of cost-effectiveness of evolocumab versus placebo was 1.96%, with a generally accepted threshold of 212,676 CNY per QALY gained. A reduction in acquisition price by approximately 70% (to less than 10,255 CNY annually) was needed to be cost-effective. Alternative scenario analyses of therapeutic benefit showed that the ICER for evolocumab in MI patients with uncontrolled familial hypercholesterolemia (FH) was 187,736 CNY per QALY gained. CONCLUSION: Evolocumab in patients with MI was not cost-effective based on the price in 2019 in China; however, treatment with evolocumab was more favorable in MI patients with FH.

[6] *Refaat H, Tantawy A*. **Low plasma adiponectin levels are associated with vulnerable plaque features in patients with acute coronary syndrome: An optical coherence tomography study**. Cardiovascular revascularization medicine : including molecular interventions 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33097459
ABSTRACT
BACKGROUND: Vulnerable plaques are the primary cause of acute coronary syndrome (ACS). The association between in-vivo plaque vulnerability and adiponectin levels in ACS still remains to be determined. OBJECTIVE: The purpose of this study was to investigate the correlation between adiponectin levels and vulnerable plaque features in ACS patients. METHODS: We enrolled 107 ACS patients admitted to our institution; 83 with Non-ST elevation ACS (NSTE-ACS) and 24 with ST-elevation myocardial infarction (STEMI). Adiponectin levels were measured in these patients. Coronary angiography and subsequent optical coherence tomography (OCT) analysis of culprit lesions were performed. RESULTS: Adiponectin level was lower in patients with complex angiographic lesions, compared to those with non-complex lesions (7.13 ± 3.04 vs. 8.94 ± 2.84 μg/ml, P = 0.002). Adiponectin level was lower in patients with plaque rupture (PR), micro-thrombi, and thin cap fibroatheroma (TCFA), compared to those with non-vulnerable features (7.19 ± 2.95 vs 8.79 ± 3.02 μg/ml, P = 0.007 & 7.29 ± 2.97 vs 8.44 ± 3.09 μg/ml, P = 0.04 and 4.76 ± 0.65 vs 9.74 ± 2.35 μg/ml, P < 0.001 μg/ml respectively). There was a significant negative correlation between adiponectin levels and lipid rich plaque extent and maximum lipid arc (r = -0.05, P < 0.001 & r = -0.03, P = 0.03, respectively). However, a significant positive correlation was observed between adiponectin levels and fibrous cap thickness (r = 0.95, P < 0.001). CONCLUSION: Low adiponectin levels were associated with complex angiographic lesions and vulnerable plaque features in ACS patients, where there was a significant correlation between it and PR, TCFA, and lipid rich plaque.

[7] *Duan M, Zhao WL, Zhou L et al.* **Omics research in vascular calcification**. Clinica chimica acta; international journal of clinical chemistry 2020; 511:319-328.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33096035
ABSTRACT
Vascular calcification (VC), the pathological process of hydroxyapatite mineral deposition in the vascular system, is closely associated with aging, atherosclerotic plaque formation, cardiovascular disease (CVD) and diabetes mellitus (DM). Studies have shown that VC is

related to cellular phenotypic changes, extracellular vesicles, disordered calcium and phosphate homeostasis, and an imbalance between inducers and inhibitors of VC. Unfortunately, there is currently no effective preventive or targeted treatment for pathologic condition. The rapid evolution of omics technology (genomics, epigenomics, transcriptomics, proteomics and metabolomics) has provided a novel approach for elucidation of pathophysiologic mechanisms in general and those associated with VC specifically. Here, we review articles published over the last twenty years and focus on the current state, challenges, limitations and future of omics in VC research and clinical practice. Highlighting potential targets based on omics technology will improve our understanding of this pathologic condition and assist in the development of potential treatment options for VC related disease.

[8] *Krysiak R, Kowalcze K, Okopień B*. **The impact of vitamin D status on cardiometabolic effects of fenofibrate in women with atherogenic dyslipidemia**. Clinical and experimental pharmacology & physiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33098674
ABSTRACT
Vitamin D deficiency is a risk factor for cardiometabolic disease. The aim of this study was to determine the role of vitamin D status in the impact of fenofibrate on plasma levels of cardiometabolic risk factors. The study population (n = 61) consisted of three matched groups of women with atherogenic dyslipidaemia: vitamin D-naïve women with vitamin D insufficiency (group A), women receiving vitamin D preparations because of vitamin D deficiency (group B), as well as vitamin D-naïve women with normal vitamin D status (group C), who were treated with micronized fenofibrate (200 mg daily). Glucose homeostasis markers, plasma lipids, as well as plasma levels of 25-hydroxyvitamin D, uric acid, high-sensitivity C-reactive protein (hsCRP), fibrinogen and homocysteine were determined at the beginning of the study and 6 months later. At entry, group A was characterized by lower levels of 25-hydroxyvitamin D, reduced insulin sensitivity and higher concentrations of uric acid, hsCRP, fibrinogen and homocysteine. Apart from a weaker effect on HDL-cholesterol and triglycerides in group A, there were no differences between the treatment arms in the effect of fenofibrate on plasma lipids. However, only in groups B and C the drug improved insulin sensitivity and reduced circulating levels of uric acid and hsCRP, as well as increased levels of 25-hydroxyvitamin D and these effects correlated with the degree of improvement in insulin sensitivity. Treatment-induced increase in homocysteine was observed only in group A. The results of the study indicate that cardiometabolic effects of fibrates may depend on the vitamin D status of patients.

[9] *Taneja K, Taneja J, Kaur C et al.* **Lipid Risk Factors in Vitiligo: Homocysteine the Connecting Link?** Clinical laboratory 2020; 66.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33073941
ABSTRACT
BACKGROUND: Vitiligo is an acquired, depigmenting skin disease with unclear, multifactorial etiopathogenesis affecting not only skin but also connected with metabolic abnormalities, including glucose and lipid abnormalities, confirming the systemic nature of the disease. Vitamin B12 and folic acid deficiencies have also been implicated in vitiligo that can lead to increased homocysteine levels in the circulation, a finding that can be expected in vitiligo. Further, an association between hyperlipidemia and hyperhomocysteinemia has been suggested in vitiligo patients showing the eminent need of management of vascular risk factors

especially in diseases with metabolic abnormalities. The present study was thus aimed to assess homocysteine levels and lipid risk factors in vitiligo patients and to study their interrelationship to predict the cardiometabolic risk in vitiligo and its management. METHODS: The present cross-sectional study included 54 case of generalized vitiligo and 54 age and gender-matched healthy adults as controls. Patients were assessed for disease activity and severity (VASI Score). All the subjects were evaluated for the lipid profile and serum homocysteine levels. RESULTS: Lipid profile analysis showed significantly higher LDL-cholesterol concentration ($p = 0.010$), significantly lower HDL-cholesterol concentration ($p = 0.003$) and significantly higher LDL/HDL ratio ($p = 0.001$) in patients with vitiligo in comparison with the control group. The mean serum homocysteine levels in vitiligo patients (18.76 ± 10.02 µmol/L) were significantly higher than in controls (10.04 ± 5.34 µmol/L) ($p = 0.000$). Serum homocysteine levels showed a positive correlation with the duration of disease which was near to significant ($p = 0.064$) and VASI score ($p = 0.000$). No significant correlation was observed between serum Hcy levels and lipid profile. CONCLUSIONS: The present study showed significantly higher Hcy levels in vitiligo patients than controls which may be a precipitating factor in the pathogenesis of vitiligo in predisposed individuals. The results of our study are also indicative of lipid disturbances in vitiligo. These findings may reflect some ongoing abnormal metabolic processes in patients with vitiligo. Therefore, we recommend routine estimation of homocysteine and lipid profile in vitiligo patients both of which should be regarded as independent significant contributing factors of cardiometabolic risk worth considering in the management of patients with vitiligo.

[10] *Schmidt AF, Carter JL, Pearce LS et al.* **PCSK9 monoclonal antibodies for the primary and secondary prevention of cardiovascular disease**. The Cochrane database of systematic reviews 2020; 10:Cd011748.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33078867

ABSTRACT

BACKGROUND: Despite the availability of effective drug therapies that reduce low-density lipoprotein (LDL)-cholesterol (LDL-C), cardiovascular disease (CVD) remains an important cause of mortality and morbidity. Therefore, additional LDL-C reduction may be warranted, especially for people who are unresponsive to, or unable to take, existing LDL-C-reducing therapies. By inhibiting the proprotein convertase subtilisin/kexin type 9 (PCSK9) enzyme, monoclonal antibodies (PCSK9 inhibitors) reduce LDL-C and CVD risk. OBJECTIVES: Primary To quantify the effects of PCSK9 inhibitors on CVD, all-cause mortality, myocardial infarction, and stroke, compared to placebo or active treatment(s) for primary and secondary prevention. Secondary To quantify the safety of PCSK9 inhibitors, with specific focus on the incidence of influenza, hypertension, type 2 diabetes, and cancer, compared to placebo or active treatment(s) for primary and secondary prevention. SEARCH METHODS: We identified studies by systematically searching CENTRAL, MEDLINE, Embase, and Web of Science in December 2019. We also searched ClinicalTrials.gov and the International Clinical Trials Registry Platform in August 2020 and screened the reference lists of included studies. This is an update of the review first published in 2017. SELECTION CRITERIA: All parallel-group and factorial randomised controlled trials (RCTs) with a follow-up of at least 24 weeks were eligible. DATA COLLECTION AND ANALYSIS: Two review authors independently reviewed and extracted data. Where data were available, we calculated pooled effect estimates. We used GRADE to assess certainty of evidence and in 'Summary of findings' tables. MAIN RESULTS:

We included 24 studies with data on 60,997 participants. Eighteen trials randomised participants to alirocumab and six to evolocumab. All participants received background lipid-lowering treatment or lifestyle counselling. Six alirocumab studies used an active treatment comparison group (the remaining used placebo), compared to three evolocumab active comparison trials. Alirocumab compared with placebo decreased the risk of CVD events, with an absolute risk difference (RD) of -2% (odds ratio (OR) 0.87, 95% confidence interval (CI) 0.80 to 0.94; 10 studies, 23,868 participants; high-certainty evidence), decreased the risk of mortality (RD -1%; OR 0.83, 95% CI 0.72 to 0.96; 12 studies, 24,797 participants; high-certainty evidence), and MI (RD -2%; OR 0.86, 95% CI 0.79 to 0.94; 9 studies, 23,352 participants; high-certainty evidence) and for any stroke (RD 0%; OR 0.73, 95% CI 0.58 to 0.91; 8 studies, 22,835 participants; high-certainty evidence). Compared to active treatment the alirocumab effects, for CVD, the RD was 1% (OR 1.37, 95% CI 0.65 to 2.87; 3 studies, 1379 participants; low-certainty evidence); for mortality, RD was -1% (OR 0.51, 95% CI 0.18 to 1.40; 5 studies, 1333 participants; low-certainty evidence); for MI, RD was 1% (OR 1.45, 95% CI 0.64 to 3.28, 5 studies, 1734 participants; low-certainty evidence); and for any stroke, RD was less than 1% (OR 0.85, 95% CI 0.13 to 5.61; 5 studies, 1734 participants; low-certainty evidence). Compared to placebo the evolocumab, for CVD, the RD was -2% (OR 0.84, 95% CI 0.78 to 0.91; 3 studies, 29,432 participants; high-certainty evidence); for mortality, RD was less than 1% (OR 1.04, 95% CI 0.91 to 1.19; 3 studies, 29,432 participants; high-certainty evidence); for MI, RD was -1% (OR 0.72, 95% CI 0.64 to 0.82; 3 studies, 29,432 participants; high-certainty evidence); and for any stroke RD was less than -1% (OR 0.79, 95% CI 0.65 to 0.94; 2 studies, 28,531 participants; high-certainty evidence). Compared to active treatment, the evolocumab effects, for any CVD event RD was less than -1% (OR 0.66, 95% CI 0.14 to 3.04; 1 study, 218 participants; very low-certainty evidence); for all-cause mortality, the RD was less than 1% (OR 0.43, 95% CI 0.14 to 1.30; 3 studies, 5223 participants; very low-certainty evidence); and for MI, RD was less than 1% (OR 0.66, 95% CI 0.23 to 1.85; 3 studies, 5003 participants; very low-certainty evidence). There were insufficient data on any stroke. AUTHORS' CONCLUSIONS: The evidence for the clinical endpoint effects of evolocumab and alirocumab were graded as high. There is a strong evidence base to prescribe PCSK9 monoclonal antibodies to people who might not be eligible for other lipid-lowering drugs, or to people who cannot meet their lipid goals on more traditional therapies, which was the main patient population of the available trials. The evidence base of PCSK9 inhibitors compared with active treatment is much weaker (low very- to low-certainty evidence) and it is unclear whether evolocumab or alirocumab might be effectively used as replacement therapies. Related, most of the available studies preferentially enrolled people with either established CVD or at a high risk already, and evidence in low- to medium-risk settings is minimal. Finally, there is very limited evidence on any potential safety issues of both evolocumab and alirocumab. While the current evidence synthesis does not reveal any adverse signals, neither does it provide evidence against such signals. This suggests careful consideration of alternative lipid lowering treatments before prescribing PCSK9 inhibitors.

[11] *Ahsan F, Oliveri F, Goud HK et al.* **Pleiotropic Effects of Statins in the Light of Non-Alcoholic Fatty Liver Disease and Non-Alcoholic Steatohepatitis**. Cureus 2020; 12:e10446.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33072455
ABSTRACT

Statins, the lipid-lowering drugs, and non-alcoholic fatty liver disease (NAFLD)/non-alcoholic steatohepatitis (NASH), a lipid-related pathology, share a complex relationship, one known to be hepatotoxic and other being hepatic injury. NASH is an unresolved mystery in terms of treatment. Could statins prove to be a promising solution due to their pleiotropic properties in addition to the cholesterol-lowering effect? This study aims to find statin effectiveness in NAFLD/NASH treatment and prevention of associated adverse outcomes. An extensive data search was done to identify the studies assessing statin effect on NAFLD/NASH and then analyzed to establish the relationship. Several studies demonstrated a reduction in NAFLD/NASH-associated inflammation and fibrosis with statin treatment. These anti-inflammatory and anti-fibrotic effects were through their pleiotropic properties, which were in addition to their cholesterol-lowering effect. In various animal studies, statins were found to improve hepatic lipotoxicity, oxidative stress, inflammatory responses, and fibrosis associated with NASH through multiple pathways. Statins exert these protective effects by recovering the gene expression level of peroxisomal proliferator-activated receptor alpha (PPARα) and therefore restore the mitochondrial and peroxisomal fatty acid oxidation (FAO). Statin treatment also increased the levels of paraoxonase 1 (PON1), an antioxidant and antiatherogenic enzyme that is reduced in NAFLD as well as encounter the hepatic lipotoxicity by resolving cholesterol crystals and Kupffer cells (KCs) with crown-like structures (CLSs). They exhibited antitumor properties by inhibiting proinflammatory cytokines and vascular proliferative factors. Moreover, they restored a healthy liver sinusoidal endothelial cell (LSEC) and hepatic stellate cells (HSC) along with inhibiting the activation of HSC via modulating inducible nitric oxide synthase (iNOS) and expressions of endothelial nitric oxide synthase (eNOS). Besides, they were protective against cardiovascular disease (CVD)-related morbidity and mortality, hepatocellular carcinoma (HCC), and metabolic syndrome (MS) associated with NAFLD/NASH. NASH and its precursor, NAFLD, could be treated and prevented with statins owing to their pleiotropic properties. This study helps to prove this by looking back at different literature and has successfully enlightened the point. Once proved through large clinical trials on humans, it could revolutionize the NASH therapy.

[12] *Alam L, Lasam G, Fishberg R*. **Achilles Tendon Xanthoma Thickness and Carotid Intima-Media Thickness in a Patient With Heterozygous Familial Hypercholesterolemia on PCSK9 Inhibition: A Case Report and Literature Review**. Cureus 2020; 12:e10497.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33094041

ABSTRACT

Ultrasound-guided measurement of carotid intima-media thickness can be used as a surrogate marker to predict future risk of atherosclerotic cardiovascular disease, and to understand the efficacy of lipid-lowering drugs. Aggressive lipid-lowering drugs such as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been shown to reduce carotid artery plaque burden, total cholesterol, and low-density lipoprotein-c in patients with heterozygous familial hypercholesterolemia (FH). We describe a patient with heterozygous FH treated with PCSK9 inhibitor over the course of two years, and the drug's impact on carotid intima-media thickness, Achilles tendon thickness, and cardiovascular disease risk reduction.

[13] *Sinning D, Landmesser U*. **Low-density Lipoprotein-Cholesterol Lowering Strategies for Prevention of Atherosclerotic Cardiovascular Disease: Focus on siRNA Treatment Targeting PCSK9 (Inclisiran)**. Current cardiology reports 2020; 22:176.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33089390
ABSTRACT
PURPOSE OF REVIEW: The aim of low-density lipoprotein-cholesterol (LDL-C) lowering therapies is to safely achieve a consistent and long-term reduction in exposure of the vasculature to atherogenic lipoproteins in order to reduce the risk of atherosclerotic cardiovascular (CV) disease and the associated CV events, such as myocardial infarctions and ischemic strokes. This review summarizes the concept and clinical development of a novel molecular approach to efficiently lower LDL-C, a synthetic small interfering ribonucleic acid (siRNA)-inclisiran-directed against proprotein convertase subtilisin-kexin type 9 (PCSK9). RECENT FINDINGS: The understanding of genes regulating atherogenic lipoproteins and their causal role in the development of atherosclerotic CV disease has substantially advanced over the past years. This has opened the possibility for development of molecular therapies targeting these atherogenic lipoproteins, in particular by RNA-targeted treatment approaches. The most advanced clinical development program is the siRNA-treatment targeting PCSK9 (inclisiran), involving more than 4000 patients in clinical studies. Phase 1 and 2 studies have identified the dose of 300 mg inclisiran for efficient LDL-C lowering. Most recently, three phase 3 studies demonstrated that a regimen of inclisiran every 6 months was feasible and reduced LDL-C by approximately 50% in patients at high or very high CV risk or with familial hypercholesterolemia. Adverse events were similar in the inclisiran and the placebo groups, except for more frequent transient injection site reactions with inclisiran than with placebo. siRNA therapy targeting PCSK9 (inclisiran) applied twice a year efficiently reduced LDL-C by approximately 50% and was safe in recent phase 3 studies. The effects of this treatment on CV outcome are currently further assessed in a large ongoing CV outcome trial.

[14] *Asfaw A, Minhas S, Khouzam AR et al.* **Fish Oil Dilemma: Does It Increase the Risk of Ventricular Arrhythmias and Death? Can Fish Oil Kill You?** Current problems in cardiology 2020:100718.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33097299
ABSTRACT
Omega-3-fatty-acids are now increasingly being used for potential beneficial anti-inflammatory effect in the treatment and management of cardiovascular disease. Eicosapentaenoic acid and Docosahexaenoic acid are 2 essential omega-3 fatty acids found predominately in fish and fish oil supplements. Despite the increased use of fish oil products for both primary and secondary prevention of cardiovascular morbidity and mortality, the available literature evidence are controversial. We searched through PubMed for studies that have investigated the impact of omega-3 fatty acids on coronary heart disease and mortality. Our systemic review suggests that most studies, which are mostly observational, have found there to be a potential benefit of omega-3 fatty acids on coronary heart disease whereas some other studies have found conflicting results. More randomized controlled studies are warranted with adequate sample size to clearly establish the risk and benefits of omega-3 fatty acids on cardiovascular disease.

[15] *Gottlieb A, Leven AS, Sowa JP et al.* **Lipoprotein and Metabolic Profiles Indicate Similar Cardiovascular Risk of Liver Steatosis and NASH**. Digestion 2020:1-11.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33080603
ABSTRACT

BACKGROUND AND AIM: Nonalcoholic fatty liver disease (NAFLD) affects about 25% of the global population, with no reliable noninvasive tests to diagnose nonalcoholic steatohepatitis (NASH) and to differentiate between NASH and nonalcoholic fatty liver (NAFL) (steatosis alone). It is unclear if NAFL and NASH differ in cardiovascular risk for patients. Here, we compared obese NAFLD patients with a healthy cohort to test whether cholesterol compounds could represent potential noninvasive markers and to estimate associated risks. METHOD: Serum samples of 46 patients with histologically confirmed NAFLD (17 NAFL, 29 NASH) who underwent bariatric surgery were compared to 32 (9 males, 21 females) healthy controls (HCs). We analyzed epidemiological data, liver enzymes, cholesterol and lipid profile, and amino acids. The latter were analyzed by nuclear magnetic resonance spectroscopy. RESULTS: Total serum and high-density lipoprotein (HDL) cholesterol were significantly lower in the NAFLD group than in HCs, with a stronger reduction in NASH. Similar observations were made for sub-specification of HDL-p, HDL-s, SHDL-p, and LHDL-p cholesterols. Low-density lipoprotein (LDL)-s and LLDL-p cholesterol were significantly reduced in NAFLD groups. Interestingly, SLDL-p cholesterol was significantly higher in the NAFL group with a stronger elevation in NASH than in HCs. The amino acids alanine, leucin, and isoleucine were significantly higher in the NAFL and NASH groups than in HCs. CONCLUSION: We show in this study that cholesterol profiles, apolipoproteins, and amino acids could function as a potential noninvasive test to screen for NAFLD or even NASH in larger populations. However, few differences in cholesterol profiles were identified between the NAFL and NASH groups, indicating similar cardiovascular risk profiles.

[16] *Chapman G, Tanner S*. **Republished: An unusually impressive atorvastatin-induced elevation of serum alkaline phosphatase**. Drug and therapeutics bulletin 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33093078
ABSTRACT

[17] *Leistner DM, Kränkel N, Meteva D et al.* **Differential immunological signature at the culprit site distinguishes acute coronary syndrome with intact from acute coronary syndrome with ruptured fibrous cap: results from the prospective translational OPTICO-ACS study**. European heart journal 2020; 41:3549-3560.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33080003
ABSTRACT
AIMS : Acute coronary syndromes with intact fibrous cap (IFC-ACS), i.e. caused by coronary plaque erosion, account for approximately one-third of ACS. However, the underlying pathophysiological mechanisms as compared with ACS caused by plaque rupture (RFC-ACS) remain largely undefined. The prospective translational OPTICO-ACS study programme investigates for the first time the microenvironment of ACS-causing culprit lesions (CL) with intact fibrous cap by molecular high-resolution intracoronary imaging and simultaneous local immunological phenotyping. METHODS AND RESULTS : The CL of 170 consecutive ACS patients were investigated by optical coherence tomography (OCT) and simultaneous immunophenotyping by flow cytometric analysis as well as by effector molecule concentration measurements across the culprit lesion gradient (ratio local/systemic levels). Within the study cohort, IFC caused 24.6% of ACS while RFC-ACS caused 75.4% as determined and validated by two independent OCT core laboratories. The IFC-CL were characterized by lower lipid content, less calcification, a thicker overlying fibrous cap, and largely localized near a coronary

bifurcation as compared with RFC-CL. The microenvironment of IFC-ACS lesions demonstrated selective enrichment in both CD4+ and CD8+ T-lymphocytes (+8.1% and +11.2%, respectively, both $P < 0.05$) as compared with RFC-ACS lesions. T-cell-associated extracellular circulating microvesicles (MV) were more pronounced in IFC-ACS lesions and a significantly higher amount of CD8+ T-lymphocytes was detectable in thrombi aspirated from IFC-culprit sites. Furthermore, IFC-ACS lesions showed increased levels of the T-cell effector molecules granzyme A (+22.4%), perforin (+58.8%), and granulysin (+75.4%) as compared with RFC plaques ($P < 0.005$). Endothelial cells subjected to culture in disturbed laminar flow conditions, i.e. to simulate coronary flow near a bifurcation, demonstrated an enhanced adhesion of CD8+T cells. Finally, both CD8+T cells and their cytotoxic effector molecules caused endothelial cell death, a key potential pathophysiological mechanism in IFC-ACS. CONCLUSIONS : The OPTICO-ACS study emphasizes a novel mechanism in the pathogenesis of IFC-ACS, favouring participation of the adaptive immune system, particularly CD4+ and CD8+ T-cells and their effector molecules. The different immune signatures identified in this study advance the understanding of coronary plaque progression and may provide a basis for future development of personalized therapeutic approaches to ACS with IFC. TRIAL REGISTRATION: The study was registered at clinicalTrials.gov (NCT03129503).

[18] *Wang X, Chen HZ, Liu WT et al.* **The association of plasma high-density lipoprotein cholesterol levels and cirrhosis development in obese patients with chronic hepatitis B: a cohort study**. European journal of gastroenterology & hepatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33079778
ABSTRACT
OBJECTIVE: Metabolic disorder is a common risk factor for cirrhosis in Asia, and it will increase the risk of cirrhosis in patients with Chronic hepatitis B (CHB). However, studies on the efficacy of plasma lipid markers which predict the happening and development of cirrhosis in obese CHB patients are limited. METHODS: In total, 3327 patients who were followed for more than 4 years' follow-up in the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine joined the program. Finally, 287 obese CHB patients were included in this study according to the results of metabolic tests. The data of baseline and follow-up were collected, and the association between them was analyzed. RESULTS: Based on the follow-up results, enrolled patients were divided into a group of cirrhosis (n = 146) and a group of noncirrhosis (n = 141). Plasma glucose and high-density lipoprotein cholesterol (HDL-C) levels in the noncirrhosis group (5.2 and 1.2 mmol/L, respectively) were significantly higher than that in the cirrhosis group (5.0 and 1.0 mmol/L, respectively), while the amount of total bile acid (TBA) in the cirrhosis group was lower than that in the cirrhosis group. Levels of HDL-C and total cholesterol were associated with liver function. Plasma HDL-C was an independent indicator of cirrhosis in patients with CHB. Patients with HDL-C levels less than 1.03 mmol/L had a 2.21-fold higher incidence rate of cirrhosis, and patients over 40 years old or the levels of HDL-C less than 1.03 mmol/L were more likely to generate cirrhosis. CONCLUSIONS: Plasma HDL-C was an appropriate marker in predicting cirrhosis for patients with CHB.

[19] *Polychronopoulos G, Tziomalos K*. **Treatment of heterozygous familial hypercholesterolemia: what does the future hold?** Expert Rev Clin Pharmacol 2020; 13:1229-1234.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33070644

ABSTRACT
INTRODUCTION: Heterozygous familial hypercholesterolemia (heFH) is a common metabolic disease associated with increased cardiovascular risk. Despite treatment with the currently available lipid-lowering agents (statins, ezetimibe, and proprotein convertase subtilisin/kexin type 9 inhibitors), a substantial proportion of patients with heFH does not achieve low-density lipoprotein cholesterol (LDL-C) targets. AREAS COVERED: The PubMed database was reviewed for relevant papers published up to August 2020. The safety and efficacy of novel agents, namely inclisiran and bempedoic acid, that lower LDL-C levels and might be useful in the management of patients with heFH are discussed. EXPERT OPINION: The prolonged lipid-lowering effect of inclisiran might improve adherence to treatment in patients with heFH. Bempedoic acid provides additional reductions in LDL-C levels in patients on high-intensity statin treatment; oral administration of this agent might be attractive to some patients. However, it is important to evaluate the effects of these agents on cardiovascular morbidity before they are incorporated in the management of heFH. The cost/benefit of treatment should also be considered, given the increasing complexity of lipid-lowering treatment.

[20] *Kirichenko TV, Markina YV, Sukhorukov VN et al.* **A Novel Insight at Atherogenesis: The Role of Microbiome**. Frontiers in cell and developmental biology 2020; 8:586189.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33072766

ABSTRACT
There is an important task of current medicine to identify mechanisms and new markers of subclinical atherosclerosis in order to develop early targets for the diagnosis and treatment of this disease, since it causes such widespread diseases as myocardial infarction, stroke, sudden death, and other common reasons of disability and mortality in developed countries. In recent years, studies of the human microbiome in different fields of medicine have become increasingly popular; there is evidence from numerous studies of the significant contribution of microbiome in different steps of atherogenesis. This review attempted to determine the current status of the databases PubMed and Scopus (until May, 2020) to highlight current ideas on the potential role of microbiome and its metabolites in atherosclerosis development, its mechanisms of action in lipids metabolism, endothelial dysfunction, inflammatory pathways, and mitochondrial dysfunction. Results of clinical studies elucidating the relationship of microbiome with subclinical atherosclerosis and cardiovascular disease considered in this article demonstrate strong association of microbiome composition and its metabolites with atherosclerosis and cardiovascular disease. Data on microbiome impact in atherogenesis open a wide perspective to develop new diagnostic and therapeutic approaches, but further comprehensive studies are necessary.

[21] *Aguilar-Palacio I, Rabanaque MJ, Maldonado L et al.* **New Male Users of Lipid-Lowering Drugs for Primary Prevention of Cardiovascular Disease: The Impact of Treatment Persistence on Morbimortality. A Longitudinal Study**. International journal of environmental research and public health 2020; 17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33092211

ABSTRACT
The objective of this study was to analyse persistence to lipid-lowering drug use for primary prevention of cardiovascular disease (CVD) in a new users cohort, to explore all-cause and cardiovascular related morbidity, comorbidity and mortality in this group and, finally, to study

the relationship between persistence and morbimortality. We selected subjects who started lipid-lowering treatment for primary prevention of CVD between 1 January 2010 and 31 December 2017 (N = 1424), and classified them as treatment-persistent or -nonpersistent. Bivariate analyses were performed to compare sociodemographic and clinical variables, morbimortality and time to event between groups. The association between morbidities was explored using comorbidity network analysis. The effect of persistence was analysed using logistic regression and Cox survival analyses. Only 38.7% of users were persistent with treatment. Persistent and nonpersistent users had similar sociodemographic and clinical profiles, although differed in age, smoking status, and glycemia. Comorbidity networks revealed that the number of co-occurring diagnoses was higher in nonpersistent than persistent users. Adjusted analyses indicated a protective effect of treatment persistence, especially against major adverse cardiovascular events (MACE), but this effect was not statistically significant. Observational studies are crucial to characterize real-world effectiveness.

[22] *Orringer CE, Tokgozoglu L, Maki KC et al.* **Transatlantic Lipid Guideline Divergence: Same Data But Different Interpretations**. Journal of the American Heart Association 2020; 9:e018189.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33092440
ABSTRACT
Despite consensus that excessive circulating concentrations of apoB-lipoproteins is a key driver for the atherosclerotic process and that treatments that low-density lipoprotein cholesterol lowering by up-regulation of low-density lipoprotein cholesterol receptor expression reduces that risk, divergent viewpoints on interpretation of study data have resulted in substantial differences in European and American lipid guideline recommendations. This article explores those differences and highlights the importance of understanding guideline-based lipid management to improve patient care and reduce the risk of clinical atherosclerotic cardiovascular disease.

[23] *Afanasieva O, Ezhov MV, Klesareva E et al.* **Effect of Evolocumab on Lipoprotein(a) and PCSK9 in Healthy Individuals with Elevated Lipoprotein(a) Level**. Journal of cardiovascular development and disease 2020; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33076542
ABSTRACT
Background and aims: The aim of this study was to investigate the influence of a single injection of Evolocumab on the dynamics of Lp(a), fractions of apoB100-containing lipoproteins, PCSK9, and their complexes in healthy individuals with elevated Lp(a) levels. Methods: This open-label, 4-week clinical study involved 10 statin-naive volunteers with Lp(a) >30 mg/dL, LDL-C < 4.9 mmol/L, and a moderate risk of cardiovascular events. The concentrations of Lp(a), lipids, PCSK9, circulating immune complexes (CIC), and plasma complexes of PCSK9 with apoB100-containing lipoproteins (Lp(a)-PCSK9 and LDL-PCSK9) were measured before and each week after Evolocumab (MABs) administration. Results: After a single dose injection of 140 mg of MABs, the median concentration of PCSK9 in serum increased from 496 to 3944 ng/mL; however, the entire pool of circulating PCSK9 remained bound with MABs for 2-3 weeks. LDL-C level decreased significantly from 3.36 mmol/L to 2.27 mmol/L during the first two weeks after the injection. Lp(a) concentrations demonstrated

multidirectional changes in different patients with the maximal decrease on the second week. There were no positive correlations between the changes in levels of Lp(a), LDL-C, and TC. The change in the amount of circulating complex of PCSK9-Lp(a) was significantly less than of PCSK9-apoB100 (-5% and -47% after 1 week, respectively). Conclusions: A single administration of monoclonal antibodies against PCSK9 (Evolocumab) in healthy individuals with hyperlipoproteinemia(a) resulted in a decrease of Lp(a) of 14%, a 5% decrease in PCSK9-Lp(a), a 36% reduction of LDL-C, a 47% decrease in PCSK9-apoB100 and a tenfold increase in total serum PCSK9 concentration.

[24] *Sukonthasarn A, Chia YC, Wang JG et al.* **The feasibility of polypill for cardiovascular disease prevention in Asian Population**. Journal of clinical hypertension (Greenwich, Conn.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33086429
ABSTRACT
Polypill is a fixed-dose combination of medications with proven benefits for the prevention of cardiovascular disease (CVD). Its role in CVD prevention has been extensively debated since the inception of this concept in 2003. There are two major kinds of polypills in clinical studies. The first is polypill that combines multiple low-dose medications for controlling only one CVD risk factor (such as high blood pressure or high serum cholesterol). These "single-purpose" polypills were mostly developed from original producers and have higher cost. The polypill that combines 3-4 pharmaceutical components, each with potential to reduce one major cardiovascular risk factors is "multi-purpose" or "cardiovascular" polypill. Using data from various clinical trials and from meta-analysis, Wald and Law claimed that this "cardiovascular" polypill when administered to every individual older than 55 years could reduce the incidence of CVD by more than 80%. Several short and intermediate to long-term studies with different cardiovascular polypills in phase II and III trials showed that they could provide better adherence, equivalent, or better risk factor control and quality of life among users as compared to usual care. One recently published randomized controlled clinical trial demonstrated the effectiveness and safety of a four-component polypill for both primary and secondary CVD prevention with acceptable number needed to treat (NNT) to prevent one major cardiovascular event. Considering the slow achievement of CVD prevention in many poor- and middle-income Asian countries and also the need to further improve compliance of antihypertensive and lipid lowering medications in many high-income Asian countries, the concept of "cardiovascular polypill" could be very useful. With further support from ongoing polypill cardiovascular outcome trials, polypill could be the foundation of the population-based strategies for CVD prevention.

[25] *Hirai K, Imamura S, Hirai A et al.* **Effect of Evolocumab on Vulnerable Coronary Plaques: A Serial Coronary Computed Tomography Angiography Study**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33080961
ABSTRACT
This study investigated the effects of evolocumab on vulnerable coronary plaques and factors associated with the change in stability and size of plaques in patients taking statins. Vulnerable coronary plaques were defined using coronary computed tomography (CT) angiography as having a density of <50 HU within the region of interest and a remodeling index ≥1.1. The

changes in minimum CT density, remodeling index, and percent stenosis of vulnerable coronary plaques after six months of evolocumab administration were retrospectively analyzed in 136 vulnerable coronary plaques from 98 patients (68 men and 30 women; mean age: 72.9 ± 8.7 years) treated with a statin. The administration of evolocumab significantly increased the minimum CT density (39.1 ± 8.1 HU to 84.9 ± 31.4 HU, $p < 0.001$), reduced the remodeling index (1.29 ± 0.11 to 1.19 ± 0.10, $p < 0.001$), and decreased the percent stenosis (27.0 ± 10.4% to 21.2 ± 9.8%, $p < 0.001$). Multiple linear regression analysis revealed that baseline percent stenosis (standard coefficient (β) = -0.391, $p = 0.002$) independently correlated with the change in minimum CT density, whereas the baseline remodeling index (β = -0.368, $p < 0.001$) independently correlated with a change in the remodeling index. Evolocumab stabilized vulnerable coronary plaques and reduced their size. These results suggest that evolocumab protects against coronary artery disease progression in patients taking statins.

[26] *Pasarikovski CR, Ku JC, Priola SM et al.* **Endovascular optical coherence tomography imaging in cerebrovascular disease**. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia 2020; 80:30-37.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33099363
ABSTRACT
Endovascular optical coherence tomography (OCT) is the highest resolution imaging modality currently available with spatial resolution of 10 μm. Although originally developed for interventional cardiology, the ability to visualize the luminal environment and anatomy, along with the stent-vessel interaction could be of great utility for various cerebrovascular diseases, and the adoption of endovascular OCT imaging in the evolving field of interventional neuroradiology seems instinctive. The purpose of this study is to conduct a systematic review of the literature regarding applications of endovascular OCT in the diagnosis and treatment of cerebrovascular diseases. In addition, the authors report their institutional experience with the use of OCT in carotid atherosclerotic disease, cerebral aneurysms, and acute ischemic stroke. A systematic review of the literature was undertaken. Peer-reviewed articles were collected through MEDLINE, Embase, Scopus, and Cochrane Central Register of Controlled Trials (CENTRAL) searches through March 2020. A total of 34 studies with 598 patients were included in the qualitative synthesis. These include 23 studies of carotid atherosclerotic disease, 7 studies of cerebral aneurysms, and 4 studies of non-aneurysmal posterior circulation pathology. OCT imaging was feasible in 94% of patients with 0.6% complication rate. Endovascular OCT appears to be safe and feasible, allowing clinicians to visualize stent-vessel interactions, aneurysmal healing, and vulnerable atherosclerotic plaque features. OCT carries great promise, however additional investigations are needed before any imposing statement can be made about the role of OCT in cerebrovascular imaging.

[27] *Ibarra-Lara L, Sánchez-Aguilar M, Del Valle-Mondragón L et al.* **Clofibrate improves myocardial ischemia-induced damage through regulation of renin-angiotensin system and favours a pro-vasodilator profile in left ventricle**. Journal of pharmacological sciences 2020; 144:218-228.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33070841
ABSTRACT
Myocardial ischemia initiates a chain of pathological conditions leading to cardiomyocyte death. Therefore, pharmacological treatment to stop ischemia-induced damage is necessary.

Fibrates, have been reported to decrease inflammatory markers and to modulate the renin-angiotensin system (RAS). Our aim was to explore if clofibrate treatment, administered one week after myocardial event, decreases MI-induced cardiac damage. Wistar rats were assigned to: 1. Sham or 2. Coronary artery ligation (MI). Seven days after, rats were subdivided to receive vehicle (V) or clofibrate [100 mg/kg (C)] daily for 7 days. Blood samples and left ventricle were analyzed. RAS components [angiotensin II, angiotensin converting enzyme (ACE), and AT(1)-receptor] decreased in MI-C compared to MI-V, while [Ang-(1-7), bradykinin, ACE-2, and AT(2)-receptor] raised in response to clofibrate treatment. Oxidative stress markers increased in MI-V rats, a profile reverted in MI-C rats. Nitric oxide (NO) pathway (Akt, eNOS, and NO) exhibits a lower participation in MI-V, but clofibrate raised NO-pathway components and its production. MI-induced fibrosis and structural damage was also improved by clofibrate-treatment. In conclusion, clofibrate administration to 7 days MI-rats exerts an antioxidant, pro-vasodilator expression profile, and anti-fibrotic effect suggesting that PPARα activation can be considered a therapeutic target to improve cardiac condition posterior to ischemia.

[28] *Vatannejad A, Salimi F, Moradi N et al.* **Evaluation of angiopoietin-like protein 3 (ANGPTL3) levels in polycystic ovary syndrome**. Life sciences 2020; 263:118595.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33075372

ABSTRACT

AIM: Angiopoietin-like protein 3 (ANGPTL3) is recognized as a regulator of lipid metabolism. However, little is known about its association with insulin resistance in polycystic ovary syndrome (PCOS) setting. The present study aimed to investigate the serum levels of ANGPTL3 and adiponectin in PCOS women compared to healthy controls. MAIN METHOD: In this study, a total of 175 premenopausal women (117 PCOS and 58 non-PCOS) were enrolled. Serum concentrations of ANGPTL3, adiponectin, fasting insulin, and other hormonal variables were measured using ELISA technique. KEY FINDINGS: Results showed that adiponectin levels were significantly lower in PCOS group than those of non-PCOS group. However, serum levels of ANGPTL3, high-sensitivity C-reactive protein (hs-CRP), and homocysteine (Hcy) were found to be higher in PCOS patients, when compared to non-PCOS ones. Moreover, serum ANGPTL3 positively correlated with BMI and serum triglyceride, while it inversely correlated with serum HDL-C in PCOS patients. SIGNIFICANCE: Our results demonstrated that increased levels of ANGPTL3 correlated with insulin resistance and dyslipidemia in PCOS patients, highlighting the need for future studies targeting its role in the pathogenesis of this disease.

[29] *Grimaudo S, Bartesaghi S, Rametta R et al.* **PCSK9 rs11591147 R46L loss-of-function variant protects against liver damage in individuals with NAFLD**. Liver international : official journal of the International Association for the Study of the Liver 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33091218

ABSTRACT

BACKGROUND AND AIMS: The proprotein convertase subtilisin/kexin type 9 (PCSK9) plays a key role in cholesterol homeostasis, and its inhibition represents an effective therapy to lower low-density lipoprotein cholesterol (LDL-C) levels. In this study, we examined the impact of the PCSK9 rs11591147 loss-of-function (LOF) variant on liver damage in a multicenter collection of patients at risk of nonalcoholic steatohepatitis (NASH), in clinical samples and experimental

models. METHODS: We considered 1874 consecutive individuals at risk of NASH as determined by histology. The SNP rs11591147, encoding for the p.R46L variant of PCSK9, was genotyped by TaqMan assays. We also evaluated 1) PCSK9 mRNA hepatic expression in human liver, and 2) the impact of a NASH-inducing diet in mice with hepatic overexpression of human PCSK9. RESULTS: Carriers of PCSK9 rs11591147 had lower circulating LDL-C levels and were protected against nonalcoholic fatty liver disease (NAFLD) (OR: 0.42; 95% CI: 0.22-0.81; P = .01), NASH (OR: 0.48; 95% CI: 0.26-0.87; P = .01) and more severe fibrosis (OR: 0.55; 95% CI: 0.32-0.94; P = .03) independently of clinical, metabolic and genetic confounding factors. PCSK9 hepatic expression was directly correlated with liver steatosis (P = .03). Finally, liver-specific overexpression of human PCSK9 in male mice drives NAFLD and fibrosis upon a dietary challenge. CONCLUSIONS: In individuals at risk of NASH, PCSK9 was induced with hepatic fat accumulation and PCSK9 rs11591147 LOF variant was protective against liver steatosis, NASH and fibrosis, suggesting that PCSK9 inhibition may be a new therapeutic strategy to treat NASH.

[30] *Jayachandran M, Qu S*. **Harnessing hyperuricemia to atherosclerosis and understanding its mechanistic dependence**. Med Res Rev 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33084092
ABSTRACT
Atherosclerosis is regarded as the disease of the arterial vasculature. The main characteristics of atherosclerosis are the abnormal accumulation of lipids, increased inflammatory cells, matrix deposits, and proliferation of smooth muscle cells. Diabetes mellitus, obesity, and hyperlipidemia are the most studied risk factors of atherosclerosis. One least studied risk factor is the uric acid (UA), a high UA in circulation is interlinked with many pathological processes. Several epidemiological studies suggest elevated UA levels as an essential biomarker in the forecast of several cardiovascular diseases. Available evidence claims that UA upholds the atherosclerosis process via disturbing lipid metabolism, reducing the nitric oxide synthesis in endothelial cells, promoting the proliferation of vascular smooth muscle cells, and overwhelms inflammation. In endothelial dysfunction and coronary artery lesions, UA is considered as an independent predictor. The updated studies on the involvement of hyperuricemia in atherosclerosis prove that treatment with xanthine oxidase (XO) inhibitors not just benefits the treatment of hyperuricemia but also reduces the burden of atherosclerosis to a greater extent. In this review, we highlight how the hyperuricemia affects vascular integrity, causes atherosclerosis, and the mechanism of action of XO inhibitors on atherosclerosis.

[31] *Rufino AT, Costa VM, Carvalho F, Fernandes E*. **Flavonoids as antiobesity agents: A review**. Med Res Rev 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33084093
ABSTRACT
Obesity is a global health problem that affects all age groups in both developing and developed countries. In recent years, the prevalence of overweight and obesity has reached pandemic levels, resulting in a dramatic increase in the incidence of various comorbidities, such as cardiovascular diseases, type 2 diabetes, and cancer, consequently leading to massive health and socioeconomic burdens. Together with lifestyle changes, antiobesity pharmacotherapy is gaining momentum as an adjunctive treatment. However, the available pharmacological approaches have limited use owing to either significant adverse effects or low

efficacy. Over the years, natural products have been an important source of lead compounds for drug discovery. Among these, flavonoids are associated with important biological effects and health-promoting activities. In this review, we discuss the modulatory effects of flavonoids on obesity and their potential mechanisms of action. The literature strongly suggests that most common flavonoids demonstrate a pronounced effect on obesity as shown by their ability to lower body weight, fat mass, and plasma triglycerides/cholesterol, both in in vitro and in vivo models. The impact of flavonoids on obesity can be observed through different mechanisms: reducing food intake and fat absorption, increasing energy expenditure, modulating lipid metabolism, or regulating gut microbiota profile. A better understanding of the known antiobesity mechanisms of flavonoids will enable their potential use to treat this medical condition. Therefore, this review focuses on the putative biological mechanisms through which flavonoids may prevent or treat obesity and highlights new perspectives on future pharmacological use.

[32] *Li T, Li X, Feng Y et al.* **The Role of Matrix Metalloproteinase-9 in Atherosclerotic Plaque Instability**. Mediators of inflammation 2020; 2020:3872367.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33082709
ABSTRACT
Matrix metalloproteinase-9 (MMP-9) belongs to the MMP family and has been widely investigated. Excessive MMP-9 expression can enhance extracellular matrix degradation and promote plaque instability. Studies have demonstrated that MMP-9 levels are higher in vulnerable plaques than in stable plaques. Additionally, several human studies have demonstrated that MMP-9 may be a predictor of atherosclerotic plaque instability and a risk factor for future adverse cardiovascular and cerebrovascular events. MMP-9 deficiency or blocking MMP-9 expression can inhibit plaque inflammation and prevent atherosclerotic plaque instability. All of these results suggest that MMP-9 may be a useful predictive biomarker for vulnerable atherosclerotic plaques, as well as a therapeutic target for preventing atherosclerotic plaque instability. In this review, we describe the structure, function, and regulation of MMP-9. We also discuss the role of MMP-9 in predicting and preventing atherosclerotic plaque instability.

[33] *Israel A, Schaffer A, Cicurel A et al.* **Large population study identifies drugs associated with reduced COVID-19 severity**. medRxiv 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33083810
ABSTRACT
BACKGROUND It may take months to years until drugs specifically designed to treat COVID-19 are available. Until then, it is crucial to identify whether existing medications could have a protective effect against severe disease. This is the objective of this large population study performed in Clalit Health Services (CHS), the largest healthcare provider in Israel. METHODS CHS centrally manages electronic health records (EHRs) including medication purchases for over 4.5 million members. Two case-control matched cohorts were assembled to assess systematically which drugs affected the risk of COVID 19 hospitalization: in both cohorts, case patients were hospitalized for COVID-19; matched control patients were taken from the general population in the first cohort, and non-hospitalized SARS-CoV-2 positive patients in the second cohort. For each medication anatomical-therapeutic-chemical (ATC) class acquired during the last month before the index-date, we computed the odds ratio (OR) for

hospitalization, 95% confidence interval (CI), and the p value, using Fisher's exact test. False discovery rate was used to adjust for multiple testing. RESULTS Several drugs and pharmacy sold items were associated with significantly reduced odds for SARS-CoV-2 hospitalization, notably ubiquinone (OR=0.185, 95% CI [0.058,0.458], p<0.001), ezetimibe (OR=0.513, 95% CI [0.375,0.688], P<0.001), rosuvastatin (OR=0.746, 95% CI [0.645,0.858], p<0.001) and flecainide (OR=0.303, 95% CI [0.080,0.813], p<0.01). Additionally, acquisition of surgical masks, latex gloves and several ophthalmological products were associated with decreased risk for hospitalization. CONCLUSION Ubiquinone, ezetimibe and rosuvastatin, all related to the cholesterol synthesis pathway were associated with reduced hospitalization risk. These findings suggest a promising protective effect which should be further investigated.

[34] *Dalli LL, Kim J, Thrift AG et al.* **Patterns of use and discontinuation of secondary prevention medications after stroke**. Neurology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33093227
ABSTRACT
OBJECTIVE: To investigate whether certain patient, acute-care, or primary-care factors are associated with medication initiation and discontinuation in the community post-stroke or TIA. METHODS: Retrospective cohort study using prospective data on adult patients with first-ever acute stroke/TIA from the Australian Stroke Clinical Registry (April 2010 to June 2014), linked with nationwide medication dispensing and Medicare claims data. Medication users were those with ≥1 dispensing in the year post-discharge. Discontinuation was assessed among medication users and defined as having no medication supply for ≥90 days in the year post-discharge. Multivariable competing risks regression, accounting for death during the observation period, was conducted to investigate factors associated with time to medication discontinuation. RESULTS: Among 17,980 registry patients with stroke/TIA, 91.4% were linked to administrative datasets. Of these, 9,817 adults with first-ever stroke/TIA were included (45.4% female, 47.6% aged ≥75 years, and 11.4% intracerebral hemorrhage). While most patients received secondary prevention medications (79.3% antihypertensive, 81.8% antithrombotic, and 82.7% lipid-lowering medication), between one-fifth and one-third discontinued treatment over the subsequent year post-discharge (20.9% antihypertensive, 34.1% antithrombotic, and 28.5% lipid-lowering medications). Prescription at hospital discharge (sub-hazard ratio [SHR]: 0.70; 95% CI: 0.62-0.79), quarterly contact with a primary-care physician (SHR: 0.62; 95% CI: 0.57-0.67), and prescription by a specialist physician (SHR: 0.87; 95% CI: 0.77-0.98) were all inversely associated with antihypertensive discontinuation. CONCLUSIONS: Patterns of use of secondary prevention medications after stroke/TIA are not optimal, with many survivors discontinuing treatment within one-year post-discharge. Improving post-discharge care for patients with stroke/TIA is needed to minimize unwarranted discontinuation.

[35] *Arenas de Larriva AP, Limia-Pérez L, Alcalá-Díaz JF et al.* **Ceruloplasmin and Coronary Heart Disease-A Systematic Review**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33096845
ABSTRACT
Several studies indicate that oxidative stress might play a central role in the initiation and maintenance of cardiovascular diseases. It remains unclear whether ceruloplasmin acts as a passive marker of inflammation or as a causal mediator. To better understand the impact of

ceruloplasmin blood levels on the risk of cardiovascular disease, and paying special attention to coronary heart disease, we conducted a search on the two most commonly used electronic databases (Medline via PubMed and EMBASE) to analyze current assessment using observational studies in the general adult population. Each study was quality rated using criteria developed by the US Preventive Services Task Force. Most of 18 eligible studies reviewed support a direct relationship between ceruloplasmin elevated levels and incidence of coronary heart disease. Our results highlight the importance of promoting clinical trials that determine the functions of ceruloplasmin as a mediator in the development of coronary heart disease and evaluate whether the treatment of elevated ceruloplasmin levels has a role in the prognosis or prevention of this condition.

[36] *Kim J, Hoang T, Kim JM et al.* **All-Cause Mortality and Cardiovascular Death between Statins and Omega-3 Supplementation: A Meta-Analysis and Network Meta-Analysis from 55 Randomized Controlled Trials**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33092130
ABSTRACT
Statins and omega-3 supplementation have shown potential benefits in preventing cardiovascular disease (CVD), but their comparative effects on mortality outcomes, in addition to primary and secondary prevention and mixed population, have not been investigated. This study aimed to examine the effect of statins and omega-3 supplementation and indirectly compare the effects of statin use and omega-3 fatty acids on all-cause mortality and CVD death. We included randomized controlled trials (RCTs) from meta-analyses published until December 2019. Pooled relative risks (RRs) and 95% confidence intervals (CIs) were calculated to indirectly compare the effect of statin use versus omega-3 supplementation in a frequentist network meta-analysis. In total, 55 RCTs were included in the final analysis. Compared with placebo, statins were significantly associated with a decreased the risk of all-cause mortality (RR = 0.90, 95% CI = 0.86-0.94) and CVD death (RR = 0.86, 95% CI = 0.80-0.92), while omega-3 supplementation showed a borderline effect on all-cause mortality (RR = 0.97, 95% CI = 0.94-1.01) but were significantly associated with a reduced risk of CVD death (RR = 0.92, 95% CI = 0.87-0.98) in the meta-analysis. The network meta-analysis found that all-cause mortality was significantly different between statin use and omega-3 supplementation for overall population (RR = 0.91, 95% CI = 0.85-0.98), but borderline for primary prevention and mixed population and nonsignificant for secondary prevention. Furthermore, there were borderline differences between statin use and omega-3 supplementation in CVD death in the total population (RR = 0.92, 95% CI = 0.82-1.04) and primary prevention (RR = 0.85, 95% CI = 0.68-1.05), but nonsignificant differences in secondary prevention (RR = 0.97, 95% CI = 0.66-1.43) and mixed population (RR = 0.92, 95% CI = 0.75-1.14). To summarize, statin use might be associated with a lower risk of all-cause mortality than omega-3 supplementation. Future direct comparisons between statin use and omega-3 supplementation are required to confirm the findings.

[37] *Santos HO, Price JC, Bueno AA*. **Beyond Fish Oil Supplementation: The Effects of Alternative Plant Sources of Omega-3 Polyunsaturated Fatty Acids upon Lipid Indexes and Cardiometabolic Biomarkers-An Overview**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33081119
ABSTRACT

Cardiovascular diseases remain a global challenge, and lipid-associated biomarkers can predict cardiovascular events. Extensive research on cardiovascular benefits of omega-3 polyunsaturated fatty acids (n3-PUFAs) is geared towards fish oil supplementation and fish-rich diets. Nevertheless, vegetarianism and veganism are becoming more popular across all segments of society, due to reasons as varied as personal, ethical and religious values, individual preferences and environment-related principles, amongst others. Due to the essentiality of PUFAs, plant sources of n3-PUFAs warrant further consideration. In this review, we have critically appraised the efficacy of plant-derived n3-PUFAs from foodstuffs and supplements upon lipid profile and selected cardiometabolic markers. Walnuts and flaxseed are the most common plant sources of n3-PUFAs, mainly alpha-linolenic acid (ALA), and feature the strongest scientific rationale for applicability into clinical practice. Furthermore, walnuts and flaxseed are sources of fibre, potassium, magnesium, and non-essential substances, including polyphenols and sterols, which in conjunction are known to ameliorate cardiovascular metabolism. ALA levels in rapeseed and soybean oils are only slight when compared to flaxseed oil. Spirulina and Chlorella, biomasses of cyanobacteria and green algae, are important sources of n3-PUFAs; however, their benefits upon cardiometabolic markers are plausibly driven by their antioxidant potential combined with their n3-PUFA content. In humans, ALA is not sufficiently bioconverted into eicosapentaenoic and docosahexaenoic acids. However, evidence suggests that plant sources of ALA are associated with favourable cardiometabolic status. ALA supplementation, or increased consumption of ALA-rich foodstuffs, combined with reduced omega-6 (n6) PUFAs intake, could improve the n3/n6 ratio and improve cardiometabolic and lipid profile.

[38] *Zhou J, Liu C, Francis M et al.* **The Causal Effects of Blood Iron and Copper on Lipid Metabolism Diseases: Evidence from Phenome-Wide Mendelian Randomization Study**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33080795
ABSTRACT
Blood levels of iron and copper, even within their normal ranges, have been associated with a wide range of clinical outcomes. The available epidemiological evidence for these associations is often inconsistent and suffers from confounding and reverse causation. This study aims to examine the causal clinical effects of blood iron and copper with Mendelian randomization (MR) analyses. Genetic instruments for the blood levels of iron and copper were curated from existing genome-wide association studies. Candidate clinical outcomes were identified based on a phenome-wide association study (PheWAS) between these genetic instruments and a wide range of phenotypes in 310,999 unrelated individuals of European ancestry from the UK Biobank. All signals passing stringent correction for multiple testing were followed by MR analyses, with replication in independent data sources where possible. We found that genetically predicted higher blood levels of iron and copper are both associated with lower risks of iron deficiency anemia (odds ratio (OR) = 0.75, 95% confidence interval (CI): 0.67-0.85, p = 1.90 × 10(-6) for iron; OR = 0.88, 95% CI: 0.78-0.98, p = 0.032 for copper), lipid metabolism disorders, and its two subcategories, hyperlipidemia (OR = 0.90, 95% CI: 0.85-0.96, p = 6.44 × 10(-4); OR = 0.92, 95% CI: 0.87-0.98, p = 5.51 × 10(-3)) and hypercholesterolemia (OR = 0.90, 95% CI: 0.84-0.95, p = 5.34 × 10(-4); OR = 0.93, 95% CI: 0.89-0.99, p = 0.022). Consistently, they are also associated with lower blood levels of total cholesterol and low-density lipoprotein cholesterol. Multiple sensitivity tests were applied to

assess the presence of pleiotropy and the robustness of causal estimates. Regardless of the approaches, consistent evidence was obtained. Moreover, the unique clinical effects of each blood mineral were identified. Notably, genetically predicated higher blood iron is associated with an enhanced risk of varicose veins (OR = 1.28, 95% CI: 1.15-1.42, p = 4.34 × 10(-6)), while blood copper is positively associated with the risk of osteoarthrosis (OR = 1.07, 95% CI: 1.02-1.13, p = 0.010). Sex-stratified MR analysis further revealed some degree of sex differences in their clinical effects. Our comparative PheWAS-MR study of iron and copper comprehensively characterized their shared and unique clinical effects, highlighting their potential causal roles in hyperlipidemia and hypercholesterolemia. Given the modifiable nature of blood mineral status and the potential for clinical intervention, these findings warrant further investigation.

[39] *Ortiz N, Díaz C*. **Mevalonate pathway as a novel target for the treatment of metastatic gastric cancer**. Oncology letters 2020; 20:320.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33093924
ABSTRACT
Gastric mucosa tumors may present as two distinct major entities: Diffuse and intestinal subtypes. There is no standard treatment for advanced or metastatic gastric cancer. The mevalonate pathway and cholesterol homeostasis are important processes in cancer cells that may be highly relevant in terms of cell growth, survival and metastatic potential. Two model cell lines representing intestinal (NCI-N87) and diffuse (Hs746T) metastatic gastric tumor histological subtypes were treated with different drugs that alter membrane lipid metabolism to determine whether cell proliferation, viability and migration were affected. The results indicated that the cells exhibited significant differences in proliferation when treated with the cholesterol-lowering drug simvastatin, but not with terbinafine, another compound that affects cholesterol synthesis. Only simvastatin affected migration in both cell lines. Reposition studies with mevalonolactone, farnesyl pyrophosphate and geranylgeranyl pyrophosphate in the presence of high and low FBS concentrations indicated that both isoprenoids and cholesterol reversed the antiproliferative effects of simvastatin in gastric cancer cells. The cell lines used in the present study had different sensitivities to several potential anti-neoplastic agents that affect the synthesis of membrane lipids. The diffuse gastric cancer cells were particularly sensitive to simvastatin, suggesting it as an option for combination treatment.

[40] *Arildsen NS, Hedenfalk I*. **Simvastatin is a potential candidate drug in ovarian clear cell carcinomas**. Oncotarget 2020; 11:3660-3674.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33088426
ABSTRACT
Ovarian clear cell carcinomas (OCCC) constitute a rare subtype of epithelial ovarian cancer, lacking efficient treatment options. Based on previous studies, we assessed the anti-proliferative effect of simvastatin, a Rho GTPase interfering drug, in three OCCC cell lines: JHOC-5, OVMANA and TOV-21G, and one high-grade serous ovarian cancer (HGSOC) cell line, Caov3. We used the Rho GTPase interfering drug CID-1067700 as a control. All OCCC cell lines were more sensitive to single-agent simvastatin than the HGSOC cells, while all cell lines were less sensitive to CID-1067700 than to simvastatin. Combinations of carboplatin and simvastatin were generally antagonistic. Most treatments inhibited migration, while only simvastatin and CID-1067700 also disrupted actin organization in the OCCC cell lines. All

treatments induced a G1 arrest in JHOC-5 and TOV-21G cells. Treatments with simvastatin consistently reduced c-Myc protein expression in all OCCC cell lines and displayed evidence of causing both caspase-mediated apoptotic cell death and autophagic response in a cell line dependent manner. Differences between cell lines in response to the treatments were observed and such differences, including e. g. prior treatment, should be investigated further. Conclusively, simvastatin efficiently controlled OCCC proliferation and migration, thus showing potential as a candidate drug for the treatment of OCCC.

[41] *Gkotzamanis V, Panagiotakos D*. **Dietary interventions and cognition: A systematic review of clinical trials**. Psychiatriki 2020; 31:248-256.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33099465
ABSTRACT
Prevalence of Alzheimer's Disease and other forms of dementia is increasing in accordance with the increase of life expectancy and the resulting world population aging, while an effective pharmaceutical treatment is pending. These facts underline the need for development of targeted interventions that could decrease the incidence of dementia. Dietary supplementation, especially sources of ω-3 fatty acids and polyphenols such as fish oil and blueberries respectively, have been reported to have a beneficial effect on cognitive functioning. The aim of this review is to summarize the most recent findings of clinical studies investigating the effect of dietary supplementation on cognitive performance and identify potential effective interventions. For this purpose, PubMed, Scopus and Google Scholar research was conducted and a total of ten studies met the selection criteria. Four of these studies investigated the effect of ω-3 fatty acid supplementation. Two of these presented significant benefits in certain domains of cognitive functions (such as working memory, space imagery efficiency perceptual speed), in full scale IQ as well as prevention of hippocampal atrophy while the remaining two did not report any improvements. Two more studies investigated the effect of polyphenol supplementation and reported minor benefits in spatial memory as well as enhanced stimulation of certain brain regions. One study compared the effect of fish oil and blueberry supplementation as well as their combination and presented cognitive benefits for both fish oil and blueberries but not for their simultaneous administration. Finally, three more studies investigated the effect of DW 2009 soybean, ashwagandha and a nutraceutical formulation and reported cognitive benefits in attention, memory and global cognition respectively for their intervention groups. In total, eight studies investigated interventions on people with Mild Cognitive Impairment or Subjective Cognitive Impairment and all of them reported significant cognitive benefits in some cognitive domains. On the contrary, the remaining two studies included individuals with diagnosed dementia reported minimal to hardly any benefits. Conclusively, the interventions of the studies reviewed seem promising for individuals at risk of dementia, but not for those who are already diagnosed with dementia. However, further research is required to validate their effect as well as determine recommended doses.

[42] *Al Ali R, Vukadinović D, Maziak W et al.* **Cardiovascular effects of waterpipe smoking: a systematic review and meta-analysis**. Reviews in cardiovascular medicine 2020; 21:453-468.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33070549
ABSTRACT

Waterpipe smoking has developed into a major and rapidly growing global tobacco epidemic affecting more than 100 million people worldwide. This study identifies and analyzes comprehensively all available data on the cardiovascular effects of waterpipe smoking. Databases PubMed, EMBASE, Web of Science, and the Cochrane Library were searched for studies published until December 2019 assessing cardiovascular effects of waterpipe smoking. We included experimental, cohort, cross-sectional and case-control studies and excluded systematic reviews, case reports/series and qualitative studies. Studies not conducted in humans or not distinguishing waterpipe smoking from other forms of smoking were also excluded. A total of 42 studies with 46 cardiovascular parameters were eligible for analysis. The meta-analysis included 31 studies with 38,037 individuals. Results showed that one waterpipe smoking session leads to immediate increases in heart rate and blood pressure ($P < 0.001$). Compared to non-smokers, waterpipe smokers had significantly lower high-density lipoprotein levels ($P < 0.001$), higher levels of low-density lipoprotein ($P = 0.04$), triglyceride ($P < 0.001$) and fasting blood glucose ($P = 0.03$) and higher heart rate ($P = 0.04$) with a tendency to have higher blood pressure. Mean heart rate, blood pressure and lipids levels did not differ between waterpipe and cigarette smokers, except for total cholesterol, being higher among waterpipe smokers ($P < 0.001$). Current level of evidence suggests that waterpipe smoking is associated with substantial adverse effects on cardiovascular system, which seem to be similar to those of cigarette smoking. Longitudinal studies are required to scrutinize the magnitude of these effects.

[43] *Schlunk F, Fischer P, Princen HMG et al.* **Effects of Inhibition or Deletion of PCSK9 (Proprotein Convertase Subtilisin/Kexin Type 9) on Intracerebral Hemorrhage Volumes in Mice**. Stroke 2020; 51:e297-e298.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33070710
ABSTRACT

[44] *Skeik N, Nowariak ME, Smith JE et al.* **Lipid-lowering therapies in peripheral artery disease: A review**. Vascular medicine (London, England) 2020:1358863x20957091.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33074778
ABSTRACT
Peripheral artery disease (PAD) is estimated to affect approximately 8.5 million individuals in the US above the age of 40, and is associated with significant morbidity, mortality, and impairment. Despite the significant adverse limb and cardiovascular (CV) outcomes seen in patients with PAD, there is typically less attention paid to risk factor modification relative to other atherosclerotic diseases such as coronary artery disease (CAD) or stroke. In the current literature, statins have been shown to reduce mortality, major adverse CV events, major adverse limb events, and improve symptomatic outcomes in patients with PAD. In addition, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are emerging as an additional lipid-lowering therapy for patients with PAD. However, despite current guideline recommendations based on growing evidence, PAD patients are consistently undertreated with lipid-lowering therapies. We provide an extensive literature review and evidence-based recommendations for the use of statins and PCSK9 inhibitors in patients with PAD.