[1] *Rodriguez VJ, Chahine A, Parrish MS et al.* **The contribution of syndemic conditions to cardiovascular disease risk**. AIDS care 2020:1-9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32397737
ABSTRACT
The syndemic conditions of low education, childhood maltreatment, depression, HIV, alcohol and cocaine use, and obesity have been established as independent risk factors for cardiovascular risk, but research examining the association between syndemic conditions and cardiovascular risk in high-risk populations is lacking. A total of N = 503 participants underwent an ultrasound of the carotid artery to assess for atherosclerotic plaque. Participants, HIV-infected (n = 202) and HIV-uninfected (n = 301) with and without a history of cocaine use, were a mean age of 36.13 years (SD = 9.51); 50% were male, and 62% were African-American. Each syndemic condition was associated with 8% greater odds of atherosclerotic plaque (OR = 1.08), 9% greater odds of systolic blood pressure (OR = 1.09), and 10% greater odds of diastolic blood pressure (OR = 1.10). Multilevel research, interventions, and public policy initiatives are needed to activate stakeholders at each level to maximize their impact at a community level among populations with high rates of syndemic conditions.

[2] *Dikariyanto V, Smith L, Francis L et al.* **Snacking on whole almonds for 6 weeks improves endothelial function and lowers LDL cholesterol but does not affect liver fat and other cardiometabolic risk factors in healthy adults: the ATTIS study, a randomized controlled trial**. The American journal of clinical nutrition 2020; 111:1178-1189.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32412597
ABSTRACT
BACKGROUND: There is convincing evidence that daily whole almond consumption lowers blood LDL cholesterol concentrations, but effects on other cardiometabolic risk factors such as endothelial function and liver fat are still to be determined. OBJECTIVES: We aimed to investigate whether isoenergetic substitution of whole almonds for control snacks with the macronutrient profile of average snack intakes, had any impact on markers of cardiometabolic health in adults aged 30-70 y at above-average risk of cardiovascular disease (CVD). METHODS: The study was a 6-wk randomized controlled, parallel-arm trial. Following a 2-wk run-in period consuming control snacks (mini-muffins), participants consumed either whole roasted almonds (n = 51) or control snacks (n = 56), providing 20% of daily estimated energy requirements. Endothelial function (flow-mediated dilation), liver fat (MRI/magnetic resonance spectroscopy), and secondary outcomes as markers of cardiometabolic disease risk were assessed at baseline and end point. RESULTS: Almonds, compared with control, increased endothelium-dependent vasodilation (mean difference 4.1%-units of measurement; 95% CI: 2.2, 5.9), but there were no differences in liver fat between groups. Plasma LDL cholesterol concentrations decreased in the almond group relative to control (mean difference -0.25 mmol/L; 95% CI: -0.45, -0.04), but there were no group differences in triglycerides, HDL cholesterol, glucose, insulin, insulin resistance, leptin, adiponectin, resistin, liver function enzymes, fetuin-A, body composition, pancreatic fat, intramyocellular lipids, fecal SCFAs, blood pressure, or 24-h heart rate variability. However, the long-phase heart rate variability parameter, very-low-frequency power, was increased during nighttime following the almond treatment compared with control (mean difference 337 ms2; 95% CI: 12, 661), indicating greater parasympathetic regulation. CONCLUSIONS: Whole almonds consumed as snacks

markedly improve endothelial function, in addition to lowering LDL cholesterol, in adults with above-average risk of CVD.This trial was registered at clinicaltrials.gov as NCT02907684.

[3] *Alder M, Bavishi A, Zumpf K et al.* **A Meta-Analysis Assessing Additional LDL-C Reduction from Addition of a Bile Acid Sequestrant to Statin Therapy**. The American journal of medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32416177
ABSTRACT
BACKGROUND: Statins are the first line therapy for reducing low-density lipoprotein cholesterol (LDL-c). However, there are secondary prevention patients who are either intolerant to maximal statin therapy or do not get adequate effects from a high-intensity statin. While data exists for the additional LDL-c lowering effects of ezetimibe, there is no data on additional LDL-c lowering of bile acid sequestrants when combined with statin therapy. OBJECTIVE: To quantify the LDL-c lowering effects of bile acid sequestrants when added to statin therapy. METHODS: Databases (Medline via PubMed, Embase, and the Cochrane Library) were searched for randomized controlled trials comparing statin therapy to statin therapy with the addition of bile acid sequestrants. Nine studies were included in the meta-analysis. A meta-regression was performed to estimate the mean difference in LDL-c between the two groups RESULTS: Without controlling for other variables, data suggests that combining statin with bile acid sequestrant increases the percentage change in LDL-c by 16.2 points on average, compared to statin use alone. CONCLUSION: In patients unable to tolerate an adequate statin dosage, bile acid sequestrants offer a viable alternative with additional LDL-c lowering benefit.

[4] *Guzman-Rivera D, Liempi A, Gonzalez-Herrera F et al.* **Simvastatin improves cardiac function through Notch1 activation in BALB/c mice with chronic Chagas cardiomyopathy**. Antimicrobial agents and chemotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393497
ABSTRACT
Background and Purpose: Chagas disease, caused by the protozoan Trypanosoma cruzi, is endemic in Latin America but distributed worldwide because of migration. Without appropriate treatment, the disease progresses from an acute asymptomatic phase to a chronic, progressive inflammatory cardiomyopathy causing heart failure and death. Despite specific trypanocidal therapy, heart damage progression cannot be stopped or reverted. As part of their pleiotropic actions, statins can modulate chagasic myocarditis by inducing the production of 15-epi-lipoxin A4 (15-epi-LXA4), a proresolution lipid mediator in inflammation. Furthermore, several reports suggest that simvastatin activates the Notch pathway after stroke in cerebral endothelial cells, enhancing blood flow by promoting angiogenesis. Thus, statins are an attractive therapeutic strategy for modulating the Notch pathway to revert the chronic heart damage induced by T. cruzi Experimental Approach: BALB/c mice chronically infected with T. cruzi were treated with 1 mg/kg/day simvastatin or 25 mug/kg/day 15-epi-LXA4 for 20 days. During the treatment period, cardiac function was evaluated by echocardiography. At 80 days postinfection, the heart tissues were assessed for Notch1 activity.Key Results: T. cruzi infection activated the Notch1 pathway, and simvastatin (but not 15-epi-lipoxin A4) produced a further increase in that activity, correlating with improvement in the ejection fraction and histopathologic findings typical of T. cruzi infection, including improvements in inflammation

and fibrosis. Moreover, simvastatin increased isolectin B4+ cells suggesting active angiogenesis in the chronically infected hearts without altering the parasitic load.Conclusions and Implications: Simvastatin, probably acting through the Notch1 pathway, decreases inflammation, improving cardiac function in chronically T. cruzi-infected mice.

[5] *Katsiki N, Banach M, Mikhailidis DP*. **Lipid-lowering therapy and renin-angiotensin-aldosterone system inhibitors in the era of the COVID-19 pandemic**. Archives of medical science : AMS 2020; 16:485-489.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32399093
ABSTRACT

[6] *Reiner Z, Hatamipour M, Banach M et al.* **Statins and the COVID-19 main protease: in silico evidence on direct interaction**. Archives of medical science : AMS 2020; 16:490-496.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32399094
ABSTRACT
Introduction: No proven drug and no immunisation are yet available for COVID-19 disease. The SARS-CoV-2 main protease (Mpro), a key coronavirus enzyme, which is a potential drug target, has been successfully crystallised. There is evidence suggesting that statins exert anti-viral activity and may block the infectivity of enveloped viruses. The aim of this study was to assess whether statins are potential COVID-19 Mpro inhibitors, using a molecular docking study. Material and methods: Molecular docking was performed using AutoDock/Vina, a computational docking program. SARS-CoV-2 Mpro was docked with all statins, while antiviral and antiretroviral drugs - favipiravir, nelfinavir, and lopinavir - were used as standards for comparison. Results: The binding energies obtained from the docking of 6LU7 with native ligand favipiravir, nelfinavir, lopinavir, simvastatin, rosuvastatin, pravastatin, pitavastatin, lovastatin, fluvastatin, and atorvastatin were -6.8, -5.8, -7.9, -7.9, -7.0, -7.7, -6.6, -8.2, -7.4, -7.7, and -6.8 kcal/mol, respectively. The number of hydrogen bonds between statins and amino acid residues of Mpro were 7, 4, and 3 for rosuvastatin, pravastatin, and atorvastatin, respectively, while other statins had two hydrogen bonds. Conclusions: These results indicate, based upon the binding energy of pitavastatin, rosuvastatin, lovastatin, and fluvastatin, that statins could be efficient SARS-CoV-2 Mpro inhibitors. This is supported by the fact that the effects of some statins, especially pitavastatin, have a binding energy that is even greater than that of protease or polymerase inhibitors. However, further research is necessary to investigate their potential use as drugs for COVID-19.

[7] *Tian X, Zuo Y, Chen S et al.* **Association of changes in lipids with risk of myocardial infarction among people without lipid-lowering therapy**. Atherosclerosis 2020; 301:69-78.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32388104
ABSTRACT
BACKGROUND AND AIMS: Although serum lipids are widely accepted as independent predictors of myocardial infarction (MI), there is insufficient evidence for associations of changes in lipid levels with MI. The present study aimed at investigating the associations between changes in lipids and incidence of MI in people without lipid-lowering therapy. METHODS: 64,031 Chinese participants (mean age: 53.42 +/- 11.95 years) without previous MI were enrolled in the study. The participants were divided into four categories based on quartiles of lipid changes. Multivariable Cox regression models were used to calculate hazard

ratios (HRs) and 95% confidence intervals (CIs) for MI. RESULTS: During a median follow-up of 7.03 years, 599 individuals developed MI. After adjustment for covariates, increased total cholesterol (TC), increased low-density lipoprotein cholesterol (LDL-C), increased non-high-density lipoprotein cholesterol (non-HDL-C), and decreased high-density lipoprotein cholesterol (HDL-C) were associated with elevated risk of MI, with HRs (95% CIs) in the highest quartile group compared with the lowest quartile group of 1.56 (1.21-2.01), 1.96 (1.49-2.57), 1.95 (1.52-2.50), and 0.69 (0.53-0.90), respectively. However, changes in triglyceride (TG) were not associated with MI risk (p = 0.8030). CONCLUSIONS: Changes in levels of TC, LDL-C, non-HDL-C, and HDL-C, but not TG, were associated with risk of MI. Early detection and control of lipid levels may be beneficial and necessary for young people and those with healthy lipid levels at baseline.

[8] *Virta J, Hellberg S, Liljenback H et al.* **Effects of dipeptidyl peptidase 4 inhibition on inflammation in atherosclerosis: A (18)F-fluorodeoxyglucose study of a mouse model of atherosclerosis and type 2 diabetes**. Atherosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32386751
ABSTRACT
BACKGROUND AND AIMS: Dipeptidyl peptidase 4 (DPP-4) inhibitors have anti-inflammatory and atheroprotective effects. We evaluated the effects of the DPP-4 inhibitor linagliptin on atherosclerotic plaque and hepatic inflammation using histology and 2-deoxy-2-[(18)F]-fluoro-d-glucose ((18)F-FDG), a positron emission tomography tracer of inflammation, in a mouse model of hypercholesterolemia and type 2 diabetes. METHODS: Igf2/Ldlr(-/-)Apob(100/100) mice were fed a high-fat diet (HFD) for 8 weeks and then randomly allocated to receive HFD (n = 14), or HFD with added linagliptin (n = 15) for additional 12 weeks. Five mice fed a chow diet were studied as an additional control. At the end of the study, glucose tolerance, aortic and liver uptake of (18)F-FDG, and histology were studied. RESULTS: Mice in linagliptin and HFD groups had similar fasting glucose concentrations, but linagliptin improved glucose tolerance. Aortas of linagliptin and HFD groups showed advanced atherosclerotic plaques with no difference in the mean intima-to-media ratio or number of macrophages in the plaques. Autoradiography showed similar (18)F-FDG uptake by atherosclerotic plaques in linagliptin and HFD groups (plaque-to-wall ratio: 1.7 +/- 0.25 vs. 1.6 +/- 0.21; p = 0.24). In the liver, linagliptin reduced the histologic inflammation score but had no effect on (18)F-FDG uptake. Compared with chow diet, uptake of (18)F-FDG was similar in the aorta, but higher in the liver after HFD. CONCLUSIONS: Linagliptin therapy improved glucose tolerance and reduced hepatic inflammation but had no effect on plaque burden or atherosclerotic inflammation, as determined by histology and (18)F-FDG uptake, in atherosclerotic mice with type 2 diabetes.

[9] *Penson PE*. **What's new in lipid-lowering pharmacology? Integrating basic and clinical research to improve patient outcomes**. British journal of clinical pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32415737
ABSTRACT

[10] *Gomes HA, Garcia P, Diogo L et al.* **Experience on statin therapy in paediatric age: retrospective study in a Portuguese referral centre**. Cardiology in the young 2020:1-12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32408915

ABSTRACT
BACKGROUND: The use of statins in children, although not frequent, is recommended in specific clinical contexts, namely, familial hypercholesterolaemia, conditions carrying a moderate-high cardiovascular risk and sub-optimal cholesterol levels after implementation of lifestyle modifications. The aim of this study is to characterise children with dyslipidaemia managed with statins, followed at a tertiary referral centre in central Portugal. METHODS AND RESULTS: The authors carried out a retrospective and descriptive study made up of 66 patients (50% males, mean age of therapy onset 11.9 years) followed up at the Cardiovascular Clinic of a tertiary referral centre between January, 2012, and May, 2018. Clinical, analytical, and echocardiographic parameters were analysed. About 60.6% had clinical and/or molecular diagnosis of familial hypercholesterolaemia. On average, each patient had three cardiovascular risk factors, obesity (31%) being most prevalent, followed by arterial hypertension (14%). Statin therapy showed a statistically significant reduction in the lipid profile, particularly in the total cholesterol (23%) and low-density lipoprotein cholesterol (30%) levels, as well as in the carotid intima-media thickness ($p = 0.015$). Hepatic and muscle integrity markers were within normal range. CONCLUSIONS: Statins are safe and efficient in the management of children with hypercholesterolaemia. Our study showed that apart from its lipid-lowering properties, it also reduced significantly the carotid intima-media thickness and, implicitly, the cardiovascular risk of these patients.

[11] *Sattari R, Palizban A, Khanahmad H*. **Single-Strand DNA-Like Oligonucleotide Aptamer Against Proprotein Convertase Subtilisin/Kexin 9 Using CE-SELEX: PCSK9 Targeting Selection**. Cardiovascular drugs and therapy / sponsored by the International Society of Cardiovascular Pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32415571

ABSTRACT
BACKGROUND: Proprotein convertase subtilisin/kexin 9 (PCSK9) serves a key regulatory function in the metabolism of low-density lipoprotein (LDL)-cholesterol (LDL-C) through interaction with the LDL receptor (LDLR) followed by its destruction that results in the elevation of the plasma levels of LDL-C. The aims of the present study were to separate and select a number of single-stranded DNA (ssDNA) aptamers against PCSK9 from a library pool ($n > 10(12)$) followed by their characterization. METHODS: The aptamers obtained from the DNA-PCSK9 complexes which presented the highest affinity against PCSK9 were separated and selected using capillary electrophoresis evolution of ligands by exponential enrichment (CE-SELEX). The selected aptamers were amplified and cloned into a T/A vector. The plasmids from the positive clones were extracted and sequenced. The Mfold web server was used to predict the secondary structure of the aptamers. RESULTS: Following three rounds of CE-SELEX, the identified anti-PCSK9 ssDNA aptamers, namely aptamer 1 (AP-1) and aptamer 2 (AP-2), presented half maximal inhibitory concentrations of 325 and 327 nM, lowest dissociation constants of 294 and 323 nM, and most negative Gibbs free energy values of -9.17 and - 8.28 kcal/mol, respectively. CONCLUSION: The results indicated that the selected aptamers (AP-1 and AP-2) induced potent inhibitory effects against PCSK9. Further in vivo studies demand to find out AP-1 and AP-2 aptamers as suitable candidates, instead of antibodies, for using in therapeutic purposes in patients with hypercholesterolemia and cardiovascular disease.

[12] *Zhang X, Xing L, Jia X et al.* **Comparative Lipid-Lowering/Increasing Efficacy of 7 Statins in Patients with Dyslipidemia, Cardiovascular Diseases, or Diabetes Mellitus: Systematic Review and Network Meta-Analyses of 50 Randomized Controlled Trials**. Cardiovascular therapeutics 2020; 2020:3987065.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32411300

ABSTRACT

Objective: The drug efficacy may differ among different statins, and evidence from head-to-head comparisons is sparse and inconsistent. The study is aimed at comparing the lipid-lowering/increasing effects of 7 different statins in patients with dyslipidemia, cardiovascular diseases, or diabetes mellitus by conducting systematic review and network meta-analyses (NMA) of the lipid changes after certain statins' use. Methods: In this study, we searched four electronic databases for randomized controlled trials (RCTs) published through February 25, 2020, comparing the lipid-lowering efficacy of no less than two of the included statins (or statin vs. placebo). Three reviewers independently extracted data in duplicate. Firstly, mixed treatment overall comparison analyses, in the form of frequentist NMAs, were conducted using STATA 15.0 software. Then, subgroup analyses were conducted according to different baseline diseases. At last, sensitivity analyses were conducted according to age and follow-up duration. The trial was registered with PROSPERO (number CRD42018108799). Results: As a result, seven statin monotherapy treatments in 50 studies (51956 participants) were used for the analyses. The statins included simvastatin (SIM), fluvastatin (FLU), atorvastatin (ATO), rosuvastatin (ROS), lovastatin (LOV), pravastatin (PRA), and pitavastatin (PIT). In terms of LDL-C lowering, rosuvastatin ranked 1(st) with a surface under cumulated ranking (SUCRA) value of 93.1%. The comparative treatment efficacy for LDL-C lowering was ROS>ATO>PIT>SIM>PRA>FLU>LOV>PLA. All of the other ranking and NMA results were reported in SUCRA plots and league tables. Conclusions: According to the NMAs, it can be concluded that rosuvastatin ranked 1(st) in LDL-C, ApoB-lowering efficacy and ApoA1-increasing efficacy. Lovastatin ranked 1(st) in TC- and TG-lowering efficacy, and fluvastatin ranked 1(st) in HDL-C-increasing efficacy. The results should be interpreted with caution due to some limitations in our review. However, they can provide references and evidence-based foundation for drug selection in both statin monotherapies and statin combination therapies.

[13] *Dei Cas M, Zulueta A, Mingione A et al.* **An Innovative Lipidomic Workflow to Investigate the Lipid Profile in a Cystic Fibrosis Cell Line**. Cells 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32408521

ABSTRACT

Altered lipid metabolism has been associated to cystic fibrosis disease, which is characterized by chronic lung inflammation and various organs dysfunction. Here, we present the validation of an untargeted lipidomics approach based on high-resolution mass spectrometry aimed at identifying those lipid species that unequivocally sign CF pathophysiology. Of n.13375 mass spectra recorded on cystic fibrosis bronchial epithelial airways epithelial cells IB3, n.7787 presented the MS/MS data, and, after software and manual validation, the final number of annotated lipids was restricted to n.1159. On these lipids, univariate and multivariate statistical approaches were employed in order to select relevant lipids for cellular phenotype discrimination between cystic fibrosis and HBE healthy cells. In cystic fibrosis IB3 cells, a pervasive alteration in the lipid metabolism revealed changes in the classes of ether-linked phospholipids, cholesterol esters, and glycosylated sphingolipids. Through functions

association, it was evidenced that lipids variation involves the moiety implicated in membrane composition, endoplasmic reticulum, mitochondria compartments, and chemical and biophysical lipids properties. This study provides a new perspective in understanding the pathogenesis of cystic fibrosis and strengthens the need to use a validated mass spectrometry-based lipidomics approach for the discovery of potential biomarkers and perturbed metabolism.

[14] *Bouzkova K*. **State of the art in diagnostics of ischemic heart disease and current recommended therapeutic approach**. Cesk Patol 2020; 56:13-17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393041
ABSTRACT
Several changes have occurred during last few years in diagnostics and treatment of the ischemic heart disease, especially due to introduction of so called high-sensitive troponins, implementation of new antiplatelet drugs, using of drug-eluting stents in percutaneous coronary interventions or novel definitions of acute myocardial infarction types. The European Society of Cardiology and Czech Society of Cardiology established new recommendations for management of both acute and chronic forms of the ischemic heart disease. Recently discovered inhibitors of the PCSK9 molecule that have been slowly introduced in the clinical practice represent a breakthrough in the treatment of dyslipidemia. Future research will certainly aim at detection of early forms of the atherosclerotic involvement of the coronary arteries.

[15] *Wu DF, Wu YX, Deng JL*. **Changes in Homocysteine Levels Affect Serum Lipid Response to Atorvastatin in Patients With Acute Coronary Syndrome: A Retrospective Observational Study**. Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis 2020; 26:1076029620920369.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32392083
ABSTRACT
OBJECTIVE: The present study investigated whether changes in serum homocysteine (Hcy) levels modify the effects of atorvastatin treatment on blood lipid parameters in patients with acute coronary syndrome (ACS). METHODS: A total of 159 patients with ACS who received regular, long-term treatment with 20 mg/d atorvastatin were included. Depending on the changes in Hcy parameters, they were divided into Hcy reduction (HR) and Hcy elevation (HE) groups. RESULTS: After long-term atorvastatin treatment, total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), apolipoprotein (Apo) B, and Hcy levels were decreased ($P < .05$), and the ApoAI level was increased ($P < .01$). Correlation and stratified analysis showed that Hcy or hyperhomocysteinemia was correlated with blood lipids. In both the HE and HR groups, the TC, LDL-C, and ApoB levels after treatment were lower than those before treatment ($P < .01$), and the ApoAI level was increased compared with that before treatment ($P < .05$). There was no difference in the reduction of TC, LDL-C, and ApoB levels or in the increase of ApoAI level (P interaction > .05) between the 2 groups. However, there was a clear opposite trend of the effect of atorvastatin on TG and high-density lipoprotein cholesterol (HDL-C) levels between the HR and HE groups (P interaction < .05). In the HR group, the HDL-C level was increased ($P < .05$), and TGs were decreased compared with those before treatment ($P < .01$). Nevertheless, in the HE group, the HDL-C level was

decreased (P < .05), and TGs (P < .05) were increased compared with those before treatment. CONCLUSION: The effects of atorvastatin on TGs and HDL-C depend on changes in Hcy levels. Patients with a reduced Hcy level after atorvastatin treatment had more favorable lipid parameters.

[16] *Gundlach K, Wolf K, Salem I et al.* **Safety of Candesartan, Amlodipine, and Atorvastatin in Combination: Interaction Study in Healthy Subjects**. Clinical pharmacology in drug development 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32388918
ABSTRACT
For efficient cardiovascular risk protection antihypertensive treatment is often combined with cholesterol-lowering treatment, although solid data of interaction and side effects are missing. This is a prospective, single-center interaction study conducted in a fixed sequence design at steady state of candesartan, amlodipine, and atorvastatin. Five-day monotherapy of candesartan 8 mg was followed by 5-day atorvastatin 40 mg monotherapy and subsequently 9-day amlodipine 5 mg monotherapy; each treatment separated by washout phases. Immediately after amlodipine monotherapy, all 3 drugs were administered concomitantly for 5 days. Pharmacokinetic parameters as well as safety were assessed. Eighteen healthy subjects enrolled and completed the study. No significant difference in the maximum concentration (Cmax) and the area the under plasma concentration-time curve (AUC) for amlodipine and AUC of atorvastatin was detected following combination versus monotherapy. Cmax of atorvastatin decreased slightly but clinically not relevantly when given in combination. A statistically significant but not below 0.80-fold decrease between candesartan following combination vs monotherapy was detected for Cmax and AUC. In general, all treatments were well tolerated. Concluding, systemic exposure of candesartan, amlodipine, and atorvastatin is not clinically significantly changed upon coadministration. These data support a fixed-dose combination of the 3 components for dual cardiovascular risk prevention.

[17] *Perkins BA*. **Sounding the alarm on rising diabetes-related amputations**. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2019; 191:E953-e954.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32392480
ABSTRACT

[18] *Huang S, Xu Q, Liu L et al.* **Effect of Green Tea and (-)-epigallocatechin Gallate on the Pharmacokinetics of Rosuvastatin**. Current drug metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32407265
ABSTRACT
BACKGROUND: Green tea can inhibit OATPs, so it may interact with the substrate of OATPs, such as rosuvastatin. OBJECTIVE: This study aimed to investigate the effects of green tea on the pharmacokinetics of rosuvastatin and its mechanism. METHODS: Male Sprague-Dawley rats received different doses of green tea extract (GTE) and (-)- epigallocatechin-3-gallate (EGCG). Caco-2 cells and OATP1B1-HEK293T cells were used in drug uptake and transport assay. The matrix concentrations of rosuvastatin and catechins were determined by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). RESULTS: GTE and EGCG were both found to increase the area under the plasma concentration-time

curve (AUC0-infinity) of rosuvastatin ((p<0.050). In the Caco-2 cell model, the uptake and transport of rosuvastatin in the GTE groups were 1.94-fold (p<0.001) and 2.11-fold (p<0.050) higher, respectively, than those of the control group. However, in the EGCG group, the uptake and transport of rosuvastatin were decreased by 22.62% and 44.19%, respectively (p<0.050). In the OATP1B1- HEK293T cell model, the OATP1B1-mediated rosuvastatin uptake was decreased by GTE to 35.02% of that in the control (p<0.050) and was decreased by EGCG to 45.61% of that in the control (p<0.050). CONCLUSION: GTE increased the systemic rosuvastatin exposure in rats. The mechanism may include an increase in rosuvastatin absorption and a decrease in liver distribution by inhibiting OATP1B1. EGCG may be the main ingredient of green tea that affects the pharmacokinetic parameters of rosuvastatin. Our results showed the importance of conducting green tea-rosuvastatin study.

[19] *Feldman DI, Pacor JM, Blumenthal RS, Nasir K*. **2019 clinical trials in lipid lowering**. Current opinion in cardiology 2020; 35:319-324.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32412963
ABSTRACT
PURPOSE OF REVIEW: Lipid-lowering therapies play a major role in reducing atherosclerotic cardiovascular disease (ASCVD). This article reviews the most recent lipid-lowering therapy trials, many of which provide a unique opportunity to further reduce low-density lipoprotein cholesterol (LDL-C) levels and ASCVD risk on top of statin therapy, and in doing so further decrease the number of future major adverse cardiovascular events. RECENT FINDINGS: Although statin therapy has been the mainstay of treatment for lowering LDL-C levels for many years, many individuals require additional or alternative options for further reducing their risk. Trials on previously studied therapies, such as PCSK9 inhibitors, and new therapies, including inclisiran, bempedoic acid and icosapent ethyl demonstrate significant potential for further lowering of LDL-C levels and risk for events on top of maximally tolerated statin therapy with favourable side effect profiles. SUMMARY: As therapies for ASCVD prevention continue to emerge, clinicians will need to identify the appropriate treatment for individuals based on their estimated risk and risk-enhancing factors. When statin therapy is either not sufficient or patients do not tolerate adequate statin therapy, relying on newer therapies, such as PCSK9-inhibitors, inclisiran, bempedoic acid and icosapent ethyl, will be critical to maximize risk factor profiles to reduce adverse outcomes.

[20] *Babinska A, Clement CC, Li Y et al.* **In vivo data: treatment with the F11R/JAM-A peptide 4D decreases mortality and reduces the generation of atherosclerotic plaques in ApoE-deficient mice**. Data in brief 2020; 30:105516.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32395574
ABSTRACT
The data in this article focus on the F11 Receptor (F11R/JAM-A; Junctional Adhesion Molecule-A; JAM-A, F11R), a cell adhesion protein constitutively expressed on the membrane surface of circulating platelets and localized within the tight junctions of healthy endothelial cells (ECs). Previous reports have shown that F11R/JAM-A plays a critical role in the adhesion of platelets to an inflamed endothelium due to its' pathological expression on the luminal surface of the cytokine-inflamed endothelium. Since platelet adhesion to an inflamed endothelium is an early step in the development of atherosclerotic plaque formation, and with time, resulting in heart attacks and stroke, we conducted a long-term, study utilizing the

atherosclerosis-prone ApoE (-/-) mice to attempt a blockade of the formation of atherosclerotic plaques by preventing the adhesion of platelets to the inflamed vasculature in vivo. Utilizing a nonhydrolyzable peptide derived from an amino acid sequence of F11R/JAM-A, peptide 4D, we have shown in culture that the adhesion of platelets to the inflamed endothelial cells could be blocked by peptide 4D. The present data demonstrate the positive health benefits of chronic peptide 4D administration to the atherosclerosis-prone ApoE(-/-) mice, and provides new information for potential use of this F11R derived peptide in the prevention of atherosclerosis. The data presented in this article provide further experimental support for the study presented in Babinska et al., Atherosclerosis 284 (2019) 92-101.

[21] *Bajaj HS, Brown RE, Jiandani D et al.* **Goal achievement of A1C and LDL in a Randomized Trial Comparing Colesevelam vs. Ezetimibe: GOAL-RCT**. Diabetes Obes Metab 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32406601
ABSTRACT
AIMS: To compare the efficacy and safety of colesevelam and ezetimibe as second-line LDL lowering options in type 2 diabetes (T2D). MATERIALS AND METHODS: GOAL-RCT is a 24-week, open label, randomized, pragmatic clinical trial. Subjects with T2D with uncontrolled A1C (7.1-10%) and LDL-c (>2.0 mmol/L) were randomized 1:1 to colesevelam 3.75 g or ezetimibe 10 mg daily. The primary composite outcome was the proportion of participants achieving LDL-c target </=2.0 mmol/L and A1C target </=7.0%. Intention to treat analysis was performed. RESULTS: 200 subjects were enrolled: mean age 59 +/- 10 years; mean A1C 8.0%; mean LDL-c 2.5 mmol/L; 97% on statin therapy. The primary composite outcome was achieved by similar proportion of participants with colesevelam (14.6%) and ezetimibe (10.5%), pnon-inferiority < 0.001, psuperiority = 0.41. LDL-c reduction from baseline was less with colesevelam compared to ezetimibe (14.0% vs. 23.2%, p < 0.01), as was the proportion of subjects achieving LDL-c target </=2.0 mmol/L (47.6% and 67.0%, respectively; p = 0.007). Mean A1C was reduced with colesevelam (-0.26 +/- 0.10%), while no change was observed with ezetimibe (difference p = 0.06). Adverse events (AE) and discontinuation rates were higher for colesevelam (20.2% and 31.1%) compared to ezetimibe (7.2% and 6.2%), respectively. CONCLUSIONS: Among subjects with T2D, the initiation of colesevelam or ezetimibe led to similar achievement of primary composite outcome (LDL-c and A1c within target), with ezetimibe recording a greater LDL-c reduction and better toleratability than colesevelam. CLINICAL TRIAL REGISTRATION: NCT02682680.

[22] *Saisho Y.* **SGLT2 Inhibitors: the Star in the Treatment of Type 2 Diabetes?** Diseases (Basel, Switzerland) 2020; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32403420
ABSTRACT
Sodium-glucose cotransporter 2 (SGLT2) inhibitors are a novel class of oral hypoglycemic agents which increase urinary glucose excretion by suppressing glucose reabsorption at the proximal tubule in the kidney. SGLT2 inhibitors lower glycated hemoglobin (HbA1c) by 0.6-0.8% (6-8 mmol/mol) without increasing the risk of hypoglycemia and induce weight loss and improve various metabolic parameters including blood pressure, lipid profile and hyperuricemia. Recent cardiovascular (CV) outcome trials have shown the improvement of CV and renal outcomes by treatment with the SGLT2 inhibitors, empagliflozin, canagliflozin, and

dapagliflozin. The mechanisms by which SGLT2 inhibitors improve CV outcome appear not to be glucose-lowering or anti-atherosclerotic effects, but rather hemodynamic effects through osmotic diuresis and natriuresis. Generally, SGLT2 inhibitors are well-tolerated, but their adverse effects include genitourinary tract infection and dehydration. Euglycemic diabetic ketoacidosis is a rare but severe adverse event for which patients under SGLT2 inhibitor treatment should be carefully monitored. The possibility of an increase in risk of lower-extremity amputation and bone fracture has also been reported with canagliflozin. Clinical trials and real-world data have suggested that SGLT2 inhibitors improve CV and renal outcomes and mortality in patients with type 2 diabetes (T2DM), especially in those with prior CV events, heart failure, or chronic kidney disease. Results of recent trials including individuals without diabetes may change the positioning of this drug as "a drug for cardiorenal protection". This review summarizes the potential of SGLT2 inhibitors and discusses their role in the treatment of T2DM.

[23] *Saha P, Shumate JL, Caldwell JG et al.* **Inter-domain dynamics drive cholesterol transport by NPC1 and NPC1L1 proteins**. eLife 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32410728
ABSTRACT
Transport of LDL-derived cholesterol from lysosomes into the cytoplasm requires NPC1 protein; NPC1L1 mediates uptake of dietary cholesterol. We introduced single disulfide bonds into NPC1 and NPC1L1 to explore the importance of inter-domain dynamics in cholesterol transport. Using a sensitive method to monitor lysosomal cholesterol efflux, we found that NPC1's N-terminal domain need not release from the rest of the protein for efficient cholesterol export. Either introducing single disulfide bonds to constrain lumenal/extracellular domains or shortening a cytoplasmic loop abolishes transport activity by both NPC1 and NPC1L1. The widely prescribed cholesterol uptake inhibitor, ezetimibe, blocks NPC1L1; we show that residues that lie at the interface between NPC1L1's three extracellular domains comprise the drug's binding site. These data support a model in which cholesterol passes through the cores of NPC1/NPC1L1 proteins; concerted movement of various domains is needed for transfer and ezetimibe blocks transport by binding to multiple domains simultaneously.

[24] *Sabouret P, Galati G, Angoulvant D et al.* **THE INTERPLAY BETWEEN CARDIOLOGY AND DIABETOLOGY: A RENEWED COLLABORATION TO OPTIMIZE CARDIOVASCULAR PREVENTION AND HEART FAILURE MANAGEMENT**. European heart journal. Cardiovascular pharmacotherapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32402065
ABSTRACT
Type 2 diabetes mellitus (T2DM) portends high risk of atherosclerotic cardiovascular events and of cardiovascular mortality, moreover this group of patients has a very high probability of developing heart failure (HF). In this review, we discuss new advances in pharmacological treatment both in cardiovascular prevention and in HF management with a special focus on T2DM patients. A large number of randomized clinical trials and metanalyses provided strong evidence about therapeutic strategies acting on glucose metabolism such as GLP-1 RA and SGLT2i and about lipid-lowering treatment such as PCSK9i and Icosapent Ethyl. Moreover, SGLT2i demonstrated strong evidence of benefit particularly in HF management both in diabetic and non-diabetic patients. The pathophysiological bases of multiple mechanisms of

benefit of this class of drug explain the unexpected and remarkable results demonstrated both by prevention trials and by trials dedicated only to HF (like DAPA-HF). These, new drugs in the cardiovascular therapeutic armamentarium are establishing a new comprehensive approach from prevention to therapy of HF, giving more emphasis on HF classification in four stages (A-->D). New therapies, which are on the horizon, promise to further reduce cardiovascular mortality and morbidity in HF patients irrespective of diabetic status.

[25] *Siniscalchi C*. **Protective role of statins during anticoagulation for venous thromboembolism: beyond their lipid lowering effect?** European journal of internal medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32389501
ABSTRACT

[26] *Munkhaugen J, Sverre E, Peersen K et al.* **Is the novel LDL-cholesterol goal <1.4 mmol/L achievable without a PCSK9 inhibitor in a chronic coronary population from clinical practice?** European journal of preventive cardiology 2020:2047487320923187.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32397790
ABSTRACT

[27] *Zhang Q, Fan X, Ye R et al.* **The Effect of Simvastatin on Gut Microbiota and Lipid Metabolism in Hyperlipidemic Rats Induced by a High-Fat Diet**. Frontiers in pharmacology 2020; 11:522.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32410994
ABSTRACT
The objective of this study was to investigate the effects of simvastatin (SIM) on lipid metabolism disorders and gut microbiota in high-fat diet-induced hyperlipidemic rats. The obtained results revealed that feeding rats with SIM (20 mg/kg/day) significantly decreased serum lipid level and inhibited hepatic lipid accumulation and steatosis. Histological analysis further indicated that SIM reduced lipid deposition in adipocytes and hepatocytes in comparison with that of the HFD group. The underlying mechanisms of SIM administration against HFD-induced hyperlipidemia were also studied by UPLC-Q-TOF/MS-based liver metabonomics coupled with pathway analysis. Metabolic pathway enrichment analysis of liver metabolites with significant difference in abundance indicated that fatty acids metabolism and amino acid metabolism were the main metabolic pathways altered by SIM administration. Meanwhile, operational taxonomic units (OTUs) analysis revealed that oral administration of SIM altered the composition of gut microbiota, including Ruminococcaceae (OTU960) and Lactobacillus (OTU152), and so on. Furthermore, SIM treatment also regulated the mRNA levels of the genes involved in lipid and cholesterol metabolism. Immunohistochemistry (IHC) analysis of the liver-related proteins (CD36, CYP7A1 and SREBP-1C) showed that oral administration of SIM could regulate the levels of the protein expression related to hepatic lipid metabolism.

[28] *Dousdampanis P, Assimakopoulos SF, Syrocosta I et al.* **Alirocumab in a high cardiovascular risk patient on hemodialysis with liver abnormalities**. Hemodial Int 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32400094
ABSTRACT

We present a male diabetic type 2 patient on hemodialysis (HD) with high cardiovascular (CVD) risk and hyperlipidemia. The patient was under cholesterol-lowering therapy with statin and ezetimibe but he was obligated to discontinue due to chronic hepatitis C virus infection. Statins and ezetimibe may exert a potential hepatotoxic effect and for this reason, we attempted to find an alternative treatment to prevent CVD. Given that a potential hepatotoxic effect has not been reported for Abs SPCK9, we administered alirocumab 150 mg every 2 weeks for a total of 8 weeks. Low-density lipoprotein levels have decreased and no side effects have been observed. In conclusion, alirocumab is a safe and efficient alternative therapy approach for HD patients with high CVD risk and liver abnormalities. We suggest that SPCK 9 inhibitors should be considered as a first line treatment for lowering cholesterol in this specific patient group.

[29] *Chang PC, Tai WC, Luo HT et al.* **Core-Shell poly-(D,l-Lactide-co-Glycolide)-chitosan Nanospheres with simvastatin-doxycycline for periodontal and osseous repair**. Int J Biol Macromol 2020; 158:627-635.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32387616
ABSTRACT
This study aimed to evaluated the potential of core-shell poly(D,l-lactide-co-glycolide)-chitosan (PLGA-chitosan) nanospheres encapsulating simvastatin (SIM) and doxycycline (DOX) for promoting periodontal and large-sized osseous defects. SIM, and/or DOX were encapsulated in PLGA-chitosan nanospheres using double emulsion technique and were delivered to sites of experimental periodontitis and large-sized mandibular osseous defects of rats for 1-4 weeks. The resultant nanospheres were ~ 200 nm diameter with distinct core-shell structure and released SIM and DOX sustainably for 28 days. DOX and SIM-DOX nanospheres significantly inhibited P. gingivalis and S. sanguinis. In experimental periodontitis sites, SIM-DOX nanospheres significantly down-regulated IL-1b and MMP-8 and significantly reduced bone loss. In mandibular osseous defects, VEGF was up-regulated, and osteogenesis was significantly augmented with SIM nanospheres treatment. In conclusion, core-shell PLGA-chitosan nanospheres released SIM and DOX sustainably. SIM-DOX and SIM nanospheres could be considered to promote the repair of infected periodontal sites and non-infected osseous defects respectively.

[30] *Hartz J, Krauss RM, Gottsater M et al.* **Lipoprotein Particle Predictors of Arterial Stiffness after 17 Years of Follow Up: The Malmo Diet and Cancer Study**. Int J Vasc Med 2020; 2020:4219180.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32411471
ABSTRACT
Background: Central arterial stiffness is a surrogate of cardiovascular risk and predicts cardiovascular mortality. Apolipoprotein B lipoproteins are also established cardiovascular risk factors. It is not known whether specific lipoprotein subclasses measured in the Malmo Diet and Cancer Study and previously shown to be associated with coronary heart disease also predict arterial stiffening after a mean period of 17 years. Methods: Lipoprotein particle analysis was performed on 2,505 men and women from Malmo, Sweden, from 1991 to 1994, and arterial stiffness was assessed by carotid-femoral pulse wave velocity (c-fPWV) on this same cohort from 2007 to 2012. Associations between c-fPWV and lipoprotein particles were determined with multiple linear regression, controlling for sex, presence of diabetes, waist-to-

hip circumference, and smoking status at baseline, as well as heart rate (measured at the carotid artery), mean arterial pressure, antihypertensive and lipid-lowering medications, C-reactive protein (CRP), and age at the time of c-fPWV measurement. Results: The results confirm that triglycerides (TG) and high-density lipoprotein cholesterol (HDL-c) but not low-density lipoprotein cholesterol (LDL-c) predict c-fPWV. We identify a positive predictive association for very small, small, and medium (high risk), but not large LDL particles. There was a negative association for large HDL particles. The relationships between c-fPWV and high-risk LDL particles were unaffected by adjusting for LDL-c or CRP and were only mildly attenuated by adjusting for the homeostatic model for insulin resistance (HOMA-IR). Due to the collinearity of very small, small, and medium LDL particles and dyslipidemia (elevated TG and decreased HDL-c), the observed relationship between c-fPWV and high-risk LDL particles became insignificant after controlling for the concentration of HDL-c, large cholesterol-rich HDL particles, and TG. Conclusions: The development of central arterial stiffness previously associated with combined dyslipidemia may be mediated in part by LDL particles, particularly the very small-, small-, and medium-sized LDL particles.

[31] *Parhofer KG*. **[Lipidology update : Evidence-based treatment of dyslipidemia]**. Internist (Berl) 2020; 61:573-586.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32394074
ABSTRACT
The treatment of elevated plasma lipids plays an important role in atherosclerosis prevention. Low-density lipoprotein (LDL) cholesterol lowering with statins and, if required, additional inhibition is of the utmost importance. Lifestyle modification plays only a minor role in LDL cholesterol lowering. Absolute cardiovascular risk determines whether and at what intensity lipid lowering therapy should be implemented. Thus, in patients at very high risk, an LDL cholesterol level <55mg/dl (<1.4mmol/l) and a 50% reduction from baseline should be achieved. With respect to elevated triglyceride concentrations, treatment goals are less clearly defined, despite the fact that elevated triglyceride concentrations are causally linked to atherosclerotic events. Lifestyle modification can significantly reduce triglyceride concentrations and are often more effective than specific triglyceride lowering medications. New lipid lowering drugs still need to prove their clinical benefit in endpoint trials.

[32] *Ghoreshi ZA, Kabirifar R, Khodarahmi A et al.* **The preventive effect of atorvastatin on liver fibrosis in the bile duct ligation rats via antioxidant activity and down-regulation of Rac1 and NOX1**. Iranian journal of basic medical sciences 2020; 23:30-35.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32395205
ABSTRACT
Objectives: Atorvastatin is a cholesterol-lowering agent capable of inhibiting 3-hydroxy-3-methylglutaryl coenzyme A reductase. Recent studies have demonstrated new facets of atorvastatin, such as antioxidant and anti-fibrotic properties. We investigated the effect of atorvastatin on hepatic injury via the measurement of the antioxidant capacity and protein expression of NOX1, Rac1-GTP, and Rac1 in a rat biliary duct ligation (BDL) model. Materials and Methods: This study is regarded as experimental interventional research in which a total of 32 adult male Wistar rats (200-250 g) were assigned to 4 groups (eight rats per group) as follows: Control group; Control + At group (15 mg\kg\day atorvastatin); BDL group, and BDL+ At group (15 mg\kg\day atorvastatin). Expression levels of Rac1, NOX1, and Rac1-GTP were

determined by western blot analysis. Besides, specific biomarkers of oxidative stress in hepatic tissues of all animals were also analyzed. Results: Atorvastatin reduced liver injury via a decrease in the expression of NOX1, Rac1-GTP, and Rac1 in the BDL group (P<0.05), while the increased contents of protein thiol groups were observed, and the protein carbonylation was decreased in atorvastatin-treated BDL rats compared to the BDL group (P<0.05). Also, administration of atorvastatin in the BDL group significantly lowered oxidative stress through increasing the activity of catalase and superoxide dismutase in comparison with the BDL group (P<0.05). Conclusion: It seems that atorvastatin has potential advantages in mitigation of liver fibrosis by a decrease in the expression of NOX1, Rac1-GTP, and Rac1, along with, a reduction in oxidative stress of liver tissues in rats induced by BDL.

[33] *Jabarpour M, Rashtchizadeh N, Ghorbani Haghjo A et al.* **Protection of renal damage by HMG-CoA inhibitors: A comparative study between atorvastatin and rosuvastatin**. Iranian journal of basic medical sciences 2020; 23:206-213.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32405364
ABSTRACT
Objectives: Hypercholesterolemia is a common metabolic disorder in developing and developed countries and is associated with the increased rates of chronic kidney disease (CKD). Statin therapy could reduce cholesterol synthesis as well as progression of CKD. Diversity between statins causes variety in pharmacokinetics and pharmacodynamics and also their pleiotropic effects. In the present investigation we aimed to evaluate the protective potentials of both atorvastatin (Ator) (as lipid-soluble statin) and rosuvastatin (Ros) (as water-soluble statin) against renal histopathological damages in the high cholesterol diet induced hypercholesterolemic rats (HCDIHR). Materials and Methods: Serum lipid profile, oxidized low density lipoprotein (OX-LDL), malondialdehyde (MDA), urea and creatinine levels, as well as renal histopathology were evaluated. Results: While Ros acted better than Ator to reduce serum low density lipoprotein cholesterol (LDL-C) (P<0.01), atherogenic index (AI) (P<0.01), MDA (P<0.01), and OX-LDL (P<0.01); no significant differences were noted in their cholesterol (P=0.72), triglyceride (TG) (P=0.79), and very low density lipoprotein cholesterol lowering (VLDL-C) (P=0.79) and high density lipoprotein cholesterol elevating effects (HDL-C) (P=0.72). Ator was more effective to reduce renal histopathologic indices compared to Ros, including accumulation of lipid droplet, glomerular foam cells, mesangial cell proliferation, renal hemorrhage, and tubulointerstitial damages in the kidneys of diet induced hypercholesterolemic rats. Conclusion: The findings underline that the lipophilic Ator may performs better than Ros in attenuating renal damages in HCDIHR.

[34] *Cheung K, Powers EM, McKillip J, Powers JG*. **Effect of statin use on incidence of eczema and atopic dermatitis: a retrospective cohort study**. Journal of the American Academy of Dermatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32407738
ABSTRACT

[35] *Lee N, Tilija Pun N, Jang WJ et al.* **Pitavastatin induces apoptosis in oral squamous cell carcinoma through activation of FOXO3a**. Journal of cellular and molecular medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32406610

ABSTRACT
Statins are a class of lipid-lowering drugs that have recently been used in drug repositioning in the treatment of human cancer. However, the underlying mechanism of statin-induced cancer cell death has not been clearly defined. In the present study, we evaluated the anticancer effect of pitavastatin on oral squamous cell carcinoma (OSCC), SCC15 and SCC4 cells and found that FOXO3a might be a direct target in pitavastatin-induced cancer cell death. Our data revealed that pitavastatin selectively suppressed cell viability and induced intrinsic apoptosis in a FOXO3a-dependent manner in SCC15 cells while no effect was observed in SCC4 cells. Notably, treatment with pitavastatin in SCC15 cells induced the nuclear translocation of FOXO3a via dual regulation of two upstream kinases, AMPK and Akt, resulting in the up-regulation of PUMA, a transcriptional target gene of FOXO3a. Furthermore, our data revealed that FOXO3a-mediated PUMA induction plays a role in pitavastatin-induced intrinsic apoptosis in SCC15 cells. Taken together, our findings suggest that pitavastatin activates the FOXO3a/PUMA apoptotic axis by regulation of nuclear translocation of FOXO3a via Akt/FOXO3a or AMPK/FOXO3a signalling. Therefore, these findings might help to elucidate the underlying mechanism of the anticancer effects of pitavastatin on OSCC.

[36] *Gallagher P, Chan KR, Rivino L, Yacoub S*. **The association of obesity and severe dengue: possible pathophysiological mechanisms**. The Journal of infection 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32413364

ABSTRACT
Dengue virus (DENV) is a medically important flavivirus and the aetiological agent of Dengue, a normally self-resolving febrile illness that, in some individuals, can progress into Severe Dengue (SD), a life-threatening disorder that manifests as organ impairment, bleeding and shock. Many different risk factors have been associated with the development of SD, one of which is obesity. In many countries where DENV is endemic, obesity is becoming more prevalent, therefore SD is becoming an increased public health concern. However, there is a paucity of research on the mechanistic links between obesity and SD. This is a narrative review based on original research and reviews sourced from PubMed and Google Scholar. Four key areas could possibly explain how obesity can promote viral pathogenesis. Firstly, obesity downregulates AMP-Protein Kinase (AMPK), which leads to an accumulation of lipids in the endoplasmic reticulum (ER) that facilitates viral replication. Secondly, the long-term production of pro-inflammatory adipokines found in obese individuals can cause endothelial and platelet dysfunction and can facilitate SD. Thirdly, obesity could also cause endothelial dysfunction in addition to chronic inflammation, through the production of reactive oxygen species (ROS) and possible damage to the glycocalyx found in the endothelium. Finally, obesity has several effects on immunomodulation that reduces NK cell function, B and T cell response and increased pre-disposition to stronger pro-inflammatory cytokine responses after viral infection. Together, these effects can lead to greater viral proliferation and greater tissue damage both of which could contribute to SD. The four mechanisms outlined in this review can be taken as reference starting points for investigating the link between obesity and SD, and to discover potential therapeutic strategies that can potentially reduce disease severity.

[37] *Yang Y, Wei C, Liu J et al.* **Atorvastatin protects against postoperative neurocognitive disorder via a peroxisome proliferator-activated receptor-gamma signaling pathway in mice**. J Int Med Res 2020; 48:300060520924251.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32412807
ABSTRACT
OBJECTIVE: Postoperative neurocognitive disorder (PND) is a main complication that is commonly seen postoperatively in elderly patients. The underlying mechanism remains unclear, although neuroinflammation has been increasingly observed in PND. Atorvastatin is a pleiotropic agent with proven anti-inflammatory effects. In this study, we investigated the effects of atorvastatin on a PND mouse model after peripheral surgery. MATERIAL AND METHODS: The mice were randomized into five groups. The PND models were established, and an open field test and fear condition test were performed. Hippocampal inflammatory cytokine expression was determined using ELISA. Peroxisome proliferator-activated receptor-gamma (PPARgamma) expression in the hippocampus was tested using qRT-PCR and western blot analysis. RESULTS: On day 1 after surgery, inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-1beta, and interleukin-6 showed a significant increase in the hippocampus, with prominent cognitive impairment. Atorvastatin treatment improved cognitive function in the mouse model, attenuated neuroinflammation, and increased PPARgamma expression in the hippocampus. However, treatment with the PPARgamma antagonist GW9662 partially reversed the protective effects of atorvastatin. CONCLUSIONS: These results indicated that atorvastatin improves several hippocampal functions and alleviates inflammation in PND mice after surgery, probably through a PPARgamma-involved signaling pathway.

[38] *Peterson LR, Jiang X, Chen L et al.* **Alterations in plasma triglycerides and ceramides: links with cardiac function in humans with type 2 diabetes**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393551
ABSTRACT
Cardiac dysfunction in type 2 diabetes (T2D) is associated with excessive fatty acid uptake, oxidation, and generation of toxic lipid species by the heart. It is not known whether decreasing lipid delivery to the heart can effect improvement in cardiac function in humans with T2D. Thus, our objective was to test the hypothesis that lowering lipid delivery to the heart would result in evidence of decreased 'lipotoxicity' - improved cardiac function, and salutary effects on plasma biomarkers of cardiovascular risk. Thus, we performed a double-blind, randomized, placebo-controlled, parallel design study of the effects of 12 weeks of fenofibrate-induced lipid-lowering on cardiac function, inflammation and oxidation biomarkers, and on the ratio of two plasma ceramides - Cer d18:1 (4E) (1OH, 3OH)/24:0 and Cer d18:1 (4E) (1OH, 3OH)/16:0 - (i.e., 'C24:0/C16:0'), which is associated with decreased risk of cardiac dysfunction and heart failure. Fenofibrate lowered plasma TG and cholesterol but did not improve heart systolic or diastolic function. Fenofibrate treatment lowered the plasma C24:0/C16:0 ceramide ratio and minimally altered oxidative stress markers but did not alter measures of inflammation. Overall, plasma TG lowering correlated with improvement of cardiac relaxation (diastolic function) as measured by tissue Doppler-derived parameter e. Moreover, lowering the plasma C24:0/C16:0 ceramide ratio was correlated with worse diastolic function. These findings indicate that fenofibrate treatment per se is not sufficient to effect changes in cardiac function; however, decreases in plasma TG may be linked to improved diastolic function. In contrast, decreases in plasma C24:0/C16:0 are linked with worsening cardiac function.

[39] *Leon-Martinez JM, Martinez-Abundis E, Gonzalez-Ortiz M, Perez-Rubio KG*. **Effect of Berberine Plus Bezafibrate Administration on the Lipid Profile of Patients with Mixed Dyslipidemia: A Pilot Clinical Trial**. Journal of medicinal food 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32397850
ABSTRACT
To evaluate the effect of berberine (BBR) plus bezafibrate administration on the lipid profile of patients with mixed dyslipidemia. A double-blind randomized pilot clinical trial with parallel groups was carried out in 36 patients, aged 30-60 years with mixed dyslipidemia [triglycerides (TG) >/=1.7 mM and total cholesterol (TC) >/=5.2 mM]. Patients were assigned to 3 groups of 12 patients each, receiving oral administration during 90 days of BBR 500 mg t.i.d., bezafibrate 400 mg b.i.d., or BBR 500 mg t.i.d. plus bezafibrate 400 mg b.i.d, respectively. Clinical evaluation, lipid profile, glucose, creatinine, and uric acid levels were measured before and after the pharmacological intervention. Kruskal-Wallis, Wilcoxon, Mann-Whitney U, and chi(2) tests were used for statistical analyses; a P </= .05 was considered statistically significant. BBR reduced TC levels. Bezafibrate decreased TG, TC, low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein (VLDL) concentrations. BBR plus bezafibrate decreased TG (2.6 +/- 0.8 vs. 1.3 +/- 0.7 mM, P = .007), TC (6.3 +/- 0.7 vs. 4.6 +/- 1.2 mM, P = .005), LDL-C (3.4 +/- 0.6 vs. 2.2 +/- 1.3 mM, P = .037), and VLDL (0.5 +/- 0.2 vs. 0.2 +/- 0.1 mM, P = .007) levels. Bezafibrate and BBR plus bezafibrate significantly decreased TG, TC, LDL-C, and VLDL concentrations, and thus, remitting the diagnosis of mixed dyslipidemia in 90% of the patients.

[40] *Ould-Nana I, Cillis M, Gizzi M et al.* **Rhabdomyolysis and acute kidney injury induced by the association of rosuvastatin and abiraterone: A case report and review of the literature**. J Oncol Pharm Pract 2020:1078155220923001.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32397905
ABSTRACT
INTRODUCTION: Abiraterone acetate is an inhibitor of androgens biosynthesis, approved as first-line treatment in castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer. Abiraterone has been rarely associated with severe rhabdomyolysis, but the mechanism of muscle toxicity is unknown. CASE REPORT: We hereby present a case of severe rhabdomyolysis resulting in acute on chronic kidney injury following abiraterone initiation in a patient previously under rosuvastatin. MANAGEMENT AND OUTCOME: Rhabdomyolysis was resolutive after rosuvastatin and abiraterone discontinuation, and kidney function recovered. There was no recurrence of muscle toxicity after re-initiation of abiraterone alone. DISCUSSION: Abiraterone selectively inhibits CYP17 as well as the hepatic transporter OATP1B1. OATP1B1 is an efflux transporter, whose function is to extract several drugs from the portal blood, allowing them to undergo hepatic metabolism. We hypothesize that abiraterone-induced inhibition of plasmatic uptake of rosuvastatin by OATP1B1 increased plasmatic concentration of rosuvastatin, leading to toxicity on muscle cells. We therefore suggest that the association between rosuvastatin and abiraterone should be avoided.

[41] *Kalra S, Priya G, Aggarwal S*. **Colesevelam in the management of type 2 diabetes**. JPMA. The Journal of the Pakistan Medical Association 2020; 70:934-936.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32400758
ABSTRACT

Colesevelam is a bile acid sequestrant, approved for the management of both dyslipidaemia and type 2 diabetes. This review discusses the potential for the use of colesevelam in the management of type 2 diabetes. Expert opinion suggests possible indications where colesevelam may add value as a glucose lowering agent. It also highlights the limitations of the drug, and precautions that must be observed while using it.

[42] *Lei L, Li X, Yuan YJ et al.* **Inhibition of proprotein convertase subtilisin/kexin type 9 attenuates 2,4,6-trinitrobenzenesulfonic acid-induced colitis via repressing toll-like receptor 4/nuclear factor-kappa B**. Kaohsiung J Med Sci 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32396274
ABSTRACT
Inflammatory bowel disease (IBD) is characterized by recurring inflammatory disorders in digestive system, and devoid of effective treatment. Proprotein convertase subtilisin/kexin type 9 (PCSK9), stimulated via inflammation whose inhibition could decrease secretion of inflammatory factors. We then determined whether inhibition of PCSK9 could improve the inflammation. First, rats model of colitis was first established via administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS), and then verified via determination of body weight loss, myeloperoxidase (MPO) activity, and histopathological analysis of colonic damage. Results showed that treatment with TNBS induced a great body weight loss, MPO activity increase, and serious colonic damage, showing an obviously character of IBD. PCSK9 was elevated in TNBS-induced rats, and PCSK9 inhibition delivered by adenovirus vector increased the body weight, decreased MPO activity, and ameliorated histological change of colon. Second, the protective effect of PCSK9 inhibition against TNBS-induced colitis was accompanied by decrease of proinflammatory factors secretion, including tumor necrosis factor-alpha, interleukin-1beta, interleukin-6, intercellular adhesion molecule 1, and monocyte chemoattractant protein-1. TNBS could activate toll-like receptor 4 (TLR4)/nuclear factor-kappa B (NF-kappaB) signaling pathway, while PCSK9 inhibition suppressed activation of TLR4/NF-kappaB in TNBS-induced rats. In conclusion, PCSK9 inhibition attenuated TNBS-induced rat colitis through anti-inflammatory effect under inactivation of TLR4/NF-kappaB, suggesting potential therapeutic strategy in IBD.

[43] *Byrne RA, Colleran R*. **Aspirin for secondary prevention of cardiovascular disease**. Lancet 2020; 395:1462-1463.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32386577
ABSTRACT

[44] *Chiarito M, Sanz-Sanchez J, Cannata F et al.* **Monotherapy with a P2Y12 inhibitor or aspirin for secondary prevention in patients with established atherosclerosis: a systematic review and meta-analysis**. Lancet 2020; 395:1487-1495.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32386592
ABSTRACT
BACKGROUND: Antiplatelet therapy is recommended among patients with established atherosclerosis. We compared monotherapy with a P2Y12 inhibitor versus aspirin for secondary prevention. METHODS: In this systematic review and meta-analysis, all randomised trials comparing P2Y12 inhibitor with aspirin monotherapy for secondary prevention in patients with cerebrovascular, coronary, or peripheral artery disease were evaluated for inclusion. On

Dec 18, 2019, we searched PubMed, Embase, BioMedCentral, Google Scholar, and the Cochrane Central Register of Controlled Trials. Additionally, we reviewed references from identified articles and searched abstracts from 2017 to 2019 presented at relevant scientific meetings. Data about year of publication, inclusion and exclusion criteria, sample size, baseline patients' features including the baseline condition determining study inclusion (ie, cerebrovascular, coronary, or peripheral artery disease), P2Y12 inhibitor type and dosage, aspirin dosage, endpoint definitions, effect estimates, follow-up duration, and percentage of patients lost to follow-up were collected. Odds ratios (ORs) and 95% CIs were used as metric of choice for treatment effects with random-effects models. Co-primary endpoints were myocardial infarction and stroke. Key secondary endpoints were all-cause death and vascular death. Heterogeneity was assessed with the I(2) index. This study is registered with PROSPERO (CRD42018115037). FINDINGS: A total of nine randomised trials were identified and included in this study, and 42 108 patients randomly allocated to a P2Y12 inhibitor (n=21 043) or aspirin (n=21 065) were included in our analyses. Patients who received a P2Y12 inhibitor had a borderline reduction for the risk of myocardial infarction compared with those who received aspirin (OR 0.81 [95% CI 0.66-0.99]; I(2)=10.9%). Risks of stroke (OR 0.93 [0.82-1.06]; I(2)=34.5%), all-cause death (OR 0.98 [0.89-1.08]; I(2)=0%), and vascular death (OR 0.97 [0.86-1.09]; I(2)=0%) did not differ between patients who received a P2Y12 inhibitor and those who received aspirin. Similarly, the risk of major bleeding (OR 0.90 [0.74-1.10]; I(2)=3.9%) did not differ between patients who received a P2Y12 inhibitor and those who received aspirin. The number needed to treat to prevent one myocardial infarction with P2Y12 inhibitor monotherapy was 244 patients. Findings were consistent regardless of the type of P2Y12 inhibitor used. INTERPRETATION: Compared with aspirin monotherapy, P2Y12 inhibitor monotherapy is associated with a risk reduction for myocardial infarction and a comparable risk of stroke in the setting of secondary prevention. The benefit of P2Y12 inhibitor monotherapy is of debatable clinical relevance, in view of the high number needed to treat to prevent a myocardial infarction and the absence of any effect on all-cause and vascular mortality. FUNDING: Italian Ministry of Education.

[45] *Feld JJ, Cypel M, Kumar D et al.* **Short-course, direct-acting antivirals and ezetimibe to prevent HCV infection in recipients of organs from HCV-infected donors: a phase 3, single-centre, open-label study**. The lancet. Gastroenterology & hepatology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32389183

ABSTRACT

BACKGROUND: An increasing percentage of potential organ donors are infected with hepatitis C virus (HCV). After transplantation from an infected donor, establishment of HCV infection in uninfected recipients is near-universal, with the requirement for post-transplant antiviral treatment. The aim of this study was to determine if antiviral drugs combined with an HCV entry blocker given before and for 7 days after transplant would be safe and reduce the likelihood of HCV infection in recipients of organs from HCV-infected donors. METHODS: HCV-uninfected organ recipients without pre-existing liver disease were treated with ezetimibe (10 mg; an HCV entry inhibitor) and glecaprevir-pibrentasvir (300 mg/120 mg) before and after transplantation from HCV-infected donors aged younger than 70 years without co-infection with HIV, hepatitis B virus, or human T-cell leukaemia virus 1 or 2. Recipients received a single dose 6-12 h before transplant and once a day for 7 days after surgery (eight doses in total). HCV RNA was assessed once a day for 14 days and then once a week until 12 weeks post-

transplant. The primary endpoint was prevention of chronic HCV infection, as evidenced by undetectable serum HCV RNA at 12 weeks after transplant, and assessed in the intention-to-treat population. Safety monitoring was according to routine post-transplant practice. 12-week data are reported for the first 30 patients. The trial is registered on ClinicalTrials.gov, NCT04017338. The trial is closed to recruitment but follow-up is ongoing. FINDINGS: 30 patients (23 men and seven women; median age 61 years (IQR 48-66) received transplants (13 lung, ten kidney, six heart, and one kidney-pancreas) from 18 HCV-infected donors. The median donor viral load was 5.11 log10IU/mL (IQR 4.55-5.63) and at least three HCV genotypes were represented (nine [50%] donors with genotype 1, two [11%] with genotype 2, five [28%] with genotype 3, and two [11%] with unknown genotype). All 30 (100%) transplant recipients met the primary endpoint of undetectable HCV RNA at 12 weeks post-transplant, and were HCV RNA-negative at last follow-up (median 36 weeks post-transplant [IQR 25-47]). Low-level viraemia was transiently detectable in 21 (67%) of 30 recipients in the early post-transplant period but not after day 14. Treatment was well tolerated with no dose reductions or treatment discontinuations; 32 serious adverse events occurred in 20 (67%) recipients, with one grade 3 elevation in alanine aminotransferase (ALT) possibly related to treatment. Non-serious transient elevations in ALT and creatine kinase during the study dosing period resolved with treatment completion. Among the serious adverse events were two recipient deaths due to causes unrelated to study drug treatment (sepsis at 49 days and subarachnoid haemorrhage at 109 days post-transplant), with neither patient ever being viraemic for HCV. INTERPRETATION: Ezetimibe combined with glecaprevir-pibrentasvir given one dose before and for 7 days after transplant prevented the establishment of chronic HCV infection in recipients of different organs from HCV-infected donors. This study shows that an ultra-short course of direct-acting antivirals and ezetimibe can prevent the establishment of chronic HCV infection in the recipient, alleviating many of the concerns with transplanting organs from HCV-infected donors. FUNDING: Canadian Institutes of Health Research; the Organ Transplant Program, University Health Network.

[46] *Goodarzi Z, Karami E, Yousefi S et al.* **Hepatoprotective effect of atorvastatin on Cadmium chloride induced hepatotoxicity in rats**. Life sciences 2020; 254:117770.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32407846

ABSTRACT

AIMS: Cadmium chloride has various industrial applications and considered an industrial and environmental pollutant. The aim of this study was to evaluate the effect of atorvastatin on Cadmium chloride-induced hepatotoxicity in male rats. MATERIALS AND METHODS: Fifty-six adult male rats, randomly were divided into 8 groups. Groups 1-3 were received atorvastatin (20 mg/kg) intragastrically for 15 days during which Cadmium chloride (1, 2, and 3 mg/kg) were given intraperitoneally from days 8 to 15. Groups 4-6 were as first three groups but animals were received vehicle of atorvastatin. Group 7 was received vehicle of atorvastatin and vehicle of Cadmium chloride and Group 8 was received atorvastatin and vehicle of Cadmium chloride according to timeline of other groups. On day 16, under full anesthesia, blood sampling was prepared from heart, and livers were dissected out to analyses the biochemical and histopathology studies. KEY FINDINGS: Cadmium chloride significantly increased aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) in the serum. Malondialdehyde (MDA) significantly increased and superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione (GSH)

significantly decreased the in the liver following Cadmium chloride administration. Atorvastatin significantly improved the levels of MDA, SOD, GPx, GSH, but not ALT, AST, and ALP in Cadmium chloride-treated rats. In histopathological studies, atorvastatin could not improve injured liver tissues induced by Cadmium chloride. SIGNIFICANCE: Atorvastatin has beneficial effects in improving Cadmium chloride-induced antioxidative enzymes disturbance which may be contribute to improving liver function in male rats.

[47] *Rosada A, Kassner U, Weidemann F et al.* **Hyperlipidemias in elderly patients: results from the Berlin Aging Study II (BASEII), a cross-sectional study**. Lipids in health and disease 2020; 19:92.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32410691
ABSTRACT
BACKGROUND: Hyperlipidemias are common and the last decades have seen substantially growing evidence of their causative role in the development of atherosclerosis and subsequent cardiovascular diseases. Since hyperlipidemias usually do not cause direct clinical symptoms, they often remain undiagnosed until a serious cardiovascular event occurs. Especially for LDL-hypercholesteremia, there are well-established treatment options available to prevent the occurrence of atherosclerosis. However, there is a lack of knowledge regarding the proper treatment of elderly patients. The goal of this study was to assess the prevalence of hyperlipidemia in a group of young and a group of elderly community-dwelling participants and to determine to what extent treatment of hyperlipidemia should be initiated or required. METHODS: Crossectional data from a total of 2151 subjects (1657 in the elderly group, mean age 69, and 494 in the young group (control group), mean age 29) of the Berlin Aging Study II (BASE-II) were available. Medical history was assessed and recorded by trained physicians and prevalence of lipid disorders was determined with laboratory tests, including a lipid-profile. RESULTS: A large proportion of subjects (39%) were unaware of an existing lipid disorder. The prevalence of hyperlipidemia was more frequent in the elderly group (76%) compared to the young group (41%). Hypercholesterolemia was the most common diagnosed disorder (64%), followed by hyperlipoproteinemia(a) (18%), hypertriglyceridemia (7%) and combined hyperlipoproteinaemia (5%). Only a minority of this cohort was treated with lipid-lowering medication (17%) and of those treatment targets according to ESC guidelines were reached only in 16.5 %. CONCLUSIONS: Hyperlipidemias appear underdiagnosed and undertreated. As the prevalence of these disorders increases with age and with regard to their role as a major modifiable risk factor for cardiovascular disease it seems to be advisable to aim for more consistent and sustainable screening and treatment of these common disorders. TRIAL REGISTRATION: BASE-II registered with the clinical trial registry Deutsches Register Klinischer Studien (DRKS00009277).

[48] *Zhang X, Stiekema LCA, Stroes ESG, Groen AK*. **Metabolic effects of PCSK9 inhibition with Evolocumab in subjects with elevated Lp(a)**. Lipids in health and disease 2020; 19:91.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393252
ABSTRACT
BACKGROUND: Epidemiological studies substantiated that subjects with elevated lipoprotein(a) [Lp(a)] have a markedly increased cardiovascular risk. Inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) lowers both LDL cholesterol (LDL-C) as well as Lp(a), albeit modestly. Effects of PCSK9 inhibition on circulating metabolites such as

lipoprotein subclasses, amino acids and fatty acids remain to be characterized. METHODS: We performed nuclear magnetic resonance (NMR) metabolomics on plasma samples derived from 30 individuals with elevated Lp(a) (> 150 mg/dL). The 30 participants were randomly assigned into two groups, placebo (N = 14) and evolocumab (N = 16). We assessed the effect of 16 weeks of evolocumab 420 mg Q4W treatment on circulating metabolites by running lognormal regression analyses, and compared this to placebo. Subsequently, we assessed the interrelationship between Lp(a) and 14 lipoprotein subclasses in response to treatment with evolocumab, by running multilevel multivariate regression analyses. RESULTS: On average, evolocumab treatment for 16 weeks resulted in a 17% (95% credible interval: 8 to 26%, P < 0.001) reduction of circulating Lp(a), coupled with substantial reduction of VLDL, IDL and LDL particles as well as their lipid contents. Interestingly, increasing concentrations of baseline Lp(a) were associated with larger reduction in triglyceride-rich VLDL particles after evolocumab treatment. CONCLUSIONS: Inhibition of PCSK9 with evolocumab markedly reduced VLDL particle concentrations in addition to lowering LDL-C. The extent of reduction in VLDL particles depended on the baseline level of Lp(a). Our findings suggest a marked effect of evolocumab on VLDL metabolism in subjects with elevated Lp(a). TRIAL REGISTRATION: Clinical trial registration information is registered at ClinicalTrials.gov on April 14, 2016 with the registration number NCT02729025.

[49] Team NGU. In: Non-surgical interventions for slowing aneurysm growth and reducing the risk of rupture: Abdominal aortic aneurysm: diagnosis and management: Evidence review E. London: National Institute for Health and Care Excellence (UK)
Copyright (c) NICE 2020.; 2020.

[50] *Di Minno MND, Gentile M, Di Minno A et al.* **Changes in carotid stiffness in patients with familial hypercholesterolemia treated with Evolocumab(R): A prospective cohort study**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32402582

ABSTRACT

BACKGROUND AND AIM: Protein convertase subtilisin kexin type 9 (PCSK-9) inhibitors demonstrated efficacy in cholesterol reduction and in the prevention of cardiovascular events. We evaluated changes in lipid profile and carotid stiffness in patients with familial hypercholesterolemia during 12 weeks of treatment with a PCSK-9 inhibitor, Evolocumab(R). METHODS AND RESULTS: Patients with familial hypercholesterolemia starting a treatment with Evolocumab(R) were included. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), small dense LDL (assessed by LDL score) and carotid stiffness were evaluated before starting treatment with Evolocumab(R) and during 12 weeks of treatment. Twenty-five subjects were enrolled (52% males, mean age 51.5 years). TC and LDL-C were reduced of 38% and 52%, respectively during treatment, with LDL score reduced of 46.1%. In parallel, carotid stiffness changed from 8.8 (IQR: 7.0-10.4) m/sec to 6.6 (IQR: 5.4-7.5) m/sec, corresponding to a median change of 21.4% ($p < 0.001$), with a significant increase in carotid distensibility (from 12.1, IQR: 8.73-19.3 kPA(-1) x 10(-3) at T0 to 21.8, IQR: 16.6-31.8 kPA(-1) x 10(-3) at T12w) corresponding to a median change of 62.8% ($p < 0.001$). A multivariate analysis showed that changes in LDL score were independently associated with changes in carotid stiffness (beta = 0.429, $p = 0.041$). CONCLUSION: Small dense LDL reduction, as assessed by LDL score, is associated with changes in carotid stiffness in patients with familial hypercholesterolemia treated with Evolocumab(R).

[51] *Scicali R, Di Pino A, Piro S et al.* **May statins and PCSK9 inhibitors be protective from COVID-19 in familial hypercholesterolemia subjects?** Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32405159
ABSTRACT

[52] *Pahlavani M, Ramalingam L, Miller EK et al.* **Discordant Dose-Dependent Metabolic Effects of Eicosapentanoic Acid in Diet-Induced Obese Mice**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32397139
ABSTRACT
Obesity is a widespread epidemic that increases the risk for several metabolic diseases. Despite several beneficial health effects of eicosapentaenoic acid (C20:5n-3, EPA), previous studies have used very high doses of EPA. In this study, dose-dependent effects of EPA on metabolic outcomes were determined in diet-induced obese mice. We used B6 male mice, fed high-fat diet (HF, 45% kcal fat) or HF diet supplemented with 9, 18, and 36 g/kg of EPA-enriched fish oil for 14 weeks. We conducted metabolic phenotyping during the feeding period, and harvested tissues and blood at termination. Only mice fed 36 g/kg of EPA significantly ($p < 0.05$) lowered body weight, fat content and epididymal fat pad weight, compared to HF. Both 18 and 36 g/kg doses of EPA significantly increased glucose clearance and insulin sensitivity, compared to HF or 9 g/kg of EPA. Locomotor activity was significantly increased with both 18 and 36 g/kg doses of EPA. Interestingly, all doses of EPA compared to HF, significantly increased energy expenditure and oxygen consumption and significantly reduced serum insulin, leptin, and triglycerides levels. These results demonstrate weight- and adiposity-independent metabolic benefits of EPA, at doses comparable to those currently used to treat hypertriglyceridemia.

[53] *Yang YJ, Qian HY, Song L et al.* **Strengthening effects of bone marrow mononuclear cells with intensive atorvastatin in acute myocardial infarction**. Open heart 2020; 7.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393654
ABSTRACT
OBJECTIVE: To test whether intensive atorvastatin (ATV) increases the efficacy of transplantation with autologous bone marrow mononuclear cells (MNCs) in patients suffering from anterior ST-elevated myocardial infarction (STEMI). METHODS: This clinical trial was under a 2x2 factorial design, enrolling 100 STEMI patients, randomly into four groups of regular (RA) or intensive ATV (IA) with MNCs or placebo. The primary endpoint was the change of left ventricular ejection fraction (LVEF) at 1-year follow-up from baseline, primarily assessed by MRI. The secondary endpoints included other parameters of cardiac function, remodelling and regeneration determined by MRI, echocardiography, positron emission tomography (PET) and biomarkers. RESULTS: All the STEMI patients with transplantation of MNCs showed significantly increased LVEF change values than those with placebo (p=0.01) with only in the IA+MNCs patients group demonstrating significantly elevation of LVEF than in the IA+placebo group (+12.6% (95%CI 10.4 to 19.3) vs +5.0% (95%CI 4.0 to 10.0), p=0.001), pointing to a better synergy between ATV and MNCs (p=0.019). PET analysis revealed significantly increased viable areas of myocardium (p=0.015), while the scar sizes (p=0.026) and blood aminoterminal pro-B-type natriuretic peptide (p<0.034) reduced. All these above

benefits of MNCs were also attributed to IA+MNCs instead of RA+MNCs group of patients with STEMI. CONCLUSIONS: Intensive ATV treatment augments the therapeutic efficacy of MNCs in patients with anterior STEMI at the convalescent stage. The treatment with the protocol of intensive ATV and MNC combination offers a clinically essential approach for myocardial infarction. TRIAL REGISTRATION NUMBER: NCT00979758.

[54] *Wang P, Chen Z, Xing D*. **Multi-parameter characterization of atherosclerotic plaques based on optical coherence tomography, photoacoustic and viscoelasticity imaging**. Optics express 2020; 28:13761-13774.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32403844
ABSTRACT
Detection of atherosclerotic plaque vulnerability is the critical step in prevention of acute coronary events. Fibrous cap thickness, lipid core size, and inflammation extent are three key parameters for assessing plaque vulnerability. Here, we report on multimodality imaging of mice aortic plaques using a system that integrates optical coherence tomography (OCT), photoacoustic imaging (PAI), and photoacoustic viscoelasticity imaging (PAVEI). The thickness of fibrous cap is accurately evaluated by OCT, and PAI helps to determine the distribution and size of lipid core. The mechanical properties of plaques are closely related to the plaque compositions and the content and distribution of macrophages, while PAVEI can characterize the plaque viscoelasticity through the phase delay of photoacoustic signal. Experimental results demonstrate that the OCT-PAI-PAVEI system can comprehensively characterize the three traits of atherosclerotic plaques, thereby identifying high-risk lesions.

[55] *Dai H, Ji X, Huang X et al.* **MiR-379 relieves myocardial injury after acute myocardial infarction by regulating tumor necrosis factor-alpha-induced protein 8**. Panminerva medica 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32414226
ABSTRACT
BACKGROUND: Acute myocardial infarction (AMI) is the myocardial avascular necrosis syndrome caused by coronary atherosclerotic plaque rupture, thrombosis or coronary artery occlusion. Therefore, it is of great significance to find new targets for the treatment of myocardial infarction. The purpose of this study was to investigate the effect of microRNA-379 (miR-379) on AMI and its mechanism. METHODS: MiR-379 mimic was used to transfect H9c2 cells and we determined the protective effect of miR-379 on H9c2 by detecting the level of apoptosis. TargetScan software was used to detect miR-379's downstream targets. We constructed siRNA to analyze the effect of miR-379's downstream targets on H9c2 cells. In addition, we used miR-379 agomir to inject the tail vein of AMI rats to verify the effect of miR-379 on rat cardiomyocytes. RESULTS: TargetScan detected that miR-379 and Tumor necrosis factor-alpha-induced protein 8 (TNFAIP8) may have binding sites and the dual luciferase reporter assay found that miR-379 binds to TNFAIP8 and inhibits its activity. MiR-379 mimic was found to reduce the expression of caspase3 and caspase9 in H9c2 cells and thereby reduce H2O2-induced cell damage. Inhibition of TNFAIP8 also significantly reduced apoptosis level and inhibited the NF-kappaB signaling pathway in H9c2 cells. Finally, miR-379 agomir was used to inject the tail vein of AMI rats and verified the protective effect of miR-379 in the heart in vivo. CONCLUSIONS: MiR-379 has a binding site with TNFAIP8 and can inhibit its activity by binding to TNFAIP8 mRNA. SiRNA-TNFAIP8 can inhibit the NF-kappaB signaling

pathway and protect myocardial cells from AMI-induced myocardial damage by reducing the apoptosis level of myocardial cells.

[56] *Kalkman HO*. **The Association Between Vascular Inflammation and Depressive Disorder. Causality, Biomarkers and Targeted Treatment**. Pharmaceuticals (Basel, Switzerland) 2020; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32408603
ABSTRACT
Diabetes, obesity, atherosclerosis, and myocardial infarction are frequently co-morbid with major depressive disorder. In the current review, it is argued that vascular inflammation is a factor that is common to all disorders and that an endothelial dysfunction of the blood-brain barrier could be involved in the induction of depression symptoms. Biomarkers for vascular inflammation include a high plasma level of C-reactive protein, soluble cell-adhesion molecules, von Willebrand factor, aldosterone, and proinflammatory cytokines like interleukin-6 or tumor necrosis factor alpha. A further possible biomarker is flow-mediated dilation of the brachial artery. Treatment of vascular inflammation is expected to prevent or to reduce symptoms of depression. Several tentative treatments for this form of depression can be envisioned: eicosapentaenoic acid (EPA), valproate, Vagus-nerve stimulation, nicotinic alpha7 agonists, and agonists of the cannabinoid CB2-receptor.

[57] *Banach M, Penson PE, Fras Z et al.* **Brief recommendations on the management of adult patients with familial hypercholesterolemia during the COVID-19 pandemic**. Pharmacological research : the official journal of the Italian Pharmacological Society 2020; 158:104891.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32389859
ABSTRACT
Individuals with Familial Hypercholesterolaemia (FH) are at very high risk of cardiovascular disease, which is associated with poor outcomes from coronavirus infections. COVID-19 puts strain on healthcare systems and may impair access to routine FH services. On behalf of the International Lipid Expert Panel (ILEP) and the European FH Patient Network (FH Europe), we present brief recommendations on the management of adult patients with FH during the COVID-19 pandemic. We discuss the implications of COVID-19 infections for FH patients, the importance of continuing lipid-lowering therapy where possible, issues relating to safety monitoring and service delivery. We summarise the evidence for additional benefits of statins and other lipid-lowering drugs during viral infections. The recommendations do not override in any way the individual responsibility of physicians to make appropriate and accurate decisions taking into account the condition of a given patient and the doses, rules, and regulations applicable to drugs and devices at the time of their prescription/use.

[58] *Maree S, du Preez JL, du Plessis LH et al.* **A novel HPLC method developed and validated for the detection and quantification of atorvastatin, fluvastatin, pitavastatin and pravastatin during transdermal delivery studies**. Pharmazie 2020; 75:163-165.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32393420
ABSTRACT
An HPLC method was developed and validated to quantify and identify several statins (atorvastatin, fluvastatin, pitavastatin and pravastatin) that were used during transdermal drug

delivery. The method proved to be most effective with a Restek Ultra C18, 250 x 4.6 mm, 5 mum column, a flow rate of 1.0 ml/min, UV detection at 240 nm and injection volume of 10 mul. The mobile phase used was acetonitrile/Milli-Q((R)) water with 0.1% orthophosphoric acid starting with 30% acetonitrile, which increased linearly to 70% (after 4 min) for up to 10 min and then re-equilibrated to start conditions. This HPLC method indicated linearity (correlation coefficient (R(2)) of 1) within the concentration range of 0.05-200.00 mug/ml and had an average recovery of 98-103%. Limit of detection (LOD) and limit of quantification (LOQ) showed that statins could still be identified at concentrations of 0.004-0.006 mug/ml with the exception of atorvastatin (quantifiable at 0.013-0.035 mug/ml). Specificity performed during method validation, confirmed that the method was suitable for accurate detection and quantification of the statins when included in the transdermal formulations with other excipients.

[59] *Masmeijer C, van Leenen K, De Cremer L et al.* **Effects of omega-3 fatty acids on immune, health and growth variables in veal calves**. Prev Vet Med 2020; 179:104979.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32388034
ABSTRACT
Under the present intensive rearing conditions, calves face a series of stressors and multiple pathogens often necessitating antimicrobial use. Multiple feed additives are currently explored for their ability to prevent disease and limit the use of antimicrobials. Supplementation of the polyunsaturated long chain n-3 fatty acids eicosapentaenoic (EPA) and docohexaenoic (DHA) from marine origin has been proposed as a strategy to improve immune function and prevent excessive inflammation reactions. The aim of this randomized clinical trial was to explore the effects of n-3 fatty acids (PUFAs) used as feed supplement on health, production and immune variables in a veal calf setting. One hundred-seventy calves were randomly assigned to 3 treatment groups: microalgae (MA, n=57, 2.5g DHA/animal/day), fish oil (FO, n=57, 2.5g EPA+DHA/animal/day)] and a control group (CON, n=56). Average daily gain (ADG), bodyweight at 12 weeks on feed and slaughter weight were determined. Health monitoring consisted of recording of clinical signs and repeated thoracic ultrasonography. After 5, 8 and 11 weeks of supplementation, the function of neutrophils, monocytes and peripheral blood mononuclear cells (PBMCs) was evaluated ex vivo by measuring reactive oxygen species (ROS) production by neutrophils and monocytes and proliferation of and cytokine release by PBMCs. Under the field conditions of this study, dietary supplementation of MA and FO showed very limited immunomodulatory effects. Feeding MA led to increased ROS production by neutrophils, Estimate (E)=0.38, Standard Error (SE)=0.14; P<0.05, compared to the control calves after 5 weeks of in-feed supplementation. FO reduced IL-6 secretion E= -0.29, SE= 0.11; P<0.05 compared to MA treated animals after 11 weeks on feed. Health and production variables were unaffected by treatments. The doses of EPA and DHA used in this study did not cause immunomodulatory changes in highly stressed calves to such an extent that this led to better health or growth of animals.

[60] *Moreira TA, Alvares-Teodoro J, Barbosa MM et al.* **Use of medicines by adults in primary care: Survey on health services in Minas Gerais, Brazil**. Rev Bras Epidemiol 2020; 23:e200025.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32401914
ABSTRACT

INTRODUCTION: Inappropriate use and increase of health care spending reinforce the need to extend our knowledge about the quality of medication use. OBJECTIVES: To describe and evaluate the profile of medication use in a representative sample of adult users of primary care services in the Unified Health System (SUS) of Minas Gerais. METHOD: Cross-sectional study, with 1,159 interviewees in 104 municipalities and 253 health care services. Data on sociodemographic characteristics, health conditions and use of medicines were collected, and these variables were stratified by age group. Univariate and multivariate analyses, using logistic regression, were conducted to identify predictors of self-medication. We set a significance level of 5% for all tests. RESULTS: The prevalence of medication use was 81.8%, with an average of 2.67 medicines per user, which increased with age. The most used drugs were losartan, hydrochlorothiazide and simvastatin, which differed between age groups. Significant self-medication was observed not only in young adults but also in the elderly. The predictors of self-medication were: being a young adult, having a higher level of education, not having chronic diseases, having worse self-perception of health and not adhering to prescription drugs. Young and elderly adults showed characteristics that made them more vulnerable in relation to the rational use of medicines. CONCLUSION: This study can contribute to improving primary care, where it identified problems related to the extent of medication use, especially among young adults and the elderly in Minas Gerais.

[61] *Prickett TCR, Troughton RW, Espiner EA*. **Effect of statin therapy on plasma C-type Natriuretic Peptides and Endothelin-1 in males with and without symptomatic coronary artery disease**. Scientific reports 2020; 10:7927.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32404888
ABSTRACT
C-type Natriuretic Peptide (CNP) and Endothelin-1 (ET-1) have reciprocal roles in maintaining vascular homeostasis and are acutely modulated by statins in human cultured endothelial cells. Whether these actions of statins in vitro are reflected in studies in vivo is unknown. In a prospective study of 66 subjects with or without post- acute coronary syndrome (ACS), plasma concentrations of bioactive CNP and bio-inactive aminoterminal proCNP (NTproCNP), ET-1, B-type Natriuretic Peptide (BNP) and high sensitivity C Reactive Protein (hsCRP) were measured together with lipids before and at intervals of 1, 2 and 7 days after commencing atorvastatin 40 mg/day - and for a further period of 6months in those with ACS. Plasma lipids fell significantly in all subjects but plasma CNP, NTproCNP and ET-1 were unchanged by atorvastatin. In ACS, baseline hsCRP, BNP and CNP but not NTproCNP or ET-1 were significantly raised compared to values in age-matched controls. The ratio of NTproCNP to CNP was significantly lower in ACS throughout the study and was unaffected by statin therapy. We conclude that conventional doses of atorvastatin do not affect plasma CNP products or ET-1. Elevated CNP after cardiac injury likely results from regulated changes in clearance, not enhanced production.

[62] *Wypasek E, Natorska J, Mazur P et al.* **Effects of rivaroxaban and dabigatran on local expression of coagulation and inflammatory factors within human aortic stenotic valves**. Vascular pharmacology 2020; 130:106679.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32387621
ABSTRACT

Literature update week 19 (2020)

BACKGROUND: Treatment with non-vitamin K antagonist oral anticoagulants (NOACs) such as dabigatran (a direct thrombin inhibitor) or rivaroxaban (a direct inhibitor of factor [F] Xa) attenuates atherosclerotic plaque progression in hypercholesterolemic mice. PURPOSE: To evaluate the effect of NOACs application on the expression of coagulation proteins in loco within stenotic aortic valves and in valve interstitial cells (VICs) from patients with severe aortic stenosis (AS). METHODS: Primary cultures of VICs obtained from 90 patients undergoing aortic valve replacement were stimulated with TNF-alpha (50 ng/mL) and pre-treated with rivaroxaban (1 and 10 ng/mL) or dabigatran (25 and 250 ng/mL). The expression of coagulation proteins was analyzed by immunofluorescence. Cytokine levels were measured by ELISA. RESULTS: FX, FXa, FVII, thrombin and PAR1/2 were present in loco within human aortic stenotic valves. Cultured VICs exhibited constant expression of FX, TF, PAR1/2. Exposure of VICs to TNF-alpha caused the upregulated expression of TF, PAR1/2 and induced expression of thrombin, FVII and FXa. FX was expressed by 80% of VICs, regardless of stimulation. Cultured VICs were able to synthesize metalloproteinases 1-3, IL-6, IL-32, IL-34, osteopontin and osteocalcin, the levels of which increased under TNF-alpha stimulation. NOACs added to culture inhibited coagulation factor and PAR1/2 expression. Moreover, NOACs down-regulated VIC-derived proteins responsible for valve calcification and extracellular matrix remodeling. CONCLUSIONS: NOACs at therapeutic concentrations may inhibit the effects of FXa and thrombin at in vitro level. It might be speculated that long-term treatment with rivaroxaban or dabigatran could attenuate the progression of AS in humans.