[1] *Xu M, Li HW, Chen H, Guo CY*. **Sex and Age Differences in Patients With Unstable Angina Pectoris: A Single-Center Retrospective Study**. The American journal of the medical sciences 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32563567
ABSTRACT
BACKGROUND: Sex and age may affect the pathogenesis of coronary heart disease, such as cardiovascular risk factors, treatment and prognosis, but this information is not well known. METHODS: This was a single-center retrospective cohort study. Patients with unstable angina pectoris between January 2013 and June 2018 were included and stratified into 4 age groups (<55, 55-64, 65-74 and ≥75 years). The cardiovascular risk factors profile, treatment and in-hospital prognosis differences by sex and age were explored. RESULTS: This study included 5,908 patients (2,198 women). The women were older than the men (mean age 67 vs. 62 years). Approximately 2 of 3 patients had ≥3 cardiovascular risk factors. Men were more likely to be smokers, and women had a higher level of total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol. Hypertension, diabetes and chronic kidney disease were more frequent in women ≥ 65 years old than in similarly aged men. Men and women less than 65 years of age had more frequent family history of coronary heart disease, higher body mass index, higher fasting plasma glucose, and higher lipid levels, especially for patients <55 years of age. More women tended to receive medical therapy than men (51.6% vs. 42.8%, P < 0.01). The overall incidence of in-hospital major adverse cardiovascular events was higher in men than in women (4.1% vs. 2.6%, P < 0.05), whereas there was no sex difference in the in-hospital cardiac mortality (0.2% vs. 0.2%, P > 0.05). CONCLUSIONS: Women had higher cholesterol levels, and were less likely to undergo revascularization therapy than similarly aged men, and elderly women had a higher prevalence of hypertension, diabetes, and chronic kidney disease than elderly men. In-hospital major adverse cardiovascular events were lower in women than in men; however, there was no sex difference in the in-hospital cardiac mortality.

[2] *Ding S, Xu S, Chen X, Wu S*. **Effects of atorvastatin combined with bivalirudin on coagulation function, cardiac function, and inflammatory factors of percutaneous coronary intervention in elderly patients with acute myocardial infarction**. Ann Palliat Med 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32576006
ABSTRACT
BACKGROUND: Acute myocardial infarction (AMI) occurs when atherosclerotic lesions which present in the coronary arteries cause the intravascular plate to rupture and with the result of myocardial ischemia, hypoxia, and infarct. The preferred treatment for AMI is currently percutaneous coronary intervention (PCI), for which the key to the success is the choice of anticoagulant and thrombolytic drugs during surgery. Here, we aim to explore the effects of atorvastatin combined with bivalirudin on coagulation function, cardiac function, and inflammatory factors in elderly patients with AMI who underwent PCI. METHODS: The clinical data of 86 AMI patients who were admitted to our hospital between February 2016 and May 2018 were retrospectively analyzed. Based on different treatments, the patients were divided into the control group and the observation group, with 43 patients in each group. The control group patients were treated with bivalirudin, and the observation group was treated with bivalirudin plus atorvastatin. Both groups of patients underwent PCI and the clinical efficacy,

coagulation function, cardiac function, inflammatory factor levels and cardiovascular events (MACE), and other clinical data were compared between the groups. RESULTS: The total clinical effective rate in the observation group was significantly higher than that in the control group (90.90% vs. 72.09%) (P<0.05). Fibrinogen (Fg) and D-dimer (D-D) levels were significantly decreased after treatment in both groups but were significantly lower in the observation group than in the control group. The prothrombin time (PT) was significantly prolonged after treatment in both groups but was significantly longer in the observation group than in the control group after treatment (P<0.05). Meanwhile, the left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) were significantly reduced after treatment in both groups but were significantly lower in the observation group than in the control group, whereas the left ventricular ejection fraction (LVEF) was significantly higher in the observation group compared with the control group after treatment (P<0.05). After treatment, serum levels of transforming growth factor-β1 (TGF-β1), tumor necrosis factor-α (TNF-α), and IL-6 were significantly reduced in both groups but the levels were significantly lower in the observation group than in the control group (P<0.05). The overall incidence of MACE in the observation group was significantly lower than that in the control group (9.30% vs. 30.23%) (P<0.05). CONCLUSIONS: Atorvastatin combined with bivalirudin can improve the efficiency of clinical treatment in elderly AMI patients who undergo PCI, while simultaneously improving blood coagulation function and reducing the occurrence of bleeding, compared with bivalrudin alone. It can also decrease the level of inflammatory factors, promote vascular recanalization, and improve myocardial ischemia, thereby reducing the incidence of MACE and improving patient prognosis.

[3] *Rodrigues MOM, Evangelista-Silva PH, Neves NN et al.* **Caloric restriction-induced weight loss with a high-fat diet does not fully recover visceral adipose tissue inflammation in previously obese C57BL/6 mice**. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32574503

ABSTRACT

Caloric restriction (CR) reduces body weight and systemic inflammation, but effects on adipose tissue under dietary lipid overload are controversial. We evaluated the effects of CR-induced weight loss with a high-fat diet (HF) on adipose tissue inflammation of obese mice. Male mice were assigned into LF (low-fat diet) and HF. After 8-wk, HF was reassigned for another 7-wk into HF - kept at HF; LFAL - switched from HF to LF ad libitum; RHF - fed HF calorie-restricted to reach LFAL body weight. Serum markers, adipocytokines, morphology, and inflammatory infiltrates in retroperitoneal adipose tissue (RAT) were accessed. LFAL and RHF reduced body weights, equaling to LF. LFAL restored almost all inflammatory markers as LF, except tumor necrosis factor-alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and adiponectin. Compared to HF, RHF lowered visceral adiposity, retroperitoneal adipocyte sizes, RAT inflammatory cell infiltration as well as TNF-α, interleukin-6, hepatic and serum C-reactive protein, which were higher than LFAL; adiponectin and MCP-1 did not change. CR with high-fat diet reduced body weight and attenuated visceral adiposity, but did not fully recover visceral tissue inflammation. Novelty bullets • Caloric restriction in a high-fat diet ameliorated visceral adiposity. • Caloric restriction in a high-fat diet did not recover visceral adipose tissue inflammation.

[4] *Arunsak B, Pratchayasakul W, Amput P et al.* **Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor exerts greater efficacy than atorvastatin on improvement of brain function and cognition in obese rats**. Archives of biochemistry and biophysics 2020; 689:108470.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32592802
ABSTRACT
The accumulation of lipid as a result of long-term consumption of a high-fat diet (HFD) may lead to metabolic and brain dysfunction. Atorvastatin, a recommended first-line lipid-lowering agent, has shown beneficial effects on metabolic and brain functions in several models. Recently, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor was approved as an effective therapeutic drug for dyslipidemia patients. However, few studies have reported on the effect of this PCSK9 inhibitor on brain function. In addition, the comparative efficacy on the improvement of metabolic and brain functions between PCSK9 inhibitor and atorvastatin in obese models have not been elucidated. We hypothesized that PCSK9 inhibitor improves metabolic and brain functions in an obese model to a greater extent than atorvastatin. Thirty-two female rats were fed with either a normal diet (ND) or HFD for 15 weeks. At week 13, ND rats were given normal saline and HFD rats were given either normal saline, atorvastatin (40 mg/kg/day) or PCSK9 inhibitor (4 mg/kg/day) for 3 weeks. Oxidative stress, blood brain barrier breakdown, microglial hyperactivity, synaptic dysplasticity, apoptosis, amyloid proteins production in the hippocampus and cognitive decline were found in HFD-fed rats. Atorvastatin and PCSK9 inhibitor therapies equally attenuated hippocampal apoptosis and amyloid protein production in HFD-fed rats. Interestingly, PCSK9 inhibitor had the greater efficacy than atorvastatin on the amelioration of hippocampal oxidative stress, blood brain barrier breakdown, microglial hyperactivity, synaptic dysplasticity in the hippocampus and cognitive decline. These findings suggest that PCSK9 inhibitor may be another drug of choice for improving brain function in the obese condition with discontinued statin therapy.

[5] *Baidžajevas K, Hadadi É, Lee B et al.* **Macrophage polarisation associated with atherosclerosis differentially affects their capacity to handle lipids**. Atherosclerosis 2020; 305:10-18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32592946
ABSTRACT
BACKGROUND AND AIMS: Lipid-rich foam cell macrophages drive atherosclerosis via several mechanisms, including inflammation, lipid uptake, lipid deposition and plaque vulnerability. The atheroma environment shapes macrophage function and phenotype; anti-inflammatory macrophages improve plaque stability while pro-inflammatory macrophages promote rupture. Current evidence suggests a variety of macrophage phenotypes occur in atherosclerotic plaques with local lipids, cytokines, oxidised phospholipids and pathogenic stimuli altering their phenotype. In this study, we addressed differential functioning of macrophage phenotypes via a systematic analysis of in vitro polarised, human monocyte-derived macrophage phenotypes, focussing on molecular events that regulate foam-cell formation. METHODS: We examined transcriptomes, protein levels and functionally determined lipid handling and foam cell formation capacity in macrophages polarised with IFNγ+LPS, IL-4, IL-10, oxPAPC and CXCL4. RESULTS: RNA sequencing of differentially polarised macrophages revealed distinct gene expression changes, with enrichment in atherosclerosis and lipid-associated pathways. Analysis of lipid processing activity showed IL-4

and IL-10 macrophages have higher lipid uptake and foam cell formation activities, while inflammatory and oxPAPC macrophages displayed lower foam cell formation. Inflammatory macrophages showed low lipid uptake, while higher lipid uptake in oxPAPC macrophages was matched by increased lipid efflux capacity. CONCLUSIONS: Atherosclerosis-associated macrophage polarisation dramatically affects lipid handling capacity underpinned by major transcriptomic changes and altered protein levels in lipid-handling gene expression. This leads to phenotype-specific differences in LDL uptake, cellular cholesterol levels and cholesterol efflux, informing how the plaque environment influences atherosclerosis progression by influencing macrophage phenotypes.

[6] *Lau P, Soubeyrand S, Hegele RA et al.* **Molecular mechanism linking a novel PCSK9 copy number variant to severe hypercholesterolemia**. Atherosclerosis 2020; 304:39-43.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32585424
ABSTRACT
BACKGROUND AND AIMS: A 42 year-old male with premature atherosclerosis, severe dyslipidemia and resistance to treatment with high dose statin and a recommended dose of a PCSK9 inhibitor, was found to have a duplication of the PCSK9 gene. However, the clinical phenotype, which included a more than 15-fold elevation in circulating PCSK9, was unexpected given that he had one additional gene copy. METHODS: Here we have carried out whole genome sequencing and transcriptional reporter assays to investigate the molecular mechanism leading to this unusual FH phenotype. RESULTS: The PCSK9 duplication was found to contain the full coding sequence but with an 829 bp shorter 3'-untranslated region (UTR) sequence. All possible rearrangements include a head-to-head fusion between a completely duplicated PCSK9 and a chromosomal region, normally situated ~80 kb away, that includes HNF4 and USF1 binding sites that could promote transcription of the PCSK9 gene. Transcriptional reporter assays demonstrated that a construct harboring the HNF4 binding site significantly increased the promoter activity by 2.5-fold with a smaller effect noted for a USF1 construct. CONCLUSIONS: Here we describe, in a patient with resistant hypercholesterolemia, a novel PCSK9 gene rearrangement that enables upregulation of PCSK9 expression by allowing proximity to an active enhancer binding to HNF4A.

[7] *Martínez Soriano B, Güemes A, Pola G et al.* **Effect of Melatonin as an Antioxidant Drug to Reverse Hepatic Steatosis: Experimental Model**. Canadian journal of gastroenterology & hepatology 2020; 2020:7315253.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32566547
ABSTRACT
INTRODUCTION: The hepatic steatosis of the nonalcoholic origin or NAFLD is increasing at present, particularly in Western countries, parallel to the increase in obesity, constituting one of the most prevalent hepatic processes in the Western society. Melatonin has been successfully tested in experimental models in mice as a drug capable of reversing steatosis. The effect of melatonin on fat metabolism can be summarized as a decrease in lipid peroxidation and a decrease in oxidative stress, biochemical phenomena intimately related to fat deposition in the hepatocyte. There are hardly any studies in large animals. OBJECTIVE: In this study, we investigate the effects of melatonin administered orally at a dose of 10 mg/kg/day to reverse established hepatic steatosis induced by a special diet in a porcine animal model. MATERIALS AND METHODS: We analyze the parameters of oxidative stress: malondialdehyde (MDA), 4-

hydroxyalkenals (4-HDA), and carbonyls, degree of fat infiltration (analyzed by direct vision by a pathologist and by means of a computer program of image treatment), and serological parameters of lipid metabolism and hepatic damage. These parameters were analyzed in animals to which hepatic steatosis was induced by means of dietary modifications. RESULTS: We have not been able to demonstrate globally a beneficial effect of melatonin in the improvement or reversal of liver steatosis once established, induced by diet in a porcine animal model. However, we have found several signs of improvement at the histological level, at the level of lipid metabolism, and at the level of oxidative stress parameters. We have verified in our study that, in the histological analysis of the liver sample by means of the program image treatment (free of subjectivity) of the animals that continue with the diet, those that consume melatonin do not increase steatosis as much as those that do not consume it significantly (p=0.002). Regarding the parameters of oxidative stress, MDA modifies in a significant manner within the group of animals that continue with the diet and take melatonin (p=0.004). As for lipid metabolism, animals that maintain the steatotic diet and take melatonin lower total and LDL cholesterol levels and increase HDL levels, although these results do not acquire statistical significance. CONCLUSIONS: In this study, it has not been possible to demonstrate a beneficial effect of melatonin in the improvement or reversal of liver steatosis once established and induced by diet in the porcine model. It is true that signs of improvement have been found at the histological level, at the level of lipid metabolism, and at the level of oxidative stress phenomena, when comparing animals with established steatosis that are treated with melatonin with those who do not take it. This work is the first study conducted in a large animal model in which the effect of melatonin is studied as a treatment in the reversal of established hepatic steatosis.

[8] *Koren MJ, Jones PH, Robinson JG et al.* **A Comparison of Ezetimibe and Evolocumab for Atherogenic Lipid Reduction in Four Patient Populations: A Pooled Efficacy and Safety Analysis of Three Phase 3 Studies**. Cardiology and therapy 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32564340

ABSTRACT

INTRODUCTION: Clinicians, payers, guideline committees, and policymakers support the use of high-intensity statins in patients at high risk for complications of cardiovascular disease (CVD). Guidelines and recommendations provide guidance on next steps for patients with inadequate low-density lipoprotein cholesterol (LDL-C) control on maximally tolerated statin or for those who are statin-intolerant. Ezetimibe and evolocumab improve CV outcomes when added to statins in high-CV-risk populations. The aim of the study was to compare evolocumab and ezetimibe for lipid-lowering efficacy and safety. METHODS: We summarized data from 1427 patients from three phase 3 evolocumab studies comparing double-blinded evolocumab vs. ezetimibe. These studies evaluated four distinct populations: those free of CVD receiving each agent as monotherapy, patients with CVD receiving add-on therapy to low- or high-intensity statin, and statin-intolerant patients. Lipid efficacy and safety were reported at week 12. RESULTS: Across the studies, evolocumab reduced LDL-C by a mean 55-61% from baseline to week 12; ezetimibe lowered LDL-C by 18-20% from baseline (mean difference = 38-43% favoring evolocumab; $p < 0.0001$). This corresponded to absolute reductions in LDL-C of 60-104 mg/dL with evolocumab vs. 17-35 mg/dL with ezetimibe. Evolocumab also significantly improved other lipids and led to a higher percentage of patients achieving LDL-C goals vs. ezetimibe. Adverse events and discontinuation rates (oral and

parenteral therapy) were balanced across groups, suggesting good tolerance and acceptance of both treatments. CONCLUSIONS: Evolocumab outperformed ezetimibe in efficacy and lipid goal attainment. Both products demonstrated good safety/tolerability. These data may help guide access decisions for high-risk patients with inadequate treatment response or intolerance to statin therapy.

[9] *Zhang XJ, Qin JJ, Cheng X et al.* **In-Hospital Use of Statins Is Associated with a Reduced Risk of Mortality among Individuals with COVID-19**. Cell Metab 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32592657
ABSTRACT
Statins are lipid-lowering therapeutics with favorable anti-inflammatory profiles and have been proposed as an adjunct therapy for COVID-19. However, statins may increase the risk of SARS-CoV-2 viral entry by inducing ACE2 expression. Here, we performed a retrospective study on 13,981 patients with COVID-19 in Hubei Province, China, among which 1,219 received statins. Based on a mixed-effect Cox model after propensity score-matching, we found that the risk for 28-day all-cause mortality was 5.2% and 9.4% in the matched statin and non-statin groups, respectively, with an adjusted hazard ratio of 0.58. The statin use-associated lower risk of mortality was also observed in the Cox time-varying model and marginal structural model analysis. These results give support for the completion of ongoing prospective studies and randomized controlled trials involving statin treatment for COVID-19, which are needed to further validate the utility of this class of drugs to combat the mortality of this pandemic.

[10] *Chmelík Z, Vaclová M, Lánská V et al.* **Analysis of incidence and prevalence of cardiovascular risk factors and evaluation of their control in epidemiological survey in the Czech Republic**. Cent Eur J Public Health 2020; 28:114-119.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32592555
ABSTRACT
OBJECTIVE: The aim of this analysis was to analyze the presence of the most important cardiovascular (CV) risk factors and to discuss patterns of LDL cholesterol management in the population studied. METHODS: We enrolled 961 males, average age of 42.9 ± 4.7, and 851 females, average age of 51.2 ± 3.6. Data on personal, pharmacological and family history, and laboratory examinations were collected. Cardiovascular (CV) risk was calculated using the Systematic Coronary Risk Evaluation (SCORE) algorithm with modifications according to the guidelines. RESULTS: The distribution of CV risk in the observed cohort was as follows: 24% of the subjects had low, 51% moderate, 17% high and 8% very high risk. The percentage of patients who reached target values of LDL cholesterol was dramatically lower in the groups with very high (1%) and high (3%) risk than in the groups with moderate (14%) or low risk (59%). Dyslipidemia was newly identified in 20% of both sexes. Arterial hypertension was newly diagnosed in 8% of males and 5% of females, and type 2 diabetes mellitus was newly diagnosed in 3% of both the males and females. Dyslipidemia was present in 39% of males and 41% of females; arterial hypertension in 43% of males and 45% of females, and type 2 diabetes mellitus was diagnosed in 11% of the subjects of both sexes. 49% of males and 31% of females were overweight and 32% of both genders were obese. There were 36% of male smokers and 22% of female smokers. 48% of the participants were pharmacologically treated. Non-pharmacological treatment was recommended to 62% of male and to 65% of female

participants. Pharmacological intervention was started in 53% of males and 51% of females. In both gender antihypertensive treatment with angiotensin-converting enzyme (ACE) inhibitors (29% of males and 27% of females) and lipid lowering therapy with a statin (28% of males, 27% of females) were the most commonly initiated treatments. In the subgroup of the 101 patients with LDL cholesterol levels > 5 mmol/L 56% were not treated with a statin. The analysis of relationship between the positive family history of any of the followed CV risks showed significant increases of the risk for arterial hypertension, type 2 diabetes mellitus and dyslipidemia. CONCLUSION: European guidelines suggest general screening for risk factors, including analysis of lipid profiles in the population of 40-year-old males and 50-year-old or postmenopausal women. Our study documents high prevalence and incidence of CV risk factors together with insufficient control of the risk factors in Czech patients of this age range. This finding suggests that preventive examinations should be undertaken earlier (e.g., in 30-year-old males and 40-year-old women). Exact timing of the preventive check-ups to yield the best cost-benefit ratio needs to be verified.

[11] *Khamlaoui W, Mehri S, Hammami S et al.* **Association Between Genetic Variants in FADS1-FADS2 and ELOVL2 and Obesity, Lipid Traits, and Fatty Acids in Tunisian Population**. Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis 2020; 26:1076029620915286.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32584610

ABSTRACT

The aim of this study was to determine whether genetic variants in FADS1/FADS2 and ELOVL2 are associated with overweight-obesity and body mass index (BMI) and to assess the association between these genetic variants and lipid profile and fatty acid levels. A total of 259 overweight-obese patients were compared to 369 healthy controls. FADS1, FADS2, and ELOVL2 genes were associated with BMI and overweight-obesity ($P \leq .001$). In an additive model, the C allele in each of these variants was associated with a lower BMI: -1.18, -0.90, and -1.23 units, respectively. Higher amounts of total cholesterol, low-density lipoprotein cholesterol, total saturated fatty acids (lauric [12:0], myristic [C14:0], palmitic [C16:0], stearic [C18:0], arachidic [20:0], lignoceric [24:0]), monounsaturated fatty acids (myristoleic [C14:1], erucic [C22:1 n-9]), and polyunsaturated fatty acids (α-linolenic [ALA, 18:3 n-3], docosahexaenoic [DHA, C22:6 n-3], eicosapentaenoic acid [EPA, C20:5n-3], arachidonic acid [AA, 20:4n-6], and conjugated linolenic acids [CLA1 and CLA2]) were shown in patients. A significant increase in D6D activities presented by 20:4n-6/18:2n-6 and 18:3n-6/18:2n-6, Δ9 desaturase (D9D) activity, estimated by the ratio 18:1n-9/18:0 and elongase activities (AE), and estimated by the ratio of docosatetraenoic/AA and DPA/EPA in patients. The C minor allele of FADS1 had significantly lower DHA. A significant decrease in stearic acid, EPA, and AE activity (docosatetraenoic/AA) was revealed in patients with the minor allele carriers of FADS2. The C minor allele of ELOVL2 had significantly lower ALA, EPA, DPA, and D6D activity (C20:4 n-6/C18:2n-6). These data suggest that variations in FADS1, FADS2, and ELOVL2 affect the risk of overweight-obesity and the level of circulating fatty acids and could point to a key molecular pathway of metabolic syndrome and its related comorbidities.

[12] *Gutierrez-Bedmar M, Olmedo P, Gil F et al.* **Low serum iron levels and risk of cardiovascular disease in high risk elderly population: Nested case-control study in the**

PREvención con DIeta MEDiterránea (PREDIMED) trial. Clinical nutrition (Edinburgh, Scotland) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32591250
ABSTRACT
BACKGROUND & AIMS: Epidemiological data on iron status and cardiovascular disease (CVD) are still controversial. The aim of this study was to determine whether low serum iron (SI) levels are associated with an increased odds of first CVD event in a population at high cardiovascular risk. METHODS: Case-control study design nested within the "PREvención con DIeta MEDiterránea" (PREDIMED) trial. A total of 207 participants diagnosed with CVD (myocardial infarction, stroke or cardiovascular death) during follow-up period (2003-2010) were matched by sex, age and intervention group to 436 controls by incidence density sampling. Median time between serum sample collection and subsequent CVD event occurrence was 0.94 years. Inductively coupled plasma mass spectrometry analysis was used to determine SI levels. In-person interviews, medical record reviews, and validated questionnaires were used to assess covariates. Multivariable-adjusted odds ratios (ORs) of CVD were calculated with conditional logistic regression. RESULTS: Mean SI levels were higher in men than in women (1224.0 μg/L vs. 1093.8 μg/L; $p < 0.001$). Among women, but not in men, the mean SI concentration was lower in cases than in controls (1008.5 μg/L vs. 1132.9 μg/L; $p = 0.030$). There was a gradual decrease in the multivariable-adjusted ORs of CVD with increasing SI levels (highest vs. lowest quartile: OR = 0.55, 95% CI: 0.32-0.93; p(trend) = 0.020). This inverse relationship was more pronounced among women (highest vs. lowest quartile: OR = 0.15, 95% CI: 0.03-0.69; p(trend) = 0.011). CONCLUSIONS: The present findings are consistent with previously reported inverse associations between SI and CVD. SI levels as an independent marker of short-term cardiovascular risk may be useful for risk assessment in older populations. TRIAL REGISTRATION: www.controlled-trials.com; International Standard Randomized Controlled Trial Number (ISRCTN): 35,739,639. Registered 5 October 2005. Retrospectively registered.

[13] *Huh KY, Kim E, Lee H et al.* **Comparison of the Pharmacokinetics of a Fixed-Dose Combination of Rosuvastatin/Metformin Sustained-Release (10/1000 mg) and Separate Tablets in Healthy Male Subjects**. Clinical pharmacology in drug development 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32579298
ABSTRACT
Fixed-dose combination (FDC) drugs with various dose combinations for the treatment of type 2 diabetes mellitus and dyslipidemia are currently in demand. We compared the pharmacokinetic (PK) profiles of the rosuvastatin/metformin sustained-release (10/1000 mg) FDC and separate tablets and evaluated the effect of food by randomized, open-label, 3-period, 6-sequence crossover studies conducted in healthy male subjects. Subjects were randomly assigned to one of the following treatments: separate tablets of 10 mg rosuvastatin and 1000 mg metformin sustained release in the fed state and the FDC in the fasted and fed states. PK samples were collected up to 72 hours postdose for rosuvastatin, N-desmethyl rosuvastatin, and metformin. The PK parameters were determined using a noncompartmental method, and the geometric mean ratio (GMR) and the 90% confidence interval (CI) of the treatments were calculated. A total of 35 subjects completed the study. The GMR and 90%CI of the peak concentration (C(max)) and area under the plasma concentration-time curve from time zero to the last measurable concentration (AUC(last)) of the FDC and the separate

tablets were within the bioequivalence criteria (0.8-1.25) for both rosuvastatin and metformin. The effect of food was statistically significant for both rosuvastatin and metformin but not expected to be of clinical significance.

[14] *Aradine E, Hou Y, Cronin CA, Chaturvedi S*. **Current Status of Dyslipidemia Treatment for Stroke Prevention**. Current neurology and neuroscience reports 2020; 20:31.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32572590
ABSTRACT
PURPOSE OF REVIEW: Elevated cholesterol is an established risk factor for ischemic stroke. The value of statins for stroke prevention has been clear for more than a decade. RECENT FINDINGS: However, the use of new medication combinations such as ezetimibe or proprotein convertase subtilisin-kexin type 9 inhibitors plus statins is increasing and the value for reducing stroke has been shown for these combination therapies. Recent data also support the strategy of lowering triglycerides for stroke prevention. A modern approach to dyslipidemia treatment and its relation to stroke prevention is summarized in this paper.

[15] *Tokgözoglu L, Zamorano JL*. **Current perspectives on the use of statins in the treatment of dyslipidaemic patients: focus on pitavastatin**. Drugs in context 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32587627
ABSTRACT
A meeting entitled 'Current Perspective on the Use of Statins in the Treatment of Dyslipidemic Patients' was held in Stresa, Italy, on 27-28th June 2019. The presentations covered the 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines on dyslipidaemia, with discussion about the importance of controlling low-density lipoprotein cholesterol (LDL-C) and the pharmacological opportunities to reach the novel lipid goals. The roles of statins to manage dyslipidaemia in patients with different cardiovascular risks were also discussed. In particular, the efficacy and safety of pitavastatin for the treatment of dyslipidaemia were reviewed, highlighting its further advantages beyond LDL-C reduction. Therefore, the impact of statins on the glycaemic profile was discussed in view of the null/lower effect of pitavastatin as compared with other statins, as well as the interaction profile with other drugs commonly used. This meeting report summarizes the main messages of the discussion with a special focus on pitavastatin, whose main features in different settings are described.

[16] *Jacob RS, de Souza Santos LV, d'Auriol M et al.* **Diazepam, metformin, omeprazole and simvastatin: a full discussion of individual and mixture acute toxicity**. Ecotoxicology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32588236
ABSTRACT
High consumption of drugs, combined with their presence in the environment, raises concerns about its consequences. Even though researches are often engaged in analyzing substances separately, that is not the environmental reality. Therefore, the aim of this study was to investigate the acute toxicity of the pharmaceuticals simvastatin, metformin, omeprazole and diazepam, and all possible mixtures between them, to the organism Aliivibrio fischeri, verifying possible synergistic or antagonistic effects and assessing byproducts formation. In terms of individual toxicity, omeprazole is the most toxic of the active ingredients, followed by simvastatin, diazepam and, finally, metformin. When the toxicity of mixtures was tested,

synergism, antagonism and hormesis were perceived, most probably generated due to byproducts formation. Moreover, it was observed that even when compounds are at concentrations below the non-observed effect concentration (NOEC), there may be toxicity to the mixture. Hence, this work points to the urgent need for more studies involving mixtures, since chemicals are subject to interactions and modifications, can mix, and potentiate or nullify the toxic effect of each other.

[17] *Abdullah S, Jarrar Y, Alhawari H et al.* **The Influence Of Endothelial Nitric Oxide Synthase (Enos) Genetic Polymorphisms On Cholesterol Blood Levels Among Type 2 Diabetic Patients On Atorvastatin Therapy**. Endocrine, metabolic & immune disorders drug targets 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32564765
ABSTRACT
BACKGROUND: Endothelial nitric oxide synthase (eNOS) plays a major role in the response of antihypercholesterol statin drugs. Genetic polymorphisms in the eNOS gene affect the activity of eNOS and thereby modulate statin response. OBJECTIVES: This study investigated the influence of major functional eNOS gene polymorphisms (rs2070744, rs1799983, and rs61722009) on the lipid profile of type 2 diabetes mellitus (T2DM) Jordanian patients treated with atorvastatin. METHODS: The sample comprised 103 T2DM patients who attended the diabetes clinic of Jordan University Hospital. The T2DM patients had regularly been taking 20 mg atorvastatin. The atorvastatin response was calculated by measuring the lipid profile before and after three months of atorvastatin treatment. The eNOS genotypes of the subjects were analyzed using polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP) assay. RESULTS: No significant association was found between eNOS genetic polymorphisms and the response to atorvastatin (ANOVA, $p > 0.05$). In addition, no significant difference in the frequency of eNOS genotypes was found between T2DM patients and healthy subjects. However, patients with eNOS rs1799983, 4a/4a, and rs61722009 G/G genotypes showed a significantly lower levels of baseline total cholesterol (TC) and low density lipoprotein (LDL) than did patients carrying the rs1799983 4b/4b or rs61722009 T/T genotype ($p < 0.05$). The eNOS rs1799983 and rs61722009 polymorphisms were in complete linkage disequilibrium ($D' = 1$). CONCLUSION: Although no association was found between eNOS genetic polymorphisms and atorvastatin response, there was a significant association between the rs1799983 and rs61722009 genotypes and baselines levels of TC and LDL in Jordanian T2DM patients. These genetic variants affect cholesterol levels and may play a role in the susceptibility to cardiovascular diseases in T2DM patients. Further studies are needed to validate these findings.

[18] *Deng Q, Li XX, Fang Y et al.* **Therapeutic Potential of Quercetin as an Antiatherosclerotic Agent in Atherosclerotic Cardiovascular Disease: A Review**. Evidence-based complementary and alternative medicine : eCAM 2020; 2020:5926381.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32565865
ABSTRACT
Atherosclerotic cardiovascular disease (ASCVD) is one of the diseases with the highest morbidity and mortality globally. It causes a huge burden on families and caregivers and high costs for medicine and surgical interventions. Given expensive surgeries and failures of most conventional treatments, medical community tries to find a more cost-effective cure. Thus,

attentions have been primarily focused on food or herbs. Quercetin (Qu) extracted from food, a flavonoid component, develops potentials of alternative or complementary medicine in atherosclerosis. Due to the wide range of health benefits, researchers have considered to apply Qu as a natural compound in therapy. This review is aimed to identify the antiatherosclerosis functions of Qu in treating ASCVD such as anti-inflammatory, antioxidant properties, effects on endothelium-dependent vasodilation, and blood lipid-lowering.

[19] *Liu D, Shen T, Ren C et al.* **The effects of atorvastatin and rosuvastatin on exercise tolerance in patients with coronary heart disease**. Expert opinion on drug safety 2020:1-6.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571108

ABSTRACT

OBJECTIVES: This study was aimed to analyze the effects of atorvastatin and rosuvastatin and different lipid-lowering intensity treatments on exercise tolerance in patients with coronary heart disease (CHD). METHODS: A retrospective analysis was conducted in 549 patients with CHD who underwent cardiopulmonary exercise testing (CPET) from February 2014 to August 2018. The CPET results of patients taking different types and doses of statins were compared from baseline to follow-up. RESULTS: No significant difference was found in baseline VO(2)peak between the rosuvastatin group and the atorvastatin group. The VO(2)peak growth of the rosuvastatin group was significantly greater than that of the atorvastatin group after treatment [1.52 ± 4.03 ml/kg/min vs 0.90 ml/kg/min (-1.60, 3.45), p = 0.018]. Multivariate analysis showed that atorvastatin was a negative independent influencing factor of ΔVO(2)peak (B = -0.665, SE = 0.321, t = -2.070, p = 0.039, 95% CI: - 1.295~-0.034). There was no significant difference between the median intensity and high-intensity lipid-lowering groups in parameters of CPET. CONCLUSIONS: The exercise tolerance improvement was more considerable for patients with CHD taking rosuvastatin compared with those taking atorvastatin. The lipid-lowering intensity of statins was not independently associated with changes in exercise tolerance in patients with CHD.

[20] *Brandts J, Ray KK*. **Bempedoic acid, an inhibitor of ATP citrate lyase for the treatment of hypercholesterolemia: early indications and potential**. Expert opinion on investigational drugs 2020:1-8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32564642

ABSTRACT

INTRODUCTION: The lowering of low-density lipoprotein cholesterol (LDL-C), regardless of the method used, results in a reduction of cardiovascular events. Bempedoic acid is a new and until now, the only approved adenosine triphosphate citrate lyase inhibitor that works through the cholesterol-synthesis pathway (similar to statins) that leads to a safe and effective reduction in LDL-C. AREAS COVERED: We review clinical phase 2 and 3 studies on bempedoic acid's lipid-lowering effect and approved indications. EXPERT OPINION: In the United States, bempedoic acid is currently approved for use in secondary prevention. In primary prevention, its approval is limited to individuals with heterozygous familial hypercholesterolemia (FH). However, its tolerability and safety profile may warrant its use in primary prevention besides FH. Even though its efficacy appears weaker than high-intensity statins, it may be a useful adjunct in individuals who achieve less than desirable LDL-C reductions with statins or who cannot tolerate statins, where bempedoic acid alone or in combination with ezetimibe may be useful alternatives.

[21] *Sorokin AV, Karathanasis SK, Yang ZH et al.* **COVID-19-Associated dyslipidemia: Implications for mechanism of impaired resolution and novel therapeutic approaches**. FASEB journal : official publication of the Federation of American Societies for Experimental Biology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32588493
ABSTRACT
The current coronavirus disease 2019 (COVID-19) pandemic presents a global challenge for managing acutely ill patients and complications from viral infection. Systemic inflammation accompanied by a "cytokine storm," hemostasis alterations and severe vasculitis have all been reported to occur with COVID-19, and emerging evidence suggests that dysregulation of lipid transport may contribute to some of these complications. Here, we aim to summarize the current understanding of the potential mechanisms related to COVID-19 dyslipidemia and propose possible adjunctive type therapeutic approaches that modulate lipids and lipoproteins. Specifically, we hypothesize that changes in the quantity and composition of high-density lipoprotein (HDL) that occurs with COVID-19 can significantly decrease the anti-inflammatory and anti-oxidative functions of HDL and could contribute to pulmonary inflammation. Furthermore, we propose that lipoproteins with oxidized phospholipids and fatty acids could lead to virus-associated organ damage via overactivation of innate immune scavenger receptors. Restoring lipoprotein function with ApoA-I raising agents or blocking relevant scavenger receptors with neutralizing antibodies could, therefore, be of value in the treatment of COVID-19. Finally, we discuss the role of omega-3 fatty acids transported by lipoproteins in generating specialized proresolving mediators and how together with anti-inflammatory drugs, they could decrease inflammation and thrombotic complications associated with COVID-19.

[22] *Gao K, Chu W, Sun J, Mao X*. **Identification of an alkaline lipase capable of better enrichment of EPA than DHA due to fatty acids selectivity and regioselectivity**. Food chemistry 2020; 330:127225.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32569931
ABSTRACT
The whole genome of Streptomyces violascens (=ATCC 27968) was sequenced and the cloning and expression of OUC-Lipase 6 were conducted in Bacillus subtilis WB800. The recombinant enzyme belongs to the lipolytic enzymes family V. OUC-Lipase 6 showed optimal activity at 30 °C and pH 9.0, and retained 90.2% of its activity in an alkaline buffer (pH 8.0, 30 °C and 96 h). OUC-Lipase 6 showed good stability under medium temperature conditions (residual activity of 68.8%, pH 8.0, 45 °C and 96 h). OUC-Lipase 6 could selectively hydrolyze fatty acids on the glyceride backbone, thus improving the contents of DHA and EPA in codfish oil. OUC-Lipase 6 also showed regioselectivity, resulting in a better enrichment efficiency for EPA than DHA. After hydrolyzing for 36 h via OUC-Lipase 6, the contents of EPA and DHA were improved to 3.24-fold and 1.98-fold, respectively.

[23] *Hu W, Li Y, Zhao Y et al.* **Telmisartan and Rosuvastatin Synergistically Ameliorate Dementia and Cognitive Impairment in Older Hypertensive Patients With Apolipoprotein E Genotype**. Frontiers in aging neuroscience 2020; 12:154.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32581766
ABSTRACT

Objective: To investigate the effect of telmisartan, rosuvastatin, or their combination on dementia and to understand the impact of apolipoprotein E (APOE) genotype on the effect of the medications in older patients with hypertension. Methods: This is a double-blind, randomized, and placebo-controlled trial using a 2 × 2 factorial design. Between April 2008 and November 2010, 1,244 hypertensive patients aged ≥60 years without cognitive impairment were recruited from communities in six cities in Shandong area, China. Patients were randomized into telmisartan and rosuvastatin administration after a 2-week washout period. APOE genotype was identified at the baseline. Possible dementia was determined using the combination of the global cognitive function and Assessment of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Results: Over an average follow-up of 7 [interquartile range (IQR): 6.7-7.2] years, telmisartan and rosuvastatin significantly reduced the cognitive impairment progression and the incidence of dementia. There was a synergistic interaction between telmisartan and rosuvastatin to reduce the cognitive impairment and the incidence of dementia (P (adjusted) < 0.001). The cognitive impairment progression and the risk of dementia were higher in the hypertensive patients with APOE ε4 allele than in those without APOE ε4 allele. Rosuvastatin medication significantly alleviated the cognitive impairment progression and the risks of dementia in patients with APOE ε4 allele. Conclusion: The combination of telmisartan and rosuvastatin might be an effective prevention and/or treatment strategy for cognitive impairment and dementia, especially in hypertensive patients with the APOE ε4 allele. Clinical Trial Registration: www.ClinicalTrials.gov, ChiCTR.org.cn, identifier ChiCTR-IOR-17013557. Registered on April 12, 2017 - Retrospectively registered, http://www.chictr.org.cn/showproj.aspx?proj=23121.

[24] *Chew H, Solomon VA, Fonteh AN*. **Involvement of Lipids in Alzheimer's Disease Pathology and Potential Therapies**. Front Physiol 2020; 11:598.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32581851

ABSTRACT

Lipids constitute the bulk of the dry mass of the brain and have been associated with healthy function as well as the most common pathological conditions of the brain. Demographic factors, genetics, and lifestyles are the major factors that influence lipid metabolism and are also the key components of lipid disruption in Alzheimer's disease (AD). Additionally, the most common genetic risk factor of AD, APOE ϵ4 genotype, is involved in lipid transport and metabolism. We propose that lipids are at the center of Alzheimer's disease pathology based on their involvement in the blood-brain barrier function, amyloid precursor protein (APP) processing, myelination, membrane remodeling, receptor signaling, inflammation, oxidation, and energy balance. Under healthy conditions, lipid homeostasis bestows a balanced cellular environment that enables the proper functioning of brain cells. However, under pathological conditions, dyshomeostasis of brain lipid composition can result in disturbed BBB, abnormal processing of APP, dysfunction in endocytosis/exocytosis/autophagocytosis, altered myelination, disturbed signaling, unbalanced energy metabolism, and enhanced inflammation. These lipid disturbances may contribute to abnormalities in brain function that are the hallmark of AD. The wide variance of lipid disturbances associated with brain function suggest that AD pathology may present as a complex interaction between several metabolic pathways that are augmented by risk factors such as age, genetics, and lifestyles. Herewith, we examine factors that influence brain lipid composition, review the association of lipids with all known facets of AD pathology, and offer pointers for potential therapies that target lipid pathways.

[25] *Augoulea A, Armeni E, Paschou SA et al.* **Breastfeeding is associated with lower subclinical atherosclerosis in postmenopausal women**. Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology 2020:1-4.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32584151
ABSTRACT
Objective: To evaluate the association between a personal history of lactation and indices of subclinical atherosclerosis in postmenopausal women.Methods: We evaluated the association between a history of breastfeeding and indices of subclinical atherosclerosis (pulse wave velocity, PWV; intima-media thickness [IMT]; atherosclerotic plaque presence) in 197 parous postmenopausal women with history of breastfeeding.Results: Women who reported breastfeeding ≥6 months when compared with women who reported breastfeeding for 1-5 months exhibited significantly lower values of common carotid artery IMT (Model R(2)=15.7%, b-coefficient = -0.170, 95% CI: -0.208-0.001, p-value = .019) and lower odds of subclinical atherosclerosis (Model X(2)=28.127, OR = 0.491, 95% CI 0.318-0.999, p-value = .049), adjusting for traditional cardiovascular risk factors.Conclusions: Postmenopausal women with a history of breastfeeding for at least 6 months have a lower prevalence of subclinical atherosclerosis, independently of traditional cardiovascular risk factors. A longer duration of breastfeeding may have a beneficial effect on subclinical atherosclerosis later in life.

[26] *Tarkin JM, Ćorović A, Wall C et al.* **Positron emission tomography imaging in cardiovascular disease**. Heart 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571959
ABSTRACT
Positron emission tomography (PET) imaging is useful in cardiovascular disease across several areas, from assessment of myocardial perfusion and viability, to highlighting atherosclerotic plaque activity and measuring the extent of cardiac innervation in heart failure. Other important roles of PET have emerged in prosthetic valve endocarditis, implanted device infection, infiltrative cardiomyopathies, aortic stenosis and cardio-oncology. Advances in scanner technology, including hybrid PET/MRI and total body PET imaging, as well as the development of novel PET tracers and cardiac-specific postprocessing techniques using artificial intelligence will undoubtedly continue to progress the field.

[27] *Melendez QM, Wooten CJ, Krishnaji ST et al.* **Identification of Novel Proteins Interacting with Proprotein Convertase Subtilisin/Kexin 9**. International journal of biomedical investigation 2020; 3.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32587953
ABSTRACT
High levels of cholesterol, especially as low-density lipoprotein (LDL), are a well-known risk factor for atherosclerotic-related diseases. The key atherogenic property of LDL is its ability to form atherosclerotic plaque. Proprotein convertase subtilisin/kexin-9 (PCSK9) is an indirect regulator of plasma LDL levels by controlling the number of LDL receptor molecules expressed at the plasma membrane, especially in the liver. Herein, we performed a combination of affinity chromatography, mass spectrometry analysis and identification, and gene expression studies to identify proteins that interact with PCSK9. Through these studies, we identified three

proteins, alpha-1-antitrypsin (A1AT), alpha-1-microglobulin/bikunin precursor (AMBP), and apolipoprotein H (APOH) expressed by C3A cells that interact with PCSK9. The expression levels of A1AT and APOH increased in cells treated with MITO+ medium, a condition previously shown to affect the function of PCSK9, as compared to treating with Regular (control) medium. However, AMBP expression did not change in response to the treatments. Additional studies are required to determine which of these proteins can modulate the expression/function of PCSK9. The identification of endogenous modulators of PCSK9's function could lead to the development of novel diagnostic tests or treatment options for patients suffering hypercholesterolemia in combination with other chronic metabolic diseases.

[28] *Jabbari A, Jafari A, Hadian M, Ghasemi M*. **Model-based Cost-effectiveness Analysis of Atorvastatin Drugs for Prevention of Cardiovascular Diseases in Iran**. International journal of preventive medicine 2020; 11:57.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32577187
ABSTRACT
BACKGROUND: Today, cardiovascular disease is one of the main causes of mortality and disability in most developed and developing countries. The prediction of the major causes of deaths all over the world at all ages shows that 61% of deaths are due to chronic diseases, of which 30% is due to cardiovascular disease. The aim of this study was to assess the cost-utility analysis of atorvastatin for the prevention of cardiovascular diseases using the Markov model. METHODS: Markov model with a lifetime horizon was developed to evaluate economic and health outcomes for atorvastatin drugs for the prevention of cardiovascular diseases for a cohort of 1,000 patients. The effectiveness indicator in this study was quality-adjusted life-years (QALYs); robustness of results was examined by one-way and probabilistic sensitivity analysis. RESULTS: The results showed that the use of atorvastatin compared to no drug intervention was highly cost-effective with USD173 per additional QALY. The results of one-way and probabilistic sensitivity analysis confirmed the results of this study. The findings of this study also showed that the highest cost items were hospitalization costs in the cardiac care unit (CCU). Also, the highest cost items in para-clinical services were related to echocardiography costs, and troponin constituted the largest cost of laboratory tests. CONCLUSIONS: Based on the results of this study, it is recommended that cardiologists use atorvastatin in the prevention of cardiovascular disease.

[29] *Wang K, Li Y, Liu G et al.* **Healthy Lifestyle for Prevention of Premature Death Among Users and Nonusers of Common Preventive Medications: A Prospective Study in 2 US Cohorts**. Journal of the American Heart Association 2020; 9:e016692.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32578485
ABSTRACT
Background It remains unknown whether individuals who regularly use preventive medications receive the same benefit from healthy lifestyle as those who do not use medications. We aimed to examine the associations of healthy lifestyle with mortality according to use of major preventive medications, including aspirin, antihypertensives, and lipid-lowering medications. Methods and Results Among 79 043 women in the Nurses' Health Study (1988-2014) and 39 544 men in the Health Professionals Follow-up Study (1986-2014), we defined a healthy lifestyle score based on body mass index, smoking, physical activity, diet, and alcohol intake. We estimated multivariable hazard ratios (HRs) and population-attributable risks of death from

any cause, cardiovascular disease, cancer, and other causes in relation to healthy lifestyle according to medication use. We documented 35 195 deaths. A similar association of healthy lifestyle score with lower all-cause mortality was observed among medication users (HR, 0.82 per unit increment; 95% CI, 0.81-0.82) and nonusers (HR, 0.81; 95% CI, 0.79-0.83) (P interaction=0.54). The fraction of premature deaths that might be prevented by adherence to the 5 healthy lifestyle factors among medication users and nonusers was 38% (95% CI, 32%-42%) and 40% (95% CI, 29%-50%) for all-cause mortality, 37% (95% CI, 27%-46%) and 45% (95% CI, 18%-66%) for cardiovascular disease mortality, and 38% (95% CI, 28%-46%) and 33% (95% CI, 14%-49%) for cancer mortality, respectively. Conclusions Adherence to a healthy lifestyle confers substantial benefit for prevention of premature death among both regular users and nonusers of preventive medications. Adherence to a healthy lifestyle remains important even among individuals regularly using preventive medications.

[30] *Arashi H, Yamaguchi J, Kawada-Watanabe E et al.* **The Effects of Lipid-Lowering Therapy on Serum Eicosapentaenoic Acid to Arachidonic Acid Ratio: An HIJ-PROPER Sub-Analysis**. Journal of cardiovascular pharmacology and therapeutics 2020:1074248420931621.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32567339
ABSTRACT
BACKGROUND: Controversy remains regarding the influence of lipid-lowering therapy on the eicosapentaenoic acid/arachidonic acid ratio. OBJECTIVE: This study aimed to clarify the effects of lipid-lowering therapy on the eicosapentaenoic acid/arachidonic acid ratio in patients with acute coronary syndrome (ACS). METHODS: This was a post hoc sub-analysis of the Heart Institute of Japan-PRoper level of lipid-lowering with pitavastatin and ezetimibe in ACS study. We compared the eicosapentaenoic acid/arachidonic acid ratio changes from baseline to the 3-month follow-up after contemporary lipid-lowering therapy with pitavastatin + ezetimibe therapy and pitavastatin mono-therapy. RESULTS: Among patients with ACS and dyslipidemia, the eicosapentaenoic acid/arachidonic acid increased significantly in the pitavastatin mono-therapy group (0.40 ± 0.26 to 0.46 ± 0.34, P < .0001) but did not increase in the pitavastatin + ezetimibe group (0.37 ± 0.22 to 0.38 ± 0.27, P = .18). When the analysis was limited to patients who received 2 mg/day of pitavastatin during the follow-up period, these trends in changes of the eicosapentaenoic acid/arachidonic acid ratio remained unchanged. Multivariate analysis showed that ezetimibe use (P = .005; β = 0.09), ST-elevation myocardial infarction (P = .04; β = -0.01), and baseline low-density lipoprotein cholesterol (LDL-C) level (P = .0003; β = 0.12) were independent predictors of the percentage change in the eicosapentaenoic acid/arachidonic acid ratio. These trends were similar even when the analysis was limited to patients who did not take statins at enrollment. CONCLUSION: Standard lipid-lowering therapy with pitavastatin mono-therapy improved the eicosapentaenoic acid/arachidonic acid ratio for patients with ACS. Intensive lipid-lowering therapy with pitavastatin + ezetimibe did not improve the eicosapentaenoic acid/arachidonic acid ratio, although LDL-C decreased significantly. Inhibition of the improvement in the eicosapentaenoic acid/arachidonic acid ratio by adding ezetimibe may affect cardiovascular disease prognosis.

[31] *Aceña Á, Franco Peláez JA, Pello Lázaro AM et al.* **PCSK9 and HS-CRP Predict Progression of Aortic Stenosis in Patients with Stable Coronary Artery Disease**. Journal of cardiovascular translational research 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32577988
ABSTRACT
It is essential to study the factors associated with the evolution of aortic stenosis progression (ASP) to develop therapies that could reduce it. We studied 283 patients 6 months after acute coronary syndrome (ACS). ASP was defined as an increase in the maximum aortic velocity of at least 0.5 m/s between the echocardiogram performed during ACS hospitalization and the last one recorded in the electronic medical registry. The median follow-up was 72.4 months. Twenty patients (7%) had ASP. A multivariate binary logistic regression analysis was performed showing that PCSK9 plasma levels (OR, 0.668 CI (0.457-0.977); p = 0.038), HS-CRP (OR, 1.034 CI (1.005-1.063); p = 0.022), the presence of dyslipidemia (OR, 4.622 CI (1.285-16.618); p = 0.019), the history of PAD (OR, 9.453 CI (1.703-52.452); p = 0.010), and GFR (OR, 0.962 CI (0.939-0.986); p = 0.002) were independent predicting factors of ASP. In patients with ischemic heart disease, low plasma levels of PCSK9 and elevated levels of HS-CRP are independent predictors of ASP.

[32] *Hori M, Takahashi A, Son C et al.* **The first Japanese cases of familial hypercholesterolemia due to a known pathogenic APOB gene variant, c.10580 G>A: p.(Arg3527Gln)**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32591292
ABSTRACT
BACKGROUND: We previously showed that patients without pathogenic variants in the LDLR and PCSK9 genes comprised approximately 40% of familial hypercholesterolemia (FH) cases. OBJECTIVE: Our aim was to identify novel causative variants in Japanese patients with FH. METHODS: Whole-exome sequencing was performed in 216 family members from 123 families without pathogenic variants in the LDLR and PCSK9 genes. Clinical and biochemical data were gathered from the family members. RESULTS: The known p.(Arg3527Gln) variant in the APOB gene was identified in one Japanese family. The other pathogenic variants in the APOB gene were not identified. The p.(Arg3527Gln) variant was not identified in the other 113 index cases without pathogenic variants in the LDLR and PCSK9 genes. The allele frequency of the p.(Arg3527Gln) variant was 0.0001 in the general Japanese population. CONCLUSION: This is the first report of Japanese cases of FH caused by a known pathogenic APOB variant, p.(Arg3527Gln).

[33] *Wang KN, Bell JS, Tan EC et al.* **Statin use and fall-related hospitalizations among residents of long-term care facilities: A case-control study**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571729
ABSTRACT
BACKGROUND: Statins are associated with muscle-related adverse events, but few studies have investigated the association with fall-related hospitalizations among residents of long-term care facilities (LTCFs). OBJECTIVE: The objective of the study is to investigate whether statin use is associated with fall-related hospitalizations from LTCFs. METHODS: A case-control study was conducted among residents aged ≥65 years admitted to hospital from 2013 to 2015. Cases (n = 332) were residents admitted for falls and fall-related injuries. Controls (n = 332) were selected from patients admitted for reasons other than cardiovascular and diabetes. Cases and controls were matched 1:1 by age (±2 years), index date of admission

(±6 months), and sex. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were estimated using conditional logistic regression, after considering for history of falls, hypertension, dementia, functional comorbidity index, polypharmacy (≥9 regular preadmission medications), and fall-risk medications. Subanalyses were performed for individual statins, dementia, and statin intensity. RESULTS: Overall, 43.1% of cases and 27.1% of controls used statins. Statins were associated with fall-related hospitalizations (aOR = 2.24, 95% CI 1.56-3.23), in particular simvastatin (aOR = 2.26, 95% CI 1.22-4.20) and atorvastatin (aOR = 2.08, 95% CI 1.33-3.24). Statins were associated with fall-related hospitalizations in residents with (aOR = 2.34, 95% CI 1.33-4.11) and without dementia (aOR = 2.30, 95% CI 1.46-3.63). There was no association between statin intensity and fall-related hospitalizations (aOR = 0.78, 95% CI 0.43-1.40). CONCLUSION: This study suggests a possible association between statin use and fall-related hospitalizations among residents living in LTCFs. However, there was minimal evidence for a relationship between statin intensity and fall-related hospitalizations. Further research is required to substantiate these hypothesis-generating findings.

[34] *Radenkovic D, Chawla S, Pirro M et al.* **Cholesterol in Relation to COVID-19: Should We Care about It?** Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32570882
ABSTRACT
Current data suggest that infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing corona virus disease-19 (COVID-19) seems to follow a more severe clinical course in patients with cardiovascular disease (CVD), hypertension, and overweight/obesity. It appears that lipid-lowering pharmacological interventions, in particular statins, might reduce the risk of cardiovascular complications caused by COVID-19 and might potentially have an additional antiviral activity. It has been shown that high cholesterol levels are associated with more lipid rafts, subdomains of the plasma membrane that can harbour angiotensin-converting enzyme 2 (ACE2) receptors for the S-protein of SARS-CoV-2. Evidence of the importance of cholesterol for viral entry into host cells could suggest a role for cholesterol-lowering therapies in reducing viral infectivity. In addition to their lipid-lowering and plaque-stabilisation effects, statins possess pleiotropic effects including anti-inflammatory, immunomodulatory, and antithrombotic activities. Lower rates of mortality and intubation have been reported in studies investigating statin therapy in influenza infection, and statin therapy was shown to increase viral clearance from the blood during chronic hepatitis C infection. Statins may also serve as potential SARS-CoV-2 main protease inhibitors, thereby contributing to the control of viral infection. In this review, we elaborate on the role of cholesterol level in the process of the coronavirus infection and provide a critical appraisal on the potential of statins in reducing the severity, duration, and complications of COVID-19.

[35] *Li N, Xu X, Mao S et al.* **Association of dyslipidaemia with Alzheimer's disease in a cohort of postmenopausal women**. J Int Med Res 2020; 48:300060520926020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32567449
ABSTRACT
OBJECTIVE: To evaluate the association between dyslipidaemia and Alzheimer's disease (AD) in a cohort of postmenopausal women. METHODS: This retrospective study analysed data from postmenopausal women with early AD (group AD) and a cohort of healthy age- and sex-matched control subjects (group NC) that were considered to be within standard limits

according to a neuropsychological assessment between March 2010 and March 2019. The primary endpoints were body mass index and lipid-related laboratory parameters, including leptin, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol, adiponectin, triglycerides, apolipoprotein A1, apolipoprotein B and apolipoprotein E4, which were evaluated using multivariate binary logistic analysis. RESULTS: The study enrolled 200 postmenopausal women with early AD (mean ± SD age 69.34 ± 6.25 years) and 180 control subjects (mean ± SD age 67.48 ± 7.42 years). Lower HDL-C and higher LDL-C were risk factors for AD. A multivariate binary logistic regression model demonstrated that lower HDL-C and higher LDL-C were the only variables associated with the development of AD (odds ratio [OR] 21.14, 95% confidence interval [CI] 2.47, 4.13; OR 36.35, 95% CI 1.24, 3.38; respectively). CONCLUSION: Both low HDL-C and high LDL-C were associated with the occurrence of AD in a cohort of postmenopausal women.

[36] *Black LP, Puskarich MA, Henson M et al.* **Quantitative and Qualitative Assessments of Cholesterol Association With Bacterial Infection Type in Sepsis and Septic Shock**. Journal of intensive care medicine 2020:885066620931473.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32578468
ABSTRACT
BACKGROUND: Reduced cholesterol levels are associated with increased organ failure and mortality in sepsis. Cholesterol levels may vary by infection type (gram negative vs positive), possibly reflecting differences in cholesterol-mediated bacterial clearance. METHODS: This was a secondary analysis of a combined data set of 2 prospective cohort studies of adult patients meeting Sepsis-3 criteria. Infection types were classified as gram negative, gram positive, or culture negative. We investigated quantitative (levels) and qualitative (dysfunctional high-density lipoprotein [HDL]) cholesterol differences. We used multivariable logistic regression to control for disease severity. RESULTS: Among 171 patients with sepsis, infections were gram negative in 67, gram positive in 46, and culture negative in 47. Both gram-negative and gram-positive infections occurred in 11 patients. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and HDL cholesterol (HDL-C) levels were lower for culture-positive sepsis at enrollment (TC, $P < .001$; LDL-C, $P < .001$; HDL-C, $P = .011$) and persisted after controlling for disease severity. Similarly, cholesterol levels were lower among culture-positive patients at 48 hours (TC, $P = .012$; LDL-C, $P = .029$; HDL-C, $P = .002$). Triglyceride (TG) levels were lower at enrollment ($P = .033$) but not at 48 hours ($P = .212$). There were no differences in dysfunctional HDL. Among bacteremic patients, cholesterol levels were lower at enrollment (TC, $P = .010$; LDL-C, $P = .010$; HDL-C, $P \leq .001$; TG, $P = .005$) and at 48 hours (LDL-C, $P = .027$; HDL-C, $P < .001$; TG, $P = .020$), except for 48 hour TC ($P = .051$). In the bacteremia subgroup, enrollment TC and LDL-C were lower for gram-negative versus gram-positive infections (TC, $P = .039$; LDL-C, $P = .023$). CONCLUSION: Cholesterol levels are significantly lower among patients with culture-positive sepsis and bacteremia.

[37] *Slhessarenko JR, Hirata M, Sousa A et al.* **Effect of Preloading With High Dose of Rosuvastatin on Serum Levels of Inflammatory Markers After Percutaneous Coronary Intervention**. J Invasive Cardiol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32568096
ABSTRACT

OBJECTIVES: We sought to assess the effects of a high loading dose of rosuvastatin (40 mg) on acute inflammatory response after coronary stenting. METHODS: Patients with stable coronary disease without statin use (≥7 days) and undergoing elective percutaneous coronary intervention (PCI) in a native coronary artery were randomized to receive a loading dose of rosuvastatin (n = 64) or not (n = 61). Blood samples were obtained before statin intake (time point A), 3 hours after medication (time point B), and 3 hours after PCI (time point C). The primary goal was the comparison in the variation of the serum inflammatory markers and their gene expression at the different time points between the two groups. RESULTS: Baseline clinical, angiographic, and procedural characteristics did not significantly differ between the groups, except for the more frequent use of postdilation in the control group (73.4% vs 90.2%; P=.02). Patients pretreated with statin showed a reduction in the serum levels of interleukin (IL)-1β (Δ = -0.491 pg/mL; Pinteraction<.001), IL-6 (Δ = -0.209 pg/mL; Pinteraction<.001), and plasminogen activator inhibitor 1 (Δ = -1.573 pg/mL; Pinteraction<.001) as well as in their genetic expression, which was not observed in the control group. Regarding high-sensitivity c-reactive protein, there was no significant variation in its value from time point A to C in patients pretreated with statin (P=.58) while it significantly increased in the control group (P=.04). CONCLUSIONS: Among patients with stable coronary artery disease undergoing PCI with stents, pretreatment with high dose of rosuvastatin resulted in significant reduction in the serum levels of important inflammatory markers and their genetic expression.

[38] *Spezani R, da Silva RR, Martins FF et al.* **Intermittent fasting, adipokines, insulin sensitivity, and hypothalamic neuropeptides in a dietary overload with high-fat or high-fructose diet in mice**. The Journal of nutritional biochemistry 2020; 83:108419.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32580132

ABSTRACT

The intermittent fasting (IF) might have benefits on metabolism and food intake. Twelve-week old C57BL/6 J mice were fed a control diet (C, 10% kcal fat), a high-fat diet (HF, 50% kcal fat) or a high-fructose diet (HFru, 50% kcal fructose) for 8 weeks, then half of the animals in each group underwent IF (24 h fed, 24 h fasting) for an additional 4 weeks. Although food intake on the fed day remained the same for all groups, all fasting groups showed a reduction in body mass compared to their counterparts. IF reduced total cholesterol, triacylglycerol, fasting glucose, fasting insulin resistance index, and plasma leptin, but increased plasma adiponectin. IF reduced Leptin gene expression in the HF-IF group, but increased proinflammatory markers in the hypothalamus, also in the C-IF group. Both groups HFru-IF and C-IF, showed alterations in the leptin signaling pathway (Leptin, OBRb, and SOCS3), mainly in the HFru-IF group, suggesting leptin resistance. NPY and POMC neuropeptides labeled the neurons of the hypothalamus by immunofluorescence, corroborating qualitatively other quantitative findings of the study. In conclusion, current results are convincing in demonstrating the IF effect on central regulation of food intake control, as shown by NPY and POMC neuropeptide expressions, resulting in a lower weight gain. Besides, IF improves glycemia, lipid metabolism, and consequently insulin and leptin resistance. However, there is increased expression of inflammatory markers in mouse hypothalamus challenged by the HF and HFru diets, which in the long term may induce adverse effects.

[39] *Ozaki Y, Morozumi T, Watanabe K et al.* **Inhibitory effect of omega-3 fatty acids on alveolar bone resorption and osteoclast differentiation**. Journal of oral science 2020; 62:298-302.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32581177
ABSTRACT
In this study, a Porphyromonas gingivalis (P.g.)-infected mouse periodontitis model was used to investigate the effect of omega-3 fatty acid intake on differentiation and maturation of cultured osteoclast. Four-week-old C57BL/6JJcl mice were divided into four groups according to the diets they were fed from the beginning of the experiment (i.e., food containing omega-3 or omega-6 fatty acids) and whether they were orally administered P.g. Thirty-three days after beginning the experiment, bone marrow cells were sampled from the femoral bone of mice from each group and differentiated into osteoclasts; the effects of the ingestion of different fatty acids were subsequently investigated. There was no statistical interaction between the different fatty acids and P.g. infection on the number of osteoclasts ($P = 0.6$). However, the fatty acid type affected the number of osteoclasts in mice ($P = 0.0013$), with the omega-3 groups demonstrating lower osteoclast numbers than the omega-6 groups. Furthermore, the addition of resolvin E1 (RvE1), which is an omega-3 fatty acid-derived lipid mediator, suppressed the differentiation of mouse cultured osteoclasts ($P < 0.0001$). Therefore, the ingestion of omega-3 fatty acids may suppress osteoclast differentiation while inhibiting bone resorption and tissue destruction due to periodontitis.

[40] *Bagheri M, Tiwari HK, Murillo AL et al.* **A lipidome-wide association study of the lipoprotein insulin resistance index**. Lipids in health and disease 2020; 19:153.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32586392
ABSTRACT
BACKGROUND: The lipoprotein insulin resistance (LPIR) score was shown to predict insulin resistance (IR) and type 2 diabetes (T2D) in healthy adults. However, the molecular basis underlying the LPIR utility for classification remains unclear. OBJECTIVE: To identify small molecule lipids associated with variation in the LPIR score, a weighted index of lipoproteins measured by nuclear magnetic resonance, in the Genetics of Lipid Lowering Drugs and Diet Network (GOLDN) study (n = 980). METHODS: Linear mixed effects models were used to test the association between the LPIR score and 413 lipid species and their principal component analysis-derived groups. Significant associations were tested for replication with homeostatic model assessment-IR (HOMA-IR), a phenotype correlated with the LPIR score ($r = 0.48$, $p < 0.001$), in the Heredity and Phenotype Intervention (HAPI) Heart Study (n = 590). RESULTS: In GOLDN, 319 lipids were associated with the LPIR score (false discovery rate-adjusted p-values ranging from $4.59 \times 10(-161)$ to $49.50 \times 10(-3)$). Factors 1 (triglycerides and diglycerides/storage lipids) and 3 (mixed lipids) were positively ($\beta = 0.025$, $p = 4.52 \times 10(-71)$ and $\beta = 0.021$, $p = 5.84 \times 10(-41)$, respectively) and factor 2 (phospholipids/non-storage lipids) was inversely ($\beta = -0.013$, $p = 2.28 \times 10(-18)$) associated with the LPIR score. These findings were replicated for HOMA-IR in the HAPI Heart Study ($\beta = 0.10$, $p = 1.21 \times 10(-02)$ for storage, $\beta = -0.13$, $p = 3.14 \times 10(-04)$ for non-storage, and $\beta = 0.19$, $p = 8.40 \times 10(-07)$ for mixed lipids). CONCLUSIONS: Non-storage lipidomics species show a significant inverse association with the LPIR metabolic dysfunction score and present a promising focus for future therapeutic and prevention studies.

[41] *Yu S, Guo X, Li GX et al.* **Lower or higher HDL-C levels are associated with cardiovascular events in the general population in rural China**. Lipids in health and disease 2020; 19:152.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32586331
ABSTRACT
BACKGROUND: The present study aims to estimate whether high-density lipoprotein cholesterol (HDL-C) is correlated with cardiovascular events (CVEs) and cardiovascular mortality (CVM) in a large sample of the general population in rural areas of China. METHODS: Adult participants (n = 10,266, age = 53.79 ± 10.49 years; 46.5% men) were enrolled from the Northeast China Rural Cardiovascular Health Study (NCRCHS). Laboratory testing, blood pressure, weight, height, and questionnaires about socioeconomic status were collected. RESULTS: In all, 585 nonfatal or fatal CVEs and 212 cardiovascular deaths were documented during a 4.66-year follow-up. Compared to the reference groups (HDL-C between 1.5 and 1.99 mmol/L), either lower or higher levels of HDL-C were correlated with an increased incidence of CVEs but not CVM [hazard ratio (HR) (the lowest) = 1.369, 95% confidence interval, 1.007-1.861; HR (the highest) = 1.044, 0.509-2.231]. Elevated CVM was seen in the lowest HDL-C category (1.840; 1.121-3.021). CONCLUSIONS: Lower or higher HDL-C was associated with a higher incidence of CVEs but not CVM in the general population of rural China. Perhaps if an appropriate level of HDL-C is maintained, CVEs can be effectively prevented.

[42] *Zhao X, Zheng H, Shan S et al.* **Association between the non-HDL-cholesterol-to-HDL-cholesterol ratio and the risk of gallbladder polyp formation among men: a retrospective cohort study**. Lipids in health and disease 2020; 19:146.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32576257
ABSTRACT
BACKGROUND: Dyslipidaemia and male sex are associated with gallbladder polyp (GBP) formation. However, the potential relation between the non-high-density lipoprotein-cholesterol-to-high-density lipoprotein-cholesterol (non-HDL-c/HDL-c) ratio and GBPs in men is unclear. METHODS: A total of 1866 eligible subjects were selected for this retrospective cohort study from Wuhan Union Hospital between April 1, 2013, and November 30, 2014. Clinical and laboratory data of subjects were collected. Patients with GBPs or cholecystectomy at baseline, with missing data for baseline lipid profiles, following abdominal ultrasonography or taking lipid-lowering drugs were excluded. The patients were divided into five groups based on their non-HDL-c/HDL-c ratios, and descriptive analyses of the baseline data were performed. A Cox proportional hazards model was applied to estimate the relationship between the non-HDL-c/HDL-c ratio and GBPs. RESULTS: After a median follow-up of 1 year, 7.34% (n = 137) of the subjects developed GBPs. Compared with subjects without GBPs, those who developed GBPs after follow-up had significantly higher triglyceride (TG) levels and non-HDL-c/HDL-c ratios. The prevalence of GBPs showed a linearity increment with age, peaked in the 30-39 years group, 40-49 years group and 50-59 years group, and then declined slightly. The results of univariate analysis showed that the non-HDL-c/HDL-c ratio (hazard ratio (HR) = 1.29, 95% confidence interval (CI), 1.05-1.60, P = 0.0159) was positively correlated with GBPs. In the fully adjusted Cox regression model, the HRs were 2.24 for quintile 2 (95% CI: 1.13-4.44, P = 0.0203), 1.50 for quintile 3 (95% CI: 0.73-3.10, P = 0.269), 2.52 for quintile 4 (95% CI: 1.26-5.01, P = 0.0087) and 2.13 for quintile 5 (95% CI: 1.04-4.37, P = 0.0397). No

interaction was found among the subgroups. CONCLUSIONS: A higher non-HDL-c/HDL-c ratio is independently related to a higher risk of GBP formation in Chinese men. Further research is needed to investigate whether this association exists in different regions and races.

[43] *Pedro-Botet J, Climent E, Benaiges D*. **Atherosclerosis and inflammation. New therapeutic approaches**. Medicina clinica 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571617
ABSTRACT
The recognition of atherogenesis as an active process rather than a passive cholesterol storage disease has underlined key inflammatory mechanisms. Hence, innate and adaptive immune responses play an important role in the onset and progression of atherosclerosis. More recently, some clinical studies were designed to address the impact of anti-inflammatory intervention strategies in reducing risk of cardiovascular disease beyond the management of classic risk factors. Therefore, we review first the pathophysiological contribution of inflammation to atherosclerosis and the effect of lipid-lowering drugs on inflammatory biomarkers. Next, we address the effect of classic anti-inflammatory drugs, pharmacological therapies targeting specific inflammatory mediators and vaccines in cardiovascular prevention.

[44] *Dozio E, Ruscica M, Vianello E et al.* **PCSK9 Expression in Epicardial Adipose Tissue: Molecular Association with Local Tissue Inflammation**. Mediators of inflammation 2020; 2020:1348913.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32565719
ABSTRACT
Epicardial adipose tissue (EAT) has the unique property to release mediators that nourish the heart in healthy conditions, an effect that becomes detrimental when volume expands and proinflammatory cytokines start to be produced. Proprotein convertase subtilisin/kexin type 9 (PCSK9), a proinflammatory mediator involved in atherosclerosis, is also produced by visceral fat. Due to the correlation of inflammation with PCSK9 and EAT enlargement, we evaluated whether PCSK9 was expressed in EAT and associated with EAT inflammation and volume. EAT samples were isolated during surgery. EAT thickness was measured by echocardiography. A microarray was used to explore EAT transcriptoma. The PCSK9 protein levels were measured by Western Blot in EAT and ELISA in plasma. PCSK9 was expressed at both the gene and protein levels in EAT. We found a positive association with EAT thickness and local proinflammatory mediators, in particular, chemokines for monocytes and lymphocytes. No association was found with the circulating PCSK9 level. The expression of PCSK9 in EAT argues that PCSK9 is part of the EAT secretome and EAT inflammation is associated with local PCSK9 expression, regardless of circulating PCSK9 levels. Whether reducing EAT inflammation or PCSK9 local levels may have beneficial effects on EAT metabolism and cardiovascular risk needs further investigations.

[45] *Kim KW, Kim SJ, Kim H et al.* **Clinical effects of slim-diet, with lifestyle modification for childhood obesity in community-based healthcare program: A case series**. Medicine (Baltimore) 2020; 99:e20817.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32590767
ABSTRACT

RATIONALE: Although there are several reports on the effect of herbal medicine on weight loss in adults, evidence supporting its efficacy and safety in obese pediatrics is insufficient. Herein, we clinically investigated the preliminary experience of community-based healthcare program in cases of childhood obesity treated with an herbal complex, Slim-diet (SD), along with lifestyle modification. PATIENT CONCERNS: Seventeen subjects with childhood obesity participated in a community-based healthcare program, which consisted of twice-a-week play type physical activity and dietary counseling program with simultaneous twice-a-day administration of SD for 4 weeks. DIAGNOSES: The data of 13 obese pediatrics (body mass index [BMI] ≥ the 95th percentile for children of the same age and sex) in their 3rd to 6th grade who finally completed at least 6 visits out of a total of 8 visits of the program including baseline and endpoint assessments were analyzed. INTERVENTIONS: Participants received 20 g of SD daily. Simultaneously, play-type physical activity program with an exercise therapist and dietary counseling with a dietitian for lifestyle modification were conducted at every visit. Body composition, blood chemistry, the Korean Youth Physical Activity Questionnaire (KYPAQ) score, and the preference for salt density and sugar content were assessed at baseline and endpoint. OUTCOMES: After SD administration, body mass index decreased from 26.74 ± 2.11 kg/m to 26.50 ± 2.20 kg/m ($P < .05$) with statistically significant increases in height, weight, and skeletal muscle mass. The results of blood chemistry and the KYPAQ score showed no significant change. The preferences for salt density were improved in 8, maintained in 2, and worsened in 3 participants and those for sugar content were improved in 6 and maintained in 7 participants with no worsening. LESSONS: In the present study, we showed the clinical effects of SD with lifestyle modification in patients with childhood obesity who participated in community-based healthcare program. Further clinical studies investigating the effects of SD are required.

[46] *Thonusin C, Pantiya P, Jaiwongkam T et al.* **A proprotein convertase subtilisin/kexin type 9 inhibitor provides comparable efficacy with lower detriment than statins on mitochondria of oxidative muscle of obese estrogen-deprived rats**. Menopause (New York, N.Y.) 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32576799
ABSTRACT
OBJECTIVES: The aim of the study was to compare the effects of atorvastatin, a proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i), and 17β-estradiol on oxidative muscle mitochondria in a model of menopause with obesity. METHODS: Female Wistar rats consumed either a standard diet (n = 12) or a high-fat/calorie diet (HFCD: n = 60). At week 13, standard diet-fed rats underwent a sham operation, whereas HFCD-fed rats underwent either a sham operation (n = 12) or an ovariectomy (n = 48). At week 19, all sham-operated rats received vehicle, and ovariectomized HFCD-fed rats received either vehicle, 40 mg/kg/d of atorvastatin, 4 mg/kg/d of PCSK9i (SBC-115076), or 50 μg/kg/d of 17β-estradiol for 3 weeks (n = 12/group). Metabolic parameters and soleus muscle physiology were investigated at the end of week 21. RESULTS: Sham-operated and ovariectomized HFCD-fed rats developed obesity, hyperlipidemia, and insulin resistance, also showing increased oxidative phosphorylation (OXPHOS) proteins, ratio of p-Drp1-to-total Drp1 protein, malondialdehyde level, mitochondrial reactive oxygen species, and mitochondrial membrane depolarization in soleus muscle. All drugs equally decreased insulin resistance, OXPHOS proteins, ratio of p-Drp1-to-total Drp1 protein, and malondialdehyde level in soleus muscle. Only atorvastatin and

PCSK9i attenuated hypertriglyceridemia, whereas 17β-estradiol had greater efficacy in preventing weight gain than the other two drugs. In addition, 17β-estradiol decreased mitochondrial reactive oxygen species and mitochondrial membrane depolarization. Atorvastatin increased ratio of cleaved caspase 3,8-to-procaspase 3,8, and cytochrome C. CONCLUSIONS: 17β-Estradiol exhibits the greatest efficacy on the attenuation of obesity with the least harmful effect on skeletal muscle in a model of menopause with obesity, yet its effect on the treatment of hyperlipidemia is inferior to those of standard lipid-lowering agents.

[47] *Zhou R, Duncan K, Lopez J et al.* **Assessing the Continuation of Glucagon-Like Peptide-1 Receptor Agonists When Weight and HBA1C Are Not Reduced**. Metab Syndr Relat Disord 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32580677
ABSTRACT
Background: Glucagon-like peptide-1 agonists (GLP-1) reportedly lower HbA1c and promote weight reduction and improve cardiovascular outcomes. The primary objective of this study was to evaluate the use of GLP-1 agents in patients and changes in HbA1c, weight loss, blood pressure, and lipoid profiles. Methods: Patient information was extracted from a regional Veteran Affairs data mart. Patients were included if they had prescriptions for at least 90 days of a GLP-1 between April 1, 2005, and December 1, 2016, and HbA1Cs and weights at both baseline and within first 15 months of therapy. Blood pressure and lipids were also measured. Pearson's correlation and multiple regression analysis were used. Results: Three hundred twenty-two patients met inclusion criteria. Average HbA1c decreased by 0.81% and weight by 4.4 kg. At 1 year, 160 patients had both weight and HbA1c measured, and of those, 92 (58%) patients had HbA1c reduction of at least 0.5% and 94 (59%) patients had <-2 kg change in weight. Fifty-seven (36%) patients met both of those outcomes. Veterans who met both weight and HbA1c outcomes were slightly, but significantly, older than those who did not meet both. No correlation was found between weight and HbA1c change at each quarter ($P > 0.05$); however, weight change was correlated with systolic blood pressure change ($P = 0.03$). Multiple regression for meeting weight and HbA1c target outcomes, and changes at quarters 1-3, all correlated to success at 1 year ($P < 0.05$). Conclusions: Weight change was independent of HbA1c changes in patients receiving GLP-1s for diabetes control. Weight loss was associated with decreases in systolic BP.

[48] *Dewidar B, Kahl S, Pafili K, Roden M*. **Metabolic liver disease in diabetes - From mechanisms to clinical trials**. Metabolism 2020:154299.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32569680
ABSTRACT
Non-alcoholic fatty liver disease (NAFLD) comprises fatty liver (steatosis), non-alcoholic steatohepatitis (NASH) and fibrosis/cirrhosis and may lead to end-stage liver failure or hepatocellular carcinoma. NAFLD is tightly associated with the most frequent metabolic disorders, such as obesity, metabolic syndrome, and type 2 diabetes mellitus (T2DM). Both multisystem diseases share several common mechanisms. Alterations of tissue communications include excessive lipid and later cytokine release by dysfunctional adipose tissue, intestinal dysbiosis and ectopic fat deposition in skeletal muscle. On the hepatocellular level, this leads to insulin resistance due to abnormal lipid handling and mitochondrial function. Over time, cellular oxidative stress and activation of inflammatory pathways, again supported

by multiorgan crosstalk, determine NAFLD progression. Recent studies show that particularly the severe insulin resistant diabetes (SIRD) subgroup (cluster) associates with NAFLD and its accelerated progression and increases the risk of diabetes-related cardiovascular and kidney diseases, underpinning the critical role of insulin resistance. Consequently, lifestyle modification and certain drug classes used to treat T2DM have demonstrated effectiveness for treating NAFLD, but also some novel therapeutic concepts may be beneficial for both NAFLD and T2DM. This review addresses the bidirectional relationship between mechanisms underlying T2DM and NAFLD, the relevance of novel biomarkers for improving the diagnostic modalities and the identification of subgroups at specific risk of disease progression. Also, the role of metabolism-related drugs in NAFLD is discussed in light of the recent clinical trials. Finally, this review highlights some challenges to be addressed by future studies on NAFLD in the context of T2DM.

[49] *Stefanovski D, Vellanki P, Smiley-Byrd DD et al.* **Population insulin sensitivity from sparsely sampled oral glucose tolerance tests**. Metabolism 2020; 110:154298.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32569679

ABSTRACT

OBJECTIVE: This work aimed to estimate population-level insulin sensitivity (S(I)) from 2-hour oral glucose tolerance tests (OGTT) with less than 7 samples. RESEARCH DESIGN AND METHODS: The current methodology combines the OGTT mathematical model developed by Dalla Man et al., with nonlinear multilevel (NLML) statistical model to estimate population-level insulin sensitivity (S(I)) from sparsely sampled datasets (3 or 4 samples per subject obtained in 120 min). To validate our novel methodology of population S(I) estimation, we simulated 50 virtual subjects. We simulated 10 observations per subject over 240 minutes. After estimating their S(I) using the OGTT model, the virtual subjects were split into two groups, subjects with S(I) above the average and ones with below average. Subsequently, the simulated data were analyzed using statistical software and employing a t-test. The mean estimates of population S(I) for the two groups of virtual subjects and their respective 95% CI were compared to the estimates obtained with our novel NLML group S(I) estimates obtained using the 3 and 4 time points per subject. To further validate the performance of the novel NLML model, a set of 34 prediabetic and 30 diabetic subjects with T2D was used. As outlined above for the in-silico subjects, differences between the prediabetic and T2D subjects in regard to S(I) was assessed using the classical two-stage approach (individual S(I) estimation followed by statistical comparison of the two groups). The average estimates obtained with the classical two-stage approach were compared to the group estimated obtained with the NLML approach using 3 (0, 60, and 120 minutes) points per subject obtained in 120 minutes. RESULTS: Unique and identifiable individual estimates of S(I) were obtained for all virtual subjects. In comparison to the subjects with above average S(I) (n=25), the subjects with simulated below average S(I) (n=25) exhibited significantly lower insulin sensitivity (P<0.001). Our novel NLML population model confirmed these findings (4-point OGTT: P<0.001; 3-point OGTT: P<0.001). In a similar fashion to the one outlined for the virtual subjects, the median insulin sensitivities estimated with the classical two-stage approach were different between the prediabetic (n=34) and T2D subjects (n=32, P=0.004). Using 3 points per subject, our novel NLML model confirmed these findings (P<0.001). CONCLUSIONS: The population estimates of S(I) from OGTT data is an effective tool to assess population insulin sensitivity and assess differences that may not be possible when calculating individual S(I) or when less than 7 samples are available.

[50] *Hollstein T, Schumann F, Kassner U*. **[HIV and dyslipidemia - reasons and therapy]**. MMW Fortschritte der Medizin 2020; 162:54-61.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32583267
ABSTRACT

[51] *Wang K, Li B, Xie Y et al.* **Statin rosuvastatin inhibits apoptosis of human coronary artery endothelial cells through upregulation of the JAK2/STAT3 signaling pathway**. Molecular medicine reports 2020; 22:2052-2062.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32582964
ABSTRACT
The purpose of the present study was to explore the potential molecular signaling pathway mediated by the statin rosuvastatin in cultured human coronary artery endothelial cells (HCAECs) induced by CoCl2. CoCl2 was used to induce the apoptosis of HCAECs. Myocardial infarction rats were established and received statin or PBS treatment. Reverse transcription-quantitative PCR, western blotting, ELISA, TUNEL assay and immunohistochemistry were used to analyze the role of statin treatment. The results showed that rosuvastatin treatment decreased apoptosis of HCAECs induced by CoCl2 by increasing anti-apoptosis Bcl-xl and Bcl-2 expression, and decreasing pro-apoptosis Bax, Bad, caspase-3 and caspase-9 expression. The myocardial ischemia rat model demonstrated that rosuvastatin treatment decreased the mitochondrial reactive oxygen species, inflammation, mitochondrial damage, lipid catabolism, heart failure and the myocardial infarction areas, but improved the cardiac function indicators, right and left ventricular ejection fraction and increased expression levels of Janus kinase (JAK) and signal transducer and activator of transcription (STAT)3 in myocardial tissue. In conclusion, the results of the current study revealed that the statin rosuvastatin presents cardioprotective effects by activation of the JAK2/STAT3 signaling pathway.

[52] *Wei T, Cheng Q, Min YL et al.* **Systemic nanoparticle delivery of CRISPR-Cas9 ribonucleoproteins for effective tissue specific genome editing**. Nature communications 2020; 11:3232.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32591530
ABSTRACT
CRISPR-Cas9 has emerged as a powerful technology that relies on Cas9/sgRNA ribonucleoprotein complexes (RNPs) to target and edit DNA. However, many therapeutic targets cannot currently be accessed due to the lack of carriers that can deliver RNPs systemically. Here, we report a generalizable methodology that allows engineering of modified lipid nanoparticles to efficiently deliver RNPs into cells and edit tissues including muscle, brain, liver, and lungs. Intravenous injection facilitated tissue-specific, multiplexed editing of six genes in mouse lungs. High carrier potency was leveraged to create organ-specific cancer models in livers and lungs of mice though facile knockout of multiple genes. The developed carriers were also able to deliver RNPs to restore dystrophin expression in DMD mice and significantly decrease serum PCSK9 level in C57BL/6 mice. Application of this generalizable strategy will facilitate broad nanoparticle development for a variety of disease targets amenable to protein delivery and precise gene correction approaches.

[53] *Castilla Guerra L, Fernández Moreno MC, Jiménez Hernández MD et al.* **Trends in the use of statins after ischaemic stroke: Have clinical practices changed?** Neurologia 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32591153
ABSTRACT
INTRODUCTION: The role of statins after ischaemic stroke changed with the publication of the SPARCL study in 2006. We analyse how this has influenced the prescription of statins in this patient population. METHODS: We conducted a retrospective study of patients discharged with ischaemic stroke at the Virgen Macarena, Virgen del Rocío, and Valme hospitals in Seville (Spain) over two periods: 1999-2001 and 2014-2016. RESULTS: The study included 1575 patients: 661 (42%) were women and mean age (standard deviation) was 69 (10) years. Patients from the later period are older (68 [10] vs 71 [11]; P=.0001); include a higher proportion of women; and present higher rates of dyslipidaemia, hypertension, and diabetes. At discharge, statins were used in 18.7% of patients (vs 86.9% in the first period; P=.0001), with high-intensity statins prescribed in 11.1% of cases (vs 54.4%; P=.0001). In both periods, atorvastatin was the most commonly prescribed statin (80mg: 6% vs 42.7%; 40mg: 5.1% vs 11.1%). In the first period, the use of statins and high-intensity statins was correlated with hypercholesterolaemia, and inversely correlated with age. In the second period, statin use was correlated with hypertension and hypercholesterolaemia, and high-intensity statin use was correlated with ischaemic heart disease and inversely correlated with age. CONCLUSION: There has been a clear change in the prescription of statins to patients with ischaemic stroke at discharge. However, many patients remain undertreated and the use of these drugs needs to be optimised.

[54] *Froylan DM, Esteban JG, Carlos PR et al.* **Prevalence of lipid control and factors associated with its poor attainment in patients with premature coronary artery disease**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571615
ABSTRACT
BACKGROUND AND AIMS: Lipid goals have become more stringent in high risk patients. However, no studies have analyzed lipid control defined as the composite achievement of goals in low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (Non-HDL-C) and apolipoproteinB-100 (ApoB-100), in patients with premature coronary artery disease (CAD). We aimed to analyze lipid control rates, and the associated factors with its poor achievement in patients with premature CAD. METHODS AND RESULTS: The study included 1196 patients with CAD diagnosed before 55 and 65 years old in men and women, respectively. The American Heart Association/American College of Cardiology (non-strict) and the American Association of Clinical Endocrinologists (strict) criteria were used to analyze lipid control rates. Sociodemographic, dietary-healthy and clinical characteristics of the patients were collected. Participants were 54 ± 8 years old, 19.7% were women, and median CAD evolution was 2.4 years. Non-strict and strict lipid control was achieved in 23.0% and 8.9% of the patients, respectively. Moreover, 46.5% and 62.8% of the patients did not achieve any lipid goal using both criteria. Sociodemographic data were not different among patients who achieved or not lipid control. Treatment adherence<85%, prescription of low- and moderate-intensity statins, and obesity were consistently associated with poor lipid control. CONCLUSIONS: Lipid control is suboptimal in patients with premature CAD. Low lipid-lowering treatment adherence, low prescription of high-intensity statins, and obesity were

independently associated with poor lipid control. Novel preventive programs and more aggressive pharmacological intervention should be implemented in order to reduce the burden of premature CAD.

[55] *Lund MAV, Thostrup AH, Frithioff-Bøjsøe C et al.* **Low-grade inflammation independently associates with cardiometabolic risk in children with overweight/obesity**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32571613
ABSTRACT
BACKGROUND AND AIMS: Pediatric obesity associates with both low-grade inflammation and cardiometabolic risk on the population level. Yet on an individual patient level, overweight/obesity does not always equal increased cardiometabolic risk. In this study, we examine whether low-grade inflammation associates with cardiometabolic risk in Danish children, independent of degree of adiposity. We further assess the value of integrating multiple inflammation markers to identify children with very-high cardiometabolic risk profiles. METHOD AND RESULTS: We studied 2192 children and adolescents aged 6-18 years from an obesity clinic cohort and a population-based cohort, in a cross-sectional study design. Anthropometry, blood pressure, pubertal stage and body composition by dual-energy X-ray absorptiometry were assessed, and biomarkers including fasting serum high sensitivity C-reactive protein (hsCRP), white blood cells (WBC), resistin, lipid profile and glucose metabolism were measured. Adjusted correlation analysis and odds ratios were calculated. We found that, independent of degree of adiposity, having high-normal inflammation marker concentrations associated with increased cardiometabolic risk: for girls, hsCRP >0.57-9.98 mg/L (mid/upper tertile) associated with ~2-fold higher odds of dyslipidemia and hepatic steatosis (vs. lower tertile). For both sexes, WBC >7.0-12.4 10(9)/L (upper tertile) associated with 2.5-fold higher odds of insulin resistance. Lastly, children with multiple inflammation markers in the high-normal range exhibited the most severe cardiometabolic risk profile. CONCLUSION: Low-grade inflammation associates with cardiometabolic risk in children independent of degree of adiposity. The associations vary with sex and inflammation marker measured. Finally, integrating multiple low-grade inflammation markers identifies a very-high-risk subgroup of children with overweight/obesity and may have clinical value.

[56] *Marquina C, Zomer E, Vargas-Torres S et al.* **Novel Treatment Strategies for Secondary Prevention of Cardiovascular Disease: A Systematic Review of Cost-Effectiveness**. PharmacoEconomics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32583316
ABSTRACT
BACKGROUND: New pharmacological therapies for the treatment of cardiovascular disease (CVD) have emerged in recent years. The high rates of CVD and the need for long-term treatment to decrease risk factors makes cost-effectiveness crucial for their successful long-term implementation. OBJECTIVE: This study assessed cost-effectiveness studies of novel pharmacological treatments (ezetimibe, proprotein convertase subtilisin/kexin type 9 [PCSK9] inhibitors, omega-3 polyunsaturated fatty acids [n-3 PUFAs], and the cardiovascular polypill) compared with standard care for the secondary prevention of CVD. METHODS: We searched seven databases and the reference list of selected literature reviews for eligible cost-effective analyses (CEA) published between January 2009 and January 2020 that evaluated the above

novel treatments versus standard care. Two independent reviewers performed the screening and evaluation in accordance with the Consolidated Health Economic Evaluation Reporting Standards statement. Cost results were adapted to 2018 US dollars (US$) to facilitate comparisons between studies. Consideration of cost-effectiveness was based on the original study criteria. RESULTS: Thirty-two studies were included in this review, most of them adopting a healthcare perspective. Studies evaluating ezetimibe, PCSK9 inhibitors and n-3 PUFAs assessed their addition to standard care compared with standard care alone, while studies analysing the polypill evaluated the replacement of multiple monotherapies for a fixed-dose combination. Ten studies reported on ezetimibe, fifteen evaluated PCSK9 inhibitors, five focused on n-3 PUFAs and seven on the polypill. From a healthcare perspective, ezetimibe was cost effective in 62.5% of the studies (incremental cost-effectiveness ratios [ICERs] ranged from US$27,195 to US$204,140), n-3 PUFAs in 60% (ICERs from US$57,128 to US$139,082) and the cardiovascular polypill in 100% (ICERs from dominant to US$30,731) compared with standard care. Conversely, only 10% of the studies considered PCSK9 inhibitors cost effective compared with standard care from a healthcare perspective (ICERs ranged from US$231,119 to US$1,223,831). Additionally, ezetimibe was cost effective in 50% of the studies, PCSK9 inhibitors in 33% and the polypill in 50% of the studies adopting a societal perspective. The key model-related parameters predicting cost-effectiveness included drug cost, time horizon, and the baseline risk of cardiovascular events. CONCLUSIONS: Based on current pricing and willingness-to-pay thresholds, most CEA studies considered ezetimibe, n-3 PUFAs and the polypill to be cost effective compared with standard care but not PCSK9 inhibitors for secondary prevention of CVD.

[57] *Fan XN, Chen LX, Xu GY*. **[The effects and mechanism of caloric restriction on energy metabolism]**. Sheng li xue bao : [Acta physiologica Sinica] 2020; 72:371-381.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32572434
ABSTRACT
Caloric restriction (CR) is explored to limit the caloric intake without malnutrition. CR can affect the levels of various metabolites in organism, such as lipids, free fatty acids, ketones, bile acids and amino acids, etc, and is thought being able to extend the lifespan, postpone and reduce the incidence of age-related disorders (e.g., type 2 diabetes, cancer and cardiovascular diseases). These effects are mainly attributed to the role of CR in energy metabolism. The mechanism of CR on energy metabolism is closely related to biological clock, hormonal production, gastrointestinal flora and inflammation. Here we briefly review the effects and mechanism of CR on energy metabolism.

[58] *Mengozzi A, Tricò D, Natali A*. **A novel method for interpreting survival analysis data: description and test on three major clinical trials on cardiovascular prevention**. Trials 2020; 21:578.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32586346
ABSTRACT
BACKGROUND: Major results of randomized clinical trials on cardiovascular prevention are currently provided in terms of relative or absolute risk reductions, including also the number needed to treat (NNT), incorrectly implying that a treatment might prevent the occurrence of the outcome/s under investigation. Provided that these results are based on survival analysis, the primary measure of which is time-to-the outcome and not the outcome itself, we sought an

alternative method to describe, analyse and interpret clinical trial results consistent with this assumption, so as to better define qualitative and quantitative heterogeneity of various therapeutic strategies in terms of their effects and costs. METHODS: The original Kaplan-Meier graphs of three major positive cardiovascular prevention trials (PROVE-IT, LIFE and HOPE) were captured from the PDF images of the article and then digitalized. We calculated the difference between the placebo and active treatment curves and plotted it as a function of time to describe the event-free time gain (Time-Gain) produced by the active treatment. By calculating the exposure to the active treatment in terms of months (MoT) as a function of time and dividing it for the corresponding time-dependent number of event-free years gained (i.e. months/12), we described the kinetics of the pharmaco-economic index MoT/y(+). The same procedure was repeated replacing MoT with the actual number of patients being treated at each time point as a function of time to obtain the NNT to gain 1 event-free year (NNT/y(+)) curve. RESULTS: The Time-Gain curves depict the kinetics of the treatment-related effect over time and possess the peculiar feature of being smooth and accurately fitted by second-order polynomial functions (a*time(2) + b*time); similarly, also the MoT/y(+) and NNT/y(+) curves can be accurately fitted by power functions (a*time(b)). These curves and indices allow to fully appreciate the quantitative and qualitative heterogeneity, both in terms of effects and costs, of the different therapeutic strategies adopted in the three trials. CONCLUSIONS: With our novel method, by exploiting original Kaplan-Meier curves from three major clinical trials on cardiovascular prevention, we generate new information on the actual consequences of choosing a therapeutic strategy vs another, thus ultimately providing the clinical gain in terms of time-dependent functions. Accurately assessing clinically and economic meaningful results from any intervention trial reporting positive results through this approach, facilitates objective comparisons and increases reliability in predicting survival among the various therapeutic options provided. TRIAL REGISTRATION: PROVE-IT (Pravastatin or Atorvastatin Evaluation and Infection Therapy (TIMI22), Clinical trial registration number: NCT00382460, date of registration: September 29, 2006, study start date: November 2000). LIFE (Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) Study, Clinical trial registration number: NCT00338260, date of registration: June 20, 2006, study start date: June 1995). HOPE (Heart Outcomes Prevention Evaluation; we could not find Clinical trial registration number and date of registration).