[1] *Kim CH, Kang SI, Shin D*. **Pharmacokinetic Interaction Between Telmisartan and Rosuvastatin/Ezetimibe After Multiple Oral Administration in Healthy Subjects**. Adv Ther 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33326064

ABSTRACT

INTRODUCTION: Telmisartan, rosuvastatin and ezetimibe are commonly recommended as combination therapies. However, the pharmacokinetic (PK) interaction among these therapeutic drugs has not been clearly reported. The objective of this study was to investigate possible interactions between telmisartan monotherapy and a fixed-dose combination (FDC) of rosuvastatin/ezetimibe. METHODS: A randomized, open-label, multiple oral dose, three-treatment, three-period, six-sequence crossover study was conducted in healthy male volunteers. Monotherapy and cotherapy with telmisartan (80 mg) or a FDC of rosuvastatin and ezetimibe (20/10 mg) were compared after once-daily treatment for 7 days. The PK profiles for telmisartan, rosuvastatin, total ezetimibe (ezetimibe + exetimibe glucuronide) and ezetimibe were evaluated up to 48 h after the last dose. There was a 14-day washout period between each treatment. RESULTS: The geometric mean ratios (GMRs) and 90% confidence intervals (CIs) for the peak plasma concentration at steady state (C(max,ss)) and area under the plasma concentration-time curve during the dosing interval at steady state (AUC(τ,ss)) were 1.258 (1.072-1.475) (P = 0.020) and 1.264 (1.167-1.370) (P < 0.001) for telmisartan, 0.796 (0.723-0.878) (P < 0.001) and 0.904 (0.842-0.970) (P = 0.021) for total ezetimibe and 1.237 (1.081-1.416) (P = 0.012) and 0.988 (0.899-1.086) (P = 0.832) for ezetimibe, respectively. With rosuvastatin, the GMR (90% CI) was 2.616 (2.287-2.992) (P < 0.001) for C(max,ss) and 1.265 (1.168-1.369) (P < 0.001) for AUC(τ,ss). No serious adverse events or clinically significant results were reported. CONCLUSIONS: The coadministration of multiple doses of telmisartan and rosuvastatin/ezetimibe led to a mild increase in systemic exposure with respect to telmisartan and rosuvastatin and a nonsignificant change in exposure to total ezetimibe and ezetimibe, which was not considered clinically significant without safety concerns. Furthermore, for the generalizability of the clinical effects, a large-scaled clinical study might be required in patients with hypertension and dyslipidemia. CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov registry number: NCT03802526.

[2] *Gomez E, Garcia Buey L, Molina E et al.* **Effectiveness and safety of obeticholic acid in a Southern European multicenter cohort of patients with primary biliary cholangitis and suboptimal response to ursodeoxycholic acid**. Alimentary pharmacology & therapeutics 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33314220

ABSTRACT

BACKGROUND: Obeticholic acid (OCA) was recently approved as the only on-label alternative for patients with primary biliary cholangitis (PBC) with intolerance or suboptimal response to ursodeoxycholic acid (UDCA). However, few data are available outside clinical trials. AIM: To assess the effectiveness and safety of OCA in a real-world cohort of patients with non-effective UDCA therapy. METHODS: Open-label, prospective, real-world, multicentre study, enrolling consecutive patients who did not meet Paris II criteria, from 18 institutions in Spain and Portugal. Effectiveness was assessed by the changes in GLOBE and UK-PBC scores from baseline. POISE and Paris II criteria were evaluated after 12 months of OCA . Liver fibrosis was evaluated by FIB-4 and AST to platelet ratio index (APRI). RESULTS: One hundred and twenty patients were eligible, median time since PBC diagnosis 9.3 (4.0-13.8) years, 21.7% had cirrhosis, and 26.7% received had previous or concomitant treatment with fibrates. Seventy-eight patients completed at least 1 year of OCA. The

Globe-PBC score decreased to 0.17 (95% CI 0.05 to 0.28; P = 0.005) and the UK-PBC score decreased to 0.81 (95% CI -0.19 to 1.80; P = 0.11). There was a significant decrease in alkaline phosphatase of 81.3 U/L (95% CI 42.5 to 120; P < 0.001), ALT 22.1 U/L (95% CI 10.4 to 33.8; P < 0.001) and bilirubin 0.12 mg/dL (95% CI 0 to 0.24; P = 0.044). FIB-4 and APRI remained stable. According to the POISE criteria, 29.5% (23 out of 78) achieved response. The adverse events rate was 35%; 11.67% discontinued (8.3% due to pruritus). CONCLUSIONS: This study supports data from phase III trials with significant improvement of PBC-Globe continuous prognostic marker score among OCA-treated patients with good tolerability.

[3] *Kazemi M, Kim JY, Parry SA et al.* **Disparities in cardio-metabolic risk between Black and White women with polycystic ovary syndrome: a systematic review and meta-analysis**. American journal of obstetrics and gynecology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33316275

ABSTRACT

OBJECTIVE: We conducted a systematic review and meta-analysis to summarize and quantitatively pool evidence on cardio-metabolic health disparities between Black and White women with polycystic ovary syndrome (PCOS) in the United States in response to the call for further delineation of these disparities in the International Evidence-based Guideline for the Assessment and Management of PCOS. DATA SOURCES: Databases of MEDLINE, Web of Science, and Scopus were searched initially through March 05, 2020, and confirmed on September 11, 2020. STUDY ELIGIBILITY CRITERIA: Observational studies documenting cardio-metabolic risk profile (glucoregulatory, lipid profile, anthropometric, and blood pressure [BP] status) in Black and White women with PCOS were included. Studies on children (<17yrs.), pregnant or menopausal-aged (>50yrs.) women were excluded. The primary outcome was fasting glucose. Further, data on major cardiovascular events (stroke, coronary heart disease, heart failure) and mortality rate (cardiovascular death, total mortality) were evaluated. STUDY APPRAISAL AND SYNTHESIS METHODS: Data were pooled by random-effects models and expressed as mean differences and 95% confidence intervals. Studies were weighted based on the inverse of the variance. Heterogeneity was evaluated by Cochran Q and I(2) statistics. Study methodologic quality was assessed by the Newcastle-Ottawa scale (NOS). RESULTS: Eleven studies (n=2851; [652 Black and 2199 White]) evaluated cardio-metabolic risk profile and all had high quality (NOS score≥8). No studies reported on cardiovascular events/mortality rate. Black women had comparable fasting glucose (-0.61 [-1.69 to 2.92] mg/dL; I(2)=62.5%), yet exhibited increased fasting insulin (6.76 [4.97 to 8.56] µIU/mL; I(2)=59.0%); homeostatic model assessment of insulin resistance (HOMA-IR;1.47 [0.86 to 2.08]; I(2)=83.2%); systolic BP (SBP,3.32 [0.34 to 6.30] mmHg; I(2)=52.0%) and decreased triglyceride (-32.56 [-54.69 to -10.42] mg/dL; I(2)=68.0%) compared to White women (All: P≤0.03). Groups exhibited comparable total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and diastolic BP (All: P≥0.06). CONCLUSIONS: Black women with PCOS have a greater tendency for an adverse cardio-metabolic risk profile (increased insulin, HOMA-IR, and SBP) despite lower triglycerides than White women. Our observations support consideration of these disparities for diagnostic, monitoring, and management practices in Black women and for future Guideline recommendations. Given the heterogeneity among studies, future research should address the relative contributions of biological, environmental, socioeconomic, and healthcare factors to the observed disparities. Further, longitudinal research is

required to address patient-pressing complications, including cardiovascular events and mortality rate in Black women with PCOS as a high-risk yet under-studied population.

[4] *Abdel-Hamid TA, AbdelLatif D, Ahmed E et al.* **Relation between Maternal and Neonatal Serum Lipid Profile and Their Impact on Birth Weight**. Am J Perinatol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33321526

ABSTRACT

OBJECTIVE: Maternal malnutrition with disturbed lipid metabolism during pregnancy may affect the fetal lipid profile. We aimed to detect the relation between maternal and neonatal serum lipid profile, as well as to detect the serum lipid profile difference between small for gestational age (SGA) infants and appropriate for gestational age (AGA) infants to disclose the impact of maternal malnutrition on birth weight. STUDY DESIGN: A cross-sectional study was conducted on 150 pregnant women coming to the labor room. Before delivery, maternal serum levels of high-density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TGs), and total cholesterol were assessed, then after delivery, cord blood samples were taken for assessment of the neonatal lipid profile. Birth weights were measured, then the neonates were divided into SGA and AGA groups. RESULTS: Serum levels of LDL, TGs, and total cholesterol in the SGA infants were lower than that in the AGA infants. A positive correlation between maternal and neonatal serum TGs levels was found. Besides, there was a positive correlation between birth weight and maternal serum levels of LDL, TGs, and total cholesterol. CONCLUSION: Maternal serum lipid profile could be an indicator of the neonatal serum lipid profile and birth weight. KEY POINTS: · SGA neonates have lower levels of serum lipids compared to AGA neonates.. · There is a positive correlation between maternal and neonatal triglycerides.. · There is a positive correlation between birth weight and maternal serum lipids..

[5] *Kelsey MD, Newby LK*. **In patients at high CV risk receiving simvastatin, the Myopathy Risk Score predicted statin-related myopathy**. Annals of internal medicine 2020; 173:Jc71.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33316194

ABSTRACT

Hopewell JC, Offer A, Haynes R, et al. Independent risk factors for simvastatin-related myopathy and relevance to different types of muscle symptom. Eur Heart J. 2020;41:3336-42. 32702748.

[6] *Chueire VB, Muscelli E*. **Effect of free fatty acids on insulin secretion, insulin sensitivity and incretin effect - a narrative review**. Archives of endocrinology and metabolism 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33320449

ABSTRACT

Deleterious effects of free fatty acids, FFAs, on insulin sensitivity are observed in vivo studies in humans. Mechanisms include impaired insulin signaling, oxidative stress, inflammation, and mitochondrial dysfunction, but the effects on insulin secretion are less well known. Our aim was to review the relationship of increased FFAs with insulin resistance, secretion and mainly with the incretin effect in humans. Narrative review. Increased endogenous or administered FFAs induce insulin resistance. FFAs effects on insulin secretion are debatable; inhibition and stimulation have been reported, depending on the type and duration of lipids exposition and the study subjects. Chronically elevated FFAs seem to decrease insulin biosynthesis, glucose-stimulated insulin secretion and β-cell glucose sensitivity. Lipids infusion decreases the response to incretins with

unchanged incretin levels in volunteers with normal glucose tolerance. In contrast, FFAs reduction by acipimox did not restore the incretin effect in type-2 diabetes, probably due to the dysfunctional β-cell. Possible mechanisms of FFAs excess on incretin effect include reduction of the expression and levels of GLP-1 (glucagon like peptide-1) receptor, reduction of connexin-36 expression thus the coordinated secretory activity in response to GLP-1, and GIP (glucose-dependent insulinotropic polypeptide) receptors downregulation in islets cells. Increased circulating FFAs impair insulin sensitivity. Effects on insulin secretion are complex and controversial. Deleterious effects on the incretin-induced potentiation of insulin secretion were reported. More investigation is needed to better understand the extent and mechanisms of β-cell impairment and insulin resistance induced by increased FFAs and how to prevent them.

[7] *Al Rifai M, Kanaya AM, Kandula NR et al.* **Distribution of calcium volume, density, number, and type of coronary vessel with calcified plaque in South Asians in the US and other race/ethnic groups: The MASALA and MESA studies**. Atherosclerosis 2021; 317:16-21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333344

ABSTRACT

BACKGROUND AND AIMS: South Asians (SA) experience disproportionately higher rates of atherosclerotic cardiovascular disease (ASCVD) events than non-Hispanic whites (NHW) and several other Asian groups. The coronary artery calcium (CAC) Agatston score may not capture the unique characteristics of coronary plaque in SA. We therefore evaluated the prevalence and patterns of advanced CAC measures (specific coronary vessel involvement, CAC volume and density) in SA versus other race/ethnicities. METHODS: We combined data from the Mediators of Atherosclerosis in South Asians Living in America (MASALA) and Multi-Ethnic Study of Atherosclerosis (MESA) cohorts. We used multivariable-adjusted linear regression models to compare advanced CAC measures between SA and other ethnicities. RESULTS: Our analyses included 7,625 individuals (810 SA, 2,622 whites, 1,893 African Americans, 1,496 Hispanics, 803 Chinese Americans) with mean (SD) age 62 (10) years and 48% men. In adjusted analyses, compared to NHW, SA had lower overall CAC volume [beta coefficient (95% CI)] [-0.46 (-0.62,-0.29)] but higher overall CAC density [0.14 (0.11,0.18)]. These trends were similar when SA were compared to non-whites (Hispanics, Chinese Americans, and African Americans). SA had higher overall [0.07 (0.03,0.12)] and right coronary artery [0.09 (0.03,0.16)] CAC density compared to non-whites, while CAC volume was not significantly different between these two groups. CONCLUSIONS: SA have lower CAC volume compared to NHW but similar compared to non-whites. Overall CAC density is higher among SA compared to NHW and non-whites. Future longitudinal studies of ASCVD events are required to confirm the prognostic significance of these findings among SA.

[8] *Gao Y, Lou Y, Liu Y et al.* **The relationship between residual cholesterol risk and plaque characteristics in patients with acute coronary syndrome: Insights from an optical coherence tomography study**. Atherosclerosis 2021; 317:10-15.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333343

ABSTRACT

BACKGROUND AND AIMS: The impact of residual cholesterol risk (RCR) on plaque characteristics is not fully understood. The study aims to explore the relationship between RCR and plaque features in patients presenting with acute coronary syndrome (ACS). METHODS: All ACS patients undergoing

pre-intervention optical coherence tomography (OCT) with high-sensitivity C-reactive protein (hs-CRP) <2 mg/L on admission were retrospectively enrolled from January to December 2017, at Beijing Anzhen Hospital, Capital Medical University. RCR was defined as low density lipoprotein cholesterol (LDL-C) ≥1.8 mmol/L. Patients were divided into the RCR and non-RCR groups according to baseline LDL-C. RESULTS: A total of 90 patients (94 vessels) were included, with 50 in the RCR group and 40 in the non-RCR group, respectively. Compared with the non-RCR group, patients in the RCR group were younger (54.0 ± 11.04 vs. 58.4 ± 9.59, p = 0.049) and had a higher incidence of multivessel disease (6.0% vs. 2.5%, p = 0.028). With regard to plaque characteristics, fibrous plaque (0.0% vs 12.5%, p = 0.003) was less and fibroatheroma (79.6% vs. 50.0%, p = 0.028) was more frequently seen in the RCR group. Patients in the RCR group were more prone to present with plaque rupture (24.1% vs 5.0%, p = 0.008). Cholesterol crystal (22.2% vs 12.5%, p = 0.226) and thin-cap fibroatheroma (25.9% vs. 12.5%, p = 0.109) were more common in the RCR group, though without statistical difference. Multivariate logistic regression showed that RCR (odds ratio [OR]: 7.95, p = 0.011) and smoking (OR: 4.08, p = 0.026) were independent risk factors of plaque rupture in our patients. CONCLUSIONS: ACS patients with RCR are more likely to have atherosclerotic plaque and plaque rupture, indicating a more vulnerable plaque phenotype.

[9] *Huang YC, Chang CC, Yeh CC et al.* **The protective effect of statins against pressure ulcers in stroke patients: A propensity-score matched study based on a real-world database**. Atherosclerosis 2021; 317:22-28.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333345
ABSTRACT
BACKGROUND AND AIMS: Limited information is available regarding the association between statins and pressure ulcers. The purpose of this study is to evaluate the beneficial effects of statins on pressure ulcers in stroke patients. METHODS: Using the claims data of Taiwan's National Health Insurance, we conducted a retrospective cohort study and identified new-onset stroke patients in 2000-2004. The propensity-score matching procedure was used to select eligible stroke patients with (n = 49,919) and without (n = 49,919) the use of statins. These two groups were followed until the end of 2009 to track the occurrence of pressure ulcers. Multivariate Cox proportional hazard models were conducted to calculate adjusted hazard rations (HRs) and 95% confidence intervals (CIs) of pressure ulcer associated with the use of statins. RESULTS: Stroke patients who used statins had a reduced risk of pressure ulcers during the follow-up period (HR 0.74, 95% CI 0.71-0.78). The association between statin use and a reduced risk of poststroke pressure ulcers was significant in men (HR 0.73, 95% CI 0.68-0.78), women (HR 0.75, 95% CI 0.71-0.80), and people aged more than 50 years. Use of lovastatin, pravastatin, rosuvastatin, atrovastatin, fluvastatin, and simvastatin was associated with reduced poststroke pressure ulcers. There was a dose-dependent decrease in the frequency of pressure ulcers with increasing quantities of statins used, from 1 prescription to ≥3 prescriptions. CONCLUSION: We raised the possibility that use of statins was associated with reduced risk of pressure ulcers in stroke patients. However, the potential beneficial effect associated with statins requires further validation using randomized clinical trials.

[10] *Korosoglou G, Chatzizisis YS, Raggi P*. **Coronary computed tomography angiography in asymptomatic patients: Still a taboo or precision medicine?** Atherosclerosis 2021; 317:47-49.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33334549

ABSTRACT

[11] *Frank-Tewaag J, Bleek J, Horenkamp-Sonntag D et al.* **Use of guideline-recommended drug therapy in patients undergoing percutaneous coronary intervention for stable coronary heart disease in Germany: a multilevel analysis of nationwide routine data**. BMJ open 2020; 10:e042886.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33318120

ABSTRACT
OBJECTIVES: To determine the prescription of guideline recommended drug therapy in patients with stable coronary heart disease (sCHD) prior to percutaneous coronary intervention (PCI) in Germany and to examine the role of patient characteristics and features of regional healthcare supply in a multilevel model. DESIGN: Secondary data analysis of factors associated with the prescription of guideline recommended drug therapy using a multilevel model to analyse regional-level effects, over and above the effects of patient-level demographic and health status. SETTING: Office-based prescriptions in the year prior to the invasive procedure. PARTICIPANTS: A linked nationwide dataset from Germany's three largest statutory health insurance funds of all patients receiving PCI in the year 2016. MAIN OUTCOME MEASURES: Patients' odds of receiving optimal medical therapy and symptom-oriented therapy within 1 year prior to PCI. RESULTS: 68.6% of patients received at least one lipid-lowering drug and one symptom-oriented therapy prior to PCI. 43.6% received at least two agents to control their symptoms. Patients who received treatment in accordance with the recommendations had a greater number of diagnosed risk factors, a more severe history of cardiac disease and used a higher volume of ambulatory office-based physician services. The prescriptions prevalence for the symptom-oriented therapies differed significantly between eastern and western Germany, with a higher prevalence in the eastern districts. CONCLUSIONS: Guidelines can only provide decision-making corridors, and the applicability of recommendations must always be assessed on a case by case basis. Nevertheless, our analysis indicates that the prevalence of prescriptions in routine practice is subject to substantial variation and that conservative therapy options are not fully exhausted prior to PCI. This suggests that there might be room for improvement in the care of patients with sCHD.

[12] *Satokar VV, Cutfield WS, Derraik JGB et al.* **Double-blind RCT of fish oil supplementation in pregnancy and lactation to improve the metabolic health in children of mothers with overweight or obesity during pregnancy: study protocol**. BMJ open 2020; 10:e041015.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33323442

ABSTRACT
INTRODUCTION: Maternal obesity during pregnancy is associated with adverse changes in body composition and metabolism in the offspring. We hypothesise that supplementation during pregnancy of overweight and obese women may help prevent the development of greater adiposity and metabolic dysfunction in children. Previous clinical trials investigating fish oil supplementation in pregnancy on metabolic outcomes and body composition of the children have not focused on the pregnancies of overweight or obese women. METHODS AND ANALYSIS: A double-blind randomised controlled trial of fish oil (providing 3 g/day of n-3 polyunsaturated fatty acids) versus an equal volume of olive oil (control) taken daily from recruitment until birth, and in breastfeeding mothers, further continued for 3 months post partum. Eligible women will have a singleton pregnancy at 12-20 weeks'

gestation and be aged 18-40 years with body mass index ≥25 kg/m(2) at baseline. We aim to recruit a minimum of 128 participants to be randomised 1:1. Clinical assessments will be performed at baseline and 30 weeks of pregnancy, including anthropometric measurements, fasting metabolic markers, measures of anxiety, physical activity, quality of life and dietary intake. Subsequent assessments will be performed when the infant is 2 weeks, 3 months and 12 months of age for anthropometry, body composition (dual-energy X-ray absorptiometry (DXA)) and blood sampling. The primary outcome of the study is a between-group difference in infant percentage body fatness, assessed by DXA, at 2 weeks of age. Secondary outcomes will include differences in anthropometric measures at each time point, percentage body fat at 3 and 12 months and homeostatic model assessment of insulin resistance at 3 months. Statistical analysis will be carried out on the principle of intention to treat. ETHICS AND DISSEMINATION: This trial was approved by the Northern A Health and Disabilities Ethics Committee, New Zealand Ministry of Health (17/NTA/154). Results will be published in a peer-reviewed journal. TRIAL REGISTRATION NUMBER: ACTRN12617001078347p; Pre-results.

[13] *Yoshida M, Nakamura K, Miyoshi T et al.* **Correction to: Combination therapy with pemafibrate (K-877) and pitavastatin improves vascular endothelial dysfunction in dahl/salt-sensitive rats fed a high-salt and high-fat diet**. Cardiovascular diabetology 2020; 19:213.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33317516
ABSTRACT

[14] *Hu D, Mao L, Tang X et al.* **Nuclear magnetic resonance reveals postprandial low-density lipoprotein cholesterol determined by enzymatic method could be a misleading indicator**. Clinica chimica acta; international journal of clinical chemistry 2020; 514:59-65.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333042
ABSTRACT
BACKGROUND: Serum concentration of low-density lipoprotein cholesterol (LDL-C) is markedly reduced after a meal. Does postprandial cholesterol in LDL truly decline via clearance of LDL particles or is there simply a redistribution of cholesterol in LDL subclasses? Thus, we sought to evaluate whether postprandial decline of LDL-C reflects a reduction of LDL particle and to assess the correlation between proprotein convertase subtilisin/kexin type 9 (PCSK9) concentration and postprandial atherogenic lipoproteins profile. METHODS: Eighty-seven persons were enrolled in this study. We measured lipid profiles by enzymatic and nuclear magnetic resonance (NMR)-based methods and serum PCSK9 concentration by enzyme-linked immunosorbent assays before and after a meal. Plasma samples were collected after a 10-h fasting and 2 and 4 h post-meal. RESULTS: Compared to the fasting status, there was significant postprandial decline of LDL-C measured enzymatically (LDL-Ce) at 2nd and 4th h [99.38 (80.43, 120.65) vs 95.51 (74.25, 117.17) vs 87.01 (69.99, 108.28) mg/dl, $p < 0.000$]. But there was no significant reduction in LDL particle and its cholesterol content (LDL-Cn) determined by NMR. Just the postprandial large LDL particle [186.45 (151.36, 229.42) vs 176.92 (147.43, 220.91) vs 181.77 (149.05, 224.17), $p < 0.000$] and its cholesterol content [19.10 (15.09, 22.37) vs 18.28 (14.59, 21.84) vs 17.79 (14.62, 22.14), $p < 0.000$] were greatly decreased at 2nd and 4th h compared to the fasting one. Interestingly, postprandial serum PCSK9 was decreased at 2nd and 4th h compared with fasting concentration [298.75 (233.25, 396.92) vs 257.34 (207.52, 342.36) vs 250.57 (215.02, 339.66) ng/ml, $p < 0.000$]. The postprandial

percent decrease in serum PCSK9 at 4th h was positively correlated to the percent decline in postprandial LDL-Ce (r = 0.252, p = 0.019) but was independently associated with the percent increase in remnant cholesterol (r = 0.262, p = 0.016). CONCLUSIONS: Postprandial decline of LDL-C determined enzymatically was not confirmed by NMR-based methods. Indeed, there exists cholesterol redistribution in LDL subclasses following a meal. The decrease of postprandial PCSK9 may be secondary to the increase in intrahepatic lipids following food intake.

[15] *Masson W, Lobo M, Lavalle-Cobo A, Molinero G*. **Effect of Bempedoic Acid on atherogenic lipids and inflammation: A meta-analysis**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33328138
ABSTRACT
BACKGROUND: Bempedoic acid is a novel non-statin drug that was developed to treat hyperlipidemia in combination with other lipid-lowering drugs in those patients who need additional lipid lowering. OBJECTIVES: (1) To investigate the lipid efficacy of bempedoic acid; (2) to analyze the anti-inflammatory effects of bempedoic acid estimated through high sensitivity C-reactive protein (hsCRP). METHODS: We performed a meta-analysis including randomized trials of bempedoic acid therapy, reporting low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B and hsCRP with a minimum of 4 weeks of follow-up. The primary endpoint was defined as the percentage change in lipids and hsCRP levels measured from baseline to follow-up, comparing groups of subjects on bempedoic acid versus placebo. RESULTS: Seven eligible trials of bempedoic acid (3892 patients) were included. The bempedoic acid therapy was associated with a significant reduction in LDL-C levels [-20.3% (CI 95% -23.5 to -17.1)]; I(2)=43%]. Similarly, a significant percentage reduction in the apolipoprotein B levels [-14.3% (CI 95% -16.4 to -12.1)]; p<0.05; I(2)=46%], non-HDL-C levels [-15.5% (CI 95% -18.1 to -13.0)]; p<0.05; I(2)=53%] and hsCRP [-23.4% (CI 95% -32.6 to -14.2)]; p<0.05; I(2)=69%] was demonstrated with the bempedoic acid use. The sensitivity analysis showed that the results were robust. CONCLUSION: Our data suggests that the use of bempedoic acid significantly reduces the levels of all atherogenic lipid markers, including LDL-C, non-HDL-C and apolipoprotein B. Furthermore, considering hsCRP levels, the drug produces an anti-inflammatory effect.

[16] *Mauri M, Calmarza P, Ibarretxe D*. **Dyslipemias and pregnancy, an update**. Clinica e investigacion en arteriosclerosis : publicacion oficial de la Sociedad Espanola de Arteriosclerosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33309071
ABSTRACT
During pregnancy there is a physiological increase in total cholesterol (TC) and triglycerides (TG) plasma concentrations, due to increased insulin resistance, oestrogens, progesterone, and placental lactogen, although their reference values are not exactly known, TG levels can increase up to 300mg/dL, and TC can go as high as 350mg/dL. When the cholesterol concentration exceeds the 95(th) percentile (familial hypercholesterolaemia (FH) and transient maternal hypercholesterolaemia), there is a predisposition to oxidative stress in foetal vessels, exposing the newborn to a greater fatty streaks formation and a higher risk of atherosclerosis. However, the current treatment of pregnant women with hyperlipidaemia consists of a diet and suspension of lipid-lowering drugs. The most

prevalent maternal hypertriglyceridaemia (HTG) is due to secondary causes, like diabetes, obesity, drugs, etc. The case of severe HTG due to genetic causes is less prevalent, and can be a higher risk of maternal-foetal complications, such as, acute pancreatitis (AP), pre-eclampsia, preterm labour, and gestational diabetes. Severe HTG-AP is a rare but potentially lethal pregnancy complication, for the mother and the foetus, usually occurs during the third trimester or in the immediate postpartum period, and there are no specific protocols for its diagnosis and treatment. In conclusion, it is crucial that dyslipidaemia during pregnancy must be carefully evaluated, not just because of the acute complications, but also because of the future cardiovascular morbidity and mortality of the newborn child. That is why the establishment of consensus protocols or guidelines is essential for its management.

[17] *Kosmas CE, Skavdis A, Sourlas A et al.* **Safety and Tolerability of PCSK9 Inhibitors: Current Insights**. Clinical pharmacology : advances and applications 2020; 12:191-202.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33335431
ABSTRACT
The current era of preventive cardiology continues to emphasize on low-density lipoprotein cholesterol (LDL-C) reduction to alleviate the burden of atherosclerotic cardiovascular disease (ASCVD). In this regard, the pharmacological inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) enzyme via monoclonal antibodies has emerged as a novel lipid-lowering therapy, leading to a marked reduction in circulating LDL-C levels and subsequent improvement of cardiovascular outcomes. As these agents are increasingly used in current clinical practice, mounting scientific and clinical evidence supports that PCSK9 inhibitors offer an excellent safety and tolerability profile with a low incidence of adverse events. Notably, the most frequently reported side effects are injection-site reactions. In contrast to statins, PCSK9 inhibitors do not appear to exert a detrimental effect on glycemic control or to increase the incidence of new-onset diabetes mellitus. Accumulating evidence also indicates that PCSK9 inhibitors are a safe, well-tolerated and effective therapeutic strategy for patients with statin intolerance. On the other hand, as PCSK9 inhibitors reduce LDL-C to unprecedented low levels, a large body of current research has examined the effects of their long-term administration on neurocognition and on levels of vitamin E and other fat-soluble vitamins, providing encouraging results. This review aims to present and discuss the current clinical and scientific evidence pertaining to the safety and tolerability of PCSK9 inhibitors.

[18] *Graudal NA, Hubeck-Graudal T, Jurgens G.* **Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride**. The Cochrane database of systematic reviews 2020; 12:Cd004022.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33314019
ABSTRACT
BACKGROUND: Recent cohort studies show that salt intake below 6 g is associated with increased mortality. These findings have not changed public recommendations to lower salt intake below 6 g, which are based on assumed blood pressure (BP) effects and no side-effects. OBJECTIVES: To assess the effects of sodium reduction on BP, and on potential side-effects (hormones and lipids) SEARCH METHODS: The Cochrane Hypertension Information Specialist searched the following databases for randomized controlled trials up to April 2018 and a top-up search in March 2020: the Cochrane Hypertension Specialised Register, the Cochrane Central Register of Controlled Trials

(CENTRAL), MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. We also contacted authors of relevant papers regarding further published and unpublished work. The searches had no language restrictions. The top-up search articles are recorded under "awaiting assessment." SELECTION CRITERIA: Studies randomizing persons to low-sodium and high-sodium diets were included if they evaluated at least one of the outcome parameters (BP, renin, aldosterone, noradrenalin, adrenalin, cholesterol, high-density lipoprotein, low-density lipoprotein and triglyceride,. DATA COLLECTION AND ANALYSIS: Two review authors independently collected data, which were analysed with Review Manager 5.3. Certainty of evidence was assessed using GRADE. MAIN RESULTS: Since the first review in 2003 the number of included references has increased from 96 to 195 (174 were in white participants). As a previous study found different BP outcomes in black and white study populations, we stratified the BP outcomes by race. The effect of sodium reduction (from 203 to 65 mmol/day) on BP in white participants was as follows: Normal blood pressure: SBP: mean difference (MD) -1.14 mmHg (95% confidence interval (CI): -1.65 to -0.63), 5982 participants, 95 trials; DBP: MD + 0.01 mmHg (95% CI: -0.37 to 0.39), 6276 participants, 96 trials. Hypertension: SBP: MD -5.71 mmHg (95% CI: -6.67 to -4.74), 3998 participants,88 trials; DBP: MD -2.87 mmHg (95% CI: -3.41 to -2.32), 4032 participants, 89 trials (all high-quality evidence). The largest bias contrast across studies was recorded for the detection bias element. A comparison of detection bias low-risk studies versus high/unclear risk studies showed no differences. The effect of sodium reduction (from 195 to 66 mmol/day) on BP in black participants was as follows: Normal blood pressure: SBP: mean difference (MD) -4.02 mmHg (95% CI:-7.37 to -0.68); DBP: MD -2.01 mmHg (95% CI:-4.37, 0.35), 253 participants, 7 trials. Hypertension: SBP: MD -6.64 mmHg (95% CI:-9.00, -4.27); DBP: MD -2.91 mmHg (95% CI:-4.52, -1.30), 398 participants, 8 trials (low-quality evidence). The effect of sodium reduction (from 217 to 103 mmol/day) on BP in Asian participants was as follows: Normal blood pressure: SBP: mean difference (MD) -1.50 mmHg (95% CI: -3.09, 0.10); DBP: MD -1.06 mmHg (95% CI:-2.53 to 0.41), 950 participants, 5 trials. Hypertension: SBP: MD -7.75 mmHg (95% CI:-11.44, -4.07); DBP: MD -2.68 mmHg (95% CI: -4.21 to -1.15), 254 participants, 8 trials (moderate-low-quality evidence). During sodium reduction renin increased 1.56 ng/mL/hour (95%CI:1.39, 1.73) in 2904 participants (82 trials); aldosterone increased 104 pg/mL (95%CI:88.4,119.7) in 2506 participants (66 trials); noradrenalin increased 62.3 pg/mL: (95%CI: 41.9, 82.8) in 878 participants (35 trials); adrenalin increased 7.55 pg/mL (95%CI: 0.85, 14.26) in 331 participants (15 trials); cholesterol increased 5.19 mg/dL (95%CI:2.1, 8.3) in 917 participants (27 trials); triglyceride increased 7.10 mg/dL (95%CI: 3.1,11.1) in 712 participants (20 trials); LDL tended to increase 2.46 mg/dl (95%CI: -1, 5.9) in 696 participants (18 trials); HDL was unchanged -0.3 mg/dl (95%CI: -1.66,1.05) in 738 participants (20 trials) (All high-quality evidence except the evidence for adrenalin). AUTHORS' CONCLUSIONS: In white participants, sodium reduction in accordance with the public recommendations resulted in mean arterial pressure (MAP) decrease of about 0.4 mmHg in participants with normal blood pressure and a MAP decrease of about 4 mmHg in participants with hypertension. Weak evidence indicated that these effects may be a little greater in black and Asian participants. The effects of sodium reduction on potential side effects (hormones and lipids) were more consistent than the effect on BP, especially in people with normal BP.

[19] *Ahmmed MK, Ahmmed F, Tian HS et al.* **Marine omega-3 (n-3) phospholipids: A comprehensive review of their properties, sources, bioavailability, and relation to brain health**. Compr Rev Food Sci Food Saf 2020; 19:64-123.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33319514

ABSTRACT
For several decades, there has been considerable interest in marine-derived long chain n-3 fatty acids (n-3 LCPUFAs) due to their outstanding health benefits. n-3 LCPUFAs can be found in nature either in triglycerides (TAGs) or in phospholipid (PL) form. From brain health point of view, PL n-3 is more bioavailable and potent compared to n-3 in TAG form, as only PL n-3 is able to cross the blood-brain barrier and can be involved in brain biochemical reactions. However, PL n-3 has been ignored in the fish oil industry and frequently removed as an impurity during degumming processes. As a result, PL products derived from marine sources are very limited compared to TAG products. Commercially, PLs are being used in pharmaceutical industries as drug carriers, in food manufacturing as emulsifiers and in cosmetic industries as skin care agents, but most of the PLs used in these applications are produced from vegetable sources that contain less (without EPA, DPA, and DHA) or sometimes no n-3 LCPUFAs. This review provides a comprehensive account of the properties, structures, and major sources of marine PLs, and provides focussed discussion of their relationship to brain health. Epidemiological, laboratory, and clinical studies on n-3 LCPUFAs enriched PLs using different model systems in relation to brain and mental health that have been published over the past few years are discussed in detail.

[20] *Wijekoon N, Wijekoon S, Bulugahapitiya U et al.* **Tolerability and effectiveness of every-other-day atorvastatin compared to daily atorvastatin in patients with muscle symptoms: A randomized controlled clinical trial**. Contemporary clinical trials communications 2020; 20:100685.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33319120

ABSTRACT
Despite limited evidence, non-daily dosing of statins is recommended for managing muscle symptoms associated with statin therapy. We assessed the tolerability and effectiveness of every-other-day atorvastatin compared to daily atorvastatin in patients having muscle symptoms associated with atorvastatin therapy. A parallel-group, outcome-assessment-blinded, randomized controlled clinical trial was conducted at Colombo South Teaching Hospital, Sri Lanka. Patients with muscle pain, tenderness or cramps alone or in combination for ≥2 weeks while on daily atorvastatin for ≥1 month, with no alternative cause, were recruited. Patient's regular atorvastatin dose was given every-other-day to those in intervention group (IG) and daily to those in control group (CG). Primary outcomes were assessed at 24 weeks and included composite of myalgia and myositis, LDL-cholesterol level and percentage reduction of LDL-cholesterol from baseline. Number recruited was 49 to IG (women:79.6%; mean-age:60.6 ± 8.7years) and 52 to CG (women:73.1%; mean-age:61.7 ± 9.8years). Mean atorvastatin dose per day was 8.6 mg (SD = 4 mg) and 17.6 mg (SD = 8.4 mg) in IG and CG, respectively. Composite of myalgia and myositis at 24 weeks was 79.6% in IG and 69.2% in CG (OR = 1.7, 95% CI 0.7-4.3; p = 0.234). IG failed to show noninferiority for mean LDL-cholesterol (difference:0.31 mmol/L; upper limit 97.5% CI:0.61 mmol/L; p for noninferiority = 0.989) and for mean percentage reduction of LDL-cholesterol from baseline (difference:3.13%; upper limit 97.5% CI:15.5%; p for noninferiority = 0.718). At 24 weeks, mean creatine kinase and discomfort due to muscle symptoms (assessed with Visual Analogue Scale) were

not different between the two groups. Findings of this study do not favor every-other-day atorvastatin as an option for managing patients with muscle symptoms associated with atorvastatin therapy.

[21] *Langslet G, Zinman B, Wanner C et al.* **Cardiovascular outcomes and LDL-cholesterol levels in EMPA-REG OUTCOME(®)**. Diabetes & vascular disease research 2020; 17:1479164120975256.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33307785

ABSTRACT

OBJECTIVE: It is well established that higher low-density lipoprotein (LDL)-cholesterol levels are associated with increased cardiovascular risk. We analyzed whether effects of empagliflozin on cardiovascular outcomes varied by different LDL-cholesterol levels at baseline in EMPA-REG OUTCOME. METHODS: Participants with type 2 diabetes and high cardiovascular risk received empagliflozin (10/25 mg) or placebo in addition to standard of care. We investigated the time to first 3P-MACE, cardiovascular death, hospitalization for heart failure (HHF) and all-cause mortality for empagliflozin versus placebo between baseline LDL-cholesterol categories <1.8, 1.8-<2.2, 2.2- <2.6, 2.6-3.0, and > 3.0 mmol/L, by a Cox regression including the interaction of baseline LDL-cholesterol category and treatment. RESULTS: Of the 7020 participants randomized and treated, 81.0% received lipid lowering therapy (77.0% statins). Mean ± SD LDL-cholesterol was 2.2 ± 0.9 mmol/L, and 38%/18%, had LDL-cholesterol <1.8/>3.0 mmol/L. Age, BMI, and HbA1c levels were balanced between the LDL-cholesterol subgroups, but those in the lowest versus highest group, had more coronary artery disease (83.0% vs 59.9%) and statin treatment (88.2% vs 50.9%). Empagliflozin consistently reduced all outcomes across LDL-cholesterol categories (all interaction p-values > 0.05). CONCLUSION: The beneficial cardiovascular effects of empagliflozin was consistent across higher and lower LDL-cholesterol levels at baseline.

[22] *Wolf P, Fellinger P, Pfleger L et al.* **Gluconeogenesis, But Not Glycogenolysis, Contributes to the Increase in Endogenous Glucose Production by SGLT-2 Inhibition**. Diabetes Care 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33318126

ABSTRACT

OBJECTIVE: Recent studies indicate that sodium-glucose cotransporter 2 (SGLT-2) inhibition increases endogenous glucose production (EGP), potentially counteracting the glucose-lowering potency, and stimulates lipid oxidation and lipolysis. However, the acute effects of SGLT-2 inhibition on hepatic glycogen, lipid, and energy metabolism have not yet been analyzed. We therefore investigated the impact of a single dose of dapagliflozin (D) or placebo (P) on hepatic glycogenolysis, hepatocellular lipid (HCL) content and mitochondrial activity (kATP). RESEARCH DESIGN AND METHODS: Ten healthy volunteers (control [CON]: age 30 ± 3 years, BMI 24 ± 1 kg/m(2), HbA(1c) 5.2 ± 0.1%) and six patients with type 2 diabetes mellitus (T2DM: age 63 ± 4 years, BMI 28 ± 1.5 kg/m(2), HbA(1c) 6.1 ± 0.5%) were investigated on two study days (CON-P vs. CON-D and T2DM-P vs. T2DM-D). (1)H/(13)C/(31)P MRS was performed before, 90-180 min (MR1), and 300-390 min (MR2) after administration of 10 mg dapagliflozin or placebo. EGP was assessed by tracer dilution techniques. RESULTS: Compared with CON-P, EGP was higher in CON-D (10.0 ± 0.3 vs. 12.4 ± 0.5 µmol kg(-1) min(-1); P < 0.05) and comparable in T2DM-D and T2DM-P (10.1 ± 0.7 vs. 10.4 ± 0.5 µmol kg(-1) min(-1); P = not significant [n.s.]). A strong correlation of EGP with glucosuria was observed (r = 0.732; P < 0.01). The insulin-to-glucagon ratio was lower after dapagliflozin in CON-D and T2DM-D compared with baseline (P < 0.05). Glycogenolysis did not differ between CON-P and

CON-D (-3.28 ± 0.49 vs. -2.53 ± 0.56 µmol kg(-1) min(-1); P = n.s.) or T2DM-P and T2DM-D (-0.74 ± 0.23 vs. -1.21 ± 0.33 µmol kg(-1) min(-1); P = n.s.), whereas gluconeogenesis was higher after dapagliflozin in CON-P compared with CON-D (6.7 ± 0.6 vs. 9.9 ± 0.6 µmol kg(-1) min(-1); P < 0.01) but not in T2DM. No significant changes in HCL and kATP were observed. CONCLUSIONS: The rise in EGP after SGLT-2 inhibition is due to increased gluconeogenesis, but not glycogenolysis. Changes in glucagon and the insulin-to-glucagon ratio are not associated with an increased hepatic glycogen breakdown. HCL and kATP are not significantly affected by a single dose of dapagliflozin.

[23] *Kebede Zelalem B, Feyisa D*. **Determinants of Statin Initiation Among Adult Diabetic Patients in Bonga, Ethiopia**. Diabetes, metabolic syndrome and obesity : targets and therapy 2020; 13:4839-4847.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33335410
ABSTRACT
BACKGROUND: Diabetes mellitus (DM) is a chronic degenerative disease associated with a high risk of chronic complications and comorbidities. According t the World Health Organization, 16.7 million people worldwide die of cardiovascular diseases each year. AIM OF THE STUDY: The aim of this study is to evaluate determinants of statin initiation among diabetic patients. METHODS: A hospital-based cross-sectional study was conducted to evaluate statin initiation and determinants in Gebre Tsadik Shewa General Hospital, Bonga, Ethiopia. This hospital covers a catchment population of about 1.4 million and offers diagnosis and treatment in outpatient and inpatient settings in different departments. Epi data 4.0.2.49 and STATA 14.2 were used for data entry and analysis. Before analysis, presence of co-linearity and model fitness were checked. Chi-square statistics were used to check adequacy of cells for binary logistic regression. Bivariate analysis was done and p <0.25 was included in a multivariate model. Finally p-value less than 0.05 was considered a significant predictor. RESULTS: A total of 120 patients were included in this study, of which 77 (64.17%) were males. The mean age and standard deviation was 47.04 ± 12.13 years with 75% of patients ≥40 years. The mean duration of illness was 10.26 ± 0.6 years. Ninety-eight (81.67%) patients had varying comorbidities. Sixty-four (53.33%) patients developed complications. The majority of patients were evaluated by a general practitioner (GP). Fifty-one (42.5%) patients started statins. Of them, 31 (60.78%) started for secondary prevention. The majority of patients had atorvastatin with moderate dosage. Government insurance (p=0.029), polypharmacy (0.008), physician level of training (0.023) and previous counseling of patients about the importance of statins (p<001) were significantly associated with initiation of statins. CONCLUSION: Only near to 40% of patients started statins. Physician reluctance and unavailability of drugs were the most common reasons not to initiate statins. The hospital tries to provide medication. Physicians should evaluate patients in need of cardio-protective drugs.

[24] *Bell DSH, Goncalves E*. **Diabetogenic effects of cardioprotective drugs**. Diabetes Obes Metab 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33319474
ABSTRACT
Drugs that protect against cardiovascular events in the patient with diabetes may also positively or negatively affect glycaemic control in the patient with established diabetes and may induce the development of diabetes in the predisposed patient. Mainly through increasing insulin resistance, beta-blockers, statins and high-dose diuretics have the potential to worsen glycaemic control.

Dihydropyridine calcium channel blockers, low-dose diuretics, vasodilating beta-blockers, alpha-blockers and pitavastatin have little or no effect on glycaemic control. Blockers of the renin-angiotensin-aldosterone system, colesevelam, ranolazine and verapamil, through slowing breakdown of bradykinin, vasodilation, increasing cholecystokinin levels, blocking sodium channels and decreasing beta cell apoptosis, may improve glycaemic control and avoid the development of diabetes.

[25] *Vlacho B, Mundet-Tudurí X, Mata-Cases M et al.* **Analysis of the effectiveness of second oral glucose-lowering therapy in routine clinical practice from the mediterranean area: A retrospective cohort study**. Diabetes Res Clin Pract 2020; 171:108616.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33310172

ABSTRACT

AIM: To compare the changes in HbA1c, the effect on body weight or both combined after the addition of a DPP-4i, SGLT-2i, or sulfonylureas (SU) to metformin in real-world condition. METHODS: We used a primary care SIDIAP database. The included subjects were matched by propensity score according to baseline age, sex, HbA1c, weight, inclusion date, diabetes duration, and kidney function. RESULTS: Mean absolute HbA1c reduction was: 1.28% for DPP4i, 1.29% for SGLT2i and 1.26% for SU. Mean weight reduction was: 1.21 kg for DPP4i, 3.47 kg for SGLT2i and 0.04 kg for SU. The proportion of patients who achieved combined target HbA1c (≥0.5%) and weight (≥3%) reductions after the addition of DPP-4i, SGLT-2i or SU, was: 24.2%, 41.3%, and 15.2%, respectively. Small differences in systolic blood pressure reduction (1.07, 3.10 and 0.96 mmHg, respectively) were observed in favour of SGLT-2i. Concerning the lipids, we observed small differences, with an HDL-cholesterol increase with SGLT-2i. CONCLUSION: Our real-world study showed that the addition of SGLT-2i to metformin was associated with greater reductions in weight and the combination target of weight-HbA1c compared to SU and DPP4 inhibitors. However, similar hypoglycaemic effectiveness was observed among the three-drug classes.

[26] *Polonskaya YV, Kashtanova EV, Murashov IS et al.* **The Influence of Calcification Factors and Endothelial-Dysfunction Factors on the Development of Unstable Atherosclerotic Plaques**. Diagnostics (Basel, Switzerland) 2020; 10.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33322310

ABSTRACT

BACKGROUND: This study aimed to evaluate changes in markers of calcification and of endothelial dysfunction during the development of calcification and instability of atherosclerotic plaques and to identify associations of calcification factors with the formation of unstable plaques. METHODS: We analyzed 44 male patients with coronary atherosclerosis who underwent endarterectomy in coronary arteries during coronary bypass surgery. The endarterectomy material (intima/media) was examined using histological and biochemical methods, and the stability and calcification degree of atherosclerotic plaques were assessed. In homogenates of the tissue samples and in blood, concentrations of osteoprotegerin, osteocalcin, osteopontin, osteonectin, monocyte-chemoattractant protein type 1 (MCP-1), soluble vascular cell adhesion molecule 1 (sVCAM-1), and E-selectin were determined by enzyme immunoassays. RESULTS: Unstable atherosclerotic plaques proved to be calcified more frequently (80.4% of plaques) than stable ones (45.0%). Osteonectin, E-selectin, and sVCAM-1 levels were lower in unstable plaques and plaques with large calcification deposits.

Osteocalcin content increased with the increasing size of the calcification deposits in plaque. Blood osteocalcin concentration directly correlated with osteocalcin concentration in atherosclerotic plaques and was higher in the blood of patients with calcified plaques in coronary arteries. CONCLUSIONS: The results provide the basis for further research on the suitability of osteocalcin as a potential biomarker of an unstable calcified atherosclerotic plaque in a coronary artery.

[27] *Meng J, Zhu Y*. **Efficacy of simvastatin plus metformin for polycystic ovary syndrome: A meta-analysis of randomized controlled trials**. Eur J Obstet Gynecol Reprod Biol 2020; 257:19-24.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33338947

ABSTRACT

INTRODUCTION: The efficacy of simvastatin plus metformin to treat polycystic ovary syndrome (PCOS) remained controversial. Therefore, we conducted this meta-analysis to explore the influence of simvastatin plus metformin versus metformin monotherapy on the treatment of PCOS. METHODS: We have searched PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases through June 2020 and included randomized controlled trials (RCTs) assessing simvastatin plus metformin versus metformin for PCOS. This meta-analysis was performed using the random-effect model. RESULTS: Five RCTs were included in the meta-analysis. Overall, compared with metformin monotherapy for PCOS, combined treatment with simvastatin plus metformin was associated with significantly reduced total testosterone (mean difference [MD] = -0.31; 95 % confidence interval [CI] = -0.50 to -0.13; P = 0.0009), leuteinizing hormone: follicle stimulating hormone (LH:FSH) ratio (MD = -0.92; 95 % CI = -1.62 to -0.23; P = 0.009) and low-density lipoprotein (LDL) cholesterol (MD = -34.90; 95 % CI = -39.33 to -30.47; P < 0.00001), but spontaneous menses per 6 months, volume of both ovaries, body mass index (BMI) and fasting glucose were found to be similar between two groups. CONCLUSIONS: Combined treatment with simvastatin plus metformin was better to treat PCOS than metformin alone as evidenced by significantly reduced total testosterone, LH:FSH ratio and LDL cholesterol.

[28] *Fan Y, Guo T, Yan F et al.* **Association of Statin Use With the In-Hospital Outcomes of 2019-Coronavirus Disease Patients: A Retrospective Study**. Frontiers in medicine 2020; 7:584870.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33330541

ABSTRACT

Background: Statins have multiple protective effects on inflammation, immunity and coagulation, and may help alleviate pneumonia. However, there was no report focusing on the association of statin use with in-hospital outcomes of patients with coronavirus disease 2019 (COVID-19). We investigated the association between the use of statins and in-hospital outcomes of patients with COVID-19. Methods: In this retrospective case series, consecutive COVID-19 patients admitted at 2 hospitals in Wuhan, China, from March 12, 2020 to April 14, 2020 were analyzed. A 1:1 matched cohort was created by propensity score-matched analysis. Demographic data, laboratory findings, comorbidities, treatments and in-hospital outcomes were collected and compared between COVID-19 patients taking and not taking statins. Result: A total of 2,147 patients with COVID-19 were enrolled in this study. Of which, 250 patients were on statin therapy. The mortality was 2.4% (6/250) for patients taking statins while 3.7% (70/1,897) for those not taking statins. In the multivariate Cox model, after adjusting for age, gender, admitted hospital, comorbidities, in-hospital medications and blood lipids, the risk was lower for mortality (adjusted HR, 0.428; 95% CI, 0.169-0.907; P = 0.029), acute respiratory distress

syndrome (ARDS) (adjusted HR, 0.371; 95% CI, 0.180-0.772; P = 0.008) or intensive care unit (ICU) care (adjusted HR, 0.319; 95% CI, 0.270-0.945; P = 0.032) in the statin group vs. the non-statin group. After propensity score-matched analysis based on 18 potential confounders, a 1:1 matched cohort (206:206) was created. In the matched cohort, the Kaplan-Meier survival curves showed that the use of statins was associated with better survival (P = 0.025). In a Cox regression model, the use of statins was associated with lower risk of mortality (unadjusted HR, 0.254; 95% CI, 0.070-0.926; P = 0.038), development of ARDS (unadjusted HR, 0.240; 95% CI, 0.087-0.657; P = 0.006), and admission of ICU (unadjusted HR, 0.349; 95% CI, 0.150-0.813; P = 0.015). The results remained consistent when being adjusted for age, gender, total cholesterol, triglyceride, low density lipoprotein cholesterol, procalcitonin, and brain natriuretic peptide. The favorable outcomes in statin users remained statistically significant in the first sensitivity analysis with comorbid diabetes being excluded in matching and in the second sensitivity analysis with chronic obstructive pulmonary disease being added in matching. Conclusion: In this retrospective analysis, the use of statins in COVID-19 patients was associated with better clinical outcomes and is recommended to be continued in patients with COVID-19.

[29] *Zhang S, Lu Z, Wu Z et al.* **Determination of a "Specific Population Who Could Benefit From Rosuvastatin": A Secondary Analysis of a Randomized Controlled Trial to Uncover the Novel Value of Rosuvastatin for the Precise Treatment of ARDS**. Frontiers in medicine 2020; 7:598621.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33335905

ABSTRACT

Background: The high heterogeneity of acute respiratory distress syndrome (ARDS) contributes to paradoxical conclusions from previous investigations of rosuvastatin for ARDS. Identification of the population (phenotype) that could benefit from rosuvastatin is a novel exploration for the precise treatment. Methods: The patient population for this analysis consisted of unique patients with ARDS enrolled in the SAILS trial (rosuvastatin vs. placebo). Phenotypes were derived using consensus k-means clustering applied to routinely available clinical variables within 6 h of hospital presentation before the patients received placebo or rosuvastatin. The Kaplan-Meier statistic was used to estimate the 90-day cumulative mortality to screen for a specific population that could benefit from rosuvastatin, with a cutoff $P < 0.05$. Results: The derivation cohort included 585 patients with ARDS. Of the patients with the four derived phenotypes, those with phenotype 3 were classified as the "specific population who could benefit from rosuvastatin" as rosuvastatin resulted in a significant reduction in 90-day cumulative mortality from ARDS [hazard ratio (HR), 0.29; 95% confidence interval (CI), 0.09-0.93; P = 0.027]. Additionally, rosuvastatin markedly improved the days free of cardiovascular failure (10.08 ± 3.79 in the rosuvastatin group vs. 7.31 ± 4.94 in the placebo group, P = 0.01) and coagulation abnormalities (13.65 ± 1.33 vs. 12.15 ± 3.77, P = 0.02) up to day 14 in the phenotype 3 cohort. Phenotype 3 was summarized as Platelet(high) & Creat(low) phenotype because these patients have a relatively higher platelet count (390.05 ± 79.43 × 10(9)/L) and lower creatinine (1.42 ± 1.08 mg/dL) than do patients classified as other phenotypes. In addition, rosuvastatin seemed to increase 90-day mortality for patients classified as phenotype 4 (HR, 2.76; 95% CI, 0.09-9.93; P = 0.076), with an adverse effect on reducing the days free of renal failure up to day 14 (4.70 ± 4.99 vs. 10.17 ± 4.69, P = 0.01). Patients in phenotype 4 showed relatively severe illness in terms of baseline features, particularly renal failure, with high serum glucose. Therefore, phenotype 4 was defined as APACHE(high) & Serum glucose(high) phenotype. Conclusions: This secondary analysis of the

SAILS trial identified that rosuvastatin seems to be harmful for patients classified as APACHE(high) & Serum glucose(high) phenotype, but benefit patients in Platelet(high) & Creat(low) phenotype, thus uncovering the novel value of rosuvastatin for the precise treatment of ARDS.

[30] *Li Z, Wang Y, Wu X et al.* **Studying the Factors of Human Carotid Atherosclerotic Plaque Rupture, by Calculating Stress/Strain in the Plaque, Based on CEUS Images: A Numerical Study**. Front Neuroinform 2020; 14:596340.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33324188

ABSTRACT

Carotid plaque neovascularization is one of the major factors for the classification of vulnerable plaque, but the axial force effects of the pulsatile blood flow on the plaque with neovessel and intraplaque hemorrhage was unclear. Together with the severity of stenosis, the fibrous cap thickness, large lipid core, and the neovascularization followed by intraplaque hemorrhage (IPH) have been regarded as high-risk features of plaque rupture. In this work, the effects of these factors were evaluated on the progression and rupture of the carotid atherosclerotic plaques. Five geometries of carotid artery plaque were developed based on contrast-enhanced ultrasound (CEUS) images, which contain two types of neovessel and IPH, and geometry without neovessel and IPH. A one-way fluid-structure interaction model was applied to compute the maximum principal stress and strain in the plaque. For that hyper-elastic and non-linear material, Yeoh 3rd Order strain energy density function was used for components of the plaque. The simulation results indicated that the maximum principal stress of plaque in the carotid artery was higher when the degree of the luminal stenosis increased and the thickness of the fibrous cap decreased. The neovessels within the plaque could introduce a 2.5% increments of deformation in the plaque under the pulsatile blood flow pressure. The IPH also contributed to the increased risk of plaque rupture that a gain of stress was 8.983, 14.526, and 34.47 kPa for the plaque with 50, 65, and 75%, respectively, when comparing stress in the plaque with IPH distributed at the middle to the shoulder of the plaque. In conclusion, neovascularization in the plaque could reduce the stability of the plaque by increasing the stress within the plaque. Also, the risk of plaque rupture increased when large luminal stenosis, thin fibrous cap, and IPH were observed.

[31] *Chen KN, He L, Zhong LM et al.* **Meta-Analysis of Dyslipidemia Management for the Prevention of Ischemic Stroke Recurrence in China**. Frontiers in neurology 2020; 11:483570.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33329292

ABSTRACT

Background: The benefit of blood cholesterol reduction for secondary prevention of ischemic stroke remains undetermined in Chinese patients. The purpose of this meta-analysis was to determine whether lipid-lowering agents including statins, fibrates, nicotinic acid, and ezetimibe reduced the risk of recurrent stroke in ischemic stroke patients in China and whether such findings could inform treatment decisions for blood lipid-lowering treatment in China. Methods: The English electronic databases PubMed, EMBASE, Cochrane Library and Chinese databases CNKI, Sino-Med, Wan Fang, and VIP were searched for studies published between January 1990 and April 2020. This meta-analysis included published data from trials that randomly assigned patients to groups treated with either blood lipid-lowering regimens or placebo. Effect comparisons were made using fixed effects model in meta-analysis and linear and spline regression were performed to identify the relative risk of stroke recurrence. The primary outcome was the reduction of total ischemic stroke events, and

relative risk values were obtained using a risk prediction equation developed from the control groups of the included trials. Results: Five studies including 4,999 individuals with available data met the inclusion criteria. Relative to the control groups, the pooled estimated odds ratio (OR) for recurrent stroke among those who received lipid-lowering therapy was 0.79 (95% confidence interval [CI]: 0.63-1.00). A 50% or greater reduction in low-density lipoprotein cholesterol (LDL-C) significantly reduced the risk of ischemic stroke recurrence (OR: 0.15 [95% CI: 0.11-0.20]). The overall beneficial effect of statin therapy was confirmed to prevent ischemic stroke with an OR of 0.51 (95% CI: 0.36-0.72). Conclusions: Effective lipid-lowering therapy could decrease the blood LDL-C level, which had a protective effect against stroke recurrence. These results support the use of predicted baseline cerebrovascular disease risk equations to inform decisions regarding blood lipid-lowering treatment in ischemic stroke patients in China.

[32] *Schiano E, Annunziata G, Ciampaglia R et al.* **Bioactive Compounds for the Management of Hypertriglyceridemia: Evidence From Clinical Trials and Putative Action Targets**. Front Nutr 2020; 7:586178.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33330588
ABSTRACT
Hypertriglyceridemia refers to the presence of elevated concentrations of triglycerides (TG) in the bloodstream (TG >200 mg/dL). This lipid alteration is known to be associated with an increased risk of atherosclerosis, contributing overall to the onset of atherosclerotic cardiovascular disease (CVD). Guidelines for the management of hypertriglyceridemia are based on both lifestyle intervention and pharmacological treatment, but poor adherence, medication-related costs and side effects can limit the success of these interventions. For this reason, the search for natural alternative approaches to reduce plasma TG levels currently represents a hot research field. This review article summarizes the most relevant clinical trials reporting the TG-reducing effect of different food-derived bioactive compounds. Furthermore, based on the evidence obtained from in vitro studies, we provide a description and classification of putative targets of action through which several bioactive compounds can exert a TG-lowering effect. Future research may lead to investigations of the efficacy of novel nutraceutical formulations consisting in a combination of bioactive compounds which contribute to the management of plasma TG levels through different action targets.

[33] *Dyson JK, Jeffreys Jones DE.* **Bezafibrate for the Treatment of Cholestatic Pruritus: Time for a Change in Management?** Gastroenterology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33340537
ABSTRACT

[34] *Watts GF, Sullivan DR, Hare DL et al.* **Integrated Guidance for Enhancing the Care of Familial Hypercholesterolaemia in Australia**. Heart, lung & circulation 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33309206
ABSTRACT
Familial hypercholesterolaemia (FH) is a dominant and highly penetrant monogenic disorder present from birth that markedly elevates plasma low-density lipoprotein (LDL)-cholesterol concentration and, if untreated, leads to premature atherosclerosis and coronary artery disease (CAD). There are approximately 100,000 people with FH in Australia. However, an overwhelming majority of those

affected remain undetected and inadequately treated, consistent with FH being a leading challenge for public health genomics. To further address the unmet need, we provide an updated guidance, presented as a series of systematically collated recommendations, on the care of patients and families with FH. These recommendations have been informed by an exponential growth in published works and new evidence over the last 5 years and are compatible with a contemporary global call to action on FH. Recommendations are given on the detection, diagnosis, assessment and management of FH in adults and children. Recommendations are also made on genetic testing and risk notification of biological relatives who should undergo cascade testing for FH. Guidance on management is based on the concepts of risk re-stratification, adherence to heart healthy lifestyles, treatment of non-cholesterol risk factors, and safe and appropriate use of LDL-cholesterol lowering therapies, including statins, ezetimibe, proprotein convertase subtilisin/kexin type 9 inhibitors and lipoprotein apheresis. Broad recommendations are also provided for the organisation and development of health care services. Recommendations on best practice need to be underpinned by good clinical judgment and shared decision making with patients and families. Models of care for FH need to be adapted to local and regional health care needs and available resources. A comprehensive and realistic implementation strategy, informed by further research, including assessments of cost-benefit, will be required to ensure that this new guidance benefits all Australian families with or at risk of FH.

[35] *Yi SW, Park SJ, Yi JJ et al.* **High-density lipoprotein cholesterol and all-cause mortality by sex and age: a prospective cohort study among 15.8 million adults**. International journal of epidemiology 2020.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33313654

ABSTRACT

BACKGROUND: The associations between high-density lipoprotein cholesterol (HDL-C) levels and all-cause mortality are unclear in young adults (<45 years) and in Asian populations. METHODS: In total, 15 860 253 Korean adults underwent routine health examinations during 2009-10 and were followed until June 2018 for all-cause mortality. Hazard ratios (HRs) were calculated using Cox proportional hazard models. RESULTS: During a mean 8.4 years of follow-up, 555 802 individuals died. U-curve associations were found between HDL-C levels and mortality, irrespective of sex or age. The HDL-C ranges associated with the lowest mortality were 40-59 and 50-69 mg/dL (1.03-1.54 and 1.29-1.80 mmol/L) in men aged <65 and ≥65 years, respectively, and the corresponding ranges were 40-69 and 50-79 mg/dL (1.03-1.80 and 1.29-2.06 mmol/L) in women aged <45 and ≥45 years, respectively. For HDL-C ranges of 60-149 mg/dL (1.55-3.86 mmol/L), each 39 mg/dL (1 mmol/L) increase in HDL-C was associated with higher mortality [men: HR = 1.39; 95% confidence interval (CI) = 1.36-1.42; women: HR = 1.15, 95% CI = 1.11-1.18], adjusting for age. These positive associations were generally stronger at younger than older ages, whereas inverse associations for HDL-C ranges <60 mg/dL (1.55 mmol/L) were strongest in middle age (45-64 years). The U-curve associations were generally unchanged after adjustment for various confounders. CONCLUSIONS: Korean adults showed U-curve associations of HDL-C with mortality, regardless of sex, and age. Younger adults had a lower optimal range and a stronger positive association with mortality than older adults in the high HDL-C range. Even moderately high HDL-C levels are not necessarily a sign of good health, especially in young adults.

[36] *Lehrer S, Rheinstein PH.* **Statins combined with niacin reduce the risk of peripheral neuropathy**. Int J Funct Nutr 2020; 1.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33330853

ABSTRACT

Statins are a class of lipid-lowering medications that reduce illness and mortality in those who are at a high risk of developing cardiovascular disease. They are the most common cholesterol-lowering drugs. A case control study published in 2002 indicated that statins may increase the risk of peripheral neuropathy. Statin users were 14-fold more likely to develop peripheral neuropathy than non-users, although the overall risk of developing neuropathy was minimal. However, a number of other studies have produced conflicting results regarding neuropathy and statins. Statins are frequently combined with niacin (vitamin B3). Due to its beneficial effects on lipid profiles, niacin has been prescribed for the prevention of heart disease for >40 years. Among the B vitamins, niacin has long been recognized as a key mediator of neuronal development and survival, and may be of value for the treatment of neuropathy. The present study aimed to assess whether the combination of niacin and statin may reduce the risk of peripheral neuropathy attributed to statins. For this purpose, data from MedWatch, the Food and Drug Administration (FDA) Safety Information and Adverse Event Reporting Program were analyzed. The online tool OpenVigil 2.1 was used to query the databases. The results revealed that the majority of statins alone were related to neuropathy. Pitavastatin was the only exception. The association with neuropathy was most pronounced in the lipophilic statins: Atorvastatin and fluvastatin. The association was weaker for other lipophilic statins, such as lovastatin and simvastatin. Two hydrophilic statins, rosuvastatin and pravastatin, exhibited a similarly weaker association with neuropathy, while no reports of any association of pitavastatin with neuropathy were found. Statins + niacin were unrelated to neuropathy. On the whole, the findings of the present study demonstrate that the controversial association of statins with neuropathy may be due to the fact that previous studies have not included the use of niacin and the potential neuroprotective effects of niacin. Multiple reports have stated that niacin is no longer beneficial for the management of hyperlipidemia and should be abandoned. However, given the apparent ability of niacin to reduce the risk of neuropathy, perhaps niacin should not be discarded before further studies are performed to provide more in depth information.

[37] *Behl T, Kaur I, Sehgal A et al.* **The Lipid Paradox as a Metabolic Checkpoint and Its Therapeutic Significance in Ameliorating the Associated Cardiovascular Risks in Rheumatoid Arthritis Patients**. International journal of molecular sciences 2020; 21.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33327502

ABSTRACT

While the most common manifestations associated with rheumatoid arthritis (RA) are synovial damage and inflammation, the systemic effects of this autoimmune disorder are life-threatening, and are prevalent in 0.5-1% of the population, mainly associated with cardiovascular disorders (CVDs). Such effects have been instigated by an altered lipid profile in RA patients, which has been reported to correlate with CV risks. Altered lipid paradox is related to inflammatory burden in RA patients. The review highlights general lipid pathways (exogenous and endogenous), along with the changes in different forms of lipids and lipoproteins in RA conditions, which further contribute to elevated risks of CVDs like ischemic heart disease, atherosclerosis, myocardial infarction etc. The authors provide a deep insight on altered levels of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein

cholesterol (HDL-C) and triglycerides (TGs) in RA patients and their consequence on the cardiovascular health of the patient. This is followed by a detailed description of the impact of anti-rheumatoid therapy on the lipid profile in RA patients, comprising DMARDs, corticosteroids, anti-TNF agents, anti-IL-6 agents, JAK inhibitors and statins. Furthermore, this review elaborates on the prospects to be considered to optimize future investigation on management of RA and treatment therapies targeting altered lipid paradigms in patients.

[38] *Daviglus ML, Ferdinand KC, López JAG et al.* **Effects of Evolocumab on Low-Density Lipoprotein Cholesterol, Non-High Density Lipoprotein Cholesterol, Apolipoprotein B, and Lipoprotein(a) by Race and Ethnicity: A Meta-Analysis of Individual Participant Data From Double-Blind and Open-Label Extension Studies**. Journal of the American Heart Association 2021; 10:e016839.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33325247
ABSTRACT
Background Prevalence of cardiovascular disease risk factors and rates of atherosclerotic cardiovascular disease outcomes vary across racial/ethnic groups. This analysis examined the effects of evolocumab on LDL-C (low-density lipoprotein cholesterol) levels and LDL-C goals achievement by race/ethnicity. Methods and Results Data from 15 phase 2 and 3 studies of treatment with evolocumab versus placebo or ezetimibe were pooled (n=7669). Results were analyzed by participant clinical characteristics and by self-identified race/ethnicity. Key outcomes included percent change from baseline in LDL-C, achievement of LDL-C <70 mg/dL, and LDL-C reduction of ≥50% at 12 weeks and at 1 to 5 years. Across 12-week studies, mean percent change in LDL-C from baseline in evolocumab-treated participants was -52% to -59% for White and -46% to -67% for non-White participants, across clinical characteristics groups. LDL-C <70 mg/dL was achieved in 43% to 84% and 62% to 94% and LDL-C reduction of ≥50% in 63% to 78% and 58% to 86%, respectively. In 1- to 5-year studies, mean percent change in LDL-C was -46% to -52% for White and -49% to -55% for non-White participants. LDL-C <70 mg/dL was achieved in 53% to 84% and 66% to 77%, and LDL-C reduction of ≥50% in 53% to 67% and 58% to 68%, respectively. The treatment effect on mean percent change in LDL-C differed only in participants with type 2 diabetes mellitus, with a larger reduction in Asian participants. The qualitative interaction P values were nonsignificant, indicating consistent directionality of effect. Conclusions Similar reduction in LDL-C levels with evolocumab was observed across racial/ethnic groups in 12-week and 1- to 5-year studies. Among those with diabetes mellitus, Asian participants had greater LDL-C reduction.

[39] *Kalra DK*. **Bridging the Racial Disparity Gap in Lipid-Lowering Therapy**. Journal of the American Heart Association 2021; 10:e019533.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33325243
ABSTRACT

[40] *Abdelaziz AA, El-Barrawy MA, El-Nagar RAM*. **Potent synergistic combination of rosuvastatin and levofloxacin against Staphylococcus aureus: in vitro and in vivo study**. J Appl Microbiol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33326676
ABSTRACT

AIMS: The present study aims to evaluate the capability of rosuvastatin to synergize with levofloxacin against Staphylococcus aureus. METHODS AND RESULTS: Rosuvastatin inhibited the growth of S. aureus with minimum inhibitory concentration of 16 μg ml(-1) . Additionally, it showed a bactericidal effect at 4x minimum inhibition concentration. Using a checkerboard method, a synergistic effect was recorded when rosuvastatin was combined with levofloxacin showing against S. aureus isolate 28 (S 28). Furthermore, this combination was also able to display a significant reduction in biofilm formation (92·8%) and suppress the production of coagulase and β-haemolysin, and virulence factors of S. aureus isolate 28. An animal model for wound infection was used to assess the therapeutic effect of the test combination, in vivo. It was found that the test combination reduced the bacterial burden in the infected wounds by 91·3%. Pathological and histological analyses have revealed a decline in cell infiltration in the excisional wound skin tissue after treatment with rosuvastatin and levofloxacin combination. CONCLUSIONS: Rosuvastatin combined with levofloxacin can be considered as a promising solution to combat S. aureus antibiotic resistance phenomenon. SIGNIFICANCE AND IMPACT OF THE STUDY: This study unveils the potential effect of rosuvastatin when used in combination with levofloxacin can be used as a topical antibacterial agent to treat S. aureus skin infections.

[41] *Schlotter F, de Freitas RCC, Rogers MA et al.* **ApoC-III is a novel inducer of calcification in human aortic valves**. The Journal of biological chemistry 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33334888
ABSTRACT
Calcific aortic valve disease (CAVD) occurs when subpopulations of valve cells undergo specific differentiation pathways, promoting tissue fibrosis and calcification. Lipoprotein particles carry oxidized lipids that promote valvular disease, but low-density lipoprotein lowering therapies have failed in clinical trials, and there are currently no pharmacological interventions available for this disease. Apolipoproteins are known promotors of atherosclerosis, butwhether they possess pathogenic properties in CAVD is less clear. To search for a possible link, we assessed 12 apolipoproteins in non-fibrotic/non-calcific (NF/NC), fibrotic, and calcific aortic valve tissues by proteomics and immunohistochemistry to understand if they were enriched in calcified areas. Eight apolipoproteins (apoA-I, apoA-II, apoA-IV, apoB, apoC-III, apoD, apoL-I and apoM) were enriched in the calcific vs. NF/NC tissues. Apo(a), apoB, apoC-III, apoE and apoJ localized within the disease-prone fibrosa and colocalized with calcific regions as detected by immunohistochemistry. Circulating apoC-III on lipoprotein(a) is a potential biomarker of aortic stenosis incidence and progression, but whether apoC-III also induces aortic valve calcification is unknown. We found that apoC-III was increased in fibrotic and calcific tissues and observed within the calcification-prone fibrosa layer as well as around calcification. In addition, we showed that apoC-III induced calcification in primary human valvular cell cultures via a mitochondrial dysfunction/inflammation-mediated pathway. This study provides a first assessment of a broad array of apolipoproteins in CAVD tissues, demonstrates that specific apolipoproteins associate with valvular calcification, and implicates apoC-III as an active, modifiable driver of CAVD beyond its potential role as a biomarker.

[42] *Hu Y, Meuret C, Martinez A et al.* **Distinct patterns of apolipoprotein C-I, C-II and C-III isoforms are associated with markers of Alzheimer's disease**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33310862

ABSTRACT
Apolipoproteins C-I, C-II and C-III interact with ApoE to regulate lipoprotein metabolism and contribute to Alzheimer's disease pathophysiology. In plasma, apoC-I and C-II exist as truncated isoforms, while apoC-III exhibits multiple glycoforms. This study aimed to 1. delineate apoC-I, C-II and C-III isoform profiles in CSF and plasma in a cohort of non-demented older individuals (n = 61), and 2. examine the effect of APOE4 on these isoforms and their correlation with CSF Aβ42, a surrogate of brain amyloid accumulation. The isoforms of the apoCs were immunoaffinity enriched and measured with MALDI-TOF mass spectrometry, revealing a significantly higher percentage of truncated apoC-I and apoC-II in CSF compared to matched plasma, with positive correlation between CSF and plasma. A greater percentage of monosialylated and disialylated apoC-III isoforms was detected in CSF, accompanied by a lower percentage of the two non-sialylated apoC-III isoforms, with significant linear correlations between CSF and plasma. Furthermore, a greater percentage of truncated apoC-I in CSF, and apoC-II in plasma and CSF, was observed in individuals carrying at least one apoE ε4 allele. Increased apoC-I and apoC-II truncations were associated with lower CSF Aβ42. Finally, monosialylated apoC-III was lower, and disialylated apoC-III greater in the CSF of ε4 carriers. Together, these results reveal distinct patterns of the apoCs isoforms in CSF, implying CSF-specific apoCs processing. These patterns were accentuated in APOE ε4 allele carriers, suggesting an association between APOE4 genotype and Alzheimer's disease pathology with apoCs processing and function in the brain.

[43] *Kamal H, Mehta BK, Ahmed MK et al.* **Laboratory factors associated with symptomatic hemorrhagic conversion of acute stroke after systemic thrombolysis**. J Neurol Sci 2020; 420:117265.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333324

ABSTRACT
BACKGROUND: Laboratory factors associated with hemorrhagic conversion (HC) after Intravenous thrombolysis with rtPA (IVT) for Acute Ischemic Stroke (AIS) remain nebulous despite advances in our knowledge of AIS. This study aimed to investigate the laboratory factors predisposing to HC in AIS patients receiving IVT. METHODS: We retrospectively reviewed the medical records of patients who received IV tPA for AIS at our comprehensive stroke center over a 9.6-year period. Besides age, gender, NIHSS, history of diabetes mellitus (DM), history of atrial fibrillation (Afib), we gathered their laboratory data including International Normalized Ratio (INR), lipid panel, serum albumin, serum creatinine, hemoglobin A1c (HbA1c), and admission blood glucose. Post-thrombolysis brain imagings were reviewed to evaluate for symptomatic ICH (sICH). The mean values of above mentioned laboratory data were compared between the group with sICH and patients with no sICH. Univariate and multivariate logistic regression were performed to evaluate the association of the laboratory findings with presence of sICH. sICH was defined as ICH causing an increase in NIHSS ≥4. RESULTS: Of the 794 subjects in this study 51 (6.4%) had sICH. In the univariate analysis, patients who developed sICH had significantly higher NIHSS on admission (14.2 ± 5.4 vs 11.2 ± 6.5, $p < .001$), LDL-cholesterol (113.3 mg/dl ±36.9 vs. 101.8 mg/dl ± 38.2, $p = .032$), HbA1c (6.9% ± 2.3 vs. 6.1 ± 1.3, $p = .003$) and lower levels of Albumin (3.5 g/dl ±0.4 vs. 3.9 g/dl ± 0.5, $p < .001$). Furthermore, a higher prevalence of history of DM (45% vs. 21.6%, $p = .020$) and Afib (25.4% vs. 10.4%, $p = .028$) was found in subjects who developed sICH. There were no significant group differences regarding age, sex, total cholesterol, blood glucose on admission, serum creatinine or

INR levels (p > .05). After adjusting for multiple covariates, lower Albumin level and and higher HbA1c were significantly associated with an increased risk for sICH development (p < .05). Chances of sICH increased by 33% for every 1 g/dl below a normal albumin level of 4.0 g/dl (p < .05). CONCLUSION: Lower endogenous albumin level and higher HbA1c have shown to predispose to a higher risk of sICH after IVT for AIS and might be good predictors of sICH post IVT.

[44] *Henzel J, Kępka C, Kruk M et al.* **High-Risk Coronary Plaque Regression After Intensive Lifestyle Intervention in Nonbstructive Coronary Disease: A Randomized Study**. JACC. Cardiovascular imaging 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33341413
ABSTRACT
OBJECTIVES: The authors sought to study the impact of diet and lifestyle intervention on changes in atherosclerotic plaque volume and composition. BACKGROUND: Lifestyle and diet modification are the leading strategies to manage coronary artery disease; however, their direct impact on atherosclerosis remains unknown. Coronary plaque composition is related to the risk of future cardiovascular events independent of stenosis severity and can be conveniently evaluated with computed tomography angiography (CTA). METHODS: We enrolled 92 patients (41% women; mean age 60 ± 7.7 years) with nonobstructive (<70% stenosis) coronary atherosclerosis identified by CTA. Participants were randomized (1:1) to either the DISCO (Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography) intervention group (systematic follow-up by a dietitian to adhere to the Dietary Approaches to Stop Hypertension nutrition model together with optimal medical therapy [OMT]) or the control group (OMT alone). In all patients, CTA was repeated after 66.9 ± 13.7 weeks. The outcome was change (Δ) in atheroma volume and plaque composition. Based on atherosclerotic tissue attenuation ranges in Hounsfield units (HU), the following components of coronary plaque were distinguished: dense calcium (>351 HU), fibrous plaque (151 to 350 HU), and fibrofatty plaque combined with necrotic core (-30 to 150 HU), referred to as noncalcified plaque. RESULTS: Percent atheroma volume increased in the control arm (Δ = +1.1 ± 3.4%; p = 0.033) versus no significant change in the experimental arm (Δ = +1.0% ± 4.2%; p = 0.127; intergroup p = 0.851). There was a reduction in noncalcified plaque in both the experimental arm (Δ = -51.3 ± 79.5 mm(3) [-1.7 ± 2.7%]; p < 0.001) and the control arm (Δ = -21.3 ± 57.7 [-0.7 ± 1.9%]; p = 0.018), which was greater in the DISCO intervention group (intergroup p = 0.045). No differences in fibrous component or dense calcium changes were observed between the groups. CONCLUSIONS: Controlled diet and lifestyle intervention together with OMT may slow the progression of atherosclerosis and reduce noncalcified plaque volume compared to OMT alone. (Dietary Intervention to Stop Coronary Atherosclerosis in Computed Tomography [DISCO-CT]; NCT02571803).

[45] *Xue C, Zhang LM, Zhou C et al.* **Effect of Statins on Renal Function and Total Kidney Volume in Autosomal Dominant Polycystic Kidney Disease**. Kidney Dis (Basel) 2020; 6:407-413.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33313061
ABSTRACT
BACKGROUND: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary nephropathy with few treatments to slow renal progression. The evidence on the effect of lipid-lowering agents (statins) on ADPKD progression remains inconclusive. METHODS: We performed a systematic review and meta-analysis by searching the PubMed, Embase, Web of

Science, and Cochrane databases (up to November 2019). Changes in estimated glomerular filtration rate (eGFR) and total kidney volume (TKV) were the primary outcomes. Mean differences (MDs) for continuous outcomes and 95% confidence intervals (CIs) were calculated by a random-effects model. RESULTS: Five clinical studies with 648 participants were included. Statins did not show significant benefits in the yearly change in eGFR (4 studies, MD = -0.13 mL/min/m(2), 95% CI: -0.78 to 0.52, p = 0.70) and the yearly change in TKV (3 studies, MD = -1.17%, 95% CI: -3.40 to 1.05, p = 0.30) compared with the control group. However, statins significantly decreased urinary protein excretion (-0.10 g/day, 95% CI: -0.16 to -0.03, p = 0.004) and serum low-density lipoprotein level (-0.34 mmol/L, 95% CI: -0.58 to -0.10, p = 0.006). CONCLUSION: Despite these proteinuria and lipid-lowering benefits, the effect of statins on ADPKD progression was uncertain.

[46] *Pereira AC*. **A roadmap for familial hypercholesterolaemia control**. Lancet Digit Health 2019; 1:e376-e377.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33323213
ABSTRACT

[47] *Barkas F, Milionis H, Anastasiou G, Liberopoulos E*. **Statins and PCSK9 inhibitors: What is their role in coronavirus disease 2019?** Medical hypotheses 2020; 146:110452.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33333472
ABSTRACT
Statins and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors interfere with several pathophysiological pathways of coronavirus disease 2019 (COVID-19). Statins may have a direct antiviral effect on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by inhibiting its main protease. Statin-induced up-regulation of angiotensin-converting enzyme 2 (ACE2) may also be beneficial, whereas cholesterol reduction might significantly suppress SARS-CoV-2 by either blocking its host-cell entry through the disruption of lipid rafts or by inhibiting its replication. Available human studies have shown beneficial effects of statins and PCSK9 inhibitors on pneumonia and sepsis. These drugs may act as immunomodulators in COVID-19 and protect against major complications, such as acute respiratory distress syndrome and cytokine release syndrome. Considering their antioxidative, anti-arrhythmic, antithrombotic properties and their beneficial effect on endothelial dysfunction, along with the increased risk of mortality of patients at high cardiovascular risk infected by SARS-CoV-2, statins and PCSK9 inhibitors might prove effective against the cardiovascular and thromboembolic complications of COVID-19. On the whole, randomized clinical trials are needed to establish routine use of statins and PCSK9 inhibitors in the treatment of SARS-CoV-2 infection. In the meantime, it is recommended that lipid-lowering therapy should not be discontinued in COVID-19 patients unless otherwise indicated.

[48] *Blacher J, Gabet A, Vallée A et al.* **Prevalence and management of hypercholesterolemia in France, the Esteban observational study**. Medicine (Baltimore) 2020; 99:e23445.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33327276
ABSTRACT
Hypercholesterolemia is a major risk factor for cardiovascular diseases. However, its management in everyday clinical practice is often suboptimal. The aims of the Esteban study were to estimate the prevalence of hypercholesterolemia and to describe its management in France in 2015.Esteban is a

cross-sectional, publicly funded survey, representative of the French population. Data were collected using questionnaires and biological and clinical examinations in 3021 adults aged 18-74.The lipid-lowering treatments were obtained by matching the individual data of the subjects included in the Esteban survey with data from the Système national de données de santé. Hypercholesterolemia was defined as either a low density lipoprotein cholesterol value higher than the goal set in the European Society of Cardiology/European Atherosclerosis Society guidelines as a function of individual cardiovascular risk level, or at least 1 delivery of lipid-lowering treatment. Adherence was defined by the proportion of days covered by the lipid-lowering treatment in the 6 months preceding clinical examination. Prevalence of hypercholesterolemia in France was 23.3% (27.8% in men, 19.0% in women). Mean low density lipoprotein cholesterol was 3.38mmol/l in French participants. Among them, 7.2% were treated (8.5% of men, 5.8% of women), while 16.1% of adults went untreated (19.3% of men, 13.2% of women). Only 29.7% of secondary prevention adults had a delivery of lipid-lowering treatments in the 6 months preceding clinical examination. Fewer than 1 in 3 treated adults were adherent, i.e. more than 80% of days covered by a treatment. This proportion reached 37.4% in the high-risk group, with no significant difference of adherence in people with or without a personal history of cardiovascular disease in this group.This study showed that hypercholesterolemia is a common metabolic disease in France, affecting 23.3% of the population. Lipid-lowering prescriptions diverged greatly from current recommendations, with less than a third of eligible patients being treated.

[49] *Takeuchi S, Takahashi Y, Asai S*. **Comparison of pleiotropic effects of statins vs fibrates on laboratory parameters in patients with dyslipidemia: A retrospective cohort study**. Medicine (Baltimore) 2020; 99:e23427.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33327270
ABSTRACT
Differences in the mechanism of action and potential pleiotropic effects between statins and fibrates would potentially drive a different effect on various laboratory parameters, but this remains controversial because of a paucity of reports comparing them. Therefore, the aim of this study was to compare the effects of statins and fibrates on laboratory parameters in Japanese patients in routine clinical practice.This retrospective cohort study included patients with dyslipidemia who had been newly treated with statin or fibrate monotherapy between January 2005 and December 2017. Patients were randomly matched into two sets of pairs by sex, age, and baseline triglyceride (TG) or low-density lipoprotein (LDL) cholesterol level. The 830 patients in TG-matched pairs (415 fibrate users and 415 matched statin users) and 1172 patients in LDL cholesterol-matched pairs (586 fibrate users and 586 matched statin users) were included in this study. Generalized estimating equations were used to estimate the effects of the drugs on serum creatinine level, estimated glomerular filtration rate (eGFR), urea nitrogen, hemoglobin A1c, aspartate aminotransferase, and alanine aminotransferase (ALT), in addition to LDL cholesterol and TG levels, and red blood cell (RBC) and platelet (PLT) counts, up to 12 months after the start of study drug administration.In TG-matched pairs, the increases in creatinine and urea nitrogen levels (P=.010 and P<.001, respectively) and the decreases in eGFR, ALT level and RBC count (P<.001, P=.003, and P=.014, respectively) were greater in fibrate users than in statin users. The decrease in PLT count was greater in statin users than in fibrate users (P<.001). The mean changes in aspartate aminotransferase and hemoglobin A1c levels were not significantly different between statin users and fibrate users. In LDL cholesterol-

matched pairs, the differences in changes of all laboratory parameter levels between statin users and fibrate users were similar to those in TG-matched pairs.We demonstrate here that fibrates have a greater effect of increasing creatinine and urea nitrogen levels and of reducing eGFR, ALT level, and RBC count than statins, and that the lowering effect on PLT count is greater with statins than with fibrates.

[50] *Zhao T, Feng X, Zhou C et al.* **Effects of atorvastatin and aspirin on post-stroke epilepsy and usage of levetiracetam**. Medicine (Baltimore) 2020; 99:e23577.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33327318
ABSTRACT
OBJECTIVE: Atorvastatin and aspirin have been used in treating different forms of epilepsy. However, their effect on post-stroke epilepsy (PSE) still needs to be validated by large-scale clinical studies. In addition, their impact on the use of the antiepileptic drug levetiracetam for post-stroke epilepsy remains to be explored. Thus, the aim of this study was to further evaluate the effect of atorvastatin and aspirin on PSE and their effect on the usage of the antiepileptic drug levetiracetam in PSE patients. METHODS: Patients, aged 65 to 85 years, with newly diagnosed post-ischemic stroke epilepsy from August 30, 2014 to August 30, 2018 were included in the study, with the exclusion of those with coexisting conditions. RESULTS: Initially, 1321 patients were included, and 780 remained in the study at the 1-year follow-up. During the study, atorvastatin treatment with or without aspirin reduced the number of clinical epileptic episodes in PSE patients. It also reduced the dosage of levetiracetam and achieved better control of epilepsy compared to levetiracetam mono-treatment. Aspirin co-treatment with levetiracetam did not result in a significant improvement. However, the combination of aspirin with atorvastatin significantly reduced the number of seizures compared to atorvastatin treatment alone. CONCLUSION: Atorvastatin and aspirin co-treatment with levetiracetam can reduce epilepsy in PSE patients and reduce the dosage of levetiracetam required for effective control of PSE.

[51] *Yelnik CM, Bruckert É*. **[Hypercholesterolemia, from screening to treatment: Who, why and how to manage]**. Rev Med Interne 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=33308860
ABSTRACT
Hypercholesterolemia refers to dyslipidemia with an increased circulating cholesterol levels. This is the most common dyslipidemia and is associated with an increased risk of developing atheromatous cardiovascular diseases. One of the major challenges in primary prevention is to define the threshold for therapeutic intervention that allow to obtain a significant clinical benefit without unnecessarily expose the patient to potential side effects of lipid-lowering treatments. It is also important to recall to screen patient for heterozygous familial hypercholesterolemia, a common genetic disease of lipid metabolism responsible for particularly severe and early coronary disease. In this article, the issues of hypercholesterolemia screening, the definition of therapeutic targets and expected benefits as well as the modalities of therapeutic management (by also addressing the problem of statin intolerance) will be addressed.