[1] *Schultes B, Ernst B, Schmid SM*. **Treating hypercholesterinemia in a patient with maternally inherited diabetes and deafness (MIDD) by the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor alirocumab**. Acta diabetologica 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34370095
ABSTRACT

[2] *Alanazi NS, Alenazi TS, Alenzi KA*. **Hepatotoxicity Induced by Fluvastatin: A Reversible Acute Cholestatic Liver Injury**. Am J Case Rep 2021; 22:e931418.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34383728
ABSTRACT
BACKGROUND Fluvastatin, a commonly prescribed statin, is indicated for treatment of hypercholesterolemia in persons at high risk for coronary, cerebrovascular, and peripheral artery disease. However, there have been rare reports of liver injury or renal failure associated with use of fluvastatin. CASE REPORT We describe the case of a 69-year-old Saudi man with a medical history of diabetes mellitus and hypercholesterolemia for 2 years, on metformin, gliclazide modified release, daily aspirin, and simvastatin. Fluvastatin 40 mg daily was administered instead of simvastatin for 7 weeks before the patient was admitted to the hospital with fatigue, weakness, abdominal pain, loss of appetite, vomiting, itching, and elevated liver enzymes. Discontinuation of fluvastatin and other combined therapies led to a decrease in liver enzymes. He was diagnosed with fluvastatin-induced cholestatic liver injury and acute kidney disease. CONCLUSIONS The Naranjo scale indicates a probable relationship between cholestatic liver injury and fluvastatin, as well as a possible relationship between cholestatic injury and gliclazide and metformin. In our case report, we describe the synergistic effect of several factors in contributing to liver injuries, such as age, long-term gliclazide intake, and fluvastatin. Accordingly, we recommend close monitoring of patients' liver and kidney function, especially in the elderly and those with polypharmacy, while allowing sufficient time for the liver function to recover from a reversible reaction to fluvastatin.

[3] *Bassuk SS, Chandler PD, Buring JE, Manson JE*. **The VITamin D and OmegA-3 TriaL (VITAL): Do Results Differ by Sex or Race/Ethnicity?** American journal of lifestyle medicine 2021; 15:372-391.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34366734
ABSTRACT
Whether vitamin D or marine omega-3 (n-3) fatty acid supplementation reduces risk of cancer or cardiovascular disease (CVD) in general populations at usual risk for these outcomes is relatively unexplored in randomized trials. The primary goal of the VITamin D and OmegA-3 TriaL (VITAL), a nationwide, randomized, placebo-controlled, 2 × 2 factorial trial of vitamin D(3) (2000 IU/day) and marine n-3 fatty acids (1 g/day) in the primary prevention of cancer and CVD among 25 871 US men aged ≥50 years and women aged ≥55 years, was to fill these knowledge gaps. Studying the influence of sex and race/ethnicity on treatment-related outcomes was a prespecified goal; such analyses help ensure that important effects are not missed and contribute to the foundation for developing targeted recommendations for supplement use. To enable investigation of potential sex- and race-specific treatment effects, trial investigators enrolled an even balance of men (n = 12 786) and women (n = 13 085) and oversampled African Americans (n = 5106). Significant or suggestive variation in intervention effects according to sex, race/ethnicity, and other participant characteristics was

observed for some, though not all, outcomes. Additional research is needed to determine which individuals may be most likely to derive a net benefit from vitamin D or n-3 fatty acid supplementation. (VITAL clinicaltrials.gov identifier: NCT01169259).

[4] *Murray JM, Pfeffer P, Seifert R et al.* **Vesseg: An Open-Source Tool for Deep Learning-Based Atherosclerotic Plaque Quantification in Histopathology Image**. Arteriosclerosis, thrombosis, and vascular biology 2021:Atvbaha121316124.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34380331

ABSTRACT

OBJECTIVE: Manual plaque segmentation in microscopy images is a time-consuming process in atherosclerosis research and potentially subject to unacceptable user-to-user variability and observer bias. We address this by releasing Vesseg a tool that includes state-of-the-art deep learning models for atherosclerotic plaque segmentation. Approach and Results: Vesseg is a containerized, extensible, open-source, and user-oriented tool. It includes 2 models, trained and tested on 1089 hematoxylin-eosin stained mouse model atherosclerotic brachiocephalic artery sections. The models were compared to 3 human raters. Vesseg can be accessed at https://vesseg.online or downloaded. The models show mean Soerensen-Dice scores of 0.91±0.15 for plaque and 0.97±0.08 for lumen pixels. The mean accuracy is 0.98±0.05. Vesseg is already in active use, generating time savings of >10 minutes per slide. CONCLUSIONS: Vesseg brings state-of-the-art deep learning methods to atherosclerosis research, providing drastic time savings, while allowing for continuous improvement of models and the underlying pipeline.

[5] *Cheraghi L, Amiri P, Vahedi-Notash G et al.* **Predisposing factors of long-term responsiveness in a cardio-metabolic cohort: Tehran Lipid and Glucose Study**. BMC Med Res Methodol 2021; 21:161.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34372764

ABSTRACT

BACKGROUND: Non-participation in cohort studies, if associated with both the exposure and occurrence of the event, can introduce bias in the estimates of interest. This study aims to identify factors associated with follow-up participation in Tehran Lipid and Glucose Study, a large-scale community-based prospective study in West Asia. METHODS: A sample of 10,368 adults from TLGS was included in the analysis. All analyses were split according to sex and age groups (20-39, 40-59, and 60 years). The associations between socio-demographic, health, and lifestyle factors with response rate were identified using the Generalized Estimating Equations model. RESULTS: Over the median of 15.7 years of follow up the response rate was 64.5%. The highest response rate was observed in those aged 40-59 years for both sexes. Current smokers had lower odds of response in both sexes for all age groups, ranging from 0.51 to 0.74, $p<0.01$. In young adults, being single ($OR=0.79$, $OR=0.57$, $p\leq0.01$, respectively for men and women) and unemployed ($OR=0.73$, $OR=0.76$, $p\leq0.01$, respectively for men and women) in both sexes, high physical activity in men ($OR=0.77$, $p<0.01$), high education ($OR=0.75$, $p=0.02$) and obesity ($OR=0.85$, $p=0.05$) in women were associated with lower response rate. For the middle-aged group, diabetes in men ($OR=0.77$, $p=0.05$) and hypertension ($OR=0.84$, $p=0.05$), and having a history of cancer ($OR=0.43$, $p=0.03$) in women were factors associated with lower response rates. Finally, interventions for both sexes ($OR=0.75$, $OR=0.77$, $p\leq0.05$, respectively for men and women) and being divorced/widow in

women (OR = 0.77, p = 0.05) were the factors associated with the lower response rate in the elderly. CONCLUSIONS: Long-term participation was influenced by socio-demographic, health, and lifestyle factors in different sex- and age-specific patterns in TLGS. Recruitment strategies targeting these factors may improve participant follow-up in longitudinal studies.

[6] *Kopolovets I, Berek P, Stefanic P et al.* **Hypothesis of "stroke-stop" formula: a tool for risk index determination in development of acute cerebrovascular disease in asymptomatic individuals with carotid stenosis**. BMC neurology 2021; 21:310.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34380459
ABSTRACT
BACKGROUND: Extracranial carotid artery disease is considered a risk factor for developing acute cerebrovascular diseases. The paper suggests the "Stroke-Stop" formula as hypothesis for the determination of the risk of developing stroke in asymptomatic individuals with carotid stenosis. The formula is based on a mathematical calculation of the major risk factors for stroke: the degree of ICA (internal carotid artery) stenosis, the morphological structure of the atherosclerotic plaque and the level of lipoprotein-associated phospholipase A2 (Lp-PLA2) concentration. METHODS: The cross sectional study included 70 patients with atherosclerotic ICA stenosis. Among vascular inflammatory markers, Lp-PLA2 was determined with concentration 252.7-328.6 mg/l. The obtained results were evaluated using descriptive statistics (the frequency, percentage ratio) as well as the one-way analysis of variance (ANOVA) and chi-square test. RESULTS: The risk of stroke development is eminently increasing with the progression of ICA stenosis and elevation of Lp-PLA2 levels. In patients with echolucent plaque, the risk of stroke development was significantly higher in correlation with patients with echogenic plaque. Based on calculations using "Stroke-Stop" formula, three main groups were generated: low (<70 points), medium (70-100 points) and high (>100 points) risk of stroke development. CONCLUSIONS: Hypothesis of "Stroke-Stop" formula is proposed for better selection of patients who should be indicated for surgical treatment and will be evaluated in prospective study. In order to verify this hypothesis, we plan to do prospective study using "Stroke-Stop" formula for ipsilateral annual stroke rate in asymptomatic individuals with carotid stenosis who receive conservative therapy.

[7] *Liao M, Jeziorski KG, Tomaszewska-Kiecana M et al.* **A phase 1, open-label, drug-drug interaction study of rucaparib with rosuvastatin and oral contraceptives in patients with advanced solid tumors**. Cancer Chemother Pharmacol 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34370076
ABSTRACT
PURPOSE: This study aimed at evaluating the effect of rucaparib on the pharmacokinetics of rosuvastatin and oral contraceptives in patients with advanced solid tumors and the safety of rucaparib with and without coadministration of rosuvastatin or oral contraceptives. METHODS: Patients received single doses of oral rosuvastatin 20 mg (Arm A) or oral contraceptives ethinylestradiol 30 μg + levonorgestrel 150 μg (Arm B) on days 1 and 19 and continuous doses of rucaparib 600 mg BID from day 5 to 23. Serial blood samples were collected with and without rucaparib for pharmacokinetic analysis. RESULTS: Thirty-six patients (n = 18 each arm) were enrolled and received at least 1 dose of study drug. In the drug-drug interaction analysis (n = 15 each arm), the geometric mean ratio (GMR) of maximum concentration (C(max)) with and without rucaparib was

1.29 for rosuvastatin, 1.09 for ethinylestradiol, and 1.19 for levonorgestrel. GMR of area under the concentration-time curve from time zero to last quantifiable measurement (AUC(0-last)) was 1.34 for rosuvastatin, 1.43 for ethinylestradiol, and 1.56 for levonorgestrel. There was no increase in frequency of treatment-emergent adverse events (TEAEs) when rucaparib was given with either of the probe drugs. In both arms, most TEAEs were mild in severity and considered unrelated to study treatment. CONCLUSION: Rucaparib 600 mg BID weakly increased the plasma exposure to rosuvastatin or oral contraceptives. Rucaparib safety profile when coadministered with rosuvastatin or oral contraceptives was consistent with that of rucaparib monotherapy. Dose adjustments of rosuvastatin and oral contraceptives are not necessary when coadministered with rucaparib. ClinicalTrials.gov NCT03954366; Date of registration May 17, 2019.

[8] *Bostrom JA, Beckman JA, Berger JS*. **Summoning STRENGTH to Question the Placebo in REDUCE-IT**. Circulation 2021; 144:407-409.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34370544
ABSTRACT

[9] *Qu H, Zhang G, Pan J et al.* **Evaluation of Lipoprotein-Associated Phospholipase A2 as a Prognostic Biomarker in Chronic Kidney Disease**. Clinical laboratory 2021; 67.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34383418
ABSTRACT
BACKGROUND: The leading cause of death in patients with chronic kidney disease (CKD) is atherosclerosis (AS). Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a biomarker of atherosclerotic plaque stability. The aim of our study was to analyze the association of Lp-PLA2 with CKD complicated with carotid atherosclerotic stenosis (CAS). METHODS: Serum specimens were collected from 77 CKD patients and 39 healthy controls. Laboratory examination results including glucose, total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and Lp-PLA2 were measured. Receiver operating characteristic (ROC) was drawn and the area under the curve (AUC) was calculated. RESULTS: Multivariate logistic regression analysis showed that age, gender, glucose, and Lp-PLA2 were considered as risks for CKD-CAS with odds ratios (OR) of 1.111 (95% CI: 1.055, 1.170), 5.123 (95% CI: 1.482, 17.714), 1.679 (95% CI: 1.123, 2.512), and 1.023 (95% CI: 1.008, 1.037), respectively. The AUC for Lp-PLA2 and glucose was 0.618 ($p = 0.014$) and 0.592 ($p = 0.057$), respectively. The best diagnostic value was archived by Lp-PLA2 with the cutoff value of 201.06 ng/mL. CONCLUSIONS: Lp-PLA2 is a potential prognostic and diagnostic biomarker for CKD-CAS.

[10] *Yuan L, Hou L, Zhang L et al.* **Clinical Evaluation and Test of a Modified Lp-PLA2 Kit in Diagnosing Atherosclerosis**. Clinical laboratory 2021; 67.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34383412
ABSTRACT
BACKGROUND: Lipoprotein-associated phospholipase A2 (Lp-PLA2) has been identified as an inflammatory marker tightly correlated with the onset of atherosclerosis. Although several methodologies have been developed to detect Lp-PLA2, including enzyme-linked immunosorbent assay, Lp-PLA2 detection is still time- and resource-consuming with poor antiinterference ability and low sensitivity. Thus, it is urgent to explore new methodology for Lp-PLA2 detection. METHODS: In

the current study, we evaluated the clinical performance of a modified Lp-PLA2 quantitative assay kit based on magnetic particle chemiluminescence, and analyzed the levels of Lp-PLA2 in atherosclerosis patients using this kit. RESULTS: Our results showed that the magnetic particle chemiluminescence method could effectively dissociate Lp-PLA2 from lipoprotein and finish the test within 20 minutes with high accuracy and good repeatability, as demonstrated by the results of linear measurement range, precision, and recovery rate. Furthermore, our preliminary data revealed that serum Lp-PLA2 levels were correlated to the presence and degree of atherosclerotic plaques. CONCLUSIONS: Lp-PLA2 could be helpful in diagnosing atherosclerosis.

[11] *Zeng D, Wu H, Huang Q et al.* **High Levels of Serum Triglyceride, Low-density Lipoprotein Cholesterol, Total Bile Acid, and Total Bilirubin are Risk Factors for Gallstones**. Clinical laboratory 2021; 67.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34383399

ABSTRACT

BACKGROUND: This study aimed to identify the risk factors for gallstone disease in the Hakka population in the Meizhou area of China. METHODS: In total, 816 patients with gallstone disease and 818 control participants were included in the study, and their serum lipid levels were measured. Data on age, gender, and risk factors for gallstone disease (such as smoking and drinking history and the prevalence of hypertension) were recorded. RESULTS: Of the 1,634 enrolled individuals, age 13 - 101 years, 727 were men and 907 were women. Serum triglyceride (TG) ($p < 0.001$), low-density lipoprotein-cholesterol (LDL-C) ($p = 0.043$), total bile acid (TBA) ($p < 0.001$), and total bilirubin (T-BIL) ($p < 0.001$) levels showed significant differences between the patients and controls. However, age, the proportion history of drinking and smoking; the prevalence of hypertension and diabetes mellitus; and serum levels of total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), apolipoprotein A1 (Apo-A1), apolipoprotein B (Apo-B), and Apo-A1/Apo-B were similar between the two groups. The frequencies of gallstones in the common bile duct ($\chi2 = 13.909$, $p < 0.001$) and intrahepatic bile ducts ($\chi2 = 8.289$, $p = 0.004$) showed significant differences between male and female patients, but the distribution of gallstones of different sizes was similar between the two groups. Serum TBA ($p < 0.001$) and T-BIL ($p < 0.001$) levels were higher in patients with gallstones in the common bile duct than in those with gallstones in the gall bladder and intrahepatic bile ducts. Logistic regression analysis indicated that participants with high serum TG, LDL-C, TBA, and T-BIL levels had a significantly higher risk of gallstone disease. CONCLUSIONS: High serum levels of TG, LDL-C, TBA, and T-BIL are found to be the main risk factors for gallstone formation in our study.

[12] *Ministrini S, Carbone F.* **PCSK9 and inflammation. Maybe a role in autoimmune diseases? Focus on rheumatoid arthritis and systemic lupus erythematosus**. Curr Med Chem 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34375179

ABSTRACT

Despite a clear epidemiological link between autoimmune disease and cardiovascular (CV) risk exists, pathophysiological explanations are extremely complex and far from being elucidated. Dysregulation of metabolic pathways and chronic low-grade inflammation represent common pathways, but CV risk still remains underestimated in patients with autoimmune diseas. Among different candidate mediators, pro-protein convertase subtilisin/kexin type 9 (PCSK9) is attracting a growing attention, due to a combined effect on lipid metabolism and inflammatory response. Study on

PCSK9 inhibitors have established a clear benefit on CV outcome without an established effect on inflammation. Conversely, evidence from sepsis and HIV infection strongly support a pro-inflammatory role of PCSK9. Still uncertain is instead the role of PCSK9 in autoimmune disease. So far reported clinical findings are controversial and likely reflect the poor knowledge of PCSK9 activity on monocyte/macrophage migration and activation. The complex signaling network around PCSK9 synthesis and metabolism may also have a role, especially concerning the involvement of scavenger receptors such as CD36. Such complexity in PCSK9 signaling seems particularly evident in autoimmune disease model. This would also potentially explain the observed independency between lipid profile and PCSK9 levels, the so-called "lipid paradox". In this narrative review we will summarize the current knowledge about the complex network of PCSK9 signaling. We will focus of upstream and downstream pathways with potential implication in autoimmune disease and potential effects of PCSK9 inhibiting strategies.

[13] *Sauder KA, Stafford JM, Ehrlich S et al.* **Disparities in Hemoglobin A(1c) Testing During the Transition to Adulthood and Association With Diabetes Outcomes in Youth-Onset Type 1 and Type 2 Diabetes: The SEARCH for Diabetes in Youth Study**. Diabetes Care 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34376501

ABSTRACT

OBJECTIVE: To identify correlates of hemoglobin A(1c) (HbA(1c)) testing frequency and associations with HbA(1c) levels and microvascular complications in youth-onset diabetes. RESEARCH DESIGN AND METHODS: The SEARCH for Diabetes in Youth study collected data from individuals diagnosed with diabetes before age 20 at 8 years (n=1,885 type 1, n=230 type 2) and 13 years (n=649 type 1, n = 84 type 2) diabetes duration. We identified correlates of reporting ≥3 HbA(1c) tests/year using logistic regression. We examined associations of HbA(1c) testing with HbA(1c) levels and microvascular complications (retinopathy, neuropathy, or nephropathy) using sequentially adjusted linear and logistic regression. RESULTS: For type 1 diabetes, odds of reporting ≥3 HbA(1c) tests/year at 8 and 13 years diabetes duration decreased with older age at diagnosis (odds ratio [OR] 0.91 [95% CI 0.88-0.95]), longer duration of diabetes (OR 0.90 [0.82-0.99]), not having a personal doctor (OR 0.44 [0.30-0.65]), and lapses in health insurance (OR 0.51 [0.27-0.96]). HbA(1c) testing ≥3 times/year over time was associated with lower HbA(1c) levels (OR -0.36% [-0.65 to -0.06]) and lower odds of microvascular complications (OR 0.64 [0.43-0.97]) at 13 years duration, but associations were attenuated after adjustment for HbA(1c) testing correlates (OR -0.17 [-0.46 to 0.13] and 0.70 [0.46-1.07], respectively). For type 2 diabetes, not seeing an endocrinologist decreased the odds of reporting ≥3 HbA(1c) tests/year over time (OR 0.19 [0.06-0.63]), but HbA(1c) testing frequency was not associated with HbA(1c) levels or microvascular complications. CONCLUSIONS: We observed disparities in HbA(1c) testing frequency predominately by health care-related factors, which were associated with diabetes outcomes in type 1 diabetes.

[14] *Bashir M, Elhadd T, Dabbous Z et al.* **Optimal glycaemic and blood pressure but not lipid targets are related to a lower prevalence of diabetic microvascular complications**. Diabetes & metabolic syndrome 2021; 15:102241.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34390975

ABSTRACT

BACKGROUND: Diabetic microvascular complications are a major cause of morbidity and are related to glycaemic control and cardiovascular risk factors. AIMS: We sought to determine the association of microvascular complications in relation to control of glycemia, blood pressure and lipids in T2DM patients attending secondary care in Qatar. METHODS: This is a cross-sectional study undertaken in patients with T2DM attending Qatar's National Diabetes Centres. Patients underwent assessment of glycemia, blood pressure and lipids and prevalence of diabetic peripheral neuropathy (DPN), retinopathy and microalbuminuria. RESULTS: We included 1114 subjects aged 52.1 ± 11.3 years with a duration of diabetes 10.0 ± 7.6 years and had a prevalence of 25.8% for DPN, 34.3% for painful DPN, 36.8% for microalbuminuria and 25.1% for retinopathy. Patients who achieved an HbA1c ≤ 7.0% compared to >7% had a significantly lower prevalence of DPN ($P < 0.01$), painful DPN ($P < 0.01$), retinopathy ($P < 0.01$) and microalbuminuria ($P < 0.007$). Patients who achieved a systolic BP ≤ 140 mmHg compared to >140 mmHg had a significantly lower prevalence of DPN ($P < 0.001$), painful DPN ($P < 0.001$), retinopathy ($P < 0.001$) and microalbuminuria ($P < 0.001$). Patients who achieved an LDL ≤2.6 mmol/l compared to >2.6 mmol/l had a significantly higher prevalence of DPN ($P < 0.03$), but no difference in other outcomes. There was no difference in microvascular complications between those who achieved a HDL-C ≥ 1.02 mmol/l, and among those who achieved triglycerides ≤1.7 mmol/l. CONCLUSIONS: Optimal control of glycemia and blood pressure, but not lipids is associated with a lower prevalence of diabetic microvascular complications.

[15] *Moon SJ, Jang HN, Kim JH, Moon MK*. **Lipid Profiles in Primary Aldosteronism Compared with Essential Hypertension: Propensity-Score Matching Study**. Endocrinol Metab (Seoul) 2021; 36:885-894.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34372626
ABSTRACT
BACKGROUND: There has been controversy regarding the association between primary aldosteronism (PA) and dyslipidemia and few studies considered the effects of diabetes and renal function on lipid metabolism. We analyzed lipid profiles of PA patients and compared them to propensity-score (PS)-matched essential hypertension (EH) patients adjusting for glycemic status and renal function. METHODS: Patients who were diagnosed with PA using a saline-infusion test at Seoul National University Hospital from 2000 to 2018 were retrospectively analyzed. EH patients who had aldosterone-renin ratio (ARR) results were selected as controls. Covariates, including diabetes, were PS-matched for patients with PA, lateralized PA, non-lateralized PA, and high ARR to EH patients, respectively. RESULTS: Among a total of 80 PA and 80 EH patients, total cholesterol (TC) and triglyceride (TG) levels were significantly lower in the PA patients than in the EH patients (least-squares mean±standard error: 185.5±4.4 mg/dL vs. 196.2±4.4 mg/dL, P=0.047, for TC; and 132.3±11.5 mg/dL vs. 157.4±11.4 mg/dL, P=0.035, for TG) in fully adjusted model (adjusting for multiple covariates, including diabetes status, glycosylated hemoglobin level, and estimated glomerular filtration rate). There were no significant differences in high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol levels between the two groups. According to increments in aldosterone levels, an increasing tendency of HDL-C and decreasing tendencies of TG and non-HDL-C were observed. CONCLUSION: PA patients had lower TC and TG levels than EH patients, independent of glycemic status and renal function.

[16] *Parthymos I, Kostapanos MS, Mikhailidis DP, Florentin M*. **Lipoprotein (a) as a treatment target for cardiovascular disease prevention and related therapeutic strategies: a critical overview**. European journal of preventive cardiology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34389859
ABSTRACT
Advances in several fields of cardiovascular (CV) medicine have produced new treatments (e.g. to treat dyslipidaemia) that have proven efficacy in terms of reducing deaths and providing a better quality of life. However, the burden of CV disease (CVD) remains high. Thus, there is a need to search for new treatment targets. Lipoprotein (a) [Lp(a)] has emerged as a potential novel target since there is evidence that it contributes to CVD events. In this narrative review, we present the current evidence of the potential causal relationship between Lp(a) and CVD and discuss the likely magnitude of Lp(a) lowering required to produce a clinical benefit. We also consider current and investigational treatments targeting Lp(a), along with the potential cost of these interventions.

[17] *Schulz R, Andreadou I, Ferdinandy P*. **Editorial: PCSK9: Importance in Physiology and Pathophysiology**. Front Physiol 2021; 12:706115.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34381377
ABSTRACT

[18] *Pincus KJ, Blackman AL, Suen SY et al.* **Statin gap in patients living with HIV: assessing dose appropriateness**. HIV medicine 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34369052
ABSTRACT
OBJECTIVES: Patients living with HIV (PLWH) are predisposed to atherosclerotic cardiovascular disease (ASCVD), resulting in concomitant antiretroviral and statin use. A statin prescribing gap for PLWH has been reported, but appropriateness of statin selection and dosing (ASD) has not been described. METHODS: This is a comparative, retrospective study reviewing ASD in PLWH vs. uninfected patients at two outpatient clinics within an academic medical centre. Adults > 21 years old indicated for statin therapy were included. The primary outcome was percentage of PLWH prescribed an appropriately dosed statin, accounting for clinical- and patient-related variables, compared with uninfected patients. The secondary outcome was to identify patient characteristics associated with inappropriately dosed statins. RESULTS: After propensity score matching, 879 PLWH and 879 uninfected patients were included for analysis. Fewer PLWH (27.8%, n = 244) were prescribed an ASD compared with uninfected patients (40.5%, n = 356, P < 0.001). Similar rates of statin omission were seen in both populations (P = 0.11). More PLWH received too low a dose compared with the uninfected population (P < 0.0064). There were lower ASD rates in PLWH for subgroups of patients with clinical ASCVD (P = 0.00013) and 10-year ASCVD risk ≥7.5% (P = 0.00055), but not in patients with low-density lipoprotein cholesterol ≥190 mg/dL or diabetes. CONCLUSIONS: Although a statin gap exists in both PLWH and uninfected patients, the clinical significance may be greater for PLWH given the increased risk of ASCVD. This study confirms a larger statin gap in PLWH, particularly when underdosing of statin medications is considered. Additional analysis is warranted to investigate reasons for the ASD gap and beneficial clinical interventions.

[19] *Plakogiannis R, Saseen JJ, Stefanidis A.* **Pharmacists' Utilization of Non-HDL-C Levels in Managing Patients With Lipid Disorders**. Hospital pharmacy 2021; 56:378-383.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34381278

ABSTRACT

Background: Since 2013 there have been cholesterol guideline changes impacting pharmacists' clinical practice in managing lipid disorders. For more than a decade, cholesterol management was based on the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol Adult Treatment Panel III guideline, highlighting non-high-density lipoprotein cholesterol (non-HDL-C) as a secondary target in persons with triglycerides ≥200 mg/dL, after low-density lipoprotein cholesterol goal attainment. The 2013 American College of Cardiology and American Heart Association (ACC/AHA) guideline differed from the traditional management of dyslipidemia, in part no longer emphasizing the utilization of non-HDL-C levels. Objective: To measure pharmacists' attitudes and behavior regarding utilization of non-HDL-C level calculation before and after the inception of the 2013 ACC/AHA cholesterol guideline. Methods: Pharmacists in the American College of Clinical Pharmacy ambulatory care listserv participated in an electronic survey in November 2013, before the inception of the 2013 ACC/AHA guideline, and again in October 2018. Results: We collected 391 usable responses from participants; 212 responses in 2013 and 179 responses in 2018. The before and after comparison revealed that respondents in 2013 reported significantly higher frequency of calculating non-HDL-C levels (mean = 1.88, SD = 0.80) than respondents in 2018 (mean = 1.66, SD = 0.79) ($P \leq .001$). Also, the frequency that non-HDL-C level calculation alters decisions regarding course of treatment was lower in the 2018 (mean = 3.50, SD = 1.06) in comparison with 2013 (mean = 3.77, SD = 0.88) ($P \leq .05$). Furthermore, pharmacists were more favorable toward the inclusion of non-HDL-C level calculation in 2018 (mean = 3.77, SD = 1.05) than in 2013 (mean = 3.13, SD = 1.33) ($P \leq .001$). Conclusion and Relevance: Clinical pharmacists' utilization of non-HDL-C levels in the clinical management of patients with hypercholesterolemia has decreased, highlighting the need for further education on the importance of evaluating non-HDL-C levels in the very high-risk atherosclerotic cardiovascular disease population.

[20] *Arnold SV, Cannon CP, de Lemos JA et al.* **What Do US Physicians and Patients Think About Lipid-Lowering Therapy and Goals of Treatment? Results From the GOULD Registry**. Journal of the American Heart Association 2021; 10:e020893.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34369165

ABSTRACT

Background Because of an increasing number and complexity of treatment options for lipid-lowering therapy in patients with atherosclerotic cardiovascular disease, guidelines recommend greater active involvement of patients in shared decision-making. However, patients' understanding and perceptions of the benefits, risks, and treatment objectives of lipid-lowering therapy are unknown. Methods and Results Structured questionnaires were conducted in 5006 US outpatients with atherosclerotic cardiovascular disease and suboptimal low-density lipoprotein cholesterol (LDL-C) control (LDL-C ≥70 mg/dL) or on a PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitor and in 113 physician providers as a part of the GOULD (Getting to an Improved Understanding of Low-Density Lipoprotein Cholesterol and Dyslipidemia Management) Registry. Mean age of the patients was 68±10 years, 60% were men, and 86% were White race. Across all patients, 63% believed heart disease was the leading cause of death in men and 46% the leading cause of death in women. Only

28% of patients thought the primary reason they were taking lipid-lowering medication was to lower the risk of heart attack or stroke, 68% did not know their approximate LDL-C level, and 69% did not know their LDL-C goal. Patients on PCSK9 inhibitors (versus LDL-C cohort), younger patients (versus age ≥65 years), and men (versus women) were somewhat more knowledgeable about their disease and its management. Most physicians (66%) felt that a lack of understanding of the importance and efficacy of statins was the primary factor contributing to nonadherence, as opposed to costs (9%) or side effects (1%). More education was the most commonly used strategy to address patient-reported side effects. Conclusions A large proportion of patients with atherosclerotic cardiovascular disease remain unaware of their underlying atherosclerotic cardiovascular disease risk, reasons for taking lipid-lowering medications, current LDL-C levels, or treatment goals. These data highlight a large education gap which, if addressed, may improve shared decision-making and treatment adherence. Registration URL: https://www.clinicaltrials.org; Unique identifier: NCT02993120.

[21] *Choi J, Sung KC, Ihm SH et al.* **Central blood pressure lowering effect of telmisartan-rosuvastatin single-pill combination in hypertensive patients combined with dyslipidemia: A pilot study**. Journal of clinical hypertension (Greenwich, Conn.) 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34384001

ABSTRACT

This multicenter, phase 4, Prospective Randomized Open, Blinded End-point (PROBE) study aimed to evaluate safety and efficacy of telmisartan/rosuvastatin single-pill combination (SPC) therapy on lowering central blood pressure (BP) compared with telmisartan monotherapy in hypertensive patients with dyslipidemia in Korea. Study was terminated earlier than planned due to COVID-19 pandemic, thus should be considered as a pilot study. Among 125 patients who met the inclusion criteria of hypertension and dyslipidemia (defined as 10-year Atherosclerotic Cardiovascular Disease risk score over 5%), 80 patients went through 4-week single-group run-in period with telmisartan 40-80 mg, then randomized to telmisartan 80 mg + rosuvastatin (10 or 20 mg) SPC group or telmisartan 80 mg monotherapy group. The central/brachial BP, brachial-ankle pulse wave velocity (baPWV), and augmentation index (AIx) were assessed at baseline and 16 weeks later. Mean brachial SBP changed from 135.80 ± 14.22 mmHg to 130.69 ± 13.23 mmHg in telmisartan/rosuvastatin group and from 134.37 ± 12.50 mmHg to 133.75 ± 12.30 mmHg in telmisartan monotherapy group without significant difference (between-group difference p = .149). Mean central SBP were reduced significantly in the telmisartan/rosuvastatin group with change from 126.72 ± 14.44 mmHg to 121.56 ± 14.56 mmHg while telmisartan monotherapy group showed no significant change (between-group difference p = .028). BaPWV changed from 1672.57 ± 371.72 m/s to 1591.75 ± 272.16 m/s in telmisartan/rosuvastatin group and from 1542.85 ± 263.70 m/s to 1586.12 ± 297.45 m/s in telmisartan group with no significance (between-group difference p = .078). Change of AIx had no significant difference (between-group difference p = .314). Both groups showed excellent compliance rate of 96.9 ± 4.5% with no significant difference in adverse rate. Telmisartan/rosuvastatin SPC therapy was more effective in lowering central BP compared with the telmisartan monotherapy. The results of this study showed benefit of additive statin therapy in hypertensive patients combined with dyslipidemia.

[22] *Lelis DF, Calzavara JVS, Santos RD et al.* **Reference values for the triglyceride to high-density lipoprotein ratio and its association with cardiometabolic diseases in a mixed adult population: The ELSA-Brasil study**. Journal of clinical lipidology 2021.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34389285

ABSTRACT

BACKGROUND: Among several lipid ratios available, the triglyceride/HDL-cholesterol (TG/HDL-C) may detect individuals at risk of cardiometabolic diseases. However, its reference values for different ethnicities are not well established. OBJECTIVE: To define sex- and ethnicity-specific reference values for TG/HDL-C ratio in a large sample of healthy multiethnic adults and test its association with cardiometabolic conditions. METHODS: An apparently healthy sample (n = 2,472), aged 35-74, free of major cardiovascular risk factors, was used to generate the reference values for the TG/HDL-C. Exclusion criteria were diabetes, elevated blood pressure, obesity, hypercholesterolemia, severe hypertriglyceridemia, and smoking history. Cut-offs based on the reference values were tested in the whole ELSA Brasil study (n = 13,245), stratified by sex and ethnicity, to identify cardiometabolic conditions. RESULTS: TG/HDL-C ratio was higher in men than women, and did not change significantly with age, regardless of sex and ethnicity. Also, black individuals showed lower levels of TG/HDL-C as compared to other ethnic groups. ROC curve showed that the cut-off based on the 75th percentile displayed better sensitivities and specificities for men and women, regardless of ethnicity. Also, the sex- and ethnicity-specific cut-offs based on the 75th percentile were significantly associated with all tested cardiometabolic conditions (hypertension, diabetes, obesity, metabolic syndrome, and insulin resistance). Also, we observed that the use of a single sex-specific cut-off (men: 2.6; women: 1.7) could be used for the different ethnicities with good reliability. CONCLUSION: The defined TG/HDL-C cut-offs (men: 2.6; women: 1.7) are reliable and showed good clinical applicability to detect cardiometabolic conditions in a multiethnic population.

[23] *Bell TA, 3rd, Liu M, Donner AJ et al.* **Antisense oligonucleotide-mediated inhibition of angiopoietin-like protein 3 increases reverse cholesterol transport in mice**. Journal of lipid research 2021; 62:100101.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371033

ABSTRACT

Supported by an abundance of experimental and genetic evidence, angiopoietin-like protein 3 (ANGPTL3) has emerged as a promising therapeutic target for cardiovascular disease. ANGPTL3 is primarily produced by the liver and is a potent modulator of plasma lipids and lipoproteins. Experimental models and subjects with loss-of-function Angptl3 mutations typically present with lower levels of HDL-C than noncarriers. The effect of ANGPTL3 on HDL-C is typically attributed to its function as an inhibitor of the enzyme endothelial lipase. The ability to facilitate reverse cholesterol transport (RCT), the transport of cholesterol from peripheral tissues back to the liver, is a proposed antiatherogenic property of HDL. However, the effect of ANGPTL3 inhibition on RCT remains unclear. Here, we performed a series of dose-response and RCT studies using an Angptl3 antisense oligonucleotide (ASO) in mouse models with varying plasma lipid profiles ranging from moderately to severely hyperlipidemic. Angptl3 ASO-mediated reduction in HDL-C was limited to the model with moderate lipidemia, where the majority of plasma cholesterol was associated with HDL. Surprisingly, regardless of the effect on HDL-C, treatment with the Angptl3 ASO enhanced RCT in all models tested. The observations from the RCT assays were confirmed in HDL clearance studies, where mice treated with the Angptl3 ASO displayed increased plasma clearance and hepatic uptake of labeled HDL. The results from our studies suggest that inhibition of ANGPTL3 not only reduces levels of proatherogenic lipids but also improves HDL-mediated RCT.

[24] *Vachal P, Duffy JL, Campeau LC et al.* **Invention of MK-8262, a Cholesteryl Ester Transfer Protein (CETP) Inhibitor Backup to Anacetrapib with Best-in-Class Properties**. Journal of medicinal chemistry 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34375108
ABSTRACT
Cholesteryl ester transfer protein (CETP) represents one of the key regulators of the homeostasis of lipid particles, including high-density lipoprotein (HDL) and low-density lipoprotein (LDL) particles. Epidemiological evidence correlates increased HDL and decreased LDL to coronary heart disease (CHD) risk reduction. This relationship is consistent with a clinical outcomes trial of a CETP inhibitor (anacetrapib) combined with standard of care (statin), which led to a 9% additional risk reduction compared to standard of care alone. We discuss here the discovery of MK-8262, a CETP inhibitor with the potential for being the best-in-class molecule. Novel in vitro and in vivo paradigms were integrated to drug discovery to guide optimization informed by a critical understanding of key clinical adverse effect profiles. We present preclinical and clinical evidence of MK-8262 safety and efficacy by means of HDL increase and LDL reduction as biomarkers for reduced CHD risk.

[25] *Jardou M, Lawson R*. **Supportive therapy during COVID-19: The proposed mechanism of short-chain fatty acids to prevent cytokine storm and multi-organ failure**. Medical hypotheses 2021; 154:110661.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34385045
ABSTRACT
The world is currently facing the COVID-19 pandemic that is taking a heavy toll on several countries. While many infected patients have a good prognosis, in some cases the progression can be serious and even lead to death. The commonly seen complications are a cytokine storm and multi-organ failure that require intensive care. The mortality of critically ill patients depends on age, sex, immune state or co-morbidities. There is an urgent need to discover a biomarker to identify early on patients at risk of developing serious complications and to find an effective treatment that could prevent disease progression and critical states. Recent investigations have pointed to the possible contribution of intestinal dysbiosis to the pathophysiology of COVID-19. Herein, we hypothesize that butyrate, a short-chain fatty acid initially produced by the gut microbiota, could be administered as supportive therapy to prevent immune system activation and disease progression.

[26] *Goicoechea M, Álvarez V, Segarra A et al.* **Lipid profile of patients treated with evolocumab in Spanish hospital nephrology units (RETOSS NEFRO)**. Nefrologia : publicacion oficial de la Sociedad Espanola Nefrologia 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34389184
ABSTRACT
BACKGROUND AND OBJECTIVE: To describe the clinical characteristics, the reasons for initiating therapy and the effects of treatment in the initial phase of evolocumab availability in the Nephrology Units of Spain. MATERIAL AND METHODS: Retrospective, observational and multicentric study that included patients initiating treatment with evolocumab (from February 2016 to August 2018), in 15 Nephrology Units in Spain. The demographic and clinical characteristics of the patients, the lipid lowering treatment and the evolution of the lipid profiles between 24 weeks pre-initiation and 12±4

weeks post-initiation of evolocumab were reviewed. RESULTS: Sixty patients were enrolled: 53.3% women; mean (SD) age, 56.9 (12.8) years, 45.0% with familial hypercholesterolemia (FH) (5.0% homozygous and 40.0% heterozygous) and 65.0% with atherosclerotic cardiovascular (CV) disease. The mean (SD) eGFR was 62.6 (30.0)ml/min/1.73m(2) (51.7% of patients had eGFR<60ml/min/1.73m(2) [CKD stage>2]), 50.0% had proteinuria (>300mg/g) and 10.0% had nephrotic syndrome. Other CV risk factors were hypertension (75.0%), diabetes (25.0%), and smoking (21.7%). A 40.0% of patients were statin intolerant. At evolocumab initiation, 41.7% of patients were on a high-intensity statin, 18.3% on moderate intensity statin and 50.0% were receiving ezetimibe. Mean (SD) LDL-c at evolocumab initiation was 179.7 (62.9)mg/dL (53.4% of patients with LDL-c≥160mg/dL and 29.3%≥190mg/dL). After 12 weeks, evolocumab resulted in LDL-c reductions of 60.1%. At week 12, 90.0% of patients reached LDL-c levels <100mg/dL, 70.0% <70mg/dL, and 55.0% <55mg/dL, while mean eGFR levels and statin use were remained stable. CONCLUSION: In Nephrology Units of Spain, evolocumab was predominantly prescribed in patients with FH, chronic renal disease (CRD>2) and secondary prevention, with LDL-c levels above those recommended by the guidelines. Evolocumab used in clinical practice significantly reduced the LDL-c levels in all patients included in the study.

[27] *Djuricic I, Calder PC*. **Beneficial Outcomes of Omega-6 and Omega-3 Polyunsaturated Fatty Acids on Human Health: An Update for 2021**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371930
ABSTRACT
Oxidative stress and inflammation have been recognized as important contributors to the risk of chronic non-communicable diseases. Polyunsaturated fatty acids (PUFAs) may regulate the antioxidant signaling pathway and modulate inflammatory processes. They also influence hepatic lipid metabolism and physiological responses of other organs, including the heart. Longitudinal prospective cohort studies demonstrate that there is an association between moderate intake of the omega-6 PUFA linoleic acid and lower risk of cardiovascular diseases (CVDs), most likely as a result of lower blood cholesterol concentration. Current evidence suggests that increasing intake of arachidonic acid (up to 1500 mg/day) has no adverse effect on platelet aggregation and blood clotting, immune function and markers of inflammation, but may benefit muscle and cognitive performance. Many studies show that higher intakes of omega-3 PUFAs, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are associated with a lower incidence of chronic diseases characterized by elevated inflammation, including CVDs. This is because of the multiple molecular and cellular actions of EPA and DHA. Intervention trials using EPA + DHA indicate benefit on CVD mortality and a significant inverse linear dose-response relationship has been found between EPA + DHA intake and CVD outcomes. In addition to their antioxidant and anti-inflammatory roles, omega-3 fatty acids are considered to regulate platelet homeostasis and lower risk of thrombosis, which together indicate their potential use in COVID-19 therapy.

[28] *Mehta S, Ruth Dugas L, Choo-Kang C et al.* **Consumption of Monounsaturated Fatty Acids Is Associated with Improved Cardiometabolic Outcomes in Four African-Origin Populations Spanning the Epidemiologic Transition**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371950
ABSTRACT

Long-chain omega-3 PUFAs, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are of increasing interest because of their favorable effect on cardiometabolic risk. This study explores the association between omega 6 and 3 fatty acids intake and cardiometabolic risk in four African-origin populations spanning the epidemiological transition. Data are obtained from a cohort of 2500 adults aged 25-45 enrolled in the Modeling the Epidemiologic Transition Study (METS), from the US, Ghana, Jamaica, and the Seychelles. Dietary intake was measured using two 24 h recalls from the Nutrient Data System for Research (NDSR). The prevalence of cardiometabolic risk was analyzed by comparing the lowest and highest quartile of omega-3 (EPA+ DHA) consumption and by comparing participants who consumed a ratio of arachidonic acid (AA)/EPA + DHA ≤4:1 and >4:1. Data were analyzed using multiple variable logistic regression adjusted for age, gender, activity, calorie intake, alcohol intake, and smoking status. The lowest quartile of EPA + DHA intake is associated with cardiometabolic risk 2.16 (1.45, 3.2), inflammation 1.59 (1.17, 2.16), and obesity 2.06 (1.50, 2.82). Additionally, consuming an AA/EPA + DHA ratio of >4:1 is also associated with cardiometabolic risk 1.80 (1.24, 2.60), inflammation 1.47 (1.06, 2.03), and obesity 1.72 (1.25, 2.39). Our findings corroborate previous research supporting a beneficial role for monounsaturated fatty acids in reducing cardiometabolic risk.

[29] *Pinto AM, MacLaughlin HL, Hall WL*. **Heart Rate Variability and Long Chain n-3 Polyunsaturated Fatty Acids in Chronic Kidney Disease Patients on Haemodialysis: A Cross-Sectional Pilot Study**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371962
ABSTRACT
Low heart rate variability (HRV) is independently associated with increased risk of sudden cardiac death (SCD) and all cardiac death in haemodialysis patients. Long chain n-3 polyunsaturated fatty acids (LC n-3 PUFA) may exert anti-arrhythmic effects. This study aimed to investigate relationships between dialysis, sleep and 24 h HRV and LC n-3 PUFA status in patients who have recently commenced haemodialysis. A cross-sectional study was conducted in adults aged 40-80 with chronic kidney disease (CKD) stage 5 (n = 45, mean age 58, SD 9, 20 females and 25 males, 39% with type 2 diabetes). Pre-dialysis blood samples were taken to measure erythrocyte and plasma fatty acid composition (wt % fatty acids). Mean erythrocyte omega-3 index was not associated with HRV following adjustment for age, BMI and use of β-blocker medication. Higher ratios of erythrocyte eicosapentaenoic acid (EPA) to docosahexaenoic acid (DHA) were associated with lower 24 h vagally-mediated beat-to-beat HRV parameters. Higher plasma EPA and docosapentaenoic acid (DPAn-3) were also associated with lower sleep-time and 24 h beat-to-beat variability. In contrast, higher plasma EPA was significantly related to higher overall and longer phase components of 24 h HRV. Further investigation is required to investigate whether patients commencing haemodialysis may have compromised conversion of EPA to DHA, which may impair vagally-mediated regulation of cardiac autonomic function, increasing risk of SCD.

[30] *Villa López G, Valero Zanuy MA, González Barrios I et al.* **Acute Hypertriglyceridemia in Patients with COVID-19 Receiving Parenteral Nutrition**. Nutrients 2021; 13.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371797
ABSTRACT

Hypertriglyceridemia is a metabolic complication associated with parenteral nutrition (PN). It is unknown if patients with acute respiratory distress syndrome (ARDS) secondary to COVID-19 are more at risk. Our aim was to describe the incidence, risk factors and clinical impact of hypertriglyceridemia in critically ill patients with ARDS-COVID-19 receiving PN. We designed a cohort study of patients with ARDS-COVID-19 infection that required admission to critical care units and nutritional support with PN. Individual PN prescriptions for macronutrients and insulin were provided. Lipid emulsion contained fish oil (SMOFlipid(®) or Lipoplus(®)). Hypertriglyceridemia was defined as plasma levels above 400 mg/dL. Eighty-seven patients, 66.6% men, 60.1 ± 10.8 years old, BMI 29.1 ± 5.6 kg/m(2), 71% of whom received lopinavir/ritonavir, 56% received Propofol and 55% received Tocilizumab were included. The incidence of hypertriglyceridemia was 37 × 100 patient-days with PN. This complication was more frequent in obese patients (OR 3.34; 95% CI, 2.35-4.33) and in those treated with lopinavir/ritonavir (OR 4.98; 95% CI, 3.60-6.29) or Propofol (OR 2.45; 95% CI, 1.55-3.35). Total mortality was 33.3%, similar between the type of lipid emulsion (p = 0.478). On average, patients with hypertriglyceridemia had a longer requirement of PN compared to the group without elevated triglycerides (TG), probably because of their longer survival (p = 0.001). TG higher than 400 mg/dL was not a protective factor for mortality (OR 0.31; 95% CI, 0.01-1.30). In conclusion, the incidence of hypertriglyceridemia was 37 × 100 patient-days with PN. The risk of this complication is associated with obesity and the use of lopinavir/ritonavir or Propofol.

[31] *S CT, Lai LC*. **Diabetic dyslipidaemia**. Practical laboratory medicine 2021; 26:e00248.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34368411
ABSTRACT
Diabetes mellitus (DM) is an escalating pandemic and an established cardiovascular risk factor. An important aspect of the interaction between DM and atherosclerotic cardiovascular disease (ASCVD) is diabetic dyslipidaemia, an atherogenic dyslipidaemia encompassing quantitative [hypertriglyceridaemia (hyperTG) and decreased high density lipoprotein cholesterol (HDL)] and qualitative [increased small dense low density lipoprotein cholesterol (sdLDL) particles, large very low density lipoprotein cholesterol (VLDL) subfraction (VLDL1) and dysfunctional HDL] modifications in lipoproteins. Much of the pathophysiology linking DM and dyslipidaemia has been elucidated. This paper aims to review the pathophysiology and management of diabetic dyslipidaemia with respect to ASCVD. Briefly, the influence of diabetic kidney disease on lipid profile and lipid changes causing type 2 diabetes mellitus are highlighted. Biomarkers of diabetic dyslipidaemia, including novel markers and clinical trials that have demonstrated that non-lipid and lipid lowering therapies can lower cardiovascular risk in diabetics are discussed. The stands of various international guidelines on lipid management in DM are emphasised. It is important to understand the underlying mechanisms of diabetic dyslipidaemia in order to develop new therapeutic strategies against dyslipidaemia and diabetes. The various international guidelines on lipid management can be used to tailor a holistic approach specific to each patient with diabetic dyslipidaemia.

[32] *Al Rifai M, Blumenthal RS, Stone NJ et al.* **Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) guidelines for management of dyslipidemia and cardiovascular disease risk reduction: Putting evidence in context**. Prog Cardiovasc Dis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34371083
ABSTRACT

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of morbidity and mortality in the United States (U.S.) and incurs significant cost to the healthcare system. Management of cholesterol remains central for ASCVD prevention and has been the focus of multiple national guidelines. In this review, we compare the American Heart Association (AHA)/American College of Cardiology (ACC) and the U.S. Department of Veterans Affairs (VA) and U.S. Department of Defense (DoD) Cholesterol guidelines. We review the evidence base that was used to generate recommendations focusing on 4 distinct themes: 1) the threshold of absolute 10-year ASCVD risk to start a clinician-patient discussion for the initiation of statin therapy in primary prevention patients; 2) the utility of coronary artery calcium score to guide clinician-patient risk discussion pertaining to the initiation of statin therapy for primary ASCVD prevention; 3) the use of moderate versus high-intensity statin therapy in patients with established ASCVD; and 4) the utility of ordering lipid panels after initiation or intensification of lipid lowering therapy to document efficacy and monitor adherence to lipid lowering therapy. We discuss why the VA/DoD and AHA/ACC may have reached different conclusions on these key issues.

[33] *Hariharan P, Dupuis J.* **Mapping gene and gene pathways associated with coronary artery disease: a CARDIoGRAM exome and multi-ancestry UK biobank analysis**. Scientific reports 2021; 11:16461.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34385509
ABSTRACT
Coronary artery disease (CAD) genome-wide association studies typically focus on single nucleotide variants (SNVs), and many potentially associated SNVs fail to reach the GWAS significance threshold. We performed gene and pathway-based association (GBA) tests on publicly available Coronary ARtery DIsease Genome wide Replication and Meta-analysis consortium Exome (n = 120,575) and multi ancestry pan UK Biobank study (n = 442,574) summary data using versatile gene-based association study (VEGAS2) and Multi-marker analysis of genomic annotation (MAGMA) to identify novel genes and pathways associated with CAD. We included only exonic SNVs and excluded regulatory regions. VEGAS2 and MAGMA ranked genes and pathways based on aggregated SNV test statistics. We used Bonferroni corrected gene and pathway significance threshold at $3.0 \times 10(-6)$ and $1.0 \times 10(-5)$, respectively. We also report the top one percent of ranked genes and pathways. We identified 17 top enriched genes with four genes (PCSK9, FAM177, LPL, ARGEF26), reaching statistical significance ($p \leq 3.0 \times 10(-6)$) using both GBA tests in two GWAS studies. In addition, our analyses identified ten genes (DUSP13, KCNJ11, CD300LF/RAB37, SLCO1B1, LRRFIP1, QSER1, UBR2, MOB3C, MST1R, and ABCC8) with previously unreported associations with CAD, although none of the single SNV associations within the genes were genome-wide significant. Among the top 1% non-lipid pathways, we detected pathways regulating coagulation, inflammation, neuronal aging, and wound healing.

[34] *Koopman JPR, Lule SA, Zziwa C et al.* **The determinants of lipid profiles in early adolescence in a Ugandan birth cohort**. Scientific reports 2021; 11:16503.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34389769
ABSTRACT
Dyslipidaemia in adolescence tracks into adulthood and is an important risk factor for cardiovascular disease. Little is known about the effects of environmental exposures and early-life exposure to

infectious diseases common to tropical regions on lipids. In 1119 early adolescent participants in the Entebbe Mother and Baby Study, we used linear regression to examine whether prenatal, childhood or adolescent factors are associated with lipid levels. Reduced high-density lipoprotein (HDL) and elevated triglyceride levels were common (prevalence 31% and 14%, respectively), but elevated low-density lipoprotein (LDL) or total cholesterol (TC) were rare. Current malaria infection was associated with lower mean LDL (adjusted ß - 0.51; 95% CI - 0.81, - 0.21), HDL (adjusted ß - 0.40; 95% CI - 0.56, - 0.23), and TC levels (adjusted ß - 0.62; 95% CI - 0.97, - 0.27), but higher mean triglyceride levels (geometric mean ratio (GMR) 1.47; 95% CI 1.18-1.84). Early-life asymptomatic malaria was associated with modest reductions in HDL and TC. Body mass index (BMI) was positively associated with LDL, TC, and triglycerides. No associations with helminth infection were found. Our findings suggest that early-life factors have only marginal effects on the lipid profile. Current malaria infection and BMI are strongly associated with lipids and important to consider when trying to improve the lipid profile.

[35] *Sleutjes JAM, van Lennep JER, van der Woude CJ, de Vries AC*. **Thromboembolic and atherosclerotic cardiovascular events in inflammatory bowel disease: epidemiology, pathogenesis and clinical management**. Therapeutic advances in gastroenterology 2021; 14:17562848211032126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34377149

ABSTRACT

Inflammatory bowel disease (IBD) is associated with an increased risk of cardiovascular disease (CVD). The increased risk of CVD concerns an increased risk of venous thromboembolism (VTE), atherosclerotic cardiovascular disease (ASCVD) and heart failure (HF), at corresponding relative risks of 2.5, 1.2 and 2.0, respectively, as compared with the general population. Especially young patients under the age of 40 years run a relatively high risk of these complications when compared with the general population. Chronic systemic inflammation causes a hypercoagulable state leading to the prothrombotic tendency characteristic of VTE, and accelerates all stages involved during atherogenesis in ASCVD. Increased awareness of VTE risk is warranted in patients with extensive colonic disease in both ulcerative colitis and Crohn's disease, as well as during hospitalization, especially when patients are scheduled for surgery. Similarly, critical periods for ASCVD events are the 3 months prior to and 3 months after an IBD-related hospital admission. The increased ASCVD risk is not fully explained by an increased prevalence of traditional risk factors and includes pro-atherogenc lipid profiles with high levels of small dense low-density lipoprotein cholesterol particles and dysfunctional high-density lipoprotein cholesterol. Risk factors associated with HF are location and extent of inflammation, female sex, and age exceeding 40 years. A dose-dependent increase of overall CVD risk has been reported for corticosteroids. Immunomodulating maintenance therapy might reduce CVD risk in IBD, not only by a direct reduction of chronic systemic inflammation but possibly also by a direct effect of IBD medication on platelet aggregation, endothelial function and lipid and glucose metabolism. More data are needed to define these effects accurately. Despite accumulating evidence on the increased CVD risk in IBD, congruent recommendations to develop preventive strategies are lacking. This literature review provides an overview of current knowledge and identifies gaps in evidence regarding CVD risk in IBD, by discussing epidemiology, pathogenesis, and clinical management.

[36] *Liu Y, Han B.* **Efficacy evaluation of PCSK9 monoclonal antibody (Evolocumab) in combination with Rosuvastatin and Ezetimibe on cholesterol levels in patients with coronary heart disease (CHD): A retrospective analysis from a single center in China**. Transpl Immunol 2021:101444.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34375677
ABSTRACT
BACKGROUND AND PURPOSE: Proprotein convertase subtilisin-kexin type 9(PCSK9) monoclonal antibody (Mab; Evolocumab) has been reported to inhibit low-density lipoprotein cholesterol (LDL-C) and Lipoprotein(a) [LP(a)] in coronary heart diseases (CHD) patients in America, Europe and Japan. However, little is known about the effect of Evolocumab in Chinese population. This retrospective study in Chinese CHD patients compared the efficacy without or with Evolocumab therapy added to the conventional treatment with a statin (Rosuvastatin) and a gut cholesterol absorption inhibitor (Ezetimibe). METHODS: CHD patients from our hospital were divided into three therapeutic groups, A) the statin monotherapy group (10 mg Rosuvastatin every night); B) the statin/cholesterol absorption inhibitor group (10 mg Rosuvastatin and 10 mg Ezetimibe daily); and C) the triple therapy with PCSK9 Mab group (10 mg Rosuvastatin daily, 10 mg Ezetimibe daily, and 140 mg Evolocumab once 2 weeks). The plasma lipid data were collected at 0, 4, 12, and 24 Week(s). The Graphpad Prism 7 program was used to perform all the statistical analysis. RESULTS: Out of 103 patients 91 were eligible for further evaluation with 31 in group A, 31 in group B, and 29 in group C. The plasma LDL-C levels were reduced only by 33.82% in the Rosuvastatin monotherapy group, 52.13% in the Rosuvastatin/Ezetimibe group, and 73.59% in the Evolocumab/Rosuvastatin/Ezetimibe group ($P<0.0001$) at 24 weeks compared to the prior therapy levels. Neither the statin therapy alone (5.95%; $P=0.6$), nor the double therapy (5.27%; $P=0.7$) affected LP(a) levels. In contrast, addition of Evolocumab to the double therapy significantly decreased LP(a) level by 37.2% ($P<0.0001$). CONCLUSION: Addition of Evolocumab to the standard double therapy in Chinese CHD patients improved the efficacy in LDL-C reduction when compared to Rosuvastatin alone or in Rosuvastatin/Ezetimibe double therapy. Furthermore, the addition of Evolocumab lowered LP(a) level in Chinese CHD patients.

[37] *Xu XQ, Luo JZ, Li XY et al.* **Effects of perioperative rosuvastatin on postoperative delirium in elderly patients: A randomized, double-blind, and placebo-controlled trial**. World journal of clinical cases 2021; 9:5909-5920.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34368309
ABSTRACT
BACKGROUND: Experimental evidence has indicated the benefits of statins for the treatment of postoperative delirium. Previously, clinical trials did not reach definite conclusions on the effects of statins on delirium. Some clinical trials have indicated that statins reduce postoperative delirium and improve outcomes, while some studies have reported negative results. AIM: To evaluate whether perioperative rosuvastatin treatment reduces the incidence of delirium and improves clinical outcomes. METHODS: This randomized, double-blind, and placebo-controlled trial was conducted in a single center in Jiangsu, China. This study enrolled patients aged greater than 60 years who received general anesthesia during elective operations and provided informed consent. A computer-generated randomization sequence (in a 1:1 ratio) was used to randomly assign patients to receive either rosuvastatin (40 mg/d) or placebo. Participants, care providers, and investigators were all

masked to group assignments. The primary endpoint was the incidence of delirium, which was assessed twice daily with the Confusion Assessment Method during the first 7 postoperative days. Analyses were performed on intention-to-treat and safety populations. RESULTS: Between January 1, 2017 and January 1, 2020, 3512 patients were assessed. A total of 821 patients were randomly assigned to receive either placebo (n = 411) or rosuvastatin (n = 410). The incidence of postoperative delirium was significantly lower in the rosuvastatin group [23 (5.6%) of 410 patients] than in the placebo group {42 (13.5%) of 411 patients [odds ratios (OR) = 0.522, 95% confidence interval (CI): 0.308-0.885; P < 0.05]}. No significant difference in 30-d all-cause mortality (6.1% vs 8.7%, OR = 0.67, 95%CI: 0.39-1.2, P = 0.147) was observed between the two groups. Rosuvastatin decreased the hospitalization time (13.8 ± 2.5 vs 14.2 ± 2.8, P = 0.03) and hospitalization expenses (9.3 ± 2.5 vs 9.8 ± 2.9, P = 0.007). No significant differences in abnormal liver enzymes (9.0% vs 7.1%, OR = 1.307, 95%CI: 0.787-2.169, P = 0.30) or rhabdomyolysis (0.73% vs 0.24%, OR = 3.020, 95%CI: 0.31-29.2, P = 0.37) were observed between the two groups. CONCLUSION: The current study suggests that perioperative rosuvastatin treatment reduces the incidence of delirium after an elective operation under general anesthesia. However, the evidence does not reveal that rosuvastatin improves clinical outcomes. The therapy is safe. Further investigation is necessary to fully understand the potential usefulness of rosuvastatin in elderly patients.

[38] *Zheng CB, Zheng ZH, Zheng YP*. **Therapeutic plasma exchange for hyperlipidemic pancreatitis: Current evidence and unmet needs**. World journal of clinical cases 2021; 9:5794-5803.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34368298
ABSTRACT
With changes in lifestyle and diet worldwide, the prevalence of hyperlipidemic acute pancreatitis (HLAP) has greatly increased, and it has become the most common cause of acute pancreatitis not due to gallstones or alcohol. There are many available therapies for HLAP, including oral lipid-lowering agents, intravenous insulin, heparin, and therapeutic plasmapheresis (TPE). It is believed that the risk and severity of HLAP increase with rising levels of serum triglycerides (TG), thus a rapid decrease in serum TG level is the key to the successful management of HLAP. TPE has emerged as an effective modality in rapidly reducing serum TG levels. However, due to its cost and accessibility, TPE remains poorly evaluated until now. Some studies revealed its efficacy in helping to treat and prevent the recurrence, while some studies suggested that TG levels were not correlated with disease severity, mortality, or length of hospital stay. Thus TPE might have no beneficial effect for the outcome. This article gives an overview of the published evidence of TPE in the treatment of HLAP and outlines current evidence regarding individual outcome predictors, adverse effects of the procedure, and TPE in special occasions such as for pregnant patients and patients with diabetic ketoacidosis. Future direction of TPE research for HLAP is also discussed in this review.

[39] *Muñoz AE, Pollarsky FD, Marino M et al.* **Addition of statins to the standard treatment in patients with cirrhosis: Safety and efficacy**. World journal of gastroenterology : WJG 2021; 27:4639-4652.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34366626
ABSTRACT

Literature update week 32 (2021)

This review summarizes the safety and efficacy of statins in patients with cirrhosis. Due to concerns about the safety of statins in patients with impaired liver function, they have recently been investigated as a potential treatment option in cirrhosis. The most clinically significant adverse event is statin-related myopathy, and this may be related to the high serum statin concentrations in the setting of severely impaired liver function. Rhabdomyolysis is the most serious and potentially life-threatening manifestation. It has recently been demonstrated that the recommended dose of simvastatin in patients with decompensated cirrhosis would be 20 mg/d because higher values, such as 40 mg/d, are associated with many adverse events, especially muscle injury. Likewise, simvastatin should not be administered to patients with Model for End-stage Liver Disease score > 12 and/or Child-Pugh class C because of the high risk of severe muscle injury. Due to the pleiotropic effects, the focus on statins has shifted from being considered harmful to something useful. Through these effects, statins could prevent liver-related morbidity and mortality in cirrhotic patients. Observational studies in large populations of patients with cirrhosis have shown that treatment with statins to decrease high cholesterol levels was associated with a reduced risk of hepatic decompensation, hepatocellular carcinoma development and death. The few randomized controlled trials in patients with cirrhosis and portal hypertension showed that statins lower portal pressure, quite likely through a reduction in hepatic resistance. Another large randomized controlled trial in patients with variceal bleeding showed that simvastatin in addition to standard of care did not prevent rebleeding but improved survival rate. Despite these encouraging outcomes, the quality of the evidence regarding the use of statins is low or very low due to the observational characteristics of most of the studies involved. Therefore, it is advisable to perform further randomized controlled trials on a large series of patients with hard clinical endpoints, using different statin types and varying doses. The objectives would be to prevent liver-related morbidity and mortality rather than treating cirrhosis complications to take additional information that makes it possible to add statins to the standard of care of these patients.