[1] *Esenwa C, Cheng NT, Lipsitz E et al.* **COVID-19-Associated Carotid Atherothrombosis and Stroke**. AJNR. American journal of neuroradiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32819896
ABSTRACT
We present a radiology-pathology case series of 3 patients with coronavirus disease 2019 (COVID-19) with acute ischemic stroke due to fulminant carotid thrombosis overlying mild atherosclerotic plaque and propose a novel stroke mechanism: COVID-associated carotid atherothrombosis.

[2] *Choi IJ, Lim S, Lee D et al.* **Relation of Proprotein Convertase Subtilisin/Kexin Type 9 to Cardiovascular Outcomes in Patients Undergoing Percutaneous Coronary Intervention**. The American journal of cardiology 2020; 133:54-60.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32798044
ABSTRACT
The pharmacological inhibition of proprotein convertase subtilisin/kexin type 9 (PCSK9) has been shown to drastically affect low-density lipoprotein cholesterol levels and associated cardiovascular diseases. However, the potential effectiveness of PCSK9 serum levels as a biomarker for cardiovascular risk remains unclear. Serum PCSK9 levels in patients who underwent percutaneous coronary intervention (PCI) may predict long-term outcomes. PCSK9 levels were measured in 749 consecutive patients with coronary artery disease undergoing PCI. These patients were classified into 2 groups according to their serum levels of PCSK9. The primary end point was a composite of the major adverse cardiac events (MACE), including cardiac death, myocardial infarction, stroke, and any revascularization. The median PCSK9 level was 302.82 ng/ml. During a median follow-up of 28.4 months, a total of 38 (5.1%) MACE was recorded, and 50 (6.7%) patients died from any cause. Multivariate Cox regression analysis showed that compared with a lower serum PCSK9 level, a higher serum PCSK9 level was independently associated with a higher rate of MACE (adjusted hazard ratio 2.290, 95% confidence interval 1.040 to 5.045, p = 0.040) and all-cause death (adjusted hazard ratio 2.511, 95% confidence interval 1.220 to 5.167, p = 0.026). Results were consistent after propensity-score matching (MACE, adjusted HR 2.236, 95% CI 1.011-5.350, p = 0.047; all-cause death, adjusted HR 2.826, 95% CI 1.258-6.349, p = 0.012). Baseline serum PCSK9 levels were associated with long-term cardiovascular clinical outcomes and mortality during the long-term follow-up after PCI in patients with coronary artery disease.

[3] *Lone AN, Khan MZ, Khan MS et al.* **Trends of Co-morbidities in Clinical Trials of Lipid Lowering Therapies**. The American journal of cardiology 2020; 133:184-185.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32811648
ABSTRACT

[4] *Yarlagadda K, Mi K, Sendil S et al.* **A 31-Year-Old Man with COVID-19-Associated Empyema and Lupus Anticoagulant**. Am J Case Rep 2020; 21:e926623.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32807764
ABSTRACT
BACKGROUND COVID-19 was declared a pandemic in March 2020 in the United States. It has been associated with high mortality and morbidity all over the world. COVID-19 can cause a significant inflammatory response leading to coagulopathy and this hypercoagulable state

has been associated with worse clinical outcomes in these patients. The published data regarding the presence of lupus anticoagulant in critically ill COVID-19-positive patients is limited and indicates varying conclusions so far. CASE REPORT Here, we present a case of a 31-year-old man who was admitted to the hospital with COVID-19 pneumonia, complicated with superadded bacterial empyema and required video-assisted thoracoscopic surgery with decortication. This patient also had prolonged prothrombin time on preoperative labs, which was not corrected with mixing study. Further workup detected positive lupus anticoagulant and anti-cardiolipin IgM along with alteration in other coagulation factor levels. The patient was treated with fresh frozen plasma and vitamin K before surgical intervention. He had an uneventful surgical course. He received prophylactic-dose low molecular weight heparin for venous thromboembolism prophylaxis and did not experience any thrombotic events while hospitalized. CONCLUSIONS COVID-19 infection creates a prothrombotic state in affected patients. The formation of micro-thrombotic emboli results in significantly increased mortality and morbidity. Routine anticoagulation with low molecular weight heparin can prevent thrombotic events and thus can improve patient outcomes. In patients with elevated prothrombin time, lupus anticoagulant/anti-cardiolipin antibody-positivity should be suspected, and anticoagulation prophylaxis should be continued perioperatively for better outcomes.

[5] *Bae SS, Chang LC, Merkin SS et al.* **Major Lipids and Future Risk of Pneumonia: 20-Year Observation of the Atherosclerosis Risk in Communities (ARIC) Study Cohort**. The American journal of medicine 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32814017

ABSTRACT
BACKGROUND: Circulating lipids have been implicated as important modulators of immune response, and altered lipid levels correlate with the severity of infection. However, long-term prognostic implications of lipid levels regarding future infection risk remain unclear. The current project aims to explore whether baseline lipid levels are associated with risk of future serious infection, measured by hospitalization for pneumonia. METHODS: A retrospective analysis was performed in 13,478 participants selected from the Atherosclerosis Risk in Communities (ARIC) study, a large community-based longitudinal cohort in the United States with a median follow-up time of >20 years. First incident of hospitalization for pneumonia was identified through hospital discharge records. Cox proportional hazard models were used to assess the association of baseline major lipid levels (total cholesterol, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], triglycerides) with time to first pneumonia hospitalization. RESULTS: A total of 1969 (14.61%) participants had a pneumonia hospitalization during a median follow-up time of 21.5 years. The hazard ratio (HR) for pneumonia hospitalization was 0.90 (95% confidence interval, 0.87-0.92) for every 10-mg/dL increase in baseline HDL-C, and 1.02 (95% confidence interval, 1.02-1.03) for every 10-mg/dL increase in baseline triglycerides. HDL-C and triglycerides both remained significant predictors of pneumonia hospitalization after multivariable adjustment. Such associations were not seen with baseline LDL-C or total cholesterol levels. CONCLUSION: Lower baseline HDL-C and higher triglyceride levels were strongly associated with increased risk of long-term pneumonia hospitalization in a large longitudinal US cohort.

[6] *Osadchuk L, Tipisova E, Kleshchev M et al.* **Study of Semen Quality, Reproductive Hormone Levels, and Lipid Levels in Men From Arkhangelsk, a City in North of European Russia**. American journal of men's health 2020; 14:1557988320939714.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812503

ABSTRACT

Male populations in the European North of Russia have not previously been investigated for semen quality. The aim of this study was to evaluate semen parameters, reproductive hormone levels, and lipid levels in volunteers from the general urban population of the European North of Russia, to compare the data published for men from the neighboring Northern or Eastern European countries, and to evaluate associations between sperm quality and serum hormonal and lipid levels. Ninety-nine volunteers aged 23-63 years residing in the city of Archangelsk were enrolled in the study. All men had blood samples drawn and completed a questionnaire concerning their health status and lifestyle; 90 men delivered semen samples. The medians for semen volume, sperm concentration, progressive motility, and normal morphology were 3.0 ml, 42.12 million/ml, 43.8%, and 6.5%, respectively. Sperm parameters below normal threshold values were found in 38.9% of participants. It seems that the sperm quality in our study group was slightly worse than in men from Finland, Norway, Sweden, or Estonia, but very similar to that in men from Denmark or Poland. The significant negative correlations of luteinizing hormone levels and positive correlations of inhibin B levels with sperm concentration and progressive motility were revealed. Higher levels of luteinizing hormone and lower levels of inhibin B were found in participants with impaired compared to normal sperm quality. No reliable links were found between serum total cholesterol, triglyceride, high and low-density lipoprotein cholesterol, and semen parameters.

[7] *Smith DD, Costantine MM*. **The role of statins in the prevention of preeclampsia**. American journal of obstetrics and gynecology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32818477

ABSTRACT

Preeclampsia is a common hypertensive disorder of pregnancy associated with considerable neonatal and maternal morbidities and mortalities. However, the exact cause of preeclampsia remains unknown; it is generally accepted that abnormal placentation resulting in the release of soluble antiangiogenic factors, coupled with increased oxidative stress and inflammation, leads to systemic endothelial dysfunction and the clinical manifestations of the disease. Statins have been found to correct similar pathophysiological pathways that underlie the development of preeclampsia. Pravastatin, specifically, has been reported in various preclinical and clinical studies to reverse the pregnancy-specific angiogenic imbalance associated with preeclampsia, to restore global endothelial health, and to prevent oxidative and inflammatory injury. Human studies have found a favorable safety profile for pravastatin, and more recent evidence does not support the previous teratogenic concerns surrounding statins in pregnancy. With reassuring and positive findings from pilot studies and strong biological plausibility, statins should be investigated in large clinical randomized-controlled trials for the prevention of preeclampsia.

[8] *Macchi C, Greco MF, Botta M et al.* **Leptin, Resistin, and Proprotein Convertase Subtilisin/Kexin Type 9: The Role of STAT3**. The American journal of pathology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32798443

ABSTRACT
In a condition of dysfunctional visceral fat depots, as in the case of obesity, alterations in adipokine levels may be detrimental for the cardiovascular system. The proinflammatory leptin and resistin adipokines have been described as possible links between obesity and atherosclerosis. The present study was aimed at evaluating whether proprotein convertase subtilisin/kexin type 9 (PCSK9), a key regulator of low-density lipoprotein metabolism, is induced by leptin and resistin through the involvement of the inflammatory pathway of STAT3. In HepG2 cells, leptin and resistin up-regulated PCSK9 gene and protein expression, as well as the phosphorylation of STAT3. Upon STAT3 silencing, leptin and resistin lost their ability to activate PCSK9. The knockdown of STAT3 did not affect the expression of leptin and resistin receptors or that of PCSK9. The analysis of the human PCSK9 promoter region showed that the two adipokines raised PCSK9 promoter activity via the involvement of a sterol regulatory element motif. In healthy males, a positive association between circulating leptin and PCSK9 levels was found only when the body mass index was <25 kg/m(2). In conclusion, this study identified STAT3 as one of the molecular regulators of leptin- and resistin-mediated transcriptional induction of PCSK9.

[9] *Taati B, Arazi H, Suzuki K*. **Oxidative Stress and Inflammation Induced by Waterpipe Tobacco Smoking Despite Possible Protective Effects of Exercise Training: A Review of the Literature**. Antioxidants (Basel, Switzerland) 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825755

ABSTRACT
The prevalence of waterpipe tobacco smoking (WTS), which is also known as ghalyan, shisha or hookah, is increasing rapidly around the world, especially among youth. Growing interest in this form of tobacco smoking can be traced, in part, to the use of flavored tobacco products, social acceptability as a safer option than cigarettes, and its consideration as a relaxation method or entertainment. However, there is a well-established association between WTS and oxidative stress that causes irreversible chronic pathological conditions such as cardiovascular and respiratory problems, as well as different types of cancers, and thus increases the risk of mortality. Clearly, induction of inflammation status through increased reactive oxygen species (ROS), which in turn leads to oxidative stress and harm to lipids, DNA, and proteins, is the most plausible mechanism to explain the potential harmful effects of WTS. Unlike WTS, well-designed exercise training programs increase ROS to the extent that it is beneficial to the body. In this study, we aimed to review available evidence on the impact of exercise training on oxidative stress and inflammation status. We also summarize the effect of acute and chronic WTS on different exercise capacities.

[10] *During A*. **Osteoporosis: A role for lipids**. Biochimie 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32818522

ABSTRACT
An inverse relationship between bone marrow (BM) adiposity and bone mass has been described in different physiological and pathological conditions, including osteoporosis (OP). In osteoporotic patients, lower bone mass density is indeed associated with higher BM fat content, suggesting a potential role for bone lipids in the OP pathogenesis. Nevertheless, some questions remain. Is that BM adiposity a cause or a consequence of the bone loss? What kinds of lipids are involved? Human data are somehow contradictories regarding bone

lipid signature related to OP, and animal data are needed to support on one or another way the human observations. Bone lipid signature associated to OP needs to be clarified if we want to understand better their roles in OP. In that context, by using an ovariectomy-induced OP murine model and looking at lipids in two bone compartments: BM and mineralized tissue (MT), our first challenge was to identify local lipid changes in relation to OP, in view to explore later the mechanisms by which those compounds could alter bone quality, particularly during the mineralization process. As the most striking data, long-term OP resulted in an accumulation of triglycerides, reduced levels of arachidonic and docosahexaenoic acids, an increase of stearoyl-CoA desaturase indices and a reduction of sphingomyelin in the MT, and potential consequences on bone properties and cell activities are discussed. The reader will appreciate that we are at an early stage of understanding the roles of lipids in the OP development and more investigations will be necessary.

[11] *Guo Y, Li Y, Liu X et al.* **Assessing the effectiveness of statin therapy for alleviating cerebral small vessel disease progression in people ≥75 years of age**. BMC geriatrics 2020; 20:292.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32807086
ABSTRACT
BACKGROUND: Statins have been recommended by several guidelines as the primary prevention medication for cardiovascular diseases. However, the benefits of statin therapy for cerebral small vessel disease (CSVD), particularly in adults ≥75 years of age, have not been fully evaluated. METHODS: We analyzed the data from a prospective population-based cohort study and a randomized, double-blind, placebo-controlled clinical trial to determine whether statin therapy might aid in slowing the progression of CSVD in adults ≥75 years of age. For the cohort study, 827 participants were considered eligible and were included in the baseline analysis. Subsequently, 781 participants were included in follow-up analysis. For the clinical trial, 227 participants were considered eligible and were used in the baseline and follow-up analyses. RESULTS: The white matter hyperintensities (WMH) volume, the WMH-to-intracranial volume (ICV) ratio, the prevalence of a Fazekas scale score ≥ 2, lacunes, enlarged perivascular spaces (EPVS), and microbleeds were significantly lower in the statin group than the non-statin group at baseline in the cohort study (all $P < 0.05$). During the follow-up period, in both the cohort and clinical trial studies, the WMH volume and WMH-to-ICV ratio were significantly lower in the statin/rosuvastatin group than the non-statin/placebo group (all $P < 0.001$). Statin therapy was associated with lower risk of WMH, lacunes, and EPVS progression than the non-statin therapy group after adjustment for confounders (all $P < 0.05$). There was no statistically significant difference in the risk of microbleeds between the statin and non-statin therapy groups (all, $P > 0.05$). CONCLUSIONS: Our findings indicated that statin therapy alleviated the progression of WMH, lacunes, and EPVS without elevating the risk of microbleeds. On the basis of the observed results, we concluded that statin therapy is an efficient and safe intervention for CSVD in adults ≥75 years of age. TRIAL REGISTRATION: Chictr.org.cn: ChiCTR-IOR-17013557 , date of trial retrospective registration November 27, 2017 and ChiCTR-EOC-017013598 , date of trial retrospective registration November 29, 2017.

[12] *Shiraishi H, Yamada K, Egawa K et al.* **Efficacy of bezafibrate for preventing myopathic attacks in patients with very long-chain acyl-CoA dehydrogenase deficiency**. Brain Dev 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32798077
ABSTRACT
BACKGROUND: Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD) is a mitochondrial fatty acid oxidation disorder that causes episodic attacks, such as general fatigue, hypotonia, myalgia, and rhabdomyolysis accompanied by lack of energy. As yet, there are no preventative drugs for these VLCADD-associated metabolic attacks. PATIENTS AND METHODS: We conducted an open-label, non-randomized, multi-center study into the effects of bezafibrate on five patients with VLCADD. Bezafibrate was administered for 4 years, and we analyzed the number of myopathic attacks requiring hospitalization and treatment infusions. RESULTS: The number of myopathic attacks requiring infusions of 24 h or longer significantly decreased during the study period. The patients' ability to conduct everyday activities was also improved by the treatment. CONCLUSION: Our findings show the potential long-term efficacy of bezafibrate in preventing myopathic attacks for patients with VLCADD.

[13] *Levintow SN, Reading SR, Saul BC et al.* **Lipid Testing Trends in the US Before and After the Release of the 2013 Cholesterol Treatment Guidelines**. Clinical epidemiology 2020; 12:835-845.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32801921
ABSTRACT
BACKGROUND: The 2013 ACC/AHA cholesterol treatment guidelines removed the recommendation to treat adults at risk of cardiovascular disease to goal levels of low-density lipoprotein cholesterol (LDL-C). We anticipated that the frequency of LDL-C testing in clinical practice would decline as a result. To test this hypothesis, we evaluated the frequency of LDL-C testing before and after the guideline release. METHODS: We used the MarketScan(®) Commercial and Medicare Supplemental claims data (1/1/2007-12/31/2016) to identify four cohorts: 1) statin initiators (any intensity), 2) high-intensity statin initiators, 3) ezetimibe initiators, and 4) patients at very high cardiovascular risk (≥2 hospitalizations for myocardial infarction or ischemic stroke, with prevalent statin use). Rates of LDL-C testing by calendar year quarter were estimated for each cohort. To estimate rates in the absence of a guideline change, we fit a time-series model to the pre-guideline rates and extrapolated to the post-guideline period, adjusting for covariates, seasonality, and time trend. RESULTS: Pre- and post-guideline rates (LDL-C tests per 1,000 persons per quarter) were 248 and 235, respectively, for 3.9 million statin initiators; 263 and 246 for 1.3 million high-intensity statin initiators; 277 and 261 for 323,544 ezetimibe initiators; and 180 and 158 for 42,108 very high-risk patients. For all cohorts, observed post-guideline rates were similar to model-predicted rates. On average, the difference between observed and predicted rates was 8.5 for patients initiating any statin; 2.6 for patients initiating a high-intensity statin; 11.4 for patients initiating ezetimibe, and -0.5 for high-risk patients. CONCLUSION: We observed no discernible impact of the release of the 2013 ACC/AHA guidelines on LDL-C testing rates. Rather, there was a gradual decline in testing rates starting prior to the guideline change and continuing throughout the study period. Our findings suggest that the guidelines had little to no impact on use of LDL-C testing.

[14] *Hansen SEJ, Madsen CM, Varbo A et al.* **Genetic Variants Associated With Increased Plasma Levels of Triglycerides, via Effects on the Lipoprotein Lipase Pathway, Increase Risk of Acute Pancreatitis**. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32801009

ABSTRACT
BACKGROUND & AIMS: Almost one third of adults in the West have increased plasma levels of triglycerides. Even mild to moderate hypertriglyceridemia (2-10 mmol/L or 177-886 mg/dL) is associated with an increased risk of acute pancreatitis. However, it is not clear whether hypertriglyceridemia is a cause or result of acute pancreatitis. Lipoprotein lipase degrades plasma triglycerides. Variants in LPL, APOA5, APOC3, ANGPTL3, and ANGPTL4, which regulate the lipoprotein lipase pathway, result in increased or reduced plasma triglyceride levels. We investigated associations between these variants and acute pancreatitis in a study of the general population. METHODS: In a prospective cohort study, men and women randomly selected from the population of Denmark were invited to complete a questionnaire, undergo a physical examination, and provide blood samples for biochemical and genetic analyses, from 2003 through 2015. We obtained triglyceride measurements from 117,427 participants. We examined for 15 genetic variants that are associated with lipoprotein lipase function in DNA samples from 102,888 participants and analyzed data from 117,427 participants in observational analyses. Diagnoses of acute pancreatitis (970 diagnoses among participants in the genetic analysis and 527 among participants in the observational study) were obtained from Danish registries. We performed a 1-sample Mendelian randomization analysis in which specific variants were used as markers of the plasma level of triglycerides to determine the association between the plasma level of triglyceride and acute pancreatitis. We calculated unweighted, internally weighted, and externally weighted allele scores for each participant by adding numbers of triglyceride-increasing alleles. RESULTS: The highest genetic allele score correlated with a higher plasma level of triglycerides of 0.54 mmol/L (48 mg/dL). Among participants with the highest vs the lowest genetic allele score, the odds ratio for acute pancreatitis was 1.55 (95% CI, 1.08-2.23). Using instrumental variable analysis, integrating the effect of genotype on both triglycerides levels and risk of acute pancreatitis, we associated higher unweighted allele scores (level of triglycerides 1 mmol/L or 89 mg/dL higher) with an increased risk of acute pancreatitis (odds ratio [OR], 1.76; 95% CI, 1.16-2.65), as well as internally weighted higher allele scores (OR, 1.41; 95% CI, 1.01-1.97) and externally weighted higher allele scores (OR, 1.44; 95% CI, 1.01-2.04). Every 1 mmol/L (89 mg/dL) increase in triglycerides was observationally associated with an increase in OR of 1.09 (95% CI, 1.05-1.14) after multivariable adjustment. CONCLUSIONS: Based on an analysis of individuals with genetic variants associated with an increased level of triglycerides, via their effects on the lipoprotein lipase pathway, we associated an increased plasma levels of triglycerides with an increased risk of acute pancreatitis. Strategies to reduce plasma levels of triglycerides, by increasing lipoprotein lipase function, might be developed for prevention of acute pancreatitis.

[15] *Balla S, Ekpo EP, Wilemon KA et al.* **Women Living with Familial Hypercholesterolemia: Challenges and Considerations Surrounding Their Care**. Current atherosclerosis reports 2020; 22:60.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32816232

ABSTRACT
PURPOSE OF REVIEW: To highlight the gender-based differences in presentation and disparities in care for women with familial hypercholesterolemia (FH). RECENT FINDINGS: Women with FH experience specific barriers to care including underrepresentation in research, significant underappreciation of risk, and interrupted therapy during childbearing. National and international registry and clinical trial data show significant healthcare disparities for women with FH. Women with FH are less likely to be on guideline-recommended high-intensity statin medications and those placed on statins are more likely to discontinue them within their first year. Women with FH are also less likely to be on regimens including non-statin agents such as PCSK9 inhibitors. As a result, women with FH are less likely to achieve target low-density lipoprotein cholesterol (LDL-C) targets, even those with prior atherosclerotic cardiovascular disease (ASCVD). FH is common, under-diagnosed, and under-treated. Disparities of care are more pronounced in women than men. Additionally, FH weighs differently on women throughout the course of their lives starting from choosing contraceptives as young girls along with lipid-lowering therapy, timing pregnancy, choosing breastfeeding or resumption of therapy, and finally deciding goals of care during menopause. Early identification and appropriate treatment prior to interruptions of therapy for childbearing can lead to marked reduction in morbidity and mortality. Women access care differently than men and increasing awareness among all providers, especially cardio-obstetricians, may improve diagnostic rates. Understanding the unique challenges women with FH face is crucial to close the gaps in care they experience.

[16] *Deoker A, Lehker A, Mukherjee D*. **Updates in Anti-anginal and Anti-ischemic Therapies for Acute Coronary Syndromes**. Current cardiology reports 2020; 22:126.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32822002

ABSTRACT
PURPOSE OF REVIEW: Acute coronary syndrome is a major health problem affecting ~ 1.5 million individuals a year in the USA. We review the contemporary role of anti-anginal and anti-ischemic therapies in the management of an individual presenting with an acute coronary syndrome. RECENT FINDINGS: Early diagnosis and appropriate evidence-based therapies significantly improve clinical outcomes in acute coronary syndrome patients. Typically, acute coronary syndrome is associated with rupture of an atherosclerotic plaque and either partial or complete thrombotic occlusion of a coronary artery. Management of an acute coronary syndrome is targeted towards this underlying pathophysiology. The last few years have seen significant advances in anti-anginal and anti-ischemic therapies in the management of patients with acute coronary syndrome. It is important to have a team effort to target risk reduction measures and to emphasize medication and dietary compliance. Long-term pharmacotherapy should include aspirin, beta-blocker, DAPT (for at least 1 year), statins, and ACE inhibitors and PCSK9 inhibitors if indicated.

[17] *Nikpayam O, Faghfouri AH, Tavakoli-Rouzbehani OM et al.* **The effect of green coffee extract supplementation on lipid profile: A systematic review of clinical trial and in-vivo studies**. Diabetes & metabolic syndrome 2020; 14:1521-1528.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32799074

ABSTRACT

BACKGROUND AND AIMS: Dyslipidemia is an important and common risk factor for cardiovascular disease and increases the risk of mortality. Green coffee extract (GCE) contains bioactive polyphenols, especially Chlorogenic acid (CGA), that due to the antioxidant characteristic, have a desirable effect on metabolic factors. This review conducted to focus on the effect of GCE on lipid profiles. METHODS: PubMed, Scopus, and web of science were searched until November 2019. All clinical studies and in-vivo studies that provide sufficient information about outcomes include to this review. RESULTS: Out of 3270 studies obtained in our searching, only 32 articles were eligible for analysis. Five double-blind, randomized clinical trial studies, two Cross-over studies, one Quasi-experimental study, and twenty animal studies were included in this systematic review-all articles evaluated according to the checklist of aim and inclusion and exclusion criteria. Generally, the results of the included studies showed there is controversy about the effect of GCE and CGA on lipid profile improvement. CONCLUSIONS: Although, a higher dosage of GCE and administration of CGA with longer duration leads to better results. However, investigating the effectiveness and safety dosage as a lipid-lowering agent needs further studies with differential dosage and periods.

[18] *Merchant RA, Chan YH, Lim JY, Morley JE*. **Prevalence of Metabolic Syndrome and Association with Grip Strength in Older Adults: Findings from the HOPE Study**. Diabetes, metabolic syndrome and obesity : targets and therapy 2020; 13:2677-2686.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821140

ABSTRACT

OBJECTIVE: To determine the prevalence of metabolic syndrome (MetS) in older adults and assess the association of MetS and adverse outcomes with handgrip strength (HGS), HGS/body weight (BWT), and HGS/body mass index (BMI). METHODS: A cross-sectional population study in Singapore. Data were collected on demographics, HGS, Timed-Up and Go (TUG), fasting glucose, lipid profile, blood pressure, waist circumference, frailty status, and cognition in 722 older adults ≥65 years old. MetS was defined using the Modified ATP III for Asians where at least three of the following conditions must be fulfilled, central obesity, high blood glucose (or diagnosed diabetes mellitus), high blood pressure (or diagnosed hypertension), low high-density lipoprotein, and high triglycerides. The waist circumference in the Modified ATP III for Asians is ≥90 cm for males or ≥80 cm for females. HGS and HGS normalized by BWT or BMI were used for the association. RESULTS: The prevalence of MetS in older adults was 41.0%, and those ≥85 years old 50.0%. The prevalence was higher in females ≥70 years old, with 8 in 10 females ≥85 years having MetS. After adjusting for age, years of education, physical exercise, as well as history of smoking and alcohol consumption, higher HGS normalized by BWT or BMI was significantly associated with lower odds of having MetS (OR: 0.51,95% CI 0.43-0.61, $p<0.01$) and (OR: 0.13, 95% CI 0.07-0.24, $p<0.01$). CONCLUSION: Almost 1 in 2 older adults had MetS, with the prevalence in females much higher than that in males over 70 years old. Our findings suggest that both HGS/BWT and HGS/BMI had a significant negative association with MetS, its components, and adverse effects. Further studies are needed to validate the association and to determine optimal cutoffs of HGS/BWT and HGS/BMI for MetS, and the effectiveness of interventions in averting the risk.

[19] *Vaccaro O, Vitale M, Costanzo S et al.* **Cardiovascular risk factors control according to diabetes status and prior cardiovascular events in patients managed in different settings**. Diabetes Res Clin Pract 2020; 168:108370.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32827595

ABSTRACT

AIMS: To document in recent cohorts the degree of control of major cardiovascular (CV) risk factors according to diabetes status and prior CV disease in different settings. METHODS: We studied men and women aged 50-75 years of whom 3028 with type 2 diabetes mellitus (T2DM) managed at diabetes clinics participants of the TOSCA.IT (NCT00700856) study recruited in 2008-2014; 742 with T2DM managed mainly in primary care and 6753 without diabetes participating in the Moli-sani (NCT03242109) study and recruited in 2005-2010 from an adult general population. RESULTS: Among people without a prior CV event people with diabetes managed at diabetes clinics have lower LDL-cholesterol and blood pressure and a more frequent use of lipid-lowering and antihypertensive medications as compared to people with diabetes managed mainly in primary care and to people without diabetes. The proportions achieving the recommended treatment targets are respectively 47.4% vs 33.4% vs 29.5% for LDL-cholesterol and 42.6% vs 9.5% vs 47.4% for blood pressure. Figures for the participants with prior CV events were 26.8% vs 15.1% vs 42.5% for LDL-cholesterol and 43.8% vs 8.5% vs 43.6% for blood pressure. CONCLUSIONS: The study documents that in modern cohorts a large proportion of people with or without diabetes does not achieve the treatment targets for LDL-cholesterol and blood pressure, both in primary and secondary CV prevention. People with diabetes attending diabetes clinics achieve a better control of major CV risk factors than those managed mainly in primary care, thus highlighting the relevant role of a structured model of care.

[20] *Bao H, Zheng N, Li Z, Zhi Y*. **Synergistic Effect of Tangeretin and Atorvastatin for Colon Cancer Combination Therapy: Targeted Delivery of These Dual Drugs Using RGD Peptide Decorated Nanocarriers**. Drug design, development and therapy 2020; 14:3057-3068.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32801644

ABSTRACT

PURPOSE: Colorectal cancer (CRC) is the third most frequently diagnosed cancer and the fourth leading cause of cancer death over the world. Nano-sized drug delivery systems are used for the treatment of cancers. The aim of this study was to develop a tangeretin (TAGE) and atorvastatin (ATST) combined nano-system decorated with RGD (RGD-ATST/TAGE CNPs) for colon cancer combination therapy. MATERIALS AND METHODS: In this study, cyclized arginine-glycine-aspartic acid sequences (RGD) contained ligand was synthesized by conjugating cyclo (Arg-Gly-Asp-d-Phe-Lys) (cRGDfK) with D-α-tocopheryl succinate dichloromethane (TOSD) using polyethylene glycol (PEG) as a linker to obtain cRGDfK-PEG-TOSD. ATST and TAGE combined nano-systems: RGD-ATST/TAGE CNPs were prepared. The combination effects as well as antitumor effects of these two agents were evaluated on colon cancer cells and mice bearing cancer models. RESULTS: Drug entrapment efficiencies of nano-systems were high (around 90%), suggesting the good loading capacity. The release profiles of ATST or TAGE from RGD-ATST/TAGE CNPs followed Higuchi model. The RGD-decorated nano-system showed more obvious cytotoxicity on HT-29 cells than the undecorated nano-system, but no obvious difference was found on normal CCD-18 cells. The

strongest synergism was observed when the weight ratio of ATST to TAGE was 1:1. In vivo biodistribution of RGD-ATST/TAGE CNPs in the tumor site is high and prominently inhibited the in vivo tumor growth. CONCLUSION: The results demonstrated that RGD-ATST/TAGE CNPs showed the most significant synergistic therapeutic efficacy, exhibited no significant toxicity to major organs and tissues, and body weight of the treated mice was stable. Therefore, the combination nano-system is a promising platform for colon cancer therapy.

[21] *Kusunoki M, Sakazaki T, Tsutsumi K et al.* **The effects of pemafibrate in Japanese patients with type 2 diabetes receiving HMG-CoA reductase inhibitors**. Endocrine, metabolic & immune disorders drug targets 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32819242
ABSTRACT
OBJECTIVE: The combination therapy of HMG-CoA reductase inhibitors (statins), which are anti-hyperlipidemia agents, and fibrates may increase the risk of hepatic dysfunction and myopathy, so this combination required careful administration for patients. In the present study, we evaluated the effects of combination therapy of pemafibrate, a novel fibrate and statins. METHODS: We administered pemafibrate for 6 months as an add-on to statin therapy in 27 type 2 diabetes patients with dyslipidemia already receiving statins for 6 months (combination group), and examined the efficacy and safety of the combination therapy in comparison with a pemafibrate monotherapy group. RESULTS: In the combination group, decrease in serum total cholesterol levels was observed after 6 months of pemafibrate treatment compared to baseline, along with increase in HDL-cholesterol. While serum triglyceride level reduced, HbA1c level was elevated in both the groups. Serum creatinine kinase level, which is an indicator of myopathy, was lowered in the combination group. In addition, decrease in □-glutamyl transpeptidase, a parameter of hepatic dysfunction, was observed in the combination group. CONCLUSION: The statin-pemafibrate combination therapy in type 2 diabetes patients with dyslipidemia improved lipid metabolism safely without increasing the risk of hepatic dysfunction and myopathy.

[22] *Cannon CP*. **Chronic kidney disease: a high-risk group that deserves intensive lipid lowering**. European heart journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32820336
ABSTRACT

[23] *Tuñón J, Steg PG, Bhatt DL et al.* **Effect of alirocumab on major adverse cardiovascular events according to renal function in patients with a recent acute coronary syndrome: prespecified analysis from the ODYSSEY OUTCOMES randomized clinical trial**. European heart journal 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32820320
ABSTRACT
AIMS: Statins reduce cardiovascular risk in patients with acute coronary syndrome (ACS) and normal-to-moderately impaired renal function. It is not known whether proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors provide similar benefit across a range of renal function. We determined whether effects of the PCSK9 inhibitor alirocumab to reduce cardiovascular events and death after ACS are influenced by renal function. METHODS AND RESULTS: ODYSSEY OUTCOMES compared alirocumab with placebo in patients with recent

ACS and dyslipidaemia despite intensive statin treatment. Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m2 was exclusionary. In 18 918 patients, baseline eGFR was 82.8 ± 17.6 mL/min/1.73 m2, and low-density lipoprotein cholesterol (LDL-C) was 92 ± 31 mg/dL. At 36 months, alirocumab decreased LDL-C by 48.5% vs. placebo but did not affect eGFR (P = 0.65). Overall, alirocumab reduced risk of the primary outcome (coronary heart disease death, non-fatal myocardial infarction, ischaemic stroke, or unstable angina requiring hospitalization) with fewer deaths. There was no interaction between continuous eGFR and treatment on the primary outcome or death (P = 0.14 and 0.59, respectively). Alirocumab reduced primary outcomes in patients with eGFR ≥90 mL/min/1.73 m2 (n = 7470; hazard ratio 0.784, 95% confidence interval 0.670-0.919; P = 0.003) and 60 to <90 (n = 9326; 0.833, 0.731-0.949; P = 0.006), but not in those with eGFR < 60 (n = 2122; 0.974, 0.805-1.178; P = 0.784). Adverse events other than local injection-site reactions were similar in both groups across all categories of eGFR. CONCLUSIONS: In patients with recent ACS, alirocumab was associated with fewer cardiovascular events and deaths across the range of renal function studied, with larger relative risk reductions in those with eGFR > 60 mL/min/1.73 m2.

[24] *Xie H, Yang K, Winston-McPherson GN et al.* **From methylene bridged diindole to carbonyl linked benzimidazoleindole: Development of potent and metabolically stable PCSK9 modulators**. European journal of medicinal chemistry 2020; 206:112678.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32823006
ABSTRACT
Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a recently validated therapeutic target for lowering low-density lipoprotein cholesterol (LDL-C). Through phenotypic screening, we previously discovered a class of small-molecules with a 2,3'-diindolymethane (DIM) skeleton that can decrease the expression of PCSK9. But these compounds have low potency and low metabolically stability. After performing structure-activity relationship (SAR) optimization by nitrogen scan, deuterium substitution and fluorine scan, we identified a series of much more potent and metabolically stable PCSK9 modulators. A preliminary in vivo pharmacokinetic study was performed for representative analogues difluorodiindolyketone (DFDIK) 12 and difluorobenzoimidazolylindolylketone (DFBIIK-1) 13. The in vitro metabolic stability correlate well with the in vivo data. The most potent compound 21 has the EC(50) of 0.15 nM. Our SAR studies also indicated that the NH on the indole ring of 21 can tolerate more function groups, which may facilitate the mechanism of action studies and also allow further improvement of the pharmacological properties.

[25] *Boreskie KF, Rose AV, Hay JL et al.* **Frailty status and cardiovascular disease risk profile in middle-aged and older females**. Experimental gerontology 2020; 140:111061.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32814098
ABSTRACT
OBJECTIVE: Frailty and pre-frailty are known to increase the risk of developing cardiovascular disease (CVD). However, the risk profiles of females are not well characterized. The aim of this study is to characterize the CVD risk profiles of robust, pre-frail and frail females. METHODS: Cross-sectional analysis of 985 females ≥55 years with no self-reported history of CVD were recruited. Frailty was assessed using the Fried Criteria with the cut-points standardized to the cohort. Framingham risk scores (FRS), the 4-test Rasmussen Disease Score (RDS), and the CANHEART health index were used to characterize composite CVD risk. Individual measures

of CVD risk included blood lipids, artery elasticity assessments, exercise blood pressure response, 6-min walk test (6MWT), sedentary time and PHQ-9 score. RESULTS: The cohort comprised of 458 (46.4%) robust, 464 (47.1%) pre-frail and 63 (6.4%) frail females with a mean age of 66 ± 6 (SD) years. Pre-frail females were at increased odds of taking diabetes medications (OR 3.04; 95% CI 1.27-7.27), hypertension medications (OR 2.02; 95% CI 1.44-2.82), having an exaggerated blood pressure response to exercise (OR 1.878; 95% CI 1.39-2.50), mild depression symptoms (OR 2.38; 95% CI 1.68-338), and lower fitness as assessed by 6MWT (OR 5.74; 95% CI 3.18-10.37), even after controlling for age and relevant medications. Pre-frail females were also at increased odds for having CVD risk scores indicating higher risk with the FRS (OR 1.52; 95% CI 1.12-2.05), the RDS (OR 1.60; 95% CI 1.21-2.10) and the CANHEART risk score (OR 3.07; 95% CI 2.04-4.62). These odds were higher when frail females were compared to their robust peers. CONCLUSION: Frailty and pre-frailty were associated with higher odds of presenting with CVD risk factors as compared to robust females, even after controlling for age.

[26] *Zhang C, Ge C, Wang J, Sun D*. **Effects of fish oil during hemodialysis on nutritional status and quality of life: a randomized double-blinded trial**. Food & nutrition research 2020; 64.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821255
ABSTRACT
BACKGROUND: Supplementation of fish oil has been shown to exert beneficial effects in patients undergoing hemodialysis. The aim of this study was to investigate the efficacy of fish oil in improving the quality of life of these patients through a randomized, double-blinded clinical trial. METHODS: Among the 103 patients enrolled in the study, a total of 74 patients were randomized to receive fish oil (intervention group) or placebo (n=37 per group). Patients received identical soft-gel capsules, with each capsule containing either 1000 mg fish oil or placebo for 4 months. Personnel responsible for data collection and analyses were blinded to the grouping. RESULTS: The reduction of protein-energy wasting (PEW) in the intervention group was significantly more prominent compared to the placebo group (P=0.023). The intervention group demonstrated significant increase in midarm circumference, arm muscle circumference, and triceps skinfold thickness after fish oil intake. The intervention group also exhibited significant differences from the placebo group in creatinine, uric acid, and serum calcium levels. Significant improvement was seen regarding the physical role and energy/figure in the intervention group. CONCLUSIONS: Our study demonstrated that fish oil intake in patient undergoing hemodialysis can significantly reduce PEW, and improve physical and biochemical parameters and quality of life, which could provide guidance to clinical management of these patients.

[27] *Sourris KC, Watson A, Jandeleit-Dahm K*. **Inhibitors of Advanced Glycation End Product (AGE) Formation and Accumulation**. Handbook of experimental pharmacology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32809100
ABSTRACT
A range of chemically different compounds are known to inhibit the formation and accumulation of advanced glycation end products (AGEs) or disrupt associated signalling pathways. There is evidence that some of these agents can provide end-organ protection in

chronic diseases including diabetes. Whilst this group of therapeutics are structurally and functionally different and have a range of mechanisms of action, they ultimately reduce the deleterious actions and the tissue burden of advanced glycation end products. To date it remains unclear if this is due to the reduction in tissue AGE levels per se or the modulation of downstream signal pathways. Some of these agents either stimulate antioxidant defence or reduce the formation of reactive oxygen species (ROS), modify lipid profiles and inhibit inflammation. A number of existing treatments for glucose lowering, hypertension and hyperlipidaemia are also known to reduce AGE formation as a by-product of their action. Targeted AGE formation inhibitors or AGE cross-link breakers have been developed and have shown beneficial effects in animal models of diabetic complications as well as other chronic conditions. However, only a few of these agents have progressed to clinical development. The failure of clinical translation highlights the importance of further investigation of the advanced glycation pathway, the diverse actions of agents which interfere with AGE formation, cross-linking or AGE receptor activation and their effect on the development and progression of chronic diseases including diabetic complications. Advanced glycation end products (AGEs) are (1) proteins or lipids that become glycated as a result of exposure to sugars or (2) non-proteinaceous oxidised lipids. They are implicated in ageing and the development, or worsening, of many degenerative diseases, such as diabetes, atherosclerosis, chronic kidney and Alzheimer's disease. Several antihypertensive and antidiabetic agents and statins also indirectly lower AGEs. Direct AGE inhibitors currently investigated include pyridoxamine and epalrestat, the inhibition of the formation of reactive dicarbonyls such as methylglyoxal as an important precursor of AGEs via increased activation of the detoxifying enzyme Glo-1 and inhibitors of NOX-derived ROS to reduce the AGE/RAGE signalling.

[28] *Sabandal MMI, Schäfer E, Aed J et al.* **Simvastatin induces adverse effects on proliferation and mineralization of human primary osteoblasts**. Head Face Med 2020; 16:18.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32819403

ABSTRACT
BACKGROUND: Frequently statins were administered to reduce the LDL-concentration in circulating blood. Especially simvastatin (SV) is an often prescribed statin. Pleiotropic effects of these drugs were reported. Thus, the aim of this study was to evaluate effects of SV on osteoblastic mineralization. METHODS: After informed consent primary osteoblasts were collected from tissue surplus after treatment of 14 individuals in the Department of Cranio-Maxillofacial Surgery, University Hospital Münster. The cells were passaged according to established protocols. Viability, mineralization capability and osteoblastic marker (alkaline phosphatase) were determined at day 9, 13 and 16 after adding various SV concentrations (0.05 µM, 0.1 µM, 0.5 µM, 1.0 µM). Statistical analysis was performed using the Kruskal-Wallis-test. RESULTS: The cell cultures showed a time and dose-dependent significantly decreased viability ($p < 0.01$) and a significantly increased mineralization ($p < 0.01$) in a late mineralization stage after adding SV. The typical alteration of the alkaline phosphatase (ALP) levels during osteogenic differentiation was not recognizable. CONCLUSIONS: The pleiotropic effects found for different SV concentrations were possibly originated from other mineralization pathways beside the ALP induced one. Additionally, possible alterations of protein expression levels during mineralization and investigation of possible deviating application of SV in other treatment fields can be considered after gaining a deeper insight in the affected mechanisms.

[29] *Han J, Bilgrami S, Ross S et al.* **Real-world lipid lowering effects of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors: A single-centre study**. International journal of cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32827563
ABSTRACT

[30] *Heidemann BE, Koopal C, Bots ML et al.* **The relation between VLDL-cholesterol and risk of cardiovascular events in patients with manifest cardiovascular disease**. International journal of cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32810544
ABSTRACT
INTRODUCTION: Apolipoprotein B containing lipoproteins are atherogenic. There is evidence that with low plasma low density lipoprotein cholesterol (LDL-C) levels residual vascular risk might be caused by triglyceride rich lipoproteins such as very-low density lipoproteins (VLDL), chylomicrons and their remnants. We investigated the relationship between VLDL-cholesterol (VLDL-C) and recurrent major adverse cardiovascular events (MACE), major adverse limb events (MALE) and all-cause mortality in a cohort of patients with cardiovascular disease. METHODS: Prospective cohort study in 8057 patients with cardiovascular disease from the UCC-SMART study. The relation between calculated VLDL-C levels and the occurrence of MACE, MALE and all-cause mortality was analyzed with Cox regression models. RESULTS: Patients mean age was 60 ± 10 years, 74% were male, 4894 (61%) had coronary artery disease, 2445 (30%) stroke, 1425 (18%) peripheral arterial disease and 684 (8%) patients had an abdominal aorta aneurysm at baseline. A total of 1535 MACE, 571 MALE and 1792 deaths were observed during a median follow up of 8.2 years (interquartile range 4.512.2). VLDL-C was not associated with risk of MACE or all-cause mortality. In the highest quartile of VLDL-C the risk was higher for major adverse limb events (MALE) (HR 1.49; 95%CI 1.16-1.93) compared to the lowest quartile, after adjustment for confounders including LDL-C and lipid lowering medication. CONCLUSION: In patients with clinically manifest cardiovascular disease plasma VLDL-C confers an increased risk for MALE, but not for MACE and all-cause mortality, independent of established risk factors including LDL-C and lipid-lowering medication.

[31] *Ahn N, Kim K*. **Can Active Aerobic Exercise Reduce the Risk of Cardiovascular Disease in Prehypertensive Elderly Women by Improving HDL Cholesterol and Inflammatory Markers?** International journal of environmental research and public health 2020; 17.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32824020
ABSTRACT
This study aims to verify the efficacy of exercise programs designed to prevent and treat hypertension-induced cardiovascular disease (CVD) by analyzing the effects of a 6-month active aerobic exercise program, administered to prehypertensive elderly women, on reducing the risk of developing CVD by enhancing their physical fitness level and improving the detailed markers of high-density lipoprotein cholesterol (HDL-C) and inflammatory markers. We assigned the elderly women (≥65 years) recruited into normal blood pressure (120-129/80-84; NBP, n = 18) and high-normal blood pressure (130-139/85-89; HNBP, n = 12) groups according to the European guidelines for the management of arterial hypertension. The

exercise program was made up of combined workouts of elastic band resistance exercise and aerobics with dance music. The program took place three times a week for six months, with each session lasting 60 min. We measured pre- and post-intervention body composition, blood pressure, physical fitness level, blood lipids profile, HDL-C, SAA, TNF-α, IL-6, IL-4, IL-15, CRP, and HSP70 and calculated the Framingham risk scores for comparison. A significant post-intervention reduction in the mean systolic blood pressure (SBP) was observed in the HNBP group ($p < 0.001$), with significant increase in HDL-C ($p < 0.01$) and significant decrease in serum amyloid A (SAA) concentration ($p < 0.01$). A significant improvement in physical fitness factors such as physical efficiency index (PEI) was also observed in the HNBP group ($p < 0.05$). The post-intervention TNF-α, IL-6, and SAA concentrations were more significantly lower in the HNBP than in the NBP group ($p < 0.05$). Compared to the baseline values, a significant decrease in SAA concentration ($p < 0.01$) and significant increase in HSP70 concentration ($p < 0.001$) were observed in the HNBP group. The HNBP group's 10-year CVD risk was also significantly reduced ($p < 0.05$). The pre-post differences in SBP and DBP were significantly correlated with those in the anti-inflammatory markers IL-4 and IL-15 ($p < 0.01$). In conclusion, the 6-month active aerobic exercise program of moderate intensity administered to prehypertensive elderly women (≥65 years) had the effect of reducing the 10-year CVD risk through a substantial reduction in SBP, overall physical fitness improvement, increase in HDL-C, decrease in SAA concentration, and substantial decrease in inflammatory biomarkers. It was also confirmed that an increase in anti-inflammatory markers, which showed a small range of increase with respect to the decrease in blood pressure, may have a major effect.

[32] *Ahmed TA, Elimam H, Alrifai AO et al.* **Rosuvastatin lyophilized tablets loaded with flexible chitosomes for improved drug bioavailability, anti-hyperlipidemic and anti-oxidant activity**. Int J Pharm 2020; 588:119791.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32827673

ABSTRACT

Rosuvastatin is a hypolipidemic drug of limited oral bioavailability. The aim was to develop rosuvastatin flexible chitosomes and loading into a pullulan-based tablet to improve the bioavailability and maximize the antihyperlipidemic and antioxidant activities. Chitosomes nanoparticles were developed and characterized. Pullulan-based lyophilized fast dissolving tablets were developed and evaluated. The tablets' outer and inner structures were morphologically investigated. In vivo disintegration of the prepared tablets was studied in healthy human volunteers. The pharmacokinetics, antihyperlipidemic, antioxidant, and biochemical markers activities were conducted after administration of the tablets into male Wister rats. Liver histopathology was also investigated. The prepared chitosomes illustrated an average particle size of 342.22 ± 2.90 nm, a zeta potential value of +28.87 ± 1.39 mV and a drug entrapment efficiency of 94.59 ± 1.62%. The developed tablets showed an acceptable quality control characteristics and in vivo disintegration time of 1.48 ± 0.439 min. Scanning electron microscopy revealed distinct porous surface and sponge-like inner structure. The chitosomes based tablets demonstrated higher relative bioavailability by more than 30% and 36% when compared with the corresponding pure rosuvastatin and the marketed drug tablets, respectively. Moreover, the chitosomes based tablets showed a significant improvement in the hepatic serum biomarkers and a dramatic decrease in the serum antioxidants in response to Poloxamer 407 intoxication. The prepared tablets did not exhibit marked histopathological changes in the hepatic tissues. Accordingly, the pullan-based lyophilized fast-dissolving tablets

loaded with chitosomes nanoparticles could be considered as a promising drug formulation for enhancing rosuvastatin bioavailability and pharmacodynamics activity.

[33] *Chen S, Wang R, Cheng M et al.* **Serum Cholesterol-Lowering Activity of β-Sitosterol Laurate Is Attributed to the Reduction of Both Cholesterol Absorption and Bile Acids Reabsorption in Hamsters**. Journal of agricultural and food chemistry 2020; 68:10003-10014.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32811147

ABSTRACT

The research was performed to delineate how β-sitosterol laurate (β-SLE) consumption influenced serum and hepatic lipids. The results showed that 220 mg/5 mL oil/kg body weight of β-SLE robustly reduced serum total triglyceride and cholesterol levels and the epididymal adipocyte size, and efficiently protected hepatic polyunsaturated fatty acids against lipid peroxidation through superoxide dismutase and glutathione transferase activity enhancement and malondialdehyde level reduction. Based on the changes of fecal cholesterol contents, fecal and hepatic bile acid (BAs) levels, and related protein expression, it was concluded that the mechanisms for lowering serum cholesterol by β-SLE involved (i) the enhanced excretion of fecal cholesterol via down-regulation of intestinal Niemann-Pick C1-like 1 protein; (ii) the increased conversion from cholesterol to primary BAs via up-regulation of cholesterol-7α-hydroxylase and sterol 27-hydroxylase, which was induced by the reduced BAs reabsorption through up-regulating ileal apical sodium-dependent bile acid transporter and ileal bile acid-binding protein.

[34] *Bergland AK, Proitsi P, Kirsebom BE et al.* **Exploration of Plasma Lipids in Mild Cognitive Impairment due to Alzheimer's Disease**. Journal of Alzheimer's disease : JAD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32804144

ABSTRACT

BACKGROUND: Lipids have important structural roles in cell membranes and changes to these membrane lipids may influence β- and γ-secretase activities and thus contribute to Alzheimer's disease (AD) pathology. OBJECTIVE: To explore baseline plasma lipid profiling in participants with mild cognitive impairment (MCI) with and without AD pathology. METHODS: We analyzed 261 plasma lipid profiles using reversed phase chromatography mass spectrometry in cerebrospinal fluid amyloid positive (Aβ+) or negative (Aβ-) participants with MCI as compared to controls. Additionally, we analyzed the potential associations of plasma lipid profiles with performance on neuropsychological tests at baseline and after two years. RESULTS: Sphingomyelin (SM) concentrations, particularly, SM(d43:2), were lower in MCI Aβ+ individuals compared to controls. Further, SM(d43:2) was also nominally reduced in MCI Aβ+ individuals compared to MCI Aβ-. No plasma lipids were associated with performance on neuropsychological tests at baseline or between the two time points after correction for multiple testing. CONCLUSION: Reduced plasma concentrations of SM were associated with AD.

[35] *Yu ZW, Li X, Wang Y et al.* **Association Between Lipid Accumulation Product and Mild Cognitive Impairment in Patients with Type 2 Diabetes**. Journal of Alzheimer's disease : JAD 2020; 77:367-374.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32804130

ABSTRACT
BACKGROUND: Diabetes may increase the risk of conversion of mild cognitive impairment (MCI) to dementia. Lipid accumulation product (LAP), an index of visceral obesity, has been shown to be a powerful predictor of insulin resistance and type 2 diabetes (T2D). However, little attention has been paid to the relationship between LAP and MCI in T2D. OBJECTIVE: We aimed to investigate the association between the LAP index and MCI in patients with T2D. METHODS: In total, 220 hospitalized patients with T2D, including 113 MCI patients and 107 patients with normal cognition, were enrolled in this cross-sectional study. We collected demographic, anthropometric, and biochemical data on each subject. The LAP index was calculated according to the following formulas: [waist circumference (WC) (cm) - 65]×triglyceride (TG) (mmol/L) for males and [WC (cm) - 58] ×TG (mmol/L) for females. RESULTS: Compared with patients with normal cognition, MCI patients were older and had a higher LAP index, WC, body mass index, and glycosylated hemoglobin A1c level, as well as a lower Montreal Cognitive Assessment score and education level ($p<0.05$). After adjusting for confounding factors, LAP index was associated with MCI (OR=1.047, 95% CI=1.031-1.063, $p<0.01$). The area under the ROC curve (AUC) for the LAP index was higher than that for WC and BMI. CONCLUSION: A high LAP index is associated with an increased risk of MCI in T2D patients. The LAP index appears to be a good indicator of risk of MCI in patients with T2D.

[36] *Ajala ON, Demler OV, Liu Y et al.* **Anti-Inflammatory HDL Function, Incident Cardiovascular Events, and Mortality: A Secondary Analysis of the JUPITER Randomized Clinical Trial**. Journal of the American Heart Association 2020; 9:e016507.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32799709

ABSTRACT
Background High-density lipoprotein (HDL) cholesterol has inverse association with cardiovascular disease. HDL possesses anti-inflammatory properties in vitro, but it is unknown whether this may be protective in individuals with inflammation. Methods and Results The functional capacity of HDL to inhibit oxidation of oxidized low-density lipoprotein (ie, the HDL inflammatory index; HII) was measured at baseline and 12 months after random allocation to rosuvastatin or placebo in a nested case-control study of the JUPITER (Justification for the Use of Statins in Prevention: An Intervention Evaluating Rosuvastatin) trial. There were 517 incident cases of cardiovascular disease and all-cause mortality compared to 517 age- and sex-matched controls. Multivariable conditional logistic regression was used to examine associations of HII with events. Median baseline HII was 0.54 (interquartile range, 0.50-0.59). Twelve months of rosuvastatin decreased HII by a mean of 5.3% (95% CI, -8.9% to -1.7%; P=0.005) versus 1.3% (95% CI, -6.5% to 4.0%; P=0.63) with placebo (P=0.22 for between-group difference). HII had a nonlinear relationship with incident events. Compared with the reference group (HII 0.5-1.0) with the lowest event rates, participants with baseline HII ≤0.5 had significantly increased risk of cardiovascular disease/mortality (adjusted hazard ratio, 1.53; 95% CI, 1.06-2.21; P=0.02). Furthermore, there was significant (P=0.002) interaction for HDL particle number with HII, such that having more HDL particles was associated with decreased risk only when HDL was anti-inflammatory. Conclusions In JUPITER participants recruited on the basis of chronic inflammation, HII was associated with incident cardiovascular disease/mortality, with an optimal anti-inflammatory HII range between 0.5 and 1.0. This nonlinear relationship of anti-inflammatory HDL function with risk may account in part for the

HDL paradox. Registration URL: https://www.clinicaltrials.gov; Unique identifier: NCT00239681.

[37] *Tada H, Takamura M, Kawashiri MA*. **Targeted Panel Sequencing will Boost Detection of Genetic Backgrounds of Familial Hypercholesterolemia in the World's Most Populous Country**. Journal of atherosclerosis and thrombosis 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32801290
ABSTRACT

[38] *Ferchaud-Roucher V, Zair Y, Aguesse A et al.* **Omega 3 Improves Both apoB100-containing Lipoprotein Turnover and their Sphingolipid Profile in Hypertriglyceridemia**. The Journal of clinical endocrinology and metabolism 2020; 105.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32805740
ABSTRACT
CONTEXT: Evidence for an association between sphingolipids and metabolic disorders is increasingly reported. Omega-3 long-chain polyunsaturated fatty acids (n-3 LC-PUFAs) improve apolipoprotein B100 (apoB100)-containing lipoprotein metabolism, but their effects on the sphingolipid content in lipoproteins remain unknown. OBJECTIVES: In subjects with hypertriglyceridemia, we analyzed the effect of n-3 LC-PUFAs on the turnover apoB100-containing lipoproteins and on their sphingolipid content and looked for the possible association between these lipid levels and apoB100-containing lipoprotein turnover parameters. METHODS: Six subjects underwent a kinetic study before and after n-3 supplementation for 2 months with 1 g of fish oil 3 times day containing 360 mg of eicosapentaenoic acid (EPA) and 240 mg of docosahexaenoic acid (DHA) in the form of triglycerides. We examined apoB100-containing lipoprotein turnover by primed perfusion labeled [5,5,5-2H3]-leucine and determined kinetic parameters using a multicompartmental model. We quantified sphingolipid species content in lipoproteins using mass spectrometry. RESULTS: Supplementation decreased very low-density lipoprotein (VLDL), triglyceride, and apoB100 concentrations. The VLDL neutral and polar lipids showed increased n-3 LC-PUFA and decreased n-6 LC-PUFA content. The conversion rate of VLDL1 to VLDL2 and of VLDL2 to LDL was increased. We measured a decrease in total apoB100 production and VLDL1 production. Supplementation reduced the total ceramide concentration in VLDL while the sphingomyelin content in LDL was increased. We found positive correlations between plasma palmitic acid and VLDL ceramide and between VLDL triglyceride and VLDL ceramide, and inverse correlations between VLDL n-3 LC-PUFA and VLDL production. CONCLUSION: Based on these results, we hypothesize that the improvement in apoB100 metabolism during n-3 LC-PUFA supplementation is contributed to by changes in sphingolipids.

[39] *Cicero AFG, Fogacci F, Bove M, Borghi C*. **Successful treatment of a patient with mitochondrial myopathy with alirocumab**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32800583
ABSTRACT
A 48-year-old man presented to our lipid clinic with statin intolerance and elevated serum creatine kinase levels, being affected by mitochondrial myopathy because of heteroplasmic mitochondrial DNA missense mutation in MTCO1 gene (m.7671T>A). He had just been treated with a coronary artery bypass 4 years before because of acute coronary syndrome, and he

had consistently high levels of both low-density lipoprotein cholesterol and triglycerides. Dyslipidemia was successfully treated using 75 mg of alirocumab subcutaneously every 2 weeks, 10 mg of ezetimibe daily, 2 g of marine omega-3 fatty acids daily, and 145 mg of micronized fenofibrate every 2 days. Although muscle weakness persisted, myalgia did not reoccur and serum creatine kinase levels remained almost stable over the time.

[40] *Sreedharan AV, Pek SLT, Tan TH et al.* **Successful pharmacological management of a child with compound heterozygous familial hypercholesterolemia and review of the recent literature**. Journal of clinical lipidology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32800790
ABSTRACT
Severe familial hypercholesterolemia (SFH) is characterized by markedly elevated low-density lipoprotein cholesterol (LDL-C) and severe early-onset cardiovascular disease if left untreated. We report on the decade-long therapeutic journey of a 15-year-old boy with SFH due to a severe compound heterozygous genotype. He presented at the age of 5 years with widespread xanthomas and LDL-C of 17.4 mmol/L. He was diagnosed with SFH, initially treated with colestyramine that was subsequently combined with simvastatin. At the age of 12 years, he was diagnosed to have supravalvular aortic stenosis and ezetimibe/atorvastatin was introduced in place of colestyramine/simvastatin. At the age of 14 years, he received triple therapy with evolocumab, initially at the recommended dose of 420 mg monthly and then reduced to 140 mg biweekly. Currently at the age of 15 years, he is on atorvastatin 40 mg ON, ezetimibe 10 mg OM, and evolocumab 140 mg biweekly, achieving LDL-C levels of 2.4 mmol/L. Genetic testing identified compound heterozygous mutations in the LDL receptor genes [c.(940 + 1_941-1) (1845 + 1_1846-1)dup] and exon 12, nucleotide c.1747 C > T, amino acid p.(His583Tyr). Medical management without lipoprotein apheresis can achieve target LDL-C in children with SFH. Our patient, who developed supravalvular aortic stenosis at the age of 12 years, needed early aggressive treatment when SFH guidelines and newer drugs for young children were unavailable. Our patient demonstrated that 140 mg biweekly of evolocumab has the same cholesterol-lowering effect as the recommended 420 mg monthly dose.

[41] *Graf C, Welzel T, Bogdanou D et al.* **Hepatitis C Clearance by Direct-Acting Antivirals Impacts Glucose and Lipid Homeostasis**. Journal of clinical medicine 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825571
ABSTRACT
BACKGROUND: Chronic hepatitis C virus (HCV) infections are causally linked with metabolic comorbidities such as insulin resistance, hepatic steatosis, and dyslipidemia. However, the clinical impact of HCV eradication achieved by direct-acting antivirals (DAAs) on glucose and lipid homeostasis is still controversial. The study aimed to prospectively investigate whether antiviral therapy of HCV with DAAs alters glucose and lipid parameters. METHODS: 50 patients with chronic HCV who were treated with DAAs were screened, and 49 were enrolled in the study. Biochemical and virological data, as well as noninvasive liver fibrosis parameters, were prospectively collected at baseline, at the end of treatment (EOT) and 12 and 24 weeks post-treatment. RESULTS: 45 of 46 patients achieved sustained virologic response (SVR). The prevalence of insulin resistance (HOMA-IR) after HCV clearance was significantly lower, compared to baseline (5.3 ± 6.1 to 2.5 ± 1.9, $p < 0.001$), which is primarily attributable to a

significant decrease of fasting insulin levels (18.9 ± 17.3 to 11.7 ± 8.7; p = 0.002). In contrast to that, HCV eradication resulted in a significant increase in cholesterol levels (total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein (HDL-C) levels) and Controlled Attenuated Score (CAP), although BMI did not significantly change over time (p = 0.95). Moreover, HOMA-IR correlated significantly with noninvasive liver fibrosis measurements at baseline und during follow-up (TE: r = 0.45; p = 0.003, pSWE: r = 0.35; p = 0.02, APRI: r = 0.44; p = 0.003, FIB-4: r = 0.41; p < 0.001). CONCLUSION: Viral eradication following DAA therapy may have beneficial effects on glucose homeostasis, whereas lipid profile seems to be worsened.

[42] *Choi JY, Na JO*. **Pharmacological Strategies beyond Statins: Ezetimibe and PCSK9 Inhibitors**. J Lipid Atheroscler 2019; 8:183-191.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821708
ABSTRACT
Dyslipidemia, highly elevated, low-density lipoprotein (LDL) cholesterol, is a major cardiovascular risk factor. Statins have been proven to effectively reduce the risk of atherosclerotic cardiovascular disease (ASCVD) and are recommended as a first-line therapy for the primary and secondary prevention of ASCVD. However, statins may not be sufficient in decreasing LDL cholesterol levels and pose a significant on-treatment residual risk of major cardiovascular events (i.e., residual cholesterol risk) according to meta-analyses of statin trials. Current guidelines for cholesterol management to achieve additional LDL cholesterol reduction and reduce ASCVD risk recommend two hyperlipidemic agents besides statins. Use of ezetimibe, a cholesterol absorption inhibitor, leads to additional LCL cholesterol reduction and decreased ASCVD risk, when added to statin therapy, without raising significant safety concerns. Furthermore, in combination with a mild-to-moderate statin intensity, ezetimibe is used in situations of statin-associated adverse effects such as myalgia and the combination therapy is relatively safer. Monoclonal antibody of proprotein convertase subtilisin/kexin type 9 (PCSK9), alirocumab, and evolocumab, have been approved to lower LDL cholesterol level. While there are drawbacks to the use of PCSK9 inhibitors, including high cost and adverse events such as injection site reaction, they significantly decreased serum LDL cholesterol levels and thereby ASCVD risks when added to maximally tolerated statin therapy.

[43] *Choi S*. **The Potential Role of Biomarkers Associated with ASCVD Risk: Risk-Enhancing Biomarkers**. J Lipid Atheroscler 2019; 8:173-182.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821707
ABSTRACT
Serum cholesterol is major risk factor and contributor to atherosclerotic cardiovascular disease (ASCVD). Therapeutic cholesterol-lowering drugs, especially statin, revealed that reduction in low-density lipoprotein cholesterol (LDL-C) produces marked reduction of ASCVD events. In the preventive scope, lower LDL-C is generally accepted as better in proven ASCVD patients and high-risk patient groups. However, in patients with low to intermediate risk without ASCVD, risk assessment is clinically guided by traditional major risk factors. In this group, the complement approach to detailed risk assessment about traditional major risk factors is needed. These non-traditional risk factors include ankle-brachial index (ABI), high-sensitivity C-reactive protein (hsCRP) level, lipoprotein(a) (Lp[a]), apolipoprotein B (apoB), or coronary artery calcium (CAC) score. CAC measurements have an additive role in the decision to use

statin therapy in non-diabetic patients 40-75 years old with intermediate risk in primary prevention. This review comprises ASCVD lipid/biomarkers other than CAC. The 2013 and 2018 American College of Cardiology/American Heart Association (ACC/AHA) guidelines suggest these factors as risk-enhancing factors to help health care providers better determine individualized risk and treatment options especially regarding abnormal biomarkers. The recent 2018 Korean guidelines for management of dyslipidemia did not include these biomarkers in clinical decision making. The current review describes the current roles of hsCRP, ABI, LP(a), and apoB in personal modulation and management of health based on the 2018 ACC/AHA guideline on the management of blood cholesterol.

[44] *Han JM, Kim HI, Lee YJ et al.* **Differing Associations between Fatty Liver and Dyslipidemia According to the Degree of Hepatic Steatosis in Korea**. J Lipid Atheroscler 2019; 8:258-266.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821716
ABSTRACT
OBJECTIVE: Fatty liver is associated with insulin resistance-related diseases, such as dyslipidemia, obesity, and type 2 diabetes. The aim of this study was to evaluate the association of dyslipidemia with fatty liver and assess the differences in these associations according to the degree of hepatic steatosis. METHODS: A total of 2,462 subjects (1,679 men and 783 women) who underwent a comprehensive health check-up (including abdominal computed tomography) from January 2010 to December 2013 were enrolled at Samsung Changwon Hospital Healthcare Center. The liver attenuation index (LAI), defined as the difference between mean hepatic and splenic attenuation, was used to assess the degree of hepatic steatosis. An LAI below 5 Hounsfield units was defined as fatty liver. RESULTS: We found that 32.2% of the study subjects had fatty liver. Serum low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG), and fasting blood glucose concentrations and glycated hemoglobin (HbA1c percentage) were significant greater in the fatty liver group compared with the non-fatty liver group, while serum high-density lipoprotein cholesterol (HDL-C) was significantly lower in the fatty liver group. Subjects with fatty liver had 1.7-fold greater risk of dyslipidemia than those without fatty liver after adjusting for age, sex, body mass index (BMI), and HbA1c. When individuals with fatty liver were analyzed by tertiles of LAI values, LDL-C, TG, fasting glucose, BMI, and HbA1c concentrations increased while HDL-C decreased with decreasing LAI tertiles. Compared with LAI tertile 3, the risk for dyslipidemia significantly increased with adjusted odds ratios of 1.42, and 1.81 in tertiles 2 and 1, respectively. CONCLUSION: Fatty liver was significantly associated with dyslipidemia and this association varied according to the degree of hepatic steatosis.

[45] *Kim H, Lee CJ, Choi D et al.* **Lipid-Lowering Efficacy and Safety of a New Generic Rosuvastatin in Koreans: an 8-Week Randomized Comparative Study with a Proprietary Rosuvastatin**. J Lipid Atheroscler 2020; 9:283-290.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821737
ABSTRACT
OBJECTIVE: The aim of this study was to investigate whether a new generic rosuvastatin is non-inferior to a proprietary one in terms of lipid-lowering efficacy. We also evaluated its non-lipid effects including adverse events. METHODS: One-hundred and fifty-eight patients with cardiovascular risks requiring pharmacological lipid-lowering therapy were screened. After a 4-

week run-in period, 126 individuals who met the lipid criteria for drug therapy were randomly assigned to receive the new generic or proprietary rosuvastatin 10 mg daily for 8 weeks. The primary outcome variables were low-density lipoprotein-cholesterol (LDL-C) reduction and LDL-C target achievement. Hematological and biochemical parameters and adverse events were assessed. RESULTS: After 8 weeks of drug treatment, the mean percentage change in LDL-C was not different between the groups (-45.5%±19.9% and -45.1%±19.0% for generic and proprietary rosuvastatin, respectively; p=0.38). The LDL-C target achievement rate was similar between the groups (75.0% and 77.1% for generic and proprietary rosuvastatin, respectively; p=0.79). The percentage change in the other lipid profiles was not significantly different. Although generic- and proprietary rosuvastatins modestly affected creatine kinase and blood pressure, respectively, the changes were all within normal ranges. Incidence of adverse events did not differ between the receivers of the 2 formulations. CONCLUSION: The new generic rosuvastatin was non-inferior to the proprietary rosuvastatin in terms of lipid-lowering efficacy. The rosuvastatin formulations did not exhibit clinically significant non-lipid effects with good safety profiles. Our study provides comprehensive data regarding 2 rosuvastatin formulations in East Asian subjects. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT03949374.

[46] *Kim J, Hoang T, Bu SY et al.* **Associations of Dietary Intake with Cardiovascular Disease, Blood Pressure, and Lipid Profile in the Korean Population: a Systematic Review and Meta-Analysis**. J Lipid Atheroscler 2020; 9:205-229.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821732
ABSTRACT
OBJECTIVE: Previous studies have separately reported the contributions of dietary factors to the risk of cardiovascular disease (CVD) and its markers, including blood pressure (BP) and lipid profile. This study systematically reviewed the current evidence on this issue in the Korean population. METHODS: Sixty-two studies from PubMed and Embase were included in this meta-analysis. We performed a random-effects model to analyze pooled odds ratios (ORs) and hazard ratios (HRs) and their 95% confidence intervals (CIs) for the consumption of 14 food items, three macro- and eight micro-nutrients, two dietary patterns, and three dietary indices. RESULTS: An analysis of pooled effect sizes from at least four individual study populations showed significant associations between coffee consumption and CVD (OR/HR, 0.71; 95% CI, 0.52-0.97) and elevated/high triglycerides (TG) (OR, 0.84; 95% CI, 0.78-0.90), sugar-sweetened beverage intake and elevated BP (OR/HR, 1.20; 95% CI, 1.09-1.33), and milk and dairy intake and elevated/high TG and low high-density lipoprotein cholesterol (HDL-C) (OR/HR, 0.82; 95% CI, 0.76-0.89 for both). Carbohydrate consumption and the low-carbohydrate-diet score were consistently related to an approximately 25% risk reduction for elevated TG and low HDL-C. A lower risk of elevated total cholesterol, but not low-density lipoprotein, was additionally observed for those with a higher low-carbohydrate-diet score. A healthy dietary pattern was only associated with a reduced risk of elevated TG in the Korea National Cancer Screenee Cohort (OR, 0.81; 95% CI, 0.67-0.98). CONCLUSION: This study showed that milk and dairy and coffee had protective effects for CVD and its risk factors, such as BP and lipid profile, while sugar-sweetened beverages exerted harmful effects.

[47] *Kim K, Lee SH*. **Effects of Statins for Primary Prevention in the Elderly: Recent Evidence**. J Lipid Atheroscler 2020; 9:1-7.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821718

ABSTRACT

The number of the elderly individuals is steeply increasing, and their absolute cardiovascular risk is higher than that of younger age groups. However, very few statin trials have included elderly patients alone. Recently, we published the SCOPE-75 study, which analyzed the effect of statins for primary prevention in elderly Koreans (>75 years). In this study, statin users showed significantly fewer cardiovascular events and a lower all-cause mortality rate, supporting more active use of statins in this population. In the current review, we further compare and discuss similar studies reported in the past decades and in recent years.

[48] *Lee I, Lee HH, Cho Y et al.* **Association Between Serum Bilirubin and the Progression of Carotid Atherosclerosis in Type 2 Diabetes**. J Lipid Atheroscler 2020; 9:195-204.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821731

ABSTRACT

OBJECTIVE: This study investigated whether serum bilirubin levels can predict the progression of carotid atherosclerosis in individuals with type 2 diabetes mellitus (T2DM). METHODS: This observational study included 1,381 subjects with T2DM in whom serial measurements of carotid intima-media thickness (CIMT) were made at 1- to 2-year intervals for 6-8 years. The progression of carotid atherosclerosis was defined as newly detected plaque lesions on repeat ultrasonography. After dividing total serum bilirubin levels into tertiles, the association between total serum bilirubin at baseline and plaque progression status was analyzed. RESULTS: Among 1,381 T2DM patients, 599 (43.4%) were categorized as having plaque progression in their carotid arteries. Those with plaque progression were significantly older; showed a higher prevalence of hypertension, abdominal obesity, and chronic kidney disease; and had a longer duration of T2DM, higher levels of total cholesterol (TC), triglycerides, and insulin resistance, and lower total bilirubin concentrations than those with no plaque progression. When total serum bilirubin levels were divided into tertiles, the highest tertile group was younger than the lowest tertile group, with higher levels of TC and high-density lipoprotein cholesterol. Multiple logistic regression analysis demonstrated that higher serum bilirubin levels were associated with a significantly lower risk of CIMT progression (odds ratio, 0.584; 95% confidence interval, 0.392-0.870; p=0.008). Age (p<0.001), body mass index (p=0.023), and TC (p=0.019) were also associated with the progression of carotid atherosclerosis in T2DM patients. CONCLUSION: Total serum bilirubin is independently associated with progression of atherosclerosis in the carotid arteries in T2DM patients.

[49] *Lee SH, Song WH, Jeong MH et al.* **Dyslipidemia and Rate of Under-Target Low-Density Lipoprotein-Cholesterol in Patients with Coronary Artery Disease in Korea**. J Lipid Atheroscler 2019; 8:242-251.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821714

ABSTRACT

OBJECTIVE: The aim of this study was to evaluate under target rates of low-density lipoprotein-cholesterol (LDL-C) in Korean patients with stable coronary artery disease (CAD) or an acute coronary syndrome (ACS) in real world practice. METHODS: Dyslipidemia International Study II was an international observational study of patients with stable CAD or an ACS. Lipid profiles and use of lipid-lowering therapy (LLT) were documented at enrollment, and for the ACS cohort, 4 months follow-up was recommended. Rates of under target LDL-C

as per European guidelines, were evaluated, and multivariate regression was performed to identify predictive factors of patients presenting under the target. RESULTS: A total of 808 patients were enrolled in Korea, 500 with stable CAD and 308 with ACS. Of these, 90.6% and 52.6% were being treated with LLT, respectively. In the stable CAD group, 40.0% were under target LDL-C, while in ACS group, the rate was 23.7%. A higher statin dose was independently associated with under target LDL-C in both groups (OR, 1.03; p=0.046 [stable CAD] and OR, 1.05; p=0.01 [ACS]). The mean statin dosage (atorvastatin equivalent) was 17 mg/day. In the 79 ACS patients who underwent the follow-up examination, the LDL-C under target rate rose to 59.5%. CONCLUSION: Only a minority of patients with stable CAD or ACS were under their target LDL-C level at enrollment. The statin dose was not sufficient in the majority of patients. These results indicate a considerable LLT gap in Korean patients with established CAD.

[50] *Moon J, Yoo S, Koh G et al.* **Efficacy and Safety of High-Dose Atorvastatin in Moderate-to-High Cardiovascular Risk Postmenopausal Korean Women with Dyslipidemia**. J Lipid Atheroscler 2020; 9:162-171.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821729
ABSTRACT
OBJECTIVE: Postmenopausal women show a more atherogenic lipid profile and elevated cardiovascular risk compared to premenopausal women. The aim of this study was to investigate the efficacy and safety of high-dose atorvastatin on the improvement of the blood lipid profile of postmenopausal women in Korea. METHODS: This study is a prospective, open-label, single-arm clinical trial that was conducted in 3 teaching hospitals. Postmenopausal women with a moderate-to-high cardiovascular risk, according to guidelines from the Korean Society of Lipid & Atherosclerosis, were enrolled. Participants were administered 20 mg of atorvastatin daily for the first 8 weeks, and if the targeted low-density lipoprotein cholesterol (LDL-C) level was not achieved, the dose was increased to 40 mg for the second 8 weeks. The primary endpoint was percentage change of LDL-C from baseline after 16 weeks of drug administration. RESULTS: Forty-four women were enrolled, 28 of whom (75.6%) had diabetes mellitus. By the end of treatment period (16 weeks) all patients had achieved LDL-C target levels, with 33 (94.2%) of the participants achieving it after only 8 weeks of administration. After 16 weeks, LDL-C decreased by 45.8±16.7% (p<0.001) from the baseline, and total cholesterol (33.2±10.9%; p<0.001), triglyceride (24.2±37.5%; p=0.001), and apolipoprotein B (34.9±15.6%; p<0.001) also significantly decreased. Blood glucose and liver enzyme levels slightly increased, but none of the participants developed serious adverse events that would cause them to prematurely withdraw from the clinical trial. CONCLUSION: 20 and 40 mg atorvastatin was effective and safe for treating dyslipidemia in postmenopausal Korean women with moderate-to-high cardiovascular risk.

[51] *Sim DS, Jeong MH, Kim HS et al.* **Intensity of Statin Treatment in Korean Patients with Acute Myocardial Infarction and Very Low LDL Cholesterol**. J Lipid Atheroscler 2019; 8:208-220.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821711
ABSTRACT
OBJECTIVE: Data on the intensity of statin therapy for patients with acute myocardial infarction (MI) and very low baseline low-density lipoprotein (LDL) cholesterol level are lacking. We sought to assess the impact of statin intensity in patients with acute MI and LDL

cholesterol <70 mg/dL. METHODS: A total of 1,086 patients with acute MI and baseline LDL cholesterol <70 mg/dL from the Korea Acute Myocardial Infarction Registry-National Institute of Health database were divided into less intensive statin (expected LDL reduction <40%, n=302) and more intensive statin (expected LDL reduction ≥40%, n=784) groups. The primary endpoint was major adverse cardiac and cerebrovascular events (MACCEs), a composite of cardiac death, MI, revascularization occurring at least 30 days after admission, and stroke, at 12 months. RESULTS: After 1:2 propensity matching, differences were not observed between less intensive (n=302) and more intensive statin (n=604) groups in incidence of cardiac death (0.3% vs. 0.3%) and hemorrhagic stroke (0.3% vs. 0.5%, p=0.727) at 12 months. Compared with the less intensive statin group, the more intensive statin group showed lower target-vessel revascularization (4.6% vs. 1.8%, p=0.027) and MACCE (11.6% vs. 7.0%, p=0.021). Major bleeding was not different between less intensive and more intensive statin groups (1.0% vs. 2.6%, p=0.118). CONCLUSION: More intensive statin therapy was associated with significantly lower major adverse cardiovascular events in patients with acute MI and very low LDL cholesterol compared with less intensive statin therapy.

[52] *Song S, Lee CJ, Oh J et al.* **Effect of Niacin on Carotid Atherosclerosis in Patients at Low-Density Lipoprotein-Cholesterol Goal but High Lipoprotein (a) Level: a 2-Year Follow-Up Study**. J Lipid Atheroscler 2019; 8:58-66.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821700
ABSTRACT
OBJECTIVE: To examine the effect of niacin on the progression of carotid intima-media thickness (IMT) in patients with high level of lipoprotein (Lp) (a). METHODS: Patients at low-density lipoprotein-cholesterol goal but with Lp (a) >25 mg/dL and mean carotid IMT >0.75 mm were included. Eligible patients were randomized at a 1:2 ratio into one of two groups for 24 months: control or 1,500 mg extended release niacin. The primary study outcomes were the percentage changes in mean and maximal carotid IMT. The percentage change in lipid profiles including Lp (a) was analyzed as a secondary study outcome. RESULTS: Among 96 randomized patients, 31 completed the study (mean age: 65 years; male: 44%). At follow-up, the percentage change in mean carotid IMT was not significantly different between the two groups (-1.4%±15.5% and -1.1%±7.3% in the control and niacin groups, respectively, p=0.95). The percentage change in maximal carotid IMT was also similar in the two groups (0.7%±16.5% and -4.4%±11.6%, respectively, p=0.35). Elevation of high-density lipoprotein-cholesterol tended to be higher in the niacin group (p=0.07), and there was a significant difference in the percentage change in hemoglobin A1c between the two groups (-1.9%±2.2% and 3.3%±6.7%, respectively, p=0.02). Reduction of Lp (a) was greater in the niacin-treated group compared to placebo, but the difference was not statistically significant. CONCLUSION: Treatment with niacin for two years did not inhibit the progression of carotid intima-media thickening in patients with high Lp (a) level. However, this study may have been underpowered to evaluate the primary study outcome.

[53] *Yvan-Charvet L, Ivanov S*. **Metabolic Reprogramming of Macrophages in Atherosclerosis: Is It All about Cholesterol?** J Lipid Atheroscler 2020; 9:231-242.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32821733
ABSTRACT

Hypercholesterolemia contributes to the chronic inflammatory response during the progression of atherosclerosis, in part by favoring cholesterol loading in macrophages and other immune cells. However, macrophages encounter a substantial amount of other lipids and nutrients after ingesting atherogenic lipoprotein particles or clearing apoptotic cells, increasing their metabolic load and impacting their behavior during atherosclerosis plaque progression. This review examines whether and how fatty acids and glucose shape the cellular metabolic reprogramming of macrophages in atherosclerosis to modulate the onset phase of inflammation and the later resolution stage, in which the balance is tipped toward tissue repair.

[54] *Huo S, Sun L, Zong G et al.* **Genetic susceptibility, dietary cholesterol intake and plasma cholesterol levels in a Chinese population**. Journal of lipid research 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32817344
ABSTRACT
Accompanied with nutrition transition, non-HDL-cholesterol (HDL-C) levels of Asian countries increased rapidly, which has caused the global epicenter of non-optimal cholesterol to shift from Western countries to Asian countries. Thus, it is critical to underline major genetic and dietary determinants. In the current study of 2,330 Chinese individuals, genetic risk scores (GRSs) were calculated for total cholesterol (TC; GRS(TC), 57 SNPs), LDL-cholesterol (LDL-C; GRS(LDL-C), 45 SNPs) and HDL-C (GRS(HDL-C), 65 SNPs) based on SNPs from the Global Lipid Genetics Consortium study. Cholesterol intake was estimated by a 74-item food frequency questionnaire. Associations of dietary cholesterol intake with plasma TC and LDL-C strengthened across quartiles of the GRS(TC) (effect sizes = -0.29, 0.34, 2.45 and 6.47; P (interaction) = 0.002) and GRS(LDL-C) (effect sizes = -1.35, 0.17, 5.45 and 6.07; P (interaction) = 0.001), respectively. Similar interactions on non-HDL-C were observed between dietary cholesterol and GRS(TC) (P (interaction) = 0.001) and GRS(LDL-C) (P (interaction) = 0.004). The adverse effects of GRS(TC) on TC (effect sizes across dietary cholesterol quartiles: 0.51, 0.82, 1.21 and 1.31; P (interaction) = 0.023) and GRS(LDL-C) on LDL-C (effect sizes across dietary cholesterol quartiles: 0.66, 0.52, 1.12 and 1.56; P (interaction) = 0.020) were more profound in those having higher cholesterol intake compared to those with lower intake. Our findings suggest significant interactions between genetic susceptibility and dietary cholesterol intake on plasma cholesterol profiles in a Chinese population.

[55] *Cornelis MC, van Dam RM*. **Habitual Coffee and Tea Consumption and Cardiometabolic Biomarkers in the UK Biobank: The Role of Beverage Types and Genetic Variation**. The Journal of nutrition 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32805014
ABSTRACT
BACKGROUND: Mechanisms linking habitual consumption of coffee and tea to the development of type 2 diabetes and cardiovascular diseases remain unclear. OBJECTIVES: We leveraged dietary, genetic, and biomarker data collected from the UK Biobank to investigate the role of different varieties of coffee and tea in cardiometabolic health. METHODS: We included data from ≤447,794 participants aged 37-73 y in 2006-2010 who provided a blood sample and completed questionnaires regarding sociodemographic factors, medical history, diet, and lifestyle. Multivariable linear regression was used to examine the association between coffee or tea consumption and blood concentrations of glycated hemoglobin, fasting glucose, total cholesterol, HDL cholesterol, LDL cholesterol, fasting

triglycerides (TGs), apoA-1, apoB, lipoprotein-a, and C-reactive protein (CRP). Lifestyle and genetic factors affecting caffeine metabolism, responses, or intake were tested for interactions with beverage intake in relation to biomarker concentrations. RESULTS: Compared with coffee nonconsumers, each additional cup of coffee was significantly associated with higher total cholesterol, HDL-cholesterol, and LDL-cholesterol concentrations and lower TG and CRP concentrations in both men and women (P-trend < 0.002). Higher consumption of espresso coffee (≥2 compared with 0 cups/d) was associated with higher LDL cholesterol in men (β: 0.110 mmol/L; 95% CI: 0.058, 0.163 mmol/L) and women (β: 0.161 mmol/L; 95% CI: 0.088, 0.234 mmol/L), whereas no substantial association was observed for instant coffee. Compared with tea nonconsumers, higher tea consumption was associated with lower total and LDL cholesterol and apoB and higher HDL cholesterol (P-trend < 0.002); these associations were similar for black and green tea. Associations were not modified by genetics. CONCLUSIONS: In the UK Biobank, consumption of certain coffee brews such as espresso had unfavorable associations with blood lipids, whereas consumption of tea had favorable associations. Findings were not modified by genetic variants affecting caffeine metabolism, suggesting a role of noncaffeine constituents of these beverages in cardiometabolic health.

[56] *Liddle DM, Hutchinson AL, Monk JM et al.* **Dietary long-chain n-3 PUFA mitigate CD4(+) T cell/adipocyte inflammatory interactions in co-culture models of obese adipose tissue**. The Journal of nutritional biochemistry 2020:108488.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32827664
ABSTRACT
Obese adipose tissue (AT) inflammation is partly driven by accumulation of CD4(+) T helper (Th)1 cells and reduced Th2 and T regulatory (Treg) subsets, which promotes macrophage chemotaxis and ensuing AT metabolic dysfunction. This study investigated CD4(+) T cell/adipocyte cytokine-mediated paracrine interactions (cross-talk) as a target for dietary intervention to mitigate obese AT inflammation. Using an in vitro co-culture model designed to recapitulate CD4(+) T cell accumulation in obese AT (5% of stromal vascular cellular fraction), 3 T3-L1 adipocytes were co-cultured with purified splenic CD4(+) T cells from C57Bl/6 mice consuming one of two isocaloric diets containing either 10% w/w safflower oil (control, CON) or 7% w/w safflower oil+3% w/w fish oil (FO) for 4 wk. (n=8-11/diet). The FO diet provided 1.9% kcal from the long-chain (LC) n-3 polyunsaturated fatty acids (PUFA) EPA and DHA, a dose that can be achieved by supplementation. Co-cultures were stimulated for 48 h with lipopolysaccharide (LPS) to mimic in vivo obese endotoxin levels, or with conditioned media collected from LPS-stimulated visceral AT isolated from CON-fed mice. In both stimulation conditions, FO reduced mRNA expression and/or secreted protein levels of Th1 markers (T-bet, IFN-γ) and increased Th2 markers (GATA3, IL-4), concomitant with reduced inflammatory cytokines (IL-1β, IL-6, IL-12p70, TNF-α), macrophage chemokines (MCP-1, MCP-3, MIP-1α, MIP-2), and levels of activated central regulators of inflammatory signaling (NF-κB, STAT-1, STAT-3) (P<.05). Therefore, CD4(+) T cell/adipocyte cross-talk represents as a potential target for LC n-3 PUFA to mitigate obese AT inflammation.

[57] *Irfan F, Karim SI*. **Co-prescription of ciprofloxacin and statins; a dangerous combination: Case Report**. JPMA. The Journal of the Pakistan Medical Association 2020; 70:1272-1274.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32799291

ABSTRACT
Drug interaction is a common clinical problem which is often underestimated by physicians. Statins are one of the commonly prescribed medicines worldwide that are generally well tolerated. Muscle-related symptoms have a varied clinical presentation which usually increases if a new medicine is co-prescribed. We report the case of a 65- year-old woman who presented with a 10-day history of extreme fatigue, slowly progressing muscle weakness and insomnia. Drug-induced myopathy was diagnosed with concomitant use of atorvastatin and ciprofloxacin. Muscle weakness improved after the medicines were withdrawn. Co-prescription of Ciprofloxacin and statin therapy appeared to have contributed to muscle weakness in this patient. Drug interaction should also be kept in mind, when managing patients on statins as it may be underappreciated as a cause of muscle weakness and its consequences can have potentially serious outcomes.

[58] *Mahassni SH, Alajlany KA*. **Water Pipe Smoking Affects Young Females and Males Differently with Some Effects on Immune System Cells, but None for C-reactive Protein, Thyroid Hormones, and Vitamin D**. J Pharm Bioallied Sci 2020; 12:31-41.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32801598
ABSTRACT
INTRODUCTION: Water pipe smoking (WPS) is a major health threat leading to higher mortality, morbidity, and incidence of many diseases, such as inflammatory, respiratory and cardiovascular diseases; and cancers. This study aimed to determine the differences in the effects of WPS on the immune system, inflammatory markers, lipids, vitamin D, and thyroid hormones in female and male WP smokers, and compared to nonsmokers of both sexes. No other studies showed the differences between female and male WP smokers for the parameters investigated here, with the exception of the lipid profile. METHODOLOGY: The study was carried on 76 randomly chosen subjects (17 female and 17 male WP smokers, 21 female and 21 male nonsmokers) living in Saudi Arabia with an age range of 20-35 years. Blood samples were collected to determine the differential complete blood counts; lipid profiles; and C-reactive protein, triiodothyronine, thyroxine, and vitamin D concentrations. RESULTS: Results showed no significant differences between female smokers and nonsmokers for all parameters. Male smokers had a significantly lower mean monocytes count and a significantly higher mean red blood cell count and hemoglobin concentration compared to male nonsmokers. Comparing females and males among smokers and nonsmokers separately, the only significant difference in the parameters that was not found in both comparisons was a significantly lower mean basophil count in female nonsmokers compared to male nonsmokers. CONCLUSION: It may be concluded that the effects of WPS were limited to males with immune cells and hematology minimally affected, and that females and males were affected differently by WPS.

[59] *Ali MK, Chwastiak L, Poongothai S et al.* **Effect of a Collaborative Care Model on Depressive Symptoms and Glycated Hemoglobin, Blood Pressure, and Serum Cholesterol Among Patients With Depression and Diabetes in India: The INDEPENDENT Randomized Clinical Trial**. Jama 2020; 324:651-662.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32809002
ABSTRACT

IMPORTANCE: Mental health comorbidities are increasing worldwide and worsen outcomes for people with diabetes, especially when care is fragmented. OBJECTIVE: To assess whether collaborative care vs usual care lowers depressive symptoms and improves cardiometabolic indices among adults with diabetes and depression. DESIGN, SETTING, AND PARTICIPANTS: Parallel, open-label, pragmatic randomized clinical trial conducted at 4 socioeconomically diverse clinics in India that recruited patients with type 2 diabetes; a Patient Health Questionnaire-9 score of at least 10 (range, 0-27); and hemoglobin A1c (HbA1c) of at least 8%, systolic blood pressure (SBP) of at least 140 mm Hg, or low-density lipoprotein (LDL) cholesterol of at least 130 mg/dL. The first patient was enrolled on March 9, 2015, and the last was enrolled on May 31, 2016; the final follow-up visit was July 14, 2018. INTERVENTIONS: Patients randomized to the intervention group (n = 196) received 12 months of self-management support from nonphysician care coordinators, decision support electronic health records facilitating physician treatment adjustments, and specialist case reviews; they were followed up for an additional 12 months without intervention. Patients in the control group (n = 208) received usual care over 24 months. MAIN OUTCOMES AND MEASURES: The primary outcome was the between-group difference in the percentage of patients at 24 months who had at least a 50% reduction in Symptom Checklist Depression Scale (SCL-20) scores (range, 0-4; higher scores indicate worse symptoms) and a reduction of at least 0.5 percentage points in HbA1c, 5 mm Hg in SBP, or 10 mg/dL in LDL cholesterol. Prespecified secondary outcomes were percentage of patients at 12 and 24 months who met treatment targets (HbA1c <7.0%, SBP <130 mm Hg, LDL cholesterol <100 mg/dL [<70 mg/dL if prior cardiovascular disease]) or had improvements in individual outcomes (≥50% reduction in SCL-20 score, ≥0.5-percentage point reduction in HbA1c, ≥5-mm Hg reduction in SBP, ≥10-mg/dL reduction in LDL cholesterol); percentage of patients who met all HbA1c, SBP, and LDL cholesterol targets; and mean reductions in SCL-20 score, Patient Health Questionnaire-9 score, HbA1c, SBP, and LDL cholesterol. RESULTS: Among 404 patients randomized (mean [SD] age, 53 [8.6] years; 165 [40.8%] men), 378 (93.5%) completed the trial. A significantly greater percentage of patients in the intervention group vs the usual care group met the primary outcome (71.6% vs 57.4%; risk difference, 16.9% [95% CI, 8.5%-25.2%]). Of 16 prespecified secondary outcomes, there were no statistically significant between-group differences in improvements in 10 outcomes at 12 months and in 13 outcomes at 24 months. Serious adverse events in the intervention and usual care groups included cardiovascular events or hospitalizations (4 [2.0%] vs 7 [3.4%]), stroke (0 vs 3 [1.4%]), death (2 [1.0%] vs 7 [3.4%]), and severe hypoglycemia (8 [4.1%] vs 0). CONCLUSIONS AND RELEVANCE: Among patients with diabetes and depression in India, a 12-month collaborative care intervention, compared with usual care, resulted in statistically significant improvements in a composite measure of depressive symptoms and cardiometabolic indices at 24 months. Further research is needed to understand the generalizability of the findings to other low- and middle-income health care settings. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02022111.

[60] *Stuijfzand WJ, van Rosendael AR, Lin FY et al.* **Stress Myocardial Perfusion Imaging vs Coronary Computed Tomographic Angiography for Diagnosis of Invasive Vessel-Specific Coronary Physiology: Predictive Modeling Results From the Computed Tomographic Evaluation of Atherosclerotic Determinants of Myocardial Ischemia (CREDENCE) Trial**. JAMA cardiology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32822476

ABSTRACT
IMPORTANCE: Stress imaging has been the standard for diagnosing functionally significant coronary artery disease. It is unknown whether novel, atherosclerotic plaque measures improve accuracy beyond coronary stenosis for diagnosing invasive fractional flow reserve (FFR) measurement. OBJECTIVE: To compare the diagnostic accuracy of comprehensive anatomic (obstructive and nonobstructive atherosclerotic plaque) vs functional imaging measures for estimating vessel-specific FFR. DESIGN, SETTING, AND PARTICIPANTS: Controlled clinical trial of diagnostic accuracy with a multicenter derivation-validation cohort of patients referred for nonemergent invasive coronary angiography. A total of 612 patients (64 [10] years; 30% women) with signs and symptoms suggestive of myocardial ischemia from 23 sites were included. Patients were recruited from 2014 to 2017. Data analysis began in August 2018. INTERVENTIONS: Patients underwent invasive coronary angiography with measurement of invasive FFR, coronary computed tomographic angiography (CCTA) quantification of atherosclerotic plaque and FFR by CT (FFR-CT), and semiquantitative scoring of rest/stress myocardial perfusion imaging (by magnetic resonance, positron emission tomography, or single photon emission CT). Multivariable generalized linear mixed models were derived and validated calculating the area under the receiver operating characteristics curve. MAIN OUTCOMES AND MEASURES: The primary end point was invasive FFR of 0.80 or less. RESULTS: Of the 612 patients, the mean (SD) age was 64 (10) years, and 426 (69.9%) were men. An invasive FFR of 0.80 or less was measured in 26.5% of 1727 vessels. In the derivation cohort, CCTA vessel-specific factors associated with FFR 0.80 or less were stenosis severity, percentage of noncalcified atheroma volume, lumen volume, the number of lesions with high-risk plaque (≥2 of low attenuation plaque, positive remodeling, napkin ring sign, or spotty calcification), and the number of lesions with stenosis greater than 30%. Fractional flow reserve-CT was not additive to this model including stenosis and atherosclerotic plaque. Significant myocardial perfusion imaging predictors were the summed rest and difference scores. In the validation cohort, the areas under the receiver operating characteristic curve were 0.81 for CCTA vs 0.67 for myocardial perfusion imaging ($P < .001$). CONCLUSIONS AND RELEVANCE: A comprehensive anatomic interpretation with CCTA, including quantification of obstructive and nonobstructive atherosclerotic plaque, was superior to functional imaging in the diagnosis of invasive FFR. Comprehensive CCTA measures improve prediction of vessel-specific coronary physiology more so than stress-induced alterations in myocardial perfusion. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02173275.

[61] *Gordon SM, Amar MJ, Jeiran K et al.* **Effect of niacin monotherapy on high density lipoprotein composition and function**. Lipids in health and disease 2020; 19:190.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825822

ABSTRACT
BACKGROUND: Niacin has modest but overall favorable effects on plasma lipids by increasing high density lipoprotein cholesterol (HDL-C) and lowering triglycerides. Clinical trials, however, evaluating niacin therapy for prevention of cardiovascular outcomes have returned mixed results. Recent evidence suggests that the HDL proteome may be a better indicator of HDL's cardioprotective function than HDL-C. The objective of this study was to evaluate the effect of niacin monotherapy on HDL protein composition and function. METHODS: A 20-week investigational study was performed with 11 participants receiving

extended-release niacin (target dose = 2 g/day) for 16-weeks followed by a 4-week washout period. HDL was isolated from participants at weeks: 0, 16, and 20. The HDL proteome was analyzed at each time point by mass spectrometry and relative protein quantification was performed by label-free precursor ion intensity measurement. RESULTS: In this cohort, niacin therapy had typical effects on routine clinical lipids (HDL-C + 16%, q < 0.01; LDL-C - 20%, q < 0.01; and triglyceride - 15%, q = 0.1). HDL proteomics revealed significant effects of niacin on 5 proteins: serum amyloid A (SAA), angiotensinogen (AGT), apolipoprotein A-II (APOA2), clusterin (CLUS), and apolipoprotein L1 (APOL1). SAA was the most prominently affected protein, increasing 3-fold in response to niacin (q = 0.008). Cholesterol efflux capacity was not significantly affected by niacin compared to baseline, however, stopping niacin resulted in a 9% increase in efflux (q < 0.05). Niacin did not impact HDL's ability to influence endothelial function. CONCLUSION: Extended-release niacin therapy, in the absence of other lipid-modifying medications, can increase HDL-associated SAA, an acute phase protein associated with HDL dysfunction.

[62] *Li Y, Liu S, Wang YT et al.* **TBL2 methylation is associated with hyper-low-density lipoprotein cholesterolemia: a case-control study**. Lipids in health and disease 2020; 19:186.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32811528
ABSTRACT
BACKGROUND: HMGCR, SCAP, SREBF1, SREBF2 and TBL2 are well-known genes that are involved in the process of lipid metabolism. However, it is not known whether epigenetic changes of these genes are associated with lipid metabolism. In this study, the methylation levels of the HMGCR, SCAP, SREBF1, SREBF2 and TBL2 genes were analyzed between samples from a hyper-low-density lipoprotein cholesterolemia (hyper-LDL) group and a control group to examine the association between the methylation levels of these genes and the risk of hyper-LDL. METHODS: In this study, a case-control approach was used to explore the association between DNA methylation and hyper-LDL. The DNA methylation levels of HMGCR, SCAP, SREBF1, SREBF2 and TBL2 genes and 231 CpG sites in the promoter regions of these genes were measured in 98 hyper-LDL participants and 89 participants without hypo-LDL. RESULTS: Compared with participants without hyper-LDL, patients with hyper-LDL TBL2 gene had lower methylation levels (11.93 vs. 12.02, P = 0.004). The methylation haplotypes with significant abundance in the TBL2 gene are tctttttttt (P = 0.034), ctttttttcct (P = 0.025), ctctttctttt (P = 0.040), cctttttttt (P = 0.028), and tctttttttttttttt. CONCLUSION: The study demonstrates that participants with hyper-LDL have lower methylation of TBL2. The results suggest that DNA methylation of TBL2 can decrease the risk for hyper-LDL in humans.

[63] *St-Amand R, Ngo Sock É T, Quinn S et al.* **Two weeks of western diet disrupts liver molecular markers of cholesterol metabolism in rats**. Lipids in health and disease 2020; 19:192.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825820
ABSTRACT
BACKGROUND: The present study was designed to test the hypothesis that in the liver, excessive fat accumulation impairs cholesterol metabolism mainly by altering the low-density lipoprotein-receptor (LDL-R) pathway. METHOD: Young male Wistar rats were fed standard

(SD), high fat (HFD; 60% kcal) or Western (WD; 40% fat + 35% sucrose (17.5% fructose)) diets for 2 or 6 weeks. RESULTS: Weight gain (~ 40 g) was observed only following 6 weeks of the obesogenic diets ($P < 0.01$). Compared to the 2-week treatment, obesogenic diets tripled fat pad weight (~ 20 vs 7 g) after 6 weeks. Hepatic triglyceride (TG) levels were greater in response to both the WD and HFD compared to the SD ($P < 0.01$) at 2 and 6 weeks and their concentrations were greater ($P < 0.05$) in WD than HFD at 2 weeks. Plasma total cholesterol levels were higher ($P < 0.05$) in animals submitted to WD. After 2 and 6 weeks, liver expression of LDL-R, proprotein convertase subtilisin/kexin 9 (PCSKk9) and sterol regulatory element binding protein 2 (SREBP2), involved in LDL-cholesterol uptake, was lower in animals submitted to WD than in others treated with HFD or SD ($P < 0.01$). Similarly, low-density lipoprotein-receptor-related protein 1 (LRP1) and acyl-CoA cholesterol acyltransferase-2 (ACAT-2) mRNA levels were lower ($P < 0.01$) among WD compared to SD-fed rats. Expression of the gene coding the main regulator of endogenous cholesterol synthesis, 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCoAR) was reduced in response to WD compared to SD and HFD at 2 ($P < 0.001$) and 6 ($P < 0.05$) weeks. Being enriched in fructose, the WD strongly promoted the expression of carbohydrate-response element binding protein (ChREBP) and acetyl-CoA carboxylase (ACC), two key regulators of de novo lipogenesis. CONCLUSION: These results show that the WD promptly increased TG levels in the liver by potentiating fat storage. This impaired the pathway of hepatic cholesterol uptake via the LDL-R axis, promoting a rapid increase in plasma total cholesterol levels. These results indicate that liver fat content is a factor involved in the regulation of plasma cholesterol.

[64] *Szeto A, Cecati M, Ahmed R et al.* **Oxytocin reduces adipose tissue inflammation in obese mice**. Lipids in health and disease 2020; 19:188.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32819381

ABSTRACT

BACKGROUND: Obesity and adipose tissue expansion is characterized by a chronic state of systemic inflammation that contributes to disease. The neuropeptide, oxytocin, working through its receptor has been shown to attenuate inflammation in sepsis, wound healing, and cardiovascular disease. The current study examined the effects of chronic oxytocin infusions on adipose tissue inflammation in a murine model of obesity, the leptin receptor-deficient (db/db) mouse. METHODS: The effect of obesity on oxytocin receptor protein and mRNA expression in adipose tissue was evaluated by Western blotting and real-time polymerase chain reaction. Mice were implanted with osmotic minipumps filled with oxytocin or vehicle for 8 weeks. At study endpoint adipose tissue inflammation was assessed by measurement of cytokine and adipokine mRNA tissue levels, adipocyte size and macrophage infiltration via histopathology, and plasma levels of adiponectin and serum amyloid A as markers of systemic inflammation. RESULTS: The expression of adipose tissue oxytocin receptor was increased in obese db/db mice compared to lean controls. In adipose tissue oxytocin infusion reduced adipocyte size, macrophage infiltration, IL-6 and TNFα mRNA expression, and increased the expression of the anti-inflammatory adipokine, adiponectin. In plasma, oxytocin infusion reduced the level of serum amyloid A, a marker of systemic inflammation, and increased circulating adiponectin. CONCLUSIONS: In an animal model of obesity and diabetes chronic oxytocin treatment led to a reduction in visceral adipose tissue inflammation and plasma markers of systemic inflammation, which may play a role in disease progression.

[65] *Casal-Lorenzo J, Sánchez-Sobrino P, Fernández-Catalina P*. **Hypercholesterolemia treated with a PCSK9 inhibitor in a patient with ischemic heart disease and McArdle disease**. Medicina clinica 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32819767
ABSTRACT

[66] *Vitturi BK, Gagliardi RJ*. **Effectiveness of statins in patients with stroke due to cervical artery dissection: A preliminary study**. Medicina clinica 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32826077
ABSTRACT
BACKGROUND: Statin therapy has become one of the most important advances in stroke secondary prevention. Nevertheless, statin therapy in patients who present an ischemic stroke following cervical artery dissection (CAD) has not yet been supported by clinical evidence. This study aimed to investigate the effect of statins on neurological outcomes after a stroke due to CAD. METHODS: We conducted a prospective cohort study including consecutive patients diagnosed with a stroke due to CAD. Subjects were classified into non-statin, simvastatin 20mg, simvastatin 40mg, and high-potency statin groups. After 2 years, the functional outcome, stroke recurrence, major cardiovascular events, and mortality were assessed. RESULTS: Among the 54 patients included in our cohort, there were 16 (29.6%) patients without statins, 22 (40.7%) with simvastatin 20mg, 12 (22.2%) with simvastatin 40mg and 4 (7.5%) with high-potency statins. Using simvastatin 40mg was associated with a significantly lower incidence of stroke recurrence. Patients with simvastatin 40mg and high-potency statins presented the best functional recovery throughout the follow-up ($p<.01$). DISCUSSION: The use of statins in patients with CAD-related stroke may improve functional outcomes in specific cases. Statins do not prevent stroke recurrence and major cardiovascular events in this type of stroke.

[67] *de Oliveira Neto AS, Souza ILA, Amorim MES et al.* **Antifungal efficacy of atorvastatin-containing emulgel in the treatment of oral and vulvovaginal candidiasis**. Med Mycol 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32823281
ABSTRACT
Drug repositioning has been an important ally in the search for new antifungal drugs. Statins are drugs that act to prevent sterol synthesis in both humans and fungi and for this reason they are promissory candidates to be repositioned to treat mycoses. In this study we evaluated the antifungal activity of atorvastatin by in vitro tests to determine the minimum inhibitory concentration against azole resistant Candida albicans and its mechanisms of action. Moreover, the efficacy of both atorvastatin-loaded oral and vaginal emulgels (0.75%, 1.5% and 3% w/w) was evaluated by means of in vivo experimental models of oral and vulvovaginal candidiasis, respectively. The results showed that atorvastatin minimal inhibitory concentration against C. albicans was 31.25 μg/ml. In oral candidiasis experiments, the group treated with oral emulgel containing 3.0% atorvastatin showcased total reduction in fungal load after nine days of treatment. Intravaginal delivery atorvastatin emulgel showed considerable effectiveness at the concentration of 3% (65% of fungal burden reduction) after nine days of treatment. From these findings, it is possible to assert that atorvastatin may be promising for drug repositioning towards the treatment of these opportunistic mycoses. LAY SUMMARY:

Atorvastatin is a statin drug that presents antifungal activity. This study showed that atorvastatin-containing oral and vaginal emulgels were able to treat vulvovaginal and oral candidiasis of infected animal model. Therefore, we showcased that atorvastatin may be a possible therapeutic agent in order to be a used to control opportunistic mucosal fungal infections caused by Candida albicans.

[68] *Rice J, Ramtekkar U*. **Integrative Management of Metabolic Syndrome in Youth Prescribed Second-Generation Antipsychotics**. Med Sci (Basel) 2020; 8.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32824428
ABSTRACT
Weight gain and metabolic syndrome are common side effects of second-generation antipsychotics and carry significant health consequences both in childhood and into adulthood. This review highlights evidence-based, non-pharmacologic interventions to assist in the management of these side effects. Such intervention categories include dietary, physical activity, sleep, stress management, and nutritional supplementation. Interventions with the highest quality evidence include increasing the consumption of fruits, vegetables, and whole grains, increasing physical activity, improving sleep, and fish oil supplementation. We suggest that clinicians work with patients on managing metabolic side effects in a patient-centered way, incorporating principles of motivational interviewing, to reduce the risk of metabolic syndrome.

[69] *Das UN*. **Can Bioactive Lipid Arachidonic Acid Prevent and Ameliorate COVID-19?** Medicina (Kaunas, Lithuania) 2020; 56.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825011
ABSTRACT
It is proposed that the bioactive lipid, arachidonic acid (AA, 20:4 n-6), can inactivate severe acute respiratory syndrome(SARS-CoV-2), facilitate M1 and M2 macrophage generation, suppress inflammation, prevent vascular endothelial cell damage, and regulate inflammation resolution processes based on the timely formation of prostaglandin E2 (PGE2) and lipoxin A4 (LXA4) based on the context. Thus, AA may be useful both to prevent and manage coronavrus disease-2019(COVID-19).

[70] *Cree-Green M, Ravi S, Carreau AM et al.* **Nonalcoholic fatty liver disease in obese adolescent females is associated with multi-tissue insulin resistance and visceral adiposity markers**. Metabol Open 2019; 2:100011.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812939
ABSTRACT
OBJECTIVE: Nonalcoholic fatty liver disease (NAFLD) is associated with insulin resistance (IR) and visceral adiposity in adults and boys, but girls with NAFLD are understudied. We sought to evaluate adipose, liver, and skeletal muscle insulin sensitivity in obese adolescent females with or without hepatic steatosis (HS) (intrahepatic triglyceride (IHTG) content >5.5%) along with cardiometabolic components typically associated with IR. STUDY DESIGN: 73 obese adolescent girls at high risk for NAFLD were enrolled. Participants underwent fasting labs, an MRI to measure IHTG and visceral fat, (31)phosphorous MR spectroscopy for muscle mitochondrial function, (1)H MR spectroscopy for intramyocellular lipid (IMCL), bicycle ergometry to assess VO(2)peak and a 4-phase hyperinsulinemic euglycemic clamp with isotope tracers to measure hepatic and peripheral IR. 29 participants had HS [age

15 yrs(13,16), BMI%ile 98.7(97.4,99.0), IHTG 10.4%(8.0,13.5)] and 44 did not [age 15 yrs(13,17), BMI%ile 98.5(96.2,99.0), IHTG 2.0%(1.1,3.0)]. RESULTS: During hyperinsulinemia, participants with HS vs. non-HS had failure to suppress free fatty acids ($p = 0.008$), endogenous glucose release ($p = 0.002$), and a lower glucose metabolic rate of disappearance (Rd) ($p = 0.012$). Girls with NALFD also had higher visceral fat ($p < 0.001$), systolic blood pressure ($p = 0.026$), triglycerides ($p = 0.02$), ALT ($p < 0.01$) and white blood cell count ($p < 0.01$), and lower adiponectin ($p = 0.02$). There was no difference between girls with and without HS in systemic glycerol turnover measured with glycerol release, or in IMCL, mitochondrial function or VO(2)peak. CONCLUSIONS: Obese adolescent girls with HS have evidence of multi-tissue IR, visceral adiposity, inflammation and multiple components of the metabolic syndrome, arguing for close cardiometabolic surveillance over time of girls with HS.

[71] *Ribeiro Dos Santos L, Baer Filho R*. **Treatment of nonalcoholic fatty liver disease with dapagliflozin in non-diabetic patients**. Metabol Open 2020; 5:100028.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812927
ABSTRACT
Steatosis, a condition characterized by excessive lipid deposition. Although usually a benign condition, steatosis mays progress to cirrhosis or hepatocellular carcinoma. Recent evidence suggests that SGLT2 inhibitors suppress the development of nonalcoholic steatohepatitis in humans, as well as in rodent models and that SGLT2 inhibitors alleviate hepatic steatosis or steatohepatitis in obese type 2 diabetic rats or mice. 14 Patients with nonalcoholic fatty liver disease used a fixed dose of 10 mg of dapagliflozin for an average of 75 days. ALT, AST, GGT, insulin, HOMA-IR, and weight levels were significantly lower after treatment. There was no significant correlation between the reduction in HOMA and the reduction in ALT values or weight reduction obtained during treatment and ALT values.

[72] *Kersten S*. **Bypassing the LDL Receptor in Familial Hypercholesterolemia**. The New England journal of medicine 2020; 383:775-776.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32813955
ABSTRACT

[73] *Raal FJ, Rosenson RS, Reeskamp LF et al.* **Evinacumab for Homozygous Familial Hypercholesterolemia**. The New England journal of medicine 2020; 383:711-720.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32813947
ABSTRACT
BACKGROUND: Homozygous familial hypercholesterolemia is characterized by premature cardiovascular disease caused by markedly elevated levels of low-density lipoprotein (LDL) cholesterol. This disorder is associated with genetic variants that result in virtually absent (null-null) or impaired (non-null) LDL-receptor activity. Loss-of-function variants in the gene encoding angiopoietin-like 3 (ANGPTL3) are associated with hypolipidemia and protection against atherosclerotic cardiovascular disease. Evinacumab, a monoclonal antibody against ANGPTL3, has shown potential benefit in patients with homozygous familial hypercholesterolemia. METHODS: In this double-blind, placebo-controlled, phase 3 trial, we randomly assigned in a 2:1 ratio 65 patients with homozygous familial hypercholesterolemia who were receiving stable lipid-lowering therapy to receive an intravenous infusion of evinacumab (at a dose of 15 mg per kilogram of body weight) every 4 weeks or placebo. The

primary outcome was the percent change from baseline in the LDL cholesterol level at week 24. RESULTS: The mean baseline LDL cholesterol level in the two groups was 255.1 mg per deciliter, despite the receipt of maximum doses of background lipid-lowering therapy. At week 24, patients in the evinacumab group had a relative reduction from baseline in the LDL cholesterol level of 47.1%, as compared with an increase of 1.9% in the placebo group, for a between-group least-squares mean difference of -49.0 percentage points (95% confidence interval [CI], -65.0 to -33.1; P<0.001); the between-group least-squares mean absolute difference in the LDL cholesterol level was -132.1 mg per deciliter (95% CI, -175.3 to -88.9; P<0.001). The LDL cholesterol level was lower in the evinacumab group than in the placebo group in patients with null-null variants (-43.4% vs. +16.2%) and in those with non-null variants (-49.1% vs. -3.8%). Adverse events were similar in the two groups. CONCLUSIONS: In patients with homozygous familial hypercholesterolemia receiving maximum doses of lipid-lowering therapy, the reduction from baseline in the LDL cholesterol level in the evinacumab group, as compared with the small increase in the placebo group, resulted in a between-group difference of 49.0 percentage points at 24 weeks. (Funded by Regeneron Pharmaceuticals; ELIPSE HoFH ClinicalTrials.gov number, NCT03399786.).

[74] *Yafasova A, Fosbøl EL, Christiansen MN et al.* **Time trends in incidence, comorbidity, and mortality of ischemic stroke in Denmark, 1996-2016**. Neurology 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32817180
ABSTRACT
OBJECTIVE: To examine whether the incidence, comorbidity, and mortality of first-time ischemic stroke changed in Denmark between 1996 and 2016 overall and according to age and sex using a nationwide cohort design. METHODS: In this cohort study, 224,617 individuals ≥18 years admitted with first-time ischemic stroke between 1996 and 2016 were identified using Danish nationwide registries. We calculated annual age-standardized incidence rates and absolute 30-day and 1-year mortality risks. Further, we calculated annual incidence rate ratios using Poisson regression, odds ratios for 30-day mortality using logistic regression, and hazard ratios for 1-year mortality using Cox regression. RESULTS: The overall age-standardized incidence rates of ischemic stroke per 1,000 person-years increased from 1996 (2.70 [95% CI, 2.65-2.76]) to 2002 (3.25 [95% CI, 3.20-3.31]) and then gradually decreased to below the initial level until 2016 (1.99 [95% CI, 1.95-2.02]). Men had higher incidence rates than women in all age groups except 18-34 and ≥85 years. Absolute mortality risk decreased between 1996 and 2016 (30-day mortality from 17.1% to 7.6% and 1-year mortality from 30.9% to 17.3%). Women between 55 and 64 and ≥85 years had higher mortality than men. Similar trends were observed for all analyses after multivariable adjustment. The prevalence of atrial fibrillation, hypertension, diabetes mellitus, and use of lipid-lowering medication increased during the study period. CONCLUSIONS: The age-standardized incidence of first-time hospitalization for ischemic stroke increased from 1996 to 2002 and then gradually decreased to below the initial level until 2016. Absolute 30-day and 1-year mortality risks decreased between 1996 and 2016. These findings correspond to increased stroke prevention awareness and introduction of new treatments during the study period.

[75] *Inglis JE, Kleckner AS, Lin PJ et al.* **Excess Body Weight and Cancer-Related Fatigue, Systemic Inflammation, and Serum Lipids in Breast Cancer Survivors**. Nutrition and cancer 2020:1-11.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812824
ABSTRACT
BACKGROUND: Cancer-related fatigue (CRF) is a common side effect impacting breast cancer survivors. Research points to a relationship between obesity and CRF in breast cancer survivors related to elevated systemic inflammation and metabolic alterations. METHODS: This cross-sectional study examined the relationship of obesity to CRF, inflammatory markers and serum lipids through a secondary analysis of a nationwide randomized controlled trial. Breast cancer survivors with CRF were categorized based on BMI category. Symptoms of CRF, inflammatory markers and serum fatty acids were assessed among groups. RESULTS: There were 105 breast cancer survivors in the analysis. BMI was positively associated with CRF based on MFSI General ($p = 0.020$; 95% C.I. 0.024, 0.273) and MFSI Physical ($p = 0.013$; 95% C.I. 0.035, 0.298) subscales. TNF-α ($p = 0.007$; 95% C.I. 0.007, 0.044), and IL-6 ($p = 0.020$; 95% C.I. 0.006, 0.073) were elevated in the obese. Monounsaturated fatty acid levels ($p = 0.047$; 95% C.I. 0.000, 0.053) and the omega-6 to omega-3 fatty acid ratio were associated with obesity ($p = 0.047$; 95% C.I. 0.002, 0.322). CONCLUSIONS: Obese breast cancer survivors had greater levels of CRF, inflammatory markers and certain fatty acids. Inflammatory markers and fatty acids were not found to have any mediating or positive association with CRF variables in this analysis. NCT02352779.

[76] *Goss AM, Gower B, Soleymani T et al.* **Effects of weight loss during a very low carbohydrate diet on specific adipose tissue depots and insulin sensitivity in older adults with obesity: a randomized clinical trial**. Nutrition & metabolism 2020; 17:64.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32817749
ABSTRACT
BACKGROUND: Insulin resistance and accumulation of visceral adipose tissue (VAT) and intermuscular adipose tissue (IMAT) place aging adults with obesity at high risk of cardio-metabolic disease. A very low carbohydrate diet (VLCD) may be a means of promoting fat loss from the visceral cavity and skeletal muscle, without compromising lean mass, and improve insulin sensitivity in aging adults with obesity. OBJECTIVE: To determine if a VLCD promotes a greater loss of fat (total, visceral and intermuscular), preserves lean mass, and improves insulin sensitivity compared to a standard CHO-based/low-fat diet (LFD) in older adults with obesity. DESIGN: Thirty-four men and women aged 60-75 years with obesity (body mass index [BMI] 30-40 kg/m(2)) were randomized to a diet prescription of either a VLCD (< 10:25:> 65% energy from CHO:protein:fat) or LFD diet (55:25:20) for 8 weeks. Body composition by dual-energy X-ray absorptiometry (DXA), fat distribution by magnetic resonance imaging (MRI), insulin sensitivity by euglycemic hyperinsulinemic clamp, and lipids by a fasting blood draw were assessed at baseline and after the intervention. RESULTS: Participants lost an average of 9.7 and 2.0% in total fat following the VLCD and LFD, respectively ($p < 0.01$). The VLCD group experienced ~ 3-fold greater loss in VAT compared to the LFD group (- 22.8% vs - 1.0%, $p < 0.001$) and a greater decrease in thigh-IMAT (- 24.4% vs - 1.0%, $p < 0.01$). The VLCD group also had significantly greater thigh skeletal muscle (SM) at 8 weeks following adjustment for change in total fat mass. Finally, the VLCD had greater increases in insulin sensitivity and HDL-C and decreases in fasting insulin and triglycerides compared to the LFD group. CONCLUSIONS: Weight loss resulting from consumption of a diet lower in CHO and higher in fat may be beneficial for older adults with obesity by depleting adipose tissue depots most strongly implicated in poor metabolic and functional outcomes and by improving insulin

sensitivity and the lipid profile. TRIAL REGISTRATION: NCT02760641. Registered 03 May 2016 - Retrospectively registered.

[77] *Trento M, Fornengo P, Amione C et al.* **Self-management education may improve blood pressure in people with type 2 diabetes. A randomized controlled clinical trial**. Nutrition, metabolism, and cardiovascular diseases : NMCD 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32811740
ABSTRACT
BACKGROUND AND AIMS: Diabetes is a suitable model to evaluate intervention programmes aimed at chronic diseases, because of its well-defined and measurable process and outcome indicators. In this study, we aimed at investigating the effects of group based self-management education on clinical and psychological variables in type 2 diabetes. METHODS AND RESULTS: Four-year randomized controlled clinical trial (ISRCTN14558376) comparing Group Care and traditional one-to-one care. Clinical and psychological variables were monitored at baseline, 2 and 4 years. Although differences between groups appear to be non-significant at univariate analysis, body weight, BMI and HbA1c, systolic and diastolic blood pressure improved in the patients followed by Group Care but not among Controls. Prescription of lipid-lowering and anti-hypertensive agents did not change among the patients on Group Care, whereas anti-hypertensives were stepped up among Controls without improving their blood pressure. Multivariable analysis suggests that blood pressure improvement among patients on Group Care was independent of BMI, duration of diabetes and antihypertensive medication, suggesting a direct effect of education, presumably by increasing adherence. The "Powerful Others" dimension of the Locus of Control worsened and fear of complications decreased among Controls. CONCLUSIONS: The results confirm that a multidisciplinary structured group educational approach improves blood pressure, presumably through better adherence to healthy lifestyle and medication, in people with type 2 diabetes. CLINICAL TRIAL REGISTRATION NUMBER: ISRCTN14558376.

[78] *Barkas F, Nomikos T, Liberopoulos E, Panagiotakos D*. **Diet and Cardiovascular Disease Risk Among Individuals with Familial Hypercholesterolemia: Systematic Review and Meta-Analysis**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32823643
ABSTRACT
BACKGROUND: Although a cholesterol-lowering diet and the addition of plant sterols and stanols are suggested for the lipid management of children and adults with familial hypercholesterolemia, there is limited evidence evaluating such interventions in this population. OBJECTIVES: To investigate the impact of cholesterol-lowering diet and other dietary interventions on the incidence or mortality of cardiovascular disease and lipid profile of patients with familial hypercholesterolemia. SEARCH METHODS: Relevant trials were identified by searching US National Library of Medicine National Institutes of Health Metabolism Trials Register and clinicaltrials.gov.gr using the following terms: diet, dietary, plant sterols, stanols, omega-3 fatty acids, fiber and familial hypercholesterolemia. SELECTION CRITERIA: Randomized controlled trials evaluating the effect of cholesterol-lowering diet or other dietary interventions in children and adults with familial hypercholesterolemia were included. DATA COLLECTION AND ANALYSIS: Two authors independently assessed the eligibility of the included trials and their bias risk and extracted the data which was

independently verified by other colleagues. RESULTS: A total of 17 trials were finally included, with a total of 376 participants across 8 comparison groups. The included trials had either a low or unclear bias risk for most of the assessed risk parameters. Cardiovascular incidence or mortality were not evaluated in any of the included trials. Among the planned comparisons regarding patients' lipidemic profile, a significant difference was noticed for the following comparisons and outcomes: omega-3 fatty acids reduced triglycerides (mean difference (MD): -0.27 mmol/L, 95% confidence interval (CI): -0.47 to -0.07, p < 0.01) when compared with placebo. A non-significant trend towards a reduction in subjects' total cholesterol (MD: -0.34, 95% CI: -0.68 to 0, mmol/L, p = 0.05) and low-density lipoprotein cholesterol (MD: -0.31, 95% CI: -0.61 to 0, mmol/L, p = 0.05) was noticed. In comparison with cholesterol-lowering diet, the additional consumption of plant stanols decreased total cholesterol (MD: -0.62 mmol/L, 95% CI: -1.13 to -0.11, p = 0.02) and low-density lipoprotein cholesterol (MD: -0.58 mmol/L, 95% CI: -1.08 to -0.09, p = 0.02). The same was by plant sterols (MD: -0.46 mmol/L, 95% CI: -0.76 to -0.17, p < 0.01 for cholesterol and MD: -0.45 mmol/L, 95% CI: -0.74 to -0.16, p < 0.01 for low-density lipoprotein cholesterol). No heterogeneity was noticed among the studies included in these analyses. CONCLUSIONS: Available trials confirm that the addition of plant sterols or stanols has a cholesterol-lowering effect on such individuals. On the other hand, supplementation with omega-3 fatty acids effectively reduces triglycerides and might have a role in lowering the cholesterol of patients with familial hypercholesterolemia. Additional studies are needed to investigate the efficacy of cholesterol-lowering diet or the addition of soya protein and dietary fibers to a cholesterol-lowering diet in patients with familial hypercholesterolemia.

[79] *Bis G, Szlasa W, Sondaj K et al.* **Lipid Complications after Hematopoietic Stem Cell Transplantation (HSCT) in Pediatric Patients**. Nutrients 2020; 12.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825002

ABSTRACT

HSCT (hematopoietic stem cell transplantation) is a widely applied method of treatment of pediatric patients with leukemia and other bone marrow-associated disorders. Metabolic disturbances can appear as procedure side effects. This study aimed to report incidence of lipid and thyroid disorders and time of their onset in pediatric patients after HSCT. There were 198 pediatric patients (123 males) aged 0.5-20 years who were subjected to HSCT. Patients were mostly diagnosed with Acute Leukemia (n = 190). The analysis of lipids, thyroid hormones, and thyroid antibodies levels comprised one month before the HSCT to last follow up visit between 2016 and 2019 (median 3.8 ± 1.8 years after HSCT). In males, the triglycerides levels increased over two times in the course of HSCT in both patients with initially low and elevated HDL (high-density lipoprotein) levels. Most of the lipid disorders occurred in six months after HSCT. Patients treated with L-thyroxine exhibited decreased LDL (low-density lipoprotein) levels. HDL remained at a lower level in males. Thyroid hormone abnormalities were evenly distributed in time until 4 years after HSCT. Patients require long term follow up including lipid metabolism and thyroid function analysis. HSCT survivors demand introduction of polyunsaturated fatty acids into the diet to reduce risk of developing the lipid complications.

[80] *Hahn HJ, Escrig JI, Shing B, Debnath A*. **In Vitro Effect of Pitavastatin and Its Synergistic Activity with Isavuconazole against Acanthamoeba castellanii**. Pathogens 2020; 9.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32825652
ABSTRACT
Acanthamoeba keratitis (AK) can occur in healthy individuals wearing contact lenses and it is a painful, blinding infection of the cornea caused by a free-living ameba Acanthamoeba. Current treatment for AK relies on a combination of chlorhexidine, propamidine isethionate, and polyhexamethylene biguanide. However, the current regimen includes an aggressive disinfectant and in 10% of cases recurrent infection ensues. Therefore, development of efficient and safe drugs is a critical unmet need to avert blindness. Acanthamoeba sterol biosynthesis includes two essential enzymes HMG-CoA reductase (HMGR) and sterol 14-demethylase (CYP51), and we earlier identified a CYP51 inhibitor isavuconazole that demonstrated nanomolar potency against A. castellanii trophozoites. In this study, we investigated the effect of well-tolerated HMGR inhibitors and identified pitavastatin that is active against trophozoites of three different clinical strains of A.castellanii. Pitavastatin demonstrated an EC(50) of 0.5 to 1.9 μM, depending on strains. Combination of pitavastatin and isavuconazole is synergistic and led to 2- to 9-fold dose reduction for pitavastatin and 11- to 4000-fold dose reduction for isavuconazole to achieve 97% of growth inhibition. Pitavastatin, either alone or in combination with isavuconazole, may lead to repurposing for the treatment of Acanthamoeba keratitis.

[81] *Orozco Morales JA, Medina Urrutia AX, Torres Tamayo M et al.* **Effects of fatty liver on the size and composition of high-density lipoprotein cholesterol subpopulations in adolescents with type 2 diabetes mellitus**. Pediatric diabetes 2020.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812688
ABSTRACT
BACKGROUND: Type 2 diabetes mellitus (T2DM) is an emerging disease in the pediatric population. The association between T2DM and non-alcoholic fatty liver disease (NAFLD) has been described. Recent evidence suggests that sizes and composition of high-density lipoprotein (HDL) may be more important that HDL-C levels in predicting coronary heart disease. There is not data regarding the HDL subclasses distribution and composition in T2DM youths with NAFLD. METHODS: This cross-sectional study included 47 adolescents with T2DM and 23 non-diabetic controls of both sexes aged 10 to 18 years. The presence of NAFLD was determined estimated proton density fat fraction (PDFF) by magnetic resonance by spectroscopy. We compared the HDL subclasses distribution (HDL2b, HDL2a, HDL3a HDL3b and HDL3c) and the HDL chemical composition (total protein, triglyceride, phospholipid, cholesteryl esters, and free cholesterol) between the groups of adolescents with T2DM and the control group. RESULTS: Patients with T2DM and NAFLD had a significantly lower proportion HDL2b (P = .040) and a higher proportion of HDL3c (P = .035); higher proportion of TG (P = .032) and a lower CE (P = .002) and FC (P < .001). A negative association was observed between PDFF and the percentages of HDL2b (r(2) = -0.341, P = .004) and the average particle size (r(2) = -0.327, P = .05), and a positive association with HDL3c subpopulations (r(2) = 0.327, P = .015); about composition inside HDL particle, a positive association with PDFF and the TG (r(2) = 0.299, P = .013) and negative with CE (r(2) = -0.265, P = .030). CONCLUSIONS: In adolescents diagnosed with T2DM, the presence of

NAFLD is associated with abnormalities in the distribution of HDL subpopulations and the lipid composition of HDL particles.

[82] *Morishima T, Tsuchiya Y, Ueda H, Ochi E*. **Muscular endurance and muscle metabolic responses to 8 weeks of omega-3 polyunsaturated fatty acids supplementation**. Physiological reports 2020; 8:e14546.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32812384
ABSTRACT
BACKGROUND: It has been well known that exercise training improves muscular endurance; however, whether nutritional strategies can be used to enhance muscular endurance remains unclear. Herein, we tested the hypothesis that 8 weeks of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) supplementation, known to promote oxygen availability and lipid metabolism, would attenuate muscular fatigue caused by numerous muscle contractions. METHODS: Nineteen healthy men were randomly assigned to a placebo group (n = 9) and fish oil group (n = 10) in a double-blind fashion. The fish oil group consumed EPA-rich fish oil that contains 600-mg EPA and 260-mg DHA per day for 8 weeks. The placebo group received matching capsules for the same duration of time. After the 8-week intervention, subjects performed muscular endurance test that was repeated knee extensions with weights equal to 40% of the subject's body weight. RESULTS: Maximal repetitions to exhaustion were recorded. In addition, maximum isometric voluntary muscle contraction (MVC), muscle metabolism using near-infrared spectroscopy, and blood lactate were measured during the test. Subjects in both groups reached exhaustion after the muscular endurance test, while the maximal repetitions did not differ between the groups. Similarly, there is no significant difference in oxygen saturation in muscle tissue (StO2), an index of muscle oxygen availability, between the groups. Also, MVC and blood lactate did not change between groups. CONCLUSION: In conclusion, the present study provided evidence that muscle fatigue caused by knee extensions cannot be attenuated by EPA and DHA supplementation in healthy subjects.

[83] *Saddiki H, Fayosse A, Cognat E et al.* **Age and the association between apolipoprotein E genotype and Alzheimer disease: A cerebrospinal fluid biomarker-based case-control study**. PLoS medicine 2020; 17:e1003289.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32817639
ABSTRACT
BACKGROUND: The ε4 allele of apolipoprotein E (APOE) gene and increasing age are two of the most important known risk factors for developing Alzheimer disease (AD). The diagnosis of AD based on clinical symptoms alone is known to have poor specificity; recently developed diagnostic criteria based on biomarkers that reflect underlying AD neuropathology allow better assessment of the strength of the associations of risk factors with AD. Accordingly, we examined the global and age-specific association between APOE genotype and AD by using the A/T/N classification, relying on the cerebrospinal fluid (CSF) levels of β-amyloid peptide (A, β-amyloid deposition), phosphorylated tau (T, pathologic tau), and total tau (N, neurodegeneration) to identify patients with AD. METHODS AND FINDINGS: This case-control study included 1,593 white AD cases (55.4% women; mean age 72.8 [range = 44-96] years) with abnormal values of CSF biomarkers from nine European memory clinics and the American Alzheimer's Disease Neuroimaging Initiative (ADNI) study. A total of 11,723

dementia-free controls (47.1% women; mean age 65.6 [range = 44-94] years) were drawn from two longitudinal cohort studies (Whitehall II and Three-City), in which incident cases of dementia over the follow-up were excluded from the control population. Odds ratio (OR) and population attributable fraction (PAF) for AD associated with APOE genotypes were determined, overall and by 5-year age categories. In total, 63.4% of patients with AD and 22.6% of population controls carried at least one APOE ε4 allele. Compared with non-ε4 carriers, heterozygous ε4 carriers had a 4.6 (95% confidence interval 4.1-5.2; $p < 0.001$) and ε4/ε4 homozygotes a 25.4 (20.4-31.2; $p < 0.001$) higher OR of AD in unadjusted analysis. This association was modified by age (p for interaction < 0.001). The PAF associated with carrying at least one ε4 allele was greatest in the 65-70 age group (69.7%) and weaker before 55 years (14.2%) and after 85 years (22.6%). The protective effect of APOE ε2 allele for AD was unaffected by age. Main study limitations are that analyses were based on white individuals and AD cases were drawn from memory centers, which may not be representative of the general population of patients with AD. CONCLUSIONS: In this study, we found that AD diagnosis based on biomarkers was associated with APOE ε4 carrier status, with a higher OR than previously reported from studies based on only clinical AD criteria. This association differs according to age, with the strongest effect at 65-70 years. These findings highlight the need for early interventions for dementia prevention to mitigate the effect of APOE ε4 at the population level.

[84] *Ooba N, Iwahashi R, Nogami A et al.* **Comparison between high and low potency statins in the incidence of open-angle glaucoma: A retrospective cohort study in Japanese working-age population**. PloS one 2020; 15:e0237617.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32804969

ABSTRACT

Some findings on the association between glaucoma and statins in the Asian population have been reported. We conducted a retrospective cohort study using health insurance claims data maintained by the JMDC Inc., which comprises data on about three million individuals representing 2.4% of the Japanese population. The association between the potency of statins and open-angle glaucoma in Japanese working-age population was examined using a commercially available health insurance claims and enrollment database. We identified 117,036 patients with a prescription of statins between January 1, 2005 and March 31, 2014; 59,535 patients were selected as new statin users. Of these, 49,671 (83%) patients without glaucoma who were prescribed statins for the first time were part of the primary analysis. New users of statin were defined as those with a prescription of statin at the beginning of the study, but without a prescription six months earlier. The cohort comprised 29,435 (59%) and 20,236 (41%) patients with a prescription of high-potency statin (atorvastatin and rosuvastatin) and low-potency statin (pravastatin, fluvastatin, pitavastatin, and simvastatin), respectively. Using Cox proportional hazards regression analysis, hazard ratios (HRs) were estimated for glaucoma adjusted for baseline characteristics. Although some baseline characteristics were not similar between the high-potency and low-potency statin groups, the standardized difference for all covariates was less than 0.1. No associations were found between high-potency statin use and glaucoma (adjusted HR = 1.08; 95% confidence interval, 0.93-1.24) in the primary analyses, using the risk for glaucoma in the low-potency statin group as reference. The risk of glaucoma with individual statin use was not significantly different from that with pravastatin. No significant association was found between high-potency statins and the

increased risk of glaucoma in Japanese working-age population. Further studies are needed to examine the association between statins and glaucoma in the elderly population.

[85] *Pellegrin M, Bouzourène K, Aubert JF et al.* **Impact of aerobic exercise type on blood flow, muscle energy metabolism, and mitochondrial biogenesis in experimental lower extremity artery disease**. Scientific reports 2020; 10:14048.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32820213
ABSTRACT
Exercise training (ET) is recommended for lower extremity artery disease (LEAD) management. However, there is still little information on the hemodynamic and metabolic adaptations by skeletal muscle with ET. We examined whether hindlimb perfusion/vascularization and muscle energy metabolism are altered differently by three types of aerobic ET. ApoE(-/-) mice with LEAD were assigned to one of four groups for 4 weeks: sedentary (SED), forced treadmill running (FTR), voluntary wheel running (VWR), or forced swimming (FS). Voluntary exercise capacity was improved and equally as efficient with FTR and VWR, but remained unchanged with FS. Neither ischemic hindlimb perfusion and oxygenation, nor arteriolar density and mRNA expression of arteriogenic-related genes differed between groups. (18)FDG PET imaging revealed no difference in the steady-state levels of phosphorylated (18)FDG in ischemic and non-ischemic hindlimb muscle between groups, nor was glycogen content or mRNA and protein expression of glucose metabolism-related genes in ischemic muscle modified. mRNA (but not protein) expression of lipid metabolism-related genes was upregulated across all exercise groups, particularly by non-ischemic muscle. Markers of mitochondrial content (mitochondrial DNA content and citrate synthase activity) as well as mRNA expression of mitochondrial biogenesis-related genes in muscle were not increased with ET. Contrary to FTR and VWR, swimming was ineffective in improving voluntary exercise capacity. The underlying hindlimb hemodynamics or muscle energy metabolism are unable to explain the benefits of running exercise.

[86] *Liang CY, Cao YP, Yan Y*. **[Blood lipid metabolic profile of overweight/obese boys aged 9-12 years]**. Zhongguo Dang Dai Er Ke Za Zhi 2020; 22:874-881.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=32800035
ABSTRACT
OBJECTIVE: To study the features of blood lipid metabolic profile in overweight/obese boys aged 9-12 years and the possible mechanism of overweight/obesity in children. METHODS: According to body mass index (BMI), 72 boys, aged 9-12 years, were divided into a control group with 42 boys and an overweight/obesity group with 30 boys. Fasting venous blood samples were collected early in the morning. BMI, waist-hip ratio, body composition, and blood lipids were measured. Ultra-performance liquid chromatography-quadrupole time-of-flight mass spectrometry technique was used to analyze the serum lipid compounds. A statistical analysis and visualization of the data were performed. RESULTS: Compared with the control group, the overweight/obesity group had significantly higher waist-hip ratio, body fat percentage, and triglyceride level ($P<0.05$) and a significantly lower level of high-density lipoprotein cholesterol ($P<0.05$). The metabolomic analysis identified 150 differentially expressed lipid compounds between the two groups, mainly glycerolipids (40.7%), glycerophospholipids (24.7%), fatty acyls (10.7%), and sphingolipids (7.3%). The levels of most of glycerolipids were significantly upregulated in the overweight/obesity group, while those of most of glycerophospholipids and

sphingolipids were downregulated in this group. Key lipids with differential expression were enriched into two KEGG metabolic pathways, i.e., ether lipid metabolism pathway and terpenoid backbone biosynthesis pathway ($P<0.05$), and might further affected the biosynthesis and metabolism of downstream coenzyme Q and other terpenoids ($P=0.06$). CONCLUSIONS: Disordered lipid metabolic profile is observed in overweight/obese boys aged 9-12 years, with increases in most glycerolipids and reductions in glycerophospholipids and sphingolipids. Overweight/obese boys may have disorders in ether lipid metabolism and biosynthesis of terpenoid and even coenzyme Q.
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