[1] *Rea F, Savaré L, Corrao G, Mancia G*. **Adherence to Lipid-Lowering Treatment by Single-Pill Combination of Statin and Ezetimibe**. Adv Ther 2021; 38:5270-5285.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34480293

ABSTRACT

INTRODUCTION: Although several studies have shown that a simplified cardiovascular drug treatment leads to better treatment adherence, limited and conflicting findings have been reported on the separate or single-pill combination of the now recommended association between a statin and ezetimibe. We addressed this issue in a large cohort of patients newly treated with statins to whom ezetimibe was additionally administered, either separately or as a single-pill combination. METHODS: A total of 256,012 patients (age 40-80 years) from the Lombardy Region (Italy) newly treated with statins during 2011-2013 were followed until 2018 to identify those to whom ezetimibe was added. The 2881 and 5351 patients who started a two-pill or a single-pill combination, respectively, of statin and ezetimibe were identified and matched for propensity score. Adherence to drug therapy at 1 year was measured as the ratio between the number of days in which the drug was available and the days of follow-up (the proportion of days covered; PDC). Patients who had a PDC > 75% or < 25% were, respectively, defined as highly and poorly adherent to drug therapy. Analysis was extended to the association between adherence and the risk of fatal/non-fatal cardiovascular events. RESULTS: Compared to those prescribed a two-pill combination, those prescribed a single-pill combination had an 87% (75-99%) greater odds of being highly adherent and a 79% (72-84%) lower odds of being poorly adherent to treatment. These advantages were manifest in all strata of age, sex, and clinical profile. The risk of cardiovascular outcomes decreased by 55% in patients with high adherence compared to those with low adherence. CONCLUSION: Patients who were prescribed a single-pill combination of statin/ezetimibe more frequently exhibit a good adherence and less frequently bad adherence to treatment than those prescribed a two-pill combination of these drugs.

[2] *Plutzky J, Benson MD, Chaney K et al.* **Population health management of low-density lipoprotein cholesterol via a remote, algorithmic, navigator-executed program**. American heart journal 2021; 243:15-27.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34481756

ABSTRACT

BACKGROUND: Implementation of guideline-directed cholesterol management remains low despite definitive evidence establishing such measures reduce cardiovascular (CV) events, especially in high atherosclerotic CV disease (ASCVD) risk patients. Modern electronic resources now exist that may help improve health care delivery. While electronic medical records (EMR) allow for population health screening, the potential for coupling EMR screening to remotely delivered algorithmic population-based management has been less studied as a way of overcoming barriers to optimal cholesterol management. METHODS: In an academically affiliated healthcare system, using EMR screening, we sought to identify 1,000 high ASCVD risk patients not meeting guideline-directed low-density lipoprotein-cholesterol (LDL-C) goals within specific system-affiliated primary care practices. Contacted patients received cholesterol education and were offered a remote, guideline-directed, algorithmic cholesterol management program executed by trained but non-licensed "navigators" under professional supervision. Navigators used telephone, proprietary software and internet resources to facilitate algorithm-driven, guideline-based medication initiation/titration, and laboratory testing until patients achieved LDL-C goals or exited the program. As a clinical effectiveness program

for cholesterol guideline implementation, comparison was made to those contacted patients who declined program-based medication management, and received education only, along with their usual care. RESULTS: 1021 patients falling into guideline-defined high ASCVD risk groups warranting statin therapy (ASCVD, type 2 diabetes, LDL ≥ 190 mg/dL, calculated 10-year ASCVD risk ≥7.5%) and not achieving guideline-defined target LDL-C levels and/or therapy were identified and contacted. Among the 698 such patients who opted for program medication management, significant LDL-C reductions occurred in the total cohort (mean -65.4 mg/dL, 45% decrease), and each high ASCVD risk subgroup: ASCVD (-57.2 mg/dL, -48.0%); diabetes mellitus (-53.1 mg/dL, -40.0%); severe hypercholesterolemia (-76.3 mg/dL, -45.7%); elevated ASCVD 10-year risk (-62.8 mg/dL, -41.1%) (P<0.001 for all), without any significant complications. Among 20% of participants with reported statin intolerance, average LDL-C decreased from baseline 143 mg/dL to 85 mg/dL using mainly statins and ezetimibe, with limited PCSK9 inhibitor use. In comparison, eligible high ASCVD risk patients who were contacted but opted for education only, a 17% LDL-C decrease occurred over a similar timeframe, with 80% remaining with an LDL-C over 100 mg/dL. CONCLUSIONS: A remote, algorithm-driven, navigator-executed cholesterol management program successfully identified high ASCVD risk undertreated patients using EMR screening and was associated with significantly improved guideline-directed LDL-C control, supporting this approach as a novel strategy for improving health care access and delivery.

[3] *Bax AM, Yoon YE, Gianni U et al.* **Plaque Character and Progression According to the Location of Coronary Atherosclerotic Plaque**. The American journal of cardiology 2021; 158:15-22.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34465463
ABSTRACT
Although acute coronary syndrome culprit lesions occur more frequently in the proximal coronary artery, whether the proximal clustering of high-risk plaque is reflected in earlier-stage atherosclerosis remains unclarified. We evaluated the longitudinal distribution of stable atherosclerotic lesions on coronary computed tomography angiography (CCTA) in 1,478 patients (mean age, 61 years; men, 58%) enrolled from a prospective multinational registry of consecutive patients undergoing serial CCTA. Of 3,202 coronary artery lesions identified, 2,140 left lesions were classified (based on the minimal lumen diameter location) into left main (LM, n = 128), proximal (n = 739), and other (n = 1,273), and 1,062 right lesions were classified into proximal (n = 355) and other (n = 707). Plaque volume (PV) was the highest in proximal lesions (median, 26.1 mm(3)), followed by LM (20.6 mm(3)) and other lesions (15.0 mm(3), p <0.001), for left lesions, and was lager in proximal (25.8 mm(3)) than in other lesions (15.2 mm(3), p <0.001) for right lesions. On both sides, proximally located lesions tended to have greater necrotic core and fibrofatty components than other lesions (left: LM, 10.6%; proximal, 5.8%; other, 3.4% of the total PV, p <0.001; right: proximal, 8.4%; other 3.1%, p <0.001), with less calcified plaque component (left: LM, 18.3%; proximal, 30.3%; other, 37.7%, p <0.001; right: proximal, 23.3%, other, 36.6%, p <0.001), and tended to progress rapidly (adjusted odds ratios: left: LM, reference; proximal, 0.95, p = 0.803; other, 0.64, p = 0.017; right: proximal, reference; other, 0.52, p <0.001). Proximally located plaques were larger, with more risky composition, and progressed more rapidly.

[4] *Chiang CW*. **Meta-analysis Comparing the Effect of Combined Omega-3+Statin Therapy Versus Statin Therapy Alone on Coronary Artery Plaques**. The American journal of cardiology 2021; 158:149-150.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34465459
ABSTRACT

[5] *Ashen MD, Carson KA, Ratchford EV*. **Coronary Calcium Scanning and Cardiovascular Risk Assessment Among Firefighters**. American journal of preventive medicine 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34456104
ABSTRACT
INTRODUCTION: Sudden cardiac death is the main cause of death among firefighters. The goal of this study is to identify firefighters at risk for cardiovascular disease using coronary artery calcium screening. METHODS: Asymptomatic firefighters aged ≥40 years without known cardiovascular disease or diabetes (N=487) were recruited from fire departments in 3 Maryland counties from 2016 to 2018, with data analysis from 2018 to 2019. The cardiovascular disease prevention program included an evaluation of blood pressure, cholesterol, BMI, fasting glucose, medications, and a coronary calcium scan. A subset (n=100) was evaluated in more detail, including family history, metabolic syndrome, diet, exercise, smoking, and atherosclerotic cardiovascular disease risk score. RESULTS: Results indicated that 191 (39%) firefighters had a coronary artery calcium score >0, of which 91% were above the average for age, sex, and ethnicity. On univariable logistic regression, older age, male sex, hypertension, BMI, and glucose were significantly ($p<0.05$) associated with a higher likelihood of having any coronary artery calcium. Multiple logistic regression found that older age; male sex; taking lipid-lowering or antihypertensive medications; and higher low-density lipoprotein cholesterol, BMI, and fasting blood glucose were significantly associated with a higher likelihood of having coronary artery calcium. Of those with coronary artery calcium, 141 (74%) were not on lipid-lowering medication. In addition, 47 (94%) of those on lipid-lowering medication had a low-density lipoprotein cholesterol >70 mg/dL. In the detailed subset, 30 (30%) had coronary artery calcium. Among these, 28 (93%) had an atherosclerotic cardiovascular disease risk score <7.5%. Thus, if atherosclerotic cardiovascular disease scores alone were used to assess risk in this subset, an opportunity would have been missed to identify and treat firefighters who may have benefited from more aggressive treatment. CONCLUSIONS: A coronary artery calcium scan may identify the firefighters at increased risk for cardiovascular disease. A comprehensive cardiovascular disease prevention program implemented early in a firefighter's career may help reduce cardiovascular disease risk and thus death and disability in this high-risk population.

[6] *Marco-Benedí V, Cenarro A, Laclaustra M et al.* **Lipoprotein(a) in hereditary hypercholesterolemia: Influence of the genetic cause, defective gene and type of mutation**. Atherosclerosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34456049
ABSTRACT
BACKGROUND AND AIMS: Lipoprotein(a) [Lp(a)] concentration in heterozygous familial hypercholesterolemia (heFH) is not well established. Whether the genetic defect responsible for heFH plays a role in Lp(a) concentration is unknown. We aimed to compare Lp(a) in controls from a healthy population, in genetically diagnosed heFH and mutation-negative hypercholesterolemia subjects, and

to assess the influence on Lp(a) of the genetic defect responsible for heFH. METHODS: We conducted a cross-sectional study, performed in a lipid clinic in Spain. We studied adults with suspected heFH and a genetic study of FH genes (LDLR, APOB, APOE and PCSK9) and controls from de Aragon Workers' Health Study. HeFH patients from the Dyslipidemia Registry of the Spanish Atherosclerosis Society (SEA) were used as validation cohort. RESULTS: Adjusted geometric means (95% confidence interval) of Lp(a) in controls (n = 1059), heFH (n = 500), and mutation-negative subjects (n = 860) were 14.9 mg/dL (13.6, 16.4), 21.9 mg/dL (18.1, 25.6) and 37.4 mg/dL (33.3, 42.1), $p < 0.001$ in all comparisons. Among heFH subjects, APOB-dependent FH showed the highest Lp(a), 36.5 mg/dL (22.0, 60.8), followed by LDLR-dependent FH, 21.7 mg/dL (17.9, 26.4). These differences were also observed in heFH from the SEA cohort. The number of plasminogen-like kringle IV type-2 repeats of LPA, the hypercholesterolemia polygenic score or LDLc concentration did not explain these differences. In LDLR-dependent FH, Lp(a) levels were not different depending on the affected protein domain. CONCLUSIONS: Lp(a) is elevated in mutation-negative subjects and in heFH. The concentration of Lp(a) in heFH varies in relation to the responsible gene. Higher Lp(a) in heFH is not explained by their higher LDLc.

[7] *Venkataraman P, Huynh Q, Nicholls SJ et al.* **Impact of a coronary artery calcium-guided statin treatment protocol on cardiovascular risk at 12 months: Results from a pragmatic, randomised controlled trial**. Atherosclerosis 2021; 334:57-65.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34482089
ABSTRACT
BACKGROUND AND AIMS: Coronary artery calcium (CAC) may encourage patients to adhere to primary prevention recommendations. This study sought to evaluate the benefit of a CAC-guided risk-management protocol in those with a family history of premature coronary artery disease (FHCAD). METHODS: In this Australian multi-centre, randomized controlled trial (Coronary Artery Calcium score: Use to Guide management of Hereditary Coronary Artery Disease, CAUGHT-CAD), asymptomatic, statin-native participants at low-intermediate cardiovascular risk with FHCAD underwent CAC assessment. Those with CAC between 1 and 400 were randomized (1:1) to disclosing the CAC result to both patient and physician and commencing atorvastatin (intervention) or blinding the CAC result with risk factor education only (control). The primary endpoint of this sub-study was change in Pooled Cohort Equation (PCE) at 12 months. RESULTS: Of 1088 participants who were scanned, 450 were randomised and 214 in both groups completed 1-year follow-up. At 1 year, PCE-risk decreased by 1.0% (95% CI 0.13 to 1.81) in the CAC-disclosed group and increased by 0.43% (95%CI 0.11-0.75) in the CAC-blinded group. LDL-C decreased in the CAC-disclosed group in both those who continued (1.5 mmol/L; 95% CI 1.36 to 1.74) and discontinued statins (0.62 mmol/L; 95% CI 0.32 to 0.92) but was unchanged in the CAC-blinded group. CONCLUSION: Participants unblinded to their CAC showed reductions in LDL irrespective of statin continuation when compared to controls at 12 months. Improvements in individual risk factors and PCE risk were also noted. CAC assessment may positively influence patients and physicians to improve risk factor control.

[8] *Vrablik M, Seifert B, Parkhomenko A et al.* **Lipid-lowering therapy use in primary and secondary care in Central and Eastern Europe: DA VINCI observational study**. Atherosclerosis 2021; 334:66-75.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34482090

ABSTRACT

BACKGROUND AND AIMS: Central and Eastern Europe (CEE) is a largely understudied region, despite having the highest cardiovascular disease mortality in Europe. This analysis aimed to assess the proportion of patients in CEE who achieved their LDL-C goals based on individual cardiovascular risk recommended by the 2016 and 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines. METHODS: The DA VINCI study was a cross-sectional observational study of primary and secondary prevention patients receiving lipid-lowering therapy across Europe between June 2017 and November 2018. RESULTS: In total, 2154 patients were enrolled from the Czech Republic (n = 509), Hungary (n = 319), Poland (n = 460), Romania (n = 259), Slovakia (n = 123) and Ukraine (n = 484). At LDL-C measurement, most patients were on either moderate- or high-intensity statin monotherapy (53% and 32%, respectively). Despite this, only 44% of patients achieved risk-based LDL-C goals recommended by the 2016 ESC/EAS guidelines, ranging from 21% in Ukraine to 50% in Hungary and Romania. Only 24% of patients overall achieved the risk-based LDL-C goals recommended by the 2019 ESC/EAS guidelines, ranging from 11% in Ukraine to 32% in Poland. CONCLUSIONS: Among patients receiving lipid-lowering therapy, more than half did not achieve their 2016 LDL-C goals. In one of the first comparative analyses evaluating 2019 risk-based goal attainment among countries in CEE, three-quarters of patients did not meet their 2019 LDL-C goals, highlighting a significant gap between guidelines and clinical practice for lipid management in CEE.

[9] *Brett T, Radford J, Heal C et al.* **Implications of new clinical practice guidance on familial hypercholesterolaemia for Australian general practitioners**. Australian journal of general practice 2021; 50:616-621.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34462766

ABSTRACT

BACKGROUND: Familial hypercholesterolaemia (FH) is a monogenic lipid disorder that may be overlooked in the diagnostic process. OBJECTIVE: The aim of this article is to review the key areas for identification and management of FH that affect Australian general practitioners (GPs). DISCUSSION: Recent consensus advice on the care of patients with FH in Australia provides an opportunity for GPs to increase their awareness and skills in diagnosing and managing FH. New Medicare Benefits Schedule items for genetic testing and Pharmaceutical Benefits Scheme listing for the use of proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors offer GPs additional supports to improve the care of patients with FH. A shared-care approach between GPs and non-GP specialists with expertise in multiple disciplines offers the best option to facilitate genetic testing and management of index cases and affected family relatives. Implementation of this guidance in the primary care setting remains an ongoing challenge and needs to be embraced as a high priority.

[10] *Yun J, Jung YH, Shin SH et al.* **Impact of very preterm birth and post-discharge growth on cardiometabolic outcomes at school age: a retrospective cohort study**. BMC pediatrics 2021; 21:373.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34465300

ABSTRACT

BACKGROUND: Adverse metabolic outcomes later in life have been reported among children or young adults who were born as preterm infants. This study was conducted to examine the impact of very preterm/very low birth weight (VP/VLBW) birth and subsequent growth after hospital discharge on cardiometabolic outcomes such as insulin resistance, fasting glucose, and systolic and diastolic blood pressure (BP) among children at 6-8 years of age. METHODS: This retrospective cohort study included children aged 6-8 years and compared those who were born at <32 weeks of gestation or weighing<1,500 g at birth (n=60) with those born at term (n=110). Body size, fat mass, BP, glucose, insulin, leptin, adiponectin, and lipid profiles were measured. Weight-for-age z-score changes between discharge and early school-age period were also calculated, and factors associated with BP, fasting glucose, and insulin resistance were analyzed. RESULTS: Children who were born VP/VLBW had significantly lower fat masses, higher systolic BP and diastolic BP, and significantly higher values of fasting glucose, insulin, and homeostatic model assessment of insulin resistance (HOMA-IR), compared to children born at term. VP/VLBW was correlated with HOMA-IR and BPs after adjusting for various factors, including fat mass index and weight-for-age z-score changes. Weight-for-age z-score changes were associated with HOMA-IR, but not with BPs. CONCLUSIONS: Although children aged 6-8 years who were born VP/VLBW showed significantly lower weight and fat mass, they had significantly higher BPs, fasting glucose, HOMA-IR, and leptin levels. The associations of VP/VLBW with cardiometabolic factors were independent of fat mass and weight gain velocity.

[11] *Soldevila-Domenech N, Forcano L, Vintró-Alcaraz C et al.* **Interplay between cognition and weight reduction in individuals following a Mediterranean Diet: Three-year follow-up of the PREDIMED-Plus trial**. Clinical nutrition (Edinburgh, Scotland) 2021; 40:5221-5237.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34474192

ABSTRACT

BACKGROUND & AIMS: Some cognitive profiles might facilitate successful weight loss and its maintenance. Also, weight reductions may result in cognitive benefits. However, little work to date has examined the interactions between cognition and weight changes in the context of interventions with the Mediterranean diet (MedDiet). We studied the within-subject longitudinal relationships between cognition, body mass index (BMI), physical activity (PA), and quality of life (QoL), in older adults following a MedDiet. METHODS: The PREDIMED-Plus is a primary prevention trial testing the effect of a lifestyle intervention program with an energy-restricted MedDiet (er-MedDiet), weight-loss goals and PA promotion on cardiovascular disease. The PREDIMED-Plus-Cognition sub-study included 487 participants (50% women, mean age 65.2 ± 4.7 years), with overweight/obesity, metabolic syndrome and normal cognitive performance at baseline. A comprehensive neurocognitive test battery was administered at baseline and after 1 and 3 years. RESULTS: Baseline higher performance in verbal memory (OR = 1.5; 95%CI 1.0, 2.1), visuoconstructive praxis and attention (OR = 1.5; 95%CI 0.9, 2.3), and inhibition (OR = 1.3; 95%CI 0.9, 1.9) were associated with a higher odd of achieving at least 8% weight loss after 3 years follow-up in participants randomized to the intervention group. There were moderate improvements in specific tests of memory and executive functions during follow-up. Higher adherence to the er-MedDiet was associated with greater improvements in memory. Women exhibited lower rates of change in global cognition, PA and QoL. Moreover, improvements in memory correlated with reductions in BMI after 1 year (β(STD) = -0.14) and with improvements in PA after 3 years (β(STD) = 0.13). Finally, participants who experienced greater improvements in executive functions and global cognition also experienced greater

improvements in their QoL. CONCLUSIONS: This study refines the understanding of the determinants and mutual interrelationships between longitudinally-assessed cognitive performance and weight loss, adding further evidence to the cognitive benefits associated with better adherence to a MedDiet. Our results also suggest that weight loss interventions tailored to the cognitive profile and gender of participants are promising avenues for future studies.

[12] *Anderson K, Nelson CH, Gong Q et al.* **Assessment of the Effect of Filgotinib on the Pharmacokinetics of Atorvastatin, Pravastatin, and Rosuvastatin in Healthy Adult Participants**. Clinical pharmacology in drug development 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34468080
ABSTRACT
Filgotinib, an oral Janus kinase-1 preferential inhibitor, is approved in Europe and Japan for adults with rheumatoid arthritis. Patients with rheumatoid arthritis are at higher risk of cardiovascular morbidity/mortality; thus, it is important to understand potential drug-drug interactions of filgotinib with lipid-lowering agents. This open-label, randomized, 2-way crossover study evaluated the pharmacokinetics of atorvastatin, pravastatin, and rosuvastatin with and without filgotinib coadministration. Healthy participants (N = 27) received single doses of atorvastatin (40 mg) and of a pravastatin (40 mg)/rosuvastatin (10 mg) cocktail-alone or with filgotinib (200 mg once daily for 11 days)-on 2 different occasions with washout in between. Serial pharmacokinetic blood samples were collected, and safety was assessed. Pharmacokinetic parameters were evaluated using 90% confidence intervals (CI) of the geometric least-squares mean (GLSM) ratio of the test treatment (statin coadministration with filgotinib) vs statin alone, with prespecified lack-of-interaction bounds of 0.70 to 1.43. Coadministration of filgotinib did not affect atorvastatin area under the plasma concentration-time curve extrapolated to infinity (AUC(inf) ; [GLSM ratios (90% CI): 0.91 (0.84-0.99)]), but maximum concentration [C(max)] was slightly lower [0.82 (0.69-0.99)]. The exposure of 2-hydroxy-atorvastatin was unaffected (GLSM ratios [90% CI], 0.98 [0.81-1.19] for C(max) ; 1.11 [1.02-1.22] for AUC(inf)). Pravastatin AUC(inf) was also unaffected (GLSM ratios, 1.22 [1.05-1.41], but C(max) was slightly higher 1.25 [1.01-1.54]). Rosuvastatin exposure was moderately higher with filgotinib coadministration-GLSM ratios (90% CI), 1.68 (1.43-1.97) for C(max) ; 1.42 (1.30-1.57) for AUC(inf) -but this was not considered clinically relevant. These results indicate that filgotinib has no clinically meaningful effect on exposure of atorvastatin, pravastatin, or rosuvastatin.

[13] *Blaum C, Brunner FJ, Goßling A et al.* **Target Populations and Treatment Cost for Bempedoic Acid and PCSK9 Inhibitors: A Simulation Study in a Contemporary CAD Cohort**. Clinical therapeutics 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34462126
ABSTRACT
PURPOSE: The lowered LDL-C treatment goal of the 2019 European Society of Cardiology dyslipidemia guidelines results in a significant increase in the projected need for cost-intensive proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors. Addition of bempedoic acid (BA) to established oral lipid-lowering medication (LLM) has the potential to enable affordable LDL-C goal attainment, particularly in patients with statin intolerance (SI). The goal of this study was to quantify the target populations for BA and PCSK9 inhibitors as well as the related treatment costs to achieve the LDL-C goal of <55 mg/dL and a ≥50% reduction assuming the addition of BA to LLM. METHODS:

This study included 1922 patients with coronary artery disease (CAD) from the contemporary observational cohort study INTERCATH. A Monte Carlo simulation incorporating an algorithm adding sequentially a statin, ezetimibe, optionally BA, and a PCSK9 inhibitor was applied to achieve the LDL-C treatment goal, with consideration of both partial and total SI. Two scenarios were simulated for both a moderate (2% full and 10% partial) and a high (12% full) rate of SI: (1) without BA; and (2) with BA. FINDINGS: Patients' mean age was 69.3 years, and the median baseline LDL-C level was 86.0 mg/dL. The need for a PCSK9 inhibitor would be 41.4% for a moderate rate of SI and 46.1% for a high rate of SI. Addition of BA would: (1) reduce the need for a PCSK9 inhibitor to 25.3% and 29.4%, thus lowering the annual overall treatment cost incurred through PCSK9 inhibitor ± BA per 1 million patients with CAD by 13.3% and 10.5%; (2) lower the cost per prevented event in the entire cohort (-5.0% and -6.3%), although at the price of fewer prevented events (-8.7% and -4.5%); and (3) reduce the cost per prevented event (-6.8% for both rates of SI) while preventing more events (7.6% and 6.9%) in the subpopulation of patients with full SI. IMPLICATIONS: Use of BA is projected to reduce the need for PCSK9 inhibitors as well as the treatment cost for add-on LLM. The subpopulation of patients with full SI might profit particularly.

[14] *Shah T, McCarthy M, Nasir I et al.* **Design and rationale of the colchicine/statin for the prevention of COVID-19 complications (COLSTAT) trial**. Contemporary clinical trials 2021:106547.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34461322

ABSTRACT

BACKGROUND: Despite improvement in the standard of care (SOC) for hospitalized COVID-19 patients, rates of morbidity and mortality remain high. There continues to be a need for easily available and cost-effective treatments. Colchicine and rosuvastatin are both safe and well-studied medications with anti-inflammatory and other pleiotropic effects that may provide additional benefits to hospitalized COVID-19 patients. METHODS AND RESULTS: The Colchicine/Statin for the Prevention of COVID-19 Complications (COLSTAT) Trial is a pragmatic, open-label, multicenter, randomized trial comparing the combination of colchicine and rosuvastatin in addition to SOC to SOC alone in hospitalized COVID-19 patients. Four centers in the Yale New Haven Health network will enroll a total of 466 patients with 1:1 randomization. The trial will utilize the electronic health record (Epic® Systems, Verona, Wisconsin, USA) at all stages including screening, randomization, intervention, event ascertainment, and follow-up. The primary endpoint is the 30-day composite of progression to severe COVID-19 disease as defined by the World Health Organization ordinal scale of clinical improvement and arterial/venous thromboembolic events. The secondary powered endpoint is the 30-day composite of death, respiratory failure requiring intubation, and myocardial injury. CONCLUSIONS: The COLSTAT trial will provide evidence on the efficacy of repurposing colchicine and rosuvastatin for the treatment of hospitalized COVID-19 patients. Moreover, it is designed to be a pragmatic trial that will demonstrate the power of using electronic health records to improve efficiency and enrollment in clinical trials in an adapting landscape. CLINICAL TRIAL REGISTRATION: NCT04472611 (https://clinicaltrials.gov/ct2/show/NCT04472611).

[15] *Jahangir A, Sahra S, Krzyzak M.* **Can Clinicians Start Prescribing Inclisiran for Hypercholesterolemia Today? A Review of Clinical Studies for Internal Medicine Physicians and Endocrinologists**. Cureus 2021; 13:e16664.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34462692

ABSTRACT
The safety profile and efficacy margin of inclisiran as a lipid-lowering drug have been assessed in clinical trials and are underway in subgroups with relevant co-morbidities. This systematic review looks at the clinical trials that have been conducted to comment on its safety and efficacy. The conclusions can serve as a guide for practicing physicians and researchers for following current and future cohorts of patients. PubMed, Cochrane, Embase, Scopus, CINAHL, Web of Science, and Clinicaltrials.gov were searched comprehensively using the terms "Inclisiran", "ALN-PCSsc", and "ALN-PCS" using the Boolean operator "OR" with data cut-off date of June 28, 2020. The outcomes of safety and efficacy were collected and charted for the systematic review. In our study, eight clinical trials were included in the final study: the ORION (1,2,7,9-11) trials and two clinical trials (phase 1 randomized clinical trials) done before ORION trials. Favourable efficacy in terms of LDL levels and PSCK9 levels was observed across all eight clinical trials. No severe adverse effects, safety concerns, or fatalities attributable directly to inclisiran were reported. Therefore, our study results suggest a positive efficacy and safety profile of inclisiran as a lipid-lowering drug in clinical trials.

[16] *D'Erasmo L, Bini S, Arca M*. **Rare Treatments for Rare Dyslipidemias: New Perspectives in the Treatment of Homozygous Familial Hypercholesterolemia (HoFH) and Familial Chylomicronemia Syndrome (FCS)**. Current atherosclerosis reports 2021; 23:65.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34468855

ABSTRACT
This review aims to summarize the most recent published literature concerning lomitapide and volanesorsen that are approved for the use in HoFH and FCS patients, respectively. Moreover, it will briefly revise the published evidence on novel, non-approved treatments that are under evaluation for the management of these rare forms of dyslipidemias RECENT FINDINGS: The definition of rare dyslipidemias identifies a large number of severe disorders of lipid metabolism of genetic origin. Among them were homozygous familial hypercholesterolemia (HoFH) (OMIM #143890) and familial chylomicronemia syndrome (FCS) (OMIM #238600), which are characterized by a markedly impaired cholesterol- and triglyceride-containing lipoproteins metabolism. They are being particularly associated with poor health outcomes and quality of life. Considering the severity of these diseases, common lipid-lowering drugs are often ineffective or do not allow to achieve the recommended lipid targets to prevent the development of complications. Nowadays, several new drugs have been found to effectively treat HoFH and FCS with an acceptable safety profile. Treating patients with HoFH and FCS remains very challenging. However, novel treatment options are emerging and might be considered in addition to conventional therapy for managing these diseases. These novel drugs will possibly change the natural history of these two rare and life-threatening diseases.

[17] *Henney NC, Banach M, Penson PE*. **RNA Silencing in the Management of Dyslipidemias**. Current atherosclerosis reports 2021; 23:69.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34468873

ABSTRACT
PURPOSE OF REVIEW: Remarkable reductions in cardiovascular morbidity and mortality have been achieved in recent decades through the widespread use of 'small-molecule' hypolipidaemic drugs such as statins and ezetimibe. An alternative approach is to perturb the production of proteins through ribonucleic acid (RNA) silencing, leading to long-lasting knock-down of specific biological

molecules. This review describes the scientific basis of RNA silencing, and critically evaluates the evidence relating to inclisiran, a small interfering RNA against proprotein convertase subtilisin kexin 9 (PCSK9). RECENT FINDINGS: Pooled analysis of three recent ORION trials has demonstrated that twice-yearly administration of inclisiran reduces LDL-C by 50% in a range of patient groups, with only mild adverse effects. Inclisiran provides safe, effective and long-lasting reductions in PCSK9 and LDL-C. The results of the phase-3 ORION-4 outcomes study are eagerly awaited. Further promising RNA silencing technologies have the potential to improve the management of dyslipidaemia.

[18] *Makhmudova U, Schulze PC, Lütjohann D, Weingärtner O*. **Phytosterols and Cardiovascular Disease**. Current atherosclerosis reports 2021; 23:68.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34468867
ABSTRACT
PURPOSE OF REVIEW: Coronary heart disease is the leading cause of mortality worldwide. Elevated blood cholesterol levels are not only the major but also the best modifiable cardiovascular risk factor. Lifestyle modifications which include a healthy diet are the cornerstone of lipid-lowering therapy. So-called functional foods supplemented with plant sterols lower blood cholesterol levels by about 10-15%. RECENT FINDINGS: In the recent revision of the ESC/EAS dyslipidemia guideline 2019, plant sterols are recommended for the first time as an adjunct to lifestyle modification to lower blood cholesterol levels. However, the German Cardiac Society (DGK) is more critical of food supplementation with plant sterols and calls for randomized controlled trials investigating hard cardiovascular outcomes. An increasing body of evidence suggests that plant sterols per se are atherogenic. This review discusses this controversy based on findings from in vitro and in vivo studies, clinical trials, and genetic evidence.

[19] *Tokgozoglu L, Kayikcioglu M*. **Familial Hypercholesterolemia: Global Burden and Approaches**. Current cardiology reports 2021; 23:151.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34480646
ABSTRACT
PURPOSE OF REVIEW: Familial hypercholesterolemia (FH) is the most common genetic metabolic disorder characterized by markedly elevated LDL-C levels from birth leading to atherosclerotic cardiovascular disease (ASCVD) and premature deaths. The purpose of this review is to share the current knowledge in the diagnosis, risk estimation, and management of patients with FH in the light of recent evidence and guideline recommendations. RECENT FINDINGS: Recent registries underscored the prevalence of FH as 1/200-250 translating to an almost 1500 million subjects suffering from FH worldwide. However, only a minority of FH patients are identified early and effectively treated. In most cases, mutations in the LDL-receptor (LDLR) gene and to a lesser degree in the apolipoprotein B-100 (APOB), proprotein convertase subtilisin/kexin type 9 (PCSK9), and the LDL-receptor adaptor protein 1 (LDLRAP1) genes cause FH. Diagnostic scores such as Dutch Lipid Clinic Network criteria using clinical manifestations are helpful in identifying FH. Traditional risk factors and high lipoprotein(a) affect the course of the disease. Vascular ultrasound imaging and coronary calcium scoring are helpful for further risk estimation of these patients. Getting to LDL-C goals is possible with currently available treatments including statins, ezetimibe, and PCSK9 inhibitors, as well as lipoprotein apheresis, lomitapide, and mipomersen in more severe phenotypes. Additionally, novel agents bempedoic acid, inclisiran, and evinacumab expanded the treatment

choices for some patients with FH. Early diagnosis and initiation of LDL-C lowering are still required to achieve the greatest reduction in ASCVD morbidity and mortality in patients with FH. FH is a common genetic disorder characterized by markedly elevated LDL-C levels from birth onward, resulting in significantly increased risk for ASCVD. Despite major advances in our understanding of the disease and effective therapies, FH is still underdiagnosed and undertreated. Early initiation of LDL-C lowering by increased awareness of FH among the healthcare professionals, patients, and the public is necessary to achieve meaningful reduction in ASCVD morbidity and mortality in these patients.

[20] *Arnold N, Koenig W*. **Persistent inflammatory residual risk despite aggressive cholesterol-lowering therapy: what is next?** Current opinion in cardiology 2021; 36:776-783.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34475328
ABSTRACT
PURPOSE OF REVIEW: To briefly summarize recently published evidence on the possible therapeutic modulation of inflammatory processes in atherosclerotic cardiovascular disease (ASCVD), focusing on the rationale for an additional randomized clinical trial, targeting both persistently elevated cholesterol and inflammatory residual risk and critically discuss still open issues and future perspectives with regard to treatment allocation. RECENT FINDINGS: Several large-scale clinical trials over the past few years have advanced our understanding of the role of inflammation in atherosclerosis, demonstrating that targeting the NLRP3 inflammasome and the IL-1β pathway indeed represent a new avenue to reduce residual risk in patients with ASCVD. However, despite optimal lipid-lowering therapy and novel options to modulate residual inflammatory risk, there are still a large number of individuals, being at high risk for recurrent ASCVD events. SUMMARY: The integration of a dual target strategy aimed at lowering the inflammatory burden in combination with aggressive lipid-modifying for those at high/very high ASCVD risk may hold potential to significantly improve patient care. However, a number of questions related to the design of such 2×2 factorial trial still needs to be answered.

[21] *Yoshida Y, Chen Z, Baudier RL et al.* **Early Menopause and Cardiovascular Disease Risk in Women With or Without Type 2 Diabetes: A Pooled Analysis of 9,374 Postmenopausal Women**. Diabetes Care 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34475032
ABSTRACT
OBJECTIVE: Early menopause may be associated with higher cardiovascular disease (CVD) risk. Type 2 diabetes mellitus (T2DM), coupled with early menopause, may result in even greater CVD risk in women. We examined CVD risk in women with early compared with normal-age menopause, with and without T2DM overall, and by race/ethnicity. RESEARCH DESIGN AND METHODS: We pooled data from the Atherosclerosis Risk in Communities study, the Multi-Ethnic Study of Atherosclerosis, and the Jackson Heart Study. We included women with data on menopausal status, menopausal age, and T2DM, excluding pre- or perimenopausal women and those with prevalent CVD. Outcomes included incident coronary heart disease (CHD), stroke, heart failure (HF), and atherosclerotic cardiovascular disease (ASCVD) (CHD or stroke). We estimated the risk associated with early (<45 years) compared with normal-age menopause using Cox proportional hazards models. Covariates included age, race/ethnicity, education, BMI, blood pressure, cholesterol, smoking, alcohol

consumption, antihypertensive medication, lipid-lowering medication, hormone therapy use, and pregnancy history. RESULTS: We included 9,374 postmenopausal women for a median follow-up of 15 years. We observed 1,068 CHD, 659 stroke, 1,412 HF, and 1,567 ASCVD events. T2DM significantly modified the effect of early menopause on CVD risk. Adjusted hazard ratios for early menopause and the outcomes were greater in women with T2DM versus those without (CHD 1.15 [95% CI 1.00, 1.33] vs. 1.09 [1.03, 1.15]; stroke 1.21 [1.04, 1.40] vs. 1.10 [1.04, 1.16]; ASCVD 1.29 [1.09, 1.51] vs. 1.10 [1.04, 1.17]; HF 1.18 [1.00, 1.39] vs. 1.09 [1.03, 1.16]). The modifying effect of T2DM on the association between early menopause and ASCVD was only statistically significant in Black compared with White women. CONCLUSIONS: Early menopause was associated with an increased risk for CVD in postmenopausal women. T2DM may further augment the risk, particularly in Black women.

[22] *Liu D, Zhong J, Wen W et al.* **Relationship Between Skeletal Muscle Mass to Visceral Fat Area Ratio and Cardiovascular Risk in Type 2 Diabetes**. Diabetes, metabolic syndrome and obesity : targets and therapy 2021; 14:3733-3742.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34471365
ABSTRACT
PURPOSE: Either visceral fat or muscle mass is identified to be correlated with cardiometabolic diseases, especially in type 2 diabetes (T2DM). But, the synergistical effect of visceral fat along with skeletal muscle on the risk of cardiovascular diseases (CVD) in T2DM still remains controversial. Thus, we investigated the relationship between skeletal muscle mass to visceral fat area ratio (SVR) and 10-yr CVD risk scores. PATIENTS AND METHODS: A total of 291 T2DM patients aged 40-80 years were enrolled in the current study. SVR was evaluated based on bioelectrical impedance measurements. Both Framingham risk score system and China-PAR risk model were applied to estimate future 10-yr CVD risk in T2DM population. RESULTS: The 10-yr CVD risk scores increased with the decreased SVR tertiles in T2DM (All $P<0.001$). SVR value was obviously lower in the high-risk group than that of low- or moderate-risk group (All $P<0.05$). However, no significant differences were observed in BMI among different CVD risk groups. Besides, SVR was correlated with Framingham risk score ($r=-0.408$; $P<0.001$) and China-PAR risk score ($r=-0.336$; $P<0.001$). HOMA-IR, triglycerides and blood pressure were also inversely related to SVR (All $P<0.05$). Furthermore, SVR value was independently correlated with both Framingham 10-yr CVD risk score ($\beta=-0.074$, $P=0.047$) and China-PAR risk score ($\beta=-0.100$, $P=0.004$) after adjustment for confounding factors, including age, gender, BMI, FPG, HbA1c, diabetes duration, albumin, creatinine, uric acid, smoking, blood pressure and blood lipid. The linear regression analysis was also conducted for men and women, respectively, indicating that the negative relationship between SVR and 10-yr CVD risk was observed in men but not in women. CONCLUSION: T2DM populations who have lower SVR value are more likely to increase CVD risk. SVR levels show marked and inverse correlation with estimated 10-yr CVD risk in T2DM, indicating that SVR could be a valuable parameter to assess the risk of CVD events in clinical practice, especially in men.

[23] *Ginsberg HN, Packard CJ, Chapman MJ et al.* **Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies-a consensus statement from the European Atherosclerosis Society**. European heart journal 2021.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34472586

ABSTRACT

Recent advances in human genetics, together with a large body of epidemiologic, preclinical, and clinical trial results, provide strong support for a causal association between triglycerides (TG), TG-rich lipoproteins (TRL), and TRL remnants, and increased risk of myocardial infarction, ischaemic stroke, and aortic valve stenosis. These data also indicate that TRL and their remnants may contribute significantly to residual cardiovascular risk in patients on optimized low-density lipoprotein (LDL)-lowering therapy. This statement critically appraises current understanding of the structure, function, and metabolism of TRL, and their pathophysiological role in atherosclerotic cardiovascular disease (ASCVD). Key points are (i) a working definition of normo- and hypertriglyceridaemic states and their relation to risk of ASCVD, (ii) a conceptual framework for the generation of remnants due to dysregulation of TRL production, lipolysis, and remodelling, as well as clearance of remnant lipoproteins from the circulation, (iii) the pleiotropic proatherogenic actions of TRL and remnants at the arterial wall, (iv) challenges in defining, quantitating, and assessing the atherogenic properties of remnant particles, and (v) exploration of the relative atherogenicity of TRL and remnants compared to LDL. Assessment of these issues provides a foundation for evaluating approaches to effectively reduce levels of TRL and remnants by targeting either production, lipolysis, or hepatic clearance, or a combination of these mechanisms. This consensus statement updates current understanding in an integrated manner, thereby providing a platform for new therapeutic paradigms targeting TRL and their remnants, with the aim of reducing the risk of ASCVD.

[24] *Dong J, Wang M, Gao J et al.* **Association between the levels of CGI-58 and lipoprotein lipase in the placenta of patients with preeclampsia**. Experimental and therapeutic medicine 2021; 22:1129.

PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34466143

ABSTRACT

Preeclampsia is an idiopathic disease of pregnancy, which seriously endangers the life of both the mother and the infant. The pathogenesis of preeclampsia has not been fully elucidated, although it is generally considered to be associated with abnormal lipid metabolism during pregnancy. Comparative gene identification-58 (CGI-58) and lipoprotein lipase (LPL) are involved in the first step of triglyceride hydrolysis and serve an important role in lipid transport in the placenta. The present study aimed therefore to investigate the association between CGI-58 and LPL in the placentas of patients with or without preeclampsia and to evaluate blood lipid levels. The patient cohort was divided into two groups, pregnant women with preeclampsia and normal pregnant women (control). According to biochemical analyses, reverse transcription-quantitative PCR, immunohistochemistry analysis and western blotting, the expression of CGI-58 and LPL in the placenta was detected, the blood lipid levels were evaluated and other clinical data were collected. Compared with the control group, triglycerides (TGs), low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (ApoB) and atherosclerotic index (AI) were significantly higher in the preeclampsia group, whereas high density lipoprotein-cholesterol (HDL-C) and apolipoprotein A (ApoA) were significantly lower ($P<0.05$). Furthermore, the expression levels of CGI-58 and LPL in the placental tissue of the preeclampsia group was significantly lower than that of the control group ($P<0.05$). Linear correlation analysis demonstrated that there was a positive association between CGI-58 and LPL ($r=0.602$; $P<0.05$), that CGI-58 was positively associated with HDL-C ($r=0.63$; $P<0.01$) but negatively associated with TG and

ApoB (r=0.840; P<0.01; and r=0.514; P<0.05, respectively), that LPL was positively associated with HDL-C (r=0.524; P<0.01) but negatively associated with TG and AI (r=0.659; P<0.01; and r=0.496; P<0.01, respectively). These results suggested that the expression of CGI-58 and LPL in the placenta was associated with the pathogenesis of preeclampsia and maternal lipids and the risk of preeclampsia was increased with decreasing expression levels of CGI-58 and LPL. Hence, CGI-58 and LPL may be used as important indicators for the diagnosis of preeclampsia and for the prevention of preeclampsia in pregnant women.

[25] *Gao Y, Li L, Yu J, Zhang Z*. **Rosuvastatin protects PC12 cells from hypoxia/reoxygenation-induced injury by inhibiting endoplasmic reticulum stress-induced apoptosis**. Experimental and therapeutic medicine 2021; 22:1189.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34475979
ABSTRACT
The endoplasmic reticulum stress (ERS) response serves an important role in cerebral ischemia-reperfusion injury (CIRI). However, to the best of the our knowledge, the effect of rosuvastatin on the ERS response in CIRI has not yet been studied. In the present study, the effect of rosuvastatin on cell damage in CIRI was investigated; furthermore, the effect of rosuvastatin on the ERS response was explored. Firstly, a hypoxia/reoxygenation (H/R)-induced cell damage model was established in PC12 cells. Cell viability was subsequently detected by a Cell Counting Kit-8 assay. A lactate dehydrogenase kit was used to detect cytotoxicity. TUNEL assay was then used to measure the extent of cell apoptosis, and western blotting was used to analyze the expression levels of the apoptosis-associated proteins Bax, Bcl-2, cleaved caspase-3 and cleaved caspase-9. In addition, western blotting was used to detect the expression levels of ERS-associated proteins, including phosphorylated (p)-protein kinase R-like endoplasmic reticulum kinase (PERK), p-eukaryotic initiation factor 2α and other proteins. Treatment with rosuvastatin led to an increased activity of H/R-induced PC12 cells and a decrease in their cytotoxicity. Rosuvastatin also led to an inhibition in apoptosis and ERS in H/R-induced PC12 cells. After administration of the ERS response activator thapsigargin (TG), TG was found to reverse the protective effect of rosuvastatin on injury of H/R-induced PC12 cells. Taken together, these findings have shown that rosuvastatin is able to protect PC12 cells from H/R-induced injury via inhibiting ERS-induced apoptosis, providing a strong theoretical basis for the use of rosuvastatin in the clinical treatment of CIRI.

[26] *Kaneko S*. **Novel approaches to pharmacological management of type 2 diabetes in Japan**. Expert opinion on pharmacotherapy 2021:1-15.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34461791
ABSTRACT
INTRODUCTION: Newly developed anti-diabetic medications have had multiple activities, beyond a blood glucose-lowering effect. Current drugs for treating type 2 diabetes mellitus (T2DM) are based on the use of gastrointestinal hormones. Representative incretin preparations, such as those with glucagon-like peptide (GLP)-1 or gastric inhibitory polypeptide (GIP) activity, aim to provide new means of controlling blood glucose levels, body weight, and lipid metabolism. In this manuscript, the pathophysiology of T2DM and the activities and characteristics of novel diabetic drugs are reviewed in the context of the Japanese population. This review also highlights the need for novel medicines to overcome the accompanying challenges. Finally, the author provides the reader with their expert

perspectives. The incidence of T2DM has been increasing in the aging of Japanese society. In older people, medical development should focus on safety, easier self-administration, and the relief of caregiver burden in terms of continuous administration. In the young, the focus should be on effectiveness, with a particular emphasis on the protection of organs, increasing the ease of adherence, and safety. Novel medicines will need to push the envelope in these areas.

[27] *Buksińska-Lisik M, Kwasiborski PJ, Ryczek R et al.* **Vitamin D Deficiency as a Predictor of a High Prevalence of Coronary Artery Disease in Pancreas Transplant Candidates With Type 1 Diabetes**. Frontiers in endocrinology 2021; 12:714728.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34456872
ABSTRACT
INTRODUCTION: Pancreas transplantation is a high-risk procedure in terms of cardiovascular complications. Therefore, identification of all cardiovascular risk factors is crucial to prevent cardiovascular complications after pancreas transplantation. Vitamin D deficiency (VDD) appears to be a potential risk factor for coronary artery disease. OBJECTIVE: To determine the prevalence of VDD in pancreas transplant candidates, and further to examine the relationship between vitamin D and the prevalence of coronary artery disease and lipid profile parameters. MATERIALS AND METHODS: This is a prospective cross-sectional study. We enrolled consecutive patients with type 1 diabetes eligible for simultaneous pancreas-kidney transplantation or pancreas transplant alone. The laboratory tests included HbA1c, lipid profile, creatinine, and total 25-hydroxyvitamin D (25(OH)D). The diagnosis of coronary artery disease was based on coronary angiography. RESULTS: The study population included 48 patients. VDD was revealed in 48% of patients and coronary artery disease in 35% of patients. The mean concentration of vitamin D in the entire cohort was 21.3 ± 9.48 ng/ml. The median value of 25(OH)D in patients with coronary artery disease was significantly lower than in patients without coronary artery disease (18.5 (11.6-21.5) vs. 24.8 (18.4-31.8) ng/ml, p = 0.018). There was a significant relationship between VDD and coronary artery disease (OR = 4.36; 95% confidence interval (CI): 1.22-15.64, p = 0.034). A patient's odds of having coronary artery disease while having a sufficient level of vitamin D was 4.36 times lower than if the patient had VDD. There was a significant relationship between VDD and hypertension (OR = 5.91; 95% CI: 1.12-31.20, p = 0.039) and hemodialysis (OR = 4.25; 95% CI: 1.25-14.5, p = 0.023). There was no significant correlation between 25(OH)D and lipid profile. CONCLUSIONS: VDD is highly prevalent in pancreas transplant candidates with type 1 diabetes. There is a significant relationship between VDD and increased prevalence of coronary disease. The lack of any significant association between serum vitamin D and lipid profile suggests that the relationship between vitamin D and coronary artery disease results from other causes.

[28] *Schuppelius B, Peters B, Ottawa A, Pivovarova-Ramich O*. **Time Restricted Eating: A Dietary Strategy to Prevent and Treat Metabolic Disturbances**. Frontiers in endocrinology 2021; 12:683140.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34456861
ABSTRACT
Time-restricted eating (TRE), a dietary approach limiting the daily eating window, has attracted increasing attention in media and research. The eating behavior in our modern society is often characterized by prolonged and erratic daily eating patterns, which might be associated with

increased risk of obesity, diabetes, and cardiovascular diseases. In contrast, recent evidence suggests that TRE might support weight loss, improve cardiometabolic health, and overall wellbeing, but the data are controversial. The present work reviews how TRE affects glucose and lipid metabolism based on clinical trials published until June 2021. A range of trials demonstrated that TRE intervention lowered fasting and postprandial glucose levels in response to a standard meal or oral glucose tolerance test, as well as mean 24-h glucose and glycemic excursions assessed using continuous glucose monitoring. In addition, fasting insulin decreases and improvement of insulin sensitivity were demonstrated. These changes were often accompanied by the decrease of blood triglyceride and cholesterol levels. However, a number of studies found that TRE had either adverse or no effects on glycemic and lipid traits, which might be explained by the different study designs (i.e., fasting/eating duration, daytime of eating, changes of calorie intake, duration of intervention) and study subject cohorts (metabolic status, age, gender, chronotype, etc.). To summarize, TRE represents an attractive and easy-to-adapt dietary strategy for the prevention and therapy of glucose and lipid metabolic disturbances. However, carefully controlled future TRE studies are needed to confirm these effects to understand the underlying mechanisms and assess the applicability of personalized interventions.

[29] *Casolo G, Gabrielli D, Colivicchi F et al.* **[ANMCO Position paper: Prognostic and therapeutic relevance of non-obstructive coronary atherosclerosis]**. Giornale italiano di cardiologia (2006) 2021; 22:767-777.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34463686
ABSTRACT
Atherosclerosis often affects the coronary arterial tree. Very often the disease does not translate in significant narrowing of the vessels, thus determining only a non-obstructive disease. This condition that is described as non-obstructive coronary artery disease (NobsCAD) should be distinguished from the absence of disease (i.e. smooth coronary arteries) as it carries a specific prognostic value. The detection and reporting of NobsCAD should prompt preventive measures that can be individualized upon the degree of the underlying burden of disease. The accompanying clinical condition, the other cardiovascular risk factors present, and the description of the severity and extent of NobsCAD should provide the framework for an individualized treatment that should also consider the best available evidences and scientific guidelines. The description of NobsCAD represents an important information to be collected whenever a coronary angiogram (both invasive and non-invasive) is performed. Treating the patient according to the presence and extent of NobsCAD offers prognostic benefits well beyond those offered by considering only the traditional cardiovascular risk factors. In order to reach this goal, NobsCAD should not be confused with the absence of coronary atherosclerosis or even ignored when detected as if it was a trivial information.

[30] *Sardari S, Fallahi F, Emadi F et al.* **Daily Consumption of Caper Fruit Along With Atorvastatin Has Synergistic Effects in Hyperlipidemic Patients: Randomized Clinical Trial**. Galen Med J 2019; 8:e1345.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34466497
ABSTRACT
BACKGROUND: Dyslipidemia leads to micro- and macro-vascular complications. Atorvastatin is the main therapeutic drug used for dyslipidemia, but it causes side effects such as new type 2 diabetes

mellitus onset and elevation of liver enzymes. Herbs may be useful in reducing atorvastatin doses. Caper fruit, an herbal drug in Persian Medicine, has hypolipidemic effects. Hence, the effect of atorvastatin therapy with and without daily caper fruit pickle (CFP) consumption was assessed on hyperlipidemia. MATERIALS AND METHODS: In this single-blinded, randomized, controlled trial, 60 hyperlipidemic patients were allocated in two groups and treated with 10 mg atorvastatin plus 40-50 g CFP (A10+CFP) or atorvastatin alone (A10) for eight weeks. Biochemical parameters were measured at baseline, 4, and eight weeks of the intervention. One-way repeated measure ANOVA and mixed ANOVA were used to measure the effect of the two treatments and the interaction between the type of treatment and time on lipid profile. RESULTS: Serum total cholesterol and low-density lipoprotein cholesterol (LDL-C) were significantly decreased in the A10+CFP group compared with the A10 group ($P<0.001$ and $P<0.001$, respectively) from baseline up to the week 8. At week 4, mean changes of LDL-C was significantly higher in the A10+CFP compared with the A10 ($P=0.01$). Adjusting for the baseline variables, the mean difference of alanine aminotransferase ($P<0.01$) and triglyceride ($P=0.003$) were significantly higher in the A10+CFP group at the end. CONCLUSION: This study reports that the intake of CFP along with atorvastatin daily may have synergistic effects which improve the lipid profile in hyperlipidemic patients.

[31] *von Eckardstein A*. **High Density Lipoproteins: Is There a Comeback as a Therapeutic Target?** Handbook of experimental pharmacology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34463854
ABSTRACT
Low plasma levels of High Density Lipoprotein (HDL) cholesterol (HDL-C) are associated with increased risks of atherosclerotic cardiovascular disease (ASCVD). In cell culture and animal models, HDL particles exert multiple potentially anti-atherogenic effects. However, drugs increasing HDL-C have failed to prevent cardiovascular endpoints. Mendelian Randomization studies neither found any genetic causality for the associations of HDL-C levels with differences in cardiovascular risk. Therefore, the causal role and, hence, utility as a therapeutic target of HDL has been questioned. However, the biomarker "HDL-C" as well as the interpretation of previous data has several important limitations: First, the inverse relationship of HDL-C with risk of ASCVD is neither linear nor continuous. Hence, neither the-higher-the-better strategies of previous drug developments nor previous linear cause-effect relationships assuming Mendelian randomization approaches appear appropriate. Second, most of the drugs previously tested do not target HDL metabolism specifically so that the futile trials question the clinical utility of the investigated drugs rather than the causal role of HDL in ASCVD. Third, the cholesterol of HDL measured as HDL-C neither exerts nor reports any HDL function. Comprehensive knowledge of structure-function-disease relationships of HDL particles and associated molecules will be a pre-requisite, to test them for their physiological and pathogenic relevance and exploit them for the diagnostic and therapeutic management of individuals at HDL-associated risk of ASCVD but also other diseases, for example diabetes, chronic kidney disease, infections, autoimmune and neurodegenerative diseases.

[32] *Begic E, Causevic M*. **Glucagon-Like Peptide-1 Receptor Agonists and Brain Vascular Function**. Heart, lung & circulation 2021; 30:1675-1680.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34479819
ABSTRACT

Prevention of cardiovascular events and regression of atherosclerotic changes are the primary aims of preventive cardiovascular medicine. Arterial thrombosis is caused by endothelial dysfunction, which disrupts vascular haemostasis. Glucagon-like peptide 1 (GLP-1) receptor agonists have been initially used as glucose lowering agents, but over time have been used for other indications due to their cardiorenal benefit, as well as their benefit in the regression of atherosclerosis process. The aim of this paper is to present the benefits of GLP-1 receptor agonists in the prevention of atherosclerotic changes, in the preservation of brain vascular function, and to show the possible role in the treatment of neurodegenerative diseases.

[33] *Tomoi Y, Soga Y, Imada K et al.* **Use of Proprotein Converse Subtilisin/Kexin Type 9 Inhibitor to Treat Cholesterol Crystal Embolisms after Catheterization: A Report of Three Cases**. Intern Med 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34471031
ABSTRACT
Cholesterol crystal embolism (CCE) is a serious complication that occurs after cardiac and vascular procedures. CCE involves multiple organs, and the prognosis and renal function of patients is poor. Although the efficacy of steroid, statin, and low-density lipoprotein apheresis has been reported, no definitive treatment has been established. We herein report three consecutive cases treated with conventional steroid therapy with proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor after catheterization. The renal function was preserved, steroid therapy was stopped, and wound healing of blue toes was achieved. PCSK9 inhibitor therapy was safe in the present patient and may be a potential treatment option for CCE.

[34] *Tien N, Wu TY, Lai JN et al.* **Influences of antidepressant medications on the risk of developing hyperlipidemia in patients with depression by a population-based cohort study and on in vitro hepatic lipogenic-related gene expression**. Journal of affective disorders 2021; 295:271-283.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34482059
ABSTRACT
BACKGROUND: Depression increases the risk of cardiovascular disease (CVD). The association between antidepressant medications (ADMs) and CVD remains controversial. Hyperlipidemia is a risk factor for CVD. We conducted a nationwide population-based retrospective cohort study to examine depression and ADM use on the risk of developing hyperlipidemia. The effects of ADMs on the expression of lipogenesis-related hepatic genes were also evaluated. METHODS: We obtained data from the Longitudinal Health Insurance Database of Taiwan on patients with new-onset depression and a comparison cohort without depression. A Cox proportional hazards regression model was used to analyze the differences in the risk of developing hyperlipidemia between these two cohorts. We also examined the influence of ADMs on the expression of lipogenesis-related hepatic genes. RESULTS: After adjustment for comorbidities and confounding factors, the case group (N = 38,322) had a higher risk for hyperlipidemia than that of the control cohort (N = 38,322) [adjusted hazards ratio (aHR) =1.16]. Patients with depression who did not receive ADM therapy exhibited a significantly higher risk of hyperlipidemia (aHR = 1.61). However, in patients with depression treated with ADMs, the risk of developing hyperlipidemia was significantly lowered compared to the patients without ADMs (all aHR < 0.81). Gene expression analysis indicated that ADMs downregulated the expression

of lipogenesis-related hepatic genes. LIMITATIONS: Unmeasured confounding risk factors for hyperlipidemia might not have been included in the study. CONCLUSIONS: ADMs reduced hyperlipidemia risk in patients with depression, partly by downregulating the expression of lipogenesis-related genes and improving the patients' lipid profiles. Early diagnosis and management of hyperlipidemia would further facilitate the prevention of CVD.

[35] *Eid WE, Sapp EH, Flerlage E, Nolan JR*. **Lower-Intensity Statins Contributing to Gaps in Care for Patients With Primary Severe Hypercholesterolemia**. Journal of the American Heart Association 2021; 10:e020800.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34465130
ABSTRACT
Background Although severe hypercholesterolemia confers a 5-fold increased long-term risk for coronary artery disease, treatment guidelines may not be fully implemented, leading to underdiagnosis and suboptimal treatment. To further understand the clinical features and gaps in treatment approaches, we analyzed electronic medical record data from a midwestern US multidisciplinary healthcare system, between 2009 and 2020. Methods and Results We retrospectively assessed the prevalence, clinical presentation, and treatment characteristics of individuals currently treated with statin therapy having a low-density lipoprotein cholesterol (LDL-C) value that is either (1) an actual maximum electronic medical record-documented LDL-C ≥190 mg/dL (group 1, n=7542) or (2) an estimated pretreatment LDL-C ≥190 mg/dL (group 2, n=7710). Comorbidities and prescribed lipid-lowering therapies were assessed. Statistical analyses identified differences among individuals within and between groups. Of records analyzed (n=266 282), 7% met the definition for primary severe hypercholesterolemia. Group 1 had more comorbidities than group 2. More individuals in both groups were treated by primary care providers (49.8%-53.0%, 32.6%-36.4%) than by specialty providers (4.1%-5.5%, 2.1%-3.3%). High-intensity lipid-lowering therapy was prescribed less frequently for group 2 than for group 1, but moderate-intensity statins were prescribed more frequently for group 2 (65%) than for group 1 (52%). Conclusions Two percent of patients in our study population being treated with low- or moderate-intensity statins have an estimated LDL-C ≥190 mg/dL (indicating severe hypercholesterolemia), but receive less aggressive treatment than patients with a maximum measured LDL-C ≥190 mg/dL.

[36] *Naito R, Daida H, Masuda D et al.* **Relation of Serum Lipoprotein(a) Levels to Lipoprotein and Apolipoprotein Profiles and Atherosclerotic Diseases in Japanese Patients with Heterozygous Familial Hypercholesterolemia: Familial Hypercholesterolemia Expert Forum (FAME) Study**. Journal of atherosclerosis and thrombosis 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34456199
ABSTRACT
AIMS: Lipoprotein(a) [Lp(a)] is a plasma lipoprotein consisting of a low-density lipoprotein (LDL)-like particle with apolipoprotein (Apo)(a), attached via a disulfide bond to Apo B100. Previous studies have shown that high Lp(a) levels are associated with an increased risk of cardiovascular disease in patients with familial hypercholesterolemia (FH). To date, limited data are available as to distribution of Lp(a) in FH and associations of Lp(a) with other lipid profiles and cardiovascular disease. Our study aimed to investigate serum Lp(a) levels in relation to other lipid profiles and clinical conditions in the national largest-ever cohort of Japanese FH patients. METHODS: This study is a secondary

analysis of the Familial Hypercholesterolemia Expert Forum (FAME) Study that includes a Japanese nationwide cohort of FH patients. In 399 patients under treatment for heterozygous FH who had a baseline measurement of serum Lp(a), the present study examined the distribution of Lp(a) levels and associations of Lp(a) with other lipid profiles and clinical conditions including coronary artery disease (CAD). RESULTS: The distribution of Lp(a) was skewed to the right with a median of 20.8 mg/dL, showing a log-normal distribution. Serum Apo B and Apo E levels were positively associated with Lp(a) levels. Age-adjusted mean of Apo B was 8.77 mg/dL higher and that of Apo E was 0.39 mg/dL higher in the highest category (40+ mg/dL) of Lp(a) than in the lowest category (＜20 mg/dL). LDL-C levels did not show such an association with Lp(a) levels. A tendency towards a positive relationship between Lp(a) and prevalent CAD was observed in men. CONCLUSION: Our study demonstrated a distribution pattern of Lp(a) in Japanese FH patients and positive relationships of Lp(a) with Apo B and Apo E levels.

[37] *Abe T, Sato K, Sekiguchi H et al.* **A case of heterozygous familial hypercholesterolemia requiring strict low-density lipoprotein cholesterol management with proprotein convertase subtilisin/kexin 9 inhibitor after coronary artery bypass grafting**. Journal of cardiology cases 2021; 24:126-130.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34466176
ABSTRACT
Heterozygous familial hypercholesterolemia (HeFH) is a common, autosomal dominant, genetic disease that results in premature atherosclerotic cardiovascular disease secondary to high-level low-density lipoprotein cholesterol (LDL-C) exposure. We present a 68-year-old male patient with HeFH who was diagnosed with acute coronary syndrome at 9 months after coronary artery bypass grafting, although his LDL-C level was decreased to 77 mg/dL from 213 mg/dL. The emergency coronary angiography revealed that all bypass grafts were occluded, and the large atherosclerotic plaque burden was observed even in right internal thoracic artery (RITA) by intravascular ultrasound examination. Emergency percutaneous coronary intervention (PCI) was performed to his RITA bypass graft. After strict LDL-C management with proprotein convertase subtilisin/kexin 9 (PCSK-9) inhibitors, re-stenosis was not observed at the PCI site and the atherosclerotic plaque burden in his graft drastically disappeared. The high-risk HeFH patients, including those suffering from coronary bypass graft stenosis despite receiving medical therapy, might need stricter management of lipid profile with PCSK-9 inhibitors. <Learning objective: Heterozygous familial hypercholesterolemia (HeFH) is one of the most common genetic disease causes of premature coronary disease. High-risk HeFH patients with multiple risk factors, including those suffering from coronary bypass graft stenosis despite receiving medical therapy, might need stricter management of lipid profile with proprotein convertase subtilisin/kexin 9inhibitors than that recommended in the guideline.>.

[38] *Leren TP, Bogsrud MP*. **The importance of cascade genetic screening for diagnosing autosomal dominant hypercholesterolemia: Results from twenty years of a national screening program in Norway**. Journal of clinical lipidology 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34479846
ABSTRACT
BACKGROUND: The most cost-effective strategy to diagnose patients with autosomal dominant hypercholesterolemia (ADH) is to perform cascade genetic screening. OBJECTIVE: To present the

cascade genetic screening program for ADH in Norway. METHODS: A national cascade genetic screening program for ADH in Norway has been operating at Unit for Cardiac and Cardiovascular Genetics, Oslo University Hospital for twenty years. This program has been run by just one genetic counsellor. We now present the main findings of this cascade genetic screening program. RESULTS: After genetic counselling, 8182 at-risk relatives have consented to genetic testing for the mutation that causes ADH in the family. Of these, 3076 (37.6%) relatives have tested positive. Among mutation-positive relatives 31.3% were on lipid-lowering therapy at the time of genetic testing. However, only 9.8% of these relatives had a value for low density lipoprotein (LDL) cholesterol below 2.5 mmol/l (97 mg/dl). At follow-up six months after genetic testing, reductions in the levels of total serum cholesterol and LDL cholesterol of 12% and 17%, respectively were observed. A total of 8811 ADH heterozygotes have been diagnosed in Norway. Thus, the number of patients diagnosed by this modest cascade genetic screening program constitutes 35% of all Norwegian ADH patients provided with a molecular genetic diagnosis. CONCLUSION: Cascade genetic screening for ADH is very effective and should be organized at a national level. Even a modest cascade genetic screening program with small resources, can result in a large number of patients being identified.

[39] *Zhang X, Chen Y, Tong N et al.* **Maternally inherited diabetes and deafness coexists with lipoprotein lipase gene mutation-associated severe hyperlipidemia that was resistant to fenofibrate and atorvastatin, but sensitive to bezafibrate: A case report**. Journal of diabetes investigation 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34460997
ABSTRACT
Maternally inherited diabetes and deafness is a rare genetic disease mainly caused by a point mutation in mitochondrial deoxyribonucleic acid. Lipoprotein lipase gene mutations are associated with familial dyslipidemias, which are difficult to manage. We reported for the first time a case that had both maternally inherited diabetes and severe hyperlipidemia caused by lipoprotein lipase gene mutation (C.347(exon3)G>C) that was resistant to fenofibrate and atorvastatin. We were able to manage the patient's hyperlipidemia with bezafibrate, and her diabetes was well controlled with insulin. In conclusion, genetic testing is helpful in identifying rare and interesting cases when clinicians suspect inheritable diseases. Additionally, when one fibrate drug is ineffective in treating hyperlipidemia, it might be worthwhile trying another fibrate.

[40] *Sanlier N, Üstün D.* **Egg consumption and health effects: A narrative review**. Journal of food science 2021; 86:4250-4261.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34472102
ABSTRACT
This study was planned and conducted to investigate the effects of egg consumption on metabolic syndrome components and potential mechanisms of action on humans. Egg, an important source of animal protein, is defined as a functional food containing various bioactive compounds that can affect the proinflammatory and anti-inflammatory pathways. As a matter of fact, the egg can show immunomodulatory, anti-inflammatory, antioxidant, anticancer, or antihypertensive effects with its bioactive components. It is claimed that egg consumption may protect individuals against metabolic syndrome by increasing HDL-C levels and reducing inflammation. The increase in egg consumption creates the perception that it may lead to cardiovascular diseases due to its cholesterol content.

However, there is insufficient evidence as to whether dietary cholesterol-lowers LDL-C. The possible potential mechanisms of egg impact on human health, MEDLINE, Embase, the Cochrane Central, www.ClinicalTrials.gov, PubMed, Science Direct, Google Scholar, and selected websites including) and databases were examined in this regard. With a view to delving into the rather mysterious relationship between egg cholesterol and blood cholesterol, it is necessary to understand the absorption of cholesterol from the egg and to know the functioning of the intestinal microbiota. Studies conducted to date have generally yielded inconsistent results regarding egg consumption and risks of CVD, diabetes, and metabolic syndrome.

[41] *Joseph P, Roshandel G, Gao P et al.* **Fixed-dose combination therapies with and without aspirin for primary prevention of cardiovascular disease: an individual participant data meta-analysis**. Lancet 2021; 398:1133-1146.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34469765

ABSTRACT
BACKGROUND: In randomised controlled trials, fixed-dose combination treatments (or polypills) have been shown to reduce a composite of cardiovascular disease outcomes in primary prevention. However, whether or not aspirin should be included, effects on specific outcomes, and effects in key subgroups are unknown. METHODS: We did an individual participant data meta-analysis of large randomised controlled trials (each with ≥1000 participants and ≥2 years of follow-up) of a fixed-dose combination treatment strategy versus control in a primary cardiovascular disease prevention population. We included trials that evaluated a fixed-dose combination strategy of at least two blood pressure lowering agents plus a statin (with or without aspirin), compared with a control strategy (either placebo or usual care). The primary outcome was time to first occurrence of a composite of cardiovascular death, myocardial infarction, stroke, or arterial revascularisation. Additional outcomes included individual cardiovascular outcomes and death from any cause. Outcomes were also evaluated in groups stratified by the inclusion of aspirin in the fixed-dose treatment strategy, and effect sizes were estimated in prespecified subgroups based on risk factors. Kaplan-Meier survival curves and Cox proportional hazard regression models were used to compare strategies. FINDINGS: Three large randomised trials were included in the analysis (TIPS-3, HOPE-3, and PolyIran), with a total of 18 162 participants. Mean age was 63·0 years (SD 7·1), and 9038 (49·8%) participants were female. Estimated 10-year cardiovascular disease risk for the population was 17·7% (8·7). During a median follow-up of 5 years, the primary outcome occurred in 276 (3·0%) participants in the fixed-dose combination strategy group compared with 445 (4·9%) in the control group (hazard ratio 0·62, 95% CI 0·53-0·73, p<0·0001). Reductions were also observed for the separate components of the primary outcome: myocardial infarction (0·52, 0·38-0·70), revascularisation (0·54, 0·36-0·80), stroke (0·59, 0·45-0·78), and cardiovascular death (0·65, 0·52-0·81). Significant reductions in the primary outcome and its components were observed in the analyses of fixed-dose combination strategies with and without aspirin, with greater reductions for strategies including aspirin. Treatment effects were similar at different lipid and blood pressure levels, and in the presence or absence of diabetes, smoking, or obesity. Gastrointestinal bleeding was uncommon but slightly more frequent in the fixed-dose combination strategy with aspirin group versus control (19 [0·4%] vs 11 [0·2%], p=0·15). The frequencies of haemorrhagic stroke (10 [0·2%] vs 15 [0·3%]), fatal bleeding (two [<0·1%] vs four [0·1%]), and peptic ulcer disease (32 [0·7%] vs 34 [0·8%]) were low and did not differ significantly between groups. Dizziness was more common with fixed-dose combination treatment (1060 [11·7%]

vs 834 [9·2%], p<0·0001). INTERPRETATION: Fixed-dose combination treatment strategies substantially reduce cardiovascular disease, myocardial infarction, stroke, revascularisation, and cardiovascular death in primary cardiovascular disease prevention. These benefits are consistent irrespective of cardiometabolic risk factors. FUNDING: Population Health Research Institute.

[42] *Berberich AJ, Ouédraogo AM, Shariff SZ et al.* **Incidence, predictors and patterns of care of patients with very severe hypertriglyceridemia in Ontario, Canada: a population-based cohort study**. Lipids in health and disease 2021; 20:98.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34479547
ABSTRACT
BACKGROUND: The incidence of severe (S-HTG) and very severe hypertriglyceridemia (VS-HTG) among Canadians is unknown. This study aimed to determine the incidence, characteristics, predictors and care patterns for individuals with VS-HTG. METHODS: Using linked administrative healthcare databases, a population-based cohort study of Ontario adults was conducted to determine incidence of new onset S-HTG (serum triglycerides (TG) >10-20 mmol/L) and VS-HTG (TG>20 mmol/L) between 2010 and 2015. Socio-demographic and clinical characteristics of those with VS-HTG were compared to those who had no measured TG value >3 mmol/L. Univariable and multivariable logistic regression were used to determine predictors for VS-HTG. Healthcare patterns were evaluated for 2 years following first incidence of TG >20 mmol/L. RESULTS: Incidence of S-HTG and VS-HTG in Ontario was 0.16 and 0.027% among 10,766,770 adults ≥18 years and 0.25 and 0.041% among 7,040,865 adults with at least one measured TG, respectively. Predictors of VS-HTG included younger age [odds ratios (OR) 0.64/decade, 95% confidence intervals (CI) 0.62-0.66], male sex (OR 3.83; 95% CI 3.5-4.1), diabetes (OR 5.38; 95% CI 4.93-5.88), hypertension (OR 1.69; 95% CI 1.54-1.86), chronic liver disease (OR 1.71; 95% CI 1.48-1.97), alcohol abuse (OR 2.47; 95% CI 1.90-3.19), obesity (OR 1.49; 95% CI 1.13-1.98), and chronic kidney disease (OR 1.39; 95% CI 1.19-1.63). CONCLUSION: The 5-year incidence of S-HTG and VS-HTG in Canadian adults was 1 in 400 and 1 in 2500, respectively. Males, those with diabetes, obese individuals and those with alcohol abuse are at highest risk for VS-HTG and may benefit from increased surveillance.

[43] *Cully M*. **Promoting APRIL interaction to control atherosclerosis**. Nature reviews. Drug discovery 2021; 20:740.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34475542
ABSTRACT

[44] *Li R, Shi T, Xing E, Qu H*. **Atorvastatin calcium tablets on inflammatory factors, hemorheology and renal function damage indexes in patients with diabetic nephropathy**. Pak J Med Sci 2021; 37:1392-1396.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34475918
ABSTRACT
OBJECTIVES: To investigate the effect of atorvastatin on inflammatory factors, hemorheology, and renal function damage in patients with diabetic nephropathy (DN). METHODS: One hundred and six DN patients who were treated in our hospital between June 2018 and August 2019 were selected and randomly grouped into observation group and control group, 53 each group. Patients in the control group were given the conventional treatment; patients in the observation group were given

atorvastatin treatment on the basis of the conventional treatment. They were treated for three months. The hemorheology indexes (whole blood viscosity, erythrocyte aggregation index, and fibrinogen (FIB)), renal function damage indexes (macrophage migration inhibitory factor (MIF), vascular cell adhesion molecule (VCAM)-1, Secreted frizzled-related protein-5 (SFRP5), and mAlb/Cr) and inflammatory factor related indexes (C-reactive protein (CRP), interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α)) were compared between the two groups before and after three months of treatment. RESULTS: After three months of treatment, the hemorheology indexes, renal function damage indexes, and inflammatory factors related indexes in the two groups changed. Compared with the control group, the whole blood viscosity, erythrocyte aggregation index, FIB, MIF, VACM-1, mAlb/Cr, CRP, IL-1, and TNF-α levels in the observation group significantly decreased, while the levels of SERP-5 significantly increased; the differences were statistically significant ($P<0.05$). CONCLUSION: Atorvastatin can effectively alleviate the renal function damage in patients with DN, reduce the level of serum inflammatory factors, and improve hemorheology, which has a good clinical application value for DN patients.

[45] *Lopes J, Santos P*. **Determinants of Non-Adherence to the Medications for Dyslipidemia: A Systematic Review**. Patient preference and adherence 2021; 15:1853-1871.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34465984

ABSTRACT

PURPOSE: Dyslipidemia is a major cardiovascular risk factor, and its control leads to less cardiovascular events. Many patients will need some medications to achieve ideal targets. Non-adherence to medications is a complex problem with high impact on their effectiveness. This study aims to identify the determinants of non-adherence to medications in patients with dyslipidemia. PATIENTS AND METHODS: We conducted a systematic review. PubMed and Scopus databases were searched for original articles, published between 2000 and 2020, using the MeSH terms "Dyslipidemias" and "Medication Adherence". RESULTS: From the initial 3502 identified articles, we selected 46 to include in the final qualitative synthesis. The determinants associated with non-adherence were lower age (≤50 years), female sex, African American ethnicity, smoking habits, being a new user of lipid-lowering medications, reporting or having concerns about lipid-lowering medication side effects and some comorbidities (chronic obstructive pulmonary disease, Alzheimer's disease/dementia, depression and diabetes). On the contrary, adherence is higher in older patients, alcohol drinking habits, taking β-blockers, having a higher number of comorbidities, having a history of cardiovascular events, cardiac interventions or revascularization procedures, having health insurance and having more provider follow-up visits. CONCLUSION: There are important identifiable determinants of non-adherence in patients with dyslipidemia. These patients benefit from a specific approach to minimize the problem and maximize the potential benefit of the prescription.

[46] *Karvaly GB, Karádi I, Vincze I et al.* **A pharmacokinetics-based approach to the monitoring of patient adherence to atorvastatin therapy**. Pharmacol Res Perspect 2021; 9:e00856.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34478238

ABSTRACT

The inadequate adherence of patients whose hyperlipidemia is treated with atorvastatin (ATR) to medical instructions presents a serious health risk. Our aim was to develop a flexible approach based on therapeutic drug monitoring (TDM), nonparametric population pharmacokinetic modeling, and

Monte Carlo simulation to differentiate adherent patients from partially and nonadherent individuals in a nonrandomized, unicentric, observational study. Sixty-five subjects were enrolled. Nonparametric, mixed-effect population pharmacokinetic models of the sums of atorvastatin and atorvastatin lactone concentrations (ATR+ATRL) and of the concentrations of the acid and lactone forms of ATR and its 2- and 4-hydroxylated pharmacologically active metabolites (ATR+MET) were elaborated by including the TDM results obtained in 128 samples collected from thirty-nine subjects. Monte Carlo simulation was performed based on the elaborated models to establish the probabilities of attaining a specific ATR+ATRL or ATR+MET concentration in the range of 0.002-10 nmol (mg dose)(-1) L(-1) at 1-24 h postdose by adherent, partially adherent, and nonadherent patients. The results of the simulations were processed to allow the estimation of the adherence of further 26 subjects who were phlebotomized at sampling times of 2-20 h postdose by calculating the probabilities of attaining the ATR+ATRL and ATR+MET concentrations measured in these subjects in adherent, partially adherent, and nonadherent individuals. The best predictive values of the estimates of adherence could be obtained with sampling at early sampling times. 61.54% and 38.46% of subjects in the adherence testing set were estimated to be fully and partially adherent, respectively, while in all cases the probability of nonadherence was extremely low. The evaluation of patient adherence to ATR therapy based on pharmacokinetic modeling and Monte Carlo simulation has important advantages over the collection of trough samples and the use of therapeutic ranges.

[47] *Siniarski A, Gajos G*. **Polyunsaturated fatty acids in cardiovascular diseases: uncertainty prevails**. Polish archives of internal medicine 2021; 131:716-723.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34463083
ABSTRACT
In the late 1970s, a lower incidence of myocardial infarction and favorable hemostatic alterations were reported in Greenland Inuits. This observation prompted investigators worldwide to continue research on the role of a specific diet in this population and sparked an ongoing discussion about the potential use of polyunsaturated fatty acids (PUFAs) in the primary prevention of cardiovascular disease (VITAL), and the secondary prevention of primarily coronary artery disease (JELIS, REDUCE-IT, OMEMI). However, the current evidence to support the preventive value of PUFAs is inconsistent. Seminal clinical trials such as the GISSI-Prevenzione, JELIS, PREDIMED, or ASCEND differed in their approach to the assessment of cardiovascular effects of n-3 PUFAs and reported divergent results. The questions remain whether eicosapentaenoic acid is the only PUFA offering cardiovascular benefits, what is the importance of PUFA dosing, and, finally, who should receive n-3 PUFA treatment. This article discusses the latest insights into n-3 PUFA use in cardiovascular disease prevention.

[48] *Zhou J, Tang G, Tang S, Yuan W*. **The effect of fish oil on inflammation markers in adult patients undergoing hemodialysis: A meta-analysis**. Semin Dial 2021.
PM: http://www.ncbi.nlm.nih.gov/pubmed/?term=34459522
ABSTRACT
OBJECTIVE: This meta-analysis was to assess the effect of fish oil supplementation on inflammation markers in adult patients receiving hemodialysis. METHODS: CENTRAL, EMBASE, MEDLINE databases were searched from inception to 10 April 2020. Two authors independently searched, selected, and screened the literature. The pooled results are represented by WMD or SMD with 95%

confidence intervals. Subgroup analysis and meta-regression were used to explore sources of heterogeneity, and sensitivity analysis was used to assess the robustness of the pooled results. Funnel plots were used to assess publication bias. RESULTS: Eleven RCT (randomized control trials) studies were included. The pooled results showed that fish oil supplementation caused a significant reduction of the CRP(C-reactive protein) level (random model: WMD, -3.36, 95%CI: -5.46 to -1.26, P = .002), especially in patients with baseline CRP ≥ 5 mg/L (random model: WMD, -4.43, 95%CI: -6.10 to -2.76, P = .00001, I(2) = 41%). Meta-regression analyses showed that CRP baseline level (CRP < 5 mg/L) was the main source of heterogeneity (P = .036). Sensitive analyses revealed that the result was hardly changed. Fish oil supplementation might not reduce the level of IL-6 (random model: WMD, -2.26, 95%CI: -19.61 to 15.09, P = .80) in four studies or the level of TNF-α (random model: SMD, -2.51, 95%CI: -6.08 to 1.06, P = .17) in three studies. CONCLUSIONS: Fish oil supplementation could reduce the level of CRP in hemodialysis patients, especially in patients with CRP ≥ 5 mg/L, but had no effects on IL-6 and TNF-α.