[1] *Kearney A, Linden K, Savage P, Menown IBA*. **Advances in Clinical Cardiology 2020: A Summary of Key Clinical Trials**. Adv Ther 2021:1-31.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33844133
***ABSTRACT***
INTRODUCTION: Despite the challenge of a global pandemic, 2020 has been an invaluable year in cardiology research with numerous important clinical trials published or presented virtually at major international meetings. This article aims to summarise these trials and place them in clinical context. METHODS: The authors reviewed clinical trials presented at major cardiology conferences during 2020 including the American College of Cardiology, European Association for Percutaneous Cardiovascular Interventions, European Society of Cardiology, Transcatheter Cardiovascular Therapeutics and the American Heart Association. Trials with a broad relevance to the cardiology community and those with potential to change current practice were included. RESULTS: A total of 87 key cardiology clinical trials were identified for inclusion. New interventional and structural cardiology data included trials evaluating bifurcation percutaneous coronary intervention (PCI) techniques, intravascular ultrasound (IVUS)-guided PCI, instantaneous wave-free (iFR) physiological assessment, new generation stents (DynamX bioadaptor), transcatheter aortic valve implantation (TAVI) in low-risk patients, and percutaneous mitral or tricuspid valve interventions. Preventative cardiology data included new data with proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors (evolocumab and alirocumab), omega-3 supplements, evinacumab and colchicine in the setting of chronic coronary artery disease. Antiplatelet data included trials evaluating both the optimal length of course following PCI and combination of antiplatelet agents and regimes including combination antithrombotic therapies for patients with atrial fibrillation (AF). Heart failure data included the use of sodium-glucose cotransporter 2 (SGLT2) inhibitors (sotagliflozin, empagliflozin and dapagliflozin) and mavacamten in hypertrophic cardiomyopathy. Electrophysiology trials included early rhythm control in AF and screening for AF. CONCLUSION: This article presents a summary of key clinical cardiology trials during the past year and should be of relevance to both clinicians and cardiology researchers.

[2] *Arnold MJ, O'Malley PG, Downs JR*. **Key Recommendations on Managing Dyslipidemia for Cardiovascular Risk Reduction: Stopping Where the Evidence Does**. American family physician 2021; 103:455-458.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33856173
***ABSTRACT***

[3] *Mason RP, Eckel RH*. **Mechanistic Insights from REDUCE-IT STRENGTHen the Case Against Triglyceride Lowering as a Strategy for Cardiovascular Disease Risk Reduction**. The American journal of medicine 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33864765
***ABSTRACT***
Elevated triglyceride (TG) levels have been linked to residual atherosclerotic cardiovascular risk in patients with controlled low-density lipoprotein cholesterol (LDL-C). However, outcome trials testing TG-lowering agents have failed to demonstrate cardiovascular risk reduction in statin-treated subjects. One such example is the recent STRENGTH trial, which tested mixed omega fatty acids (n3-FAs, 4g/d) in high-risk patients with elevated TGs. Similar to trials using fibrates and niacin,

STRENGTH failed despite effective TG-lowering. Results from these studies have contributed to skepticism about the use of TG-lowering therapy for cardiovascular risk. But new mechanistic insights are provided by the REDUCE-IT trial that used icosapent ethyl (IPE), a purified formulation of the n3-FA eicosapentaenoic acid (EPA). In high-risk patients, IPE reduced a composite of cardiovascular events (25%, P<0.001) in a manner not predicted by TG-lowering. Benefits with IPE appear linked to broad pleiotropic actions associated with on-treatment EPA levels. These studies indicate that while TGs are a potential biomarker of cardiovascular risk, there is no evidence that TG-lowering itself is an effective strategy for reducing such risk.

[4] *Vilahur G, Sutelman P, Mendieta G et al.* **Triglyceride-induced cardiac lipotoxicity is mitigated by Silybum marianum**. Atherosclerosis 2021; 324:91-101.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33857761

***ABSTRACT***

BACKGROUND AND AIMS: Silybum marianum (SM) is an herbal product with cytoprotective and antioxidant properties. We have previously demonstrated that SM ameliorates ventricular remodeling and improves cardiac performance. Here, we evaluated whether SM could exert beneficial effects against cardiac lipotoxicity in a pig model of closed-chest myocardial infarction (MI). METHODS: Study 1 investigated the effect of SM administration on lipid profile and any potential SM-related adverse effects. Animals received SM or placebo during 10 days and were afterward sacrificed. Study 2 evaluated the effectiveness of SM daily administration in reducing cardiac lipotoxicity in animals subjected to a 1.5h myocardial infarction (MI), who were subsequently reperfused for 2.5h and euthanized or kept under study for three weeks and then sacrificed. RESULTS: Animals administered a 10-day SM regime presented a sharp decline in plasma triglyceride levels vs. controls, with no other modifications in lipid profile. The decrease in triglyceride concentration was accompanied by a marked reduction in triglyceride intestinal absorption and glycoprotein-P expression. Three weeks post-MI the triglyceride content in the ischemic myocardium of the SM-treated animals was significantly lower than in the ischemic myocardium of placebo-controls. This effect was associated with an enhanced cardiac expression of PPARγ and triglyceride clearance receptors. This long-term SM-administration induced a lower expression of lipid receptors in subcutaneous adipose tissue. No SM-related side-effects were registered. CONCLUSION: SM administration reduces plasma triglyceride levels through attenuation of triglyceride intestinal absorption and modulates cardiac lipotoxicity in the ischemic myocardium, likely contributing to improve ventricular remodeling.

[5] *Alidadi M, Montecucco F, Jamialahmadi T et al.* **Beneficial Effect of Statin Therapy on Arterial Stiffness**. BioMed research international 2021; 2021:5548310.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33860033

***ABSTRACT***

Arterial stiffness describes the increased rigidity of the arterial wall that occurs as a consequence of biological aging and several diseases. Numerous studies have demonstrated that parameters to assess arterial stiffness, especially pulse-wave velocity, are predictive of those individuals that will suffer cardiovascular morbidity and mortality. Statin therapy may be a pharmacological strategy to improve arterial elasticity. It has been shown that the positive benefits of statin therapy on cardiovascular disease is attributable not only to their lipid-lowering capacity but also to various pleiotropic effects, such as their anti-inflammatory, antiproliferative, antioxidant, and antithrombotic

properties. Additionally, statins reduce endothelial dysfunction, improve vascular and myocardial remodeling, and stabilize atherosclerotic plaque. The aim of the present review was to summarize the evidence from human studies showing the effects of statins on arterial stiffness.

[6] *Ghaffar MT, Radhakrishna A, Ali I, Whelan B*. **Statin-induced necrotising autoimmune myopathy: a rare complication of statin therapy**. BMJ case reports 2021; 14.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33858894
***ABSTRACT***
Statin-induced necrotising autoimmune myopathy (SINAM), a rare complication of statin use, presents with significant proximal muscle weakness and raised creatine kinase (CK) levels (50-100 times). This is different from other musculoskeletal conditions caused by statin use. Anti-hydroxy-methyl-glutaryl-coenzyme A reductase (HMG-CoA) reductase antibody is usually positive in SINAM and it generally indicates good response to immunosuppressive medications. We report a case of a 52-year-old man who presented with a 2-month history of significant upper and lower extremity proximal muscle weakness and a CK level of >10 000. He was started on atorvastatin for myocardial infarction 3 years ago. MRI pelvis, including proximal thigh, showed diffuse muscle oedema to all muscle groups. Muscle biopsy was suggestive of necrotising myopathy. His HMG-CoA reductase antibody was also positive. His treatment regimen consisted of immunosuppressants, including steroids. He also required extensive physiotherapy and showed response to treatment when reviewed in the outpatient clinic 9 months later.

[7] *Cacciottolo PJ, Kostapanos MS, Hernan Sancho E et al.* **Investigating the Lowest Threshold of Vascular Benefits from LDL Cholesterol Lowering with a PCSK9 mAb Inhibitor (Alirocumab) in Patients with Stable Cardiovascular Disease (INTENSITY-HIGH): protocol and study rationale for a randomised, open label, parallel group, mechanistic study**. BMJ open 2021; 11:e037457.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33849844
***ABSTRACT***
INTRODUCTION: Elevated low-density lipoprotein cholesterol (LDL-C) is a strong independent risk predictor of cardiovascular (CV) events, while interventions to reduce it remain the only evidence-based approach to reduce CV morbidity and mortality. Secondary prevention statin trials in combination with ezetimibe and/or proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors showed that there is no 'J shaped curve' in LDL-C levels with regard to CV outcomes. The lowest threshold beyond which reduction of LDL-C confers no further CV benefits has not been identified.The INTENSITY-HIGH study seeks to explore physiological mechanisms mediating CV benefits of LDL-C lowering by PCSK9 inhibition in patients with established cardiovascular disease (CVD). The study examines the changes in measures of endothelial function and vascular inflammation imaging following intervention with PCSK9 and against standard of care. METHODS AND ANALYSIS: This is a single-centre, randomised, open label, parallel group, mechanistic physiological study. It will include approximately 60 subjects with established CVD, with LDL-C of <4.1 mmol/L on high-intensity statins. All eligible participants will undergo 18-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) scanning of the aorta and carotid arteries, as well as baseline endothelial function assessment. Subsequently, they will be randomised on a 1:1 basis to either alirocumab 150 mg or ezetimibe 10 mg/day. Repeat FDG-PET/CT scan and vascular assessments will be undertaken after 8 weeks of treatment. Any changes in these parameters will be

correlated with changes in lipid levels and systemic inflammation biomarkers. ETHICS AND DISSEMINATION: The study received a favourable opinion from the Wales Research Ethics Committee 4, was registered on clinicaltrials.gov and conformed to International Conference for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice. The results of this study will be reported through peer-reviewed journals and conference presentations. TRIAL REGISTRATION NUMBER: NCT03355027.

[8] *Xu M, Demuyakor A, Hu S et al.* **Is the effect of atorvastatin 60 mg on stabilization of lipid-rich plaque equivalent to that of rosuvastatin 10 mg? A serial optical coherence tomography combined with intravascular ultrasound imaging**. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions 2021; 97 Suppl 2:1097-1107.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33864710

***ABSTRACT***

OBJECTIVES: This study aimed to compare the effect of atorvastatin 60 (AT60) mg to that of rosuvastatin 10 (RT10) mg on the morphological changes in lipid-rich plaques (LRPs) and plaque volume, using serial optical coherence tomography (OCT) and intravascular ultrasound imaging (IVUS). BACKGROUND: Intensive lipid lowering therapy by statin provides more clinical benefit compared to that of moderate lipid lowering therapy. METHODS: Fifty patients who underwent OCT and IVUS at baseline, 6, and 12 months were grouped by statin therapy into the AT60 mg (n = 27) and RT10 mg (n = 23) groups. The relationships between absolute and percentage changes in biomarkers and fibrous cap thickness (FCT) during follow-up were investigated using a simple regression analysis. RESULTS: At 6 months, the mean low-density lipoprotein cholesterol level reduced from 113.5 to 65.5 mg/dl (AT60 mg group) and 100.2 to 72.2 mg/dl (RT10 mg groups). A continuous increase in FCT from baseline to 12 months was observed in both groups ($p < .001$, $p < .001$, respectively). Mean lipid arc significantly decreased in both AT60 mg (189.0 ± 55.9°, 170.9 ± 60.2°, 155.6 ± 50.6°, $p < .001$) and RT10 mg (160.0 ± 45.6°, 151.2 ± 48.5°, 141.1 ± 52.9°, $p = .010$) groups. Plaque burden did not change significantly in both groups. CONCLUSIONS: Lipid-lowering therapy effect with AT60 mg was equivalent to that of RT10 mg in terms of change in plaque morphology. AT60 mg showed more intensive low-density lipid cholesterol level reduction compared to RT10 mg while RT10 mg was effective in increasing the high-density lipid cholesterol level. Both statin therapies could effectively stabilize LRPs.

[9] *Cha D, Wang F, Mukerji B, Mukerji V*. **Statin-Induced Necrotizing Autoimmune Myositis: Diagnosis and Management**. Cureus 2021; 13:e13787.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33842161

***ABSTRACT***

Statins are among the most frequently prescribed drugs as they effectively lower cardiovascular mortality. Atherosclerotic plaques are stabilized and lipid levels are lowered, as statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Patients placed on these drugs frequently report muscle aches, but true myositis that would call for discontinuance of the drug is actually uncommon. Workup for statin-induced myositis would require ruling out other causes of myositis and muscular dystrophies, and this can often be perplexing for the primary care physician to whom these patients initially present. This case report and recommendations may serve as a helpful guide.

[10] *Giglio RV, Stoian AP, Patti AM et al.* **Genetic and Epigenetic Biomarkers For Diagnosis, Prognosis and Treatment Of Metabolic Syndrome**. Current pharmaceutical design 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33845722
***ABSTRACT***
BACKGROUND: Metabolic syndrome is a clinical condition that deserves special attention because it puts the individual at high cardiovascular risk, especially heart attack and stroke. Considering the precision medicine, it would be advisable to valuate the individual cardio-metabolic risk by estimating the coesistence of risk factors (abdominal obesity, low level of High- Density Lipoprotein Cholesterol, High Triglycerides, and small dense Low-Density Lipoproteins sub-classes, hypertension, and elevated fasting glycemia), which could engrave on metabolism increasing cardiovascular mortality. OBJECTIVE: To identify genetic and epigenetic biomarkers may assist in the possibility of helping follow-up strategies and other measures of prevention, and in metabolic risk. METHODS: We searched for studies which valued the combination between epigenetic biomarkers and all factors of cardio-metabolic risk. RESULTS: Numerous researches have investigated the molecular start of metabolic alterations, focusing on the epigenetic mark, as methylation of DNA, histone modifications and non.coding RNAs. It has been found that DNA methylation is the most searched epigenetic sign in the human genome concerning the control of gene expression. CONCLUSION: For the screening, diagnosis, and prognosis of metabolic syndrome and the prescription of personalized medicine, the DNA methylation biomarkers specify for subjects have been recognized as an ensuring tool. While these results are promising, further investigations are needed to unravel the complicated synergic association of the genome, epigenome and the situations related to metabolic pathology.

[11] *Rocha BA, Carneiro LOB, Vespasiano A, Horta MCR*. **Detection of calcified carotid atheroma on panoramic dental radiography and its confirmation by Doppler ultrasound**. Einstein (Sao Paulo) 2021; 19:eAI5707.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33852676
***ABSTRACT***

[12] Feingold KR. The Effect of Diet on Cardiovascular Disease and Lipid and Lipoprotein Levels. In: Endotext. Edited by: Feingold KR, Anawalt B, Boyce A *et al.* South Dartmouth (MA): MDText.com, Inc.
Copyright © 2000-2021, MDText.com, Inc.; 2000.
[13] *Duong MT, Nasrallah IM, Wolk DA et al.* **Cholesterol, Atherosclerosis, and APOE in Vascular Contributions to Cognitive Impairment and Dementia (VCID): Potential Mechanisms and Therapy**. Frontiers in aging neuroscience 2021; 13:647990.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33841127
***ABSTRACT***
Vascular contributions to cognitive impairment and dementia (VCID) are a common cause of cognitive decline, yet limited therapies exist. This cerebrovascular disease results in neurodegeneration via acute, chronic, local, and systemic mechanisms. The etiology of VCID is complex, with a significant impact from atherosclerosis. Risk factors including hypercholesterolemia and hypertension promote intracranial atherosclerotic disease and carotid artery stenosis (CAS), which disrupt cerebral blood flow and trigger ischemic strokes and VCID. Apolipoprotein E (APOE) is

a cholesterol and phospholipid carrier present in plasma and various tissues. APOE is implicated in dyslipidemia and Alzheimer disease (AD); however, its connection with VCID is less understood. Few experimental models for VCID exist, so much of the present information has been drawn from clinical studies. Here, we review the literature with a focus on the clinical aspects of atherosclerotic cerebrovascular disease and build a working model for the pathogenesis of VCID. We describe potential intermediate steps in this model, linking cholesterol, atherosclerosis, and APOE with VCID. APOE4 is a minor isoform of APOE that promotes lipid dyshomeostasis in astrocytes and microglia, leading to chronic neuroinflammation. APOE4 disturbs lipid homeostasis in macrophages and smooth muscle cells, thus exacerbating systemic inflammation and promoting atherosclerotic plaque formation. Additionally, APOE4 may contribute to stromal activation of endothelial cells and pericytes that disturb the blood-brain barrier (BBB). These and other risk factors together lead to chronic inflammation, atherosclerosis, VCID, and neurodegeneration. Finally, we discuss potential cholesterol metabolism based approaches for future VCID treatment.

[14] *Zhang X, Peng X, Li L et al.* **Persistent Cigarette Smoking Attenuates Plaque Stabilization in Response to Lipid-Lowering Therapy: A Serial Optical Coherence Tomography Study**. Frontiers in cardiovascular medicine 2021; 8:616568.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33859999
***ABSTRACT***
Objective: This study aimed to investigate the effect of smoking on morphological changes in non-culprit plaques in acute coronary syndrome (ACS) patients at 1 year after percutaneous coronary intervention (PCI), using optical coherence tomography (OCT). Background: Cigarette smoking is an important risk factor for coronary artery disease. However, the reasons for the high risk of re-infarction and worsened health among patients who continue to smoke after PCI remain unclear. Methods: A total of 129 non-culprit plaques were identified from 97 ACS patients who underwent OCT imaging at the time of PCI and at 1-year follow-up. Patients were divided into the following three groups according to their smoking status at 1-year follow-up: persistent smoking group (n = 26), smoking cessation group (n = 29), and nonsmoking group (n = 42). Medical history, serum cholesterol level, coronary angiography data, and OCT-determined plaque morphology were analyzed among the three groups. Results: Relative to baseline levels, the total cholesterol and low-density lipoprotein cholesterol levels significantly decreased in all three groups at 1-year follow-up after statin therapy ($p < 0.05$). The persistent smoking group had a relatively smaller fibrous cap thickness (FCT) and a higher incidence of thin-cap fibroatheroma (TCFA) than the other two groups at 1-year follow-up ($p < 0.05$), although the FCT increased and the incidence of TCFA decreased in all three groups. Conclusions: Persistent smoking is associated with an attenuated effect of statin therapy on plaque stabilization in ACS patients.

[15] *Arca M, Di Fusco SA*. **[Dyslipidemias: new therapeutic targets and relevance of combination therapies]**. Giornale italiano di cardiologia (2006) 2021; 22:5s-8s.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33847312
***ABSTRACT***
Based on growing evidence showing a better prognosis in individuals with lower levels of low-density lipoprotein cholesterol (LDL-C), updated 2019 European Society of Cardiology guidelines have further reduced LDL-C targets in patients with higher cardiovascular risk. National and international

observational clinical studies demonstrated a significant gap between goals recommended by international guidelines and LDL-C levels achieved in the real world, especially in patient populations at higher risk. Combination treatment strategies with more lipid-lowering drugs represent effective and safe options for the achievement of recommended targets. The introduction of new drugs, such as bempedoic acid, further expands the available therapeutic armamentarium for hypercholesterolemia management.

[16] *Di Fusco SA, Scicchitano P, Colivicchi F*. **[Opportunities and perspectives for bempedoic acid use in clinical practice]**. Giornale italiano di cardiologia (2006) 2021; 22:22s-27s.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33847315
***ABSTRACT***
Bempedoic acid is a new lipid-lowering drug that inhibits cholesterol biosynthesis in liver cells selectively. Results from phase 2 and phase 3 studies showed a complementary effect on LDL-cholesterol lowering when combining bempedoic acid and ezetimibe without increasing side effects. Moreover, bempedoic acid seems to represent a good treatment option for the management of hypercholesterolemia, especially in patients at increased risk of cardiovascular events, such as patients with impaired glucose metabolism, elderly patients, patients with prior acute coronary syndrome, and patients with familial hypercholesterolemia. Based on the scientific evidence, this paper provides practical recommendations on the management of hypercholesterolemia with bempedoic acid.

[17] *Faggiano P, Bernardi N*. **[Bempedoic acid: clinical data]**. Giornale italiano di cardiologia (2006) 2021; 22:15s-21s.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33847314
***ABSTRACT***
The efficacy and safety of bempedoic acid, including the occurrence of muscle-related adverse events, have been addressed by phase 2 and phase 3 clinical trials. Phase 3 clinical trials demonstrated that in patients with atherosclerotic cardiovascular disease and/or familial hypercholesterolemia who were treated with statins at maximum tolerated dose, with or without further lipid-lowering drugs, bempedoic acid treatment was associated with a significant reduction in low-density lipoprotein cholesterol in different groups of patients with a favorable safety profile. An ongoing phase 3 study is currently evaluating the effect of longer-term (median duration of 3-4 years) treatment with bempedoic acid on the incidence of cardiovascular events.

[18] *Baragetti A, Bonacina F, Catapano AL, Norata GD*. **Effect of Lipids and Lipoproteins on Hematopoietic Cell Metabolism and Commitment in Atherosclerosis**. Immunometabolism 2021; 3:e210014.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33859831
***ABSTRACT***
Hematopoiesis is the process that leads to multiple leukocyte lineage generation within the bone marrow. This process is maintained throughout life thanks to a nonstochastic division of hematopoietic stem cells (HSCs), where during each division, one daughter cell retains pluripotency while the other differentiates into a restricted multipotent progenitor (MPP) that converts into mature, committed circulating cell. This process is tightly regulated at the level of cellular metabolism and the

shift from anaerobic glycolysis, typical of quiescent HSC, to oxidative metabolism fosters HSCs proliferation and commitment. Systemic and local factors influencing metabolism alter HSCs balance under pathological conditions, with chronic metabolic and inflammatory diseases driving HSCs commitment toward activated blood immune cell subsets. This is the case of atherosclerosis, where impaired systemic lipid metabolism affects HSCs epigenetics that reflects into increased differentiation toward activated circulating subsets. Aim of this review is to discuss the impact of lipids and lipoproteins on HSCs pathophysiology, with a focus on the molecular mechanisms influencing cellular metabolism. A better understanding of these aspects will shed light on innovative strategies to target atherosclerosis-associated inflammation.

[19] *Agstam S, Agarwal T, Gupta A, Bansal S*. **Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors in aortic stenosis - Is this the light at the end of the tunnel for patients with aortic stenosis?** Indian Heart J 2021; 73:249-252.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33865531

***ABSTRACT***

The exploratory analysis of FOURIER trial has offered a ray of hope for patients with nonrheumatic aortic stenosis (AS). At present, the only definitive treatment of severe AS is aortic valve replacement (AVR). Despite transaortic valvular replacement revolutionizing the treatment of AS, it still remains a progressive condition, with no disease-modifying pharmacotherapy. Angiotensin-converting-enzyme inhibitors, angiotensin receptor blockers, eplerenone, nitrates and statins all have been tried previously but failed to slow down the progression of aortic stenosis. Recently, there has been an emerging role of lipoprotein A [Lp(a)] in the pathogenesis of AS. This raises the possibility that long-term therapy with specific emphasis on Lp(a) reduction may reduce or slow the progression of AS.

[20] *Zelniker TA, Morrow DA, Scirica BM et al.* **Plasma Omega-3 Fatty Acids and the Risk of Cardiovascular Events in Patients After an Acute Coronary Syndrome in MERLIN-TIMI 36**. Journal of the American Heart Association 2021; 10:e017401.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33840228

***ABSTRACT***

Background Plasma omega-3 polyunsaturated fatty acids (ω3-PUFAs) have been shown to be inversely correlated with the risk of cardiovascular death in primary prevention. The risk relationship in the setting of an acute coronary syndrome is less well established. Methods and Results Baseline plasma ω3-PUFA composition (α-linolenic acid, eicosapentaenoic acid, docosapentaenoic acid, and docosahexaenoic acid) was assessed through gas chromatography with flame ionization detection in a case-cohort study involving 203 patients with cardiovascular death, 325 with myocardial infarction, 271 with ventricular tachycardia, and 161 with atrial fibrillation, and a random sample of 1612 event-free subjects as controls from MERLIN-TIMI 36 (Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST-Elevation-Acute Coronary Syndrome-Thrombolysis in Myocardial Infarction 36), a trial of patients hospitalized with non-ST-segment-elevation -acute coronary syndrome. After inverse-probability-weighted multivariable adjustment including all traditional risk factors, a higher relative proportion of long-chain ω3-PUFAs (eicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid) were associated with 18% lower odds of cardiovascular death (adjusted [adj] odds ratio [OR] per 1 SD, 0.82; 95% CI, 0.68-0.98) that was primarily driven by 27% lower odds of sudden cardiac death (adj OR per 1 SD, 0.73; 95% CI, 0.55-0.97). Long-chain ω3-PUFA levels in the

top quartile were associated with 51% lower odds of cardiovascular death (adj OR 0.49; 95% CI, 0.27-0.86) and 63% lower odds of sudden cardiac death (adj OR, 0.37; 95% CI, 0.16-0.56). An attenuated relationship was seen for α-linolenic acid and subsequent odds of cardiovascular (adj OR, 0.92; 95% CI, 0.74-1.14) and sudden cardiac death (adj OR, 0.91; 95% CI, 0.67-1.25). No significant relationship was observed between any ω3-PUFAs and the odds of cardiovascular death unrelated to sudden cardiac death, myocardial infarction, atrial fibrillation, or early post-acute coronary syndrome ventricular tachycardia. Conclusions In patients after non-ST-segment-elevation-acute coronary syndrome, plasma long-chain ω3-PUFAs are inversely associated with lower odds of sudden cardiac death, independent of traditional risk factors and lipids. Registration URL: https://www.clinicaltrials.gov. Unique identifier: NCT00099788.

[21] *Toda Kato E, Goto S*. **The TIMI Study Group's Contributions to the Advancement of Cardiology -With Focus on Atherosclerotic Cardiovascular Disease**. Journal of atherosclerosis and thrombosis 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33853997
***ABSTRACT***
Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality across the world, warranting continuous research in this field. The elucidation of the atherogenesis mechanism is considered one of the most relevant scientific accomplishments of the last century. This has led to the clinical development of various novel therapeutic interventions for patients with or at risk of ASCVD, in which randomized clinical trials played a crucial role.The Thrombolysis in Myocardial Infarction (TIMI) Study Group was initially established to conduct a clinical trial studying thrombolysis for treatment of myocardial infarction. However, over the years, the TIMI Study Group has expanded their research interests to include antithrombotic therapy, lipid lowering, anti-diabetes, anti-obesity, and even heart failure. By leading large-scale, international, randomized, controlled trials of novel therapeutics, the TIMI Study Group has helped shape the very practice of cardiovascular medicine for over a quarter of a century, and decades of research continue to provide future promise for further advancement. Through a mutual goal to improve the care of ASCVD patients, the Japanese scientific community has become one of the important contributors to the TIMI Study Group's clinical research.In this review article, the authors aim to summarize major research lead by the TIMI Study Group in the ASCVD field.

[22] *Hao D, Wang H, Zang Y et al.* **Mechanism of Glycans Modulating Cholesteryl Ester Transfer Protein: Unveiled by Molecular Dynamics Simulation**. J Chem Inf Model 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33858135
***ABSTRACT***
Inhibition of the cholesteryl ester transfer protein (CETP) has been considered as a promising way for the treatment of cardiovascular disease (CVD) for three decades. However, clinical trials of several CETP inhibitors with various potencies have been marginally successful at best, raising doubts on the target drugability of CETP. The in-depth understanding of the glycosylated CETP structure could be beneficial to more definitive descriptions of the CETP function and the underlying mechanism. In this work, large-scale molecular dynamics simulations were performed to thoroughly explore the mechanism of glycans modulating CETP. Here, the extensive simulation results intensely suggest that glycan88 tends to assist CETP in forming a continuous tunnel throughout interacting with the

upper-right region of the N-barrel, while it also could prevent the formation of a continuous tunnel by swinging toward the right-rear of the N-barrel. Furthermore, glycan240 formed stable H-bonds with Helix-B and might further stabilize the central cavity of CETP. Furthermore, the nonspecific involvement of the hydroxyl groups from the various glycans with protein core interactions and the similar influence of different glycans trapped at similar regions on the protein structure suggest that physiological glycan may lead to a similar effect. This study would provide valuable insights into devising novel methods for CVD treatment targeting CETP and functional studies about glycosylation for other systems.

[23] *Reddy LL, Shah SAV, Ponde CK et al.* **Screening of PCSK9 and LDLR genetic variants in Familial Hypercholesterolemia (FH) patients in India**. J Hum Genet 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33864011

***ABSTRACT***

Familial Hypercholesterolemia (FH) is an autosomal, dominant, inherited disorder characterized by severely elevated LDL-cholesterol (LDL-C) levels with high risk for Coronary Artery Disease (CAD). There are limited genetic studies especially on genes other than Low Density Lipoprotein receptor (LDLR) conducted in Indian population. Thus, our aim was to screen the entire Proprotein Convertase Subtilisin/Kexin type 9 gene (PCSK9) gene & hotspot exons 3, 4 and 9 of LDLR gene in FH cases and controls. 50 FH cases were categorized into definite, probable and possible cases according to Dutch Lipid Network Criteria (DLNC) who were gender matched with 50 healthy controls. All 12 exons of PCSK9, and hotspot exons 3, 4 & 9 of LDLR gene were screened through High Resolution Melt (HRM) curve analysis. Enzyme linked immunosorbent assay was performed to measure circulating PCSK9 levels. Total cholesterol and LDL-C were significantly high in all three groups of cases. Total 8 nonpathogenic variants in exon 1, 5, 7 and 9 of the PCSK9 gene were detected. In LDLR gene, 3 known pathogenic and 1 benign variant were found in exon 3 & 4. In FH cases, PCSK9 levels were significantly high compared to controls ($P = 0.0001$), and were directly correlated to LDL-C ($P = 0.0001$) and Total Cholesterol ($P = 0.0001$). Our study is first to screen the entire PCSK9 gene in western part of India. Since no pathogenic variants were identified, it is possible that PCSK9 variants are clinically less relevant. However, 3 known pathogenic variants were found in the LDLR gene. These findings support our understanding of the genetic spectrum of FH in India.

[24] *Hammoud S, Saad I, Karam R et al.* **Impact of Ramadan Intermittent Fasting on the Heart Rate Variability and Cardiovascular Parameters of Patients with Controlled Hypertension**. J Nutr Metab 2021; 2021:6610455.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33859841

***ABSTRACT***

BACKGROUND: Conflicting results are reported on the effect of Ramadan fasting on the cardiovascular health of patients with hypertension, a highly prevalent cardiovascular disease risk factor. This research aimed to evaluate the impact of fasting on cardiac health and heart rate variability (as a measure of cardiac stress) of hypertensive patients. METHODS: Patients with controlled hypertension were followed in a prospective cohort during and after Ramadan. Lipid panel and blood glucose were measured at the end of each phase. Blood pressure and heart rate variability were monitored in the morning, afternoon, and evening of each follow-up day. RESULTS: The study included 58 subjects (mean age: $54 \pm 11.5$ years, 52% male). Fasting did not affect body composition,

lipid panel parameters, and blood pressure of hypertensive subjects; males only presented lower body weight and hip circumference during Ramadan. Blood glucose was significantly higher during Ramadan. Fasting significantly increased HRV during the afternoon period. CONCLUSIONS: Ramadan intermittent fasting reduces cardiac stress among hypertensive patients controlled by and adherent to hypertensive medication, without affecting their hypertensive state.

[25] *Williams MC, Kwiecinski J, Doris M et al.* **Sex-Specific Computed Tomography Coronary Plaque Characterization and Risk of Myocardial Infarction**. JACC. Cardiovascular imaging 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33865779

***ABSTRACT***

OBJECTIVES: This study was designed to investigate whether coronary computed tomography angiography assessments of coronary plaque might explain differences in the prognosis of men and women presenting with chest pain. BACKGROUND: Important sex differences exist in coronary artery disease. Women presenting with chest pain have different risk factors, symptoms, prevalence of coronary artery disease and prognosis compared to men. METHODS: Within a multicenter randomized controlled trial, we explored sex differences in stenosis, adverse plaque characteristics (positive remodeling, low-attenuation plaque, spotty calcification, or napkin ring sign) and quantitative assessment of total, calcified, noncalcified and low-attenuation plaque burden. RESULTS: Of the 1,769 participants who underwent coronary computed tomography angiography, 772 (43%) were female. Women were more likely to have normal coronary arteries and less likely to have adverse plaque characteristics ($p < 0.001$ for all). They had lower total, calcified, noncalcified, and low-attenuation plaque burdens ($p < 0.001$ for all) and were less likely to have a low-attenuation plaque burden >4% (41% vs. 59%; $p < 0.001$). Over a median follow-up of 4.7 years, myocardial infarction (MI) occurred in 11 women (1.4%) and 30 men (3%). In those who had MI, women had similar total, noncalcified, and low-attenuation plaque burdens as men, but men had higher calcified plaque burden. Low-attenuation plaque burden predicted MI (hazard ratio: 1.60; 95% confidence interval: 1.10 to 2.34; $p = 0.015$), independent of calcium score, obstructive disease, cardiovascular risk score, and sex. CONCLUSIONS: Women presenting with stable chest pain have less atherosclerotic plaque of all subtypes compared to men and a lower risk of subsequent MI. However, quantitative low-attenuation plaque is as strong a predictor of subsequent MI in women as in men. (Scottish Computed Tomography of the HEART Trial [SCOT-HEART]; NCT01149590).

[26] *Agarkov NM, Okhotnikov OI, Korneeva SI et al.* **Psychological Continuum of Elderly Patients Suffering from Arterial Hypertension with Metabolic Syndrome, Against the Background of Chronotherapy with a Fixed Combination of Amlodipine, Lisinopril and Rosuvastatin**. Kardiologiia 2021; 61:36-41.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33849417

***ABSTRACT***

Aim To study the psychological continuum in elderly patients with arterial hypertension associated with metabolic syndrome during the chronotherapy with a fixed combination (FC) of amlodipine, lisinopril, and rosuvastatin.Material and methods In the inpatient conditions, 63 patients aged 60-74 years with arterial hypertension associated with metabolic syndrome were treated with chronotherapy with a FC of amlodipine, lisinopril, and rosuvastatin (5/10/10 mg/day in the evening). These patients composed the main group. The control group (58 patients aged 60-74

years with arterial hypertension associated with metabolic syndrome) was treated with the FC of amlodipine, lisinopril, and rosuvastatin at the same dose of 5/10/10 mg/day in the morning.Results At one year, the disorders of psychological continuum were significantly decreased with the chronotherapy (evening dosing) with the antihypertensive FC of amlodipine, lisinopril, and rosuvastatin compared to the traditional treatment (morning dosing) at the same dose of 5/10/10 mg/day in both groups. With the chronotherapeutic approach, the dynamic of cognitive disorders in patients aged 60-74 years with arterial hypertension associated with metabolic syndrome was characterized by a significant increase in the Mini-Mental-State-Examination scale score from 17.8±0.3 at baseline to 23.5±0.4 with the evening dosing (p<0.001) vs. the increase from 16.9±0.3 to 20.4±0.4 (p<0.001) with the morning dosing. The situational anxiety score decreased from 40.0±2.2 to 30.6±1.8 (p<0.05) and from 40.8±2.5 to 33.5±1.9 (p<0.05), and the trait anxiety score decreased from 48.8±2.0 to 26.4±1.9 (p<0.001) and from 44.9±1.9 to 30.7±1.7 (p<0.01) with the evening and morning dosing, respectively. Depressive disorders slightly decreased with the chronotherapy by 14.1% vs. 7.7% with the traditional regimen; nevertheless, they were consistent with depressive spectrum disorders in both groups.Conclusion The study results showed a higher effectiveness of the chronotherapeutic treatment compared to the traditional treatment with FC of amlodipine, lisinopril, and rosuvastatin in arterial hypertension with metabolic syndrome.

[27] *Zubareva MY, Malyshev PP, Ansheles AA, Sergienko IV*. **[Assessment of Risk Factors for Atherosclerosis in Individuals of Different Categories of Cardiovascular Risk Using the Aterostop Calculator]**. Kardiologiia 2021; 61:12-17.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33849413
***ABSTRACT***
Aim To analyze first results of using the Aterostop calculator for a comprehensive evaluation of the risk for cardiovascular diseases (CVD).Material and methods A cross-sectional study analyzed major and additional risk factors in 460 subjects without apparent disease and in patients with documented CVD of atherosclerotic origin using the application (calculator) Aterostop developed in the National Medical Research Center of Cardiology in Moscow, Russia.Results 45.4% of evaluated persons belonged to the categories of very high and extreme risk. Age and frequencies of smoking, arterial hypertension, and diabetes mellitus (DM) increased with the increase in risk; the growth of DM was exponential. 129 (28%) individuals used lipid-lowering medications at the time of study. Their plasma levels of low-density lipoprotein cholesterol (LDL-C) were significantly lower than in those who did not received this treatment. However, achieving the target level was inversely proportional to the risk: the greatest proportion of individuals who reached the LDL-C target was in the category of low risk and the smallest proportion was in the category of extreme risk (75% vs. 3.7%, respectively).Conclusion The results obtained with the calculator Aterostop were consistent with earlier reports of insufficient effectiveness of primary and secondary prevention of atherosclerotic CVDs, which requires more tight and fruitful cooperation of the physician and the patient.

[28] *Parhofer KG*. **[Lipoprotein(a)]**. MMW Fortschritte der Medizin 2021; 163:44-45.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33844224
***ABSTRACT***

[29] *Natarajan P, Pampana A, Graham SE et al.* **Chromosome Xq23 is associated with lower atherogenic lipid concentrations and favorable cardiometabolic indices**. Nature communications 2021; 12:2182.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33846329
***ABSTRACT***
Autosomal genetic analyses of blood lipids have yielded key insights for coronary heart disease (CHD). However, X chromosome genetic variation is understudied for blood lipids in large sample sizes. We now analyze genetic and blood lipid data in a high-coverage whole X chromosome sequencing study of 65,322 multi-ancestry participants and perform replication among 456,893 European participants. Common alleles on chromosome Xq23 are strongly associated with reduced total cholesterol, LDL cholesterol, and triglycerides (min $P = 8.5 \times 10(-72)$), with similar effects for males and females. Chromosome Xq23 lipid-lowering alleles are associated with reduced odds for CHD among 42,545 cases and 591,247 controls ($P = 1.7 \times 10(-4)$), and reduced odds for diabetes mellitus type 2 among 54,095 cases and 573,885 controls ($P = 1.4 \times 10(-5)$). Although we observe an association with increased BMI, waist-to-hip ratio adjusted for BMI is reduced, bioimpedance analyses indicate increased gluteofemoral fat, and abdominal MRI analyses indicate reduced visceral adiposity. Co-localization analyses strongly correlate increased CHRDL1 gene expression, particularly in adipose tissue, with reduced concentrations of blood lipids.

[30] *Nurmohamed NS, Collard D, Balder JW et al.* **From evidence to practice: development of web-based Dutch lipid reference values**. Neth Heart J 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33844162
***ABSTRACT***
INTRODUCTION: In the Netherlands, the total number of yearly measured lipid profiles exceeds 500,000. While lipid values are strongly affected by age and sex, until recently, no up-to-date age- and sex-specific lipid reference values were available. We describe the translation of big-cohort lipid data into accessible reference values, which can be easily incorporated in daily clinical practice. METHODS: Lipid values (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides) from all healthy adults and children in the LifeLines cohort were used to generate age- and sex-specific percentiles. A combination of RStudio, Cascading Style Sheets and HyperText Markup Language was used to interactively display the percentiles in a responsive web layout. RESULTS: After exclusion of subjects reporting cardiovascular disease or lipid-lowering therapy at baseline, 141,611 subjects were included. On the website, input fields were created for age, sex and all main plasma lipids. Upon input of these values, corresponding percentiles are calculated, and output is displayed in a table and an interactive graph for each lipid. The website has been made available in both Dutch and English and can be accessed at www.lipidtools.com . CONCLUSION: We constructed the first searchable, national lipid reference value tool with graphical display in the Netherlands to use in screening for dyslipidaemias and to reduce the underuse of lipid-lowering therapy in Dutch primary prevention. This study illustrates that data collected in big-cohort studies can be made easily accessible with modern digital techniques and preludes the digital health revolution yet to come.

[31] *Saadatagah S, Jose M, Dikilitas O et al.* **Genetic basis of hypercholesterolemia in adults**. NPJ genomic medicine 2021; 6:28.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33854068

***ABSTRACT***
We investigated monogenic and polygenic causes of hypercholesterolemia in a population-based cohort, excluding secondary hypercholesterolemia, and using an established framework to identify pathogenic variants. We studied 1682 individuals (50.2 ± 8.6 years, 41.3% males) from southeast Minnesota with primary hypercholesterolemia (low-density lipoprotein cholesterol (LDL-C) ≥155 mg/dl in the absence of identifiable secondary causes). Familial hypercholesterolemia (FH) phenotype was defined as a Dutch Lipid Clinic Network (DLCN) score ≥6. Participants underwent sequencing of LDLR, APOB, and PCSK9, and genotyping of 12 LDL-C-associated single-nucleotide variants to construct a polygenic score (PGS) for LDL-C. The presence of a pathogenic/likely pathogenic variant was considered monogenic etiology and a PGS ≥90th percentile was considered polygenic etiology. The mean LDL-C level was 187.3 ± 32.3 mg/dl and phenotypic FH was present in 8.4% of the cohort. An identifiable genetic etiology was present in 17.1% individuals (monogenic in 1.5% and polygenic in 15.6%). Phenotypic and genetic FH showed poor overlap. Only 26% of those who met the clinical criteria of FH had an identifiable genetic etiology and of those with an identifiable genetic etiology only 12.9% met clinical criteria for FH. Genetic factors explained 7.4% of the variance in LDL-C. In conclusion, in adults with primary hypercholesterolemia, 17.1% had an identifiable genetic etiology and the overlap between phenotypic and genetic FH was modest.

[32] *Salazar-Tortosa DF, Pascual-Gamarra JM, Labayen I et al.* **Interplay of physical activity and genetic variants of the endothelial lipase on cardiovascular disease risk factors**. Pediatric research 2021.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33859368

***ABSTRACT***
BACKGROUND: The aim of this study was to investigate the association of endothelial lipase gene (LIPG) polymorphisms with cardiovascular disease (CVD) risk factors in adolescents and their interaction with physical activity. METHODS: Six polymorphisms of LIPG were genotyped in 1057 European adolescents (12-18 years old) enrolled in the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) Study. CVD risk factors related to lipid profile, blood pressure, adiposity and glucose regulation were recorded. Physical activity was objectively measured by accelerometry. RESULTS: The major C allele of rs2000813, the minor T allele of rs2276269 and the minor G allele of rs9951026 were associated with lower levels of several CVD risk factors related to lipid profile. We also found a significant association of the TTACA LIPG haplotype (rs2000812, rs2000813, rs8093249, rs2276269 and rs9951026) with higher concentrations of low-density cholesterol and apolipoprotein B. Finally, the interaction between physical activity and the polymorphisms rs2000813, rs2276269 and rs9951026 had a significant influence on several CVD risk factors. CONCLUSIONS: LIPG polymorphisms were significantly associated with CVD risk factors in European adolescents. Interestingly, alleles of these polymorphisms were associated with a better cardiovascular profile in physically active adolescents only. High physical activity may reduce the development of CVD, modulating its genetic risk. IMPACT: Using gene-phenotype and gene × environment analyses, we detected associations between the endothelial lipase gene and cardiovascular risk factors, along with interactions with physical activity. This study shows that physical activity may modulate the influence of LIPG gene on cardiovascular risk in adolescents. These results bring insights into the mechanisms by which physical activity positively influences CVD in adolescents.

[33] *Moreno-Sepúlveda J, Capponi M*. **[The impact on metabolic and reproductive diseases of low-carbohydrate and ketogenic diets]**. Revista medica de Chile 2020; 148:1630-1639.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33844769

***ABSTRACT***

With low carbohydrate diets glucose becomes unavailable as a source of energy for our body, leading to the production of ketones from fatty acids in the liver. The increase in plasma ketones is known as nutritional ketosis. The available evidence from basic and clinical studies indicates that both low carbohydrate and high fat low carbohydrate diets are effective for weight loss and are better than non-intervention. However, low carbohydrate diet and ketogenic diets induce unique metabolic changes and consistently improve some markers of cardiovascular risk, lowering elevated blood glucose, insulin, triglycerides, ApoB and saturated fat concentrations, reducing small dense LDL particle numbers, glycated hemoglobin levels, blood pressure and body weight while increasing HDL-cholesterol concentrations and reversing non-alcoholic fatty liver disease. Low carbohydrate diets are an efficient strategy for the management of obesity and metabolic syndrome. They may also benefit patients with polycystic ovary syndrome. They must be prescribed by trained professionals to balance the risks and benefits for each individual patient. Future research is required to improve the knowledge about individual responses to dietary interventions, their safety, tolerance, efficacy and long-term effects.

[34] *Li Y, Deng S, Liu B et al.* **The effects of lipid-lowering therapy on coronary plaque regression: a systematic review and meta-analysis**. Scientific reports 2021; 11:7999.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33846492

***ABSTRACT***

To assess the influence of lipid-lowering therapy on coronary plaque volume, and to identify the LDL and HDL targets for plaque regression to provide a comprehensive overview. The databases searched (from inception to 15 July 2020) to identify prospective studies investigating the impact of lipid-lowering therapy on coronary plaque volume and including quantitative measurement of plaque volume by intravascular ultrasound after treatment. Thirty-one studies that included 4997 patients were selected in the final analysis. Patients had significantly lower TAV (SMD: 0.123 mm(3); 95% CI 0.059, 0.187; P = 0.000) and PAV (SMD: 0.123%; 95% CI 0.035, 0.212; P = 0.006) at follow-up. According to the subgroup analyses, TAV was significantly reduced in the LDL < 80 mg/dL and HDL > 45 mg/dL group (SMD: 0.163 mm(3); 95% CI 0.092, 0.234; P = 0.000), and PAV was significantly reduced in the LDL < 90 mg/dL and HDL > 45 mg/dL group (SMD: 0.186%; 95% CI 0.081, 0.291; P = 0.001).Thirty-one studies that included 4997 patients were selected in the final analysis. Patients had significantly lower TAV (SMD: 0.123 mm(3); 95% CI 0.059, 0.187; P = 0.000) and PAV (SMD: 0.123%; 95% CI 0.035, 0.212; P = 0.006) at follow-up. According to the subgroup analyses, TAV was significantly reduced in the LDL < 80 mg/dL and HDL > 45 mg/dL group (SMD: 0.163 mm(3); 95% CI 0.092, 0.234; P = 0.000), and PAV was significantly reduced in the LDL < 90 mg/dL and HDL > 45 mg/dL group (SMD: 0.186%; 95% CI 0.081, 0.291; P = 0.001). Our meta-analysis suggests that not only should LDL be reduced to a target level of < 80 mg/dL, but HDL should be increased to a target level of > 45 mg/dL to regress coronary plaques.Trial Registration PROSPERO identifier: CRD42019146170.

[35] *Luo JY, Fang BB, Du GL et al.* **Association between MIF gene promoter rs755622 and susceptibility to coronary artery disease and inflammatory cytokines in the Chinese Han population**. Scientific reports 2021; 11:8050.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33850223

***ABSTRACT***
Macrophage migration inhibitory factor (MIF) is an essential mediator of atherosclerotic plaque progression and instability leading to intracoronary thrombosis, therefore contributing to coronary artery disease (CAD). In this study, we investigated the relationship between MIF gene polymorphism and CAD in Chinese Han population. Three single nucleotide polymorphisms (SNP, rs755622, rs1007888 and rs2096525) of MIF gene were genotyped by TaqMan genotyping assay in 1120 control participants and 1176 CAD patients. Coronary angiography was performed in all CAD patients and Gensini score was used to assess the severity of coronary artery lesions. The plasma levels of MIF and other inflammatory mediators were measured by ELISA. The CAD patients had a higher frequency of CC genotype and C allele of rs755622 compared with that in control subjects (CC genotype: 6.5% vs. 3.9%, P = 0.008, C allele: 24.0% vs. 20.6%, P = 0.005). The rs755622 CC genotype was associated with an increased risk of CAD (OR: 1.804, 95%CI: 1.221-2.664, P = 0.003). CAD patients with a variation of rs755622 CC genotype had significantly higher Gensini score compared with patients with GG or CG genotype (all P < 0.05). In addition, the circulating MIF level was highest in CAD patients carrying rs755622 CC genotype (40.7 ± 4.2 ng/mL) and then followed by GC (37.9 ± 3.4 ng/mL) or GG genotype (36.9 ± 3.7 ng/mL, all P < 0.01). Our study showed an essential relationship between the MIF gene rs755622 variation and CAD in Chinese Han population. Individuals who carrying MIF gene rs755622 CC genotype were more susceptible to CAD and had more severe coronary artery lesion. This variation also had a potential influence in circulating MIF levels.

[36] *Zhu H, Wang H, Jia Y et al.* **Increased serum calcium levels are associated with carotid atherosclerotic plaque in normocalcaemic individuals with type 2 diabetes**. Therapeutic advances in endocrinology and metabolism 2021; 12:2042018821995369.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33854752

***ABSTRACT***
BACKGROUND: Patients with type 2 diabetes mellitus (T2DM) have an elevated risk of atherosclerotic cardiovascular disease. Although previous data have suggested that serum calcium levels could be involved in T2DM and cardiovascular disease, whether this applies in T2DM patients with atherosclerosis remains unclear. This study therefore aimed to investigate the relationship between serum calcium levels within the physiological ranges and carotid atherosclerotic plaque in T2DM patients. METHODS: A total of 594 normocalcaemic in-patients with T2DM were recruited, of whom 231 had carotid atherosclerotic plaque. Serum calcium levels were measured and carotid ultrasonography was performed. RESULTS: Patients with plaque had significantly higher serum albumin-corrected calcium than those without plaque [9.02 (8.78-9.34) mg/dL versus 8.86 (8.66-9.06) mg/dL, p < 0.001]. As serum albumin-corrected calcium levels increased across tertiles, the percentage of plaque increased (27.6%, 35.5%, and 55.7%; p < 0.001). Logistic regression showed that serum albumin-corrected calcium levels were independently and positively correlated with the presence of plaque, but not parathyroid hormone levels. Compared with patients in the lowest serum calcium tertiles, the odds ratio for plaque in patients in the upper quartile was 2.47 (95% confidence

interval 1.51-4.03, p<0.001) after adjustment for potential confounders. CONCLUSION: Serum albumin-corrected calcium levels are elevated in patients with T2DM and carotid atherosclerotic plaques.

[37] *Chen Y, Xiong N, Wang X et al.* **Efficiency of atorvastatin on in-hospital mortality of patients with acute aortic dissection (AAD): study protocol for a randomized, open-label, superiority clinical trial**. Trials 2021; 22:281.
**PM:** http://www.ncbi.nlm.nih.gov/pubmed/?term=33853639
***ABSTRACT***
BACKGROUND: Dyslipidemia and local inflammation at sites of lipid deposition on blood vessel walls have been demonstrated to be risk factors for patients with acute aortic dissection (AAD). Statins have anti-inflammatory and lipid-lowering effects, which suggest that statins may play an important role in the prevention and treatment of AAD. Some retrospective studies show that statins can protect patients with aortic dissection. However, the effect of statins on the survival of AAD patients has been scarcely investigated, especially in randomized trials. In this study, we will perform a randomized clinical trial to understand whether statins can reduce in-hospital mortality of AAD patients.
METHODS: A total of 384 subjects diagnosed with AAD in the First Affiliated Hospital of Shantou University Medical College will be recruited. Participants will be randomly divided into an atorvastatin-treated or control group. The primary outcome will be the in-hospital mortality at 30 days.
DISCUSSION: This study is designed to verify the efficacy of atorvastatin on reducing in-hospital mortality of patients with AAD. The aim is to provide a new means of improving survival as a complement to conventional drug therapy. TRIAL REGISTRATION: Chinese Clinical Trials Registry ChiCTR1900023515 . Registered on 1 June 2019.