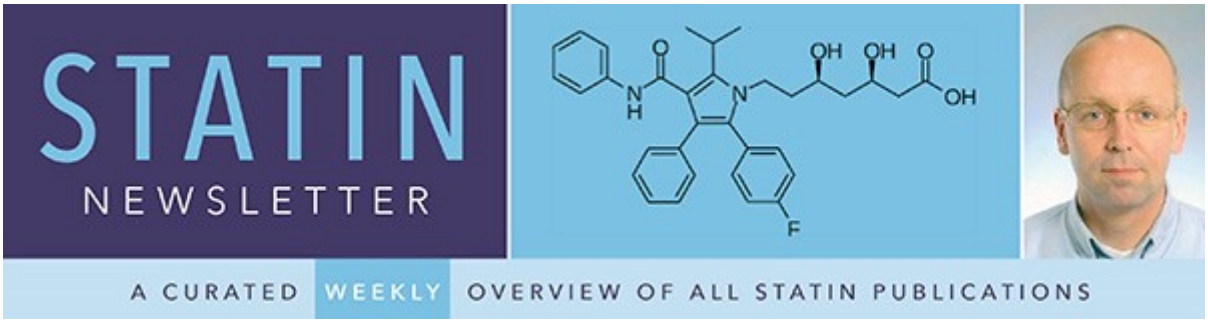

Update week 41 & 42 - 2022

Dr. Peter Lansberg is a Dutch lipidologist, educator and innovator. He has been instrumental in setting up The Dutch National Lipid Clinic Network, the Dutch Lipid Clinic Criteria for Familial Hypercholesterolemia (FH), and the Dutch National FH screening program

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The Statin Newsletter will keep you up-to-date with all recent statin publications. Based on a curated approach to select relevant articles.

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Key Publications

1. **The effect of statins on viral infections**
2. **If earlier is better. CV risk screening at younger age is detrimental**
3. **Inflammation and statins in PAD patients**
4. **hsTn a biomarker with potential - IMPROVE-IT sub analysis**
5. **Pleiotropic effects of lipid lowering drugs fiction or fact?**

Viral infection risk and statins

Statin therapy may reduce the risk of viral infections and related hospitalisations in patients with hyperlipidemia, according to a study in Taiwan. Researchers conducted a retrospective cohort study using data from Taiwan's National Health Insurance Research Database, and identified 20,202 patients with hyperlipidemia, which they divided into two groups: statin users and non-users. The risk of viral infection was found to be 40% lower in statin users than in non-users after adjustment for potential confounders, and the risk reduced as the duration of statin treatment increased. The study also found that statin therapy was associated with a lower risk of viral infection in all age groups in both men and women. Statins are known to have cholesterol-independent, immunomodulatory effects, and previous in vitro studies have suggested that statins may have antiviral effects. These findings add to the growing body of evidence that statin therapy may be beneficial in reducing the risk of viral infections, including COVID-19. However, more research is needed to confirm these findings and to understand the mechanisms by which statins may exert their antiviral effects.

Wu BR, Chen DH, Liao WC *et al.* **Statin Therapy and the Risk of Viral Infection: A Retrospective Population-Based Cohort Study.** Journal of clinical medicine 2022; 11. http://www.ncbi.nlm.nih.gov/pubmed/?term=36233493

Is screening for ASCVD risk at an earlier age cost-effective

The objective of this study was to evaluate the cost-effectiveness of screening strategies for cardiovascular diseases (CVD) in the Spanish National Health Service (NHS). The authors used an analytic decision model to estimate the costs and benefits of one-time screening strategies that varied by screening age, sex, and the threshold for initiating statin therapy (either "uniform" or "age-adjusted"). Health benefit was measured in quality-adjusted life years (QALYs). The authors used data from the European Prospective Investigation into Cancer and Nutrition (EPIC-CVD), a large multi-center nested case-cohort study, to estimate transition rates, and unit costs were taken from the Spanish health system. The authors found that the most efficient one-time screening strategy was to screen men and women at age 40 using a uniform risk threshold for initiating statin treatment (with an incremental cost-effectiveness ratio of €3,274/QALY for men and €6,085/QALY for women). They also found that reallocating statin treatment to younger individuals at high risk for their age and sex would not offset the benefit of treating older individuals with the same resources. The authors concluded that one-time screening for CVD using a uniform risk threshold appears cost-effective compared to no systematic screening. However, they note that the results are sensitive to assumptions about CVD incidence rates and should be evaluated in clinical studies.Špacírová Z, Kaptoge S, García-Mochón L *et al.* The cost-effectiveness of a uniform versus age-based threshold for one-off screening for prevention of cardiovascular disease. The European journal of health economics : HEPAC : health economics in prevention and care 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36239877

Statins in PAD – is inflammation a key biomarker?

This study aimed to investigate the effect of statins on the prognosis of patients with peripheral artery disease (PAD) who underwent endovascular therapy (EVT). The study included 560 patients with PAD, 285 of whom were taking statins and 275 of whom were not. The patients were divided into four groups based on their C-reactive protein (CRP) level at the time of EVT: low CRP (<0.1 mg/dL), intermediate-low CRP (0.1-0.3 mg/dL), intermediate-high CRP (0.3-1.0 mg/dL), and high CRP (>1.0 mg/dL). The primary endpoint was a composite of death and major amputation, and the event rates were compared between statin users and non-users in each CRP category. Overall, statin users had a lower event rate than non-users (p=0.02). However, the event rates did not differ significantly between the two groups in the low, intermediate-low, and intermediate-high CRP categories. In the high CRP category, statin users had a lower event rate than non-users (p=0.002). In this group, statin use was independently associated with the primary endpoint (hazard ratio: 0.28 [95% confidence interval: 0.14-0.55]). These results suggest that statins may have favorable prognostic effects in PAD patients with highly elevated CRP levels but not those with low-to-moderate CRP levels.
Shibahashi E, Jujo K, Mizobuchi K *et al.* Prognostic Impact of Statins on Patients With Peripheral Artery Disease With Elevated C-Reactive Protein Levels. Am J Cardiol 2023; 186:142-149. http://www.ncbi.nlm.nih.gov/pubmed/?term=36257842

High-Sensitivity Cardiac Troponin T; a relevant biomarker in IMPROVE-IT

High-sensitivity troponin (hsTn) is a protein found in the heart that is released into the bloodstream when the heart is damaged. Elevated levels of hsTn in the blood have been linked to an increased risk of future cardiovascular events, such as heart attack and stroke, in patients with chronic coronary syndromes. However, little is known about the association between changes in serial hsTn levels and subsequent cardiovascular events in these patients. The Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) was a clinical trial that enrolled 18,144 patients hospitalized for acute coronary syndrome (ACS) across 1147 sites in 39 countries. The current biomarker substudy analyzed data from 6035 participants who consented to the substudy and had hsTnT levels measured at months 1 and 4. The primary outcomes of interest were cardiovascular death, myocardial infarction (MI), stroke, or hospitalization for heart failure (HHF). The researchers found that changes in hsTnT between month one and month four

were associated with a gradient of risk for future cardiovascular events across the range of starting month one hsTnT values. Specifically, an absolute increase in hsTnT of 7 ng/L or more was associated with a more than 3-fold greater risk of the composite outcome. In comparison, decreases of 7 ng/L or more were associated with similar to lower risk compared with stable values. This association was also observed when analyzed based on relative percent and continuous change. These findings suggest that serial assessment of hsTnT may be useful in refining risk stratification and guiding therapy decisions in patients with prior ACS.

Patel SM, Qamar A, Giugliano RP *et al.* **Association of Serial High-Sensitivity Cardiac Troponin T With Subsequent Cardiovascular Events in Patients Stabilized After Acute Coronary Syndrome: A Secondary Analysis From IMPROVE-IT**. JAMA cardiology 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36260325

Visualizing the non-lipid lowering effects of statins and PCSK9ab

Statins are a commonly prescribed medication for patients with coronary artery disease, as they effectively reduce blood cholesterol levels. However, some patients may be intolerant to statins and may require alternative treatment options, such as proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i). In addition to their lipid-lowering effects, statins may also have non-lipid, cardio-protective effects, including improving cardiac nerve integrity, blood flow and reducing inflammation in congestive heart failure (CHF) patients. These effects can be visualized and monitored using nuclear cardiac radiotracers, such as 123I-metaiodobenzylguanidine (MIBG) and 18F-AF78 for cardiac nerve function, 18F-flurpiridaz for determining coronary flow, and 68Ga-PentixaFor for detecting inflammation. These imaging techniques allow in vivo monitoring of statin-induced cardioprotection beyond lipid profiling in CHF patients and help identify patients who may benefit from alternative treatment options. In addition, statins may also exhibit anti-inflammatory effects, which can be monitored using inflammatory-targeted radiotracers such as 68Ga-PentixaFor. This radiotracer can provide predictive information about the inflammatory burden in the infarcted area and may be able to identify high-risk patients prone to later major cardiovascular events. Comparing patients with and without statins after myocardial infarction and guideline-compatible intervention, the anti-inflammatory effects of statins can be determined in vivo. Overall, molecular cardiac imaging techniques may help optimize statin treatment and improve patient outcomes.

Higuchi T, Serfling SE, Rowe SP, Werner RA. **Therapeutic Effects of Lipid Lowering Medications on Myocardial Blood Flow, Inflammation, and Sympathetic Nerve Activity Using Nuclear Techniques.** Current cardiology reports 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36227406

Relevant Publications

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Basic Science

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