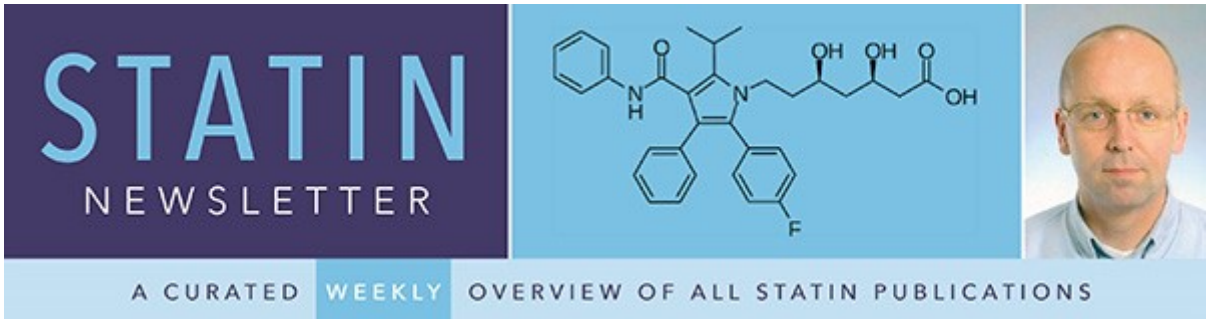

Update week 45 & 46 - 2022

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. **Benefits of statins in AF patient using OAC**
2. **Managing statin intolerance - practical recommendations**
3. **aim for an LDL-c of 50-75 mg/dl; or "the lower the better"?**
4. **Stop dietary supplements and take a statin!**
5. **Can statins prevent dementia?**

Bleeding risk in statin using AF patients on anti-coagulants

This study aimed to investigate the effects of statins in patients with non-valvular atrial fibrillation (NVAF) taking oral anticoagulants (OACs). The study was a historical multicenter registry of patients with NVAF taking OACs in Japan, and 7826 patients were registered on 26 February 2013 and followed until 25 February 2017. The study found that statins were administered in 2599 (33%) patients. The statin group was more likely to have paroxysmal AF, hypertension, diabetes mellitus, and dyslipidemia than the no-statin group. The cumulative incidence of major bleeding was 6.9% and 8.1% (p = 0.06). The study found that statins significantly reduced the risk of major bleeding, all-cause mortality, and ischemic events in patients with NVAF taking OACs. Their additive benefits should be considered in routine practice and thus be further researched.Uchida K, Ueda S, Sakakibara F *et al.* Statins Reduce Bleeding Risk in Patients Taking Oral Anticoagulants for Nonvalvular Atrial Fibrillation: A Retrospective Registry Study. Am J Cardiovasc Drugs 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36380115

Statin intolerance – a practical guidance

Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of morbidity and mortality, and statins have become a crucial approach for ASCVD risk reduction and are

among the most prescribed medications in the United States. Despite the well-documented benefits of statins, many patients stop taking them, with adverse muscle symptoms being a commonly cited reason. This is an issue because discontinuation of statins is associated with an increase in CVD events. The nocebo effect, which is the patient's perception of harm, can also play a role in statin intolerance. The aim of this article is to review the extent and factors contributing to statin intolerance, discuss real versus nocebo effects, and describe treatment strategies for patients intolerant to statins. Current and upcoming lipid-lowering therapies such as ezetimibe, PCSK9 inhibitors, bempedoic acid, and inclisiran can be effective in helping patients at risk of ASCVD achieve their lipid goals when they are unable to do so with a maximally tolerated statin. Trials studying the efficacy and long-term outcomes of these agents are needed to guide clinical practice. Employing shared decision-making with patients can go a long way towards building trust and improving the odds of therapeutic success.

Martirossian AN, Goldberg AC. **Management of patients with statin intolerance.** Best practice & research. Clinical endocrinology & metabolism 2022:101714. http://www.ncbi.nlm.nih.gov/pubmed/?term=36345572

Is an LDL-c of 50-75 mg/dl the “sweet spot”?

A subanalysis of the REAL-CAD study suggests that a "threshold" value of low-density lipoprotein cholesterol (LDL-C) might exist for the secondary prevention of cardiovascular events in Japanese patients with coronary artery disease (CAD). The study found that the risk of cardiovascular events decreased monotonically until the LDL-C level was lowered to 70 mg/dL, but when the level was further reduced, the risk was independent of LDL-C. This suggests that the "The lower, the better" hypothesis does not always apply to Japanese CAD patients. The study used a novel method called the "bottoming-out model" which divided the patients into six categories by LDL-C level at six months and calculated event rates and multivariable-adjusted hazard ratios within each category. The results of this study suggest that there might be a threshold value of LDL-C around 50-75 mg/dL for primary composite outcomes.

Sakuma M, Iimuro S, Shinozaki T *et al.* **Optimal target of LDL cholesterol level for statin treatment: challenges to monotonic relationship with cardiovascular events.** BMC Med 2022; 20:441. http://www.ncbi.nlm.nih.gov/pubmed/?term=36372869

Dietary supplements; Fa(c)ts vs fiction

This study is a randomized, placebo-controlled trial that compared the efficacy of a low-dose statin, rosuvastatin 5mg daily, with placebo and 6 common dietary supplements in impacting lipid and inflammatory biomarkers among adults with no history of atherosclerotic cardiovascular disease (ASCVD), an LDL-C of 70 to 189 mg/dL, and an increased 10-year risk of ASCVD. The supplements tested were fish oil, cinnamon, garlic, turmeric, plant sterols, and red yeast rice. The primary endpoint was the percent change in LDL-C from baseline for rosuvastatin 5 mg daily compared with placebo and each supplement after 28 days. The study found that the percent LDL-C reduction with rosuvastatin was greater than all supplements and placebo ($P < 0.001$). The difference in LDL-C reduction with rosuvastatin compared with placebo was 35.2% (95% CI: 41.3% to 29.1%; $P < 0.001$). None of the dietary supplements demonstrated a significant decrease in LDL-C compared with placebo. Adverse event rates were similar across study groups. The study concludes that among individuals with increased 10-year risk for ASCVD, rosuvastatin 5 mg daily lowered LDL-C significantly more than placebo, fish oil, cinnamon, garlic, turmeric, plant sterols, and red yeast rice.

Laffin LJ, Bruemmer D, Garcia M *et al.* **Comparative Effects of Low-Dose Rosuvastatin, Placebo, and Dietary Supplements on Lipids and Inflammatory Biomarkers.** J Am Coll Cardiol 2023; 81:1-12. http://www.ncbi.nlm.nih.gov/pubmed/?term=36351465

Risk of dementia higher in those with low LDL-c; but the opposite with statins.

This study explores the association between cholesterol levels and dementia risk according to the presence of diabetes and statin use. The study used data from the Korean National

Health Insurance Service datasets from 2002 to 2017, and evaluated the hazard of dementia in individuals aged 40 and older who underwent health examinations in 2009 (N = 6,883,494). During a median 8.33 years, 263,185 dementia cases were detected. The study found that in statin non-users with or without diabetes, the hazards of all-cause dementia were highest for those in the lowest quartile or quintile of low-density lipoprotein-cholesterol (LDL-C) level, showing an inverted J-shaped relationship. However, this trend was not observed in statin users regardless of the presence of diabetes, with an increasing trend in the hazards of all-cause dementia according to increasing LDL-C quartile or quintile. The study also found that in statin users with diabetes, even very low LDL-C level was not associated with an increased risk of all-cause dementia. The study suggests that the trend of low LDL-C level being associated with an increased risk of dementia in statin non-users is not likely to be clinically relevant and rather, an advance in LDL-C levels is associated with an increase in the hazard of all-cause dementia in statin users, regardless of the presence of diabetes. Lee YB, Kim MY, Han K *et al.* **Association between cholesterol levels and dementia risk according to the presence of diabetes and statin use: a nationwide cohort study.** Scientific reports 2022; 12:19383. http://www.ncbi.nlm.nih.gov/pubmed/?term=36371594

Relevant Publications

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Basic Science

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