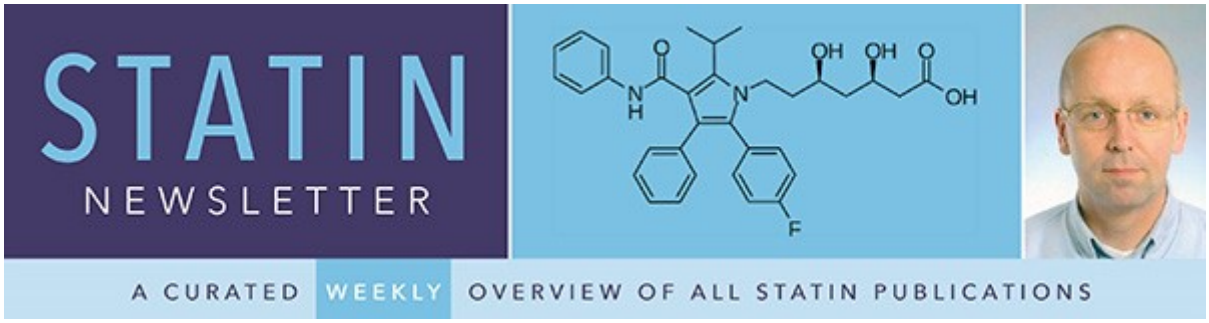

Update week 37 & 38 - 2023

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. **Effects of low LDL-c on hemorrhagic stroke and dementia - Scientific statement AHA**
2. **Statins in patients with end stage renal disease + PAD**
3. **Variability in plasma lipids more pronounced in patients using statins + ezetimibe compared to high-intensity statin mono-therapy**.

Join us in Prague!

Key publications

AHA Scientific statement on LDL-c, dementia, and haemorrhagic stroke

The scientific statement titled "Impact of Aggressive Reduction of LDL-C on the Brain" by the American Heart Association provides a comprehensive evaluation of contemporary evidence on the association between aggressive LDL-C lowering and the risk of cognitive impairment and hemorrhagic stroke. This systematic review of randomized controlled trials and observational studies, summarizes the current state of knowledge on this topic. The statement highlights that while aggressive LDL-C lowering has been shown to reduce the risk of cardiovascular events, there is limited evidence on its impact on the brain. The statement also notes that there is conflicting evidence on the association between statin use and cognitive impairment, and that the potential toxic effects of aggressive LDL-C lowering on the brain need to be further investigated. One of the key findings is the lack of evidence to support the hypothesis that aggressive LDL-C lowering leads to cognitive impairment or dementia. While some studies have suggested a possible association between statin use and cognitive impairment, these studies have limitations, such as small sample sizes and short follow-up periods. Contrasting studies found no association between statin use and cognitive impairment, and that the evidence on this topic is conflicting. The association between aggressive LDL-C lowering and hemorrhagic stroke is unclear. While some studies have suggested an increased risk of hemorrhagic stroke with statin use, however the number of participants with hemorrhagic stroke in these studies was small, and that the between-group differences were not significant. Several studies have found no association between statin use and hemorrhagic stroke, and that the evidence on this topic is also conflicting. Overall, the scientific statement provides a valuable summary of the current state of knowledge on the impact of aggressive LDL-C lowering on the brain and highlights the need for further research in this area. The statement provides recommendations for clinicians and researchers, including the need for further studies to evaluate the long-term effects of aggressive LDL-C lowering on the brain, and the need for more research on the potential mechanisms underlying the association between LDL-C lowering and cognitive impairment.

Aggressive LDL-C Lowering and the Brain: Impact on Risk for Dementia and Hemorrhagic Stroke: A Scientific Statement From the American Heart Association. Arterioscler Thromb Vasc Biol **2023; Goldstein LB, Toth PP, Dearborn-Tomazos JL *et al.***
http://www.ncbi.nlm.nih.gov/pubmed/?term=37706297

Statins are protecting end stage renal disease + PAD patients

In this study the authors aimed to ascertain the therapeutic role of statins in patients afflicted with both Peripheral Artery Disease (PAD) and End-Stage Renal Disease (ESRD). The analysis utilized data from Taiwan's National Health Insurance Research Database and used propensity score matching to equate baseline characteristics between statin users and nonusers. While the overall rates of limb events and major adverse cardiovascular events (MACEs) remained consistent between both groups, strikingly, the group on statins showcased reduced rates of limb amputation, stroke, cardiovascular death, and overall death. This was despite a higher incidence of angioplasty for PAD in the statin group. These findings contrast with some earlier studies that found limited cardiovascular benefits of statins in ESRD patients. It's crucial to highlight that PAD and ESRD patients form a high-risk population demanding rigorous medical intervention. This research posits that despite the controversies surrounding the use of statins in ESRD patients, those with co-existing PAD may indeed benefit from statin therapy. However, limitations such as the non-consideration of statin type, dosage, and duration, and lack of detailed patient biomarker data require that these findings be interpreted with caution. The potential therapeutic advantage of statins for secondary prevention in ESRD patients with PAD certainly warrants further exploration.

Protective Effects of Statins on Limb and Cardiovascular Outcomes in Patients with Peripheral Artery Disease and End-Stage Renal Disease. Acta Cardiologica Sinica **2023;**

39:755-764Lu CR, Lu SY, Lin SY *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37720404

Statin + ezetimibe or high intensity statin? Variability in plasma lipids favors the latter.

This retrospective study assessed the variability in plasma lipids in 1,275 patients with coronary atherosclerosis disease (CAD) on either intensive statin therapy or conventional-dose statins combined with ezetimibe, over a decade. The key finding indicates that intensive statin therapy offers less variability in key lipid parameters such as total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and non-HDL-C compared to the combination therapy. Less variability might correlate with more consistent drug effects and potentially fewer cardiovascular events, considering lipid variability has emerged as a reliable predictor of such events.

While this insight is invaluable, the study's retrospective nature poses inherent limitations. Changes in lipid management guidelines over the 10-year enrollment period might introduce inconsistencies in patient treatment strategies. Also, baseline differences in LDL levels among groups could introduce confounding factors. Furthermore, the potential influence of varying diets and environments on lipid levels during different follow-up times isn't accounted for. As variability in ezetimibe's effects might relate to dietary changes, a controlled, prospective trial would provide a more definitive assessment. In essence, while the study underscores the potential benefits of intensive statin therapy over combination therapy in lipid variability, the methodological constraints warrant a cautious interpretation. Future randomized controlled trials will be instrumental in cementing these findings.

Variability in Plasma Lipids Between Intensive Statin Therapy and Conventional-Dose Statins Combined with Ezetimibe Therapy in Patients with Coronary Atherosclerosis Disease. Int Heart J 2023; Jin J, Shan L, Wang M *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37704407

Relevant Publications

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2. Early Computed Tomography Coronary Angiography and Preventative Treatment in Patients with Suspected Acute Coronary Syndrome A secondary analysis of the RAPID-CTCA trial. Am Heart J 2023; Wang KL, Meah MN, Bularga A *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37709109
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