



Update week 49 & 50 - 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

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. **Statins prevent NAFLD - NASH - Fibrosis**
2. **OMT important in Elderly post-PCI patients**
3. **When to start novel lipid lowering drugs**
4. **No increased cerebral bleeding risk observed in statin users**
5. **Proteomics confirm pleiotropic benefits of statins**

Evidence linking statin uses to prevent NAFLD, NASH and fibrosis

The use of statins, drugs commonly prescribed to lower cholesterol levels, may prevent non-alcoholic fatty liver disease (NAFLD) and lower the prevalence of non-alcoholic steatohepatitis (NASH) and fibrosis in patients with NAFLD, according to a new study. The study, which was performed on a large general population in the Rotterdam Study and a group of biopsy-proven NAFLD patients in the PERSONS cohort, found that statin use was inversely associated with NAFLD in the general population, NASH in the NAFLD group, and fibrosis in both groups. The results were then pooled with available literature in a meta-analysis, which showed significant inverse associations with NASH and fibrosis. In vitro experiments also showed that statins significantly reduced lipid droplet accumulation in human liver organoids and downregulated pro-inflammatory cytokines in macrophages. The study concluded that statin use was associated with a lower prevalence of NASH and fibrosis and might prevent NAFLD, and this may be due to their anti-lipid and anti-inflammatory effects

Ayada I, van Kleef LA, Zhang H *et al.* **Dissecting the multifaceted impact of statin use on fatty liver disease: a multidimensional study.** *EBioMedicine* 2023; 87:104392.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=36502575>

OMT important; even in elderly post-PCI patients

A new study has revealed that optimal medical therapy (OMT) after percutaneous coronary intervention (PCI) has beneficial effects on long-term clinical outcomes in patients aged over 80 years with coronary artery disease (CAD). The study found that the use of OMT in these patients was associated with a significant reduction in the risk of adverse clinical events after PCI, including all-cause death and nonfatal myocardial infarction (MI). The study was a multicenter observational study and analyzed the time to the first major adverse clinical event, including death or nonfatal MI, for up to 3 years after PCI using multicenter registry data. The data included 1,056 patients aged over 80 years successfully treated with PCI. OMT was defined as a combination of antiplatelet drug, statin, beta-blocker, and angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker. The results showed that the beneficial effects of OMT on the risk of adverse clinical events remained significant in the propensity score-matched data, suggesting that OMT might be safe and effective for well selected patients aged over 80 years with CAD treated by PCI.

Nakamura T, Horikoshi T, Kobayahi T *et al.* **Optimal medical therapy after percutaneous coronary intervention in very elderly patients with coronary artery disease.** *Int J Cardiol Cardiovasc Risk Prev* 2023; 16:200162. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36506909>

When to add novel lipid lowering drugs; a step by step approach

Dyslipidemia is a significant risk factor for atherosclerotic cardiovascular disease (ASCVD). Despite an increase in high-intensity statin prescription, a substantial number of patients are still unable to reach the recommended goals. Several new lipid-lowering medications have been approved in the past decade including PCSK9 inhibitors, ATP-citrate lyase inhibitors, angiopoietin-like 3 inhibitors, lomitapide, and icosapent ethyl. Although approved, these drugs are under-prescribed worldwide due to cost, lack of cardiovascular outcomes, or unfamiliarity among clinicians. In this review, a practical stepwise approach is proposed to help clinicians prescribe these novel lipid-lowering medications to achieve treatment goals and reduce the risk of ASCVD. Advances in gene silencing technology, such as antisense oligonucleotides and siRNA, are being used to target genes that play a crucial role in dyslipidemia. New lipid-modifying agents that target other lipids besides LDL-C, including HDL-C, TG, and Lp(a), are also being explored. It is essential to have proper knowledge about these newer agents to reach treatment goals and reduce morbidity and mortality from ASCVD. Additional outcomes data and future guideline recommendations may shed light on the future of ASCVD risk reduction.

Kakavand H, Aghakouchakzadeh M, Shahi A *et al.* **A stepwise approach to prescribing novel lipid-lowering medications.** *J Clin Lipidol* 2022; 16:822-832. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36522804>

Cerebral bleeding risk with statin therapy – meta-analysis

A meta-analysis of 29 randomized controlled trials with 145,929 participants found that statin therapy is not associated with increased risk of bleeding or intracranial hemorrhage (ICH). The meta-analysis followed participants for a median of 3.65 years for bleeding events and 3.95 years for ICH. Although there was a subgroup analysis that showed an increased risk of ICH in patients with a prior stroke, these results were not robust and could be driven by a single study. The meta-analysis aimed to address the concern of bleeding events in statin therapy by pooling data from large sample size RCTs with a follow-up duration of more than three months to decrease the possibility of random error. The result supports the notion that statin therapy is not associated with the risk of bleeding or ICH.

Liu X, Zhu H, Zheng H *et al.* **Statin therapy and the risk of all bleeding and intracranial hemorrhage: A meta-analysis of randomized controlled studies.** *J Evid Based Med* 2022; 15:373-384. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36510635>

Proteomic analyses reveals the pleiotropic effects of statins

A new study has compared the proteome of statin users to non-users in order to determine whether statin use is associated with proteins unrelated to lipid metabolism. The study found that statin users had 11 enriched and 11 depleted protein levels compared to non-users, with many of the proteins having previously been linked to various non-

cardiovascular conditions. The results of the study suggest that statins have a pleiotropic effect on the body, influencing not just lipid metabolism, but also other biological processes related to conditions such as neurologic function, diabetes, metabolism, and cancer. The study provides valuable information on the potential biological mechanisms underlying the pleiotropic effect of statins, which will inform future efforts to identify statin users at risk of rare non-atherosclerotic outcomes and to identify the health benefits of statin use independent of LDL-C reduction.

Bohn B, Lutsey PL, Tang W *et al.* A proteomic approach for investigating the pleiotropic effects of statins in the atherosclerosis risk in communities (ARIC) study. J Proteomics 2023; 272:104788. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36470581>

Relevant Publications

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3. Becchetti C, Dirchwolf M, Berzigotti A, Bosch J. Letter: PCSK9 inhibitor for liver transplant patients during the post-statin era? Authors' reply. Alimentary pharmacology & therapeutics 2023; 57:187-188. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36480715>
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5. Dixon DL. The impact of PCSK9 modulation on cardiovascular outcomes: recent advances and the managed care implications. The American journal of managed care 2022; 28:S139-s147. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36493346>
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Basic Science

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