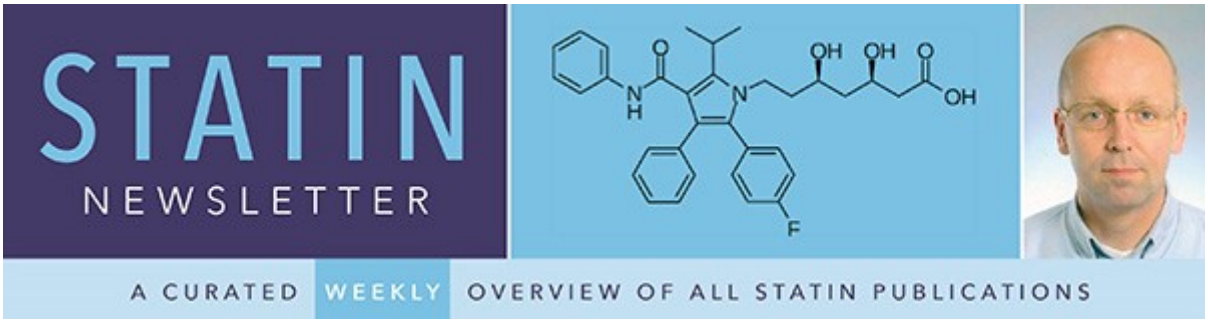

Update week 09 & 10 - 2023

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. **Can statins be prescribed to high risk pregnant wome?**
2. **Staitns and New Onset diabets - the facts versus beliefs**
3. **A personalized apporach to improve high-intensity statins use**
4. **Treat-to-target or fire-and-forget**
5. **It is the inflammation stupid!**

Statins in Pregnancy – case studies and review

This study reviews 13 pregnant women with familial hypercholesterolemia (FH) between 2007 and 2021, noting good maternal and fetal outcomes but significant loss of statin treatment time due to discontinuation during preconception, pregnancy, and lactation. The authors suggest that continuing statin therapy up to conception and even during pregnancy in higher-risk patients may be justified, given increasing evidence supporting statin therapy's safety during pregnancy. However, more long-term maternal and fetal data are needed for routine statin use during pregnancy. The authors advocate for guideline-informed models of care covering family planning and pregnancy for women with FH.
Familial hypercholesterolaemia in pregnancy: Australian case series and review. Aust N Z J Obstet Gynaecol 2023; Nangrahary M, Graham DF, Pang J *et al.*
http://www.ncbi.nlm.nih.gov/pubmed/?term=36883608

Statins and new onset diabetes – what have we learned?

Statins, lipid-lowering agents, have been linked to a small but significant increase in the risk of developing type 2 diabetes. The risk is higher with greater statin intensities and in patients with more diabetes risk factors at baseline. However, the cardiovascular benefits of statins outweigh their impact on diabetes risk, with one extra diabetes case occurring per

100-200 statin recipients over 5 years, while the benefits on major vascular outcomes are ~10-fold greater. The underlying mechanisms for the increased diabetes risk remain uncertain, and more research is needed. Clinically, doctors should counsel patients about the potential for a modest increase in diabetes risk when starting statins and advise them that lifestyle improvements can mitigate this risk and further lower cardiovascular risks. They should also monitor patients' HbA1c or fasting glucose levels after starting statin treatment to diagnose pre-diabetes or new diabetes and treat accordingly.

Statins and diabetes: What are the connections? Best practice & research. Clinical endocrinology & metabolism 2023:101749Sattar N. http://www.ncbi.nlm.nih.gov/pubmed/?term=36858834

Improving high-intensity statin prescribing by personalized reminders

A cluster-RCT study in the Department of Veterans Affairs aimed to assess if personalized reminders could improve high-intensity statin (HIS) use in patients with atherosclerotic cardiovascular disease (ASCVD). The intervention involved sending individualized reminders to primary care clinicians 2-7 days before patients' visits or outside of the primary care visit. A total of 27 primary care clinics were randomized, with 14 assigned to the intervention and 13 to usual care. The results revealed that the intervention led to a significant increase in HIS use and statin adherence in ASCVD patients. The overall effect size was modest, but it was much higher among the 53% of eligible patients who received a reminder. Limitations included stringent algorithms to limit alert fatigue, a low number of synchronous reminders, clinician dropout, the lack of a clinical decision support algorithm, and cognitive demands on clinicians due to the ongoing COVID-19 pandemic. This study demonstrates how informatics-driven interventions can improve evidence-based care delivery in large healthcare systems.

Cluster Randomized Trial Of A Personalized Clinical Decision Support Intervention To Improve Statin Prescribing In Patients With Atherosclerotic Cardiovascular Disease (PCDS Statin). Circulation 2023; Virani SS, Ramsey DJ, Westerman D *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36871214

Treat-to-target of fire-and-forget?

This randomized clinical trial examined whether a treat-to-target strategy for LDL-C (low-density lipoprotein cholesterol) levels is noninferior to high-intensity statin therapy in patients with coronary artery disease (CAD). The study involved 4341 patients (98.7%) with CAD, who were assigned to either a treat-to-target group with an LDL-C goal of 50-70 mg/dL or a high-intensity statin group. The primary endpoint was a 3-year composite of death, myocardial infarction, stroke, or coronary revascularization. Results showed that the primary endpoint occurred in 8.1% of the treat-to-target group and 8.7% of the high-intensity statin group. The difference between the two groups met the prespecified noninferiority margin of 3.0 percentage points. The study concluded that among patients with CAD, the treat-to-target LDL-C strategy was noninferior to the high-intensity statin strategy for major clinical outcomes. This supports the suitability of a treat-to-target strategy that allows a tailored approach, considering individual variability in drug response to statin therapy.

Treat-to-Target or High-Intensity Statin in Patients With Coronary Artery Disease: A Randomized Clinical Trial. Jama 2023; Hong SJ, Lee YJ, Lee SJ *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36877807

in statin treated patients Inflammation was a superior residual risk factor compared to LDL-c

In a collaborative analysis of three randomized trials, inflammation and cholesterol were assessed as predictors of cardiovascular events among patients receiving statin therapy. The study involved 31,245 patients from the multinational PROMINENT, REDUCE-IT, and STRENGTH trials. The results showed that residual inflammatory risk, assessed by high-sensitivity C-reactive protein (CRP), was significantly associated with major adverse cardiovascular events, cardiovascular mortality, and all-cause mortality. In contrast, residual cholesterol risk, assessed by low-density lipoprotein cholesterol (LDLC), had a neutral

relationship with major adverse cardiovascular events and a low magnitude relationship with cardiovascular and all-cause death. The findings suggest that among patients receiving contemporary statins, inflammation measured by high-sensitivity CRP is a stronger predictor of future cardiovascular events and death than cholesterol measured by LDLC. This has implications for selecting adjunctive treatments beyond statin therapy and suggests that combined use of aggressive lipid-lowering and inflammation-inhibiting therapies may be needed to further reduce atherosclerotic risk.
Inflammation and cholesterol as predictors of cardiovascular events among patients receiving statin therapy: a collaborative analysis of three randomised trials. Lancet 2023; Ridker PM, Bhatt DL, Pradhan AD *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36893777
Inflammation contributes to cardiovascular risk in patients receiving statin therapy. Lancet 2023; Tardif JC, Samuel M. http://www.ncbi.nlm.nih.gov/pubmed/?term=36893776

Relevant Publications

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Basic Science

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