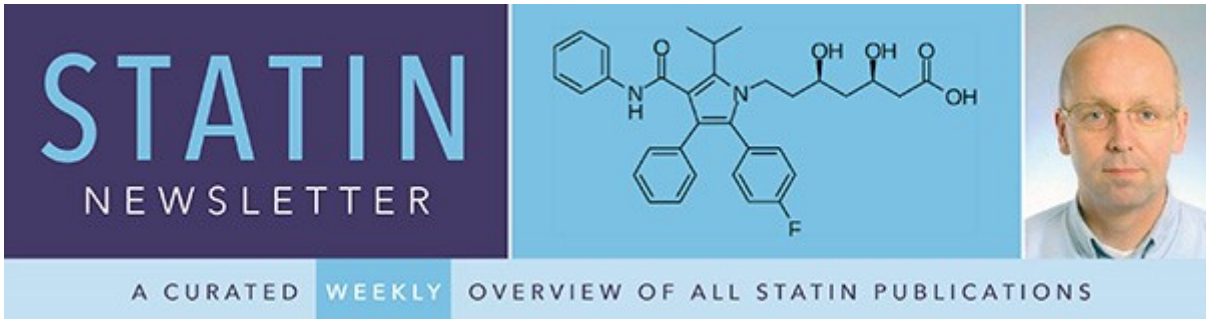

Update week 057& 08 - 2023

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. **In utero exposure to pravastatin not associated with neurodevelopmental disorders**
2. **The continuing saga of statins and Alzheimer disease**
3. **Guideline directed management largely ignorede in US post-PVI patients**
4. **Statins post aSAH - a meta-analysis**
5. **Can statins, and aspirin, help to prevent pre-eclampsia**

Safety of pravastatin after in utero exposure

A study conducted by researchers at the University of Texas Medical Branch at Galveston and published in the American Journal of Obstetrics and Gynecology examined the long-term neuromotor, cognitive, and behavioral outcomes of children exposed to pravastatin in-utero during the second and third trimesters of pregnancy. Pravastatin is a medication used to prevent preeclampsia in high-risk pregnancies, and the study aimed to determine the effect of antenatal pravastatin treatment on the child's health, growth, and neurodevelopment. The results showed that pravastatin treatment did not affect the child's growth, report of developmental or medical complications, or behavior. Children born to mothers treated with pravastatin had no limitations in motor assessment or manual abilities, general conceptual ability scores, or behavior. There was no identifiable long-term neurodevelopmental safety signal with the use of pravastatin during pregnancy, and the study supports the previously demonstrated favorable pregnancy and neonatal risk-benefit analysis in this high-risk cohort. Although the results are limited by the sample size of the original trial, the study justifies continued research using pravastatin in clinical trials. The researchers noted that preventing adverse pregnancy outcomes may improve the intrauterine environment and prevent the fetal programming of long-term adverse neurodevelopmental outcomes, and pravastatin has shown potential to reduce the long-

term adverse effects of fetal programming on neurodevelopmental, cardiovascular, and metabolic function in children born prematurely to individuals with preeclampsia.
Long-Term Neurodevelopmental Follow-up of Children Exposed to Pravastatin in-Utero. American journal of obstetrics and gynecology 2023; Costantine MM, Clifton RG, Boekhoudt TM *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36842489

Can statin promote or reduce amyloid beta in the brain?

The effect of statins on Alzheimer's disease (AD) has been the subject of much research, with studies reporting contradictory findings. This longitudinal study aimed to investigate the effect of statin drugs on amyloid β (Aβ) deposition and metabolism rate in patients with AD, mild cognitive impairment (MCI), and healthy controls (HC). The study analysed the data of 828 participants, including 178 HC, 492 MCI, and 158 AD individuals, over a four-year period, with baseline and longitudinal [18F] AV45 and 18-fluorodeoxyglucose PET standard uptake value ratio (SUVR) measures investigated. The results revealed that there was no significant difference in baseline Aβ deposition and metabolism rate between statin users and non-users among the HC, MCI, and AD subjects. However, the study found that using statins might be beneficial in slowing down or stabilising Aβ deposition in healthy individuals. Nonetheless, the study suggests that statins fail to slow down Aβ deposition once the clinical symptoms of cognitive impairment appear. The study recommends further investigation to assess the effect of statins on Aβ deposition and metabolism over a longer period.
Does statin use affect amyloid beta deposition and brain metabolism? CNS Neurosci Ther 2023; Nabizadeh F, Valizadeh P, Balabandian M. http://www.ncbi.nlm.nih.gov/pubmed/?term=36786148

Insufficient guideline-directed therapy in US post-PVI patients.

A new study has found that almost half of patients undergoing peripheral vascular interventions (PVI) in the US are not receiving guideline-directed medical therapy (GDMT), putting them at greater risk of mortality and amputation. PVI is a procedure used to treat peripheral artery disease (PAD), which affects over 8.5 million Americans. PAD patients are recommended to receive GDMT, including statin therapy, antiplatelet therapy, and hypertension medication, in order to manage cardiovascular risk. The study found that patients who did not receive GDMT had a 40% increased risk of mortality and a 20% increased risk of major amputation following PVI compared to those who did. GDMT rates also varied significantly between health systems and providers. The study highlights the need for quality improvement efforts in vascular care to focus on ensuring that patients undergoing PVI receive GDMT. The authors recommend designing and testing quality improvement metrics and reinforcement structures that take a multifactorial approach, including case management, audit and feedback with incentives, decision support tools, and educational materials. They suggest that a paradigm shift is needed to integrate vascular care with case management strategies that provide holistic, high-quality evidence-based care to successfully address PAD patients' multitude of risk factors.
Guideline-Directed Medical Therapy and Long-Term Mortality and Amputation Outcomes in Patients Undergoing Peripheral Vascular Interventions. JACC Cardiovasc Interv 2023; 16:332-343Smolderen KG, Romain G, Provance JB *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36792257

Meta-analysis on the effects of statins in aSAH patients

A new study has found that statins, commonly used to reduce cholesterol levels, could significantly decrease the incidence of ischemic cerebrovascular events (ICEs) and enhance functional prognosis in patients with aneurysmal subarachnoid hemorrhage (aSAH). The study applied Bayesian network meta-analysis to analyze the optimal dosage and type of statins for aSAH patients. A total of 2,569 patients from 14 studies were included in the analysis, and the outcomes were the incidence of ICEs and functional prognosis. The analysis revealed that statin use significantly improved functional prognosis in patients with aSAH, and statins significantly reduced the incidence of ICEs. Pravastatin at 40 mg/d was the most effective in reducing the incidence of ICEs compared to placebo and simvastatin, presenting a significantly lower rate of incidence than the latter. The study concluded that

statins could be recommended as an effective adjuvant therapy for aSAH, reducing the incidence of ICEs, and enhancing functional prognosis. The study also suggested that diverse types and dosages of statins showed distinct efficacies. The authors emphasized that large-scale randomized controlled trials are needed to explore the effects of different types and dosages of statins on ICEs incidence in patients with aSAH to provide optimal treatment options for clinicians. The limitations of the study were also noted, including the mixed use of observational studies and RCTs, limited direct comparisons of statin types and doses, and the need for more reliable conclusions based on larger sample RCTs.
Impacts of Statin Therapy Strategies on Incidence of Ischemic Cerebrovascular Events in Patients With Aneurysmal Subarachnoid Hemorrhage: A Systematic Review and Bayesian Network Meta-Analysis. Neurosurgery 2023; Zhong S, Liu T, Zhai Q *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36794961

Prevention of pre-eclampsia – the role of aspirin and pravastatin

Preeclampsia (PE) is a severe hypertensive disorder that affects up to 8% of pregnancies and is a leading cause of maternal mortality worldwide. It can cause end-organ damage and lead to complications for both the mother and fetus, resulting in a substantial financial burden on the healthcare system. Racial and ethnic disparities exist in the prevalence and burden of PE, with Non-Hispanic Black individuals developing the condition at higher rates and having higher case fatality rates. The pathogenesis of PE is multifactorial, involving genetic, immunologic, and environmental factors, as well as abnormal placentation, leading to an imbalance of angiogenic and antiangiogenic factors, endothelial cell dysfunction, and activation of the coagulation system. The use of aspirin and statins for the prevention of PE has been investigated. Aspirin is currently recommended for high-risk pregnancies, but the optimal dosage and timing have not been determined. Pravastatin has emerged as a potential agent for the prevention of PE, with more randomized trials supporting its effectiveness and safety. However, further research is needed to better understand the pathology of the disease and develop targeted therapies with limited side effects.
Aspirin and Pravastatin for Preeclampsia Prevention in High-Risk Pregnancy. Obstet Gynecol Clin North Am 2023; 50:79-88Eid J, Rood KM, Costantine MM. http://www.ncbi.nlm.nih.gov/pubmed/?term=36822711

Relevant Publications

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2. Pharmacogenetic Testing in a 70-Year-Old Woman with Polypharmacy and Multiple Comorbidities: A Case Report. Am J Case Rep 2023; 24:e938850Jessop JP, Russell J, DeJesus A *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36804920
3. Long-Term Neurodevelopmental Follow-up of Children Exposed to Pravastatin in-Utero. American journal of obstetrics and gynecology 2023; Costantine MM, Clifton RG, Boekhoudt TM *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=36842489
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