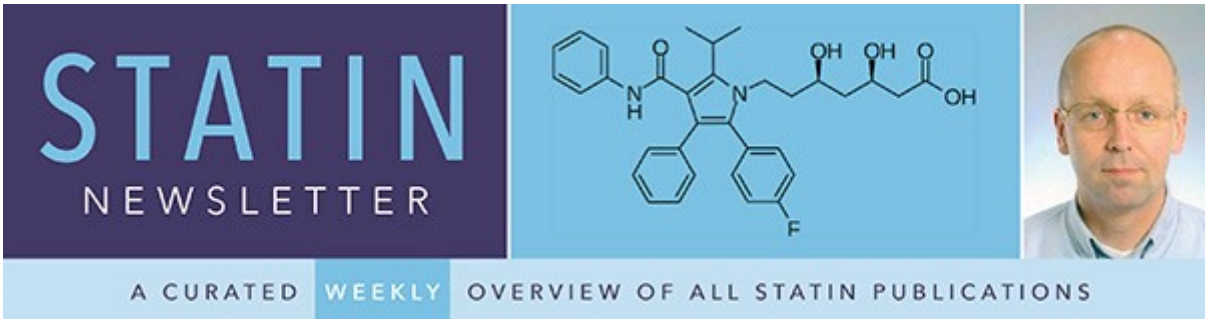

Update week 21 & 22 - 2023

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. **Are the kidneys protected or harmed by statins?**
2. **Short term use of PCSK9ab is Post PCI - ACS pateints**
3. **Is high a LDL-c beter for those that survive an AMI? The LDL paradox explained**
4. **What physicians think they do is not what they actually do - Adhering to guidelines targets**
5. **New models for early detection of drug induced myotoxicity**

Join us at the WCIM 2024 in Prague

Renal harm or benefits in diabetics using statins?

This retrospective study evaluates the role of statin initiation in the development of kidney disease in type 2 diabetes mellitus (DM) patients. Based on data collected in a Chinese multi-centre cohort study, statin initiation was linked with a significant decrease in the risk of developing diabetic kidney disease (DKD) and kidney function decline. The study also found that the association was stronger in those with better control of LDL-C. The findings contradict earlier research which suggested statins might not reduce kidney disease risk or could even have adverse detrimental renal effects. The strength of this study lies in its large sample size, real-world based data source, inclusion of diverse disease phenotypes, and hard kidney outcomes. However, the study has limitations, including potential uncontrolled factors affecting kidney outcomes, potential for ascertainment bias, and limited generalizability due to the specificity of the Chinese population. The authors call for more research to enrich our understanding on the protective renal effects of specific statins and newer lipid-lowering drugs.

Statin initiation and risk of incident kidney disease in patients with diabetes. **CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne 2023; 195:E729-e738Zhou S, Su L, Xu R *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37247880**

Impact of 3 months PCSK9ab in post PCI ACS pateints

This study evaluated if expensive PCSK9 focused interventions could be used be used for a limited period in post PCI-ACS patients. Patients were using lipid-lowering therapy (LLT) but often fail to reach the recommended low-density lipoprotein cholesterol (LDL-C) target level. In this study patients were randomised to 3 months of lipid lowering therapy (LLT) with a PCSK9 antibody followed by conventional LLT or 12 months of conventional LLT. The trial included a total of 124 patients. The primary endpoint was a composite of death, myocardial infarction, stroke, unstable angina, and ischemia-driven revascularization. The primary composite outcome occurred in 9.7% and 14.5% of the patients in the with- and without-PCSK9-antibody groups, respectively (hazard ratio: 0.70(0.25 to 1.97; p = 0.498) the results suggest that the addition of PCSK9 antibodies did not significantly alter the primary composite outcome or hospitalization rates, despite very intensive lowering LDL-C levels in the first 3 months. While these findings suggest the feasibility of short-term PCSK9 antibody treatment, the authors caution that the study's small scale and potential biases necessitate further, more rigorous testing. They suggest that longer-term studies with larger patient populations would provide a more definitive understanding of the potential benefits and risks of PCSK9 antibody administration in this context.

Feasibility of Short-Term Aggressive Lipid-Lowering Therapy with the PCSK9 Antibody in Acute Coronary Syndrome. **J Cardiovasc Dev Dis 2023; 10Yamashita S, Sakamoto A, Shoji S *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37233171**

The LDL-c paradox in MI survivors explained.

Using data from the SWEDEHEART study, the authors set out to explore the LDL-c paradox. They provide a nuanced understanding of this frequently debated observation of improved survival in MI patients with the highest LDL-c plasma concentrations. Their findings suggest that patients with high LDL-C levels at the time of MI have lower mortality and morbidity rates, mainly due to their younger age, fewer comorbidities, and the modifiability of LDL-C. However, these patients also exhibit an increased risk of recurrent nonfatal MI, supporting the causative role of LDL-C in ischemic heart disease. The study reveals that low LDL-C levels could be a sign of overall frailty and advanced biological age, often accompanied by numerous comorbidities, hence the poorer prognosis. However, reducing LDL-C levels post-MI still contributes to reduced mortality, underlining the importance of lipid-lowering treatments, irrespective of the initial LDL-C level at the time of MI. The study, therefore, reveals a complex interplay between LDL-C levels, patient age, comorbidity burden, and post-MI outcomes, calling for personalized patient management.

Elevated low-density lipoprotein cholesterol: An inverse marker of morbidity and mortality

in patients with myocardial infarction. Journal of internal medicine 2023; Schubert J, Lindahl B, Melhus H *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37254886

Physicians' perception of LDL-c control does not reflect reality

Physicians tend to overestimate the quality of their care, in the context of adhering to guideline recommendations. In this study the discrepancy between physicians' perceptions and actual LDL cholesterol control among dyslipidemia patients in Spain was explored. Physicians overestimated LDL cholesterol control rates (62% perceived vs. 31% actual), suggesting a misunderstanding of the extent of dyslipidemia control, which may contribute to therapeutic inertia. Inadequate intensification of lipid-lowering therapy (LLT) was identified as a major cause for patients not achieving LDL cholesterol goals. Furthermore, cardiovascular risk was frequently underestimated, influencing the prescription of less stringent LDL-c targets. The study suggests that measures such as improved education for physicians, better CV risk stratification, and enhancement of patient adherence to lipid lowering therapy may help bridge this gap. The need for additional or new LLT options was also highlighted to improve the LDL cholesterol control rate. While the study was insightful, it relied mainly on physicians' perceptions and experiences which may present bias, and its findings may be limited to countries with similar healthcare systems to Spain.

Impact of physician's perception about LDL cholesterol control in clinical practice when treating patients in Spain. Atherosclerosis 2023; 375:38-44Cosín-Sales J, Campuzano Ruiz R, Díaz Díaz JL *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=37245425

Developing new models for detecting drug-induced myotoxic effects

Drug-induced rhabdomyolysis is a severe and rare adverse event that poses significant risks to patients. The authors review the United States Food and Drug Administration Adverse Event Reporting System (FAERS) that logged 27,140 rhabdomyolysis cases from 2004 to 31 March 2020. Based on their findings in FAERS they identify 14 drugs frequently reported in 6583 rhabdomyolysis cases and to investigate whether mitochondrial toxicity is a common pathway of drug-induced rhabdomyolysis by these drugs. Fenofibrate, risperidone, pregabalin, propofol, and simvastatin lactone drugs were identified as mitotoxic and underwent further investigation, The authors emphasize the need for effective screening methods during drug development to identify potential myotoxicants and prevent serious muscle toxicity. The study utilizes FAERS to generate a list of suspect drugs and investigates their impact on mitochondrial function using skeletal muscle cell models. The article provides valuable insights into the global incidence of rhabdomyolysis, its implications for the healthcare system and pharmaceutical industry, and the economic costs associated with such adverse events. It highlights the limitations of the FAERS database for data analysis and the challenges in establishing causality between reported events and specific drugs. Their findings suggest that drug-induced mitochondrial dysfunction may play a significant role in the development of severe skeletal muscle toxicity. The study identifies several drugs that induce mitochondrial dysfunction through the inhibition of electron transport chain activity. However, the article acknowledges the need for further validation of the findings using primary human cell models and emphasizes that the proposed screening method should serve as an initial tier of testing rather than a conclusive assessment. This review contributes to the understanding of drug-induced rhabdomyolysis and highlights the importance of early detection and prevention of skeletal muscle adverse events during drug development.

Muscle-Related Adverse Events Associated With PCSK9 Inhibitors in a Veteran Population. Federal practitioner : for the health care professionals of the VA, DoD, and PHS 2023; 40:62-67Cencetti J, Abramowitz C, Spoonhower H. http://www.ncbi.nlm.nih.gov/pubmed/?term=37222994

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Basic Science

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