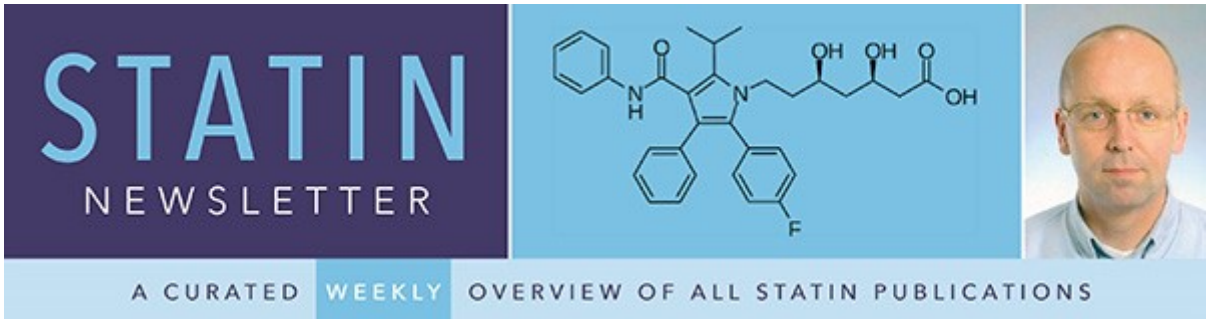

Update week 27 & 28 - 2022

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

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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. **Long term use of statins and plasma glucose**
2. **CKD and ststins a new piece of the puzzle**
3. **PCSK9ab for elective post PCI shows no benefit**
4. **How to bridge treatment inertia in developing economies**
5. **Evaluating major guidelines; what should be changed**

Statins and fasting glucose – more than meet the eye.

For some patients and physicians, the reported glycaemic changes in statin users can be a significant hurdle to initiating or continuing high-dose high-intensity statins. Most reports have been based on relatively short-time use of statins. In this retrospective analysis of electronic health records, the effects of statins on fasting glucose (FG) were evaluated. Simvastatin, lovastatin, atorvastatin, and pravastatin were included in this analysis; no data on rosuvastatin and pitavastatin was presented. Statin-users before and after initiating statins and statin never-users were compared. A total of 593,130 FG measurements from 87,151 individuals were measured during a median follow-up of 20 years. There were 42,678 never-users and 44,473 statin users with 730,031 statin prescriptions. The calculated annual increase in FG was 0.14 mg/dl, with insignificant differences between statins. The authors concluded that based on their findings, the effect of statins on glucose metabolism was modest. For most patients, long-term statin use was associated with only a tiny increase in FG. In patients whose pre-statin FG levels are normal, the risk of developing new-onset diabetes is small.

Haldar T, Oni-Orisan A, Hoffmann TJ *et al.* Modest effect of statins on fasting glucose in a longitudinal electronic health record based cohort. Cardiovascular diabetology 2022; 21:132. http://www.ncbi.nlm.nih.gov/pubmed/?term=35836181

Statins reduce new onset CKD and eGFR decline in elderly Chinese patients

Currently, what we know about the effects of statins on renal function is confusing. Reports claiming harm are quoted as frequently as reports showing protective effects. Statins are not equal; patients using high-dose rosuvastatin are more prone to developing renal issues such as proteinuria and hematuria than patients using atorvastatin. In this retrospective Chinese Analysis of the Research on Community Elderly Population of Tongji University (RECEPT) study, patients with normal renal function (eGFR >60) were divided into statin users and nonusers. Based on propensity score matching, 604 patients using statins were compared to 604 controls. New onset CKD was observed less frequently in the statin users, HR: 0.73 (0.59 to 0.91, p<0.01) in the unmatched cohort and 0.75 (0.59 to 0.97, p=0.02) in the matched cohort. Both statin users and nonusers with dyslipidemia experienced more new-onset CKD (p<0.05). Though no data was available on statin type and dosage, the findings of this study suggest that statins help slow down the eGFR decline and decrease risk of new-onset CKD.

Zhao M, Ren L, Zhou Z *et al.* The Association Between Statin Use and Risk of Chronic Kidney Disease in Community-Dwelling Older People in Shanghai, China. Clinical epidemiology 2022; 14:779-788. http://www.ncbi.nlm.nih.gov/pubmed/?term=35782995

PCSK9ab fail to protect IMR in stable CAD patients that had an elective PCI

The use of PCSK9ab is gaining momentum, particularly in the setting of ACS and patients with highly elevated LDL-c, e.g., FH. Although both statins share LDL-c lowering properties, non-LDL-c-related properties seem to differ. In this small Japanese study, 100 stable CAD patients scheduled for a PCI were randomized to evolocumab (N=54) every two weeks for 2-6 weeks or no evolocumab (N=46). All patients used statins. The study's primary endpoint was the index of microvascular resistance (IMR) after PCI. Troponin T at baseline and 24 hours after PCI. No difference in the primary endpoint was noted. The geometric mean IMR was 20.6 (17.2-24.6) in the evolocumab group and 20.6 (17.0-25.0) in the control group (p=0.98). The post-PCI troponin T levels were similar as well, 0.054 (CI: 0.041-0.071 ng/ml) vs 0.054 (0.038-0.077 ng/ml; p=0.99). Major periprocedural MI's were observed in 44.4% of the patients using evolocumab and 44.2% in the control arm (P=1.00). Evolocumab pre-treatment failed to avert periprocedural microvascular dysfunction in stable CAD patients post PCI using statins.

Ishihara M, Asakura M, Hibi K *et al.* Evolocumab for prevention of microvascular dysfunction in patients undergoing percutaneous coronary intervention: the randomised, open-label EVOCATION trial. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35837711

The gap between Real World and guideline recommended lipid-management

Adequately managing risk is challenging in developed economies; the situation is even direr in developing economies such as India and Sri Lanka. This is reflected by the real-world data collected in a small cross-sectional study by the University Medical Clinic and Endocrine Clinic at Colombo South Teaching Hospital in Sri Lanka. Diabetic patients were included from February to April 2021. Of the 471 patients, 441 used statins (93.6%), and 30 patients did not take statins. High-dose high-intensity statins (HD-HIS) should have been prescribed to HD-HIS; only 3 (173%) were using them. Moderate statins dosage/intensity were used by 152 (93.25%), 4 patients (2.45%) used low-intensity statins, and 4 patients (2.45%) did not take any statin. Patients diagnosed with ASCVD and DM2 (N=155, 32.91%) were considered very high risk and should have an LDL-c < 50 mg/dL; this was achieved by 17 (10.97%) of the patients. Problems with DM and ASCVD start to occur at a much younger age compared to Western countries; the mean age of the participants was 59.05 (± 9.24) years; the mean duration of diabetes was 10.97 (±9.57%) years, pointing to the need of earlier detection and intervention. The authors concluded that despite the observation that

statin use was common in diabetic patients, only a small number of patients were able to reach international guideline-recommended targets. These findings underline the need to educate and convince health care professionals why lipid management in high-risk patients is critical and needs to improve drastically

Matthias AT, Kaushalya J, Somathilake G, Garusinghe C. **Utilization of statins in patients with type 2 diabetes mellitus: the practice in a lower middle income South Asian country.** Int J Diabetes Dev Ctries 2022:1-7. http://www.ncbi.nlm.nih.gov/pubmed/?term=35822081

Evaluating the performance of currently used guidelines for starting statins

Lipid management guidelines emphasize a 10-year risk cut-off point to determine eligibility for drug initiation in patients at risk for ASCVD. Treating patients affected with a high CVD risk and the atherosclerotic burden was accepted as a cost-effective approach to prevent serious complications. Despite effective pharmacological agents to reduce LDL-c cholesterol to unprecedented levels, the residual risk remains high despite low LDL-c plasma concentrations. A shift towards preserving health instead of fighting disease revealed the significant impact of initiating LDL-c lowering earlier in life. Using data collected in the Copenhagen General Population study, the authors show the shortcomings of the currently used risk scores to adequately recognize patients who would benefit from statins. Comparing the SCORE-1, the SCORE-2, the US PCE, and the UK QRISK3 models. The sensitivity of the European-ESC guidelines was improved by lowering the treatment thresholds; the threshold of European-SCORE2 should be reduced to 5% overall to match US-ACC/AHA, to 6% to match UK-NICE, and to 7% to match 2019 European-ESC/EAS guidelines. The new treatment thresholds of the 2021 European-ESC guidelines reduce the eligibility for statins in a primary prevention setting significantly. To improve the overall performance of the European primary prevention guideline for statins in low-risk European countries, lower treatment thresholds should be implemented in future guidelines.

Mortensen MB, Tybjærg-Hansen A, Nordestgaard BG. **Statin Eligibility for Primary Prevention of Cardiovascular Disease According to 2021 European Prevention Guidelines Compared With Other International Guidelines.** JAMA cardiology 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35793078

Navar AM, Fonarow GC, Pencina MJ. **Time to Revisit Using 10-Year Risk to Guide Statin Therapy.** JAMA cardiology 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=35793080

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Basic Science

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