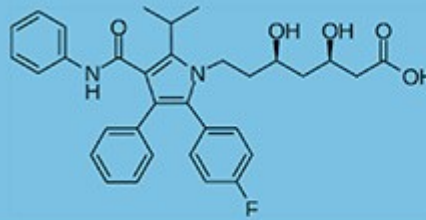


STATIN NEWSLETTER



A CURATED WEEKLY OVERVIEW OF ALL STATIN PUBLICATIONS

Update week 11 & 12 - 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

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. **SGLT2i and statins; a strong and safe combo.**
2. **Statins and glycemic control - what can we expect to see?**
3. **Can we predict who will, and who will not adhere to statins.**
4. **Pharmacists can improve statin adherence in diabetic patients**
5. **The SWEDEHEART registry: statins after ACS in CKD patients?**

The risk of muscle toxicity when combining SGLT2i with a statin

Concomitant use of statins sodium-glucose co-transporter 2 inhibitors (SGLT2i) is frequently observed in type 2 diabetics likely to see substantial benefit from both drug classes. In this study "Concomitant use of statins and SGLT2i and the risk of myotoxicity investigates the potential interaction between SGLT2i and statins and their risk for myotoxicity. The study uses data from the Food and Drug Administration Adverse Event Reporting System (FAERS) from 2013 to 2021 and estimates several measures of disproportionate reporting of myopathy and rhabdomyolysis associated with concomitant use of SGLT2i and statins. The study finds no increased risk of myotoxicity reporting associated with concomitant use of SGLT2 inhibitors and statins. Previously detected weak safety signals with specific SGLT2 inhibitor-statin pairs were not detected in this study after using various signal detection methods, and also restricting the study period. These results support previous work and argue against a potential interaction between these commonly used medications. The study contributes to the field by using a 'customized' definition of myopathy, which improves specificity and assessing the reporting risk of rhabdomyolysis. It also used a combination of frequentist and Bayesian signal detection methods and explored the potential impact of stimulated reporting, which is an inherent challenge in pharmacovigilance analyses. However, the study has limitations, including reporting bias

and confounding. The absence of a signal does not guarantee the safety of a drug or a drug interaction, but the totality of available evidence supports the notion that an excess myotoxic risk due to the concomitant use of statins and SGLT2 inhibitors is not likely. The study's results should raise awareness about the importance of accounting for stimulated reporting in pharmacovigilance analyses.

Concomitant use of statins and sodium-glucose co-transporter 2 inhibitors and the risk of myotoxicity reporting - A disproportionality analysis. *Br J Clin Pharmacol* 2023; Gravel CA, Krewski D, Mattison DR *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=36912450>

Meta-analysis on the effect of statins on glycaemic control

In this systematic review and meta-analysis studied the effects of statin therapy on glycemic control and insulin resistance were evaluated. The analysis included 67 studies, investigating over 25,000 individuals. Results indicated that statins increased glycosylated hemoglobin (HbA1c) levels and homeostatic model insulin resistance (HOMA-IR) index in both individuals with altered and normal glycemic control. The type or dosage of statins did not seem to influence the diabetogenic effect. This study confirmed the diabetogenic effect of statins found in previous analyses. Atorvastatin consistently worsened glucose metabolism while pravastatin was only diabetogenic in insulin-resistant individuals. The analysis did not find an association between statin dosage or duration and the diabetogenic effect of statins. Though the underlying mechanisms of statins diabetogenic effect are not fully understood, several theories have been postulated, including inhibition of CoQ10 synthesis, reduced capacity to synthesize fatty acids, increased fat and calorie intake, and impaired skeletal muscle GLUT4 translocation. More research is needed to determine the specific mechanisms involved in statins' diabetogenic effect.

Effects of statin therapy on glycemic control and insulin resistance: A systematic review and meta-analysis. *Eur J Pharmacol* 2023:175672 Alvarez-Jimenez L, Morales-Palomo F, Moreno-Cabañas A *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=36965747>

Who will stop taking statins? A risk prediction model

Non-adherence to statin therapy is common in patients with a history of acute coronary syndrome (ACS), and it is associated with adverse cardiovascular outcomes. In this study, researchers aimed to develop a risk score that predicts statin non-adherence using routinely collected data during hospital admission for ACS. The study involved 19,942 patients hospitalised for ACS, and the risk score was based on a multivariable Poisson regression model that identified risk factors associated with the statin Medication Possession Ratio (MPR) 6-18 months after hospital discharge. The results showed that statin non-adherence (MPR <0.8) occurred in 24% of patients. Patients with a history of cardiovascular disease (CVD) who were not taking a statin on ACS admission were more likely to have MPR <0.8 than those with low-density lipoprotein (LDL) cholesterol <2 mmol/L who were taking a statin. Other independent risk factors for non-adherence included age <45 years, female sex, disadvantaged ethnic groups, and no coronary revascularisation during the ACS admission. The risk score, which included nine variables, had a C-statistic of 0.67. Patients in the highest quartile of the risk score had a 45% chance of MPR <0.8, while those in the lowest quartile had a 12% chance. The study concludes that the risk score generated from routinely collected data can identify patients at higher risk of statin non-adherence during follow-up. It suggests that the risk score could be used to target inpatient and outpatient interventions to improve medication adherence. The risk score may help clinicians to identify patients who require additional support to adhere to their medication regimen, such as culturally appropriate education, and digital health services.

A Risk Model to Predict Statin Non-Adherence Following an Acute Coronary Syndrome. *Heart, lung & circulation* 2023; Liao YB, Lee M, Poppe KK *et al.*

<http://www.ncbi.nlm.nih.gov/pubmed/?term=36933980>

The role of community pharmacist to improve statin adherence in diabetics.

The GuIDE-S study evaluated the impact of a community pharmacist intervention on statin adherence in new users with type 2 diabetes (T2D). The study aimed to initiate statin therapy and optimize statin adherence through education, monitoring, and communication with

patients' other healthcare providers. The study involved community pharmacy staff proactively identifying adult patients with T2D who were not prescribed a statin, and patients received individualized education and follow-up and monitoring for one year. Adherence was defined as the proportion of days covered (PDC) by a statin over 12 months. The study found that patients in the intervention group were 21.2% more likely to have PDC of 80% or higher, and the adjusted average PDC was 3.1% higher in the intervention group than the control group. However, the differences were not statistically significant. Several strategies have been found to improve medication adherence, including pharmacist interventions for patients with diabetes and patients taking lipid-lowering medications such as statins. Community pharmacists have an opportunity to deliver medication adherence interventions given that they are highly accessible and have more frequent contact with patients than most other health care providers. The GuIDE-S intervention incorporated evidence-based components that improve medication adherence, such as education, ongoing follow-up, and monitoring and communication with patients' other health care providers. The study has limitations, including the use of pharmacy-based fill data rather than claims data, and pharmacies were not randomized to study arms. Future research should evaluate core adherence intervention components and implementation strategies that optimize fidelity to improve the effect of community pharmacist interventions to improve statin adherence in people with T2D.

Community pharmacist intervention to optimize statin adherence in diabetes care: The GuIDE-S study. *Journal of the American Pharmacists Association : JAPhA* 2023; Bacci JL, Marcum ZA, Rodriguez P *et al.* <http://www.ncbi.nlm.nih.gov/pubmed/?term=36933697>

Effect of statins in ACS patients with renal disease – SWEDEHEART registry

The use of statins in patients with chronic kidney disease (CKD) and acute coronary syndromes (ACS) remains controversial. CKD patients may exhibit reduced benefits from statins due to reduced low-density lipoprotein (LDL) levels. A recent study aimed to clarify the gaps in the issue by analysing the outcomes of statin discontinuation in CKD patients during the first year following ACS and comparing the long-term outcomes of high-dose statins versus low-moderate intensity statins. The study analysed data from the Swedish national registry SWEDEHEART, which included 142,962 patients admitted with a first diagnosis of acute myocardial infarction (AMI) between 2005-2016. The study found that the use of high-dose statins in CKD patients reduced the risk of reinfarction, stroke, and all-cause mortality regardless of renal function, compared to low-moderate intensity statins. However, the benefits of high-dose statins were not observed in patients with eGFR <30 mL/min. The study also found that discontinuation rates of statin therapy among kidney function groups were similar, regardless of statin intensity. The study's findings highlight the importance of using statins to improve long-term outcomes in CKD patients with ACS. Despite some limitations, the study suggests that statins have pleiotropic effects, including anti-inflammatory, antioxidant, and endothelial-protective effects, which may reduce the inflammatory burden and improve glomerular hemodynamics. Further clinical studies are needed to clarify the issue, possibly aimed at identifying possible biomarkers of statins action on renal function. The study also suggests a more critical approach to deprescribing and a change in the paradigm regarding the use of statins as life-saving therapy in CKD patients.

Statin therapy after myocardial infarction in patients with renal failure: the longer, the merrier! *Journal of cardiovascular pharmacology* 2023; Spadafora L, Crimi G, Porto I, Biondi-Zoccai G. <http://www.ncbi.nlm.nih.gov/pubmed/?term=36930569>

Relevant Publications

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Basic Science

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