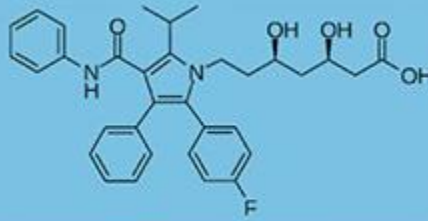


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IAS STATIN
NEWSLETTER



INTERNATIONAL
ATHEROSCLEROSIS
SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 01, 2021



Curated by Peter Lansberg,
a Dutch lipidologist and educator, and
reviewed by prof. Philip Barter, Past President of the
International Atherosclerosis Society.

The IAS statin literature update will keep you up-to-date with all recent statin publications, using a curated approach to select relevant articles.

Key publications

Reprogramming the nocebo effects of statins

Statin side effects remain one of the most critical hurdles to ensure long term adherence and persistence. Strategies to improve compliance focus on lab results and explain the findings of the randomized controlled clinical trial. In this short review, an innovative approach is suggested based on evidence-based pain management strategies. The nocebo concept is a relatively new model to explain the frequently reported side effects in statin users based on expectation and misinterpretation. The suggested 5 step approach: 1. build a trust relationship, 2. manage expectations, 3. Stop statin until symptoms resolve 4. rechallenge with statin 5. repeat steps 1-4 if symptoms recur. In the recently published SAMSON study, patients received four bottles containing placebo, atorvastatin 20 mg or no tablets. Every two weeks, patients had to use one bottle in

random order. Symptom intensity (1-100) was 8 during empty bottle weeks, 15.4 during placebo, and 16.3 during statin weeks. The P-value between statin use and placebo was 0.39. At the end of this one-year study, patients were given the data on their own experiences. Half of the statin-intolerant patients successfully restarted their statin therapy <6 months after the study stopped. Brain pathways mediate the statin nocebo response; both trust and appropriate information can re-program negative expectations and benefits of using statins.

Robinson JG. **The neuropsychology of statin intolerance.** Nat Rev Cardiol 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33408360>

Motivational interviewing to improve adherence

Another powerful approach to promote medication adherence is motivational interviewing (MI). In this study pharmacy students received a two-day training and were handed MI scripts. Based on the administrative claims database, 152 non-adherent statin users received MI and were compared to 304 controls. The initial call took on average 10-15 minutes duration; three follow-up calls were between 3-5 minutes. The primary outcome was adherence to antidiabetic/antihypertensive medication, based on the proportion of days covered >0.80. Despite the successful improvement in statins compliance, published in an earlier study, antidiabetic/antihypertensive medication's impact proved less successful. The antidiabetic group had 53 intervention patients and 102 controls. The antihypertensive group had 80 intervention patients and 159 controls. No significant improvement in adherence was observed. Predictors for improved adherence were baseline adherence in the antidiabetic; OR = 6.5 (P < 0.0001) and antihypertensive; OR = 4.1 (P = 0.0001 & β = 0.09; P = 0.008) users. Physician specialty OR = 3.902 (P = 0.01 & β = 0.09; P = 0.015) among antidiabetic users and age >70 years; OR = 2.148 (P = 0.025) among antihypertensive users. It is not completely understood why an MI strategy successfully improved statin adherence but failed to improve adherence to antidiabetic/antihypertensive medication. The authors suggested that different adherence barriers for different medications need to be explored, and a more target approach might help address specific issues. The sample size in this second evaluation was significantly smaller than the statin MI intervention, which could explain the less favorable outcome.

Mohan A, Vadhariya A, Majd Z *et al.* **Impact of a motivational interviewing intervention targeting statins on adherence to concurrent hypertension or diabetes medications.**

Patient education and counseling 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33402279>

VA centres differ significantly in statin and antiplatelet prescriptions for young ASCVD patients

Patients affected with premature (< 55 years in men; < 60 years in women) and extremely premature (< age 40 years) atherosclerotic complications are classified as extremely high CVD risk. Universally secondary prevention guidelines emphasize strict control of platelet aggregation (aspirin, clopidogrel, ticagrelor, prasugrel, and ticlopidine) and continued use of high dose, high-intensity statins. Data collected in the nationwide Veterans with premaTure AtheroscLerosis (VITAL) registry was re-evaluated to discern differences between the 130 VA healthcare facilities and their use of statins antiplatelets as well as statin adherence. Included were 135 703 patients with premature and 7716 with extremely premature ASCVD. Overall, the median prescription rate (IQR) for statins, high intensity statins (HIS) and antiplatelets was 0.73 (0.70–0.75), 0.36 (0.32–0.41), and 0.77 (0.73–0.81), respectively. The median rate ratios (MRR), a measure of the likelihood that two random facilities differ in any statin, HIS, and antiplatelet use, were 1.53 (1.44–1.60), 1.58 (1.49–1.66), and 1.49 (1.42–1.56), respectively, showing 53, 58, and 49% facility-level variation. Similar outcomes were noted in those categorized as extremely premature ASCVD. These findings underline the lack of proper guideline dictated prescription of well-established and simple prescribable drugs such as HIS and antiplatelets. Urgent interventions are warranted to optimize care in young ASCVD VA patients.

Mahtta D, Lee MT, Ramsey DJ *et al.* Significant Facility-Level Variation in Utilization of and Adherence with Secondary Prevention Therapies Among Patients with Premature Atherosclerotic Cardiovascular Disease: Insights from the VITAL (Veterans with premaTure AtheroscLerosis) Registry7. *Cardiovasc Drugs Ther* 2021.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=33400053>

Inflammation & atherosclerosis

Atherosclerosis and inflammation have been studied and debated since Rudolph Virchow published his pivotal paper in 1858. Peter Libby, the 21st-century godfather on this topic, published this updated review that provides a broad overview of our current understanding of this complicated topic and innovative therapeutic options that will become available in the foreseeable future. The article provides a historical overview of a century and a half of research and thousands of papers on this intriguing topic. Clear, and well, lustrated, explanations on immune response, relevant biomarkers as well anti-inflammatory therapies Potential promising biomarkers such as interleukin 1, -2 -6,-18

and the NLRP3 inflammasome have been successfully targeted and could open up new therapeutic avenues for very high CVD risk patients most likely to benefit from these interventions. The recent outcome studies with canakinumab and colchicine showed exciting results and confirmed inflammation as an independent risk factor for atherosclerosis. Based on current findings, anti-inflammatory strategies to prevent ASCVD complications are likely to become incorporated in personalized patient management and future ASCVD risk management guidelines.

Libby P. **Inflammation in Atherosclerosis-No Longer a Theory.** *Clinical chemistry* 2021; 67:131-142. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33393629>

Statins and DVT/PE recurrence

Venous thromboembolism (VTE) are commonly occurring cardiovascular complications, managed/prevented with anticoagulant medication. Despite the currently available effective drugs, recurrences are frequently reported, with estimates of 7% at six months and 40% over a follow-up period of 10-years. The shortcoming of effective anticoagulation therapy is the increased risk of hemorrhagic complications. Alternative approaches to prevent VTE recurrences are explored in this meta-analysis of observational statin studies that reported VTE outcomes. Of the 14 studies selected for this analysis, 12 qualified for the meta-analysis. Overall statins use was associated with a reduced risk of VTE-recurrences; pooled adjusted HR: 0.76 (0.69-0.83); these results were robust in sensitivity analyses and free of significant publication bias. The differences remained statistically significant when only patients after anticoagulant withdrawal were explored; pooled adjusted HR: 0.78 (0.70-0.88). Separating deep venous thromboembolism patients from those that suffered PE's, those that used statins were better protected: pooled adjusted HR: 0.71 (0.62-0.81) and HR: 0.80 (0.66-0.97; P = 0.027), respectively. All-cause mortality was significantly lower in VTE patients on statins vs. those that did not use statins, adjusted HR: 0.65 (0.56-0.77). Even a trend towards a lower risk for bleeding complications was noted, adjusted HR: 0.88 (0.73–1.07). Based on their findings, the authors suggested that statins could potentially reduce the risk for VTE recurrences. Observational data cannot establish a causal relationship between interventions and outcomes; hence randomized trials are urgently warranted to prove or refute these promising findings.

Li R, Yuan M, Yu S *et al.* **Effect of statins on the risk of recurrent venous thromboembolism: A systematic review and meta-analysis.** *Pharmacol Res* 2021:105413. <http://www.ncbi.nlm.nih.gov/pubmed/?term=33412275>

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