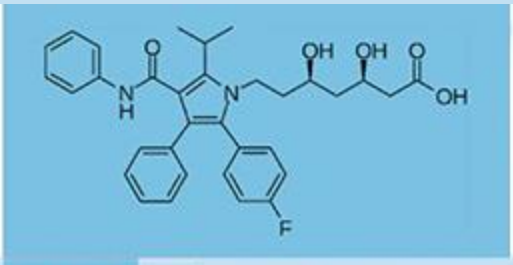
# IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 15, 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

### Aligning patient's perceptions to improve statin adherence

**Patient's perceptions of statin therapy can promote or deter adherence. Attitudes and beliefs of non-adherent patients were evaluated in this self-administered cross-sectional survey. In 2019 173 patients were recruited from two US academic centers and nationwide internet advertisements. Of the 173 participants, 49 (28.3%) were classified as secondary prevention. Prescriptions were never filled by 99 (57.2%), 74 (42.8%) collected their prescriptions but never took the statins, and more than half failed to inform their physician they were not taking their medication. Most interviewed preferred alternatives to statins, diet/exercise (N=134; 77.4%), natural remedies/supplements (N=125; 72.3%). Motivation for statins use was significantly hampered. Fear of statin dependence/addiction was noted by**

98 (56.6%), 27 (15.6%) were reluctant to take statins based on CVD risk estimates, 50 (28.9%) selected a risk threshold of >20%, and 23 (13.3%) would consider taking statins if the CVD risk estimate was >50%. Based on these findings, the authors underlined the importance of shared-decision making and assessing patients' attitudes about statins, improving the alignment of CVD risk management strategies.

Tarn DM, Pletcher MJ, Tosqui R *et al.* Primary nonadherence to statin medications: Survey of patient perspectives. Preventive medicine reports 2021; 22:101357. http://www.ncbi.nlm.nih.gov/pubmed/?term=33842201

## Statin use in hospitalized COVID-19 patients associated with improved mortality

To evaluate the protective effects of statins in CVOID-19 patients, a single cohort observational study was conducted in 1179 hospitalized patens with PCR confirmed SARS-CoV-2. Endpoints were 28-day mortality, ICU admission, and hospital discharge. Patients were divided into 4 groups; a. never used a statin (N=360), B. initiated statins (311); C. continued statins (466), and D. discontinued statins (42). Mortality risk was significantly reduced in statin users; HR: 0.566 (0.372-0.863; p=0.008). Patients that were started on statins and those that continued statins during hospitalization reduced their 18-mortality; HR: 0.493 (0.253-0.963; p=0.038) and HR: 0.270 (0.114-0.637; p=0.003), respectively. Sensitivity analysis showed improved mortality in those >65 years, not in patients <65 years. Based on these observational findings combined with the proven safety and global availability of statins, a randomized controlled trial is warranted.

Memel ZN, Lee JJ, Foulkes AS *et al.* Statins Are Associated with Improved 28-day Mortality in Patients Hospitalized with SARS-CoV-2 Infection. medRxiv 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33851192

## Meta-analysis of statin implementation strategies

Statins are one of the major pharmacological pillars to reduce CVD risk. Despite the solid scientific evidence base underlining the importance of high-dose high-intensity statins, many patients at risk for CVD are poorly managed. This meta-analysis reviews the success of different strategies to improve statin use. Evaluated were LDL-C (concentration and target achievement), statin prescribing, and statin adherence (percentage and target achievement). A total of 258 different strategies were used in 86 trials. The medium number of strategies used in the trials was 3 (1-13). Implementation tactics did not always include key characteristics. Temporarily was noted in 59%, dose in 52%, affected outcomes in 9%, and justification in 6%. Only 31 trials reported at least 1 of 3 outcomes; The major outcomes were a. reduced LDL-c standardized mean difference (SMD) − 0.17 (− 0.27 to − 0.07, p = 0.0006; OR:1.33, (1.13 to 1.58, p = 0.0008), b. increased statin prescriptions; OR 2.21 (1.60 to

3.06, p < 0.0001); OR 2.21 (1.60 to 3.06, p < 0.0001), and c. improved adherence SMD:0.13 (0.06 to 0.19; p = 0.0002; OR 1.30 (1.04 to 1.63, p = 0.023). Including more implementation strategies was associated with improved efficacy outcomes. The authors concluded that statin implementation strategies for hypercholesterolemic patients are published but reported poorly and have limited generalizability. Improved study design and standardized efficacy endpoints are needed to fill this relevant gap in current understanding.

Jones LK, Tilberry S, Gregor C *et al.* Implementation strategies to improve statin utilization in individuals with hypercholesterolemia: a systematic review and meta-analysis. Implement Sci 2021; 16:40. http://www.ncbi.nlm.nih.gov/pubmed/?term=33849601

## What can we expected from a structure lifestyle intervention strategy?

All major CVD risk management guidelines put large emphasis on lifestyle improvement in combination with the appropriate pharmacological management when indicate. In this prospective Cardiovascular Health Program (CHP) registry participants were followed for 12 months to evaluate the impact of a structured and personalized therapeutic lifestyle change (TLC) program. The TLC consisted of a half-day interactive workshop, face-to-face instructions with certified health coaches four times over 6 months and monthly telephone coaching for an additional 6 months. Of the 965 participants that started, 648 (67%) completed the program all measure outcomes improved; better dietary behaviours rose from 53% to 86%, Improved exercise 44% to 66%, perceived stress 65% to 79%, and sleep quality 28% to 49%. In those with abnormal anthropomorphic measurements at baseline, BMI improved in 63%, waist circumference in 71% (men) and 74% (women), systolic BP in 69% and diastolic BP in 71%. Patients with abnormal lab test showed better outcomes as well, total cholesterol in 74%, LDL-c in 65%, triglycerides in 86%, fasting glucose in 72% and insulin resistance in 71%. Carotid intima media thickness improved or showed no change in 70%. Sleep quality and longer total sleep time improved as well. The promising outcomes of this CHP Registry warrants a larger and longer duration study to determine its scalability, cost-effectiveness, and effects on MACE completed the intervention.Eliasson A, Kashani M, Vernalis M. Results of a prospective cardiovascular disease prevention program. Preventive medicine reports 2021; 22:101344. http://www.ncbi.nlm.nih.gov/pubmed/?term=33842199

## Reviewing statins effects on arterial stiffness

Statins are very effective LDL-c lowering drugs, but their effects are not limited to reducing plasma lipids but can improve relevant vascular characteristics. In this review, the authors present our current understanding of the effects of statins on arterial stiffness. An increase in arterial stiffness, measured by flow-mediated dilatation and pulse-wave velocity, is

**associated with an increase in CVD risk. Statins purportedly have various pleiotropic effects, including anti-inflammatory, anti-proliferative, ant-oxidant, and anti-thrombotic properties. The authors review evidence from human studies showing conflicting outcomes in different studies. They review studies from all the currently available statins and compare the different statins. They highlight potential mechanisms that could explain these effects on vascular elasticity. Better designed, more extensive studies of longer duration are needed to properly evaluate both class effect as well as differences between statins and dosage of statins on arterial stiffness.**

**Alidadi M, Montecucco F, Jamialahmadi T *et al.* Beneficial Effect of Statin Therapy on Arterial Stiffness. BioMed research international 2021; 2021:5548310.**
http://www.ncbi.nlm.nih.gov/pubmed/?term=33860033

# Relevant publications


1. **Zhang X, Peng X, Li L *et al.* Persistent Cigarette Smoking Attenuates Plaque Stabilization in Response to Lipid-Lowering Therapy: A Serial Optical Coherence Tomography Study. Frontiers in cardiovascular medicine 2021; 8:616568.** http://www.ncbi.nlm.nih.gov/pubmed/?term=33859999
2. **Xu M, Demuyakor A, Hu S *et al.* Is the effect of atorvastatin 60 mg on stabilization of lipid-rich plaque equivalent to that of rosuvastatin 10 mg? A serial optical coherence tomography combined with intravascular ultrasound imaging. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions 2021; 97 Suppl 2:1097-1107.** http://www.ncbi.nlm.nih.gov/pubmed/?term=33864710
3. **Mason RP, Eckel RH. Mechanistic Insights from REDUCE-IT STRENGTHen the Case Against Triglyceride Lowering as a Strategy for Cardiovascular Disease Risk Reduction. Am J Med 2021.** http://www.ncbi.nlm.nih.gov/pubmed/?term=33864765
4. **Liu MM, Peng J, Cao YX *et al.* The difference between fasting and non-fasting lipid measurements is not related to statin treatment. Annals of translational medicine 2021; 9:386.** http://www.ncbi.nlm.nih.gov/pubmed/?term=33842607
5. **Kim SY, Song YS, Wee JH *et al.* Evaluation of the relationship between previous statin use and thyroid cancer using Korean National Health Insurance Service-Health Screening Cohort data. Scientific reports 2021; 11:7912.** http://www.ncbi.nlm.nih.gov/pubmed/?term=33846511
6. **Hasanvand A, Ahmadizar F, Abbaszadeh A *et al.* Neuroprotective and Anti-inflammatory Role of Atorvastatin and Its Interaction with Nitric Oxide (NO) in**

Chronic Constriction Injury-induced Neuropathic Pain. Iranian journal of pharmaceutical research : IJPR 2020; 19:67-75. http://www.ncbi.nlm.nih.gov/pubmed/?term=33841522

7. Feng JL, Dixon-Suen SC, Jordan SJ, Webb PM. Is there sufficient evidence to recommend women diagnosed with endometrial cancer take a statin: Results from an Australian record-linkage study. Gynecologic oncology 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33846016
8. Cha D, Wang F, Mukerji B, Mukerji V. Statin-Induced Necrotizing Autoimmune Myositis: Diagnosis and Management. Cureus 2021; 13:e13787. http://www.ncbi.nlm.nih.gov/pubmed/?term=33842161
9. Campos-Staffico AM, Cordwin D, Ding Y *et al.* Fewer patients receive recommendations for pharmacotherapy in primary prevention using the 2018 atherosclerotic cardiovascular disease risk estimator. Prev Med 2021:106555. http://www.ncbi.nlm.nih.gov/pubmed/?term=33862035
10. Zubareva MY, Malyshev PP, Ansheles AA, Sergienko IV. [Assessment of Risk Factors for Atherosclerosis in Individuals of Different Categories of Cardiovascular Risk Using the Aterostop Calculator]. Kardiologiia 2021; 61:12-17. http://www.ncbi.nlm.nih.gov/pubmed/?term=33849413
11. Wu B, Zhou JH, Wang WX *et al.* Association Analysis of Hyperlipidemia with the 28-Day All-Cause Mortality of COVID-19 in Hospitalized Patients. Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih / Chinese Academy of Medical Sciences 2021; 36:17-26. http://www.ncbi.nlm.nih.gov/pubmed/?term=33853705
12. Wang Y, Jones G, Hill C *et al.* Effect of atorvastatin on knee cartilage volume in patients with symptomatic knee osteoarthritis: results from a randomised placebo-controlled trial. Arthritis & rheumatology (Hoboken, N.J.) 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33844449
13. Kuang YL, Theusch E, R MK, M WM. Identifying genetic modulators of statin response using subject-derived lymphoblastoid cell lines. Pharmacogenomics 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33858191
14. Hernar I, Graue M, Richards DA *et al.* Use of patient-reported outcome measures (PROMs) in clinical diabetes consultations: the DiaPROM randomised controlled pilot trial. BMJ Open 2021; 11:e042353. http://www.ncbi.nlm.nih.gov/pubmed/?term=33853796
15. Hellemans L, Mertens B, Hias J *et al.* Age is just a number: the concept of time to benefit in older adults. Eur J Hosp Pharm 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33863810
16. Ghaffar MT, Radhakrishna A, Ali I, Whelan B. Statin-induced necrotising autoimmune myopathy: a rare complication of statin therapy. BMJ case reports 2021; 14. http://www.ncbi.nlm.nih.gov/pubmed/?term=33858894
17. Chen Y, Xiong N, Wang X *et al.* Efficiency of atorvastatin on in-hospital mortality of patients with acute aortic dissection (AAD): study protocol for a randomized, open-label, superiority clinical trial. Trials 2021; 22:281. http://www.ncbi.nlm.nih.gov/pubmed/?term=33853639
18. Cacciottolo PJ, Kostapanos MS, Hernan Sancho E *et al.* Investigating the Lowest Threshold of Vascular Benefits from LDL Cholesterol Lowering with a PCSK9 mAb

Inhibitor (Alirocumab) in Patients with Stable Cardiovascular Disease (INTENSITY-HIGH): protocol and study rationale for a randomised, open label, parallel group, mechanistic study. BMJ Open 2021; 11:e037457. http://www.ncbi.nlm.nih.gov/pubmed/?term=33849844

# Basic Science publications

1. Jo JH, Park HS, Lee DH *et al.* Rosuvastatin inhibits the apoptosis of platelet-derived growth factor-stimulated vascular smooth muscle cells by inhibiting p38 via autophagy. J Pharmacol Exp Ther 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33846234
2. Fu CN, Song JW, Song ZP *et al.* Excessive expression of miR-1a by statin causes skeletal injury through targeting mitogen-activated protein kinase kinase kinase 1. Aging 2021; 13:11470-11490. http://www.ncbi.nlm.nih.gov/pubmed/?term=33864447
3. Evangelista FF, Costa-Ferreira W, Mantelo FM *et al.* Rosuvastatin revert memory impairment and anxiogenic-like effect in mice infected with the chronic ME-49 strain of Toxoplasma gondii. PLoS One 2021; 16:e0250079. http://www.ncbi.nlm.nih.gov/pubmed/?term=33857221
4. Bai L, Wang Y, Huo J *et al.* Simvastatin accelerated motoneurons death in SOD1(G93A) mice through inhibiting Rab7-mediated maturation of late autophagic vacuoles. Cell death & disease 2021; 12:392. http://www.ncbi.nlm.nih.gov/pubmed/?term=33846297

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