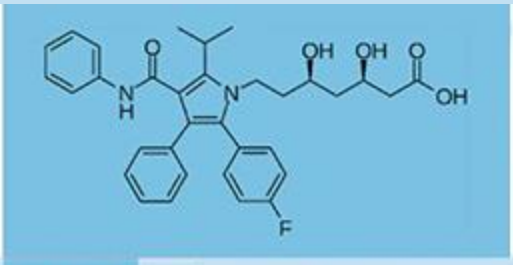
IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 16, 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

Should we shift from LDL-c to Apo B?

Calculating CVD risk based on plasma lipids has zoomed in on LDL particles and the lipids, cholesterol, and apolipoproteins they carry. What would provide the most accurate assessment of risk? Should we switch from the fractions we have become accustomed to, LDL-cholesterol or even non-HDL-cholesterol (total cholesterol minus HDL-cholesterol), and embrace apo B as our new gold standard. In this review, by three leading experts measuring lipoproteins, the Apo B fraction stands out as the preferred choice. The authors share current updates on Mendelian randomization studies and patients that used statins combined with ezetimibe and/or PCSK9ab to improve lipids and CVD risk. Their advice is unequivocally to switch to apolipoprotein B instead of measuring lipid fractions carried by lipoproteins. Has the LDL-c paradigm become obsolete? Is it time to re-focus our strategies in studies, guidelines, and clinical practice on what the authors qualify as a superior marker, apo B?

Sniderman A, Langlois M, Cobbaert C. Update on apolipoprotein B. Curr Opin Lipidol 2021.
http://www.ncbi.nlm.nih.gov/pubmed/?term=33870931

Statins protect undetermined embolic stroke patients

The benefits of high-dose high-intensity statins in patients that suffered an ischemic stroke are firmly established, based on the SPARCL trial. Evidence on statin benefits in non-atherosclerotic strokes was only noted in observational studies and a post-hoc, underpowered explorative analysis in the SPARCL study. Patients with an embolic stroke of undermined source (ESUS), recorded Athens Stroke Registry, were prospectively followed for stroke recurrence, MACE, and death for a period of up to 10-years. Of the 264 discharged ESUS patients, 89 (33.7%) were prescribed a statin. After a follow-up period of 4 years, Statin use was protective for all three endpoints. Stroke recurrence; 3.58 vs. 7.23/100 patient-years; HR: 0.48 (0.26–0.90), MACE 4.98 vs. 9.89/100 patient-years; HR: 0.49 (0.29–0.85), and death 3.93 vs. 8.21/100 patient-years, HR: 0.50 (0.28–0.89). similar reductions were observed after multivariate analyses. The authors concluded that ESUS patients discharged with a statin have a reduced risk for stroke recurrence, MACE, and death compared to post ESUS patients not taking statins after leaving the hospital.

Sagris D, Perlepe K, Leventis I *et al.* Statin treatment and outcomes after embolic stroke of undetermined source. Internal and emergency medicine 2021.
http://www.ncbi.nlm.nih.gov/pubmed/?term=33895939

Societal economic impact of lipid lowering therapy accrued over the last 20 years

The benefits of lipid-lowering therapy (LLT) have far-reaching effects on a societal level. In this article, the authors estimated the benefits and costs of LLT's for primary and secondary prevention patients between 1987 (when statins were introduced) and 2014, the most recent year of available observational data. Data from NHANES (1999-2014) Medical Expenditure Panel Survey (MEPS) and LLT clinical trials were used to calculate LLT expenditures and value of prevented hospitalizations, CVD events, and other utilization-related outcomes. The combination of statins plus ezetimibe prevented 2.8 million non-fatal heart attacks and 1.7 million non-fatal strokes (1987-2014). Statin use generated $2.6 trillion in societal value through deaths avoided; 85% of this value has accrued in patients. The meaningful societal impact of lipid-lowering therapy by statins, ezetimibe, and PCSK9ab have not been given the attention they deserve. The reduction of costs associated with the prevention of both fatal and non-fatal events are meaningful and deserve the acknowledgment provided by the data presented in this overview article.

MacEwan JP, Zhao LM, Everson K *et al.* Two steps forward, one step back: 50 years of societal value from LDL-C-lowering therapies. The American journal of managed care 2021; 27:162-168. http://www.ncbi.nlm.nih.gov/pubmed/?term=33877775

Suboptimal secondary prevention in women with premature ASCVD

Simple secondary prevention seems to be less stringent in females compared to men. This US study evaluated the use of statins, an antiplatelet drug, in female and male veterans diagnosed with premature ASCVD. Between October 1, 2014, to September 30, 2015, in 147 600 veterans with premature ASCVD (ischemic heart disease [IHD), ischemic cerebral vascular disease [ICVD], and peripheral artery disease [PAD]). In total, 10 413 women and 137 187 men with premature ASCVD (age <55 years) and 1340 women and 8145 men with extremely premature ASCVD (age <40 years) were evaluated in a retrospective cross-sectional design analysis. For antiplatelets use, the adjusted OR's for women compared to men was 0.47 (045-0.50, any statin 0.62 (0.59-0.66), for high-intensity statins 0.63 (0.59-0.66) and women were less statin adherent as well 0.68 vs. 0.73. Similar patterns were observed for premature CVD and PAD. In those with extremely premature ASCVD, the adjusted odds ratio for antiplatelet use in women was 0.61 (0.53-0.70), any statin 0.51 (0.44-0.58), and high-intensity statin use 0.45 (0.37-0.54). No sex differences were noted for statin adherence in those with premature ICVD, premature PAD, or extremely premature ASCVD. This study confirms that basic secondary prevention strategies are suboptimal in women with premature and extremely premature ASCVD. These findings warrant structural improved patient-centered interventions to improve proper preventive management in women.
Lee MT, Mahtta D, Ramsey DJ *et al.* Sex-Related Disparities in Cardiovascular Health Care Among Patients With Premature Atherosclerotic Cardiovascular Disease. JAMA cardiology 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33881448

EAS task force practical guide on combination lipid-lowering therapy

The introduction of new effective lipid-lowering drugs requires changes in current medical management. The European Atherosclerosis Society Task Force has released an update on combination lipid-modifying therapy in high- and very-high-risk patients. This practical guide provides clinicians a simple, evidence-based overview on the use of drug combinations needed to improve guideline dictated lipid goals. The statin-ezetimibe combo is the first step in managing elevated LDL-c and adding PCSK9ab therapy if suggested if LDL-c remains too high. For those with abnormal TG's (200 – 500 mg/dL), statins plus either a fibrate or a high dose omega-3 fatty acid (icosapent ethyl) may be an alternative. Diabetic patients can benefit from fibrates to reduce their risk for macro-and microvascular complications. Integration of these approaches into routine practice has the potential to improve the implementation of guideline-recommended management of elevated LDL-cholesterol and TG levels, ultimately reduce the associated risk of ASCV complications.
Averna M, Banach M, Bruckert E *et al.* Practical guidance for combination lipid-modifying therapy in high- and very-high-risk patients: A statement from a European Atherosclerosis

Society Task Force. Atherosclerosis 2021; 325:99-109.
http://www.ncbi.nlm.nih.gov/pubmed/?term=33892925

Relevant publications

1. Zhu Y, Gou H, Ma L *et al.* Effects of double-dose statin therapy for the prevention of post-stroke epilepsy: A prospective clinical study. Seizure 2021; 88:138-142. http://www.ncbi.nlm.nih.gov/pubmed/?term=33895389
2. Yang YL, Leu HB, Yin WH *et al.* Adherence to Healthy Lifestyle Improved Clinical Outcomes in Coronary Artery Disease Patients After Coronary Intervention. Journal of the Chinese Medical Association : JCMA 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33871387
3. Wang N, Harris K, Chalmers J *et al.* Combination blood pressure lowering in the presence or absence of background statin and aspirin therapy: a combined analysis of PROGRESS and ADVANCE Trials. J Hypertens 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33883461
4. Tomlinson B, Patil NG, Fok M, Lam CWK. Role of PCSK9 Inhibitors in Patients with Familial Hypercholesterolemia. Endocrinol Metab (Seoul) 2021; 36:279-295. http://www.ncbi.nlm.nih.gov/pubmed/?term=33866776
5. Singh J, Wozniak A, Cotler SJ *et al.* Combined Use of Aspirin and Statin is Associated With a Decreased Incidence of Hepatocellular Carcinoma. Journal of clinical gastroenterology 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33883511
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7. Okumus T, Pala AA, Taner T, Aydin U. Effects of Preoperative Statin on the Frequency of Ventricular Fibrillation and C-Reactive Protein Level in Patients Undergoing Isolated Coronary Artery Bypass Grafting. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP 2021; 30:373-378. http://www.ncbi.nlm.nih.gov/pubmed/?term=33866719
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9. Meier S, Frick M, Liu M *et al.* Reduced adrenal stress response in patients on PCSK9 inhibitor therapy. Atherosclerosis 2021; 325:63-68. http://www.ncbi.nlm.nih.gov/pubmed/?term=33892329
10. Lin TK, Huang JY, Pan LF, Jong GP. Gender- and age-related differences of statin use on incident dementia in patients with rheumatoid arthritis: a Nationwide

population-based cohort study. Lipids Health Dis 2021; 20:37. http://www.ncbi.nlm.nih.gov/pubmed/?term=33879179
11. Lalagkas PN, Poulentzas G, Kontogiorgis C, Douros A. Potential drug-drug interaction between sodium-glucose co-transporter 2 inhibitors and statins: pharmacological and clinical evidence. Expert Opin Drug Metab Toxicol 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33888031
12. Koskinas KC, Mach F, Räber L. Lipid-lowering therapy and percutaneous coronary interventions. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology 2021; 16:1389-1403. http://www.ncbi.nlm.nih.gov/pubmed/?term=33875408
13. Kim JH, Wee JH, Choi HG *et al.* Association between statin medication and asthma/asthma exacerbation in a national health screening cohort. The journal of allergy and clinical immunology. In practice 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33894391
14. Guo LL, Chen YQ, Lin QZ *et al.* Non-HDL-C Is More Stable Than LDL-C in Assessing the Percent Attainment of Non-fasting Lipid for Coronary Heart Disease Patients. Frontiers in cardiovascular medicine 2021; 8:649181. http://www.ncbi.nlm.nih.gov/pubmed/?term=33869310
15. Engell AE, Svendsen ALO, Lind BS *et al.* Drug-drug interactions between vitamin K antagonists and statins: a systematic review. Eur J Clin Pharmacol 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33895864
16. Danese MD, Pemberton-Ross P, Catterick D, Villa G. Estimation of the increased risk associated with recurrent events or polyvascular atherosclerotic cardiovascular disease in the United Kingdom. Eur J Prev Cardiol 2021; 28:335-343. http://www.ncbi.nlm.nih.gov/pubmed/?term=33891694
17. Curfman G, Shehada E. Icosapent ethyl: scientific and legal controversies. Open heart 2021; 8. http://www.ncbi.nlm.nih.gov/pubmed/?term=33888593
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29. Gormley M, Yarmolinsky J, Dudding T *et al.* Using genetic variants to evaluate the causal effect of cholesterol lowering on head and neck cancer risk: A Mendelian randomization study. PLoS Genet 2021; 17:e1009525. http://www.ncbi.nlm.nih.gov/pubmed/?term=33886544
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Basic Science publications

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metabolic syndrome and obesity : targets and therapy 2021; 14:1631-1645. http://www.ncbi.nlm.nih.gov/pubmed/?term=33880049

2. Zheng P, Ding Y, Lu F *et al.* Atorvastatin reverses high cholesterol-induced cardiac remodeling and regulates mitochondrial quality-control in a cholesterol-independent manner: an experimental study. Clin Exp Pharmacol Physiol 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33891707
3. Xu HR, Yang Q, Xiang SY *et al.* Rosuvastatin Enhances Alveolar Fluid Clearance in Lipopolysaccharide-Induced Acute Lung Injury by Activating the Expression of Sodium Channel and Na,K-ATPase via the PI3K/AKT/Nedd4-2 Pathway. J Inflamm Res 2021; 14:1537-1549. http://www.ncbi.nlm.nih.gov/pubmed/?term=33889010
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6. Jin H, Ji Y, Cui Y *et al.* Simvastatin-Incorporated Drug Delivery Systems for Bone Regeneration. ACS biomaterials science & engineering 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=33877804
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