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.


**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 patients 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.


**Meta-analysis of statin implementation strategies**

Statin 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.


**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](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.


Relevant publications

6. Hasanvand A, Ahmadian F, Abbaszadeh A et al. Neuroprotective and Anti-inflammatory Role of Atorvastatin and Its Interaction with Nitric Oxide (NO) in


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.


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**Basic Science publications**


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.  
   **Aging** 2021; 13:11470-11490.  

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*.  

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.  

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