LDL-C: Lower for Longer is Better

Key Takeaways



Early, intensive reduction of LDL-cholesterol (LDL-C) is recommended and can have significant clinical impact on reducing the risk of ASCVD and recurrent events

LDL-lowering contributes to plaque regression and stabilization as shown in studies using coronary angiography and intravascular ultrasound

The long-term risk of cardiovascular events is significantly influenced by LDL levels over the course of a life

What is the LDL-cholesterol hypothesis?

This hypothesis refers to the concept that **elevated LDL-C is a key risk factor** for the development of atherosclerosis and cardiovascular disease.

What is it founded on?

- Cholesterol deposits constitute a significant component of atherosclerotic plaque
- Strong evidence indicates that the cholesterol found in plaque is delivered there by LDL particles
- Reducing LDL-C levels can result in significant regression of coronary atherosclerosis as shown in angiographically monitored trials
- LDL-lowering contributes to plaque stabilization according to studies using coronary angiography and intravascular ultrasound

What are the clinically relevant implications?

- A measure of exposure to cholesterol over time is superior to a static measure of cholesterol at a given time
- The long-term risk of cardiovascular events is significantly influenced by LDL levels over the course of a life

Why should LDL-C be aggressively managed as early as possible?

Lifetime exposure to LDL-C associated with greater risk



Observations from large Mendelian randomization studies have emphasized the concept of area under the cholesterol curve. The concept of cholesterolyears represents the cumulative lifetime exposure of the arterial wall to LDL-C. It considers the product of the magnitude and duration of exposure to LDL-C over time to estimate the risk of ASCVD.

Evolution of evidence over 25 years supporting lower treatment targets



Lower LDL-C for longer is better for reducing the risk of ASCVD and recurrent events





References: Goldstein JL, Brown MS. A century of cholesterol and coronaries: from plaques to genes to statins. Cell. 2015;161(1):161-172. doi:10.1016/j.cell.2015.01.036; Goldberg LJ, Sharma G, Fisher EA. Atherosclerosis: Making a U Turn. Annu Rev Med. 2020;71:191-201. doi:10.1146/annurev-med-042418-011108; D'Ascenzo F, et al. Atherosclerotic coronary plaque regression and the risk of adverse cardiovascular events: a meta-regression of randomized clinical trials. Atherosclerosis. 2013;226(1):178-185. doi:10.1016/j.atherosclerosis.2012.10.065; Shapiro MD & Bhatt DL, "Cholesterol-Years" for ASCVD risk prediction and treatment. J Am Coll Cardiol. 2020;76(13):1517-1512. doi:10.1016/j.jacc.2020.07.059