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Study compares CV risk reduction of statin vs nonstatin therapies used for lowering LDL-C

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In a study appearing in the September 27 issue of *JAMA*, Marc S. Sabatine, M.D., M.P.H., of Brigham and Women's Hospital, Harvard Medical School, Boston, and colleagues evaluated the association between lowering low-density lipoprotein cholesterol (LDL-C) and relative cardiovascular risk reduction across different statin and nonstatin therapies.

Low-density lipoprotein cholesterol is a well-established risk factor for cardiovascular disease. The clinical benefit of lowering LDL-C with statins remains widely accepted. In contrast, the comparative clinical benefit of nonstatin therapies that reduce LDL-C remains uncertain. For this study, the authors conducted a review and meta-analysis of 49 trials that met criteria for inclusion. The study included a total of 312,175 participants with 39,645 major vascular events and 9 different interventions to lower LDL-C.

The interventions were divided into 4 groups: (1) statins; (2) nonstatin therapies that ultimately work predominantly through upregulation of LDL receptor expression (i.e., diet, bile acid sequestrants, ileal bypass, and ezetimibe); (3) interventions that do not reduce LDL-C levels primarily through upregulation of LDL receptor expression (i.e., fibrates, niacin, cholesteryl ester transfer protein [CETP] inhibitors); and (4) PCSK9 inhibitors, which upregulate LDL-C clearance through the LDL receptor, but for which dedicated cardiovascular outcome trials

have not yet been completed (and were considered separately to evaluate how the data to date compare with established therapies that upregulate LDL receptor expression).

The authors found that there was a similar association between absolute reductions in LDL-C and lower relative risks for major vascular events (a composite of cardiovascular death, acute heart attack or other acute coronary syndrome, coronary revascularization, or stroke) across therapies that lead to upregulation of LDL receptor expression. Each 1-mmol/L (39 mg/dL) reduction in LDL-C was associated with a 23 percent relative reduction in the risk of major vascular events. There was also a significant linear association between achieved LDL-C and the rate of cardiovascular outcomes over the range of LDL-C studied.

"The implications of these results deserve careful consideration in light of the strength of the available trial evidence for different types of therapies. As per current guidelines, when tolerated, statins should be the first-line therapy given the large reductions observed for LDL-C, the excellent safety profile, the demonstrated clinical benefit, and low cost (now that most are generic). However, the data in the present meta-regression analysis raise the possibility that other interventions, especially those that ultimately act predominantly through upregulation of LDL receptor expression, may provide additional options and may potentially be associated with the same relative clinical benefit per each 1-mmol/L reduction in LDL-C," the authors write.

More information: *JAMA*, DOI: 10.1001/jama.2016.13985