Abstracts

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Statins and All-Cause Mortality in High-Risk Primary Prevention: A Meta-analysis of 11 Randomized Controlled Trials Involving 65,229 Participants


Conclusion: There is no benefit of statin therapy on all-cause mortality in a high-risk primary prevention setting.

Summary: The justification for the use of Statins in Prevention Intervention Trial Evaluating Rosuvastatin (JUPITER) reported that patients with comparatively low levels of low-density lipoprotein (LDL) cholesterol (<130 mg/dL) and baseline levels of high-sensitivity C-reactive protein (HS-CRP; > 2 mg/L) reduced all-cause mortality by 20% (Ridker PM, N Engl J Med 2008;359:2195-207). However, the JUPITER findings have been questioned as occurring by chance or as being an exaggerated observation (Yusuf S, Lancet 2009;373:1152-5). The authors undertook a new metaanalysis of published clinical trials (including information previously unpublished by such studies) to assess whether statins reduce all-cause mortality in the setting of high-risk primary prevention populations. The goal was to determine if statin therapy reduces all-cause mortality in intermediate- to high-risk individuals without a history of cardiovascular disease, from a public health perspective. The authors identified trials for the analysis through computerized literature searches of MEDLINE and Cochrane databases from January 1970 to May 2009. Trials had to be prospective, randomized, and controlled in individuals free from cardiovascular disease at baseline. Data were extracted for the number of patients randomized and for mean duration of follow-up. The number of incident deaths was obtained through the principle publication or by correspondence with investigators. For the analysis, 11 studies were identified and data combined from the studies, with the sample effects pooled using a random-effects model. Given the recent JUPITER versus PRINCE trial data, the authors conducted a systematic review and meta-analysis of all randomized trials of statins in high-risk primary prevention populations. The authors found no evidence of benefit on mortality or other endpoints for statins in primary prevention populations compared to placebo or no treatment. The authors concluded that the use of statins in primary prevention should be reconsidered and that alternative strategies for reducing cardiovascular risk should be considered.

Data were available on 65,229 participants followed-up for approximately 244,000 person-years, during which 2793 deaths occurred. Use of statins in this high-risk primary prevention setting was not associated with a statistically significant reduction (RR, 0.91; 95% CI, 0.83-1.01) in all-cause mortality. There was no statistical evidence of heterogeneity among studies (P = 0.73). The authors compared the use of statins in primary prevention to other strategies, such as aspirin, antihypertensive therapy, or intensive lifestyle modification, and found that statins were not as effective as these other interventions in reducing all-cause mortality.

Comment: Three-quarters of patients who take statins take them for primary prevention. Depending on perspective, their study has enormous implications for expenditures (from payers perspective) or revenue (from industry perspective). An editorial by Dr Lee A. Green in the same issue of Archives of Internal Medicine (2010;170:1007-8), points out this advocates for lipid lowering therapy for primary preventionfeel benefit would likely accrue over a longer time of observation. Skeptics postulate little incremental benefit will accrue later. Accompanying the Ray et al meta-analysis is another article in the same issue of Archives of Internal Medicine by de Lourgeri et al., “Cholesterol Lowering, Cardiovascular Diseases, and the Rosuvastatin-JUPITER Controversy, A Critical Reappraisal” (2010;170:1032-6), in which the authors point out that the JUPITER trial is the only trial that has shown benefit for primary prevention with statins. These authors are highly critical of the JUPITER trial in terms of industry control, industry-performed statistical analysis, conflicts of interest of the authors, and premature ending of the trial. It may be that statins for primary prevention of cardiovascular disease in patients at risk is not the “home run” everyone believes it is. When used for primary prevention, the only beneficiaries of statin therapy may be the pharmaceutical industry and their stockholders!