Letter by Wells and Eisenberg Regarding Article, “Statins for the Primary Prevention of Cardiovascular Events in Women With Elevated High-Sensitivity C-Reactive Protein or Dyslipidemia: Results From the Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) and Meta-Analysis of Women From Primary Prevention Trials”

To the Editor:

We read with interest the article by Mora and colleagues\(^1\) that makes a notable contribution by providing a women-specific meta-analysis of statins in a primary prevention context. An important issue is the combining of Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) with other statin studies. Three prior meta-analyses of primary prevention for women, 2 of which are quite recent, yielded no significant cardioprotective effect.\(^2\)\(^–\)\(^4\) For coronary heart disease events (with exclusion of the Heart Protection Study as not being primary prevention), Petretta et al\(^3\) report a relative risk of 0.96, a 95% confidence interval of 0.83 to 1.10, and a \(P\) value for heterogeneity of 0.557. Eisenberg and Wells\(^4\) report a relative risk of 0.98, a 95% confidence interval of 0.84 to 1.13, and a \(P\) value for heterogeneity of 0.584. In the study of Mora et al, the 95% confidence interval for women in JUPITER for total cardiovascular disease is 0.37 to 0.80. This does not overlap with the confidence intervals for either of the other recent meta-analyses and, in our opinion, raises a question about combining JUPITER with the other studies. The \(P\) value for heterogeneity in the cardiovascular disease analysis of Mora et al is 0.053, which is arguably too low, in our opinion, to support combining JUPITER given evidence of homogeneity in prior studies. Furthermore, JUPITER drives the cardioprotective effect in Figure 2B in the article by Mora et al, and therefore the decision to combine JUPITER is critical to their results. Indeed, the other studies in Figure 2B, individually and collectively, show no statistically significant cardiovascular disease benefit. The possible distinctiveness of JUPITER may derive from its patient pool. JUPITER excluded subjects with elevated cholesterol and required subjects to have elevated C-reactive protein. Practicing physicians might hesitate to prescribe, for example, atorvastatin for women with elevated cholesterol on the basis of this meta-analysis, whose results are driven by 1 study of a different drug that lacked any patients with high cholesterol. Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), the key atorvastatin primary prevention clinical trial, showed increased risk of cardiac incidents for women. Carotid Atorvastatin Study in Hyperlipidemic Post-Menopausal Women: A Randomized Evaluation of Atorvastatin, Versus Placebo (CASHMERE) limited to postmenopausal women, showed no benefit for atorvastatin, although Pfizer has not publicized the results. By focusing on women, Mora and colleagues contribute importantly to the study of possible differences, or lack of differences, between men and women.

Disclosures

None.

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