Letter by Vos et al Regarding Article, "Primary Prevention With Statin Therapy in the Elderly: New Meta-Analyses From the Contemporary JUPITER and HOPE-3 Randomized Trials"

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To the Editor:

We read with interest the article by Ridker et al[1] that proposes, based on 2 rosuvastatin trials, JUPITER (Justification for Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) and HOPE-3 (Heart Outcomes Prevention Evaluation), that there would be a probable statin mortality benefit in primary prevention in the elderly.[2,3] The article relies on the combined end point of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death, but without separating these nonequipoise end points. In fact, the *P* values for fewer cardiovascular deaths in these 2 studies were *P*=0.37 and *P*=0.34, respectively. There were ≈105 000 patient-years of observation, statin or placebo, and it must therefore be concluded that the statin did not reduce cardiovascular mortality. There is no evidence that this could be different in any age group. The article deviates from cardiovascular mortality by mentioning that JUPITER ended with an all-cause mortality reduction (–20%, *P*=0.02). This finding was from fewer cancer deaths, a finding not found in any other statin trial. In fact, the JUPITER steering committee "…believes that [the reduced cancer mortality finding] was likely the play of chance…"[4] Supporting this belief was the finding that there was no reduction in "newly diagnosed cancer" (*P*=0.51).[2] Without this chance cancer finding, the *P* value for all-cause mortality becomes *P*=0.21, whereas it was *P*=0.32 in HOPE-3, approaching the highly nonsignificant *P* values for cardiovascular deaths in both megatrials. We propose that the benefit in these trials may well be related to the well-known nitroglycerin-mimicking effects of statins, promoting the nitric oxide/endothelial nitric oxide synthase pathways in vasculature and in blood cells. This nitric oxide effect may well explain the almost universal finding of statins not lowering mortality, while reducing nonfatal events, as in JUPITER and HOPE-3.[5] The article ends by suggesting that there is "the potential for a modest effect in longevity" from statins in the elderly. This is highly doubtful based on JUPITER and HOPE-3. Therefore, it now becomes vitally important to examine statin trials with a focus on all-cause mortality (such as numbers needed to treat per group) and on the precise roles of nitric oxide.[5]

DISCLOSURES

None.

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Circulation is available at http://circ.ahajournals.org.

Circulation. 2017;136:1454–1455. DOI: 10.1161/CIRCULATIONAHA.117.029008

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