

## **Questioning the beneficial effects of statin therapy in patients with advanced chronic kidney disease. *Author reply***

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In our meta-analysis of individual participant data from 28 trials of statin-based therapy there was a significant trend towards smaller relative risk reductions for the composite outcome of major vascular events (myocardial infarction or death from coronary heart disease, stroke or coronary revascularisation) with declining estimated glomerular filtration rate (eGFR).<sup>1</sup> Whilst a trend was present for major coronary events, neither of the corresponding trends for coronary revascularisation procedures and stroke were statistically significant. Since the number of coronary revascularisations and stroke were relatively small among those with advanced chronic kidney disease (CKD), however, it is not possible to determine reliably whether the trends in relative risk reductions differ for specific vascular events.

Contrary to the assertion by Mascitelli and Goldstein, the precise nature of the relationship between eGFR and the relative effects of statin therapy on coronary procedures is not important when considering how intensively to lower low-density lipoprotein (LDL) cholesterol in patients with CKD. Previous meta-analyses conducted by the Cholesterol Treatment Trialists' (CTT) Collaboration have shown that the absolute benefit of statin therapy on major vascular events is determined by 2 factors: (i) the achieved absolute reduction in LDL cholesterol and (ii) the absolute risk of major vascular events.<sup>2</sup> The results of the Study of Heart and Renal Protection (SHARP) demonstrated that the same relationship holds among patients with CKD.<sup>3</sup> Since our meta-analysis showed that the relative risk reduction in major vascular events *per mmol/L reduction* in LDL cholesterol diminishes as eGFR falls, it is possible to compensate for this diminution by seeking the largest possible LDL cholesterol reduction (ie, the first of the 2 factors determining absolute benefit) with an intensive statin-based regimen.

Such a strategy is worthwhile because the second factor determining the absolute benefit of a statin regimen, the baseline risk of atherosclerotic disease, is high among patients with CKD.<sup>4</sup> In the Editorial accompanying our article<sup>5</sup>, the figure underestimated the absolute benefits that could realistically be achieved in patients with CKD since the rates were calculated from SHARP, which excluded high-risk patients with known CHD. In routine

practice the absolute risk of major atherosclerotic events is likely to be substantially higher, and when an intensive statin-based regimen is used to yield larger absolute reductions in LDL cholesterol, the potential absolute benefits in patients with advanced CKD may be as large as those observed in other high risk populations.

## References

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