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As detailed in our article, we classified all adverse events using the Medical Dictionary for Regulatory Activities and they were further categorised by degree of certainty (definite, probable or possible) according to pre-specified definitions. The frequency of most adverse events, including all those assigned by system organ classification to musculo-skeletal and connective tissue disorders, was similar in both phases of the trial (7-9%) but, using the more specific and adjudicated definitions for muscle-related adverse events, the frequency was slightly lower in the non-blinded phase (1-2%) than the blinded phase (2%). However, it is incorrect to assert that this is due to some selection bias. For example, the statin-users in the non-blinded phase had similar rates of muscle-related adverse events when, during the blinded randomized phase, they were allocated to a statin or placebo (1.72 per 100 person-years) or placebo (1.80 per 100 person-years; $p=0.636$). Furthermore, following their decision of whether to continue, discontinue or commence a statin in the non-blinded phase, there was little difference in the reported muscle-related adverse events amongst those previously assigned to statin therapy (1.32 per 100 person-years), or placebo (1.20 per 100 person-years; $p=0.500$). Indeed, the small excess in the reported rates amongst users who were previously assigned atorvastatin further strengthens our hypothesis of a 'nocebo' effect, as the explanation for the excess reporting of muscle-related adverse events in statin users during the non-blinded phase of the trial.

Reference

1. Gupta A, Thompson D, Whitehouse A, et al. Adverse events associated with unblinded, but not with blinded, statin therapy in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA): a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase. *Lancet*. 2017;389:2473-81.

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