



LETTERS

STATINS FOR PEOPLE AT LOW RISK

N-of-1 approach to determine when adverse effects are caused by statins

Shah Ebrahim honorary professor of public health¹, George Davey Smith director²

¹London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK; ²Medical Research Council Integrative Epidemiology Unit, University of Bristol, Bristol, UK

McPherson finds it shocking that a Cochrane review group is not interested in seeking data on adverse events associated with statins. If he read our Cochrane reviews on statins he would see that findings related to adverse events are reported. What is more shocking is that a systematic review of the adverse effects of statins using observational and randomised trial evidence that we submitted to *The BMJ* was rejected without review. The review was published and concluded: "The absolute excess risk of the observed harmful unintended effects of statins is very small compared to the beneficial effects of statins on major cardiovascular events." Perhaps these findings did not chime well with *The BMJ* s editors, who have taken a stand against widespread use of statins.

Doctors and patients often attribute adverse effects to statins, but the evidence we have from trials indicates that "Only a small minority of symptoms reported on statins are genuinely due to the statins: almost all would occur just as frequently on placebo." The Cholesterol Treatment Trialists' (CTT) collaboration has developed a detailed protocol for collecting all relevant data from trials for a definitive study of the adverse effects of statins. CTT has engaged with a wide range of collaborators, including the Cochrane Heart Group, in setting up this new study.

This work will take some time to complete. In the meantime, further evidence is available from n-of-1 trials in which eight

patients who had experienced myalgia symptoms while taking statins were randomly and blindly swapped between placebo and statin over repeat three week periods. The frequency and severity of symptoms were indistinguishable when these patients were taking statins or placebo, making it unlikely that statins were causal. The authors suggested that doctors might find it helpful to use an n-of-1 approach to determine which patients' adverse effects are caused by statins, a view with which we concur.

Competing interests: SE was coordinating editor of the Cochrane Heart Group from 1996 to 2014. Both SE and GDS take statins.

- McPherson K. Need for proper trial protocols to assess side effects of drugs. BMJ 2015;351:h4303. (11 August.)
- Taylor F, Huffman MD, Macedo A, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev 2013;1:CD004816.
- 3 Macedo A, Taylor F, Casas JP, et al. Unintended effects of statins from observational studies in the general population: systematic review and meta-analysis. BMC Med 2014;12:51.
- 4 Finegold JA, Manisty CH, Goldacre B, et al. What proportion of symptomatic side effects in patients taking statins are genuinely caused by the drug? Systematic review of randomized placebo-controlled trials to aid individual patient choice. Eur J Prevent Cardiol 2014;21 464-74.
- 5 Joy TR, Monjed A, Zou GY, et al. N-of-1 (single-patient) trials for statin-related myalgia. Ann Intern Med 2014;160:301.

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