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Correspondence

Reply to: "Comments on 'Optimising treatment of hyperlipidaemia: Quantitative evaluation of UK, USA and European guidelines taking account of both LDL cholesterol levels and cardiovascular disease risk' "

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To the Editor,

We are grateful to Dr Shah for his appreciative comments about our article [1]. He raises a number of important points. However, these stem from issues arising as consequences of the guidelines themselves. The purpose of our paper was to determine which guidance was most appropriate for cholesterol-lowering medication in people throughout the range of LDL cholesterol, from below to above average, at differing degrees of atherosclerotic cardiovascular disease (CVD) risk. Our main conclusion was that for people whose LDL cholesterol was < 4 mmol/l (154 mg/dl), fixed dose atorvastatin 20 mg daily (or an equally efficacious dose of another statin) was optimal, whereas for those with LDL cholesterol ≥4 mmol/l, treatment aimed at a target of < 1.8 mmol/l (70 mg/dl) was more clinically effective. For some very high risk patients, a target LDL cholesterol of < 1.4 mmol/l (55 mg/dl) [2], and this was potentially even more effective.

Dr Shah raises the question of when lowering cholesterol with drug therapy becomes worthwhile for an individual patient and for the clinical commitment of physician and nurses. The current guidelines are *ex cathedra* on this subject. As clinicians ourselves, we would feel comfortable in offering statin therapy when the number who needs treatment for 10 years to prevent one CVD event (NNT) is < 30 (equivalent to preventing > 3.3 events per 100 people treated). Current guidelines, which do not take LDL cholesterol into account, would offer treatment to some people whose likelihood of benefit is low, and deny it to others who stand to gain greatly. For example, the NNT is 49 for someone prescribed atorvastatin 20 mg daily at 7.5% 10-year CVD risk, with an initial LDL cholesterol of 3 mmol/l, while at the same CVD risk, the NNT is only 21 in a patient with a pre-treatment LDL cholesterol of 6 mmol/l treated to a target of 1.8 mmol/l.

Another issue raised by Dr Shah is how low to go. Possible adverse effects of persistently low LDL cholesterol remain a concern, although evidence from genetic causes of low cholesterol and from acquired disorders leading to hypocholesterolaemia is generally reassuring [3]. When the gain in CVD events prevented from achieving low LDL cholesterol is real, as in patients at substantially elevated CVD risk (> 40% in the next 10 years), potential adverse effects pale into insignificance. Ironically, most of the debate, however, has focussed on these high risk patients. What has rarely been considered [4] is that some guidelines advocating fixed dose statin would offer atorvastatin 20 mg daily, which typically lowers LDL cholesterol by 43%, to people with initial LDL cholesterol < 3.2 mmol/l, whose 10-year CVD risk is only 7.5%. Thus, the LDL cholesterol of someone whose pre-treatment was 2.5 mmol/l would be decreased to 1.4mmol/l to little purpose [5].

Clearly, future guidelines would benefit from algorithms aiding clinical decisions, which are not simply intended to estimate CVD risk, but also incorporate initial LDL cholesterol concentration and compute the most suitable treatment plan (fixed dose statin or treatment aimed at specific LDL cholesterol targets).

Conflict of interest

Handrean Soran and Paul N Durrington have served as consultants to pharmaceutical companies marketing lipid-lowering drugs, and have received travel expenses, payment for speaking at meetings and funding for research from some of these companies. Safwaan Adam has nothing to declare.

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