*The authors' reply:*

We would like to address the comments of Drs Messerli and Grossman as follows.

1. Since the MRC study,[1] several long-term double-blind studies have compared the major classes of antihypertensive drugs (thiazides, β-blockers, calcium channel antagonists, ACE inhibitors and α-blockers), and overall showed no consistent or important differences between them as regards hypertensive efficacy, adverse effects or quality of life.[2-5] Trials that have compared different classes of drugs directly as regards reduction in cardiovascular events have shown no consistent differences between regimens based on different drug classes.[6,7,8,9,10] In general, these outcome trials have shown reductions in coronary events by 16% and in cardiovascular mortality by 21%, although the reduction in coronary events observed in all trials was less than the 20 to 25% reduction predicted from epidemiological observations.[11] The reasons are not clear, but in relation to β-blockers, may relate to the metabolic disturbance discussed such as weight gain, lipid abnormalities and changes in diabetic control. The question as to whether metabolically neutral agents will improve outcome with regard to coronary events will hopefully be answered by large comparative trials such as Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)[12] and Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT).[13]

2. We agree that the diabetic population are at particular risk from the complications of hypertension, particularly in relation to coronary morbidity and mortality.

3. We disagree that the UKPDS study[14] had no effect on coronary heart disease. What it did show was that the group assigned to tight blood pressure control had a reduction in risk of 21% in the aggregate end-point for myocardial infarction compared with less tight control. Although the result was not statistically significant, the reduction in myocardial infarction by one-fifth is still encouraging. In addition, when all macrovascular diseases were combined, including myocardial infarction, sudden death, stroke and peripheral vascular disease, the group assigned to tight blood pressure control had a 34% reduction in risk compared with the group assigned to less tight control. Importantly, β-blockers were as effective as ACE inhibitors at reducing these complications.[15] What it would seem to suggest is that the patients with diabetes mellitus and hypertension need aggressive blood pressure control before they will reap the benefits of improved outcome, probably because they are at such high risk to start with. In keeping with this, in the cohort with diabetes mellitus of the Hypertension Optimal Treatment (HOT) study,[16] blood pressure lowering improved cardiovascular outcome and, importantly, there were 50% fewer cardiovascular end-points when diastolic blood pressure was titrated beyond <90 mmHg to <80 mmHg.

4. We consider that we have discussed fully the adverse effects of β-blockers which may make them unattractive in some patients with diabetes mellitus. We would reiterate that the hazards of hyperlipidaemia and lipid abnormalities may have been exaggerated in the past and have to be balanced against the known cardioprotective effects of these agents. In addition, newer, more cardioselective agents, particularly those with additional properties such as nitric oxide release, may be indicated in those patients with diabetes mellitus who also have peripheral vascular disease. Finally, the clear message in patients with diabetes mellitus and hypertension, both from the HOT[16] and UKPDS studies,[14,15] is that the lower the blood pressure the better the outcome. This is unlikely to be achieved without the use of 2 or more agents one of which will often be a β-blocker.

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