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## The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease

### Aspirin for Primary Prevention in Diabetes

**26 October 2008**

Dear Editor

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The excellent study by Belch et al (BMJ 2008;337:a1840) suggests that aspirin is not universally indicated for primary prevention of vascular events in diabetic patients. Biologically, there is no difference in the action of antiplatelet drugs for primary or secondary prevention – the major difference is in the event rate and therefore the power of study needed to show benefit. Arguably, the patients in the study had atherosclerotic disease and were therefore secondary prevention patients. With baseline risk factors (smoking, blood pressure, cholesterol) as presented, many patients in this study would have been above the 1.5% per year risk threshold where benefit of aspirin outweighs risk. 1 The event rate documented was considerably short of that predicted, and this may have been due to increased use of statins and other cardioprotective drugs during the study – no data are given for this. Benefits of aspirin in high-risk patients are significant, 2 but less than those projected for statins. 3

Increased risk of haemorrhagic events is an inevitable consequence of deriving benefit from the antiplatelet effects of aspirin. There was no increased risk of dyspeptic symptoms or gastrointestinal haemorrhage with aspirin in Belch's study in spite of the fact that the numbers and length of follow-up were sufficient to expect adverse effects to be detected. 4 Compliance and aspirin resistance are two factors not addressed in the study, but which could affect response. At least a quarter of patients treated with aspirin may be resistant, and this translates into decreased protection from cardiovascular events. 5 Because of increased platelet reactivity, aspirin resistance appears to be even more common in diabetic patients and may be overcome by increasing the dose or prescribing an additional antiplatelet drug. 6 Presumably, aspirin-resistant patients, while not benefiting from treatment, are also not susceptible to haemorrhagic side effects.

Diabetic patients are at high risk of macrovascular complications, but trials must take account of the interaction between drugs and changing clinical practice. Although aspirin is cheap and safe, it is not always effective. The time may have come to consider monitoring platelet function in patients with aspirin – as other forms of anticoagulation are monitored. Aggregometry is simple and cheap, but requires standardisation. Current evidence does not allow us to preclude an effect of aspirin in primary prevention of vascular events in diabetes, but neither does it support universal prescription of aspirin despite the very high risk experienced by diabetic patients.

Conflicts of Interest:

The authors have no conflicts of interest to declare

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