The Use of Aspirin in Primary Prevention of Cardiovascular Disease

Statement from the British Hypertension Society January 2010

The use of aspirin to prevent future cardiovascular events in those with a prior history of cardiovascular disease is recommended by all relevant guidelines and is supported by a strong evidence base. However, there has been much publicity and debate resulting from recent reports questioning the benefits of aspirin use in those with no history of prior cardiovascular disease, including those with diabetes (1,2,3), particularly in the context of the known increase in risk of gastrointestinal bleeding.

The current BHS Guidelines, published in 2004 (BHS IV), recommend that all patients suitable for secondary prevention strategies (those with prior history of cardiovascular disease), including those with type 2 diabetes of greater than 10 years duration, or over 50 years, have a sufficient level of cardiovascular disease risk to benefit from aspirin therapy, and should be considered for low -dose aspirin (75mg daily) unless they have specific contraindications to aspirin use.

For primary prevention, the balance of benefits vs harm mandate that patients need to be aged over 50 years and have a CVD risk level ≥ 20% over 10 years to shift the balance in favour of benefit. Thus, for primary prevention, low- dose aspirin should only be offered to hypertensive patients aged over 50 years whose blood pressure has been controlled to the audit standard (<150/90 mmHg) and who have a baseline CVD risk ≥20% over 10 years and no contraindication to aspirin use. These recommendations were strongly influenced by the assessment of the benefit and harm of low-dose aspirin in well treated hypertensive subjects at different levels of baseline CVD risk (5). In these analyses the benefit *vs* harm was neutral at a 10 year CVD risk of about 10%, but favoured benefit at higher levels of risk.

The recently published updated meta-analysis using individual participant data from the original trials of the use of aspirin in primary prevention (1), reported an overall proportional risk reduction in serious vascular events of 12% (0.51% aspirin vs 0.57% control per year, p=0.0001) due mainly to a reduction of about one fifth in non-fatal myocardial infarction (0.18% vs0.23% per year, p<0.0001). However, this benefit was offset by an increase in major gastrointestinal and extracranial bleeds (0.10% *vs* 0.07% per year, p<0.0001). Thus the absolute reduction in the risk of vascular events is only about twice as large as the absolute increase in bleeding. As the authors of the meta-analysis point out, most of the patients recruited into these primary prevention trials were not taking statins, which would have reduced their absolute risk of vascular events without any increase in harm. Even in those patients at higher risk the number of vascular events was too few to allow any reliable conclusions to be drawn.

In a further report of a meta-analysis of trials of aspirin use in the primary prevention of cardiovascular events in people with diabetes (2) which included 3 new trials since the last BHS guidelines were published, there was a non-significant trend for benefit on all cardiovascular events (HR 0.90, CI 0.81-1.00), but a significant reduction in the risk of myocardial infarction in men (HR

0.57, CI 0.34-0.94) but not women (HR 1.08,CI 0.71-1.65). The evidence from these trials for harm associated with aspirin was inconsistent.

The most recent trial to report – The AAA Study, published in abstract form only to date (3), of low-dose aspirin in the prevention of cardiovascular events and death in subjects with asymptomatic atherosclerosis, demonstrated no benefit of 100 mg aspirin in a placebo- controlled trial in almost 29,000 patients but there was a non significant excess of major haemorrhage in the aspirin treated group. Further details on this trial are awaited.

Recently the Medicines and Healthcare Products Regulatory Agency (MHRA) has issued a statement that reminds physicians and the public that aspirin is only licensed for the secondary prevention of cardiovascular disease, and that if aspirin is used in primary prevention, the balance of benefits and risks should be considered for each individual, particularly the presence of risk factors for cardiovascular disease and the risk of gastrointestinal bleeding.

On the basis of these findings and reports, and until new information becomes available from ongoing trials, the BHS Working Party reaffirms its earlier recommendations that aspirin use in the prevention of cardiovascular disease in hypertensive people should be restricted to patients with prior history of cardiovascular disease and, in primary prevention (including those with diabetes), to those aged over 50 years with 10 year cardiovascular risk of at least 20%. As advocated by MHRA, physicians should weigh up the benefits and risks of low dose aspirin in all individuals. An accurate quantitative assessment of 10 year cardiovascular risk is essential before prescribing aspirin for the primary prevention of cardiovascular disease.

References

1. Antithrombotic Trialists' (ATT) Collaboration. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *Lancet* 2009;373:1849-1860.

2. De Berardis G, Sacco M, Strippoli GFM, Pellegrini F, Graziano G, Tognoni G and Nicolucci A. Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. *BMJ* 2009;339:b4531

3. Fowkes FGR, Price JF, Stewart MCW, Butcher I, Leng GC, Pell ACH, Sandercock PAG, Fox KAA, Lowe GDO, Murray GD for the Aspirin for Asymptomatic Atherosclerosis Trialists. AAA: Randomised controlled trial of low dose aspirin in the prevention of cardiovascular events and death in subjects with asymptomatic atherosclerosis. http://www.escardio.org/congresses/esc-2009/congress-reports/Pages/706001-706002-fowkes-patrono.aspx

4. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS and Thom S McG. British Hypertension Society Guidelines. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV. *J Hum Hypertens* 2004;18:139-185.

5. Zanchetti A, Hansson L, Dahlof B, Julius S, Menard J, Warnold I, Wedel H; HOT Study Group. Benefit and harm of low-dose aspirin in well-treated hypertensives at different baseline cardiovascular risk. *J Hypertens* 2002;11:2301-2307.