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Authors' reply: Nonselective nonsteroidal anti-inflammatory drugs and increased cardiovascular events: stress could be the explanation

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Dr Sutton [1] is right to consider the broad picture, although some of the associations he suggests are on present evidence, somewhat speculative. I would like to stress that our paper was not written to undermine or attack nonsteroidal anti-inflammatory drugs (NSAIDs) but to contribute to a balanced assessment of their benefits and risk. In this context, although we did not study selective cyclo-oxygenase (COX)-2 inhibitors, our data taken with that of others, suggest that myocardial infarction is not necessarily a price to pay for the gastrointestinal benefits of cyclo-oxygenase selectivity.

Reference

- 1 Sutton JA. Nonselective nonsteroidal anti-inflammatory drugs and increased cardiovascular events: stress could be the explanation. *Br J Clin Pharmacol* 2007; 501.

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Authors' reply: Nonselective nonsteroidal anti-inflammatory drugs and increased cardiovascular events: emotional stress could be the explanation

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We noted with interest the comments of Dr Sutton [1] that 'a Google search on aldosterone, stress, mood pro-

duced '52 000 English or French pages' in 0.33 s' and that our paper [2] 'made no mention of stress as a possible cause of increases in aldosterone during NSAID treatment'. Our research [2] was conducted *in vitro* using human kidney (and liver) microsomes and demonstrated that nonselective NSAIDs inhibit the glucuronidation of aldosterone, predicating an increase in plasma and tissue (renal) aldosterone concentration *in vivo*. To suggest that stress is an explanation for our *in vitro* data indicates that Dr Sutton either did not read or understand the article and its conclusions. Although aldosterone synthesis and secretion is regulated principally by angiotensin II, extracellular potassium and ACTH we concur with Dr Sutton that other factors can stimulate or inhibit aldosterone production *in vivo* including catecholamines, 5-hydroxytryptamine, heparin and vasoactive intestinal polypeptide [3]. Undoubtedly aldosterone is a key cardiovascular hormone contributing to the pathophysiology of heart failure [3] and the development of hypertension [4]. The potential for a synergistic effect of NSAIDs and 'stress' on aldosterone concentration *in vivo* might lead us to conclude that in stressful situations the adage 'take an aspirin and lie down' should be revised simply to 'lie down'!

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