

## **RISK OF MYOCARDIAL INFARCTION, STROKE AND VASCULAR DEATH ASSOCIATED WITH COXIBS AND TRADITIONAL NSAIDS**

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We conducted a meta-analysis of tabular data from all published and unpublished randomized trials including a comparison of a coxib versus placebo, or a coxib versus a traditional NSAID, of at least four weeks duration, and which recorded information on vascular events. Individual trialists and companies provided information on the number of patients randomized, numbers of vascular events, and the person time of follow-up for each randomized group.

In placebo comparisons, allocation to a coxib was associated with a 36% increased incidence of vascular events (rate ratio [RR] 1.36 [95% CI: 1.09 – 1.69];  $p=0.006$ ) with no statistically significant heterogeneity among the different coxibs. This excess risk of vascular events was derived chiefly from a 2-fold increased risk of myocardial infarction (RR=1.86 [95% CI: 1.35 – 2.56];  $p=0.0001$ ). Among trials of at least one year duration (mean 2.7 years) the proportional increase in vascular events was 45% (RR=1.45 [95% CI 1.12–1.89];  $p=0.005$ ). Overall, there was no significant difference in the incidence of vascular events between a coxib and any traditional NSAID (RR=1.16 [95% CI: 0.97– 1.38];  $p=0.1$ ), but there was evidence of a difference between naproxen and the other traditional NSAIDs. In indirect comparisons with placebo, diclofenac and ibuprofen were each associated with a 1.6-fold increased risk of vascular events (both  $p\leq 0.05$ ), while naproxen did not increase the incidence of vascular events (RR=0.86 [95% CI 0.62-1.21];  $p=0.4$ ).

### **Conclusions**

Coxibs and some traditional NSAIDs moderately increase the risk of vascular events, particularly myocardial infarction, but there remains considerable uncertainty about the magnitude of this hazard for particular drug regimens