Correspondence

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Cardiovascular Thrombotic Events in Controlled, Clinical Trials of Rofecoxib

To the Editor:

As editors of a journal devoted to the promotion of evidence-based medicine, we search for and abstract the most relevant (valid and clinically important) reports originally published in the top English language medical journals. For the last few years, we have been following reports regarding the clinical use, efficacy, and potential side effects of selective COX-2 inhibitors. On the basis of inappropriate methodology, we have recently rejected the publication by Mukherjee et al1 from our abstracts. In the recent report, Konstam et al2 provided data on the relative rate of cardiovascular events in controlled trials of rofecoxib. To better appraise the validity of their conclusion, we wish to ask the authors for information on 3 aspects of their analysis.

What are the results of an intent-to-treat analysis in which all patients randomized to a given treatment were analyzed? The analysis, as reported by the authors, was a “modified intention-to-treat approach” in which patients were included only if they received at least 1 dose of the study drug. We do not consider those 2 analyses equivalent.

If results of intent-to-treat analysis are not available, 2 further issues gain importance. First, what was the proportion of patients removed from analysis after randomization because they did not take any dose of the drug? Second, were patients and caregivers blinded to treatment allocation in all trials (the authors state that outcome-assessors were blinded)? If not, what are the results of analysis looking at the group of blinded trials?

Finally, if one were to allow the use of aspirin in all trials, the expected result would be the lack of difference in cardiovascular events (vide CLASS trial3). From Table 1, it appears that in trials involving almost 10,000 patients, use of aspirin was actually allowed. What are the results of analysis looking only at the trials in which use of aspirin was not allowed?

We would greatly appreciate help in resolving these questions.

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Circulation. 2002;106:e18
doi: 10.1161/01.CIR.0000023454.92028.12
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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