Expression of Concern: Bombardier et al., "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis," N Engl J Med 2000;343:1520-8.

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We have recently obtained information regarding inaccuracies in data in the report of the VIGOR (Vioxx Gastrointestinal Outcomes Research) study by Bombardier et al.[1] that raise concern about certain conclusions in the article.

The VIGOR study was designed primarily to compare gastrointestinal events in patients with rheumatoid arthritis randomly assigned to treatment with rofecoxib (Vioxx) or naproxen (Naprosyn), but data on cardiovascular events were also monitored. Three myocardial infarctions, all in the rofecoxib group, were not included in the data submitted to the *Journal.* The editors first became aware of the additional myocardial infarctions in 2001 when updated data were made public by the Food and Drug Administration.

Until the end of November 2005, we believed that these were late events that were not known to the authors in time to be included in the article published in the *Journal* on November 23, 2000. It now appears, however, from a memorandum dated July 5, 2000, that was obtained by subpoena in the Vioxx litigation and made available to the *Journal,* that at least two of the authors knew about the three additional myocardial infarctions at least two weeks before the authors submitted the first of two revisions and 4½ months before publication of the article. Given this memorandum, it appears that there was ample time to include the data on these three additional infarctions in the article.

The fact that these three myocardial infarctions were not included made certain calculations and conclusions in the article incorrect. Although only summary percentages, not actual numbers of myocardial infarctions, were included in the *Journal* article, the following tables display the numerical data without (Table 1) and with (Table 2) the three myocardial infarctions.

Lack of inclusion of the three events resulted in an understatement of the difference in risk of myocardial infarction between the rofecoxib and naproxen groups (presented in the article as a reduction in the risk with naproxen but shown here as an increase in the risk with rofecoxib). It also resulted in the misleading conclusion that there was a difference in the risk of myocardial infarction between the aspirin indicated and aspirin not indicated groups.

Table 1. Data on Myocardial Infarctions Omitting the Three Events.*

Study Group	Person-Years of Exposure	No. of Myocardial Infarctions	Relative Risk	95% CI
Total				
Rofecoxib	2315	17	4.25	1.39 to 17.37
Naproxen	2316	4		
Aspirin indicated				
Rofecoxib	95	8	∞	1.65 to ∞
Naproxen	92	0		
Aspirin not indicated				
Rofecoxib	2220	9	2.25	0.63 to 10.02
Naproxen	2224	4		

* The numbers of person-years of exposure as of February 10, 2000, have been estimated. Relative risks were estimated by Poisson regression; confidence intervals were calculated by the exact method.

Table 2. Data on Myocardial Infarctions Including the Three Events.*

Study Group	Person-Years of Exposure	No. of Myocardial Infarctions	Relative Risk	95% CI
Total				
Rofecoxib	2698	20	5.00	1.68 to 20.13
Naproxen	2699	4		
Aspirin indicated				
Rofecoxib	105	8	∞	1.66 to ∞
Naproxen	102	0		
Aspirin not indicated				
Rofecoxib	2593	12	3.00	0.91 to 12.78
Naproxen	2597	4		

* Relative risks were estimated by Poisson regression; confidence intervals were calculated by the exact method.

In addition, the memorandum of July 5, 2000, contained other data on cardiovascular adverse events that we believe would have been relevant to the article. We determined from a computer diskette that some of these data were deleted from the VIGOR manuscript two days before it was initially submitted to the *Journal* on May 18, 2000.

Taken together, these inaccuracies and deletions call into question the integrity of the data on adverse cardiovascular events in this article. We have asked the authors to submit a correction to the *Journal.*

1. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. N Engl J Med 2000;343:1520-8.