

Letter to the Editors

Safety of ibuprofen vs. paracetamol

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What are readers and the public to make of the study by de Vries *et al.* [1]? At a glance, it appears that the safety profiles of ibuprofen, paracetamol and the combination of the two drugs are similar. Do the results of this study, funded by the principal manufacturer of ibuprofen, hold up to closer scrutiny?

This was not a prospective randomized controlled trial. It was a retrospective observational study. Importantly, we cannot assume that individuals were equally likely to have been prescribed the three options studied (ibuprofen alone, paracetamol alone or concomitant ibuprofen and paracetamol). There are some major confounding effects at play here. One might anticipate, for instance, that patients with a history of heart disease, peptic ulcers or renal disease would be less likely to have been prescribed a nonsteroidal anti-inflammatory drug (NSAID), compared with paracetamol, in the first place. Indeed, it is clear from table 1 of the publication that there were large and statistically significant differences between the patients retrospectively allocated to the three groups across a number of baseline variables, including age and a past history of heart failure, ischaemic heart disease, cerebrovascular disease and upper gastrointestinal disease.

There is brief mention, without clarity, of statistical adjustments for risk factors of the safety outcomes. Statistical adjustment can serve a useful function, but it cannot transform observational studies into natural experiments, and often involves very subjective judgments [2].

Confusingly, the authors also defined 'paracetamol only' patients as those with no prescriptions for ibuprofen, other NSAIDs and aspirin in the preceding 6 months, yet table 1 shows that one-third of these patients had used NSAIDs in the preceding 6 months.

Competing Interests

There are no competing interests to declare.

REFERENCES

- 1 De Vries F, Setakis E, van Staa TP. Concomitant use of ibuprofen and paracetamol and the risk of major clinical safety outcomes. *Br J Clin Pharmacol* 2010; 70: 429–38.
- 2 Christenfeld NJ, Sloan RP, Carroll D, Greenland S. Risk factors, confounding, and the illusion of statistical control. *Psychosom Med* 2004; 66: 868–75.

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