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Letter to the Editors

Reply to letter by Peterson & Naunton [safety of ibuprofen *vs.* paracetamol]

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Peterson & Naunton correctly observe that our study was not a randomized clinical trial (RCT) and that there is a potential for bias in observational studies. What are readers and the public to make of these general comments? Should we just discard observational evidence and wait for evidence to emerge from RCTs, as implied by Peterson & Naunton? In 1983, the renowned clinical epidemiologist Feinstein noted that 'despite the magnificent scientific achievements of randomized clinical trials, the foundation for a basic science of patient care will also require major attention to the events and observations that occur in the ordinary circumstances of clinical practice' [1]. There are often substantial differences in the patients recruited into clinical trials and those in actual clinical practice. As an example, a recent analysis found that users of selective Cox-2 inhibitors were very different from patients participating in large RCTs. Most of these users in actual clinical practice would not have been eligible for inclusion into the pivotal RCTs, as they only used the medicines intermittently and for short periods of time [2]. There is insufficient RCT evidence for several of the outcomes evaluated in our study [3]. Of course, observational studies can yield incorrect answers, as highlighted by the controversies around hormone therapy. The challenge is to conduct an evidence-based assessment of bias rather than to merely speculate on potential biases. We tried to minimize the effects of bias by applying a variety of approaches, including an evaluation of patterns of risk. The risk factors used in the statistical analyses were selected *a priori* on the basis of likely association with outcome and ability to measure in our data source. The fit of statistical models was checked. Rigorously conducted observational studies are important as they reflect the real-life experiences with medication.

Competing Interests

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References

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3 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.

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