Reviewer's report

Title: Incomplete evidence: the inadequacy of databases in tracing published adverse drug reactions in clinical trials

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Reviewer: Mr Phil Wiffen

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after revision, which I do not need to see

This is a useful methodology paper and will inform those who are not familiar with the pitfalls. The study highlights another difficulty of searching databases in order to retrieve all the evidence for a review and/or met-analysis. The different levels of ADR reporting between databases is a valuable warning to users.

The authors state that RCTs can potentially provide high quality estimates of the frequencies of adverse effects (Background section)

However the point that the authors do not adequately cover concerns the appropriateness of RCTs as a means of estimating ADRs. This is particularly so because a large proportion of their selected studies were single dose regimes and so there was either insufficient exposure to a medicine or too short a time frame for ADRs to manifest unless extremely common. The reader could draw the conclusion by inference that RCTs are THE place to gather ADR data. A comment on valuable and reliable methods of assessing ADRs would be useful.

One minor point relates to the coined term 'index-bias' On page 7 the authors state that failure to identify papers by searching will lead to an over-estimation of rate or severity of ADRs. Surely this could equally be underestimation.

Competing interests:

None declared.