
Improving the credibility of reporting industry-sponsored research

Reports of ghostwriting, guest authorship, selective or biased disclosure of research results, and inaccurate or incomplete reporting of potential conflicts of interest have damaged the credibility of industry-sponsored clinical research.¹ For example, an analysis of the financial conflicts of interest of members of the American Psychiatric Association who are responsible for updating the Diagnostic and Statistical Manual of Mental Disorders (DSM) showed that nearly 70% of those responsible for version 5 of the DSM had financial relationships with pharmaceutical companies.^{2,3} This has raised concerns that so many experts responsible for defining mental health conditions and treatments have financial ties to pharmaceutical companies.^{2,3}

Pharmaceutical companies are trying to improve this by using recommendations from groups such as the International Committee of Medical Journal Editors (ICMJE), the Good Publication Practice guidelines, the Committee on Publication Ethics, the EQUATOR (Enhancing the QUALity and Transparency Of health Resources) Network, and the Medical Publishing Insights and Practices (MPIP).¹ Even though important improvements have been made, a negative view of industry-sponsored research remains. In 2010, the MPIP convened a debate with journal editors and industry representatives to resolve this issue. Mansi *et al.*¹ report the 10 recommendations suggested for improving the quality and transparency of industry-sponsored clinical research reporting; these recommendations would also improve the reporting of other clinical research publications, regardless of how they were funded. The findings are summarized below.

Recommendation 1: Ensure clinical studies and publications address clinically important questions

Credibility is compromised when clinical research is intended for marketing purposes rather than advancing scientific and medical knowledge. Sponsors could enhance transparency and credibility by

better explaining the rationale behind the research and to ensure that research is designed to answer important clinical and scientific questions.¹

Recommendation 2: Make public all results, including negative or unfavourable ones, in a timely fashion, while avoiding redundancy

Many industry sponsors have committed to disclosing the results of all clinical studies through trial registries. The ability to cross-reference trial registries, results databases, and all related publications informs the scientific community whether studies are completed or are under way and discourages selective reporting.¹

Dissemination of negative, confirmatory, or inconclusive results can be challenging, but they can be very valuable in the progress of science and can prevent redundancy. They could be published in journals dedicated to these studies (perhaps in open-access format), abridged article formats more suitable to them, and/or specific reviewing mechanisms focused on scientific validity as opposed to 'impact'. Many of these potential solutions are currently being explored and developed by journals and publishers.¹

Recommendation 3: Improve understanding and disclosure of authors' potential conflicts of interest

The processes for disclosing authors' potential conflicts of interest have recently improved. Journal editors and sponsors should support the use of the updated ICMJE Conflict of Interest Reporting Form. A centralized, publicly accessible disclosure database may also be a possibility in the future.¹

Even though the processes have improved, the *PloS Medicine* Editors have raised the question as to whether or not disclosure worsens bias. They acknowledge that disclosure is preferable to non-disclosure but they also report that it may be a limited strategy in mitigating bias.² Disclosure shifts 'secret bias' to 'open bias'; a reader may be blinded by the amount of information provided; and that by disclosing a conflict of interest, it may be viewed that a person no longer needs to

manage their conflict.³ Loewenstein *et al.*⁴ have demonstrated that patients think that doctors would not intentionally mislead them and they tend to not discount advice even when they know there is a conflict of interest.

Recommendation 4: Educate authors on how to develop quality manuscripts and meet journal expectations

Researchers may lack formal writing training or knowledge of reporting guidelines, for example the Consolidated Standards of Reporting Trials (CONSORT) requirements, which affects the quality of manuscripts. To address this, best practice guides could be widely disseminated to industry and academic authors. For example, the MPIP's Authors Submission Toolkit can help authors navigate the manuscript development and submission process, and EQUATOR's author resource library can provide guidance on research reporting.¹

Recommendation 5: Improve disclosure of authorship contributions and writing assistance and continue education on best publication practices to end ghostwriting and guest authorship

Research sponsors have improved their credibility by recognising the positive role that professional writers can play in manuscript development, acknowledging them appropriately as authors or contributors (in accordance with ICMJE guidelines) and disclosing their names, affiliations, and potential conflicts of interest. Everyone must work towards zero tolerance of ghostwriting and guest authorship.¹

Recommendation 6: Report adverse event data more transparently and in a more clinically meaningful manner

The commonly used phrases of 'no clinically significant adverse events' and 'no unexpected adverse events' lack clinical relevance, particularly regarding rare adverse events that may be important for agents used over a long period in large populations. Everyone would benefit from more uniform reporting guidelines that clearly specify the type and format of adverse event data to be reported. In addition, journals may need to revisit their manuscript length policies if they wish this information to be present in the main document. Authors should also be made aware of the need to balance the strength of adverse event claims versus the features and limitations of trial design.¹

Recommendation 7: Provide access to more complete protocol information

Some journals request submission of a clinical study protocol and some also publish them online to provide greater transparency to readers. However, making protocols publicly available raises issues that require further discussion, for example protection of intellectual property. Also, protocols are often amended as a trial progresses and public disclosure of multiple versions may cause confusion.¹

Recommendation 8: Transparently report statistical methods used in analysis

Statistical methods are assessed as part of the peer review process for many journals. Sponsors should ensure that authors provide adequate information about the chosen methods based on the prespecified study design, and how they were applied to the final data set. The issue of statistical analysis reporting warrants further discussion to explore how journals can develop policies that raise standards for all clinical publications, independent of the financial support or authorship.¹

Recommendation 9: Ensure authors can access complete study data, know how to do so, and can attest to this

Authors need to be able to explain important details of study design and analysis or prove their access to raw data.¹

Recommendation 10: Support the sharing of prior reviews from other journals

The MPIP's Authors' Submission Toolkit suggests that when submitting a rejected manuscript to another journal, a copy of the previous manuscript and reviewers' comments could be provided to show that suggestions have been incorporated. Some journals already encourage the sharing of previous reviews as it improves transparency, avoids duplication, and increases the quality of subsequent submissions.¹

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Journal round-up

While working on a paper for a colleague, I stumbled across the following information in the Instructions to Authors provided by the journal *Hypertension*¹:

'Recent Advances in Hypertension. These articles are intended to highlight, provide further perspective, and enhance the overall significance of recent studies published in *Hypertension* that contribute to our understanding of hypertension and related areas. ... References should generally be restricted to those published in *Hypertension* during the last 2-3 years'.

The requirement that the references be limited to articles published in *Hypertension* struck me as strange since many of the most highly cited studies on hypertension are published in general medical journals. Of the 25 most frequently cited articles published since 2010 whose titles include the word 'hypertension', eight were published in *JAMA*, *The Lancet*, or the *New England Journal of Medicine*; only one was published in *Hypertension* (data from Web of Science, Thomson Reuters; information correct as of 18 July 2012).

Perhaps this is merely some kind of exercise in vanity, a way of bigging up *Hypertension* and its contribution to the medical literature. One thing's for sure though: it does the journal's impact factor no harm at all.

According to a set of international standards for editors agreed upon at the Second World Conference on Research Integrity, held in Singapore in 2010, 'Editors should not attempt to inappropriately influence their journal's ranking ... it is inappropriate to demand that references to that journal's articles are included except for genuine scholarly reasons'.²

Whatever *Hypertension's* reasons for insisting on the referencing of its own articles, they certainly do not appear to be scholarly.

My exploration of the *Hypertension* website led me to a staggering case of image recycling/manipulation

involving multiple articles published in leading journals including *Circulation*, *Kidney International*, and *Hypertension*.³⁻⁵

The articles, which come from a single lab in Japan, feature industrial-scale reuse of immunofluorescence and histology images, and Western and Northern blot bands. A number of the journals involved (*Hypertension* included) have published Expressions of Concern. Retractions will surely follow.

How many more such cases will come to light over the coming years?

While doing a spot of research on plagiarism (a favourite topic of mine), I came across a promising looking source in *Journal of Visual Communication in Medicine*.⁶ When I attempted to access it, however, I was informed that access for 24 hours would set me back US\$86.00. This is the highest such fee I have ever come across. To put it into perspective, an annual individual subscription to *Medical Writing* costs US\$85.00.³ (Individual *Medical Writing* articles cost US\$48.00 plus tax.)

To the relief of my bank manager, I will not be paying to find out what wisdom the *J Vis Commun Med* article contains. Luckily, excellent resources on ethical aspects of writing are available free of charge.⁷

How refreshing it was to read an editorial in the *Journal of Clinical Oncology*⁸ which questioned and indeed criticized the research methodology of recent trials - trials reported in none other than the *Journal of Clinical Oncology*.

The editorial highlighted the following issues with different trials:

1. reliance on significance test results for hazard ratios when choosing the optimum treatment regimen;
2. use of a design that was inappropriate to address a trial's stated goals; and
3. selection of an inadequate primary outcome.

Identifying ways of improving trial designs and data interpretation can only be a good thing. Good work, guys!

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