

Highlighting recent proposed best practice for statisticians in the reporting and publication of pharmaceutical industry sponsored clinical trials

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Abstract

In this paper we highlight recent recommendations for statisticians as to best practice for the reporting of clinical trials sponsored by the pharmaceutical industry. Recommendations are made covering: independent review; author responsibilities and recognition; publication timing; freedom to act; conflicts of interest; full author access to data and trial registration. Although the recommendations are made from a statistical perspective we hope that their applicability can be recognised in the wider pharmaceutical trials community, which is the purpose for writing this article.

Introduction

Motivated by an article in *Journal of the American Medical Association (JAMA)* on the reporting of industry sponsored clinical trials written by the journal's editors [1] we have made proposals for best practice for statisticians in the reporting and publication of pharmaceutical industry sponsored clinical trials. The initial impetus for writing these proposals was an invited paper session at the 2009 Statisticians in the Pharmaceutical Industry (PSI) Conference in Brighton, which we were invited to organise. The title of the session was 'Reporting of industry trials: JAMA, its impact, and the way forward'. We soon realised, however, that the topic was considerably broader than the session title encompassed and we believed that, while the JAMA editors may have been writing with respect to some genuine concerns, the situation had moved on since the original 2005 article.

Therefore, as part of the conference session we also evaluated the current situation with respect to the potential for bias in the reporting of industry sponsored trials, as well as the current level of public disclosure of industry sponsored trials [2,3]. From the start of our collaboration we were of the opinion that the best approach to addressing concerns with the reporting of industry sponsored trials was to be proactive in addressing any potential issues. We therefore worked together to form proposals for best practice for statisticians in the reporting of trials. The proposals themselves only represent the views of the authors, but it is our hope that the publication of these proposals will ignite a more general debate amongst trial statisticians from pharmaceutical companies and other sponsoring groups. These proposals were published first in *Pharmaceutical Statistics* [4] and we would encourage the reader to access this article along with accompanying commentaries.

Best practice for statisticians in the reporting and publication of industry sponsored clinical trials

Recommendations for best practice should promote the role of all authors in taking responsibility for the planning, design, conduct, analysis and reporting of a trial even if, in most instances, the trial statistician principally takes responsibility for the full and accurate reporting of the results and the statistical interpretation. It is in this context that we make the following recommendations. These are taken directly from reference [4].

1. The statistical author should be responsible for the statistical aspects of the paper

The authoring statistician should take responsibility for the statistical content of the paper. This should include but is not restricted to the correct statement of the trial objective and endpoints, the sample size justification, patient flow, analysis data set definition (e.g. Intent to Treat, per Protocol), presentation of the results and statistical interpretation of the results. It is also important that the paper appropriately identifies the methods that were planned in the original protocol and justifies any deviations from this in the final analysis results that appear in the paper.

2. The person responsible for statistical aspects of the trial should be recognised as an author

Subject to the framework for authorship established by the International Committee of Medical Journal Editors (ICMJE)[5] the statistician who is responsible for the design, conduct, analysis and reporting of a clinical trial should be identified and named as an author of the publication. They should be appropriately qualified and experienced. Where papers are submitted with no statistician declared as an author this should be noted and justified. If the trial has included a Data Monitoring Committee (DMC), the trial statistician should ensure that any statistician member of the DMC and any statisticians supporting the work of the DMC are identified and their role in the trial should be summarised. This should include the specific duties of the DMC statistician and the recommendations that they contributed to.

3. Protocols should be published and/or made publicly available in a timely manner

There should be a clear means for journal reviewers and editors to confirm the pre-defined study objectives, endpoints >

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- > and methods of analysis through having access to a publicly available protocol. This would enable them to confirm whether the published record of the trial adds, changes or omits important elements of the trial as conceived and set out in the protocol. It would also make clear where any results have been held back or retrospectively added. Publishing these details on a publicly accessible trial registry goes some way to addressing this and it is recommended that it be routine practice to include the pre-defined statistical methods of analysis for key trial outcome measures. The trial statistician should ensure that the protocol materials published include all the relevant details so that a subsequent reviewer can readily identify the trial objective, endpoints, design, sample size and proposed method of analysis for the primary endpoint.

4. Financial and other conflicts of interest should be disclosed

There should be a clear statement identifying who sponsored the trial. The trial statistician could be a sponsor company employee and/or employee of a contract research organisation who has been contracted by the sponsor to take the role of the trial statistician. They could also be an employee of an academic organisation who is running the trial with an industrial sponsor. Along with the other co-authors, the trial statistician should declare any financial interest and conflict of interest in terms of their employment status together with any direct and indirect financial interests in the sponsor and/or other relevant companies.

5. The authors should have freedom to act

The primary investigator and other co-authors should not be pressured by any sponsor company, either contractually or otherwise, to suppress the publication of trial results, or present the trial in a manner that they feel to be inappropriate. Freedom to act is particularly relevant to the trial statistician. There should be no impediment to the trial statistician in their role as author to appropriately presenting trial results. The trial statistician should understand that by being an author they are taking professional responsibility for the accurate reporting of the trial and the results as presented are a true and fair reflection of the outcome of the trial.

All URLs in *TWS* are active in the online version

TWS is published online before print in the Members Only section of the EMWA website (www.emwa.org). All URLs in the online version of the journal are live and provide a direct link to the respective websites.

6. All authors should have full access to trial data

The authors of the trial manuscript should have appropriate access to the data collected during the trial and should have played full part in the interpretation of the results from the trial. In particular they should have access to the data set used for the analysis and they should have access to the results of all of the analyses that have been conducted. An important duty for the trial statistician is to ensure that the data and results of the trial are presented to each of the authors in a timely manner. They should also ensure that the authors can access and understand the results and should facilitate communication between all authors to satisfactorily address any questions.

7. The trial results should be published

All trials should have their results published in publicly accessible registries designed for the purpose. This should also be done in a timely fashion after the completion of the trial (no more than one year after last subject last visit is good practice). As appropriate it is recommended that the trials are also published in peer review journals. Any publication should be identified and linked to the previously published trial protocol. The trial statistician should ensure that the results are made publicly available in a manner that is understandable to the wider medical community and is complete such that all results are disclosed and others are able to use the results in further research (e.g. meta analyses).

8. Independent statistical review should be highlighted

Many industry sponsored clinical trials undergo some form of statistical review by independent experts and / or regulators (e.g. available from published FDA Advisory Panel materials and European Public Assessment Reports) both in the design and in the review of the results. Where this takes place, the nature and scope of independent review should be described in the published manuscript. Where the review has been paid for, a statement should be made clarifying the nature of the relationship between sponsor and expert.

The above proposals were written with industry sponsored trials in mind, but it is clear that they are relevant to all trials, both industry and public sector sponsored. Many of the recommendations are generic and their intention is to improve the quality of reporting of studies and reduce bias.

Conclusions

When we wrote the proposals set out in [4] and described above we did so with the intention of encouraging debate. We hope also that the recommendations will form a basis for good publication practice for statistical authors, particularly those in the pharmaceutical industry, as well as for disciplines outside of statistics.

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Contributors:

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Conflicts of interest:

All of us are professional statisticians. All of us except ST and SJ currently work for the pharmaceutical industry; ST is currently a consultant to and has in the past received financial support from the pharmaceutical industry. SJ currently consults to the pharmaceutical industry for which his school receives payment and he indirectly benefits, and he gives courses from which he directly benefits. All of us are members of various academic and professional societies that receive financial support from the pharmaceutical industry.

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Medical writers, statisticians, and authorship

The medical writing community has long been aware of the important ethical issues surrounding authorship of clinical trial publications. However, as medical writers, we are often watching this debate from the sidelines, as we do not usually qualify for authorship of the papers we write (although we sometimes do). The main focus of medical writers' efforts in this area has been to promote awareness of the importance of properly attributing authorship of papers and to ensure that medical writers' contributions are made in an ethical and transparent manner, as recommended in EMWA's guidelines on publications [1].

The article by Steven Julious and coauthors explains some of the steps that industry statisticians (through their professional association, PSI) have recently been taking to ensure that statisticians also fulfil their role in publications in an ethical manner. PSI are to be congratulated on this initiative, which is described in more detail in the series of 3 papers published in *Pharmaceutical Statistics* cited in Steven's article. Statisticians are extremely important contributors to clinical trial publications, and the best practice recommendations are a welcome step towards ensuring that their contributions improve the quality of publications.

I hope all EMWA members will be aware of these guidelines when writing publications of clinical trial results and will do their best to ensure that the project statistician is named as an author of the paper. Medical writers may not often be authors of papers, but they still have a vital role to play in supporting statisticians and other authors and promoting ethical practices.

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Reference:

1. Jacobs A, Wager E. European Medical Writers Association (EMWA) guidelines on the role of medical writers in developing peer-reviewed publications. *Curr Med Res Opin* 2005;21(2):317-321.

'Ough'

'Ough' can be pronounced in eight different ways all of which feature in the following sentence: A tough, dough-faced ploughman strode through the streets of Scarborough, coughing and hiccoughing thoughtfully.