Journal watch

Transparency and bias in reporting clinical trial results, meta-analyses, conflicts of interest and medical publications, and more on ghostwriting

by Melanie Lee

Transparency and bias in reporting clinical trial results

The International Committee of Medical Journal Editors (ICMJE) requires, as a precondition of consideration for publication, that investigators register clinical trials in a public registry before patient enrolment. Mathieu and colleagues [1] have compared the primary outcomes specified in trial registries with the results reported in published articles in high impact factor journals. They found that just 45.5% of the 323 included trials were adequately registered; 315 of these showed some discrepancies between the registered and published outcomes. The authors concluded that selective outcome reporting is prevalent.

Kanaan and colleagues [2] have examined the tendency of peer-reviewed surgical journals to publish positive reports or negative and inconclusive outcomes as a function of the impact factor of the journal. They reviewed 2,457 articles from 15 journals and found an inverse correlation between impact factor and publications of negative or inconclusive reports. They concluded that journals with a lower impact factor may therefore play an important role in maintaining balanced reporting of studies; this is important, as the available published evidence is generally the basis for essential decision making in medical care. Erick Turner [3] has evaluated multiple publication of positive versus negative trial results in review articles, extending previous work on selective publication focusing on duloxetine. He found that positive trials were fully published, whereas negative trial results were bundled with positive trials in review articles. This significantly skewed the apparent weight of evidence favouring drug efficacy.

Meta-analyses

Systematic reviews of clinical trial results, preferably with meta-analyses, are regarded as the most reliable resource when making decisions about disease prevention and treatment. However, data extraction can be complicated, and different observers may get different results. Tendel and colleagues [4] report the results of an observer agreement study that aimed to study inter-observer variation related to the extraction of continuous and numerical rating scale data from trial reports for use in meta-analyses. Five experienced methodologists and five PhD students independently extracted data from trial reports used for a random sample of ten Cochrane reviews that presented a result as a standardised mean difference (SMD). They found that disagreements were common and often larger than the effect of commonly used treatments, and concluded that meta-analyses using SMDs are prone to observer variation. They suggest that more detailed review protocols, more than one observer, and statistical expertises are required to improve the reliability of meta-analyses.

Dissemination biases, more commonly known as publication biases, arise from suppression of whole studies, selective reporting of outcomes or subgroups, data 'massaging' (e.g. selective exclusion of patients from the analysis), and biases regarding timelines. Publication bias can be a problem when doing meta-analyses. To address this problem, statistical methods have been developed both to detect publication bias and to correct for suspected publication bias. Moreno and colleagues [5] have assessed the performance of novel contour enhanced funnel plots (a scatter plot of effect size versus associated standard error) and a regression based adjustment method to detect and adjust for publication biases. They have done a secondary analysis of a published systematic literature review using this novel method, and included analysis using established statistical methods for comparison. They concluded that the novel method worked convincingly, and suggest that it may become an important tool in combating publication biases.

Conflicts of interest and medical publications

Conflicts of interest (COIs) are currently being widely discussed in relation to publication of clinical trials in medical journals. COIs, authorship, and disclosure in industry-related scientific publications are discussed in a commentary by Laurence Hirsch [6], and are also the subject of an accompanying editorial by William Lanier [7]. Laurence Hirsch argues that disclosure policies vary between journals, and that their implementation is asymptomatic and biased. William Lanier makes the point that high-quality industry-sponsored research benefits journals, patients, and clinicians, and that industry benefits by being able to publish in credible journals. Therefore, authors and industry should seek out medical journals that have high publication standards that are applied equally to all parties.

Moher and colleagues [8] have developed a financial conflicts of interest (fCOI) checklist. The checklist contains four sections (administrative, study, personal financial, and author information) that are divided into six modules. It is intended to be completed by an investigator for an individual study, with different modules being completed

at different transition points over the course of the study. The checklist takes less than 20 minutes to complete. The authors invite comments and suggestions to improve the checklist.

More on ghostwriting

In an editorial in *PLoS Medicine* [9], the *PLoS Medicine* editors discuss ghostwriting in medical publications, and question the effectiveness of current policies for eliminating ghostwriting. The World Association of Medical Writers policy on ghostwriting is available at http://www.wame.org/resources/policies#ghost, and the European Medical Writers Association guidelines are available at http://www.emwa.org. ICMJE criteria for authorship in biomedical publications are available at http://www.icmje.org/#author.

The results of the *Pharma Marketing News* online 'Pharma-Sponsored Medical Article Ghost Writing Survey' have been published [10]. From 21–31 August 2009 there were 83 responses to the survey, which asked participants to what degree they agreed or disagreed with nine statements regarding issues surrounding ghostwriting and medical publications sponsored by drug companies. Selective comments from respondents are also discussed. The survey has now been re-opened for further comments (see http://bit.ly/2BYB2b).

Finally, Woolley and colleagues [11] have quantified how involved declared medical writers and the pharmaceutical industry have been in publications retracted for misconduct. A PubMed search was used to identify publications retracted for either misconduct or mistake. 463 retractions were reviewed, and 213 (46%) of these were misconduct retractions. Statistical analysis showed that the involvement of declared medical writers or the pharmaceutical industry in misconduct retractions was very low or non-existent. In comparison with mistake retractions, misconduct retractions were significantly involved with absence of a declared medical writer or pharmaceutical industry involvement (odds ratio {OR}, [95% confidence interval {CI}]; 3.74 [1.66, 8.40]), single authorship (OR [95% CI]; 2.04 [1.01, 4.12]), first author having at least one other retraction (OR [95% CI]; 2.05 [1.35, 3.11]), or an affiliation with a low/middle-income country (OR [95% CI]; 2.34 [1.18, 4.63]).

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MedComms Networking

MedComms Networking is an informal initiative, led by Peter Llewellyn of NetworkPharma. It encourages networking and dialogue amongst individuals working in and around specialist medical education, medical communications and medical publishing businesses primarily based in the UK. For more information please visit http://www.MedCommsNetworking.co.uk and please help spread the word.

A medical writer's blog

I have recently joined the Web 2.0 age and started writing a blog. Much of it will, I hope, be of interest to medical writers. I have so far blogged on a range of topics, including medical writing ethics, the way some medical stories are reported in the popular media (i.e. very badly), my experiences as a member of a research ethics committee, and some of the trials and tribulations of running a medical writing company. The blog is open for anyone to leave comments (there's no need to register), and it would be splendid to hear what other medical writers think of my musings. So please do come and read what I have to say, and tell me what you think, at http://dianthus.co.uk/dianthus-medical-blog.