

Editorial Policies for Clinical Trials and the Continued Changes in Medical Journalism

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The importance of randomized clinical trials is acknowledged by most physicians, professional organizations, and federal agencies. Clinical trials influence practice and are at the pinnacle of the evidence pyramid, either alone or as part of meta-analyses. However, many threats to the validity and scientific integrity of clinical trials can occur in their design, implementation, analysis, and reporting. Examples include modifications in primary and secondary outcomes or analytic approaches after the trial begins or after initial examination of data; manipulation and falsification of data; incomplete reporting of all available trial outcomes and selective reporting of important serious adverse events; and failure to report the results of trials with negative or unfavorable results.

Current best practice to ensure scientific validity in the design and conduct of clinical trials includes prespecification of the trial protocol, an associated statistical analytic plan, careful documentation of any changes in the protocol, and oversight by institutional review boards (IRBs) and data and safety monitoring committees. Best practice for reporting of clinical trials includes emphasis on the primary outcomes; distinguishing between secondary outcomes and post hoc analyses; careful attention to statistical issues, such as maintaining fidelity to the original statistical analysis plan and appropriate treatment of missing data; complete reporting of adverse events; and balanced, objective interpretation of the study findings.

Many changes have occurred in the reporting of clinical trials over the last decade and have served to address many of these threats to validity. Trial registration, mandated since 2005 by the International Committee of Medical Journal Editors,¹ has reduced the likelihood of suppressed trials and has helped improve the fidelity of clinical trial analysis and reporting, such as reducing selective or altered reporting of major outcomes. The CONSORT statement was released in 1996,² revised in 2001³ and 2010,⁴ with extensions that focus on non-inferiority trials in 2006⁵ and 2012,⁶ cluster randomized trials (2012),⁷ and patient-reported outcomes (2013),⁸ and has been widely adopted by most medical journals as a mechanism to improve and standardize reporting of clinical trials.

In addition, more widespread availability and detailed review of trial protocols and statistical analytic plans has helped clarify the intention of investigators at the time studies are designed, and along with gradual increases in the amount of data sharing, have facilitated the ability of reviewers and journal editors to assess the scientific validity of studies. Following the approval of new drugs, the US Food and Drug Administration

(FDA), which requires submission of complete data from trials of products under consideration for approval, is making trial data more readily and easily accessible (Erica Jefferson, deputy director of the FDA office of public affairs, written communication, May 16, 2013). Likewise, the European Medicines Agency announced plans to provide access to all clinical trial data sets submitted by industry in applications for new product registration, and some pharmaceutical companies have announced plans to make data available to appropriate groups upon request. Collectively these changes have led to a substantial improvement in reporting, assessment, and transparency of clinical trials.

In 2005 *JAMA* adopted and modified a number of policies regarding conflicts of interest, financial aspects of research, and the role of sponsors in funded research.⁹ These policies—which included a requirement for independent statistical analysis by an academic biostatistician for industry-sponsored and industry-analyzed studies—were developed during a time when several high-profile trials had evidence of problems with data integrity, inappropriately conducted statistical analyses, and incomplete reporting of major findings. Over time some of these policies have been modified and strengthened¹⁰ but have been perceived by some in academia and industry as creating barriers to publication of important trial results. Moreover, over the past 2 years, our experience has been that the conduct of additional analyses by independent academic biostatisticians generally did not result in meaningful changes in the study results.

Accordingly, we are once again modifying one of the policies. *JAMA* will evaluate and consider for publication clinical trials that are analyzed by statisticians employed by or contracted by the study sponsor, without requiring independent statistical analysis by an academic biostatistician. Advances over the past decade in standards of clinical trial reporting, enhanced understanding of the threats to validity of clinical research, increasing data transparency, and our experience support the change in policy.

We will continue to require submission of a copy of the trial protocol and statistical analytic plan with all amendments, and we will require trials to be appropriately registered in an approved publicly accessible database. Any changes to the protocol, analysis plan, or trial registration that occurred after the trial began need to be explained in detail and justified with appropriate documentation. *JAMA* editorial review will continue to include close examination of these documents for discrepancies with the submitted manuscript and diligent evaluation and scrutiny of all scien-

tific reports.¹¹ If concerns are raised in the process of editorial evaluation, we reserve the right to request the entire data set from authors to conduct our own statistical analysis. As stated in an editorial earlier this year,¹² we prefer that investigators at academic institutions rather than employees of the study sponsor be responsible for preparing the manuscripts and analyzing data from clinical trials. Indeed, that is the practice at many leading research institutions. As with all manuscripts, the first priority in decisions about publication will always be the integrity of the research.

Many important changes in medical journalism have occurred over the past decade. The presentation of information

has moved from print to web to mobile, with audio and video media. The open access movement continues to expand. Alternative metrics to measure the impact of articles and journals and other new initiatives—such as COUNTER, ALLTrials, FundRef, ORCID, data crawlers, and plagiarism detection software—and increasing concerns about both intellectual and financial conflict of interest and bias are other important issues that journal editors must consider. *JAMA* will continue to discuss and debate these new ideas and communicate with our readers about changes we make in major editorial policies. Journals must evolve as the science that is the heart and soul of journals changes.

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