Quality of Registration for Clinical Trials Published in Emergency Medicine Journals

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Study objective: In 2005, the International Committee of Medical Journal Editors established clinical trial registration as a requirement for articles submitted to member journals, with the goal of improving the transparency of clinical research. The objective of this study is to characterize the registration of clinical trials published in emergency medicine journals.

Methods: Randomized trials involving human subjects and published between June 1, 2008, and May 31, 2011 in the 5 emergency medicine journals with the highest impact factors were included. We assessed the clarity of registered primary outcomes, timing of registration relative to patient enrollment, and consistency between registered and published outcomes.

Results: Of the 123 trials included, registry entries were identified for 57 (46%). Of the 57 registered studies, 45 (79%) were registered after the initiation of subject enrollment, 9 (16%) had registered outcomes that were unclear, and 26 (46%) had discrepancies between registered and published outcomes. Only 5 studies were registered before patient enrollment with a clear primary outcome that was consistent with the published primary outcome. *Annals of Emergency Medicine* was the only journal in which the majority of trials were registered.

Conclusion: Current compliance with clinical trial registration guidelines is poor among trials published in emergency medicine journals. [Ann Emerg Med. 2012;60:458-464.]

Please see page 459 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background and Importance

Randomized trials are the most reliable form of establishing causality and as such are a critical source of knowledge in medical research. Clinical trial registries are publicly accessible, searchable databases that make information about clinical trials available to the scientific community and general public. Registries include a description of the study population, the intervention, and the measured primary outcome.

Trial registration is intended to improve research transparency through 2 mechanisms. First, registration allows subsequent investigators to assess for publication bias by providing information about all studies conducted on a particular topic regardless of whether the results were published. Thus, although studies with statistically significant results are more likely than those with nonsignificant results to be published,[1-3] this form of publication bias can be overcome by using registries to learn about studies that have been conducted but not published. Second, by maintaining a public record of the intended primary outcome, registries help to combat the common problem of authors changing the primary outcome to report an outcome for which there is a statistically significant difference.[4-7] These mechanisms for improving clinical trial transparency are effective only if trials are registered, if registration takes place before subject enrollment, and if the published primary outcome is the same as the registered primary outcome.

In an attempt to encourage trial registration, the International Committee of Medical Journal Editors (ICMJE) has required since July 2005 that all prospective interventional trials involving human participants be registered before any participants have been enrolled to be considered for publication in ICMJE member journals.[8] These journals include major general medical journals such as the *New England Journal of Medicine*, the *Journal of the American Medical Association*, and the *Lancet*. Other journals were encouraged to enact similar policies, and the requirement for registration of clinical trials before beginning

Editor's Capsule Summary

What is already known on this topic

Trial registration is an important mechanism for controlling publication bias and ensuring that researchers follow their research protocol and disclose deviations when they do not.

What question this study addressed

Whether clinical trials published in 5 high-impact emergency medicine journals are compliant with trial registration policies.

What this study adds to our knowledge

Only 46% of 123 trials were registered, 75% in this journal, 30% in the other 4. Only 5 trials were registered properly and completely, 4 in this journal.

How this is relevant to clinical practice

This will not change clinical practice but demonstrates that researchers and journals in emergency medicine need to improve their quality control about trial registration.

subject enrollment has been incorporated into both the ICMJE's "Uniform Requirements for Manuscripts Submitted to Biomedical Journals"[9] and the Consolidated Standards of Reporting Trials (CONSORT) statement guiding the reporting of randomized controlled trials.[10] These recommendations have been endorsed by the highest-impact-factor emergency medicine journals, including *Annals of Emergency Medicine*,[11] *Academic Emergency Medicine*,[12] *Resuscitation*,[13] *Injury*,[14] and the *American Journal of Emergency Medicine*.[15] Trial registration was further emphasized in 2007 with the signing of the United States Food and Drug Administration Amendment Act.[16] This legislation, which pertains to most trials performed in the United States involving drugs and devices subject to Food and Drug Administration regulation, including phase 2 to 4 clinical trials, made trial registration a requirement by federal law.[17]

Goals of This Investigation

Despite the important rationale for trial registration and the presence of clearly stated guidelines, there is evidence that both author compliance with study registration standards and editorial enforcement of these policies remain poor across a wide range of general and specialty-specific medical journals.[18-20] Compliance with recommendations about trial registration among studies published in emergency medicine journals has not been described. The goal of this investigation was to assess the quality of registration of randomized clinical trials published in emergency medicine journals.

MATERIALS AND METHODS

Study Design

This was a retrospective observational study of randomized controlled trials indexed to PubMed between June 1, 2008, and May 31, 2011. We included articles published in *Annals of Emergency Medicine, Resuscitation*, *Academic Emergency Medicine*, *Injury*, and the *American Journal of Emergency Medicine*. These journals were selected because they are classified by Journal Citation Reports as having the 5 highest impact factors among emergency medicine journals.[21] Observational studies, meta-analyses, commentaries, and studies with no full-text article available were excluded. Articles describing secondary analyses of data published elsewhere were also excluded, as were animal, in vitro, and simulation-based studies.

A structured MEDLINE through PubMed search for articles from the selected journals classified as "randomized controlled trials" was performed with the assistance of a medical librarian. We also searched these 5 journals for the unrestricted PubMed search term "random*." Abstracts were reviewed for each of the articles identified by this search. Full texts of articles were reviewed by one of the study authors (C.W.J.) for all abstracts that appeared to be potentially eligible for the study. Trials that met inclusion criteria after a review of the complete article were included for analysis.

A single investigator (C.W.J.) extracted data from each included article by using a standardized form. The investigator was blinded to all registry data until article abstraction was completed. Data collected from each article included the primary outcome or outcomes, secondary outcomes, date of journal submission, dates of subject enrollment, sample size, funding source, and author disclosures of any conflicts of interest. In articles with no explicitly stated primary outcome, the outcome used when calculating power was considered to be the primary outcome. For studies with multiple primary outcomes, each explicitly labeled primary outcome was recorded. A primary outcome was not recorded if one was not clearly identified in the published article and no power calculation was reported.

Registry entries were identified and data extraction was performed by 2 research assistants. Before conducting registry searches, each research assistant completed an educational module consisting of background information related to study registration, a list of the major trial registry Web sites, instructions for searching registry databases and matching registry entries with their corresponding articles, and instructions for abstracting data from registry entries. Research assistants were also required to successfully complete data extractions on 2 nonstudy registry entries before conducting registry searches for the study.

The first step in the search for a registration entry was to search the article for a trial registration number. If no trial registration number was provided, Clinicaltrials.gov, the World Health Organization International Clinical Trials Registry