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Availability of results from clinical research: Failing policy efforts

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Abstract *Objectives:* Trial registration has a great potential to increase research transparency and public access to research results. This study examined the availability of results either in journal publications or in the trial registry from all studies registered at ClinicalTrials.gov.

Methods: All 137,612 records from ClinicalTrials.gov in December 2012 were merged with all 19,158 PubMed records containing registration numbers in the indexing field or in the abstracts. A multivariate analysis was conducted to examine the association between the availability of the results with study and participant characteristics available in registration records.

Results: Fewer than 10% of the registered studies and 15% of the registered and completed studies had published results. The highest publication rate of 22.4% was for randomized trials completed between 2005 (starting year for structured indexing in PubMed of study registration) and 2010. For 86% of overall and 78% of completed registered studies, no results were available in ClinicalTrials.gov or in journal publications. Studies funded by industry vs. other funding sources and drug studies vs. all studies of other interventions were published less often after adjustment for study type, subject characteristics, or posting of results in ClinicalTrials.gov.

Conclusion: Existing policy does not ensure availability of results from clinical research. International policy revisions should charge principal investigators with ensuring that the approved protocols and posted data elements are aligned and that results are available from all conducted studies.

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1. Introduction

Clinical research aims to inform clinical and policy decision-making by providing valid evidence for treatment benefits and harms [1—4]. However, when conclusions about treatment benefits and harms are based on incomplete evidence, biased decisions and ineffective health care can result [5]. Bias in the publication of studies that show impressive results can exaggerate the benefits of examined treatments [6—10].

Several policy initiatives have tried to improve transparency and ensure wider availability of results from clinical research. The Food and Drug Administration Modernization Act of 1997 required that the NIH create a trial registry — ClinicalTrials.gov — for drug efficacy studies approved with Investigational New Drug applications. In 2000, the National Library of Medicine at the National Institutes of Health launched ClinicalTrials.gov and opened it to the public via the Internet, and Congress mandated the registration of all clinical trials of pharmacological treatments for serious or life-threatening diseases at the ClinicalTrials.gov online database [11—14]. Then in 2005, the International Committee of Medical Journal Editors (ICMJE) and the World Association of Medical Editors made registration a condition of publication for all clinical studies [15]. Finally, the International Clinical Trials Registry Platform (ICTRP) was developed to include 13 primary registries which met the requirements of the ICMJE in providing 20 items with ''the minimum amount of trial information that must appear in a register in order for a given trial to be considered fully registered'' (see Supplementary Appendix 1, also available at http://www.who.int/ictrp/network/trds/en/index.html).

Ensuring the public access to the results from clinical studies, the Food and Drug Administration Amendments Act (FDAAA) of 2007 mandated posting of the results from applicable clinical trials (e.g., interventional, non-phase I trials of drugs and devices subject to FDA regulation) on ClinicalTrials.gov within 1 or 2 years of study completion [16].

Nonetheless, publication of the results in journal articles remains voluntary. Less than half of the NIH-funded registered trials are published in a peer-reviewed journal within 30 months of trial completion [17]. Only 29% of completed registered studies involving children and 53% of NIH-funded trials have been published [18].

Previous research used time-consuming manual searchers of the publications in various subsets of registered studies (i.e., by source of funding [17], study participants [18], and specific health conditions) [19]. In contrast, this paper examines result availability from all studies registered with ClinicalTrials.gov to answer the question: *Do existing policies in research registration, publication, and indexing guarantee access to the results?* This study defines ''availability of the results'' as publication in the journals indexed on Medline or posting the results with ClinicalTrials.gov

2. Methods

For this study, ClinicalTrials.gov registration records were linked with Medline publication records by a unique registered study identifier (number of clinical trial or NCT). First, all records of the registered studies with no time restriction were downloaded from ClinicalTrials.gov from February 2000 to December 2012 (Appendix 2). All 20 fields required by the ICMJE were downloaded. The frequency of study types, design, funding, participant characteristics, and posting of the results were analyzed relying on information provided by the investigators in registration records [20]. Accuracy of the data in ClinicalTrials.gov can be confirmed only by comparing the posted data elements with those approved by the institutional review boards, which was beyond the scope of this study. For validation purposes, ambiguous data (e.g., enrollment values of more than 99,999 participants or negative publication time intervals when publications occurred before studies started subject recruitment) were excluded from the validated analyses.

In contrast with the previous research focusing on clinical trials only [21], all registered studies were analyzed irrespective of study design, funding, subject characteristics or market status of the examined treatments assuming that all clinical research evidence is important for decision-making (Appendix 2). The study design was categorized: as randomized trial when the study design field mentioned random allocation of participants into the treatment groups; as non-random studies when investigators did not explicitly mention randomization; and as unknown study design when investigators left this field blank. Interventions were categorized as drug, procedure, radiation, biologics, or behavioral according to the categories in ClinicalTrials.gov. Study findings were categorized into two categories: industry funding category included all studies funded by pharmaceutical or device companies exclusively or in combination with individuals, universities, or community-based orga-