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## TIME TO PUBLICATION AMONG COMPLETED CLINICAL TRIALS

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### To the Editor:

Prior studies have shown that 25% to 50% of clinical trials are never published.<sup>1–4</sup> However, among those published, we know little about the length of time required for publication in the peer-reviewed biomedical literature after study completion. Ioannidis previously demonstrated that a sample of randomized phase 2 and 3 trials conducted between 1986 and 1996 required nearly 2.5 years for publication,<sup>5</sup> while our more recent study of National Institutes of Health (NIH)-funded trials found that average time to publication was almost two years.<sup>4</sup> We sought to determine time to publication for a recent and representative sample of trials published in 2009.

## METHODS

We examined clinical trials published during the 2009 calendar year that were indexed via MEDLINE and linked to a [ClinicalTrials.gov](http://ClinicalTrials.gov) identifier (NCT Number).<sup>6</sup> We excluded articles that were not the first publication reporting on the clinical trial by reviewing article text for citations to and searching MEDLINE for earlier trial publications. We imputed completion dates based on the subject enrollment dates and the longest period of follow-up required for any outcome measure reported in the article. For trials without enrollment dates, we used the completion date provided on [ClinicalTrials.gov](http://ClinicalTrials.gov); this date was not used

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**Conflicts of interest:** Dr. Ross reports that he is a member of a scientific advisory board for FAIR Health, Inc. Dr. Krumholz reports that he chairs a scientific advisory board for UnitedHealthcare. Drs. Zarin and Tse report that they are Director and Program Analyst, respectively, for [ClinicalTrials.gov](http://ClinicalTrials.gov).

**Author contributions:** Drs. Ross, Tse, Zarin, and Krumholz were responsible for the conception and design of this work. Drs. Ross, Lampropulos, Mocanu, and Tse were responsible for acquisition of data. Dr. Ross drafted the manuscript, conducted the statistical analysis, and provided supervision. Dr. Krumholz obtained funding. All authors participated in the analysis and interpretation of the data and critically revised the manuscript for important intellectual content.

uniformly because our prior work demonstrated its unreliability.<sup>3</sup> We determined publication dates using MEDLINE, using on-line publication dates for articles made available ahead of print. Because [ClinicalTrials.gov](http://ClinicalTrials.gov) reports completion dates in month/year format, publication dates were similarly recorded for purposes of calculating time to publication.

We obtained additional information through the National Library of Medicine, using the [ClinicalTrials.gov](http://ClinicalTrials.gov) identifier, including data elements reporting lead sponsor, study design, and condition studied (Online Table). We obtained journal impact factors from Web of Knowledge (Thomson Reuters, New York, NY). We used Kruskal-Wallis tests to compare median times to publication between trial characteristic categories using a type I error rate of 0.003 to account for multiple comparisons (n=16). Statistical analysis was performed using JMP 7.0.1 (SAS Institute, Inc., Cary, NC).

## RESULTS

There were 1336 clinical trials published during the 2009 calendar year, indexed via MEDLINE and linked to a [ClinicalTrials.gov](http://ClinicalTrials.gov) identifier. The majority was funded by non-profit organizations and enrolled more than 100 subjects (Online Table). Nearly half were published in journals with an impact factor less than five.

Median time to publication was 21 months with an interquartile range of 13–32 months (Figure) and modest differences across types of trials (Online Table). For instance, median time to publication was longer among trials funded by industry when compared with trials funded by government and non-profit organizations (24 versus 20 months;  $p<0.001$ ), but was shorter among trials enrolling 1000 subjects or more when compared with trials enrolling 100 subjects or fewer and trials enrolling between 100 and 1000 subjects (18, 20 and 23 months, respectively;  $p<0.001$ ) and was shorter among trials published in journals with an impact factor greater than 10 when compared with trials published in journals with an impact factor less than 10 (17 versus 23 months;  $p<0.001$ ).

## DISCUSSION

We found, on average, nearly two years passed between completion and publication of clinical trials, across all trial funders. Moreover, given our study was necessarily limited to examining time to publication among completed trials that were eventually published, this estimate is conservative. First, we studied trials registered in and linked to [ClinicalTrials.gov](http://ClinicalTrials.gov), a select group of studies. Because of policies in place as of 2005, many may have been registered to ensure compliance with International Committee of Medical Journal Editors requirements for publication<sup>7</sup> and thus more likely to publish in a timely manner. Second, we only studied trials that were published (and indexed via MEDLINE and linked to [ClinicalTrials.gov](http://ClinicalTrials.gov) identifiers). Between 50% and 70% of studies registered in [ClinicalTrials.gov](http://ClinicalTrials.gov) are eventually published many years after trial completion;<sup>3,4</sup> 30% to 50% are never published.

Differences across trial types were generally modest and indicate that timely dissemination of research needs to be uniformly prioritized to enhance science. Many steps must be successfully taken between trial completion and publication, including data management, statistical analysis, and writing, along with processes out of investigators' control, such as peer review. The substantial variation in publication time, from months to years, suggests that there may be opportunities to improve the speed and efficiency with which investigators publish completed studies.

We cannot rule out that study findings may have been disseminated through means other than publication, including scientific meeting presentations. However, with the exception of public results reporting, these alternative dissemination strategies lead to limited public awareness of the research. Given the time required to publish results from these clinical trials, our findings support current federal initiatives requiring results reporting of clinical studies within 12 months of trial completion<sup>8</sup> to ensure the timely dissemination of clinical science.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

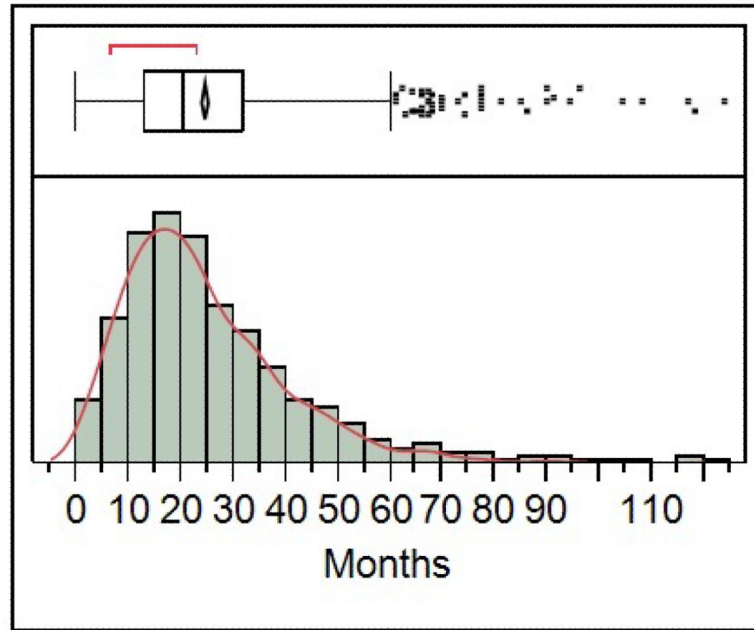
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**Figure.** Time to publication after completion among clinical trials registered in [ClinicalTrials.gov](http://ClinicalTrials.gov) and published in the biomedical literature (cited in MEDLINE).