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Journal of Clinical Epidemiology ■ (2017) ■

Journal of Clinical Epidemiology

REVIEW ARTICLE

Favorable and publicly funded studies are more likely to be published: a systematic review and meta-analysis

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Accepted 16 August 2017; Published online xxxx

Abstract

Objectives: The aim of this study was to identify and quantify the characteristics of studies associated with the likelihood of publication.

Study Design and Setting: We searched for manuscripts that tracked cohorts of clinical studies (''cohorts'') that from launch to publication. We explored the association of study characteristics with the probability of publication via traditional meta-analyses and meta-regression using random effects models.

Results: The literature review identified 85 cohorts of studies that met our inclusion criteria. The probability of publication was significantly higher for studies whose characteristics were favorable (odds ratio [OR] = 2.04; 95% confidence interval [CI]: 1.62, 2.57) or statistically significant (OR = 2.07; 95% CI: 1.52, 2.81), had a multicenter design (OR = 1.32; 95% CI: 1.16, 1.45), and were of later regulatory phase (3/4 vs. 1/2, OR = 1.34; 95% CI: 1.14, 1.49). Industry funding was modestly associated with lower (OR = 0.81; 95% CI: 0.67, 0.99) probability of publication. An exploratory analysis of effect modification revealed that the effect of the study characteristic ''favorable results'' on likelihood for publication was stronger for industry-funded studies.

Conclusion: The study characteristics of favorable and significant results were associated with greater probability of publication.

Keywords: Publication bias; Meta-regression; Meta-analysis; Meta-epidemiology; Result favorability; Statistical significance

1. Introduction

Publication bias represents a threat to the central tenet of evidence-based medicine: that systematic review of published evidence can create an accurate estimate of the true safety and efficacy of an intervention. In fact, many studies go unpublished, and those studies that do go unpublished are likely systematically different from those that are published [1−3]. The problem is widespread in medicine: only half of studies monitored by Institutional Review Boards (IRBs) are widely disseminated once results are available [4−10], and nearly 60% of all trials submitted to the US Food and Drug Administration for marketing approval never reach full publication [11]. Less than complete publication of all studies might be explained as representing a random sampling of all studies conducted, were it not for the fact that those studies that have positive, significant, or novel results are much more likely to be published than studies with negative, null, or replicated results [1−3]. This has the effect of creating a sample of studies that may overstate the effectiveness and safety of many interventions.

This phenomenon is compounded when the available trials are compiled in a systematic review and meta-analysis. The need for access to complete clinical trial data for systematic reviews is such that the National Academy of Medicine has recently published its report titled, ''Sharing Clinical Trial Data.'' As the academy explained ''Clinical trials are essential to determining the safety and efficacy of new health treatments, but limited data sharing prevents maximum utilization of knowledge gained.'' In short, the current system fails to provide an adequate return on the investments of trial participants, investigators, and sponsors.'' [12].

Conflict of interest: All authors declare that they have no conflict of interests.

Funding: This work was supported by unrestricted predoctoral grants from the PhRMA Foundation and the American Foundation for Pharmaceutical Education.

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http://dx.doi.org/10.1016/j.jclinepi.2017.08.004

What is new?

Key findings

- The probability of publication was significantly higher for studies whose results were favorable or statistically significant, had a multicenter design, and were of later regulatory phase.
- Industry funding was modestly associated with lower probability of publication.
- Overall rate of publication was widely variable based on how cohorts of studies were identified and tracked.

What this adds to what was known?

- An exploratory analysis of effect modification revealed that the effect of the study characteristic ''favorable results'' on likelihood for publication was stronger for industry-funded studies.

What is the implication and what should change now?

- Given that publication bias still remains problematic, development of new methods to incentivize publication should be developed and evaluated.

Failure to publish has strong implications for researchers, clinicians, and patients. We know that publication is strongly correlated with the study treatment's effect size, direction and significance [1−3], as well as sponsorship [13]. To the extent that we can predict the likelihood that a systematic review will be biased, we can adjust for this misdirection [14−17].

To better understand these relationships, we performed a systematic review of manuscripts that followed cohorts of studies from one of five stated prepublication milestones. A previous review [2] has attempted a similar objective, but it is over 8 years old and does not include many of the most recent investigations on this topic. Additionally, previous reviews have only evaluated the effect of one study characteristic at a time [18,19]. While this form of analysis is helpful, it presents a limited picture. To address these shortcomings, we have conducted an updated and comprehensive review that includes seven study characteristics that may influence publication.

2. Material and methods

This systematic review targeted published manuscripts that report on cohorts of studies that estimate the proportion of included studies published by a specified time point and identified study characteristics of the studies in each cohort associated with publication in a peer-reviewed journal. The unit of analysis was a clinical study. Manuscripts were eligible for inclusion if they assessed a cohort of studies systematically identified and tracked using one of five prepublication milestones (tracking methods) and then tracked these studies forward to publication (considered as a binary outcome rather than time to publication) in a peer-reviewed journal. All manuscripts included in our review included both published and unpublished studies in the cohorts they reported on.

As a study is planned and moves into execution and ultimately analysis, it creates numerous records that can be identified and tracked over time. For our analysis, we defined five methods of prepublication study tracking, herein after referred to as ''tracking method'': funding record, ethics committee approval, clinical trial registration, abstract presentation at a conference, and submission to a regulatory authority (Fig. 1). Before a trial begins to recruit patients it is funded, the organization providing the funding (manufacturer, government agency, or nonprofit funding organization) will be aware of the progress of the trial and track its progress to results, even when it goes unpublished. Studies tracked using this method can be combined in a cohort of studies. After receiving funding, trial investigators receive initial approval and oversight from an IRB or ethics committee. The IRB will have a thorough record of the study that allows for assessment of eventual publication. A third source for identifying and tracking cohorts of studies is registries such as Clinicaltrials.gov which, as a consequence of having been made mandatory in recent years, has records on a large number of studies, although the amount of information reported may be limited [20,21]. The fourth source of identification and tracking is abstracts presented at conferences. These abstracts provide partial and sometimes interim results limited to a certain scientific area. Finally, there are submissions for new products to regulatory agencies such as the US Food and Drug Administration or the European Medicines Agency. Consistent with the work of others [18]. our method for categorization of study tracking used these five methods, and we subgrouped studies by these five methods to determine if these methods of identification and tracking influenced the proportion of studies in each cohort that were published.

While publication bias can be defined in many ways [22]. for the purposes of this study, we used the binary outcome of publication in a peer-reviewed journal. We did not consider gray literature publication as a means of dissemination as these reports are often less accessible, more difficult to extract, and not used in most systematic reviews. To be considered for quantitative pooling, each identified manuscript was required to follow a cohort of studies from inception to publication. Each manuscript was only included if it reported study characteristics (predictor variables) for both the published and unpublished studies. The seven study characteristics included in our analysis as independent variables were: result favorability (defined as in previous studies as a positive result for the experimental arm, with or without statistical