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Citation bias favoring statistically significant studies was present in medical research

Anne-Sophie Jannot[a,*], Thomas Agoritsas[a,b], Angèle Gayet-Ageron[a], Thomas V. Perneger[a]

[a]CRC & Division of Clinical Epidemiology, Department of Health and Community Medicine, University of Geneva and University Hospitals of Geneva, Rue Gabrielle Perret-Gentil 6, 1211 GENEVE 14, Switzerland

[b]Division of General Internal Medicine, University Hospitals of Geneva, Geneva, Switzerland

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Abstract

Objective: Statistically significant studies may be cited more than negative studies on the same topic. We aimed to assess here whether such citation bias is present across the medical literature.

Study Design and Setting: We conducted a cohort study of the association between statistical significance and citations. We selected all therapeutic intervention studies included in meta-analyses published between January and March 2010 in the Cochrane database, and retrieved citation counts of all individual studies using ISI Web of Knowledge. The association between the statistical significance of each study and the number of citations it received between 2008 and 2010 was assessed in mixed Poisson models.

Results: We identified 89 research questions addressed in 458 eligible articles. Significant studies were cited twice as often as nonsignificant studies (multiplicative effect of significance: 2.14, 95% confidence interval: 1.38−3.33). This association was partly because of the higher impact factor of journals where significant studies are published (adjusted multiplicative effect of significance: 1.14, 95% confidence interval: 0.87−1.51).

Conclusion: A citation bias favoring significant results occurs in medical research. As a consequence, treatments may seem more effective to the readers of medical literature than they really are.

Keywords: Systematic bias; Medical literature analysis and retrieval system; Regression analysis; Journal impact factor; Meta-analysis; Publication bias

1. Introduction

Citation counts are sometimes used to judge the quality and societal impact of medical research. However, study attributes other than scientific merit drive citations [1]. For instance, positive or statistically significant findings may be cited more often than negative or nonsignificant studies on the same topic. This phenomenon, which we call ‘‘citation bias,’’ may distort the perception of available scientific evidence among the users of scientific literature. Citation bias is less extreme than but analogous to publication bias [2], which occurs when the chance for a study to be published is increased if its outcome is statistically significant. As an illustration, Emerson et al. [3] showed that a fabricated manuscript with a significant outcome was more likely to be recommended for publication than an otherwise identical manuscript reporting no difference between treatments. In the same vein, it is possible that of two published articles, identical except for the statistical significance of the main finding, the ‘‘significant’’ study would be cited more often than the nonsignificant study. Such a citation bias, if it exists, would influence the construction of scientific knowledge [4].

To date, citation bias favoring more significant studies has only been shown for some medical topics [5−8]. Whether citation bias is a more general phenomenon remains unclear. In this study, we used a broad set of clinical questions reviewed in the *Cochrane Database of Systematic Reviews* to evaluate if statistical significance was associated with citation counts.

2. Materials and methods

2.1. Data

We conducted a cohort study by retrieving all citations of relevant publications pooled in meta-analyses on a broad set of medical questions assessing the efficacy of various interventions.

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* Corresponding author. Tel.: +41 22 372 90 38; fax: +41 22 372 90 35.
E-mail address: anne-sophie.jannot@hcuge.ch (A.-S. Jannot).

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What is new?

Key findings

- Citation bias favoring significant results exists across medical fields. This bias is mediated by the impact factor of the journal where the article is published, as statistically significant findings are more likely published in journals with higher impact factors.

What this adds to what was known?

- To date, citation bias has been reported for specific topics. Our study shows that it is a general phenomenon in medical research.

What is the implication and what should change now?

- Looking for references in articles to explore the literature on a specific question should be avoided owing to a possible citation bias, as treatments may thus seem more effective to the readers of medical literature than they really are.

In November 2011, we extracted all reviews on therapeutic interventions from the *Cochrane Database of Systematic Reviews* published in January, February, and March 2010. We chose Cochrane reviews because of their well-established quality and methodological rigor [9]. To assess the current citation bias, we focused on a recent period and restricted the search to reviews with the record status of ''new review'' or ''new search.'' In each of the selected reviews, we used the first forest plot appearing in the publication that met the following criteria: at least two retrievable publications in ISI Web of Knowledge published before 2008, a binary outcome, availability of the numbers of patients in the two treatment groups (experimental and control or placebo), and the numbers of patients experiencing the outcome in each treatment group. If such a forest plot was not available, then the review was excluded.

To allow sufficient opportunity for citation, we selected only articles published until end of 2007 in each forest plot. For each article, we extracted the denominators and numerators for risks (numbers of events and the numbers of patients in each study arm). The outcome for which these numbers were extracted was the one analyzed in the forest plot and not necessarily the primary outcome of the publication. We also retrieved whether the pooled effect of the meta-analysis was statistically significant or not, assessed here as a proxy of the true effect of the intervention. We extracted the delay in years since publication. Finally, we obtained the journal's impact factor from the ISI Web of Knowledge 2010 Journal Citation Reports. When the journal was no longer published, we used the last available impact factor in ISI. We categorized meta-analyses in seven clinical fields: cancer, cardiovascular disease, infectious disease, neurology, mother and child, psychiatry, and other.

The dependent variable was the number of citations accrued by each article from 2008 to 2010 according to the ISI Web of Knowledge. We subtracted the Cochrane Review citation used to identify the relevant publications from the total number of citations, if found among the citing articles.

The main predictor was the statistical significance of each individual study defined as the *P*-value of the χ^2 (or exact test when necessary), testing the contrast between the two study arms for the outcome retrieved by the meta-analysis and dichotomized at the threshold of 0.05.

The theoretical framework we used to guide the analysis is represented in Fig. 1: the citation count depends directly on the journal's impact factor; the publication year; the research question and the medical area; and through different pathways (both indirect and direct) on sample size, the odds-ratio that characterizes the association between treatment and outcome, and its statistical significance. One example of such an indirect pathway is the relationship between the significance of the study and the citation count: a significant result may be published in a more prominent journal, which in itself may lead to more citations.

2.2. Statistical analysis

As citations are count data, we used a mixed Poisson regression model assessing the predictors (fixed effects) associated with citation counts. The clinical question (i.e., the corresponding meta-analysis used to identify relevant publications) was taken as a random effect (random intercept) in the model.

The independent variables (fixed effects) in the model were the statistical significance of the result, the delay since the study publication, the logarithm of the study sample size, the logarithm of the journal's impact factor, the clinical field, the logarithm of the odds ratio of the association between the study outcome and the study arm, and the significance of the pooled effect for the meta-analysis (significant vs. nonsignificant). We used logarithmic transformations where indicated to improve the fit of linear models based on examination of scatter plots against the logarithm of citation counts. Regression coefficients were estimated using penalized quasi likelihood to take into account overdispersion (function glmmPQL, package MASS, R 2.13.2; R Development Core Team, Vienna, Austria).

We first performed mixed-model univariate analyses with each independent variable. Regression coefficients for the different clinical fields were standardized by subtracting the mean coefficient of all medical fields. We then performed a multivariate analysis with all variables that had been shown to be significantly associated with statistical significance in univariate analyses.

To test whether the impact factor mediated the effect of the significance of the study on citation count (Fig. 1), we