Journal of Clinical Epidemiology 68 (2015) 87–93

Journal of Clinical Epidemiology

Citations alone were enough to predict favorable conclusions in reviews of neuraminidase inhibitors

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Accepted 12 September 2014; Published online 22 October 2014

Abstract

Objectives: To examine the use of supervised machine learning to identify biases in evidence selection and determine if citation information can predict favorable conclusions in reviews about neuraminidase inhibitors.

Study Design and Setting: Reviews of neuraminidase inhibitors published during January 2005 to May 2013 were identified by searching PubMed. In a blinded evaluation, the reviews were classified as favorable if investigators agreed that they supported the use of neuraminidase inhibitors for prophylaxis or treatment of influenza. Reference lists were used to identify all unique citations to primary articles. Three classification methods were tested for their ability to predict favorable conclusions using only citation information.

Results: Citations to 4,574 articles were identified in 152 reviews of neuraminidase inhibitors, and 93 (61%) of these reviews were graded as favorable. Primary articles describing drug resistance were among the citations that were underrepresented in favorable reviews. The most accurate classifier predicted favorable conclusions with 96.2% accuracy, using citations to only 24 of 4,574 articles.

Conclusion: Favorable conclusions in reviews about neuraminidase inhibitors can be predicted using only information about the articles they cite. The approach highlights how evidence exclusion shapes conclusions in reviews and provides a method to evaluate citation practices in a corpus of reviews.

Keywords: Neuraminidase inhibitors; Bibliometrics; Evidence synthesis; Reviews as a topic; Citation analysis; Supervised machine learning

1. Introduction

Variation in the inclusion of evidence can lead to flawed or unreliable conclusions in reviews and other peer-reviewed articles [1,2]. The resulting disagreement across reviews or guidelines may erode trust in evidence-based medicine and reduce the quality of clinical decision making. There has been considerable disagreement, for example, across reviews about the clinical use of neuraminidase inhibitors for the prophylaxis and treatment of influenza: some reviewers strongly recommend the use of these drugs [3–5], whereas others conclude that they provide only modest benefit and question the ability to draw any meaningful conclusions from the limited available evidence [6,7].

For oseltamivir, the most commonly prescribed neuraminidase inhibitor, the evidence supporting its use has been mired in controversy [8]. Certain data used to support claims made by the company producing the drug were not released to the public [8], and concerns have been raised about the conflicts of interest held by members of the World Health Organization advisory panel that recommended stockpiling the drug in case of a pandemic [9].

Differences in the way evidence is selected for inclusion in literature reviews that could affect the conclusions are described as reference or inclusion bias [2,10]. These biases come in many forms, including the preferential inclusion of studies with positive outcomes and statistically significant results [11–13], from high-impact journals or authors with financial conflicts of interest [14–17], or disproportionate levels of self-citation [18,19]. Citation network analyses have been used to examine the incidence and potential

Funding: This study was supported by National Health and Medical Research Council Program Grant 568612 and Project Grant 1045065. The sponsors had no role in the study.

Conflict of interest: None.

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http://dx.doi.org/10.1016/j.jclinepi.2014.09.014
0895-4356/

What is new?

- It is possible to accurately predict favorable conclusions in reviews about neuraminidase inhibitors using only information about what is included in their reference lists.
- Citation network analyses have been used to identify biases in reviews by comparing the selection of evidence across a corpus of reviews, but little is known about the effects of citation biases on review conclusions and recommendations.
- Machine learning classification methods applied across a corpus of reviews may be used to identify primary studies that are overrepresented or underrepresented in reviews with favorable conclusions.
- Extensions to the approach presented here may provide new methods for automatically evaluating the entire evidence base of interventions for which systemic citation bias is suspected.

implications of differences in evidence selection [1,20–24]. However, little is known about how the biases in evidence selection may affect the conclusions of reviews.

Supervised machine learning has been used to examine analogous problems. A Bayesian classifier was found to be capable of predicting conclusions that individual decision makers reached, based solely on the articles to which they were exposed [25]. Another example using four types of classifiers showed that machine learning could predict which articles should be screened for inclusion in systematic reviews [26].

We sought to measure the association between the primary articles cited in reviews of neuraminidase inhibitors and the likelihood of a conclusion favoring the use of the drugs for influenza, evaluating classifiers trained to predict conclusions based only on the reference lists of the reviews. The classifiers were used to identify the citations that best distinguish favorable reviews from all others, revealing how the inclusion of specific primary evidence may have influenced conclusions.

2. Methods

2.1. Study data

Reviews were identified in PubMed by searching all English-language articles published since January 2005 for keywords "influenza" and at least one of "neuraminidase inhibitors," "oseltamivir," "zanamivir," "peramivir," or "laninamivir," or their synonyms, in the title, abstract, or keywords and then restricting the set to include only articles for which the publication type was a review. The final search was performed in May 2013 and identified 211 articles. Because there were no further restrictions on the form of the reviews, the set included narrative reviews that did not include explicit search criteria or the reporting of reasons for excluding some published articles. Of the 211 that were identified, 59 were excluded by consensus (Diana Arachi, Joel Hudgins, and F.T.B.) because they did not review the clinical use of neuraminidase inhibitors (these included reviews of drug development, manufacture, or drugs from other classes), producing a set of 152 reviews about the clinical use of neuraminidase inhibitors for influenza.

Two reviewers independently examined the full text of each review (blinded to the authors and affiliations, citations, journal and formatting, acknowledgments, and conflicts of interest) and rated each review as favorable, unfavorable, or neutral to the use of neuraminidase inhibitors for the prophylaxis or treatment of influenza. The two reviewers were guided by answering questions about the presentation of evidence in relation to efficacy, safety, and resistance and the presence of recommendations for clinical use. When the two evaluators independently agreed that a review was favorable, the review was classified as favorable—all other reviews were assigned to the alternative group. Among the 152 reviews, 93 (61%) were deemed to be favorable and 59 (39%) were assigned to the alternate group.

All primary articles cited by the reviews were retrieved and verified manually. Publication dates were also recorded for each article. There were 4,574 unique articles cited in the reviews. The total number of citations from the set of reviews to these articles was 10,086; 3,112 were cited once, 582 were cited twice, and 880 were cited three times or more. The most commonly cited article was cited 46 times—in 30% of the reviews (Fig. 1). Before applying machine learning to train and test classifiers, we examined the distribution of citations to identify which primary articles were overrepresented or underrepresented among favorable reviews. To do this, while accounting for publication dates,

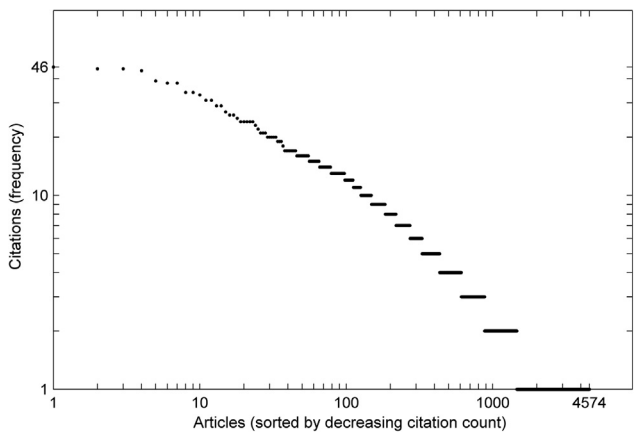

Fig. 1. The distribution of citations to each of 4,574 unique articles from the 152 reviews on the clinical use of neuraminidase inhibitors.