

ORIGINAL ARTICLE

Inadequate diversity of information resources searched in US-affiliated systematic reviews and meta-analyses: 2005–2016

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Abstract

Objective: Systematic reviews and meta-analyses (SRMAs) rely upon comprehensive searches into diverse resources that catalog primary studies. However, since what constitutes a comprehensive search is unclear, we examined trends in databases searched from 2005–2016, surrounding the publication of search guidelines in 2013, and associations between resources searched and evidence of publication bias in SRMAs involving human subjects.

Study Design: To ensure comparability of included SRMAs over the 12 years in the face of a near 100-fold increase of international SRMAs (mainly genetic studies from China) during this period, we focused on USA-affiliated SRMAs, manually reviewing 100 randomly selected SRMAs from those published in each year. After excluding articles (mainly for inadequate detail or out-of-scope methods), we identified factors associated with the databases searched, used network analysis to see which resources were simultaneously searched, and used logistic regression to link information sources searched with a lower chance of finding publication bias.

Results: Among 817 SRMA articles studied, the common resources used were Medline (95%), EMBASE (44%), and Cochrane (41%). Methods journal SRMAs were most likely to use registries and grey literature resources. We found substantial co-searching of resources with only published materials, and not complemented by searches of registries and the grey literature. The 2013 guideline did not substantially increase searching of registries and grey literature resources to retrieve primary studies for the SRMAs. When used to augment Medline, Scopus (in all SRMAs) and ClinicalTrials.gov (in SRMAs with safety outcomes) were negatively associated with publication bias.

Conclusions: Even SRMAs that search multiple sources tend to search similar resources. Our study supports searching Scopus and CTG in addition to Medline to reduce the chance of publication bias. © 2018 Published by Elsevier Inc.

Keywords: Systematic review; Meta-analysis; Evidence synthesis; Trial registries; Grey literature; Literature databases; Publication bias

1. Introduction

An increasing number of bibliographic databases cataloging biomedical literature have made the job of meta-analysis researchers to search for primary studies less arduous [1]. Bolstered by this ease of electronic literature searches, however, although publications of systematic reviews and meta-analyses (SRMAs) have increased exponentially over the last decade, there has not been comparable improvement in methodological rigor or reporting standards [2]. Meanwhile, studies linking favorable meta-analysis outcomes with financial conflicts of interest of authors have highlighted the susceptibility of SRMAs to manipulation [3–5]. Amidst these findings, while some

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What is new?**Key findings**

- In evidence synthesis for systematic reviews and meta-analyses (SRMAs), only journals focusing on research methods, and not general medical journals, are associated with searching diverse information resources.
- Promulgation of search guidelines have not substantially increased search of diverse resources.
- When searched alongside Medline, Scopus (in all SRMAs) and ClinicalTrials.gov (in SRMAs with safety outcomes) were negatively associated with publication bias.

What this adds to what was known?

- While searching multiple resources is widespread, this work finds that most systematic reviews search databases with overlapping coverage, a practice that has not changed in the last decade.
- This work also provides the evidence to justify the use of certain resources in SRMAs by examining the association of various resources with occurrence of publication bias.

What is the implication and what should change now?

- This work shows that mere guidelines may not be sufficient to increase searching of diverse, non-overlapping resources in SRMAs. All journals publishing SRMAs, and not just the ones focusing on research methods, should encourage searching of resources that are likely to find unpublished research.
- Scopus (in all SRMAs) and ClinicalTrials.gov (in SRMAs with safety outcomes) should be searched during evidence synthesis.

have questioned the position of SRMAs as the highest level of evidence [6], others have called for ensuring greater objectivity and reproducibility in producing them [7]. A way to ensure the objectivity of SRMA results is to perform comprehensive searches into resources mining primary literature [8]. However, what constitutes a comprehensive search remains open to interpretation [9] and potential manipulation.

The purpose of an SRMA is to summarize all scientifically generated evidence on a topic of interest. A systematic search for data from a diverse body of evidence is fundamental to serve that purpose. In addition to extracting data from published studies, it is important to search

unpublished studies (also known as gray literature) as research shows that the latter have smaller treatment effects than published studies [10,11] and that inclusion of unpublished results can change conclusions of meta-analyses [12,13]. Conversely, failure to include unpublished data biases the results toward a positive treatment effect (also known as publication bias) [14,15]. However, publication bias affects even the best SRMAs, as shown by Kicinski and colleagues in a sample of 1,106 Cochrane SRMAs, using a Bayesian hierarchical selection model [16]. Thus, research into the evolving use and relative importance of information resources mining published and unpublished research can improve the scientific rigor of evidence synthesis.

Although including both published and unpublished data is important for validity, in practice, neither is searching the unpublished data easy [17–19] nor are guidelines suggesting resources to be searched for unpublished data consistent among each other [20]. Most popular biomedical search engines mine only published studies, and little consensus exists regarding which resources to look into for unpublished data [9,21]. Among the sources of unpublished studies, trial registries established to mine data from clinical studies have emerged as a rich source of information over the last decade. Registries store information from studies regardless of the success of their outcomes, making them an important source for unpublished research [8]. Clinical trials of drugs, biologics, and devices must be registered in study registries including ClinicalTrials.gov [22]. ClinicalTrials.gov, launched in 2000, is currently the world's largest clinical study registry and contains information from clinical trials of products that are subject to Food and Drug Administration (FDA) regulation [23]. Other trial registries can be accessed through the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), a portal to 16 trial registries managed by various national regulatory bodies [24]. Additional repositories of trial reports can include regulatory body reports (FDA databases), grant databases, and manufacturer web sites [8]. Sources of gray literature that are not clinical trials include conference abstracts, dissertations, book chapters, policy documents, and specialized gray literature databases, among others [19]. Although studies have documented the underuse of registries [2,25–28], factors that may lead to more widespread inclusion of such resources in search strategies have not been studied.

In this study, we tracked the self-reported use of various information resources in SRMAs published between 2005 and 2016 and identified the factors associated with their use. We also examined the information resources simultaneously searched for the SRMAs through the years. In addition, we looked into the effect of best practice guidelines in the use of registries. Finally, we examined the use of information resources that are associated with low publication bias.

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