Most meta-analyses of drug interventions have narrow scopes and many focus on specific agents

Anna-Bettina Haidich[a], Dimitrios Pilalas[b], Despina G. Contopoulos-Ioannidis[c,d], John P.A. Ioannidis[e,f,g,*]

[a]Department of Hygiene and Epidemiology, School of Medicine, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece
[b]Infectious Diseases Division, 1st Department of Internal Medicine, AHEPA University Hospital, School of Medicine, Aristotle University of Thessaloniki, 54636 Thessaloniki, Greece
[c]Division of Infectious Diseases, Department of Pediatrics, Stanford University School of Medicine, Stanford, CA 94305, USA
[d]Health Policy Research, Palo Alto Medical Foundation Research Institute, Palo Alto, CA, USA
[e]Stanford Prevention Research Center, Department of Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA
[f]Department of Health Research and Policy, Stanford University School of Medicine, Stanford, CA 94305, USA
[g]Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, CA 94305, USA

Abstract

Objective: To assess the extent to which meta-analysis publications of drugs and biologics focus on specific named agents or even only a single agent, and identify characteristics associated with such focus.

Study Design and Setting: We evaluated 499 articles with meta-analyses published in 2010 and estimated how many did not cover all the available comparisons of tested interventions for a given condition (not all-inclusive); focused on specific named agent(s), or focused strictly on comparisons of only one specific active agent vs. placebo/no treatment or different doses/schedules.

Results: Of 499 eligible articles, 403 (80.8%) were not all-inclusive, 214 (42.9%) covered only specific named agent(s), and 74 (14.8%) examined only comparisons with one active agent vs. placebo/no treatment or different doses/schedules. Only 39 articles (7.8%) covered all possible indications for the examined agent(s). After adjusting for type of treatment/field, focus on specific named agent(s) was associated with publication in journal venues (odds ratio [OR]: 1.95; 95% confidence interval [CI]: 1.17−3.26) vs. Cochrane, industry sponsoring (OR: 3.94; 95% CI: 1.66−10.66), and individual patient data analyses (OR: 6.59; 95% CI: 2.24−19.39). Individual patient data analyses primarily (29/34) focused on specific named agent(s).

Conclusion: The scope of meta-analysis publications frequently is narrow and shaped to serve particular agents. © 2013 Published by Elsevier Inc.

Keywords: Meta-analysis; Randomized controlled trials; Evidence-based medicine; Bias; Industry; Research agenda

1. Introduction

Meta-analysis has evolved into a popular, influential research design with a substantial impact on the formulation of medical practice and health policy [1−6]. Hundreds of systematic reviews and meta-analyses of clinical trials are published every year. Their quality, updating, potential biases, and correlates of these features have been the subject of several empirical evaluations [7−13]. An important issue that has not received due attention to date is whether these reviews address the whole evidence that is pertinent to the management of the medical conditions of interest, or focus on specific fragments of the evidence. Systematic reviews and meta-analyses may vary a lot in the extent to which they are restrictive or not about their inclusion

What is new?

Key findings
- More than 80% of the meta-analysis publications did not consider all the available comparisons of tested interventions for the condition of interest.

- Almost half of the meta-analysis publications focused only on specific agents, and 15% focused strictly on comparisons that involved only a single agent vs. placebo/no treatment or different doses/schedules of administration, although additional agents were available for the same condition.

- Individual patient data analyses primarily focused on specific agents, and such analyses seemed to be popular for the industry to support.

What this adds to what was known?
- Despite the availability of methods to compile and synthesize evidence on multiple interventions on the same disease, most meta-analyses still have a narrow scope, and many focus inappropriately to a few or even single agent among many available.

What is the implication and what should change now?
- More inclusive systematic reviews and meta-analyses should be encouraged, offering a wider view of the available options.

criteria [14], and about the types of comparisons and settings that they try to cover [15]. For most diseases nowadays, there are multiple interventions that can be considered, and many of them have been tested in randomized controlled trials (RCTs). Systematic reviews and meta-analyses would be most informative, if they can address all the potential options and evaluate their relative advantages and disadvantages, so that the reader can see the wider picture of the evidence. This can be done either by performing meta-analyses on all the diverse available pair-wise comparisons of different interventions and/or settings [16,17] or more formally in multiple treatment comparison (network) meta-analyses [18,19]. On the other hand, some systematic reviewers may have a preference to limit the scope of their reviews on a few specific agents or even a single one. Such a restricted view of the evidence may avoid criticisms of "putting together apples and oranges." However, this practice may be misleading because other options for managing the same condition are not considered.

Here, we aimed to assess the extent to which recent meta-analysis publications of drugs and biologics focus on the limited evidence pertaining to specific named agents or even only to a single agent. We also assessed which characteristics of these published meta-analyses are associated with narrow agendas focused only on specific agents.

2. Methods

2.1. Identification and eligibility of relevant meta-analyses

We aimed to generate a reproducible, systematic sample of meta-analyses of RCTs published in 2010 rather than to perform an exhaustive search to include every single meta-analysis published in that year. The year 2010 was selected as being the most recent when our protocol was designed. A PubMed search with the key terms "meta-analysis [PT] AND 2010 [DP] AND trial*" was performed on November 28, 2010. Two investigators (A.B.H. and D.P.) screened the search results independently to identify publications where any quantitative synthesis of studies was performed. The publication title, abstract, and full text (if deemed necessary) were examined to determine eligibility.

Eligible publications included at least one meta-analysis (quantitative synthesis) of studies among which at least one was an RCT. Eligible interventions included drugs or biologic agents; drug-eluting stents were also considered eligible. Publications where the interventions evaluated were limited to surgery, radiotherapy, blood derivatives, nutritional, behavioral, anesthesia procedures (e.g., epidural vs. general), acupuncture, and herbal medicine were excluded. However, we included publications where any of these types of interventions were covered along with drugs and/or biologic agents. Whenever updates of Cochrane reviews were available during the same year, only the most recent one was included. Only full-article publications were considered eligible. We excluded letters; systematic reviews without meta-analysis; and publications in languages other than English, French, Spanish, German, or Italian.

Our search and eligibility criteria focused on publications that included quantitative syntheses of the data and excluded systematic reviews without meta-analyses. Many meta-analysis publications are conducted without necessarily a full systematic review. For example, some are pooled analyses of a number of trials on the same drug, and we explicitly wanted to capture those because these would be classic examples of narrow-scope publications. Moreover, systematic reviews without meta-analyses are often difficult to separate from nonsystematic reviews, and it is difficult to define what the exact boundaries and eligibility criteria are for the examined trials and comparisons.

2.2. Data extraction

The following information was recorded: first author, publication venue (*Cochrane Database of Systematic Reviews* or journal); type of condition; whether the meta-analysis focus pertained only to efficacy, safety (harms), or both; source of