ELSEVIER

Journal of Clinical Epidemiology 64 (2011) 1168−1177

Journal of Clinical Epidemiology

Finding evidence for comparing medical interventions: AHRQ and the Effective Health Care Program

Rose Relevo*, Howard Balshem

Scientific Resource Center, AHRQ Effective Health Care Program, Oregon Evidence-based Practice Center, Oregon Health and Science University, 3181 SW Sam Jackson Park Road, Mail code: BICC, Portland, OR 97239-3098, USA

Accepted 16 November 2010; Published online 17 June 2011

Abstract

Objective: This article discusses search methodology to identify evidence for comparative effectiveness reviews (CERs) as practiced by the Effective Health Care program.

Study Design and Setting: Review.

Results: Search methods described attempt to overcome the bias inherent in the publication and distribution of clinical evidence. Bibliographic databases and search strategies are discussed with special emphasis on searching for observational studies and harms data. Other techniques described include the use of key articles, citation tracking, hand searching, and personal communications. Strategies for locating gray literature, such as clinical trial protocols and regulatory information, are described. Search reporting and other practical matters are also discussed.

Conclusion: Better reporting and further research on search strategies is needed to develop additional evidence-based recommendations.

Keywords: Comparative effectiveness reviews; Gray literature; Controlled vocabulary; Avoiding bias; Bibliographic databases; Expert searching

1. Introduction

Although, this article both describes and advises on the process of literature searching in support of comparative effectiveness reviews (CERs) for the Effective Health Care program, it does not address searching for previously published systematic reviews, which is discussed in other articles in this series [1,2].

Searches to support systematic reviews often require judgment calls about where to search, how to balance recall and precision, and when the point of diminishing returns has been reached. Searchers with more experience with complex search strategies are better equipped to make these decisions [3]. A number of reviews of the quality of systematic reviews suggest that those reviews that employed a librarian or other professional searcher had better reporting of and more complex search strategies [4−6].

Table 1 describes the various search activities discussed in this paper and identifies who is responsible for performing each of these tasks. As is evident from the table, the Evidence-based Practice Center (EPC) conducting the review is responsible for most of these activities. Because the EPC is involved in the development of the key questions, is familiar with the literature, and consults with experts regarding studies relevant to the topic, the EPC is in the best position to develop the required search strategies. Because gray literature can provide primary documents to verify published results, EPCs should routinely search regulatory data, clinical trial registries, and conference papers and abstracts for all CERs. This has been a centralized activity conducted by the Scientific Resource Center (SRC), but is now an activity conducted by the EPCs. However, one aspect of the search strategy benefits from centralization. Centralizing the request to drug and device manufacturers for data on their products—what we call the Scientific Information Packet (SIP)—ensures that all requests to industry are conducted in the same manner; this also minimizes or eliminates contact between manufacturers and the EPC involved in writing the report.

* Corresponding author. Tel.: +503-220-8262 ×51318; fax: +503-494-4551.

E-mail address: relevo@ohsu.edu (R. Relevo).

0895-4356/$ - see front matter
doi: 10.1016/j.jclinepi.2010.11.022

Table 1. Centralized and disseminated tasks in the AHRQ effective health care program

Activity	Sources	Who does it
Key questions and analytic framework	N/A	Evidence-based practice center
Gray literature search	Clinical trial registries Regulatory information Conference proceedings	Evidence-based practice center
Scientific information packets	Manufacturers of products under review	Scientific resource center
Main literature search	MEDLINE (plus in-process and other un-indexed citations) Cochrane central register of controlled trials	Evidence-based practice center
Specialized database search	Variable (see Appendix B on the journal's Web site at www.elsevier.com)	Evidence-based practice center
Forward citation search	Scopus Web of Science Google Scholar	Evidence-based practice center
Backward citations (reading references)	Results of main literature search	Evidence-based practice center
Hand search	Targeted journals	Evidence-based practice center
Corresponding with researchers	Publication authors	Evidence-based practice center

2. Regulatory and clinical trials searching

In addition to searching for studies that have been formally published (as described below), a comprehensive search will include a search of the gray literature [7,8]. Gray literature is defined as, ''that which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers'' [9]. Gray literature can include abstracts presented at conferences, unpublished trial data, government documents, or manufacturer information. Gray literature is, by definition, not systematically identified, stored, or indexed and therefore it can be difficult to locate.

The primary goal of the gray literature search is to identify and overcome publication and reporting bias [10,11]. Published literature does not always accurately represent trial results. Often, only articles with positive results are published, whereas those with ''null'' or negative results are not; and, even when studies are published, reporting can be biased in many other ways. Systematic reviews and meta-analysis based solely on published literature that report positive results will exaggerate any estimate of effectiveness. McAuley et al. [12] has shown an exaggerated estimate of 12% when gray literature is excluded, and Hopewell et al. [13] found a 9% exaggeration.

The usefulness of the gray literature naturally varies by topic, but it is particularly helpful in areas where there is a little published evidence, where the field or intervention is new or changing [14], when the topic is interdisciplinary [15], and with alternative medicine [16,17].

Despite these reasons to include gray literature, there are also potential problems. From a practical standpoint, gray literature is the least efficient body to search [18] and may not turn up more evidence to evaluate. Even if gray literature is located it may be of low quality or may not contain usable data [19]. Often unpublished studies are (or at least are perceived to be) of lower quality [17,20], although there is limited evidence to support this [13].

Because we have found them to be the most useful for identifying primary documents to compare with published results, the SRC routinely searches the following three types of gray literature for all CERs: regulatory data, clinical trial registries, and conference papers and abstracts.

2.1. Regulatory data

The approval process for new drugs and devices involves submission to the Food and Drug Administration (FDA) of data that may not be published elsewhere. These approval documents—which can be found at Drugs@FDA.gov—may help identify publication bias even when complete methodological details of unpublished trials are not available [21,22]. This information is not available before a drug's approval and may be redacted. When they are available, reviewers can compare results of published and unpublished trials, identify inconsistencies, and often find additional data. In one meta-analysis, investigators found that published trials reported larger estimates for the efficacy of quinine than did FDA documents [23]. Similar discrepancies have been found by Turner et al. [24] for the efficacy of antidepressants.

The SRC identifies for potential inclusion of all available medical and statistical reviews for all drugs under consideration, regardless of indication. This is partly because it is difficult to distinguish specific indications in the database, but also because the actual clinical data within the reviews may cover more than one indication, and harms data are of importance regardless of indication. In addition to searching for regulatory documents from the FDA, the SRC also searches the Health Canada Drug Products Database [25] and the European Medicines Agency's European Public Assessment Reports [26].

2.2. Trial registries

Online trial registries such as ClinicalTrials.gov may include results of completed but unpublished clinical trials.