Meta-analyses: Caveat Lector

Shojania KG, Sampson M, Ansari MT, et al. How quickly do systematic reviews go out of date? A survival analysis. Ann Intern Med 2007;147:224–33.

Study Overview

Objective. To determine the average length of time until a published systematic review requires updating due to important changes in evidence.

Design. Survival analysis of a sample of quantitative systematic reviews published from 1995 to 2005 and indexed in *ACP Journal Club*.

Study selection. Systematic reviews were eligible for inclusion if they (1) evaluated the benefit or harm of a specific drug, class of drug, device, or procedure; (2) were randomized or quasi-randomized controlled trials; and (3) provided a point estimate and confidence interval for ≥ 1 outcome. To identify if there was new evidence that would require updating the systematic review, the study authors conducted systematic searches using electronic databases, including Ovid, PubMed, and Scopus.

Main outcome measures. The presence of a quantitative or qualitative signal for updating a published systematic review. A quantitative signal was defined as a change in statistical significance or a change in effect size of at least 50% when data from 1 or more new trials were combined with data in the systematic review. Qualitative signals included new information (eg, about harms, new therapies, evidence certainty) that could potentially invalidate the previous systematic review or changes in evidence that could significantly impact clinical decision making. Qualitative signals were identified using explicit criteria for comparing language in the initial systematic review with language in subsequent reviews, guidelines, or trials.

Main results. 651 potential systematic reviews were identified, and 100 were selected for review using a quasi-random process. A quantitative signal occurred in 20 of 100 systematic reviews. A qualitative signal occurred in 54 reviews, including 8 that qualified as potentially invalidating results of the original review. Overall, a qualitative or quantitative change occurred in 57% of the reviews (95% confidence interval, 47%–67%). The median length of time between publication and identification of a signal for updating was 5.5 years. A signal for updating occurred within 2 years for 23% of reviews and within 1 year for 15% of reviews. A signal had already occurred at the time of publication in 7% of reviews.

Conclusion. In a sample of high-quality, clinically relevant systematic reviews, signals for updating occur frequently and within a short time after the original review is published.

Commentary

Over the last 2 decades, the role of the meta-analysis has been firmly established [1]. This analytic tool is used to summarize data across similar studies, identify areas where additional studies are needed, and understand heterogeneity between studies. The application of this technique in diverse areas has lead to a proliferation in the number of published meta-analyses. But, with greater use of this technique has come greater misuse [2]. In fact, we may invest too much faith in the potential of meta-analyses to generate conclusive, actionable evidence; we should remember that meta-analyses are a form of observational study—with each identified study as an "observation"—and thus they are susceptible to problems of observational studies, such as selection bias (ie, publication bias). Researchers have begun to note these limitations, hence this Agency for Healthcare Research and Quality–funded study by Shojania et al of the "survival time" of meta-analyses.

This study developed techniques de novo to evaluate the clinical longevity of meta-analyses. The authors used *ACP Journal Club* to identify meta-analyses for inclusion in the study. The journal indexes a tiny fraction of the medical literature, attempting to capture the most clinically important and highest quality data from "core" journals [3]. The meta-analyses included by Shojania et al were quasi-randomly selected from among 651 potential reviews; 325 studies were screened to achieve the requisite sample of 100 with the appropriate characteristics. In effect, the sample chosen by Shojania et al represents the "best of the best" (ie, meta-analyses held to the highest methodologic standards that have been vetted and reviewed not only by a top-tier journal but again by a team of researchers who publish *ACP Journal Club*). Relative to this sample, the larger universe of meta-analyses would consist of reviews with much more variable quality, and therefore this study's generalization to this end suggests even less confidence in the longevity of findings from meta-analyses.

In assessing the results of this study, it is important to note that the authors did not consult clinical experts in the field for each individual review, nor did they definitively determine whether the evidence itself had changed (ie, they

only identified signals suggesting an update was necessary). Despite the aforementioned limitations, the results of the Shojania et al study suggest that meta-analyses may have a relatively short shelf-life. One of 5 meta-analyses examined in this select group had quantitative signals for updating, with a median survival time of 5.5 years. Including qualitative signals for updating, a total of 57% of the meta-analyses required updating. In multiple regression analysis, the authors were not able to identify the characteristics of an individual meta-analysis that predicted the need for updating within the first 2 years from publication. In addition, meta-analyses of cardiovascular topics and those with substantial "activity" in the field (defined as an increase in the total number of patients studied by a factor of > 2) had even shorter median survival times.

Applications for Clinical Practice

This important overview provides us with a better understanding of the fallibility of meta-analyses. As aggregations of "high-quality" and purportedly homogeneous data, meta-analyses have occasionally been given top ranking in the hierarchy of evidence. This study finds that this ranking may not be deserved and does so in a highly selected sample of the "best" and most clinically important systematic reviews. Clinicians should have less faith in a meta-analysis than in a high-quality randomized trial in which the dimensions of methodologic quality are better understood. Researchers should note that the use of systematic reviews over 1 year old may require an updated literature search so as not to miss important studies. And meta-analysts have a rich fodder of older reviews that may require updating.

—Review by JB Jones, MBA (Geisinger Center for Health Research, Danville, PA), and Nirav R. Shah, MD, MPH

References

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