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Meta-analyses of pain studies: What we have learned

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A B S T R A C T

Meta-analysis is a statistical procedure that integrates the results of at least two independent studies. The biggest threats to meta-analysis are publication bias due to missing studies with negative results and low-quality evidence due to methodological limitations imposed by included studies. Tools to improve the quality of meta-analysis have been developed by the Cochrane Collaboration and by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Meta-analyses of trials have demonstrated that pain responses in patients with chronic pain, following treatment, are not normally distributed but have a bimodal distribution with the majority of patients having either very little or very good pain relief. The benefit can be detected within 2–4 weeks following drug administration. Further, the efficacy of drug and physical treatments is hampered by high placebo response rates, with modest average benefits with active treatments over placebo in both parallel and crossover design trials.

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Introduction

Currently, most clinicians find that the amount of information in the medical literature is currently overwhelming. New studies are constantly being published, and clinicians are finding it nearly impossible to stay current, even in their own area of specialty [1]. Increasing numbers of review articles are therefore published that summarize the literature on a given topic to keep researchers and clinicians up to date. A narrative review using both informal and subjective methods to collect and interpret the evidence is often written by experts in the field. By contrast, a systematic review (SR) is a critical assessment and evaluation of all research studies that address a particular clinical issue using specific criteria that provide a validated and organized method of locating, assembling, and evaluating the body of literature on a particular topic. An SR typically includes a description of the findings of the collection of research studies, and it may also include a quantitative pooling of data, called a meta-analysis [2].

High-quality evidence-based guidelines are based on SRs with meta-analyses conducted for the topics of the guideline, for example, the Canadian [3,4] and German [4–11] guidelines on opioid therapy in chronic noncancer pain (CNCP). Meta-analyses are increasingly being used to provide evidence of safety and efficacy for new drugs by drug regulatory agencies [12].

The number of SRs with meta-analysis in the area of pain research increased substantially by seven- to eightfold in the last decade. A PubMed search of the word "meta-analysis and chronic pain" in the title yielded 22 articles in the year 2000 and 154 articles in 2014 (see Fig. 1).

Meta-analysis is a powerful but also controversial tool because several conditions are critical to a sound meta-analysis, and small violations of those conditions can lead to misleading results and conclusions [1]. Pain therapists and researchers, therefore, should be acquainted with the methods and pitfalls of SRs with meta-analysis.

The aims of the article are as follows: (a) to introduce the basic concepts of meta-analysis, (b) to discuss its caveats, and (c) to highlight lessons learned from recent meta-analyses of randomized controlled trials (RCTs) in chronic pain conditions for study investigators and clinicians.

The potential of meta-analyses

Meta-analysis is a statistical procedure that integrates the results of several (at least two) independent studies considered to be "combinable." Meta-analysis should be viewed as an observational study of the evidence [13]. Meta-analyses can be performed with RCTs as well as with observational studies. The main objectives of a meta-analysis are as follows [1,14]:

- Summarizing and integrating results from a number of individual studies
- Analyzing differences in the results among studies
- Overcoming small sample sizes of individual studies to detect effects of interest

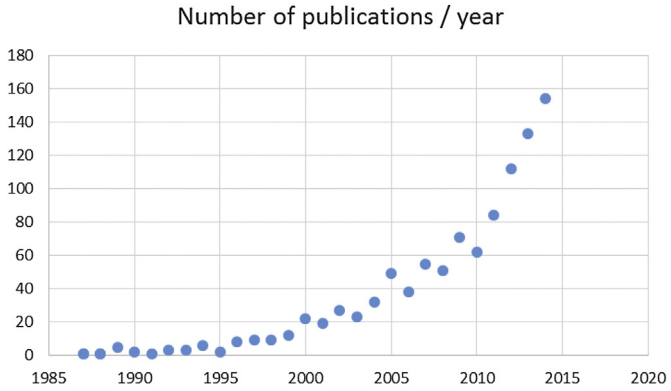

Fig. 1. Hits for "Meta-analysis and chronic pain" in PubMed from 1987 to 2014.