META-ANALYSIS: INDISPENSABLE TOOL OR WEAPON OF MASS CONFUSION?

Meta-analysis is a mathematical methodology developed in education science and psychology research in the 1970s and applied in medicine since the 1980s. The aim is to combine data from different studies on a given topic so as to produce a quantified synthesis. Meta-analyses are often very helpful in orthopedics as it is not easy for us to put together large cohorts with a minimum follow-up that is long enough to be convincing (implants, surgery in young mobile patients, etc.). A meta-analysis means collating several separate studies so as to increase the number of patients and thus provide a more precise answer to the question under study. This requires as exhaustive a search of publications on the topic of interest as possible, whether they are referenced or not: it is up to the author to compile the “list of listed references” from the selected articles, including books, congress abstracts or whatever. The studies included in the meta-analysis should apply closely related experimental conditions but may have different or indeed contradictory results. A meta-analysis is not the same thing as a systematic analysis of the literature, which reviews articles following strict selection criteria but is not necessarily seeking to be exhaustive and does not enable treatment effects (in therapeutic trials) to be quantified, as the data are not aggregated and weighted by any mathematical method. Meta-analysis thus represents a distinct progress over mere literature reviews.

In theory, a meta-analysis should be able to resolve a doubt or worry as to the effectiveness of such and such a treatment or diagnostic test when results prove contradictory, and should seek to account for the discrepancies. The method may also serve to show that the present state of knowledge does not allow any conclusion to be drawn and that further research is called for. Adding together and weighting different cohorts enables subgroup analysis and thus screening for patient groups able to obtain maximal benefit from a given treatment, or on the contrary for whom it should be contraindicated.

Meta-analysis is thus genuine research based on systematic weighted study of the included cohorts or groups, rather than a simple agglomeration of cases. As with any other clinical study, it must adhere to a rigorous methodology, as it is not exempt from possible bias such as incomplete exhaustiveness in study retrieval, publication bias (negative results being less frequently published), poor quality in the selected studies or studies lacking data on the parameters under analysis.

To clarify meta-analysis methodology, a group of clinicians, methodologists and statisticians drew up a structured diagram of meta-analysis construction and validation, with a precise and rigorous check-list that was updated in 2009 and named Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) [1]. The Cochrane collaboration also produced a strict methodology, the Cochrane Handbook for Systematic Reviews of Interventions, with computerized tools for systematic data extraction (GRADEpro and GRADE profiler) and statistical analysis in line with good practice guidelines (Review Manager software: RevMan Version 5.1; The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark). The present references [2] and [3] also contain important elements for statistical analysis, and reference [4] contains a critique of quality scoring as a means of selecting studies for meta-analysis.

As the technique grows ever more popular, the number of articles and repetitions of meta-analyses on identical topics can be seen to be increasing, sometimes with divergent findings. This causes real problems, as it is often very hard, from the information to be found in the article, to analyze and understand the reasons for such divergence. Some biases are easy to detect, such a selecting or not selecting certain articles (omission, differences in selection criteria laid out in the Methods sections, or just good old-fashioned bias), but usually the reasons are more subtle and it requires the precious help of a statistician or epidemiologist to trace to origin of the discordance (which usually comes down to lack of exhaustiveness and the variable quality and heterogeneity of the included studies, or, as the saying goes, “garbage in, garbage out’’). This is true for all large-circulation journals, and has incited the Journal of Bone and Joint Surgery
and Clinical Orthopaedics, to name but two, to draw up rules that any meta-analysis being submitted must adhere to.

Apart from the methodological principles mentioned above, it would therefore seem useful to point out a few basics.

(1) The “danger” of meta-analysis lies not so much in the tool itself as the undue confidence the final results may inspire. We need to learn to interpret meta-analyses in the light of their limitations, as with any clinical trial. It must always be borne in mind that the qualitative description of the included studies and the limitations of the literature highlighted by the meta-analysis (heterogeneity, publication bias, etc.) may well be much more important than the final result itself. We need to change our way of critical reading!

(2) One needs to be very careful in writing up a meta-analysis: although very often read only by practitioners or researchers, it may also fall into the hands of a public health or political decision-maker. Depending on its rigor and the viewpoint taken, a given meta-analysis may be more or less informative, more or less debatable, and thus go beyond the strict field of evidence-based medicine.

(3) Before submitting a meta-analysis, like any clinical study, one single question has to be raised: is the question that is being addressed one of everyday practice and are the results representative of the patients actually encountered in real life? i.e., are the results of clinical interest?

(4) To avoid the above-mentioned sources of bias, a meta-analysis must imperatively be seen as a multidisciplinary undertaking, involving clinicians from the field in question and methodologists (including statisticians and/or epidemiologists). Whereas an original clinical study necessarily involves clinical specialists in its field, who are the only ones to have access to the relevant population, a meta-analysis may in principle be conducted by a physician, a methodologist or a decision-maker without extensive knowledge of the pathology concerned or of the ever more complex techniques of surgery; “I may not practice or have any experience, but I can talk about this and tell you what you should be doing” is only just an exaggeration. Such an attitude, taking no account of the specificities of surgical practice, can only lead to mistaken interpretations and conclusions.

Finally, should we not on the one hand begin our research by analyzing the various meta-analyses and draw up a research protocol for future studies so as to be able to provide a definite answer to a given question and avoid adding yet another study to all those already available, increasing the risk of confusion and disagreement, and on the other hand limit the number of patients included in our trials and research?

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


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