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Why the Meta Analysis is Original and How does it Provide the Best Evidence?

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Abstract

Meta-analyses play a fundamental role in evidence-based healthcare. Compared to other study designs (such as randomized controlled trials or cohort studies), the meta-analysis comes in at the top of the 'levels of evidence' pyramid in evidence-based healthcare. This is a pyramid which enables us to weigh up the different levels of evidence available to us. Meta-analysis contributes to many aspects of different research, for example: 1) Meta analysis is not a method as the combination of the studies like as review study. It produces new knowledge instead of summarizing what is already known, 2) Meta-analysis is considered as an original article. Because it covers the original statistical methods. Therefore the results of Meta-analysis also are original, 3) It is the best evidence method, 4) It develops new scientific tools, 5) It provides guidelines for solving problems by using big sample size, 6) Combines the results of studies that are reverse and also puts the end point for these contrasting results, 7) Increases the statistical power by combining different studies, 8) It leads a higher statistical power and more robust point estimate than is possible from the measure derived from any individual study, 9) It produces a new weighted average of the included study results, 10) It is limited to the quality of studies that are included, 11) To provide a more precise and new estimate of the overall treatment effects.
There are two main models in meta-analysis: the fixed effects model and the random effects model. To determine which model to use, whether the model's prerequisites were met by the characteristics of the research studies included in the meta-analysis were considered. Because the source of heterogeneity is often unexplained therefore if the source of heterogeneity can not be explained, in this case it is recommended to use a random effects model. At the result, if there is no heterogeneity, the fixed effects model is used. If there is heterogeneity, random effects model should be preferred.
As a result, we can say that meta-analysis will be encountered in research for future and it is a significant original method with many benefits.

Key words: Meta analysis, Best evidence, Original study

Introduction

Meta-analysis contributes to many aspects of different research, for example:

1. Meta-analysis is not a method as the combination of the studies like as review study. It produces new knowledge instead of summar izing what is already known.

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2. Meta-analysis is considered as an original article. Because it covers the original statistical methods. Therefore the results of Meta-analysis also are original.
3. It is the best evidence method.
4. It develops new scientific tools.
5. It provides guidelines for solving problems by using big sample size.
6. Combines the results of studies that are reverse and also puts the end point for these contrasting results.
7. Increases the statistical power by combining different studies.
8. It leads a higher statistical power and more robust point estimate than is possible from the measure derived from any individual study.
9. It produces a new weighted average of the included study results
10. It is limited to the quality of studies that are included
11. To provide a more precise new estimate of the overall treatment effects

Meta-analyses play a fundamental role in evidence-based healthcare. Compared to other study designs (such as randomized controlled trials or cohort studies), the meta-analysis comes in at the top of the 'levels of evidence' pyramid in evidence-based healthcare. This is a pyramid which enables us to weigh up the different levels of evidence available to us. As we go up the pyramid, each level of evidence is less subject to bias than the level below it. Outcomes from a meta-analysis may include a more precise estimate of the effect of treatment or risk factor for disease, or other outcomes, than any individual study contributing to the pooled analysis. Therefore, meta-analyses can be seen as the pinnacle of healthcare evidence (1).

Important medical questions are typically studied more than once, often by different research teams in different locations. In many instances, the results of these multiple small studies of an issue are diverse and conflicting, which makes the clinical decision-making difficult. The need to arrive at decisions affecting clinical practise fostered the momentum toward "evidence-based medicine (2).

Evidence-based clinical practice guidelines represent statements developed to improve the quality of care, patient access, treatment outcomes, appropriateness of care, efficiency and effectiveness and achieve cost containment by improving the cost benefit ratio (3).

Literature Search

As is the case of a clinical trial, a systematic review must be carefully designed in order to avoid the possibility of biases and errors that may affect the results. It is therefore necessary to define the aims of the analysis and the rules and methods that are necessary to achieve them. In order to search effectively, it is crucial to choose the correct key words that will precisely identify the topic of our investigation (4).

The conclusions of a meta-analysis depend strongly on the quality of the studies identified to estimate the pooled effect. The internal validity may be affected by errors and incorrect evaluations during all the phases of a clinical trial (selection, performance, attrition, detection bias), so

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the assessment of the risk of study bias is a central step when one carries out a meta-analysis. The quality of randomized clinical trials should be evaluated with regard to randomization, adequate blinding and explanation for dropouts and withdrawals, which addresses the issues of both internal validity (minimization of bias) and external validity (ability to generalize results) (5-7).

As with the planning of any study, the study design of a meta-analysis determines the validity of its results. The Quality of Reporting of Meta-analyses (QUOROM) statement was published to provide guidelines for conducting meta-analyses, with the goal of improving the quality of published meta-analyses of randomized trials. A checklist assessing the quality of a meta-analysis has also been developed by the QUOROM group and is available online (8).

"**Quality" gives us an estimate of the likelihood that the results are a valid estimate of the truth.** An important characteristic of meta-analysis is that the results are determined both by the management of the meta-analysis process and by the features of studies included. The scientific rigor of potential primary studies varies considerably and the common objection to meta-analytic summaries is that they combine results from studies of different quality. Randomized controlled trials provide the best evidence of the efficacy of medical intervention, even if the validity of their results depends on the correct manner in which to conduct the study and on the control of bias. In fact, the interpretation and application of the results depends on the proper conduct of the randomization process, the description of the patients accepted as well as of the patients not accepted in the trial, the experimental and supplementary treatment regimens, those who withdrew, the blinding method used (where appropriate), testing of how well the rules have been followed and the use of proper statistical analysis (9, 10).

Meta-analyses can only be as valid as the studies selected for the systematic review. When high-quality studies are available and the methodology of the meta-analysis is sound, the conclusions of the review are likely to be reliable. On the contrary, when the methodological quality of the available studies is insufficient, then conclusions drawn from quantitative combining of these data might also be inadequate (11).

The biggest potential source of type I error (increase of false positive results) in meta-analysis is probably **publication bias**. This occurs when, in clinical literature, statistically significant "positive" results have either a better chance of being published, are published earlier or in journals with higher impact factors, and are more likely to be cited by others (7).

Statistical Methods for Meta-Analysis

Since systematic reviews summarize current knowledge, they might help identify areas lacking adequate evidence, and thereby produce promising new research questions. Meta-analyses often measure heterogeneity between studies, for instance, Cochran's Q, a statistic

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that is based on the χ^2 test, or the I^2 statistic (expressed as a value between 0% and 100%) that tells us what proportion of the total variation across studies is beyond chance. These estimates can have large uncertainty, which must be taken into account when interpreting evidence (12-14).

Meta-analysis may be used to estimate an overall effect across a number of similar studies. A number of statistical techniques are currently used to combine individual study results. The simplest of these is based on a fixed effects model, which assumes the true effect is the same for all studies. A random effect model, however, allows the true effect to vary across studies, with the mean true effect the parameter of interest (15).

There are two main models in meta-analysis: the fixed effects model and the random effects model. To determine which model to use, whether the model's prerequisites were met by the characteristics of the research studies included in the meta-analysis were considered. The fixed effects model covers the assumption that the research is the same in terms of functionality, and the objective is to estimate the effect size for only one population defined. If it is believed that the research is not equal in terms of functionality, and if generalizations through the estimated effect size are to be made for greater populations, then the model that should be used is the random effects model (16).

Because the source of heterogeneity is often unexplained therefore if the source of heterogeneity can not be explained, in this case it is recommended to use a random effects model. At the result, if there is no heterogeneity, the fixed effects model is used. If there is heterogeneity, random effects model should be preferred.

Most meta-analyses within the field of medical research have been conducted on randomized controlled trials (17).

Basu A. has recommended the following nine steps of meta analysis for a successful outcomes (18):

1.Frame a question (based on a theory)
2. Run a search (on Pubmed/Medline, Google Scholar, other sources)
3. Read the abstract and title of the individual papers.
4. Abstract information from the selected set of final articles.
5. Determine the quality of the information in these articles. This is done using a judgment of their internal validity but also using the GRADE criteria
6. Determine the extent to which these articles are heterogeneous
7. Estimate the summary effect size in the form of Odds Ratio and using both fixed and random effects models and construct a forest plot
8. Determine the extent to which these articles have publication bias and run a funnel plot
9. Conduct subgroup analyses and meta regression to test if there are subsets of research that capture the summary effects

Meta analysis can be very useful decision-making tools for healthcare professionals. They objectively summarize large amounts of information, identifying

gaps in medical research, and identifying benefcial or harmful interventions which will be useful for clinicians, researchers, and even for public and policymakers.

Moreover, standards by which to conduct and report meta-analyses of observational studies have been published to improve the quality of reporting (19,20).

Conclusion

This research review's purpose is to help the reader understand different aspects on the using meta analysis and make clarity to understand whether that is original study or not.

The conduct of a meta-analysis requires a team, which should include both statisticians and knowledgeable medical experts. Whilst the statisticians equipped with the technical knowledge, the medical expert has an important role to play in such activities as identifying the trials, defining the eligibility criteria for trials to be included, defining potential sources of heterogeneity and interpreting the results (21).

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