CE

Interpreting and Using Meta-Analysis in Clinical Practice

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Systematic reviews, which can include a meta-analysis, are considered the gold standard for determination of best practice. Meta-analysis combines the results from many primary studies to identify patterns among the individual study results and then assesses the overall effectiveness of a specific healthcare intervention. The purpose of this article was to describe the process of performing a meta-analysis, discuss advantages and disadvantages of meta-analyses, and interpret the results of a meta-analysis from current research relevant to orthopaedic nursing practice.

In many healthcare situations, it is common to find several primary studies that have attempted to answer similar questions, yet the differing populations and settings, and contradictory findings, make an overall understanding of the results difficult to apply in clinical practice. Meta-analysis, the statistical technique used in systematic review, provides a solution to this dilemma. A systematic review synthesizes a relevant body of research to "make clear what is known and not known about the potential benefits and harms of alternative drugs, devices, and other healthcare services, and combines the results from many primary studies, usually randomized controlled trials (RCT)" (Eden, Levit, Berg, & Morton, 2010). In this way, the overall effectiveness of a specific healthcare intervention can be determined. The appeal of meta-analysis is that it combines all available research on one topic into a larger study with many participants, increasing the power of the findings. By pooling the results from smaller studies into a larger study, a meta-analysis provides a precise estimate of the outcome of the intervention. A meta-analysis can be used as a guide to answer the question: "Does what we are doing make a difference to X?" even if "X" has been measured across a range of different populations and settings. By statistically combining study results, a common treatment effect of one intervention compared with another (usually the standard of care or a control intervention) and the magnitude of that treatment effect can be calculated.

Meta-analysis provides the foundation for evidence-based practice as its results can be used to determine a best practice recommendation or to address controversy in particular interventions. For example, Yang, Li, He, Wang, and Xu (2012) reviewed the results of 12 randomized controlled trials on minimally invasive total hip arthroplasty (MITHA) to determine the efficacy of this procedure given the potential for risk of postsurgical complications compared with those of the traditional method. Using the data from 12 studies, a meta-analysis was conducted indicating that there were no significant differences in either of the groups for complications (dislocations, nerve injury, infection, deep vein thrombosis, proximal femoral fracture) or revision rate ($P > .05$). It was concluded that posterior MITHA seems to be a safe surgical procedure, without increased risk of postoperative complication rates despite a limited visualization of the surgical field.

The Process of a Meta-Analysis

Meta-analysis is an essential component of a systematic review or a comparative effectiveness review. As such, a meta-analysis uses a similar rigorous methodology as is required of experimental research studies (DeCoster, 2009). Like any other research process, a number of steps are required (see Table 1). These steps include the formation of a research question, searching the literature, appraising the quality of primary studies, extracting data, calculating effect sizes, analyzing data, drawing conclusions, and reporting results (Holly, Salmond, & Saimbert, 2012; Polit & Beck, 2012).

The process of combining the results of primary studies increases the statistical power of detecting a true relationship between an intervention and a control and provides results that are more objective than those provided by a narrative review. Many primary studies are conducted on small samples and their results do not show statistical significance for the effectiveness of the intervention. For example, in Yang et al. (2012), the total sample size for the meta-analysis was 1044 patients. However, the range in the 12 primary studies

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TABLE 1. STEPS IN A META-ANALYSIS

1. Formulate a question
2. Search the literature using key words
3. Selection of studies (using inclusion and exclusion criteria)

   Based on quality appraisal criteria

   Include unpublished studies to avoid publication bias
4. Decide which dependent variables or summary measures will be extracted. For instance,

   Differences (discrete data)

   Means (continuous data)

   Use a data extraction tool to extract all data
5. Select a model for data analysis

   Fixed effect model

   The fixed effect model provides a weighted average of the study estimates. Larger studies get larger weights than smaller studies and if the studies within the meta-analysis are dominated by a very large study, it receives essentially all the weight and smaller studies are ignored. This model should be used when the intent is to generalize only to the review population.

   Random effects model

   A common model used to synthesize heterogeneous research is the random effects model of meta-analysis. This model uses the confidence interval (a measure of preciseness) to determine the weight each study is given. This model should be used when the intent is to generalize to a larger population.
6. Interpret results and draw conclusions

   Results of a meta-analysis are graphically displayed in a Forest Plot

   The conclusions drawn from a meta-analysis can be used as best practice recommendations, if appropriate

was 52–455 patients. By combining study results into a meta-analysis, a larger, more powerful sample was realized and the effect size calculated was more credible.

A meta-analysis can be undertaken to answer clinical practice questions from either a narrow focus or a broad focus (see Table 2). Questions from a narrow focus look at comparing two interventions using a common outcome to determine the overall effect of the new intervention on a specific population, for example, mortality, fall rates, or surgical site infection. The Yang et al. (2012) study is an example of a narrow focus as their outcome of interest was complications following MITHA. However, a review can also answer broader questions than those in individual studies. Questions with a broad focus could look at numerous interventions or treatments for a common condition to identify the best intervention; this method would likely include multiple meta-analyses using subgroups and combining similar interventions together. Broad questions could also explore diverse interventions that use a common outcome measure to answer the question of whether a type of intervention works. While a meta-analysis from a broad perspective can seek to determine an overall class effect of an intervention, this is done at the expense of precision to generalize the results to a broader population (Naylor, 1988). For example, Fransen and

TABLE 2. EXAMPLE OF A NARROW AND BROAD FOCUS IN SYSTEMATIC REVIEWS

Focus	Objective	Example
Narrow	To compare the minimally invasive total hip arthroplasty with conventional or traditional total hip arthroplasty with respect to complications and postoperative results.	Yang, B., Li, H., He, X., Wang, G., & Xu, S. (2012). Minimally invasive surgical approaches and traditional total hip arthroplasty: A meta-analysis of radiological and complications outcomes. *PLoS ONE, 7*(5), e37947.
Broad	To determine whether land-based therapeutic exercise is beneficial for people with knee osteoarthritis in terms of reducing joint pain or improved physical function	Fransen, M., & McConnell, S. (2008). Exercise for osteoarthritis of the knee. *The Cochrane Database of Systematic Reviews, 4*, CD004376.

McConnell (2008) examined the effects of solid surface exercise interventions designed to reduce pain and improve physical function in patients with osteoarthritis. The exercise interventions varied among the included studies and included aerobic exercise programs, walking programs, muscle strengthening programs, and tai chi classes. Programs were also administered in varying formats including individual attention, group classes, or self-administered at home and over varying periods of time. The authors performed an overall meta-analysis as well as subgroup analyses and concluded that solid surface exercise interventions had at least short-term benefits.

Advantages of a Meta-Analysis

Synthesized data from meta-analyses are usually more beneficial for clinicians than the results of a narrative review. Narrative reviews use vague criteria and subjective decisions on the part of the reviewer as to how individual study findings are weighted when integrating results and drawing conclusion. Different reviewers could draw different conclusions from the same evidence. In a meta-analysis, decisions are transparent and the statistical analysis used creates an objective measure of integrated quantitative evidence, which can then be repeated and verified.

When discussing studies in a narrative review, it may be difficult to compare the effects of studies that use varying metrics to measure a similar outcome. On the contrary, meta-analysis converts the results of primary studies into a common metric: the effect size, so that different measures from primary studies can be compared against each other, therefore, providing greater meaning to the conclusions. A meta-analysis can assist clinicians in determining whether an intervention works or not.

Meta-analyses can increase the external validity or the ability to generalize conclusions. Primary studies that have high internal validity, where the outcome is attributed to the intervention delivered, may lack in external validity. Studies selected for inclusion in a meta-analysis undergo a rigorous appraisal process to ensure that there are minimal threats to the internal validity. Combining primary studies of varying sample sizes and levels of significance increases the variation in the overall sample, allowing the results of the meta-analysis to be generalized to a wider population (Holly et al., 2012).

Disadvantages of a Meta-Analysis

The main criticism about meta-analyses is that authors attempt to combine "apples and oranges" (Polit & Beck, 2012, p. 655). The decision on which study results should and should not be combined is left to the subjective judgment of the authors. The main assumption when combining the results of primary studies is that the studies are homogeneous in terms of populations, interventions, controls, and outcomes. Although there are inherently differences between primary studies that address a common clinical question, those differences should not be so vast that combining their results produces meaningless conclusions. However, the questions asked by a systematic review, and answered through meta-analysis, are often broader in nature than those addressed in individual studies. Combining studies of various *fruit* may contribute valuable information to answer the question at hand (Borenstein, Hedges, Higgins, & Rothstein, 2009). It is inherent in the nature of a meta-analysis to allow the reviewer to formally investigate these differences through subgroup analysis.

Meta-analyses are criticized as losing the qualitative distinctions between individual studies (Holly et al., 2012). These may be more readily apparent in a narrative review. A meta-analysis, however, does not discount these qualitative distinctions, but instead codes them as moderating variables allowing for their influences to be empirically tested (DeCoster, 2009).

Another criticism of meta-analyses occurs when a reviewer attempts to combine studies of varying effects. If there were wide variances in the effect sizes among primary studies, for example, half the studies favoring the intervention group and half the studies favoring the control group, combing the results in meta-analysis would not be appropriate as the combined effect size would be misleading (Polit & Beck, 2012). Assessing for these variations, called heterogeneity, between primary studies is an important step in conducting a meta-analysis. In this case where heterogeneity in study results is present, it may be more beneficial to explore the difference in study results through subgroup analyses or in a narrative review.

Meta-analyses may contain a biased sample of studies that answer a particular clinical question (Borenstein et al., 2009). When assessing primary studies for inclusion in the meta-analysis, biases, such as selection, performance, detection, and attrition biases, should be carefully evaluated for their effect on the study design. In addition, every attempt should be made to locate all published and unpublished studies that answer the question of interest to limit the effects of publication bias, where only favorable studies are published and unfavorable results get left in the researcher's file drawer. By combining results of both published and unpublished studies and those with significant and nonsignificant results, the true effect size of an intervention can be determined, providing substance to any recommendations made as a result of the meta-analysis findings.

Many of the criticisms of meta-analyses are also true for narrative reviews (Borenstein et al., 2009). It is the systematic approach and transparency in conducting a meta-analysis that helps address the innate challenges in combining results of primary studies and creating meaningful conclusions.

Interpreting the Outcomes of a Meta-Analysis

The results of a meta-analysis are graphically displayed in a Forest Plot (see Figure 1). In a Forest Plot, the effect size and their confidence intervals of primary studies and the summary effect of the combination of these studies are graphically represented as favoring either the intervention or the control. The weight given to the effect size indicates the influence a study has on the combined treatment effect (Holly et al., 2012). Weight is a factor of sample size; studies with larger samples usually have greater precision and therefore are given

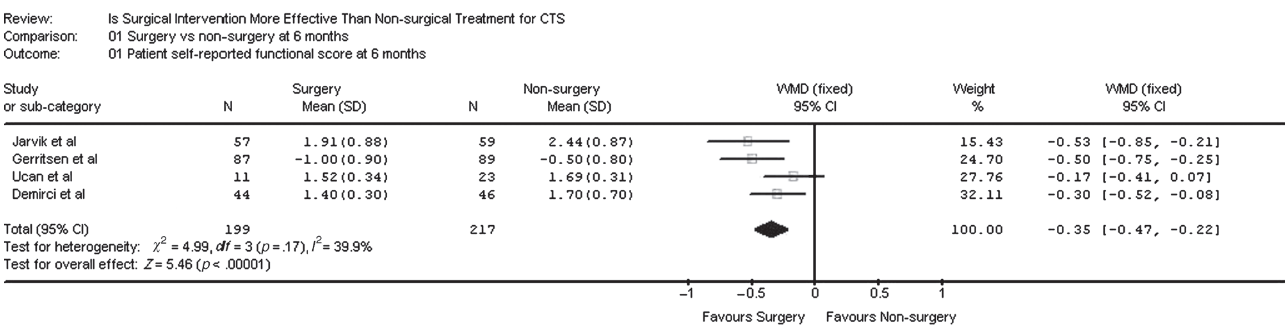

FIGURE 1. Patient self-reported functional improvement at 6 months. From "Is Surgical Intervention More Effective Than Non-surgical Treatment for Carpal Tunnel Syndrome? A Systematic Review," by Q. Shi and J. C. McDermid, 2011, *Journal of Orthopaedic Surgery and Research*, *6*, 17. doi:10.1186/1749–799X-6-17. The electronic version of this article can be found at: http://www.josr-online.com/content/6/1/17.

TABLE 3. QUESTIONS FOR INTERPRETING A FOREST PLOT

1. How many primary studies were in the review?
2. How many subjects were in the total review?
3. What is the summary effect size?
4. What is the confidence interval of the summary effect size?
5. Is it safe to recommend the results of this review?

Note. Adapted from *Comprehensive Systematic Review for Advanced Nursing Practice*, by C. Holly, S. W. Salmond, and M. K. Saimbert, 2012, New York: Springer Publishing Company, pp. 183–184.

more weight. A meta-analysis provides for a means to explore differences in effects between studies and to identify heterogeneity among study results (The Joanna Briggs Institute, 2011). There are several questions to ask to interpret the Forest Plot (see Table 3). These questions are used to determine whether recommendations based on the results of a meta-analysis are best practice.

The Forest Plot in Figure 1 presents the results of a meta-analysis on the effectiveness of surgical versus nonsurgical treatment for carpal tunnel syndrome (CTS; Shi & McDermid, 2011). Although surgical intervention is considered as the definitive treatment for CTS, it is not always considered first. Conservative intervention, such as drugs, physical therapy, or wrist splints, may provide sufficient relief and may be a patient preference due to concerns about the discomfort, inconvenience, or safety of surgery (Shi & McDermid, 2011).

There are seven studies in this systematic review; five are randomized controlled trials and two are controlled (not randomized) trials. The meta-analysis in Figure 1 is the combined results of four of these seven studies on patients' self-report of functional improvement 6 months following conservative or surgical treatment for CTS. This is an analysis of a subgroup of studies that included data related to the outcome of interest: patients' self-report on functional improvement. Included in this analysis were 416 total subjects: 199 in the surgical group and 217 in the nonsurgical group. The summary effect can be determined by looking at the placement of the diamond-shaped graphic. The vertical dark line at zero (0) on this graph is the null hypothesis. In other words, if the review results (represented by the diamond) cross this vertical line, the results are not significant. However, in this study, the diamond is fully on the left, indicating that the results of this meta-analysis are significant. It was concluded that surgical intervention had superior benefit over conservative treatment based on patient self-reports 6 months after treatment.

The numerical value of the effect size results are seen in the column labeled "WMD" for weighted mean difference. The summary effect of −0.35 demonstrated a larger treatment benefit for surgical intervention compared with nonsurgical intervention at 6 months on patient self-reported functional status. To determine the precision of these results, the confidence intervals for the overall results are provided in the column labeled "WMD (95% CI)." The confidence interval (CI) is a range of values based on the sample that represent where results would fall if it were possible to have results on the entire population, that is, every patient who has ever had either a surgical procedure for CTS or who were treated conservatively. This is known as the 95% confidence interval. The values at either end of the range are known as the confidence limits. A wide CI implies less accuracy or precision of the results, while a narrower CI provides greater certainty in the results. In this review, the results demonstrate that the CI of the summary effect is narrow (95% CI [−0.47, −0.22]). In addition, the CI does not contain the value of zero (0), the null hypothesis, indicating that the results are statistically significant. This can also be seen visually as the pointed tips of the diamond shape represent that the two ends of the CI do not cross the null hypothesis.

The results of this meta-analysis demonstrate that surgical treatment of patients with CTS is beneficial over conservative treatment (drugs, physical therapy, wrist splints) in terms of functional improvement and can be recommended as a best practice. This was determined by examining the effect size (Z score parameters >2.0); the CI does not include zero (0), representing the null hypothesis; and the diamond graphic is on the side that favors surgery.

Summary

Systematic reviews, which include a meta-analysis, are considered the gold standard for determination of best practice. Although other considerations are included in point-of-care decisions, such as patient preference and healthcare provider judgment, the results of a meta-analysis provide objective evidence upon which to base these decisions.

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