

General Steps in Systematic Review and Meta-Analysis

A Guide for AAFPRS Fellows

The systematic review is a new category of fellowship research project. A systematic review is a complete literature review based on a clearly formatted research question. In the performance of the systematic review all relevant studies are identified, and appraised for their quality. The data from all of the selected studies are then summarized. The *systematic, explicit, and transparent* approach distinguishes them from other reviews, and minimizes bias. This type of framework also produces findings that have significant impact on clinical questions and practices. This type of research is critical to the future of evidence based facial plastic surgery.

“Meta-analysis” is a statistical technique for combining findings from two or more independent studies. It can be performed on the aggregate data from a group of reviews if the outcome data are similar enough to perform formal, quantitative statistical analysis. Meta-analysis is most often used to determine the effectiveness of clinical interventions, providing an estimate of the treatment effect while taking into consideration the weight of individual studies. Complete meta-analyses evaluate for heterogeneity of studies and perform a sensitivity analysis on the results. When a meta-analysis of aggregate data is performed results may appear that were not identified in the individual analyses alone.

Systematic reviews and meta-analyses inform clinical practice guidelines that make treatment recommendations based on evidence. Systematic reviews of randomized controlled trials, for example, are considered the highest level of evidence. Given their importance to knowledge translation, we appreciate the need to promote this type of research by our academy membership.

Steps:

- 1) Prepare a detailed, *a priori*, research protocol
 - a. Ask a question using the “PICO” format. PICO denotes patient, intervention, comparison, and outcome.
 - b. An example of the PICO format would be “In patients with keloids, does treatment with 5-FU and kenalog as compared to kenalog alone improve keloid treatment as defined by keloid size and symptoms?”, where patients with keloids is the patient group, kenalog with 5-FU is the intervention, kenalog alone is the comparison group, and keloid size and symptoms is the outcome”

- 2) Specify inclusion/exclusion criteria
 - a. Specify methodologic criteria, i.e., include only randomized controlled trials, exclude languages other than English
 - b. Specify clinical criteria, i.e., exclude revision cases and those with prior radiation treatment, include all primary keloids less than 2 cm
- 3) Search the literature and document the search strategy
 - a. The search strategy should be extensive and documented well enough that a reader could reproduce the search on their own after reading the paper. This is similar to describing a research protocol well enough that anyone could repeat the experiment after reading the methods section of the paper.
 - b. All potential data sources should be included, thus computerized and print searches should be performed
 - c. List all databases queried, start/end dates, the search strategy, inclusion of unpublished literature, i.e. PubMed, EMBASE, and the Cochrane Library were searched from 1955 through October 2014
- 4) Determine which papers meet the pre-defined inclusion/exclusion criteria
 - a. Should be evaluated by minimum of two independent reviewers
 - b. Limits selection bias
- 5) Assess the quality of the included studies
 - a. Assess the papers for possible sources of bias that can either exaggerate or underestimate the effect of the intervention. In *randomized* studies confounding factors are expected to be randomly distributed throughout the intervention and comparison groups, but in observational studies they may be unevenly distributed, i.e. the kenalog alone group may have poorer results because the keloids in that group were different than those in the intervention group
 - b. Higher quality studies are those that are prospective, utilize robust methods to assess interventions and outcomes (such as validated scales and instruments), and attempt to control for confounding
 - c. In facial plastic surgery the number of RCTs to include in systematic reviews may be low, so the quality assessment will be critical
- 6) Summarize the evidence
 - a. Determine if the studies have similar outcome measures that can be analyzed in aggregate, i.e. a similar keloid QOL survey was performed in 4 of the 10 papers identified, so the QOL scores can be aggregated.

When this is true a “meta-analysis” of the aggregate data can be performed.

- b. When meta-analysis is performed *forest plots* (figure 1) are included to show the impact of individual studies relative to one another. The precision of a study is related to the number of patients included.
- c. The I^2 test (figure 2) for heterogeneity will determine how much heterogeneity there is between the studies. Studies with low heterogeneity can be analyzed with a fixed effects model, whereas those with high heterogeneity should be evaluated with a random-effects model, though if the heterogeneity is too high they should probably not be combined. Unfortunately there is not an accepted objective cutoff for heterogeneity
- d. When the data are not similar enough to combine and perform a meta-analysis, the individual study results are described
- e. Conclusions are drawn based on consideration of all identified data, whether meta-analysis was performed or not.

Figure 1: A Typical Forest Plot

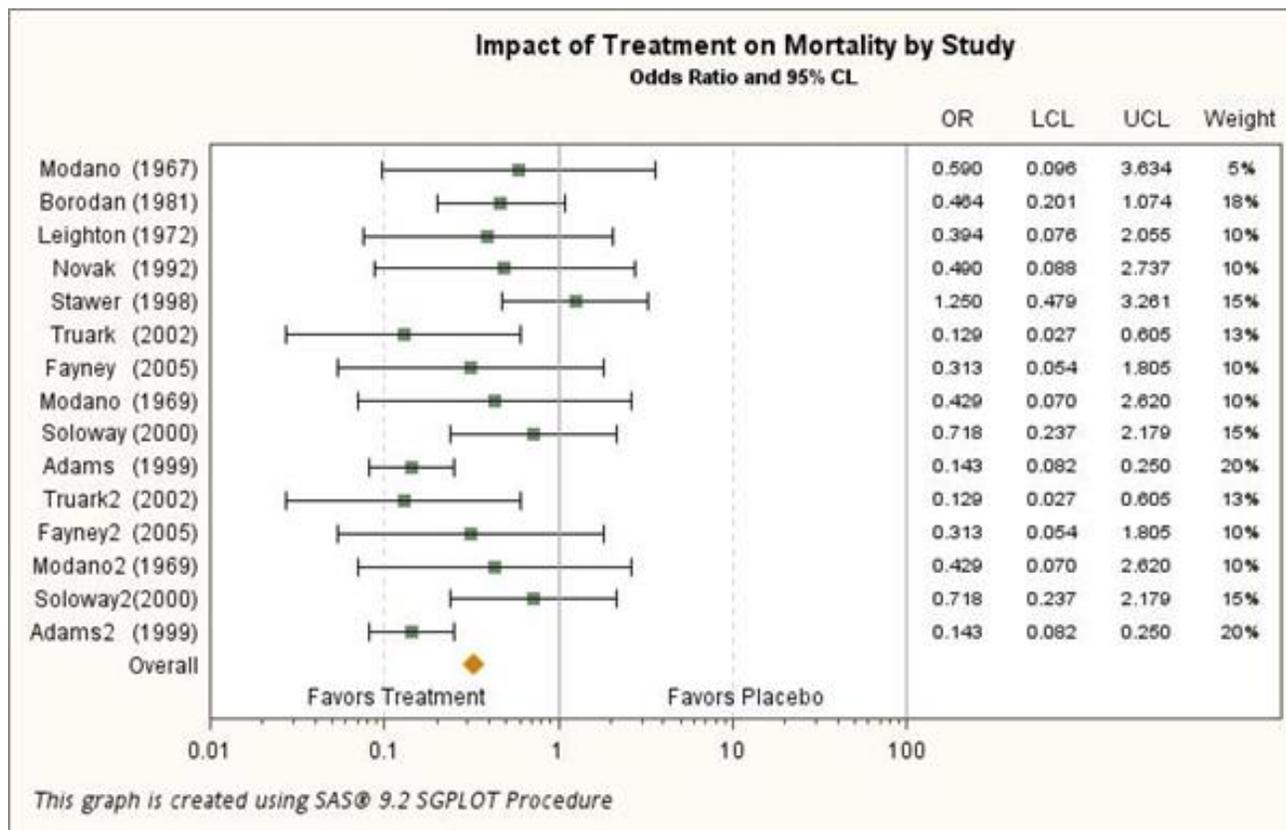


Figure 2: The I² Test for Heterogeneity

