
Meta-Analysis

Hem/Onc Journal Club

March 14th, 2011

Meta-analysis overview

- What is it? A meta-analysis is a quantitative review and synthesis of results of related but independent studies.
- Why do one?
 - ▷ Improve power to detect a treatment effect.
 - ▷ Estimate average effect, especially in studies with equivocal conclusions.
 - ▷ Estimate benefit in patient subgroups.
 - ▷ Some combination of the above.

Beginning a meta-analysis

- Establish study **objective**.
- Establish clear definitions of
 - ▷ Research **outcome**
 - ▷ **Treatment** or intervention
 - ▷ Study **population**
- Establish types of **studies** to include in the analysis.

- Objective “... to address questions about the efficacy of adjuvant taxane-based therapy, particularly in relevant subgroups of EBC patients.”
- Outcome
 - ▷ DFS including “... second primary breast cancers, local or distant recurrences of the original cancer, or death, unless otherwise specified (Table 1).”
 - ▷ OS
- Treatment Taxane-anthracycline versus anthracycline in adjuvant setting.
- Population Early breast cancer.
- Studies Randomized trials.

The literature search - identifying studies

- What?
 - ▷ Published literature
 - ▷ Unpublished literature

Q Why include un-published studies?

A To avoid *publication bias*: The bias resulting from the tendency to selectively publish results that are statistically significant.

- Where?
 - ▷ Citation indexes
 - ▷ Abstract databases
 - ▷ Clinical trials registries
 - ▷ Conference proceedings

- Published studies
 - ▷ PubMed (2000 to 2006)
 - ▷ text words: “breast cancer and (paclitaxel or docetaxel).”
- Unpublished studies - abstracts/presentations at
 - ▷ ASCO (2000 to 2006)
 - ▷ San Antonio Breast Cancer Symposium (2000 to 2005)

Combining the studies

- Identify a summary measure common to all studies.
- Combine the measures to obtain an overall summary measure.
- Obtain measures of uncertainty (e.g. 95% CI).

- Summary measure was hazard ratio (HR)
- Brief review of HR
 - ▷ Hazard quantifies the risk of death (assuming endpoint of interest is OS)
 - ▷ Hazard ratio quantifies the relative risk of death comparing treated to control patients
 - ▷ $0 < HR < 1$ means risk of death for treated subjects is less than that for control patients
 - ▷ $HR > 1$ means risk of death for treated subjects is greater than that for control patients
- Difficulties in consistency of information reported across studies (see 'Data Extraction' section)

Pooling the information

- Use a weighted average approach (see 'Data Synthesis' section).
- Weights are inversely proportional to the variance of the estimated summary measure.
- Summary statistics measured with greater variability contribute less to the pooled estimate.
- Random effects modeling approach used when there is substantial heterogeneity across subjects.
- Fixed effects modeling approach used if there is not substantial between-study heterogeneity.

Displaying results

Results are typically displayed using forest plots.