

Meta-analysis of controlled and uncontrolled studies: a case study and simulation results

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For the synthesis of evidence, it is sometimes desirable to rely not only on RCTs but also to include results from other sources as well. This may be the case when a search through the literature reveals, besides a few controlled studies, a large number of non-controlled, single-arm studies. Although these studies are less reliable, they can add valuable information. Therefore, an attempt should be made to incorporate the information coming from the single arm studies in the synthesis.

There are meta-analytic methods developed for the combination of comparative studies and single arm studies [1, 2]. The proposed models contain an estimate for each treatment arm, the treatment effects can be either fixed or random, and a random effect baseline term is included. One model assumes normally distributed effects where else in the second model the normality assumption is relaxed. We implemented the models in R.

We did a simulation study in order to study the influence of the additional information on the summary estimate and we applied the models to data on therapy-associated complications - myelodysplastic syndrome and acute myeloid leukaemia - of patients with Non-Hodgkin Lymphoma. In the latter case, the data were extracted mainly from non-comparative studies and from only three comparative studies. These three trials compared conventional chemotherapy with chemotherapy and autologous stem-cell transplantation. Differences in the results of the two models will be discussed and compared to the classical DerSimonian and Laird method.

References

[1] Begg, C. B. (1991), "A Model for Incorporating Historical Controls into a Meta-Analysis", *Biometrics*, 47, 899-906

[2] Li, Z. and Begg, C. B. (1994), "Random Effects Models for Combining Results from Controlled and Uncontrolled Studies in a Meta-Analysis", *American Statistical Association*, 89, 1523-1527