Random effect meta-analysis of individual patient time-to-event outcomes

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Objectives: Random-effect meta-analysis is considered as a powerful tool for investigating the possible sources of heterogeneity caused by unmeasured covariates. The meta-analysis of IPD can be performed by employing either a one-stage or a two-stage approach. We first investigate the current methods. We explore the performance of the one-stage and two-stage methods under different conditions and compare methods for estimating the parameters in a random effect model for time-to-event data.

Methods: Articles are searched and retrieved from the database of MEDLINE (Ovid) using keywords random effect, survival data, survival outcome time-to-event, cluster, frailty and multi centre effect.

We apply the common one-stage (Vaida, F. and R. Xu 2000, Ripatti, S. and J. Palmgren 2000, Abrahantes, J.C. and T. Burzykowski 2005, Tudur-smith et al 2005, Bowden et al 2011, Ha et al 2012, Simmonds et al 2013) and two-stage (log-rank test, fixed effect Cox model) methodology of IPD meta-analysis using 5 randomised control trials investigating the use of two anti-epileptic drugs: Carbamazepine (CBZ) and Sodium Valproate (SV).

Results: After analysing full text we have got 40 eligible studies, where studies 8 were based on parametric, 26 semi-parametric and 5 on non-parametric methods. We applied 7 one-stage and 2 two-stage methods for the estimation of the random effects models. Similar estimates were obtained for logHR and its standard error but some of the methods underestimate between trial variance parameter.

Conclusion: There are many alternative approaches for random effect meta-analysis of IPD time-to-event outcomes, and results can vary. Inferences and some suggestions based on the performance of the methods are proposed.