Basel Biometric Section of the Austro-Swiss Region of the International Biometric Society

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BBS Seminar IPD meta-analysis of treatment-covariate interaction with a continuous predictor

18 June 2013, 16:00 – 17:30

Actelion Pharmaceuticals, Hegenheimermattweg 95, 4123 Allschwil, Switzerland

PROGRAM

16:00 – 17:30 **A method for IPD meta-analysis of treatment-covariate interaction with a continuous predictor in randomised trials**

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Aims

In clinical trials, there is considerable interest in investigating whether a treatment effect is similar in all patients, or that some prognostic variable indicates a differential response to treatment. To examine this, a continuous predictor is usually categorized into groups according to one or more cut-points. Several weaknesses of categorisation are well known. To avoid the disadvantages of cut-points and to retain full information of the variable, it is preferable to keep continuous variables continuous in the analysis. We propose a statistical procedure to handle such situations when individual patient data (IPD) are available from several studies and we will illustrate practical issues using an IPD meta-analysis of three randomised trials in acute lung injury as an example.

Methods

For continuous variables, the multivariable fractional polynomial interaction (MFPI) method provides a treatment effect function, that is a measure of the treatment effect on the continuous scale of the covariate (R+S 2004, S+R 2007). MFPI is applicable to most of the popular regression models, including Cox and logistic regression. A meta-analysis approach for

averaging risk functions across several studies has recently been proposed (S+R 2011). Here we combine the two techniques to produce a method of IPD meta-analysis in which treatment-effect functions are averaged across studies. Issues such as type I error of MFPI (R+S 2013), influential points or the role of differences in patient populations across studies will be discussed. More details can be found in the registered protocol (Kasenda et al 2012).

Results

We used the new approach to investigate four potential treatment effect modifiers in a meta-analysis of IPD from three randomised trials in acute lung injury, where the main outcome of interest was 60-day in-hospital mortality. In contrast to cut-point based analyses, the results give more detailed insight into whether treatment effects are influenced by any of the four factors considered.

Conclusions

The proposed method appears to be first to address the problem of retaining full information when performing IPD meta-analyses to examine continuous effect modifiers in randomised trials. Early experience suggests that it is a promising approach with broad applications. Adjustment for confounders is possible with MFPI, therefore this approach also allows investigating interactions between a binary (extension to categorical variable is straightforward) and a continuous variable in observational studies. Functions from several observational studies can be averaged as illustrated for randomised trials here.

References

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