SENSITIVITY ANALYSIS FOR INFORMATIVELY MISSING DATA IN META-ANALYSIS

I. White

Institute of Public Health, Cambridge, UK

† E-mail: ian.white@mrc-bsu.cam.ac.uk

Any clinical trial with missing outcome data is susceptible to bias if the odds ratio between missingness and outcome (the informative missing odds ratio or IMOR) differs from one in one or more trial arms. Starting from the assumption that the IMORs in a two-arm trial equal one, sensitivity analysis should explore both the impact of equal IMORs in the two arms and the impact of differences between the IMORs. Alternatively, plausible prior beliefs may be placed on the arm-specific IMORs, which may be correlated but need not be equal, and these prior beliefs may be used in a Bayesian analysis. Typically this will have little impact on the point estimate but widen uncertainty.

In meta-analysis of randomised trials, there are four dimensions for sensitivity analysis. First, one may explore the impact of IMORs that are equal in all trials. Second, one may take the IMORs to be independent between trials, and use plausible prior beliefs about the IMORs to inflate the trial-specific standard errors. The impact of this is typically to reduce the weight given to trials with more missing data. Both sensitivity analyses should separately consider the cases where the IMORs are equal or different in both arms.

We show how these sensitivity analyses may be implemented either in a two-stage procedure or in a single hierarchical model. The methods are illustrated in a meta-analysis of drug trials in the treatment of schizophrenia.