USING DOUBLE ROBUST ESTIMATORS TO PROVIDE UNBIASED AS-TREATED EFFECTS IN RANDOMISED TRIALS

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Valid causal inference remains the key goal motivating the analysis of data from observational studies and randomised clinical trials (RCTs). Recent advances in the development of models of causation have been made in statistics and econometrics focusing on the average treatment effect, alongside the capacity to cope with different selection effects, principally confounding, missing data and non-adherence to random allocation.

Marginal structural models (MSMs) were originally introduced to adjust for time-dependent confounders in observational studies. We hypothesise that MSMs can be innovatively applied for the analysis of non-adherence in RCTs, since they provide unbiased estimates of as-treated effects, conditional on subject's previous exposure history. Estimating the causal parameters from a MSM can be achieved by g-computation, inverse probability of treatment weighting or double robust (DR) estimators. DR procedures allow for unbiased estimators under the misspecification of either the outcome model or the exposure model, and can offer increased efficiency.

DR estimated MSMs and their implementation are demonstrated using a simulation study, and the CUtLASS trial which compared the efficacy of the old and the newer atypical neuroleptics in patients suffering from severe schizophrenia. We demonstrate the use of a new Stata program for computing DR estimators in pretest-posttest studies.

MSMs are shown to be applicable for analysing non-adherence in RCTs, and both analyses show the DR estimator to be more efficient than alternative estimators, and retain the DR property under model misspecification. The analysis of the CUtLASS trials reveals that the class of atypicals perform no better than conventional neuroleptics with respect to quality of life and symptom severity.