LOOKING FOR A FEW GOOD MEDIATORS: CAUSAL ANALYSES OF MULTIPLE MEDIATION FACTORS IN RANDOMIZED TRIALS WITH STRUCTURAL MEAN MODELS

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We present a linear structural mean model approach for analyzing multiple mediators of a randomized baseline intervention's effect on a univariate follow-up outcome. Unlike standard mediation analyses, our approach does not assume that the mediating factors are randomly assigned to individuals by taking advantage of baseline randomization. The proposed G-estimation procedure represents an extension of the work on treatment non-adherence by Robins and Greenland (1992) and Ten Have et al. (2004) to estimation of direct and indirect effects of a randomized baseline factor. Simulations show good test and confidence interval performance under unmeasured confounding, in contrast to standard mediation approaches. An application is presented in the context of estimating the mediating effects by anti-depressant medication, psychotherapy, and primary care visits of an intent-to-treat effect of a randomized encouragement intervention on follow-up Hamilton depression scores.

Robins, J.M. and Greenland, S. (1992) Identifiability and exchangeability for direct and indirect effects. Epidemiology, 3: 142-155. Ten Have, T.R, Elliott, M., Joffe M., Zanutto, E., and Datto, M.C. (2004) Causal models for randomized physician encouragement trials in treating primary care depression. Journal of the American Statistical Association, 99:8-16.