Pharmacological Treatment of Adult Attention-Deficit/Hyperactivity Disorder (ADHD) in a Longitudinal Observational Study: Estimated Treatment Effect Strengthened by Improved Covariate Balance

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ABSTRACT

An improved method for estimation of causal effects from observational data is demonstrated. Applications in medicine have been few, and the purpose of the present study is to contribute new clinical insight by means of this new and more sophisticated analysis. Long term effect of medication for adult ADHD patients is not resolved. A model with causal parameters to represent effect of medication was formulated, which accounts for time-varying confounding and selection-bias from loss to follow-up. The popular marginal structural model (MSM) for causal inference, of Robins et al., adjusts for time-varying confounding, but suffers from lack of robustness for misspecification in the weights. Recent work by Imai and Ratkovic [1][2] achieves robustness in the MSM, through improved covariate balance (CBMSM). The CBMSM (freely available software) was compared with a standard fit of a MSM and a naive regression model, to give a robust estimate of the true treatment effect in 250 previously non-medicated adults, treated for one year, in a specialized ADHD outpatient clinic in Norway. Covariate balance was greatly improved, resulting in a stronger treatment effect than without this improvement. In terms of treatment effect per week, early stages seemed to have the strongest influence. An estimated average reduction of 4 units on the symptom scale assessed at 12 weeks, for hypothetical medication in the 9 - 12 weeks period compared to no medication in this period, was found. The treatment effect persisted throughout the whole year, with an estimated average reduction of 0.7 units per week on symptoms assessed at one year, for hypothetical medication in the last 13 weeks of the year, compared to no medication in this period. The present findings support a strong and causal direct and indirect effect of pharmacological treatment of adults with ADHD on improvement in symptoms, and with a stronger treatment effect than has been reported.