Diagnostics for Informative Censoring in Efficacy and Effectiveness Trials of Schizophrenia Therapy

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The gold-standard for analyzing randomized trials is the intent-to-treat design. This is often unattainable in trials of schizophrenia therapy where study dropout often exceeds 33%. When dropout is related to poor efficacy (or emergent side-effects), it is often described as “informative” because it predicts treatment effectiveness (or safety). Moreover, if such dropout differs across treatment arms, then treatment effect estimates are liable to bias. We will develop and apply diagnostics for informative censoring in (i) a short-term placebo-controlled efficacy trial of 6 mg/day or 12 mg/day paliperidone vs. placebo in 361 schizoaffective patients over 6 weeks, and (ii) a long-term comparative effectiveness trial of four atypical antipsychotics vs. perphenazine over 18 months in 1432 patients (Clinical Antipsychotic Trial Intervention Effectiveness study). In both trials we will outline and apply three diagnostics: (1) how censoring relates to both assigned treatment and prior covariates that predict the outcome (2) whether covariates themselves are affected by assigned treatment—an indication that covariate adjustment is insufficient to remove bias (3) the performance of inverse probability weights for censoring to remove bias from study dropout. These metrics will be succinctly reported with intuitive plots that summarize the metrics over person-time. Software and documentation for the Statistical Analytic System (SAS) will be developed and made freely available. This work has the potential to greatly aid the transparent reporting and analysis of randomized trials in schizophrenia.