NCT02188121

Protocol Title: Clinical trial to reduce cardiovascular health risks in patients with serious mental illness

Statistical Analysis Plan Date: 02/10/2018

Background: This trial focuses on SMI patients who are potentially eligible for cardiovascular prevention therapy (through statin and angiotensin medications such as angiotensin receptor blockers or ARBs) but who have not yet received it. The trial compares a prevention strategy intervention with usual care with respect to use of therapy. The trial includes those on partial therapy and excludes those with detected cardiovascular disease or diabetes, and assesses whether the intervention increases cardiovascular prevention use relative to usual care.

Eligibility summary: Eligibility criteria include a diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder; second generation antipsychotic (2GA) therapy within the past six months before trial entry; and mental health care at one of the study sites at the time of trial entry. We exclude subjects who already have a diagnosis of diabetes or cardiovascular disease; who already are receiving therapy with both statins and angiotensin medications (i.e., the same therapeutic drug classes as used in the intervention); or who have contraindications to both drug classes.

Primary study outcome: The main outcome is use of the cardiovascular prevention medications over the 12-months after study initiation. For each individual, we define the primary outcome as the proportion of the 12 follow-up months during which she/he either received any of the prescribed medication or the medication became clinically contraindicated after trial entry (as decided by the treating physician). We will assess the outcome using medication counts at each study visit (i.e., at the 3-, 6-, 9-, and 12-month study visit), supplemented by subject self-reports and the clinic chart review. For subjects who are eligible to receive both statins and ARB medications at baseline, we will calculate the number of days that they receive both medications during the 12 months of follow-up. For subjects who are eligible to receive only one of the two medications at baseline (i.e., because of pre-existing therapy with or because of contraindications to the other prevention medication before trial entry), we will calculate the number of days that they receive the medication during the 12 months of follow-up, with the same approach for addressing changes in subsequent eligibility.

Analysis of the primary study outcome: The primary analysis will follow the intention-to-treat (ITT) principle. We will use regression analysis to estimate the mean average of the primary outcome in each group and the difference between the mean outcomes, along with its 95% confidence interval and using the p-value for a null hypothesis. If clinically meaningful imbalances are detected in baseline covariates despite randomization, we will adjust for those covariates. If necessary, we will adjust for selection bias due to loss to follow-up via inverse-probability weighting. In supplemental analyses to the main ITT approach, we also will conduct appropriately adjusted per-protocol analyses. We will use STATA 13.0 for all analyses. We also will examine a number of pre-specified subgroup analyses, in which we examine whether the intervention might be more effective among those SMI patients who are more likely to receive fragmented care or less likely to be adherent to complex treatment regimens, e.g., SMI patients with Medicaid versus those with commercial health insurance.