Statistical Analysis Plan: In-Home Care for Patients with PSP and Related Disorders

NCT03552484

3-18-2019

Outcome ascertainment

Primary outcomes. The EQ5D will be completed at Visits 1-4 for program patients and annually for controls. This scale measures 5 domains of quality of life: *mobility, self care, usual activities, pain/discomfort, anxiety/depression*; each domain is scored from 1 to 5, with higher scores indicating better function. The scale also includes one item measuring overall self-rated health on a visual analogue scale (VAS) from 0 to 100, where 100 is "best health you can imagine". This generic scale has been studied in PSP and related disorders and is available in an online format, supporting the feasibility of our control group. Change will be assessed in each EQ5D domain and in the VAS between baseline and 1 year. The instrument will also be administered at Visits 2 and 3 to avoid missing data if dyads are lost to follow-up prior to Visit 4. The MCSI will be completed at Visits 1-4 for caregivers, and annually for control caregivers. This scale is scored from 0-72, with 20-29 indicating moderate strain, 30 or higher indicating severe strain. MCSI scores will be evaluated as both continuous and categorical variables.

Demographics and confounders. include *race, ethnicity, education, insurance,* for patients and caregivers respectively; *living situation* (home or nursing facility), *diagnosis, diagnosis duration* (from year of onset or diagnosis, if onset unknown), and *comorbidities*.

Other variables of interest. The following items will be evaluated in program patients only: *hallucinations, motor severity* (*UPDRS, HY*), and *satisfaction* with the program (*Client Satisfaction Index-Short Form, CSI-SF*) administered to patients and caregivers.

Power calculation: Based on pilot recruitment, we anticipate enrolling 20 patients in home visits over 12 months, with a 15% drop out rate, yielding 17 patients at 12 months. We anticipate enrolling 100 control patients and 60 control caregivers, with a 20% drop out rate, yielding 80 patient and 48 caregiver controls. To detect a minimum clinically important difference of 6.5-8.0 in the EQ5D VAS, assuming a baseline mean of 37, standard deviation of 18, power of 0.80 and two-sided alpha of 0.05, we would require 42-63 patients.

Data management: The primary data will be entered into a HIPAA-compliant database (**REDCap**), with quarterly audits for fidelity. Data will be exported to Stata 14 for analysis.

Data analysis:

Descriptive statistics. We will describe the demographics, disease characteristics, QoL, and caregiver strain at baseline in patients and caregivers. Categorical variables will be summarized by frequencies and percentages. Continuous variables will be assessed for normality and summarized by mean and standard deviation, or median and interquartile range. Adequacy of matching will be evaluated using chi-square and *t*-tests.

Bivariate analyses. Change in EQ5D subscores and VAS over 1 year will be compared between groups, stratified by diagnosis, by two-sample *t*-test or nonparametric Wilcoxon rank sum test. If a subject dies or is lost to follow-up, the last values of the EQ5D will be carried forward. We will analyze the association with change in EQ5D for each demographic, confounder, and covariate via chi square or multivariate ANOVA, as appropriate. We will compare change in MCSI over 1 year by group, stratified by diagnosis; if lost to follow-up, the last MCSI value will be carried forward.

Multivariable analyses**.** We will construct a linear regression model with change in EQ5D domains and VAS as sequential dependent variables, and treatment status as the primary independent variable, stratifying by diagnosis. We will build complex models to assess the contributions of each significant covariate. Model building will include manual stepwise, backward elimination checking for multicollinearity and confounding. We will construct similar models wherein MCSI change is the dependent variable.