Women's Treatment and Early Recovery (MBRP-W)

NCT02977988

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Statistical Analysis Plan

Measures for data capture

Discharge Status. Following routine site protocol, the SUD site treatment team (i.e., certified SUD counselor, masters-level clinician therapist, and team supervisor masters-level therapist; the latter two registered with the Board of Behavioral Sciences) decided on a case-by- case basis if a client developed the necessary skills to complete residential treatment. One of three clinical progress designations was documented in a patient's chart at discharge based on their progress. *Completer*: patient completed course of treatment, met treatment goals and were sufficiently stable (i.e., developed sufficient coping skills, attended groups, adhered to requirements on days away from the facility such as calling in, returning on time and negative drug screen) to transition to stepped-down care. *Non-completer with satisfactory progress*: patient left treatment before completion of the treatment plan and be- fore achieving all treatment goals, but deemed by the clinical team as having made important progress toward treatment goals and improved stability. *Non-completer without satisfactory progress*: patient left treatment before completion of the treatment plan and the clinical team determined that little or no progress was made toward achieving treatment goals (i.e., left early in treatment without being able to re- ceive many services, administratively discharged due to multiple oc- casions of relapse as assessed by drug screens without changes in be- havior, repeatedly violated residential treatment rules such as bringing drugs on site). *In-residence*: patient remained in treatment at the residential treatment facility at the end of the analytic period (i.e., day 150). It was not possible to blind the discharge team to group assignment; however, the study was presented to the discharge team as a test of two alternative intervention approaches in an effort to prevent any unbalanced expectation of treatment benefit.

Days until discharge. We used site discharge records to calculate the number of days in residential treatment beginning from the study intervention start date (day 0) and ending at day 150. We selected an analytic time period to approximate the average length of stay at the SUD treatment site (5.5 months).

Data analysis

Power analysis yielded an estimated sample size of 200 to 225 needed to detect a medium-sized effect (hazard ratio = 0.52 to 0.54) for residential treatment retention using a log-rank test with a two- sided 5% significance level and 80% power, given the probability of remaining in the treatment program in the control group is 50%. We conducted standard statistical diagnosis and performed descriptive analyses of background variables, assessed variable distributional properties, plotted means of the continuous outcome variables at each time point, and assessed internal consistency and test–retest reliability of study scales. We verified the adequacy of randomization on demo- graphic and clinical covariates, and identified variables found to differ between groups at $p < .20$ (Table 1) to include them as model covariates. Based on this criteria, the covariates included in all adjusted models were number of mental health diagnoses (i.e., SUD only, 1 co- morbid mental health dx, 2 + comorbid mental health dx), adulthood trauma exposure (LSC-R), PTSD diagnosis by DSM-5, and PTSD symptom score (PSS-SR), as well as a study design feature (i.e., days in residential treatment prior to study intervention start date obtained from clinic records) to account for exposure to residential treatment prior to the start of our study intervention.

To examine the differential risk of the outcome event (i.e., patient left treatment before completion of the treatment plan and made little or no progress toward achieving treatment goals based on clinical team determination), we applied Kaplan-Meier survival analysis using an intent-to-treat (ITT) approach with time starting on the first day of the study intervention and

ending 150 days later. Participants with the discharge status of completer, non-completer with significant progress, and in-residence were coded as 1 for “retention”. Participants with the discharge status of non-completers without significant progress were coded as 0 for “non-retention”. Our examination of the survival curves revealed that group curves crossed at 50 days from the start of the intervention, which indicated the need for a piecewise model. Thus, a multivariable, 2-piece model (i.e., Piece 1 predicting outcome events during day 0 to 50 and Piece 2 predicting outcome events for days 51 to 150) was calculated. The first piece of the model coincided with the study intervention period and the second piece to the post-intervention period. Adjusted Cox proportional hazards regression (PROC PHREG), with days as the time scale, provide estimates of hazard ratios (HR) and the 95% confidence intervals (CI) for the non-retention outcome event. HR effect size estimates are categorized as small (0.77), medium (0.53), and large (0.36) (Amaro et al., 2016). We conducted logistic regression (PROC LOGISTIC) to test for group differences in satisfactory progress among the subgroup of non-completers. We used general linear mixed models (PROC MIXED) to examine differential changes in the self-re- ported mechanism of action variables from pre-intervention to post-intervention by group, adjusting for covariates. We used Pearson r to test for correlation between class attendance (as a dosage variable) and change in mechanisms of action measure scores. Pearson r effect sizes are small (.10), moderate (0.30), or large (0.50). All analyses were conducted in SAS version 9.4 (SAS Institute). All models used a maximum likelihood estimated approach to account for missingness.

Substance Use and Relapse

To quantify substance use at the three assessment points (baseline, postintervention, and follow-up), our trained study staff used the TLFB measure, which is a comprehensive retrospective calendar-based vali- dated semistructured interview measure of daily substance use (29). From TLFB data, we calculated substance use from study intervention start date

through the day of the last intervention session date (6 weeks later) and from intervention end date to 7 months later (8.5-month follow-up period in total). The interview window for postintervention assessment was 1 to 14 days after the intervention end, and for the follow-up assessment, the window was 7–9 months after the intervention end, and this variability was dependent on participant availability. This allowed for the quantification of daily substance use from study intervention start date to study end point. TLFB data allowed us to operationalize three sub- stance use outcomes for any drug use and alcohol to intoxication as well as methamphetamine and cannabis/marijuana, including the following: time to first use, quantified as days until first any drug use or alcohol intoxication; days of use, quantified as the total number of days in which any drugs were used or alcohol intoxication occurred, and relapse status, quantified according to a) abstinent, did not use during the period after the study intervention; b) lapse, used after study intervention but did not revert to regular use on one-third or less of days after first use; and c) relapse, used substance after the study intervention and continued to use regularly on more than one-third of days from first use.

Alcohol and Drug Use Confirmation Tests

Breathalyzer (for alcohol) and urine (for drug) samples were col- lected at postintervention and follow-up. We calculated agreement rates for any and each drug (excluding alcohol) against TLFB self- report. Only two participants had a positive Breathalyzer result. For urinalysis, we compared TLFB drug use reports for 3 days be- fore the urinalysis date against the urinalysis result.

Data Analysis

Our analytic sample size of 200 was powered to detect a medium-sized effect (Cox regression hazard ratio [HR] = 0.51) for days until first drug use with a two-sided $p < .05$ significance level,

80% power, and a 35% probability of substance use in the control group. Our ITT analysis of N = 200 did not include the 25 women randomized to a study group who never showed up to the first class and were thus excluded from analysis based on receiving no dose of the in- tervention. Prediction models included clinical covariates identi- fied a priori as having conceptual relevance for their impact on the effect of study intervention on recovery (i.e., number of mental health diagnoses coded as SUD only, one co-morbid mental health diagnosis, two or more comorbid mental health diagnoses, adult- hood trauma exposure [summed domain score from Life Stressor Checklist Revised], PTSD diagnosis via the Diagnostic and Statis- tical Manual of Mental Disorders [5th Edition], and PTSD symp- tom score [PTSD symptom Scale Self Report]). These models also adjust for an inherent study design variable (i.e., days in residential treatment before study intervention start date). Unadjusted models as effect size confirmation is located in the online supplement. We use the piecewise Cox regression PHREG procedure in SAS version 9.4 (SAS Institute) to model time periods during and after the study intervention (i.e., piece 1 predicting outcome events during the in- tervention period and piece 2 predicting outcome events after the intervention). Resulting HR effect sizes are interpreted as small (0.77), medium (0.53), and large (0.36) (35). Next, because of the zero-inflated distribution of days of substance use, we use negative binomial hurdle models to estimate any use (versus ab- stinence) and days of use among users simultaneously (36). Finally, we compute unadjusted and adjusted proportional estimates for group differences in relapse status (i.e., abstinent, lapse, relapse), and effect size is expressed as odds ratios (ORs).