Confirming the Efficacy/Mechanism of Family Therapy for Children with Low Weight Avoidant/Restrictive Food Intake Disorder (ARFID)

Statistical Analysis Plan

NCT04450771

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Data Analysis

Aims:

Aim 1: To conduct an RCT involving children and adolescents between the ages of 6 and 12 years of age with DSM 5 ARFID and weight below 88% of EBW comparing FBT-ARFID with medical management to manualized Non-Specific Care (NSC) with medical management.

Aim 2: To examine early change in parental self-efficacy as a mediator of treatment effect (FBT-ARFID vs. NSC on outcome). Changes in parental re-feeding behavior will be explored to see if it is a possible mechanism of FBT-ARFID using a mediator analysis.

Aim 3: To explore moderators of treatment outcome. All baseline variables will be explored as potential predictors and/or moderators of outcome.

Data Analytic Plan:

The core analysis strategy in this project is longitudinal mixed effects modeling, where we fully utilize repeatedly measured primary and secondary outcomes. Specifically, we will use piecewise modeling allowing for two segments of change over time (baseline to EOT, follow up period). For robust maximum likelihood estimation of mixed effects models, the Mplus program version 8 or above will be used. The data analytic plan for each Aim is as follows:

For **Aim 1**, we will conduct mixed effects modeling utilizing all available repeated measures of %EBW. We will use a random intercept/slope model with and without conditional on relevant covariates that are potential predictors of %EBW. If the trajectory shape turns out nonlinear, we will apply polynomial growth models. All individuals who had outcome data at one or more assessments will be included in our analysis. The results of these analyses can be easily converted to group difference at each assessment point including EOT. For our primary Aim 1, power is estimated based on mixed effects growth modeling focusing on the change in %EBW from baseline to EOT. Preliminary data showed a large ES (Cohen's d=-0.87) regarding the treatment effect (FBT-ARFID vs NSC) on %EBW. Given the preliminary nature, we plan to use a conservative, but still clinically meaningful ES of d=0.5 at EOT for primary power estimation. We assumed gradually increasing attrition over longitudinal assessments (25% by EOT). We assumed ICC=0.6 for the correlation across repeated measures of %EBW, which is a conservative estimate based on our previous eating disorder studies.16-19 Under this scenario, with an initial N=100, the estimated power to detect the difference in %EBW at EOT between the FBT-ARFID and NSC conditions is 0.84 (alpha=.05, two-tailed).

In **Aim 2**, we will examine whether earlier change (from baseline to 6 weeks) in parent self-efficacy mediates the effect of treatment on %EBW. We will follow the eligibility and analytical criteria of MacArthur approach for mediator analysis, which will be embedded in our mixed effects models. As a way of sensitivity analysis, we will also employ modern causal mediation approaches that utilize potential outcomes and propensity scores. Mediator assessment will occur at baseline and every 2 weeks during the first 6 weeks of treatment to allow detection of change in parental self-efficacy prior to outcome as required by the MacArthur mediational model. We will also explore whether parental re-feeding behavior during mealtimes is a possible mediator by examining changes in coded mealtime behavior from baseline to 6 weeks. In the mixed effects modeling framework, we will also examine the association between the parallel

growth processes of parent self-efficacy, mealtime behavior and %EBW throughout the entire study period, which will complement mediation analysis. In Aim 2, mediation will be examined by a set of two tests, 1) whether treatment (FBT-ARFID vs NSC) significantly induces changes in parent self-efficacy (eligibility criteria for mediators) and 2) whether the change in self-efficacy are correlated with improvement in %EBW. While preliminary data showed a large effect of treatment on parent self-efficacy by 6 weeks (d=1.5), given the preliminary nature of these data, we assumed a large but more conservative effect size of d=0.7 for the first step of mediation investigation (target engagement). Preliminary data also showed a large ES (Spearman correlation=0.46) regarding the association between the early change in self-efficacy and improvement in %EBW. Given this preliminary data, we used a conservative ES of r=0.35 for the second step of mediation investigation (target validation). Under this scenario, the estimated power to show target engagement is 0.84 (alpha=.05, two-tailed) and the estimated power to show target validation is 0.88 (alpha=.05, two-tailed). With these two steps together, we are well positioned to confirm the mediation mechanism.

In **Aim 3** (exploratory), we will examine potential moderators of treatment effect. In particular, we are interested in baseline patient age, parental self-efficacy, severity scores on the PARDI, psychiatric co-morbidity, and family structure. For this investigation, we will employ the MacArthur framework for moderator analysis, following the eligibility and analytical criteria for determining moderators. Finally, we will examine if improvements will be maintained at 6 months post EOT for primary and secondary outcomes using longitudinal mixed effects modeling. For exploratory moderator investigation in Aim 3, we will put more emphasis on gathering information on hypothesis generation and clinical significance (effect size) rather than on making inference based on statistical significance (i.e., p-values).