Wise Social Psychological Interventions to Improve Outcomes of Behavioral Weight Control in Children With Obesity

Statistical Analysis Plan

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Study Design: two-arm, parallel group, randomized controlled trial.

Primary Hypothesis: Compared to children randomized to receive a usual care behavioral pediatric weight management program alone, children randomized to receive a usual care behavioral pediatric weight management program plus the wise social psychological interventions will have a significantly attenuated BMI trajectory over 6 months.

Primary Outcome: Body mass index (BMI) trajectory over the 6-months duration of the study for each participant.

Primary Analysis, Statistical Model and Approach: We will use mixed effects linear regression techniques to address our aims. Such models are typically utilized in the clinical trials setting where repeated measurements are proposed.[154,155] Specifically, we will regress BMI at a given time point on study arm, days since randomization, and an interaction between study arm and days since randomization. Also included in the model are a subject-specific random effect to account for the correlation of measurements over time within a subject and a group-specific random effect to account for the correlation among outcomes across subjects assigned to the same group and behavior coaches. Both random effects are assumed to be normally distributed. Finally, we include the randomization factors: sex and race/ethnicity. The proposed model can be expressed as:

$$BMI_{ij} = \beta 0 + \gamma_i + \delta_{j(i)} + \beta 1\ treatment_i + \beta 2\ time_{ijk} + \beta 3\ treatment_i \times time_{ijk} + \beta 4\ sex_i + \beta 5\ ethnicity_i + \varepsilon_{ijk},$$

where ε_{ijk} is the random error term assumed to follow a normal distribution for the k^{th} observation corresponding to the i^{th} child assigned to the j^{th} group, γ_i is the subject-specific random intercept corresponding to the i^{th} child, and $\delta_{j(i)}$ is the group-specific random intercept corresponding to the j^{th} group in which the i^{th} child is nested. We are interested in drawing inference around $\beta 3$ that represents the difference in BMI trajectory over time between the two study arms. For this purpose, we will use a two-sided Wald test at the 0.05 level of significance. Our mixed effects regression approach most closely matches the study design and stratified randomization, and has advantages over a t-test endpoint analysis and other repeated measures analysis approaches for trial data including repeated measures ANOVA; it uses all available data, can accommodate differential lengths of follow-up, irregular measurement intervals, and missing data under reasonably flexible assumptions regarding the missing data mechanism.[156,157]

Intent-to-Treat: We will adhere to intent-to-treat principles. All participants randomized will be included in the analysis and analyzed according to their original treatment assignment. While we expect limited loss to follow-up, our analysis allows subjects without complete data to be included in the analysis for their partially observed period. Such an analysis relies on a flexible assumption about missingness, namely that the data are missing related to observed features only (MAR). As a sensitivity analysis, we will also rely on multiple imputation-based methods that repeatedly impute values for those with incomplete data prior to fitting the mixed effects linear regression model. The imputation model can consider a large number of features (beyond those included in the primary analysis model). The sensitivity analysis will provide insight into the robustness of our findings to missingness and how missing data are handled.

Detectable Difference, Sample Size, and Power: We will randomize a total of 160 participants (80 per study arm). We estimate sufficient power to address our aims. Estimates of power were performed using simulations (1000 simulations per scenario), which allowed us to consider a wide range of plausible assumptions and conditions, varying the sample size, retention rates, ICCs within individuals, ICCs within groups, BMI standard deviations, and combinations of trajectories of BMI decreases and increases and in the treatment and control groups. Across a wide range of assumptions and our planned total sample size of 160 children, or 80 children per study arm, we have at least 80% power to detect clinically meaningful differences in trajectories of 0.4 kg/m2 or greater per 24 weeks. For example, a 0.6 BMI increase over 24 weeks in the control group and a 0.2 BMI increase over 24 weeks in the treatment group.