

**An Open-Label Clinical Trial Conducted Via Telepsychiatry of Complementary and Alternative Treatments (Omega-3 Fatty Acids and Inositol vs. N-acetylcysteine) for the Management of Emotional Dysregulation in Youth**

**NCT03911414**

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## Statistical Methods

Participants were included in the analysis based on a modified intent to treat analysis plan with the criterion that participants had to be exposed to the study medications for  $\geq 2$  weeks. Baseline clinical characteristics were examined using Pearson's chi-squared test for dichotomous measures and truncated Poisson regression models for continuous measures (CBCL-AAA and CBCL-AT: lower level [ll] of truncation=150, upper level [ul] of truncation=270; SRS: ll=30, ul=90; BRIEF: ll=30, ul=100; YMRS: ul=60; CDI: ul=40). Primary efficacy measures of mania and depression, as well as secondary measures of autism symptoms and executive functioning, were analyzed using mixed-effects Poisson regression models with robust standard errors to account for the repeated measures on each participant. These models predict the outcome measure of interest from the study group, study week (continuous), and the study group-by-study week interaction, which is the primary effect of interest. Secondary efficacy measures of mania and depression assessed at endpoint were examined using logistic regression models predicting the outcome of interest from the study group. Adverse events (AEs) were analyzed using a Poisson regression model for AE counts and Fisher's exact tests for AE prevalence. All analyses were two-tailed with an alpha level of 0.05 and conducted using Stata (Version 18.1) (StataCorp, 2023).

We also examined the moderating effect of 1) the CBCL Autistic Traits (AT) profile defined by a combined T-score  $\geq 195$  on the CBCL Withdrawn/Depressed, Social Problems, and Thought Problems scales, and 2) the CBCL-Bipolar (BP) profile defined by a combined T-score  $\geq 210$  on the CBCL Aggressive Behavior, Attention Problems, and Anxious/Depressed scales. To examine these moderating effects, we added a 3-way interaction term between study group, study visit, and CBCL profile group to each of the models for the primary and secondary outcomes of interest. The moderating effects of the CBCL-AT and CBCL-BP profiles were examined separately