Protocol NX-21270

Cover Sheet

Official Title: Boost Study 21270 (Cognition)

ClinicalTrials.gov ID (NCT number): NCT05990335

Document Date: April 17, 2022

Document Description: Statistical Analysis Plan

1. Study Design and Power

The study design reflects an interventional, between-subjects and within subjects mixed design, with major variables of high/low group intervention/control after exposure to cognition exercises under the custom mHealth application configurations denoted as “Group I” and “Group C” respectively.

The enrollment target is 120 participants as described in the Protocol, for a total of 30 participants per group. Sample size is based on a power analysis conducted on Steele et al, 2019; which indicated the need for a final sample of at least 25 participants per group to achieve an observed power > 0.8 to detect a moderate effect size of 0.3-0.4 at an alpha level of 0.05.

During pre-screening, participants who are invited but choose not to accept enrollment in the study may be replaced by screening additional participants and selecting individuals that fall within the originally defined ranges. Any participants who disenroll in the first 2 weeks may be replaced with new subjects (rolling basis) to minimize overall participant loss. With an enrollment of 30 participants per group, this will allow an additional loss of 5 participants per group while still achieving the final target sample size.

2. Analysis Methodology

Upon completion of the study, a comprehensive analysis will include pre-specified analyses:

A. Task Completion (primary) endpoint will be evaluated per Group, as whole-number percentage of subjects completing minimum usage, per week. Mean and standard deviation will be reported for each Group.

B. Task Performance (secondary) endpoint will be calculated from cognition index scores as mean and standard error, per Group, as a differences-based analysis for the subgroup of subjects completing all study weeks per arm; using, as appropriate, a multi-level model to account for individual differences per Kirkpatrick et al, 2018, provided that random effects within models are not overparameterized (Bates et al, 2016). As appropriate, we will perform analysis checks for overparameterization to minimize loss of statistical power in an exploratory analysis of between groups data.

C. Recordation and qualitative assessment of adverse events and actions taken by the investigators in response to AEs or SAEs, per IRB requirements.

3. Archival

This study is to be performed in full compliance with the protocol and applicable oversight body and regulatory requirements. All required study documentation and data records will be archived in accordance with preauthorized policies and procedures.

Documentation and data will be stored and archived in a secure format for at least 2 years and for the duration required by the Sponsor and collaborating sites.