Official Title of the study: **Web Based Tools to Improve Medication Continuity in Adolescents With ADHD**

NCT number: **NCT04173000**

Document name: **Statistical Analysis Plan**

Date of the document: **5/19/2022**

The results of the Web Based Tools study will be assessed as described in this document. This statistical analysis plan begins with an overview of the key components of the study, including its design, objectives, and outcomes measures. This is followed by a detailed description of the statistical analyses that will be utilized to address study hypotheses.

1. **Overview of study:** This study is a 4-month open label trial to test whether an intervention engages the mechanism underlying medication continuity and improves outcomes. Adolescents and their parents that agree to participate in the study will receive the intervention (MeHealth for ADHD software with medication continuity tools). We planned to enroll a total of 20 adolescents aged 11-15 with ADHD with poor medication continuity who receive care from one of the 24 pediatricians recruited from ~8 practices who currently use the MeHealth for ADHD portal.

1.1 Study Objective: Test a multi-component intervention that systematically identifies and targets aspects of the Unified Theory of Behavior Change (UTBC) model most relevant for each adolescent with poor ADHD medication continuity.

Working hypothesis 1: Medication continuity will be higher at the end of the study compared to the baseline period.

Working hypothesis 2: Use of the intervention components will be related to improved outcomes as measured by change in the Unified Theory of Behavior Change factors.

1.2 Outcome measures

Primary

- Medication continuity as measured by proportion of days covered with medicine during the 4-month trial.
    - Number of days covered with medicine is calculated from audit of prescriptions dispensed.

Secondary

- Change in pre-intention factors of Unified Theory of Behavior Change at baseline and approximately 4 months later.
    - Adolescent and parent self-report on a 5- or 7-point scale, depending on the item. Individual items measure specific attitudes, subjective norms, and perceived behavioral control. Higher scores indicate a stronger belief.
- Change in intention to take/give ADHD medicine regularly at baseline and approximately 4 months later.
    - Adolescent and parent self-report on 7-point scale. Higher scores indicate a stronger intention.
- Change in adolescent-report of medication barriers at baseline and approximately 4 months later.
    - Adolescent self-report on Adolescent Medication Barriers Scale using 5-point Likert scale. Higher score means less barriers.
- Change in parent-report of medication barriers at baseline and approximately 4 months later.
    - Parent self-report on Parent Medication Barriers scale using 5-point Likert scale. Higher score means less barriers.

- Change in medication diversion at baseline and approximately 4 months later.
    - Adolescent self-report of the number of occasions of giving away, trading, or selling ADHD medicine to someone for whom it was not prescribed.
- Change in Decision Making Involvement Scale at baseline and approximately 4 months later.
    - Adolescent and Parent self-report. The scale contains the following subscales: "Child Seek" (e.g. child asks for an opinion or information from the parent), "Child Express" (e.g. child expresses an opinion or information to the parent), "Parent Seek" (e.g. parent asks for an opinion or information from child), "Parent Express" (e.g. parent expresses advice, an opinion, or information to the child), and "Joint/Options" (e.g. negotiation and brainstorming between child and parent). Each subscale produces a score which ranges from 1 to 4 with higher scores indicating more of that behavior.

1.3 Intervention Fidelity measures

- Fidelity to intended use of intervention components during the 4-month trial.
    - Proportion of intervention components completed relative to the components that were recommended by the portal based on adolescent/parent responses to the assessment battery.

1.4 Schedule of visits and time points of interest

- Baseline survey (baseline, after consent, usually a few days after)
- Medication continuity over past year obtained at baseline
- End of study survey (4 months post study start date)
- Medication continuity at end of study (average of 4 months)

1.5 Data Management

CCHMC CRC will guide data management for this project as described in the study protocol.

1.6 Interim Safety Analyses

No interim analyses are planned for this study.

2. Statistical Reports

2.1 Report Generation

2.1.1 Software

All statistical analyses will be performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) under Microsoft Windows operating system

2.2 Analysis Populations

2.2.1 Screen Failures

Subjects who are recruited but do not meet initial eligibility criteria and subjects who give informed written consent but after obtaining dispensing records are determined ineligible are considered screen failures. Screen failures will not be included in the analysis.

2.2.2 Completion

Subjects will be considered to have completed the study once the patient completes the 4-month post survey or study end date on 5/24/21.

2.2.3 Outliers

The data management and statistical analysis teams will identify subjects having data values that appear to be potential outliers. These values will be sent to the research coordinators for verification. Clear identification of a value as an outlier will be based on medical judgment as well as on statistical grounds. In the event that outlier values are identified, any analysis using the actual values will be followed by an analysis that reduces the outlier effect.

2.2.4 Missing data

We will use pharmacy dispensing records to calculate our primary outcome for all study participants unless consent is withdrawn.

For secondary outcomes, missing outcome data could occur for several reasons such as item nonresponse, lost to follow-up, and data collection errors. The average score of the total number of available items within a factor score will be used to account for missing outcome data.

2.2.5 Protocol Violations/Withdrawals

If a study participant is to be excluded/dropped from the study database and/or analysis, the PIs/coordinators will provide to the statistical analysis team the following: 1) the specific reason for dropout (e.g., withdrawal, protocol violation), in as much detail as possible; 2) who decided that the participant would be excluded; and 3) whether the exclusion involves some or all types of participation.

2.3 Statistical Report Contents

The following section outlines the contents of the final statistical analysis. For all analyses, baseline is defined as the measurement collected during the baseline survey. Subjects who are enrolled in the study and are eligible will be analyzed.

2.3.1 Description of study population

<u>Sample size:</u>
The total number of subjects who are consented/registered and withdrawn will be given. A summary of subjects who were withdrawn will be provided.

<u>Demographics and Clinical Characteristics, Patient and Parent:</u>
Demographic and clinical characteristics as measured at baseline will be summarized. Variables to be summarized are: parent age, parent race and ethnicity, parent sex, child sex, child age, child race and ethnicity. Variables will be summarized using descriptive statistics appropriate for each type of data item.

2.3.2 Primary outcome analysis

Primary outcome: Medication continuity as measured by proportion of days covered with medicine during the 4-month trial.

- Number of days covered with medicine is calculated from audit of prescriptions dispensed.

For the primary outcome, the dependent variable will be a proportion of the number of days covered with ADHD medicine during the 4-month trial.

2.3.3 Secondary outcome analyses

- Change in pre-intention factors of Unified Theory of Behavior Change at baseline and approximately 4 months later.

The dependent variable will be the change in adolescent and parent self-report of pre-intention factors. Items were reported using a 5- or 7-point scale, depending on the item, which was then re-scaled to a 5-point scale for ease of interpretation.

- Change in intention to take/give ADHD medicine regularly at baseline and approximately 4 months later.

The dependent variable will be the change in the intention to take/give ADHD medicine. Items were reported using a 7-point scale, which were then re-scaled to be on a 5-point scale for ease of interpretation.

- Change in adolescent-report of medication barriers at baseline and approximately 4 months later.

The dependent variable will be the change in adolescent-report of medication barriers. Items were reverse coded so that higher scores mean less barriers.

- Change in parent-report of medication barriers at baseline and approximately 4 months later.

The dependent variable will be the change in parent-report of medication barriers. Items were reverse coded so that higher scores mean less barriers.

- Change in medication diversion at baseline and approximately 4 months later.

The dependent variable will be the change in medication diversion.

- Change in Decision Making Involvement Scale at baseline and approximately 4 months later.

The dependent variable will be the change in parent and adolescent-report of the Decision Making Involvement Scale subscale scores.

2.3.4 Intervention Fidelity measures

The following will be summarized as mean and full range:

- Proportion of intervention components completed relative to the component that were recommended by the portal based on adolescent/parent responses to the assessment battery.