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Effectiveness Trial of an E-Health Intervention To Support Diabetes Care in Minority Youth (3Ms)

3/20/23

Study Protocol with Statistical Analysis Plan

The effectiveness trial is a multi-site clinical trial using a randomized, controlled, repeated measures design to test the effects of a computer delivered eHealth parenting intervention to improve health outcomes among African American adolescents with type 1 diabetes (T1D). The study will be conducted at 3 clinics in the Detroit area and 4 clinics in the Chicago area. 212 African American (AA) adolescents with type 1 diabetes and their primary caregivers will be enrolled. Study consent and the baseline assessment session will be completed in the diabetes clinic at the time of a regularly scheduled medical appointment Families will be randomized to one of two arms: *The 3Ms* intervention (to increase parental motivation for monitoring of adolescent DSM) or *standard control*. Participants will be allocated to the treatment arm using block randomization within 8 strata defined by the four sites and HbA1c level (most recent HbA1c $\leq$9.5% vs. >9.5%). Within these strata, the software will randomly assign participants to conditions in a 1:1 ratio to ensure equivalence in each condition.

Parents will complete the first intervention session in the diabetes clinic immediately after baseline data collection and randomization. The subsequent two intervention sessions will also be conducted during regularly scheduled diabetes clinic visits and can be completed any time in the 12-month window after baseline assessment. American Diabetes Association standards of care for youth with diabetes specify that visits to a diabetes specialty care center should occur quarterly; therefore, participants should be seen in clinic four times in a 12-month window. *The 3Ms* intervention is designed to be delivered over nine months should families receive diabetes care at the recommended frequency. Data collection will occur on a different schedule than intervention sessions and will occur at regularly scheduled visits conducted at six months and 12 months after baseline data collection. It is also important to note that while the 12-month data collection visit will typically occur 12 months from baseline, it must also occur at least 30 days from the date of the last intervention session (so that any changes in HbA1c occurring as a result of the intervention can be detected). The data analyses to be used in the study can accommodate varying lengths of time between data collection sessions. A final data collection session will be conducted 18 months after baseline to assess stability of intervention effects in the 6 months after intervention completion.

Participants will be 212 African American adolescents aged 10 years, 0 months -13 years 11 months diagnosed with T1D for a minimum of six months, and their parents. Given that this is an effectiveness trial, exclusion criteria are kept to a minimum so that transportability to real-world settings is adequately assessed. No exclusions will be made due to co-morbid mental health problems (e.g. ADHD, conduct disorder, depression), with the exception of schizophrenia/other psychosis, current suicidality or homicidality. Adolescents with cognitive impairments are also excluded if those impairments are severe enough to result in inability to complete research measures or impact their independence with diabetes care. Finally, if potential subjects have diabetes secondary to another chronic medical illness (e.g. cystic fibrosis) and their medical management differs substantially from that of most children with type 1 diabetes, they will be excluded.

All measures will be administered at baseline, 6, 12 and 18 months. The primary outcome glycemic control will be measured via hemoglobin A1c (HbA1c). HbA1c will be obtained using the Accubase A1c test kit manufactured by Diabetes Technologies. The Accubase test is FDA approved and uses a capillary tube blood collection method instead of venipuncture. It is therefore suitable for home-based data collection. High performance liquid chromatography (HPLC) is used to analyze the blood sample. Samples are stable for up to 30 days unrefrigerated and vials are bar coded to ensure confidentiality but minimize the likelihood of data loss. Secondary outcomes are measures by questionnaire self-report and/ or parent report.

In the preliminary study, the pooled standard deviation estimate for HbA1c change was 1.34%. If a sample size for the planned analyses is approximated by a t-test for the change in HbA1c from baseline to 12 or 18 months, a sample size of 97 per study arm will allow difference of 0.6% in HbA1c (based on our pilot data and the clinical significance of a 0.5% change), to be detected with 80% power (alpha = 0.025). If 106 families are enrolled per arm, a net sample size of 97 allows for 8% subject attrition/loss to follow-up. Our retention rates in our pilot study were 94%. A sample of this size is also sufficient to identify moderator variables that account for 7% increment in outcome variance using moderated regression analysis. Since outcome data will be collected during home visits, and even patients with incomplete data will contribute to the effective net sample size, the planned sample size is considered feasible with a total of 212 participants enrolled (106 *3Ms*, 106 control).

The primary outcome will be analyzed using the linear mixed effect model (LME) for repeated measures. Contrasts on the repeated measures [baseline minus 6-month, baseline minus 12-month (end of treatment), and baseline minus 18-month (6-month follow-up)] will partition the main effect of time. Three single degree of freedom contrasts will be defined by crossing the treatment arm factor with each time contrast; the latter two contrasts will test the primary hypotheses at intervention completion and six-month follow-up. The analysis will

be intent-to-treat (ITT) and will include all randomized participants regardless of the intervention dose received. In addition, attrition will be minimized by retention methods used successfully in our prior studies. Potential control variables include sociodemographic and clinical variables. If the baseline values are not equal for the intervention and control groups, we will consider adding covariates before testing the intervention effect.
Moderated regression analysis will be used to investigate variables that might moderate treatment effects (e.g. youth executive functioning, youth depression,or level of family conflict). Product terms involving the moderator and the time x treatment contrasts will be added to the LME model one at a time. These interaction contrasts will estimate the increment in outcome variance accounted for by the moderator.