Statistical Analysis Plan

ACT1ON Phase 2 (SMART Pilot) and Phase 3 (Efficacy Trial Development)

NCT03651622

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Analytic approach: The overarching objective of this study was, in addition to comparing three dietary approaches for co-management of glycemia and weight among young adults with type 1 diabetes, to identify individual-level characteristics that might drive response to a particular diet approach. Due to the COVID-19 pandemic, we recruited n=68 instead of the planned n=72 study participants, which led to the following changes in our analytic plan:

The updated analytic plan consists of the following descriptive and modeled approaches:

- Pre-COVID diet period 1 (Randomization 1): Model outcomes using generalized linear models (PROC GLM) in SAS due to lack of repeated measures
- All data, both pre- and post-COVID: Generalized estimating equations (PROC GEE) in SAS accounting for repeated measures
- Response variables for all models: Change for each of three diet periods for each of the primary and secondary outcomes:
    - Primary outcomes:
        - Weight (kg)
        - Hemoglobin A1c (%)
        - Percent time in clinical hypoglycemia (54-60 mg/dL)
    - Secondary outcomes:
        - Body fat percentage
        - Percent time in target glucose range (70-180 mg/dL)

Pre-COVID, diet period 1 (Randomization 1) only:

- Descriptive analysis
    - Change in primary and secondary outcomes for each diet period *irrespective of diet* (PROC MEANS in SAS), paired t-test for overall changes in outcomes.
    - Examine change in primary and secondary outcomes separately for each diet assignment in each of the three diet periods (PROC MEANS in SAS, paired t-test for each diet).
- Modeled analysis (PROC GLM in SAS)
    - Change in primary and secondary outcomes for pre-COVID diet period 1 according to randomized diet assignment, and adjusted for site, baseline level of the outcome, and gender, which was imbalanced across diet assignments at baseline. Use this model to test for differences between diets.

All data, both pre- and post-COVID:

- Descriptive analysis

    - Change in primary and secondary outcomes for each diet period (i.e., each randomization) *irrespective of* diet (PROC MEANS), paired t-test for overall change in outcomes
    - Examine change in primary and secondary outcomes separately for each diet in each of the three diet (i.e., randomization) periods (PROC MEANS, paired t-test for each diet) and look at mean differences between diets (PROC MEANS).
    - Examine change in primary and secondary outcomes separately for each site and each gender in each of the three diet (i.e., randomization) periods (PROC MEANS, paired t-test for change within each stratum per diet period).

- Modeled Analysis (PROC GEE in SAS)
    - Change in primary and secondary outcomes between diet periods (i.e., randomization periods) accounting for diet assignment and adjusted for site, the baseline level of the outcome, duration (months) between each diet period given that duration varied widely during the pandemic, a COVID indicator (yes/no), diet period (1, 2, or 3), and gender.

Planned analysis: consider analytic approaches that will allow for identification of individual-level characteristics that may predict individual response to a given diet assignment.