Statistical Analysis Plan

Title: Type 2 Diabetes and Binge Eating Disorder (BED)

ClinicalTrials.gov ID: NCT06325670

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Better treatment of type 2 diabetes and Binge Eating Disorder: Statistical Analysis Plan

1. Background

Primary Objective: The purpose of this pilot study is to evaluate the effect of cognitive behavioral therapy (CBT) on the number of weekly binge eating episodes among individuals with binge eating disorder (BED) and type 2 diabetes. As this is a pilot RCT, the focus will be on estimating effect sizes and identifying trends rather than testing hypotheses. The aim is to gather information on the potential effect of the intervention, which can inform the design of a future full-scale RCT.

2. Methods

Study design: This study is a non-blinded trial with a parallel design, where participants are randomized to either intervention (Cognitive Behavioral Therapy, CBT) or a waitlist control group. The aim of the design is to assess whether CBT is superior to the waitlist control group in terms of reducing weekly binge eating episodes. The intervention group will receive CBT over 16 weeks, while the control group will not receive treatment during the study period. The design allows for a direct comparison between the two groups to assess the effect of CBT, while also providing information on the feasibility of the intervention and potential effect sizes. This pilot study aims to gather data that can inform a potential future full-scale RCT.

3. Outcome Measures

Primary Outcome:

- **Number of binge eating episodes per week**: The number of binge eating episodes per week will be assessed by changes in the average number of episodes, measured using the validated EDE-Q (Eating Disorder Examination Questionnaire). The questionnaire covers both symptoms and behaviors related to binge eating and eating disorders in general, and it is used as a standardized measure to assess both the frequency and intensity of binge eating episodes.

Secondary Outcomes:

- **HbA1c**: Glycemic control will be measured by changes in HbA1c levels, assessed through blood tests, where HbA1c represents the average blood glucose over the past 2-3 months. HbA1c will be measured via blood tests at Odense University Hospital (OUH).
- **Time in Range (TiR) and Time Above Range (TAR) / Time Below Range (TBR)**: Glycemic control will also be assessed using continuous glucose monitoring (CGM), which measures how long the participant's blood glucose stays within the desired range (TiR), as well as the time spent above and below the target range (TAR and TBR). The CGM sensor is blinded and is worn by participants for one week before being returned to OUH.
- **BED-Q**: Binge eating symptoms and behaviors will be assessed using the BED-Q (Binge Eating Disorder Questionnaire), a self-report tool that evaluates both the frequency and intensity of binge eating episodes.
- **EDE-Q**: Eating disorder symptoms will be further assessed with the EDE-Q, one of the most widely used tools in binge eating research.
- **MDI**: Depressive symptoms will be assessed using the Major Depression Inventory (MDI), a self-report questionnaire that measures symptoms of depression based on clinically defined criteria.

- **PAID-20:** The Problem Areas in Diabetes-20 will be used to assess diabetes-related distress, where participants report feelings and difficulties related to their diabetes treatment and management.
- **Lipid Profile**: Blood tests will be used to measure the lipid profile, including levels of total cholesterol, triglycerides, and HDL cholesterol.
- **BMI**: Weight and BMI will be measured via self-report on the EDE-Q, as weight will not be measured directly in the study. This choice has been made because weight loss is not the goal of the intervention, and to avoid influencing participants' expectations.
- **Blood Pressure**: Systolic and diastolic blood pressure will be measured using an automatic blood pressure monitor, providing information on changes in cardiovascular risk. Blood pressure will be measured using the MAM function (Multi-Measurement Mode) in calm clinical settings at OUH.

4. Statistical Analysis

4.1 Primary Analysis

Since this is a pilot study, the primary analyses will be exploratory and reported as descriptive statistics and inferential analyses. Changes in weekly binge eating episodes between groups will be estimated by:

- Mean and standard deviation for each group at both baseline and post-intervention
- Effect size calculated with Cohen's d to quantify the difference between groups
- 95% confidence intervals for the estimated effects
- Mixed-effects models: A mixed-effects model will be used to assess intraindividual changes in the number of binge episodes over time, accounting for both the intervention effect and individual differences. This model will allow time and group effects to be included as factors, and individual variation will also be considered. As this is a pilot study, the analysis will be exploratory and will not aim to test formal hypotheses with sufficient statistical power.
- Given the potential risk of reduced statistical power due to the limited sample size, alternative statistical methods, such as paired t-tests or Wilcoxon signed-rank tests, will be considered if necessary.

As there is insufficient power to draw definitive conclusions about the intervention's effect, the focus will be on identifying trends and possible effect sizes that can inform a future full-scale RCT.

4.2 Sensitivity and Secondary Analyses

Sensitivity analyses will be conducted to examine the robustness of the results, including handling missing data via multiple imputations. Additionally, an evaluation will be made to determine how deviations from the original inclusion criteria may have affected the results. Secondary exploratory analyses will investigate potential mediators and moderators of the intervention effect, such as baseline levels of binge eating, depressive symptoms, and diabetes-related distress, as well as individual characteristics (e.g., age and gender).

4.3 Handling of Missing Data

Missing data will be handled by multiple imputations under the assumption of missing at random (MAR). This will ensure that missing data do not introduce bias into the results. Imputation will be performed on the relevant variables, and both baseline and follow-up data will be included in the imputation model.