A Multicenter Randomized Controlled Trial comparing the Efficacy of Transanal Irrigation versus Standard Bowel Care in patients with Parkinson Disease and severe constipation. Impact on Gut Microbiome and Motor Disorders. TAI-PD Study.

Organization's Unique Protocol ID 187/2025/Disp/AOUFe

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Statistical aspects

Sample size calculation

We determined the sample size on the primary endpoint defined as the mean difference in the Cleveland Clinic (Wexner) constipation scale between treatment arms. A two-sided t-test has been considered for two independent samples according to the following parameters:

- A type I error probability of 0.05
- Overall power of 0.8

The literature evidenced that comparing TAI with CBM (Conservative Bowel Management or SBC) at the termination of the study, the mean (SD) scores were as follows: Cleveland Clinic constipation scoring system (range, 0-30, 30 = severe symptoms) was 10.3 versus 13.2 (SD=4.4), corresponding to a standardized effect size of 0.66 [33].

The achieved study size consists of 38 patients per study arm. Adjusting for a dropout of 20%, 94 patients will be included in the trial (47 per arm).

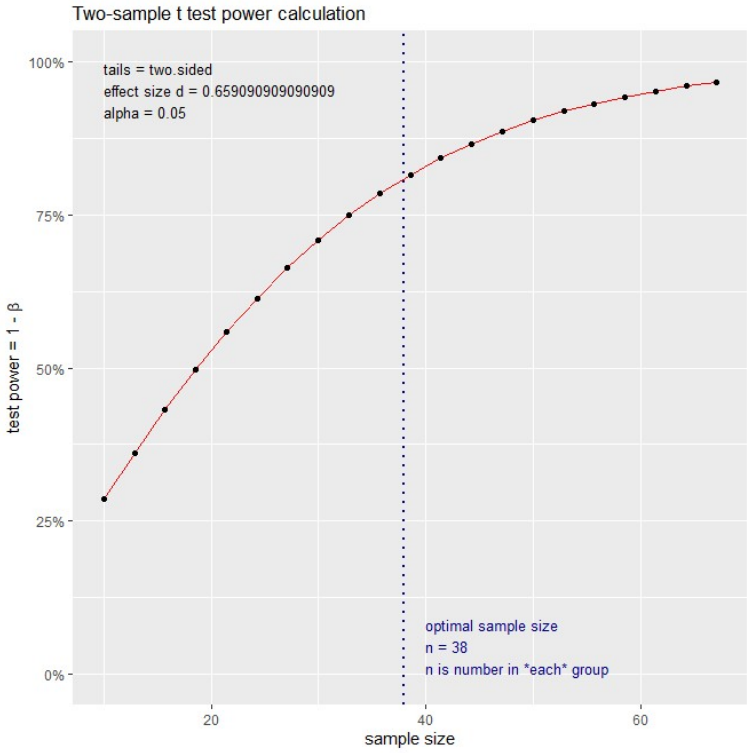


Figure 1 Statistical power according to sample size.

The computations have been performed using R 3.4.2 software and the package [34].

Statistical Analysis

Baseline data will be synthesized as median (I and III quartiles) for continuous variables and percentages (absolute numbers) for qualitative ones.

The primary efficacy analyses will consider mixed-effects models to assess the impact of TAI compared to SBC on the constipation scores among Parkinson's Disease patients. These models are adept at handling the complexities associated with repeated measures data, such as the correlation between observations taken from the same patient over time.

For binary outcomes, logistic regression models will be adapted to a mixed-model framework to evaluate changes in dichotomous outcomes across different time points. This will involve examining

the likelihood of achieving a specific clinical threshold, such as significant improvement in bowel symptom scores.

Regarding the gut microbiota data, the statistical approach will focus on changes in microbial diversity and composition due to the interventions. This analysis will be conducted using multivariate techniques suited for ecological data, such as Principal Coordinates Analysis (PCoA) to visualize differences and similarities in microbial communities. The statistical significance of these differences will be tested using permutation tests based on pseudo-F ratios. Moreover, to assess the relative abundance of different microbial taxa, the team will employ generalized linear mixed models, providing a way to account for the repeated measures structure of microbiota data.

Adjustments for multiple comparisons will be made using the Benjamini-Hochberg procedure to control the false discovery rate, ensuring the reliability of the conclusions drawn about the microbiome's role in the treatment effects observed.

The primary outcome will be evaluated on the Intent-to-Treat population ITT.

A significance level of 0.05 will be considered to perform the final inference. Analyses will be conducted with R 3.4.2 [34].