1 **The effect of high intensity interval training and surgical weight loss on distal symmetric**

2 **polyneuropathy outcomes.**

3 **July 2, 2025**

4 Statistical analysis

5 Our primary analysis was to determine the effect of HIIT and bariatric surgery on change in

6 IENFD of the proximal thigh during follow-up compared to the control group. Thus, the primary

7 covariate of interest was the interaction effect between follow-up time and treatment group.

8 Analysis of other outcomes was considered secondary analysis.

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10 Descriptive statistics were used to summarize participant demographic information at baseline.

11 Within participant change was reported for metabolic phenotyping and neuropathy outcomes.

12 For continuous variables, change was determined by subtracting baseline values from those at 2

13 year follow up visit. For categorical variables, change was determined as those that improved

14 from baseline to 2 year follow up visit. Paired t tests were used to compare within-participant

15 change for continuous variables and the Wilcoxon signed rank test was used to compare within-

16 participant change for ordinal categorical variables. Welch two sample t-tests (for continuous

17 variables) and Persons's chi-squared tests (for categorical variables) were used to compare the

18 within-participant change between each treatment and the no treatment group.

19 To account for non-compliance bias, the overall exercise compliance proportion was calculated

20 by adding the total compliant visits between baseline and the 2 year follow up visit and dividing

21 it by the total number of expected compliant visits in this period among those in HIIT

1   intervention group. Time varying compliance proportions specific to each follow up visit was

2   also calculated in a similar way by only considering the HIIT sessions occurring within each

3   follow up window. Compliance proportion was categorized into three groups: less than half a

4   session HIIT per week, less than one HIIT session per week and one or more HIIT session per

5   week. Compliance was assigned as zero for those not in HIIT intervention group.

6   Linear, poisson and zero inflation poisson mixed models were fitted to determine the effect of

7   each treatment with time on neuropathy outcomes. Since patients were not randomized to receive

8   surgery, we predicted the odds of receiving surgery using demographics and all models were

9   adjusted for this exposure. In addition, IENDF models were also adjusted separately for

10   circumferences at the biopsy locations. Sensitivity analysis was carried out to account for the

11   effect of exercise compliance on neuropathy outcomes. We carried out a couple of different

12   approaches: 1. Linear regression models to assess the association between treatment and within-

13   participant change in outcomes between baseline and 2-year visit. Exercise was modelled using

14   compliance proportions. 2. Linear, poisson and zero inflation poisson mixed models were rerun

15   separately using exercise compliance proportions as numerical and categorical variables. A two

16   tailed p-value with a cut-off of 0.05 was used to indicate statistical significance. All analyses

17   were completed using R version (4.4.3)