

Title: Are Today's Continuous Glucose Monitoring Precise and Can They be Used to Reveal and Reduce Glycaemic Variability?

NCT: NCT03842683

Date: August 31th 2018

APPENDIX 1: ANALYSIS PLAN

More of the investigation are of an exploratory and descriptive nature without use of treatment arm and the below information is therefore not always feasible to provide.

Endpoints: Difference between PG and IG. Number of Level 1 and 2 CGM hypoglycaemic events. Time in range of CGM and PG values. Sensitivity and specificity of different models.

Analysis Set: In an intention-to-“participate” manner all non-missing data will be used in these investigations. Imputation of missing values will in some cases be necessary, see below.

Statistical models: Difference analysis will be carried out using 2-sample t-tests or more advanced models such as ANOVA or MMRM with adjustment of sex, BMI, geographical region etc. where applicable. Machine learning approaches will include models such as Kernel SVM and neural networks with PCA, SEPCOR and forward selection for feature elimination.

Transformation of data: Transformations of data will be necessary to “fit” data into the machine learning models. For example, this will include splitting up data in training and evaluation data. If data are not normally distributed, logarithmic transformation may in most cases be performed.

Handling of missing data: Multiple imputation will be used when applicable, but for signal imputation, simpler methods will be used. For example, to get pairs of CGM and glucose meter data, linear interpolation of “missing” CGM data at the time points of glucose meter data may be applied.

Multiplicity issues: For multiple hypotheses testing simple Bonferroni corrections will be made to control the type 1 errors when applicable.