



## Statistical Analysis Plan

Study Code: UDDGait  
SAP Version: 1.0

Date: February 4th, 2020

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# Statistical Analysis Plan

Study Code: UDDGait

Study Title: UDDGait paper III

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SAP version: 1.0

Changes from last version: N/A

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## Introduction

The present statistical analysis plan (SAP) outlines statistical description and analysis for paper III from the UDDGait study (1). The paper will present data from the baseline and the follow-up at two years after baseline for patients with subjective cognitive impairment (SCI) or mild cognitive impairment (MCI) at baseline. Results will be compiled into a statistical report for which the output tables and figures are displayed in Table 3.

## Abbreviations and Variable List

### Abbreviations

CDT	Clock Drawing Test
UDDGait	Uppsala-Dalarna Dementia and Gait study
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
SAP	Statistical Analysis Plan
SCI	Subjective Cognitive Impairment
TUG	Timed Up and Go test

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## Variable List

Table 1. Variable list (all variables measured at baseline if not otherwise stated)

Variable (unit)	Variable scale <sup>1</sup>	Variable rôle	SAS name
Age (years)	C	Confounder	D005
Age group (<72 years/>=72 years)	D	Strata	AGEGR
Gender	D	Confounder	D006
Education (high/low)	D	Confounder	D008
Diagnoses at two years (dementia/non-dementia)	D	Outcome	F10C
MMSE	C	Confounder	D041
TUG single task, s	C	Predictor	D021
TUG dual task animals, s	C	Predictor	D023
TUG dual task animals, number of correct animals	C	Predictor	D024
TUG dual task cost animals, %	C	Predictor	D023C
TUG dual task animals, number of animals per 10s	C	Predictor	D023S
TUG dual task months, s	C	Predictor	D027
TUG dual task animals, number of correct months	C	Predictor	D028
TUG dual task costs months, %	C	Predictor	D027C
TUG dual task months, number of months per 10s	C	Predictor	D027S
Diagnoses (SCI/MCI)	D		D10GR4
Marital status	D		D007
CDT	C		D042
Word flow	C		D043
Bohannon's balance test	C		D050
Depression scale	C		D046
Height	C		D011
TMT A	D		D044
TMT B	D		D045
GMF help	C		D047
GMF pain	C		D048
GMF anxiety	C		D049
Hand grip	C		D051

<sup>1</sup>C = continuous variable, D = dichotomous variable.

## Study Objectives and Endpoints

### Objectives

#### Primary Objectives

The primary objective is to investigate if dual task variables are associated with incident dementia from baseline to follow-up after two years for patients with subjective cognitive impairment (SCI) or mild cognitive impairment (MCI) at baseline, unadjusted and adjusted for age, gender, education level and Mini Mental State Examination (MMSE). Further, this objective will be examined in younger (< 72 years) and older (>= 72 years) patients.

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## ***Endpoint***

### **Primary Endpoint**

The primary endpoint is the dichotomous variable diagnoses of dementia *vs.* non-dementia at the two years follow-up.

## **Study Design**

The study design is prospective longitudinal.

## **Definition of Analysis Population**

The study population to be analysed consists of the study patients with diagnoses SCI or MCI at baseline and for whom a dementia diagnosis could be determined at two years after baseline.

## **Statistical Description and Analysis**

### ***Derived variables***

The measures “animals/10 s” and “months/10 s” were calculated as  $10^*(\text{TUGdt number of words}/\text{TUGdt time score})$ . Dual-task cost, i.e. the relative time difference between TUGst and TUGdt, was calculated as  $100^*(\text{TUGdt time score} - \text{TUGst time score})/\text{TUGst time score}$ .

### ***Baseline Characteristics***

All baseline variables in Table 1 will be summarized for the whole study population and by incident dementia (yes/no) at two years follow-up. Further, all baseline variables in Table 1 will be summarized by younger (< 72 years) and older ( $\geq 72$  years) patients for the whole age stratum and by incident dementia (yes/no) at two years follow-up. The continuous variables will be described with number of observations, number of missing observations, mean, standard deviation, median and minimum and maximum values. Dichotomous and categorical variables will be described with numbers, number of missing observations, and percentages.

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## **Primary Analyses**

All statistical tests and confidence intervals are two-sided (where applicable) and the region  $p < 0.05$  is used to declare a statistically significant result. No adjustments for multiple tests will be made. No imputations of missing data will be made.

## **Estimated Effects**

The aims of the analyses of the primary and secondary endpoints will be investigated with estimated logistic regression models. The results from the models will be presented, for each continuous predictor, as estimated odds ratios, with 95 % confidence intervals, of a one standard deviation impaired change of the predictor, and a p value for test of the null hypothesis that the true odds ratio is unity. Impaired changes imply that for the time scores of TUG single task, s, TUG dual task animals, s TUG dual task months, s as well as TUG dual task cost animals, %, and TUG dual task cost months, %, the ORs express the risk increase per one standard deviation *increase* of the variable. Whereas for the number of animals and number of months, as well as “animals/10 s” and “months/10 s” the ORs express the risk increase per one standard deviation *decrease* of the variable.

Logistic regressions will be estimated univariate for each TUG variable and with adjustment for age, gender, education and MMSE.

## **Logistic Regression Models**

The logistic regression models to be estimated are shown in Table 2.

**Table 2. Logistic regression models**

Objective	Outcome(s)	Predictors
Primary	Incident dementia	Each dual task predictor individually
Primary	Incident dementia	Each dual task predictor individually, and age, gender, education and MMSE
Primary	Incident dementia	Each dual task predictor individually stratified by age groups < 72 years and $\geq 72$ years
Primary	Incident dementia	Each dual task predictor individually and age, gender, education and MMSE stratified by age groups < 72 years and $\geq 72$ years

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## **Receiving Operator Characteristics Curves**

Results from the models will be presented with estimated effects and 95 % confidence intervals and p values.

Predictive capacity for each TUG variable will be illustrated with receiving operator characteristics (ROC) curves and c statistics (areas under ROC curves). These curves will be presented univariate and with the incremental effect of the TUG variable over a model with age, gender, education and MMSE.

The above described analyses will also be presented stratified by age groups < 72 years and  $\geq 72$  years.

## ***Output Shell***

In the following table the names and contents of output tables and figures are displayed.

**Table 3. Output shell**

Table	Content
Table 1a	Descriptive table for all variables, in total and by incident dementia (yes/no)
Table 1b	Descriptive table for all variables, in total and by incident dementia (yes/no) stratified by age groups < 72 years and $\geq 72$ years
Table 2	Results of logistic regression models in SAP Table 2
Figure 1.1-1.9	ROC curve for each TUG variable
Figure 2.2-2.9	ROC curve for the incremental predictive capacity for each TUG variable over the model with age, gender, education and MMSE
Figure 3.1-3.9	ROC curve for each TUG variable stratified by age groups < 72 years and $\geq 72$ years
Figure 4.1-4.9	ROC curve for the incremental predictive capacity for each TUG variable over the model with age, gender, education and MMSE stratified by age groups < 72 years and $\geq 72$ years

## **References**

1. Project plan UDDGait

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