

## Appendix 1

All secondary study parameters are listed below, along with a description of the questionnaires/ instruments that will be used for their assessment.

### General disease information:

- Disease severity: see motor symptoms.
- Disease stage: will be established with the Hoehn & Yahr scale. This is a 0 to 5 scale: “asymptomatic (score 0)”, “only unilateral involvement (score 1)”, “bilateral involvement without impairment of balance (score 2)”, “light to mild bilateral involvement, some postural instability and physically independent (score 3)”, “severe disability, still able to walk independent (score 4)”, and “wheelchair or bed bounded without help (score 5)”, in which a higher number means a more developed disease stage<sup>1</sup>.
- Levodopa equivalent daily dosage (LEDD): this is, according to Tomlinson, a “summation of each individual antiparkinsonian drug aligned to 100mg immediate release L-dopa, by means of individual conversion factors”<sup>2,3</sup>.
- Presynaptic dopaminergic loss: will be analysed by means of DAT-SPECT, when applicable.

### Motor symptoms:

- Motor symptoms: will be analysed with the Movement Disorder Society Unified Parkinson Disease Rating Scale III (MDS-UPDRS III)<sup>4</sup>. This involves an examination of motor function, performed by an examiner (e.g., neurologist, trained nurse, or trained research assistant). The patient has to complete 18 motoric tasks. Subsequently, the examiner scores the tasks from 0 till 4: “normal (score 0)”, “slight (score 1)”, “mild (score 2)”, “moderate (score 3)”, and “severe (score 4)” motor problems for that specific part. Finally, a summation of each individual task is established, after that a classification can be made: “mild (score  $\leq$  32)”, “moderate (score 33-58)”, and “severe (score  $\geq$  59)” motor problems<sup>5</sup>.

### Non-motor symptoms:

- Anxiety: will be registered through the Parkinson Anxiety Scale (PAS)<sup>6</sup>. The PAS consists of 3 questionnaires (persistent anxiety, episodic anxiety, and avoidance behavior), with in total 12 questions. There are 5 response options, scored as 0 till 4: “never (score 0)”, “occasionally (score 1)”, “sometimes (score 2)”, “frequently (score 3)”, and “always (score 4)”. Afterwards, 4 groups can be made: “generalized anxiety disorder (score  $\geq$  11 on that subscale)”, “episodic anxiety (score  $\geq$  6 on that subscale)”, “avoidance behavior (score  $\geq$  5 on that subscale)”, and “any anxiety disorder score (score  $\geq$  14)”.
- Apathy: will be measured by means of the apathy evaluation scale (AES)<sup>7</sup>. This scale has 14 statements, with 4 response options: “not at all (score 0)”, “slightly (score 1)”, “somewhat (score 2)”, and “a lot (score 3)”. A total sum score of 42 can be reached. When a higher score is reached, apathy plays a bigger role. The cut off point for “high apathy score” is 14 points.
- Cognitive function: will be analysed by means of the Montreal Cognitive Assessment (MoCA)<sup>8,9</sup> and the Parkinson’s Disease Cognitive Functional Rating Scale, (PD-CFRS)<sup>10,11</sup>. The MoCA is a screening instrument for cognitive dysfunctions on different aspects, such as memory or language, which exist of 11 items in 8 different domains. The examiner (e.g., neurologist, trained nurse, or trained research assistant). scores

each item individually. A sum score of 30 can be reached, wherein a score of 26 or above represents a normal cognitive function and a score above 21 represents a mild cognitive impairment. The PD-CFRS exists of 12 questions with four response options, scored as follows: “No (score 0)”, “Sometimes (score 1)”, “A lot (score 2)” and “not applicable”. All questions answered with “not applicable” will be scored with the mean of all the other questions. A total score of 0-24 can be reached, a higher score means more cognitive problems. The total score will be used.

- **Depression:** will be registered through the Beck Depression Inventory (BDI-II)<sup>12,13,14</sup>. The BDI-II exists of 21 questions with four response options, scored as 0 till 4 (for example: “I do not feel sad”, “I feel sad much of the time”, “I am sad the whole time”, and “I am sad or so unhappy that I can’t stand it”). A maximum of 63 points can be assembled. Afterwards, 4 groups can be made: “none or minimal (score 0-13)”, “light (score 14-19)”, “moderate (score 20-28)”, and “severe (score 29-63)” depressive symptoms.
- **Impulsive-compulsive behavior:** will be analysed by means of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease-Rating Scale (QUIP-RS)<sup>15</sup>. This questionnaire has 7 subscales and in total 28 questions, with 5 response options scored 0 till 4: “never (score 0)”, “occasionally (score 1)”, “sometimes (score 2)”, “frequently (score 3)”, and “a lot (score 4)”. For a combined impulse control disorder, 4 subscales are combined. A total sum score of 64 can be reached, a higher score indicating more impulsive-compulsive behavior. When 10 points or above are registered, an impulse control disorder is present.
- **Psychosis:** will be measured by means of Parkinson’s disease-adapted scale for assessment of positive symptoms (SAPS-PD)<sup>16</sup>. This 9-item observer-rated scale is scored from 0 till 5: “none (score 0)”, “possible (score 1)”, “mild (score 2)”, “mediocre (score 3)”, “explicit (score 4)”, and “severe (score 5)”, including a part about hallucinations and a part about disillusion. A higher sum score means a probable presence of psychosis. The total score will be used.
- **Quality of sleep:** is analysed by means of two types of questionnaires that are used in this study to assess this construct. The STOP-BANG-NL<sup>17</sup> questionnaire that screens for the risk for moderate to severe obstructive sleep apnea (OSA), and the Scales for Outcomes PD Sleep (SCOPA-sleep)<sup>18</sup> that screens for quality of sleep during the night and sleepiness during the day. The STOP-BANG-NL consists of 8 questions, with 2 response options: yes (score 1) and no (score 0). The total score ranges from 0-8, a classification can be made: “low risk for OSA (score < 3)”, “intermediate risk (score 3-4)” and “severe risk for OSA (≥ 5)”<sup>17</sup>. The SCOPA-Sleep questionnaire consists of 6 questions about daytime sleepiness, with 4 response options scored from 0 till 3: “never (score 0)”, “sometimes (score 1)”, “frequently (score 2)”, and “a lot (score 3)”, and 5 questions about night time sleep, with 4 response options scored from 0 till 3: “not at all (score 0)”, “somewhat (score 1)”, “quite (score 2)”, and “a lot (score 3)”. A higher score means more daytime sleepiness and/or more nighttime sleep problems.

**Oral health and dysfunction:**

- **Reflux:** will be analysed with the Gastroesophageal Reflux Disease Questionnaire (GERD-Q NL)<sup>19</sup>. This is a self-administered questionnaire with 4 graded Likert scales scored from 0-3 for predictors of GERD, and 2

reverse Likert scales scored from 3-0 for negative predictors of GERD. The response options are as follows: "0 days (score 0 or 3)", "1 day (score 1 or 2)", "2-3 days (score 2 or 1)", and "4-7 days (score 3 or 0)" dependent on a (reverse) likert scale. When a score of  $\geq 8$  is reached, there is a suspicion for GERD.

- **Saliva:** based on the Saliva Check Buffer® (GC EUROPE N.V), the quantity and quality (pH and buffer capacity) of saliva will be screened<sup>20</sup>. The buffer capacity stands for the capability of saliva to neutralize the environment of the mouth. Both saliva in rest and saliva that is stimulated during chewing will be investigated. An overview of the normal values is given in appendix 3. Additionally, in the clinical examination, a dry mouth screening by means of the Clinical Oral Dryness Score (CODS) will be performed, which includes a 10-item observer-rated dichotomous outcome questionnaire: "present (score 1)" and "absent (score 0)". When a summation is performed, the following cut-off points are applicable: "mild dryness (score 0-3)", "moderate dryness (score 4-6)", and "severe dryness (score >6)".
- **TMD-pain intensity:** will be analysed with the use of the Graded Chronic Pain Scale (GCPS)<sup>21</sup>. This is a 7-item questionnaire. Six items have an ordinal scale from 0 till 10, in which 0 stands for "no pain" and 10 for "the worst pain ever". Additionally, the amount of days that were disabling because of the pain in the last 30 days are noted. When scoring, 5 classifications can be made: "no pain (grade 0)", "low disability, low intensity (grade 1)", "low disability, high intensity (grade 2)", "high disability, moderately limiting (grade 3)", and "high disability-severely limiting (grade 4)".
- **Tooth Wear:** will be analysed with the screening module of the Tooth Wear Screening Index (TWES)<sup>22</sup> that quantifies the amount of tooth wear in 6 sextants of the mouth (right side, front, and left side of the upper jaw and the lower jaw) from 0 till 4: "no wear (score 0)", "visible wear within the enamel (score 1)", "visible wear with dentin exposure and loss of clinical crown height of  $\leq 1/3$  (score 2)", "loss of crown height  $>1/3$  but  $<2/3$  (score 3)" and "loss of crown height  $\geq 2/3$  (score 4)"<sup>23</sup>. Additionally, the palatal side of the upper front is also graded from 0 till 2: "no tooth wear (score 0)", "tooth wear confined to the enamel (score 1)", and "tooth wear with dentin exposure (score 2)". All numbers are scored per tooth and are not summed. The highest number will be used for analysis.

#### Miscellaneous:

- **Lifestyle factors (smoking, alcohol, drugs):** will be gathered by means of self-report in the standard-care questionnaire of the VUmc. Use of alcohol is noted as units per week. In case of smoking and use of drugs will be both quantified as a nominal variable (participants do (not) smoke and/or use drugs).
- **Quality of life:** will be analysed with the Parkinson's Disease Questionnaire – 8 (PDQ-8)<sup>24</sup>, by means of 8 questions about quality of life regarding PD. Participants can answer at an ordinal 5-item scale, with scores from 0 till 4: "Never (score 0)", "Occasionally (score 1)", "Sometimes (score 2)", "Often (score 3)", and "Always (score 4)". A score from 0 till 32 can be reached. When a higher score is applicable, poor health-related quality of life is present. The total score will be used.
- **Somatic symptoms:** will be analysed with the Patient Health Questionnaire – 15 (PHQ15)<sup>25</sup>. Severity of somatization is evaluated by means of 13 questions about somatic symptoms divided in 3 subscales, with scores 0 till 2: "not at all (score 0)", "bothered a little (score 1)", and "bothered a lot (score 2)". Additionally, two questions about sleep and tiredness are present, which are also divided in 3 subscales

with scores 0 till 2: “not at all (score 0)”, “several days (score 1)”, and “more than half of the days/nearly every day (score 2)”. Scores of 0, 5, and 15 are the cut-off points for “low”, “median”, and “high somatic symptom severity”, respectively.

## Appendix 2

The following formula was used for the sample size calculation:

$$n = (Z^2P(1-P))/d^2$$

Z = Z statistic for a level of confidence

P = expected prevalence or proportion (in proportion of one)

d = precision

For the level of confidence of 95%, Z value is 1.96.

With an assumed prevalence of 46% (WB according pilot study), P is 0.46

With a precision of +/-5 percentage points (0.05), d should be set at 0.05.

The numbers for the secondary aims are obtained when reaching the sample size for the primary aim. The approach for the sample size calculation of the secondary aims are as follows:

Since no clinical data of the variables that will be studied are available yet in a population with PD, an effect size is not known for our outcome measures. Nevertheless, in a recent questionnaire-based study, an association between PD on the one hand and bruxism and TMD pain on the other was reported<sup>26</sup>. The prevalence found for these outcome measures were 46.0%, 24.3%, and 29.5% for awake bruxism, sleep bruxism, and TMD pain, respectively. In the current study, a total of 6 independent categorized variables (see Table 4) will be analysed to determine if they are associated with the presence of probable and definite bruxism and/or TMD pain in patients with PD, by means of logistic and linear regression analyses (see statistical approach). We assume that only four predictors will be eligible for multivariate analysis, because (i) only predictors with the strongest associations are included, and (ii) predictors will drop out due to their probable association with each other. The literature about numbers of observations in participants per variable (events) in a logistic regression analysis indicated that for each predictor in a regression analysis, data from 10-20 events is needed<sup>27</sup>. Consequently, 15 events are chosen and thus (4x15=) 60 events are needed. Based on the prevalence of the recent questionnaire-based pilot study<sup>26</sup>, a minimum of 130 participants (60 events/0.46 (= prevalence of awake bruxism)) and a maximum of 246 participants (60 events/0.243 (=prevalence of sleep bruxism)) are needed<sup>26</sup>. For the linear regression, this estimate of the sample size is sufficient to detect medium and large effect sizes<sup>28</sup>. Because this is a wide range, an interim analysis will be done after the inclusion of at least 130 participants or a maximum of 6 months.

### Appendix 3

Cut off points for Saliva Check Buffer (GC EUROPE N.V), to determine whether the quantity and composition of saliva deviate from normal values.

Saliva type	Volume (ml)	interpretation	pH	interpretation	Buffercapacity	Interpretation
During rest	1. >0.50	1. Hypersalivation	1. >7.5	1. Abnormal	1. 10-12	1. Normal/high
	2. 0.50-0.25	2. Normal	2. 7.5-6.8	2. Normal	2. 6-9	2. Low
	3. 0.24-0.10	3. Risk	3. 6.7-6.5	3. Risk	3. 0.5	3. Very low
	4. <0.10	4. Pathologic	4. <6.5	4. Pathologic		
During chewing	1. >2.00	1. Hypersalivation	1. >8.0	1. Abnormal	1. 10-12	1. Normal/high
	2. 2.00-0.75	2. Normal	2. 8.0-7.0	2. Normal	2. 6-9	2. Low
	3. 0.74-0.50	3. Risk	3. 6.9-6.5	3. Risk	3. 0-5	3. Very low
	4. <0.50	4. Pathologic	4. <6.5	4. Pathologic		

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