**PROBAST**

Study:

Combined accelerometer and genetic analysis to differentiate essential tremor from Parkinson’s disease

Step 2: Type of prediction study

**Is the study a diagnostic or a prognostic study?**

**Diagnostic**

**Is the study a development only, development and validation or validation only study?**

**Development only**

**What is the model of interest?**

Linear model

**What is the outcome of interest?**

Differentiate PD and ET

Step 3: Assess risk of bias

**Domain 1: Participants**

**Describe the sources of data and criteria for participant selection**

Inclusion criteria for the study were an established clinical diagnosis of PD or ET, ability to provide informed consent, and willingness to have a blood draw. Exclusion criteria included: (1) presence of dementia, (2) presence of other known neurological disorders besides PD or ET, or (3) history of bone marrow transplant.

**1.1 Were appropriate data sources used, e.g. cohort, RCT or nested case-control study data?**

**Y**

**1.2 Were all inclusions and exclusions of participants appropriate?**

Y

**Risk of bias introduced by selection of participants:**

Low

**Rationale of bias rating**

Proper inclusion and exclusion criteria

**Domain 2: Predictors**

**List and describe predictors included in the final model, e.g. definition and timing of assessment**

Participants were asked to wear the smart-watch on their tremor dominant hand, and keep the smartphone in their possession, at all waking hours of the day for a period of two weeks to avoid any disconnections. Participants were also given the contact information of our research coordinator, and IT helpdesk to assist with repairing of devices in case of any failures. Since, some of our participants were older and not very tech savvy, we also monitored their daily gameplays, and contacted them if we noticed missing data for consecutive 2 to 3 days.

Participants were asked to perform a cognitive attention task, which also initiated the collection of raw accelerometer data, three times a day; (1) upon waking in the morning prior to consuming medication, (2) in the afternoon 1 h after consuming medication, or at1 PM if not medicated, and (3) in the evening, immediately prior to sleep.

**2.1 Were predictors defined and assessed in a similar way for all participants?**

Y

**2.2 Were predictor assessments made without knowledge of outcome data?**

Y

**2.3 Are all predictors available at the time the model intended to be used?**

Y

**Risk of bias introduced by predictors or their assessment**

Low

**Rationale of bias rating**

**Domain 3: Outcome**

**Describe the outcome, how it was defined and determined, and the time interval between predictor assessment and outcome determination:**

PD vs ET. Determined via medical diagnosis.

**3.1 Was the outcome determined appropriately?**

Y

**3.2 Was a pre-specified or standard outcome definition used?**

Y

**3.3 Were predictors excluded from the outcome definition?**

Y

**3.4 Was the outcome defined and determined in a similar way for all participants?**

Y

**3.5 Was the outcome determined without knowledge of predictor information?**

Y

**3.6 Was the time interval between predictor assessment and outcome determination appropriate?**

Y

**Risk of bias introduced by the outcome or its determination**

L

**Rationale of bias rating**

Medical diagnosis for PD and ET. Reliable labeling.

**Domain 4: Analysis**

**Describe number of participants, number of candidate predictors, outcome events and events per candidate predictor**

Initially, 40 subjects with PD and 27 patients with ET were recruited for the study. Movement data collection failed for three ET subjects and seven PD subjects leaving a final cohort of 33 subjects with a diagnosis of PD and24 subjects with a diagnosis of ET.

**Describe how the model was developed, predictor selection and risk group definition**

**Describe whether and how the model was validated, either internally (cross validation, random split sample) or externally (e.g. temporal validation, geographical validation, different setting, different type of participants)**

Not described

**Describe the performance measures of the model, e.g. calibration, discrimination, classification, net benefit, and whether they were adjusted for optimism**

AUC, SEN, SPE, R2, P

**Describe any participants who were excluded from the analysis**

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**Describe missing data on predictors and outcomes as well as methods used for missing data**

Not described

**4.1 Were there a reasonable number of participants with the outcome?**

N

**4.2 Were continuous and categorical predictors handled appropriately?**

Y

**4.3 Were all enrolled participants included in the analysis?**

N

**4.4 Were participants with missing data handled appropriately?**

U

**4.5 Was selection of predictors based on univariable analysis avoided?**

Y

**4.6 Were complexities in the data (e.g. censoring, competing risks, sampling of controls)**

**accounted for appropriately?**

Y

**4.7 Were relevant model performance measures evaluated appropriately?**

Y

**4.8 Were model overfitting and optimism in model performance accounted for?**

N

**4.9 Do predictors and their assigned weights in the final model correspond to the results**

**from multivariable analysis?**

Y

**Risk of bias introduced by the analysis**

High

**Rationale of bias rating**

Little outcomes, validation approach not described. Unclear how missing data were handled

**Overall Risk of bias**

High