**PROBAST**

Study:

Towards Wearable-based Hypoglycemia Detection and Warning in Diabetes

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?**

Gradient boosting

**What is the outcome of interest?**

Hypoglycemia detection

Step 3: Assess risk of bias

**Domain 1: Participants**

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

We conducted a proof-of-concept study with one otherwise healthy individual with T1DM.

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

N

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

Y

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

High

**Rationale of bias rating**

Pilot study with only one patient. High risk and low generalizability

**Domain 2: Predictors**

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

Heart rate variability from wearable

**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**

Independent of outcome and applicable

**Domain 3: Outcome**

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

The model input are the heart rate and HRV features and the classification task is defined as a binary decision between normal BG levels (negative) and hypoglycemia (positive). For our analysis, we define hypoglycemia as observations with a BG level of <3.9mmol/L

**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**

Low

**Rationale of bias rating**

Standard hypoglycemia outcome.

**Domain 4: Analysis**

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

1 patient. The data cleaning and pre-processing resulted in a total of 74,552 obser-vations of which 15,168 (20.4%) belong to the positive class (hypoglycemia).

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

Gradient boosting decision tree

**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 well described. Simple train-test split likely.

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

AUC, ACC, Sen, Spe

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

None

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

BG measurements were re-sampled by piece-wise linear interpolation to match the frequency of physiological data.

**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?**

Y

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

Y

**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**

Only one patient. Validation approach unclear.

**Overall Risk of bias**

High