# SUPPLEMENTARY MATERIAL

Figure S1: Each plot shows instability of calibration curves for 1000 example models developed using a particular sample size (100, 200, 500, 888, 1000 or 5000) when each model is applied to the same population of 100000 individuals: each example model was produced from a logistic regression (LR) with either a full model with no penalisation ('unshrunk LR'), a full model followed by a uniform shrinkage ('shrunken LR'), or with a LASSO penalty fitted to a different random sample of individuals from a population with a true overall risk of 0.5, based on a true model with a linear prediction of LP = 0.5X1+0.3X2+0.3X3+0.25X4+0.25X5 + 0(Z1+…+Z10) where X1, …, X5~N(0,1) and 10 noise variables (Z1, …, Z10 ~ N(0,1)).

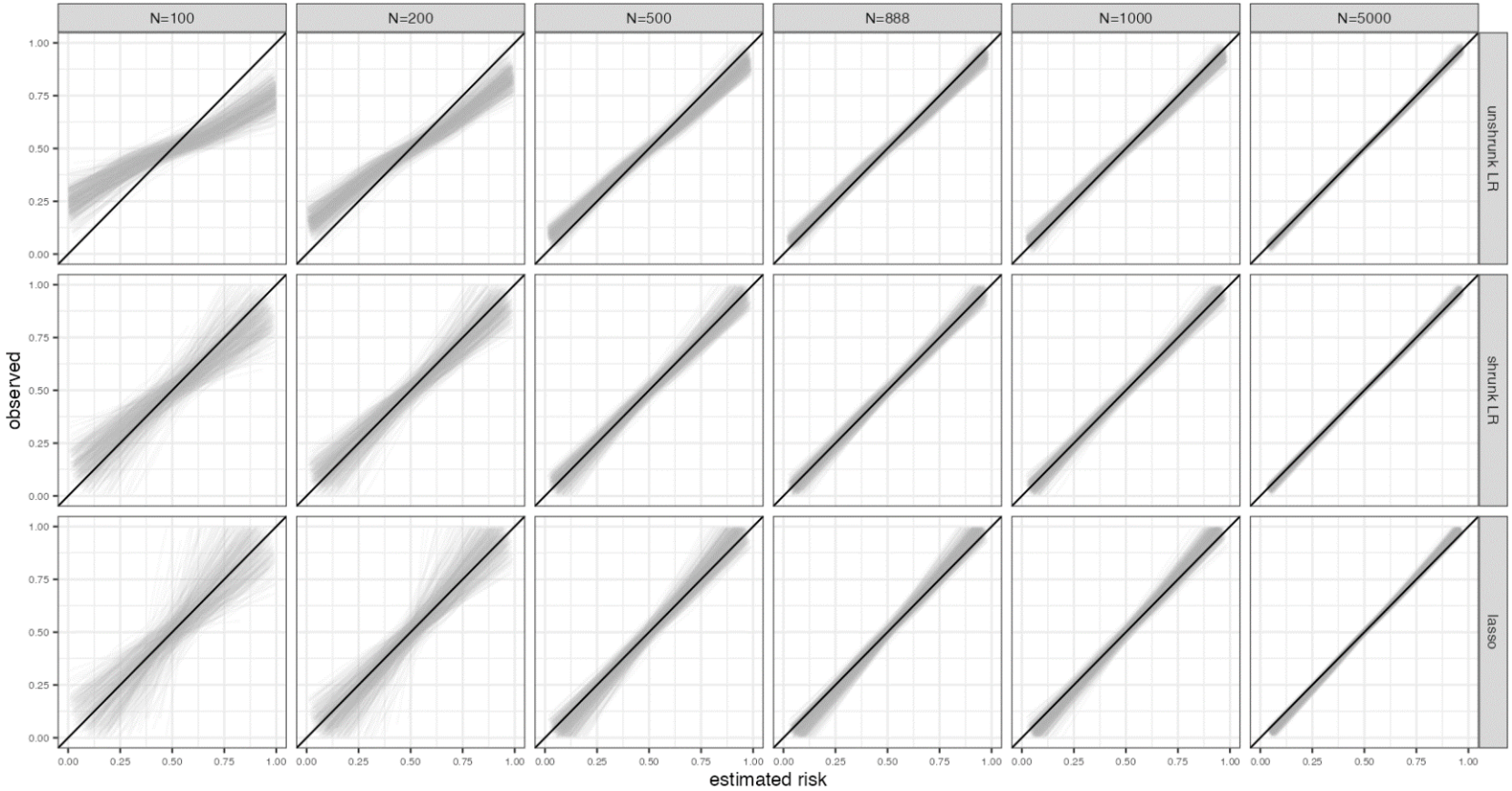


**Figure S2: Instability plots and measures for three prediction models developed using 752 participants (53 events) and 7 candidate predictors (see Sections 4.3 and 4.4)**

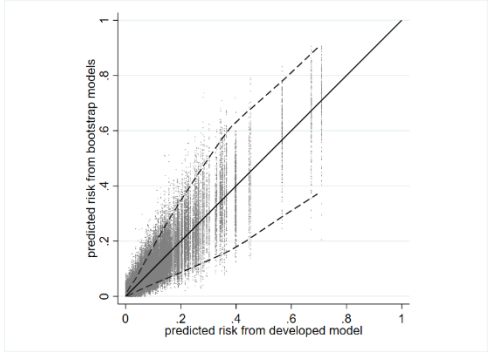
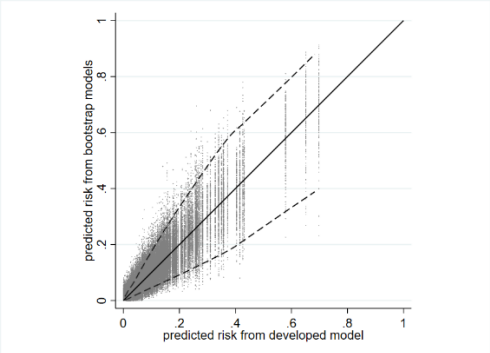
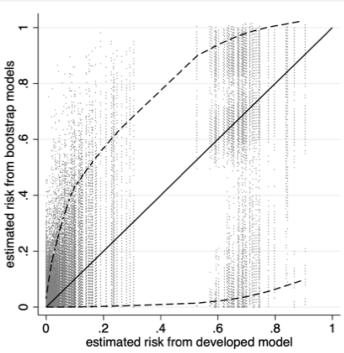
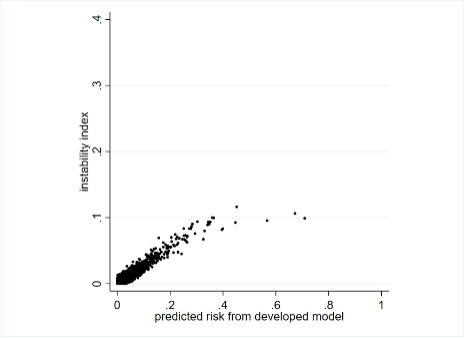
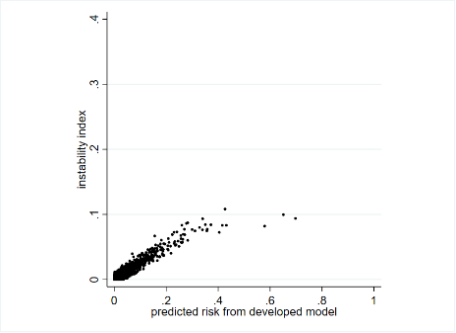
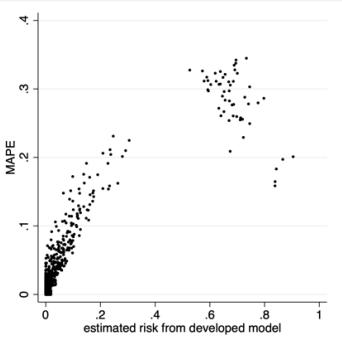
| | (a) logistic regression with LASSO | (a) unpenalised logistic regression followed by uniform shrinkage of predictor effects | (c) Random forest (100 trees, unlimited depth) |
|---|---|---|---|
| **Prediction instability plot** |  |  |  |
| **MAPE instability plot** |  |  |  |
| **Average MAPE** | 0.019 | 0.018 | 0.047 |

Figure S3: Instability plots and measures for a prediction model developed using random forest (7 predictors) in 752 participants, using a variety of hyperparameter tuning options of (a) software defaults, (b) defaults but with tree depth of 3, and (c) allowing tuning to be tailored

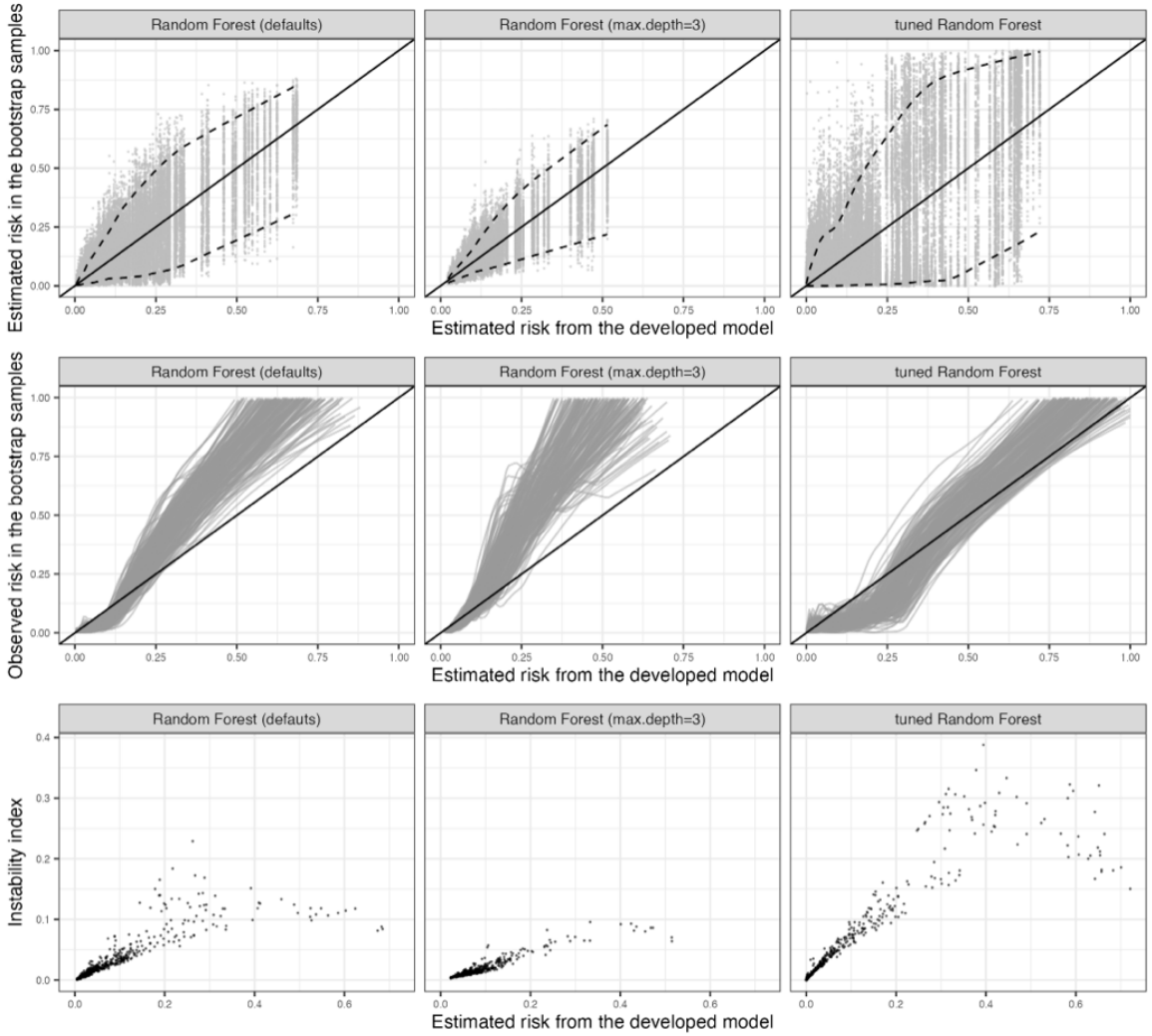
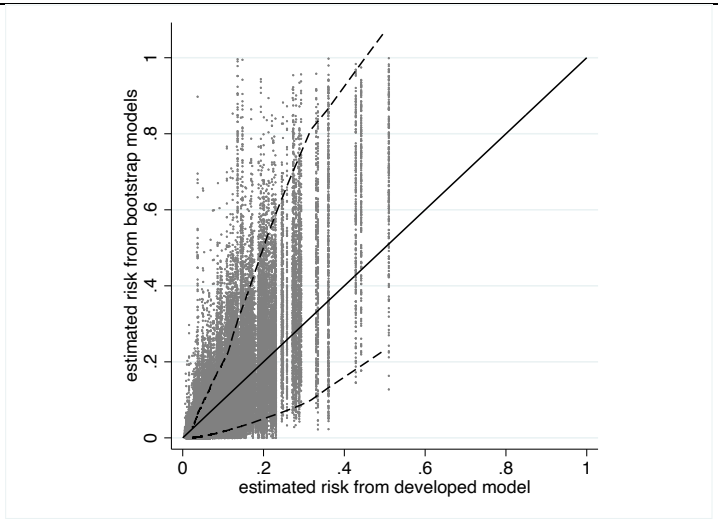
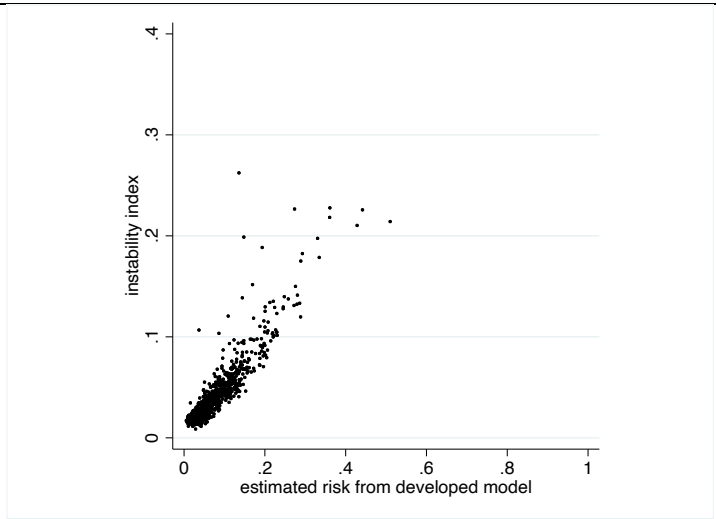


**Figure S4: Instability plots and measures for a prediction model developed using random forest (7 predictors, 100 trees, depth 3) in 452 participants, followed by recalibration in 300 participants**

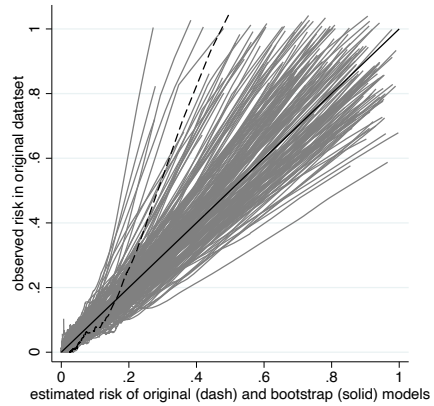
Prediction instability plot




MAPE (mean 0.045)




Calibration instability plot




Calibration instability plot when using all 752 participants for model development without recalibration

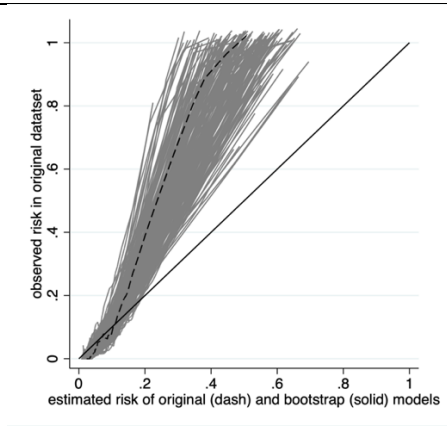


**Figure S5: Instability plots and measures to examine fairness of a LASSO prediction model in males and females separately (see Section 5.1)**

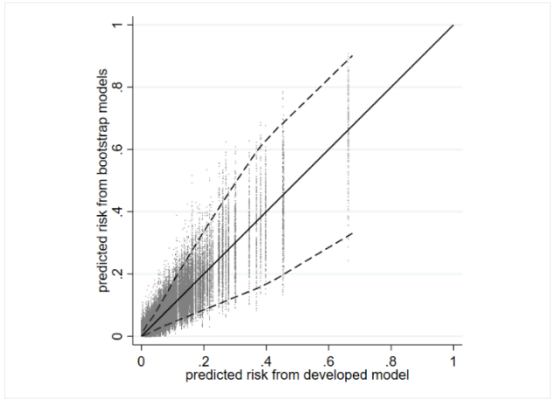
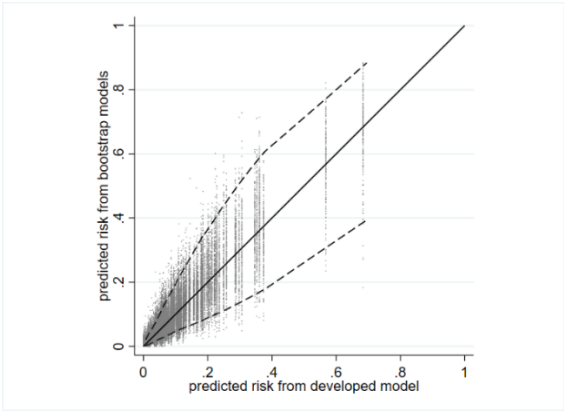
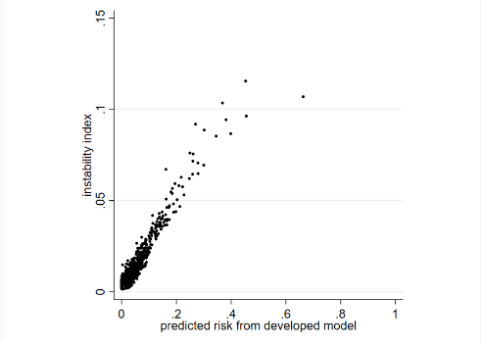
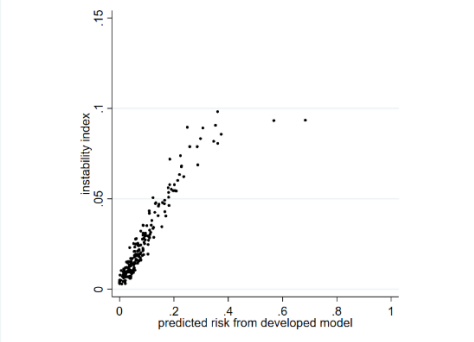
| | Males | Females |
|---|---|---|
| **Prediction instability plot** |  |  |
| **MAPE instability plot** |  |  |
| **Average MAPE** | 0.017 | 0.027 |

**Figure S6: Histogram of C-statistics from applying the LASSO model in Section 5.2 to the bootstrap samples**

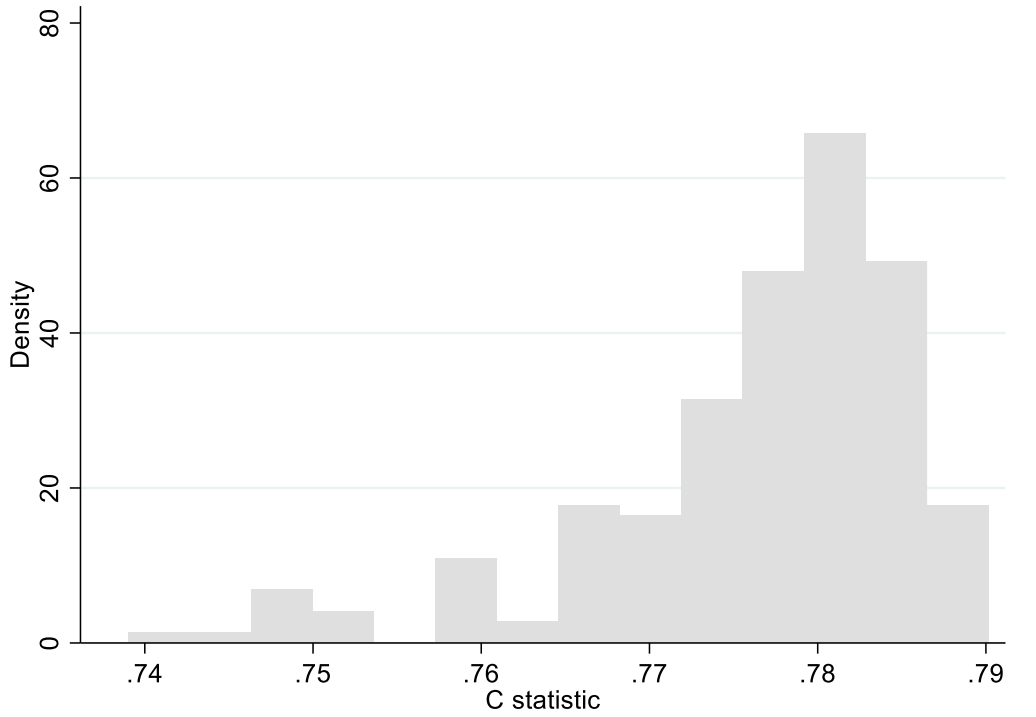
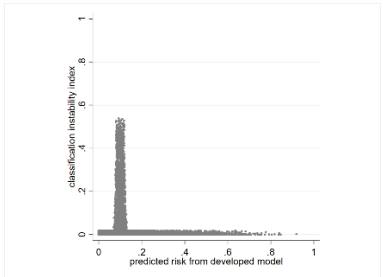
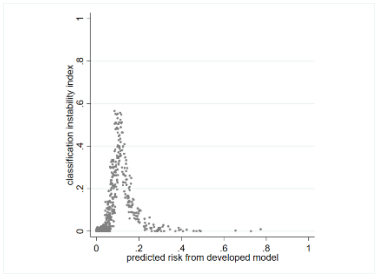
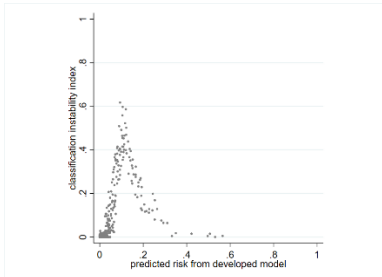
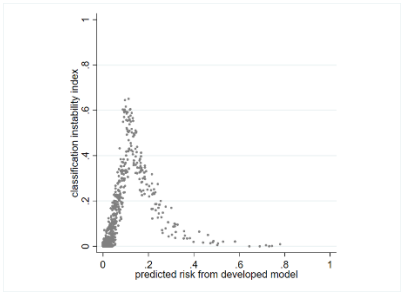
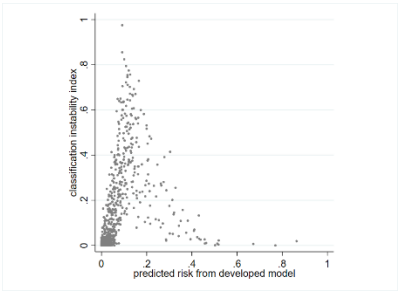
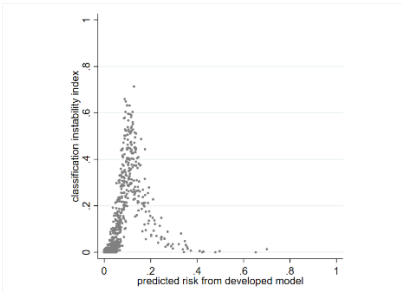
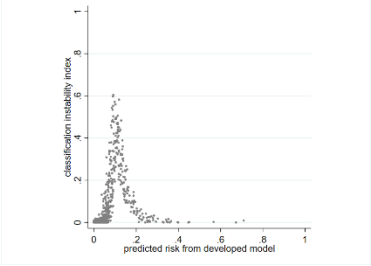
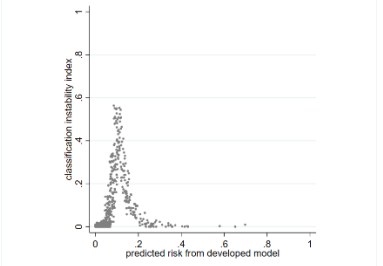
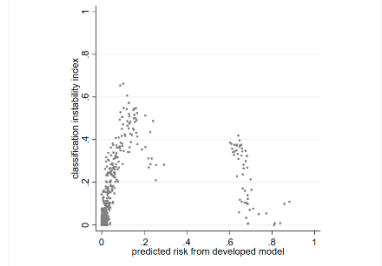
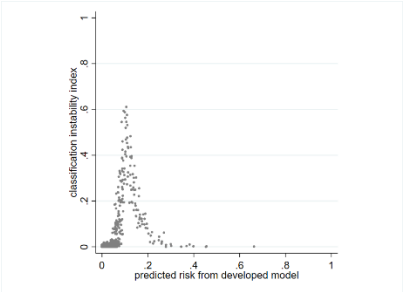
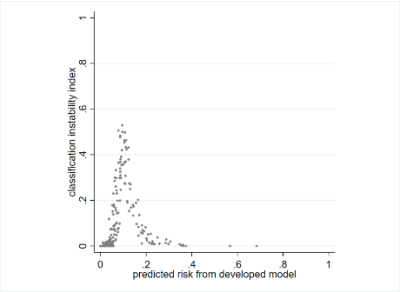


**Figure S7: Classification instability plots for various models from the case studies of Section 4.**

| | | |
|---|---|---|
| **Large sample size**<br>40830 patients, 2851 events<br>7 predictor parameters | **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters | **Small sample size**<br>300 patients 21 events<br>7 predictor parameters |
|  |  |  |
| 752 patients, 53 events<br>7 predictor + 20 noise<br>Force all predictors in | 752 patients, 53 events<br>7 predictor + 20 noise<br>Backwards selection | 752 patients, 53 events<br>7 predictor + 20 noise<br>LASSO |
|  |  |  |
| **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters<br>LASSO | **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters<br>Uniform | **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters<br>Random forest |
|  |  |  |

| **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters<br>LASSO - males | **Minimum recommended**<br>752 patients, 53 events<br>7 predictor parameters<br>LASSO - females | |
|---|---|---|
|  |  | |