Medical Risk Prediction Models

With Ties To Machine Learning

In memory of my very good friend Michael W Kattan

Outline [1]

- Why should I care about statistical prediction models?
- I am going to make a prediction model. What do I need to know?
- How should I prepare for modeling?
- I am ready to build a prediction model
- Does my model predict accurately?
- How do I decide between rival models?
- What would make me an expert?
- Can't the computer just take care of all of this?

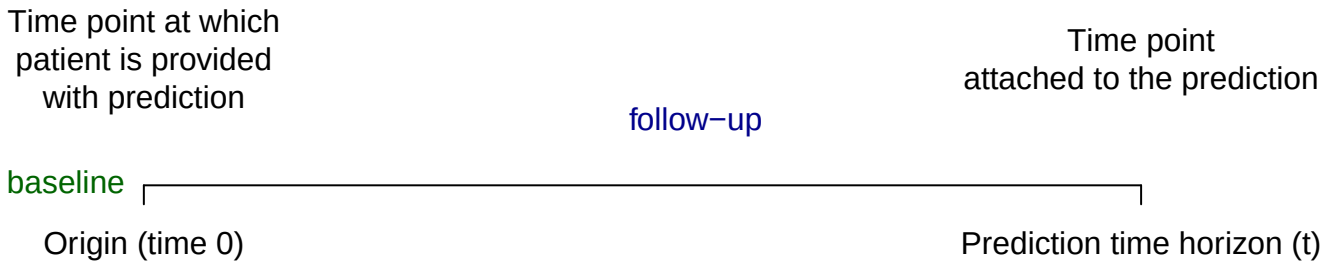
[1] Medical risk prediction models: with ties to machine learning. Chapman and Hall/CRC, 2021.

Right on

The only useful function of a statistician is to make predictions, and thus to provide a basis for action – W. Edwards Deming

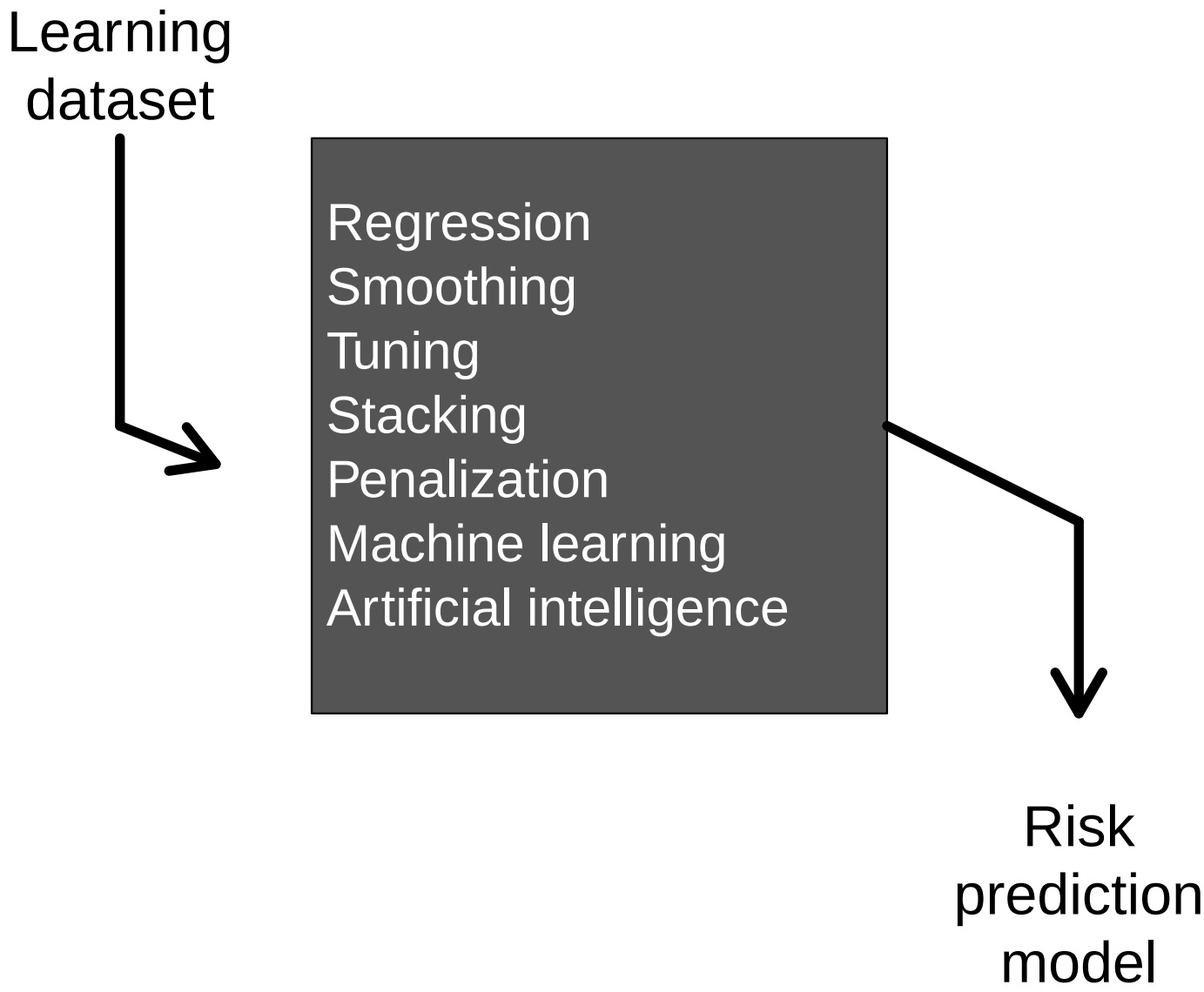
There are many ways to make a model, and every modeling expert has preferences regarding the general approach and tuning.

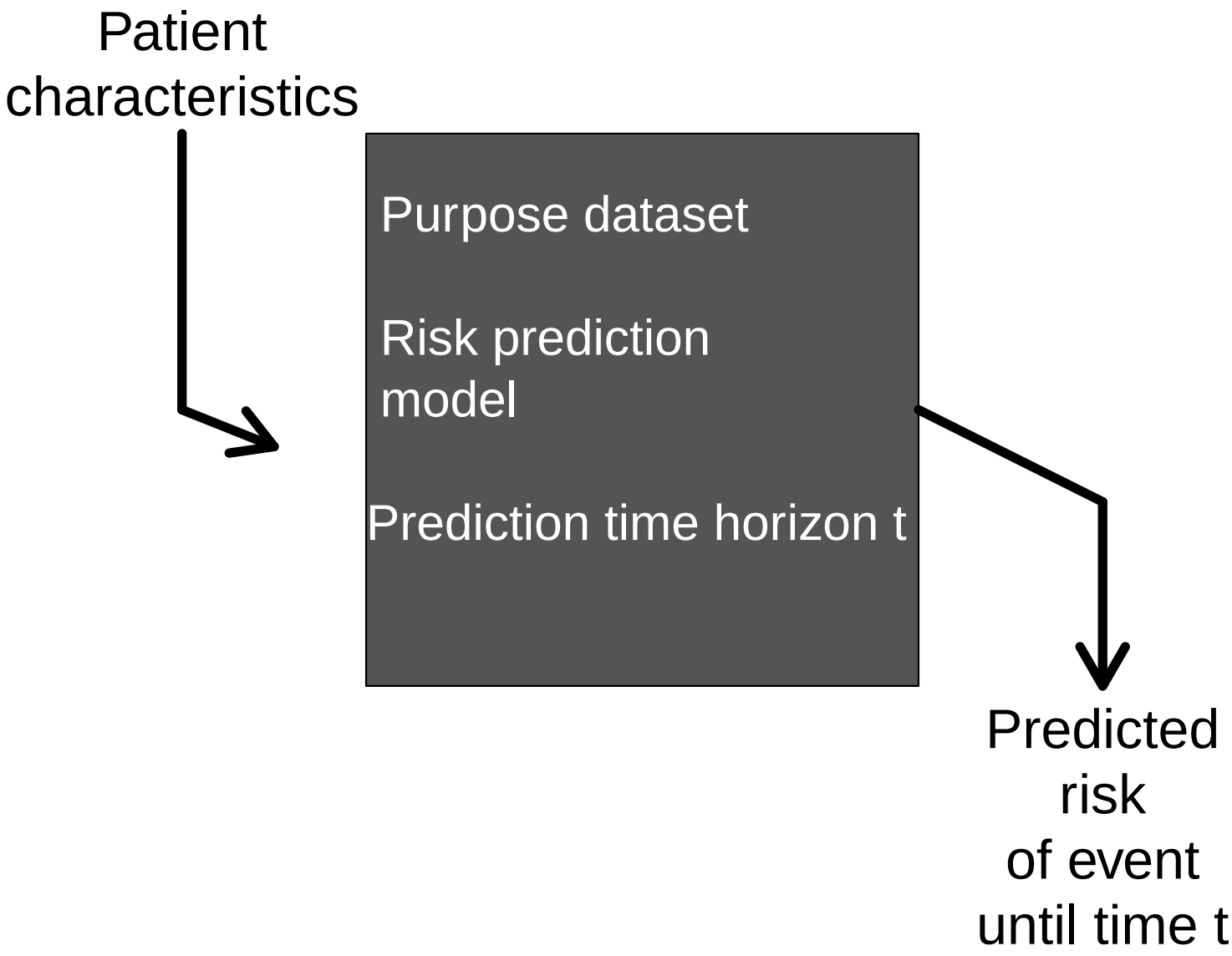
Prediction model timeline



Censored means that patient was event free at the last contact but not followed until prediction time horizon t. Event can still happen but this is not observed.

Competing risk means that patient will never experience the event.


Learning
dataset
Regression
Smoothing
Tuning
Stacking
Penalization
Machine learning
Artificial intelligence
Risk
prediction
model


Patient characteristics
Purpose dataset
Risk prediction model
Prediction time horizon t
Predicted risk of event until time t

Notation

Outcome

$$Y(t) = \begin{cases} 0 & \text{event-free or competing risk} \\ 1 & \text{event of interest before time t} \end{cases}$$

Predictors $X = (X^1, \ldots, X^p)$

Dataset $D_n = (Y_1(t), X_1, Y_2(t), X_2, \ldots, Y_n(t), X_n)$

Building the model $r : D_n \mapsto r(D_n) = \hat{M}_n$

Using the model $\hat{M}_n : X_{new} \mapsto \hat{M}_n(X_{new}) \in [0, 1]$

Example: logistic regression $\hat{M}_n(X) = \text{expit}(\hat{\alpha}_n + \hat{\beta}_n X)$

Measuring prediction performance [2]

Calibration:

$$p \mapsto P\{Y_i(t) = 1 | \hat{M}_n(X_i) = p\}$$

Discrimination:

$$\text{AUC}(t) = \text{P}(\hat{M}_n(X_i) \geq \hat{M}_n(X_j) | Y_i(t) = 1, Y_j(t) = 0)$$

Overall accuracy:

$$\text{Brier score}(t) = \text{E}\left\{ Y_i(t) - \hat{M}_n(X_i) \right\}^2$$

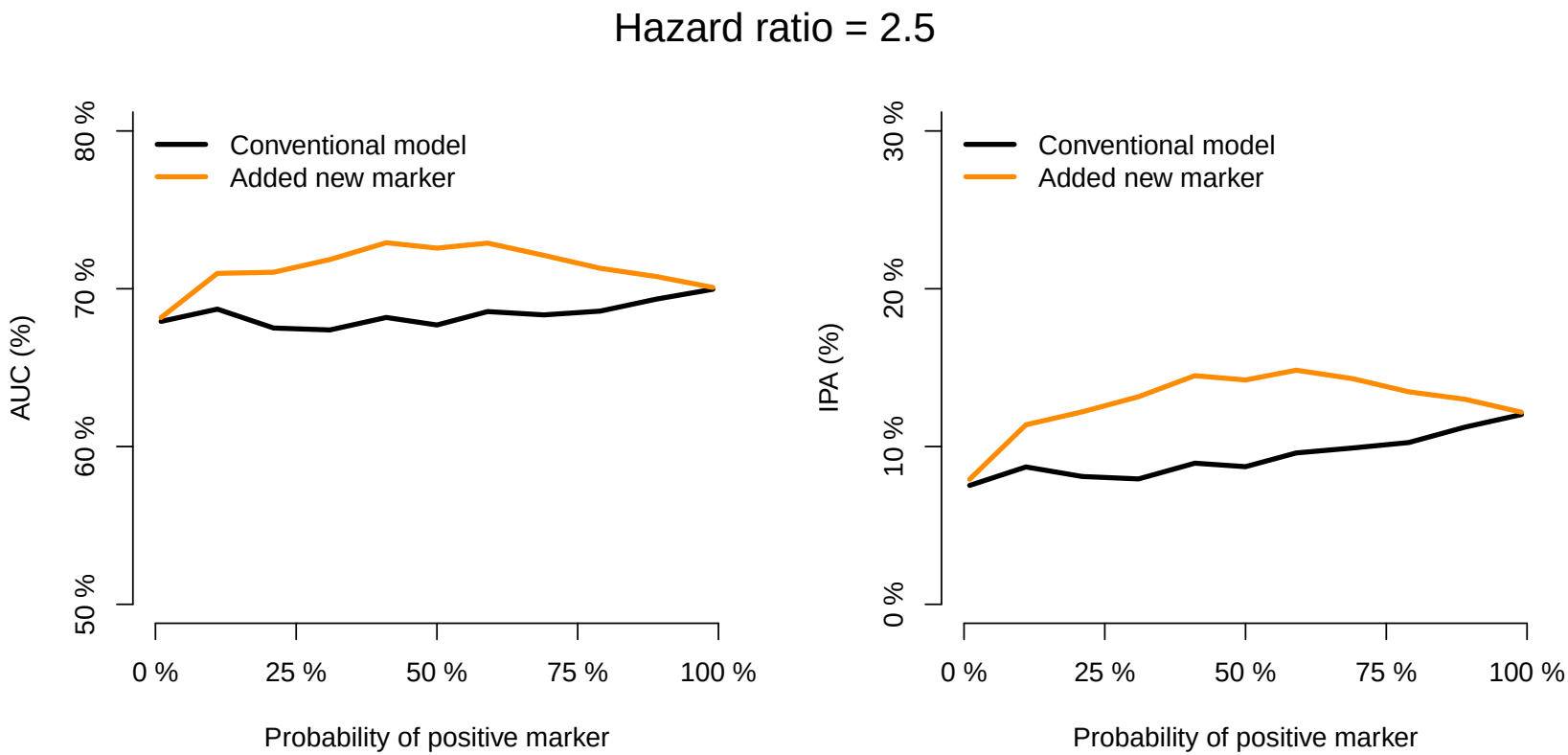
[2] The probability and expectation are taken with respect to i, j not D_n

Interpretation of a prediction performance measure should always involve a benchmark, ideally that set by a rival prediction model.

AUROC	Category
0.9-1.0	Very good
0.8-0.9	Good
0.7-0.8	Fair
0.6-0.7	Poor
0.5-0.6	Fail

In a homogeneous population, even the best possible model can have low discrimination ability (AUC/AUCROC). In a heterogeneous population, even a bad model can have a high AUC.

Don't blame the metric



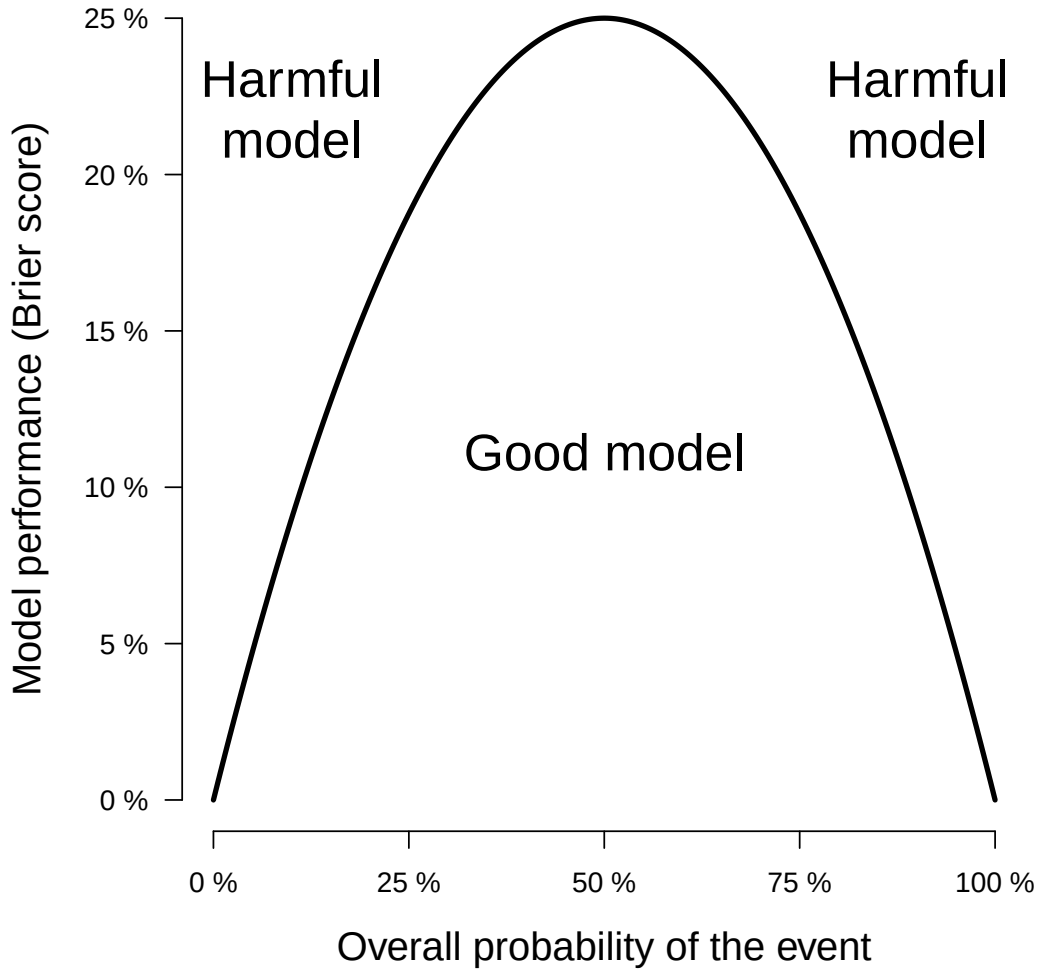
Rare biomarkers do not show change overall predictive performance

Benchmark values for the AUC (concordance index) and Brier score at any fixed prediction time horizon t.

Benchmark prediction	AUC	Brier score	Interpretation
50% always	50%	25%	useless or harmful
Overall event probability always	50%	see Figure	useless
Coin toss	50%	50%	harmful
Uniform [0,1]	50%	33%	harmful

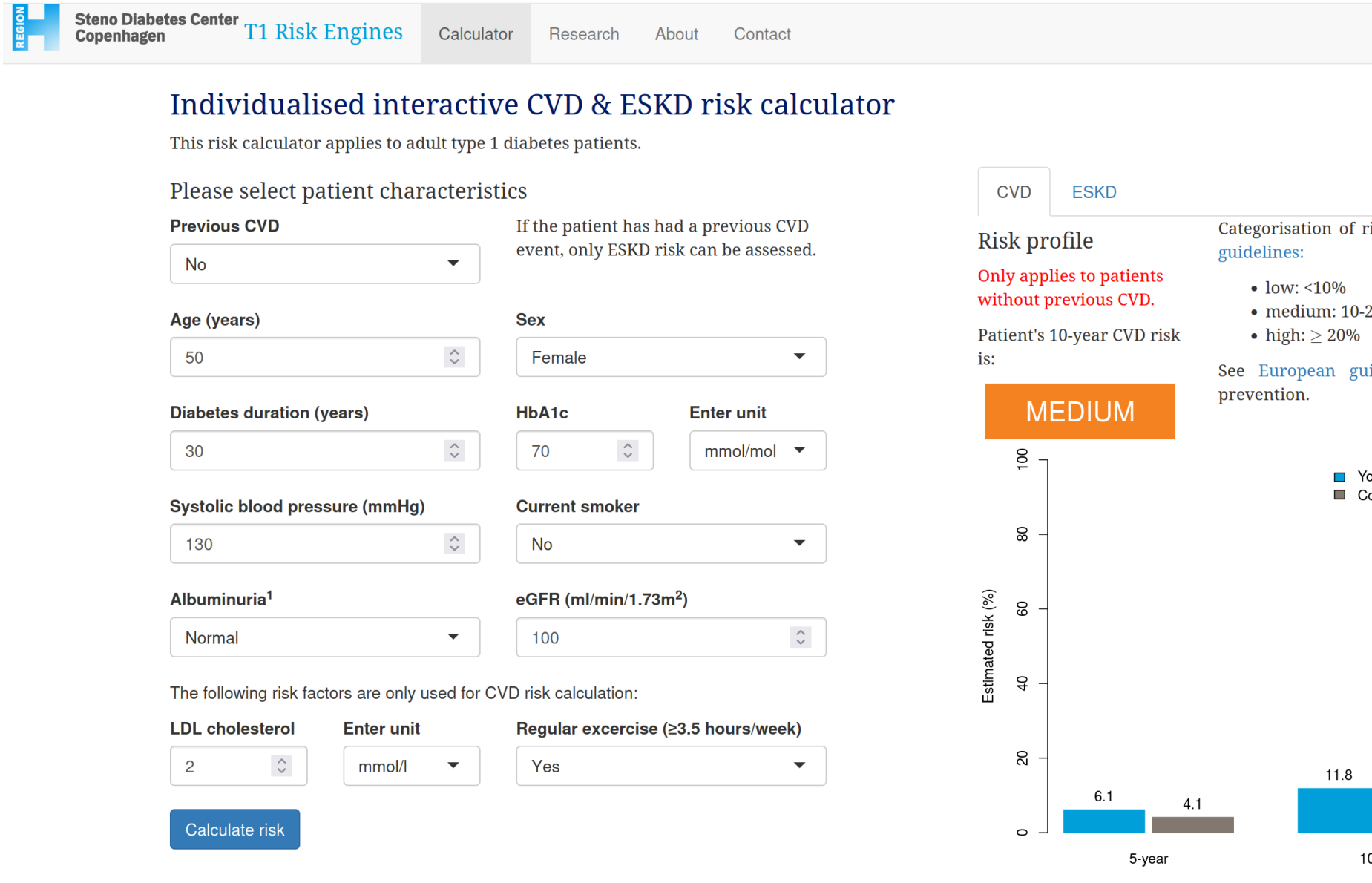
Being a rank statistic, the AUC is blind to miscalibration of the predicted risks. Hence, it cannot stand alone to assess models with respect to predictive accuracy.

Benchmark: the null model ignores the predictor variables



A good model outperforms the null model.

Steno type 1 diabetes risk engine



Example

```
library(riskRegression)
train <- readRDS("./practicals/data/type1-diabetes-train.rds")
test <- readRDS("./practicals/data/type1-diabetes-test.rds")
head(train)
```

Example

```
library(riskRegression)
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head(train)
```

	pid	age	sex_male	diabetes_duration	smoking	motion	steno_prs
1	train-28abed0e	52.92496	0	40.74757	0	0	-0.13899942
2	train-f07f8cea	42.70053	0	36.11731	0	1	0.40351668
3	train-f343cabb	47.57017	0	29.81477	0	0	0.54502533
4	train-beb0e521	50.20713	0	40.73831	0	0	0.23982291
5	train-05d45f09	40.76193	0	22.58828	0	1	-0.55949839
6	train-82772fab	45.96690	0	28.94583	0	1	0.04637945

	eGFR_pre_trt	statin	HBA1C_post_trt	urine_albumin_post_trt	LDL_post_trt	SBP_po
1	104.03674	0	49.51156	95.958599	8.816790	116
2	90.13102	0	35.53323	44.175849	6.772076	97
3	102.67096	0	75.10901	96.535995	6.853455	135
4	113.77416	0	72.04421	39.454438	4.687593	130
5	104.25661	0	28.79908	5.671578	1.392458	105
6	98.40765	0	68.75695	230.856313	1.389660	124

Conventional model and experimental model

```
# Logistic regression similar to Steno 1 risk engine
    formula
conventional_model <- glm(cvd_5year~sex_male + age +
    diabetes_duration + smoking + motion + HBA1C_post_
    trt + urine_albumin_post_trt + LDL_post_trt + SBP_
    post_trt + eGFR_post_trt,
              data = train, family = "binomial")
# Logistic regression with interactions and reduced
    number of variables
experimental_model <- glm(cvd_5year~sex_male *SBP_post
    _trt + age + I(age>40) * eGFR_post_trt + diabetes_
    duration + smoking + motion,
              data = train, family = "binomial")
```

Predicted risks for a single subject

```
data.frame("subject id" = c(24,24),
           "model" = c("conventional","experimental"),
           "risk prediction" = c(predictRisk(
    conventional_model,newdata = test[24,]),
                                 predictRisk(
    experimental_model,newdata = test[24,])))
```

```
  subject.id        model risk.prediction
1         24 conventional       0.1826537
2         24 experimental       0.4429426
```

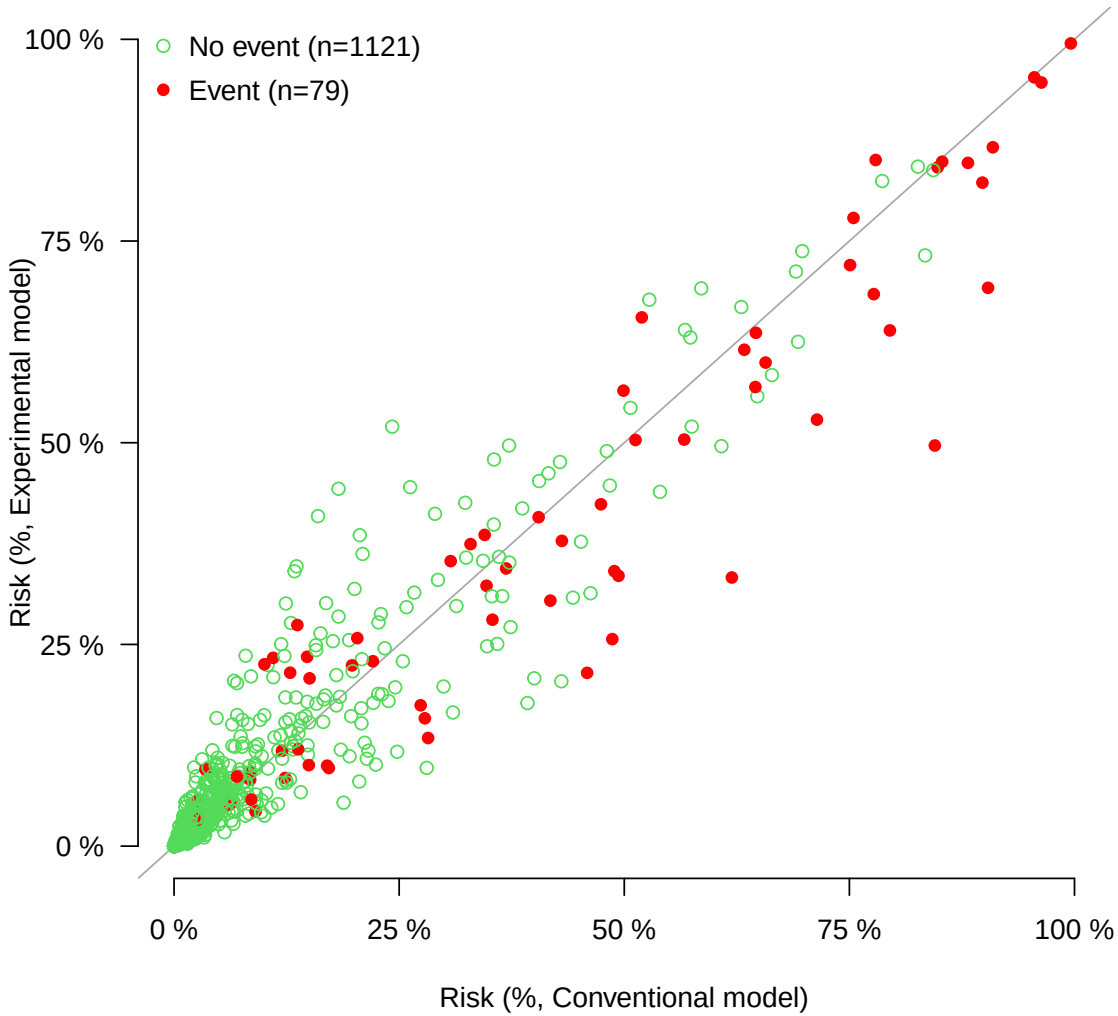
Evaluating model performance

```
x <- Score(list("Conventional model" = conventional_
    model,"Experimental model" = experimental_model),
            data = test,
            formula = cvd_5year~1,
            summary = "risks",
            plots = c("roc","cal"))
summary(x,what = "score")
```

```
$score
Key: <Model>
                  Model           AUC (%)      Brier (%)
                 <fctr>            <char>         <char>
1:          Null model               <NA> 6.1 [4.9;7.4]
2: Conventional model 88.3 [84.6;92.0] 4.6 [3.7;5.5]
3: Experimental model 87.8 [84.1;91.5] 4.9 [4.0;5.8]
```

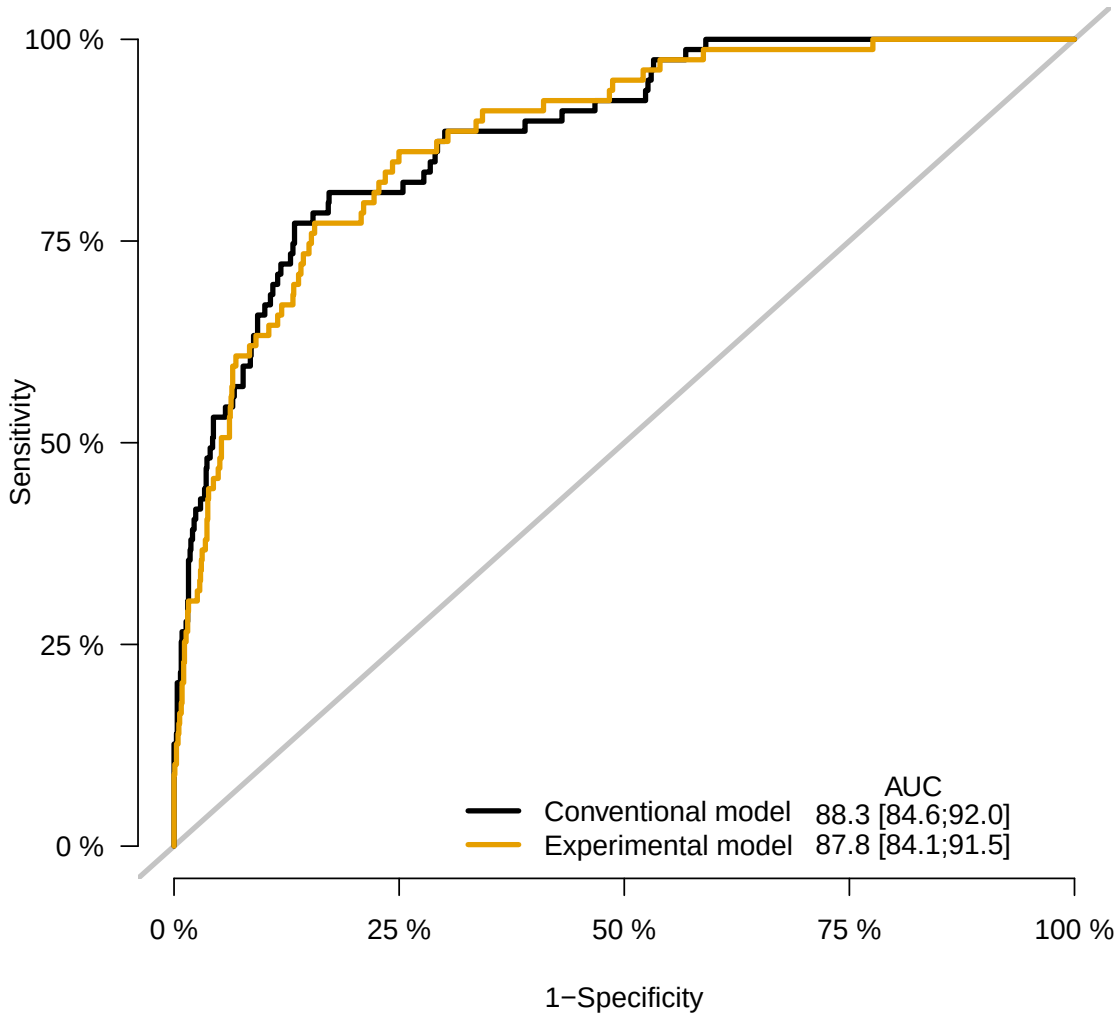
Predicted risks

```
plotRisk(x)
```



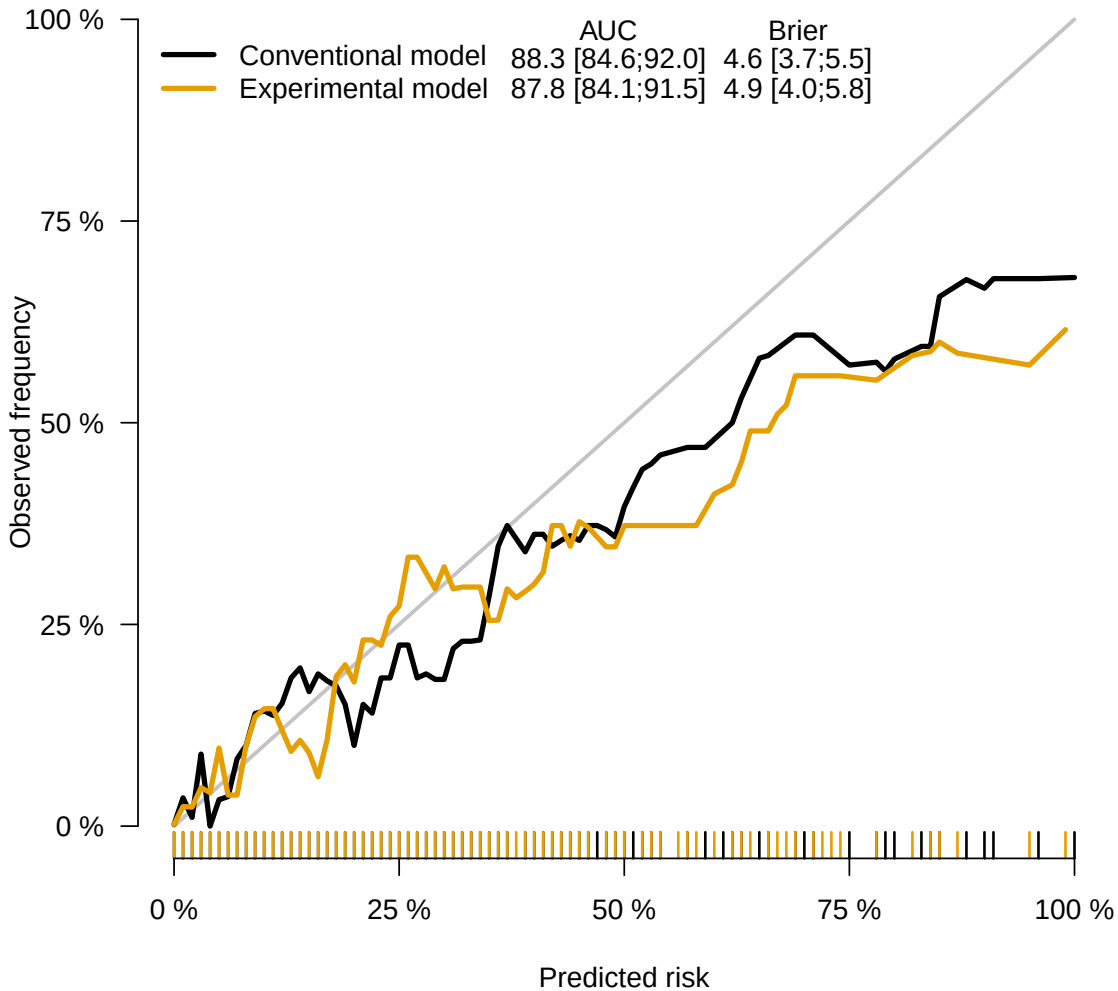
Discrimination

```
plotROC(x)
```



Calibration

```
plotCalibration(x)
```



Uncertainty

A medical risk prediction model finds people in the data set who were alike the current person, i.e., with similar values of the risk predictors, and summarizes what happened to them as a probability:

Dear patient, if we had 100 patients exactly like you we would expect 17 to experience the event within the next 5 years.

A probabilistic prediction has built-in uncertainty

But, we expect more reliable predictions for people who are well represented in the data set than people at the border of the data set.

Summary and outlook

A medical risk prediction model predicts the probability with which an event occurs until a fixed prediction time horizon.

Prediction performance (metrics) can be used to decide between rival models.

The values of the prediction performance metrics do not have a direct clinical interpretation!

How useful a model is depends on what it is used for ...