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# THE HARMS OF CLASS IMBALANCE CORRECTIONS FOR MACHINE LEARNING BASED PREDICTION MODELS: A SIMULATION STUDY.

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A PREPRINT

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May 1, 2024

## **Abstract**

Risk prediction models are increasingly used in healthcare to aid in clinical decision making. In most clinical contexts, model calibration (i.e., assessing the reliability of risk estimates) is critical. Data available for model development are often not perfectly balanced with respect to the modeled outcome (i.e., individuals with vs. without the event of interest are not equally represented in the data). It is common for researchers to correct this class imbalance, yet, the effect of such imbalance corrections on the calibration of machine learning models is largely unknown. We studied the effect of imbalance corrections on model calibration for a variety of machine learning algorithms. Using extensive Monte Carlo simulations we

compared the out-of-sample predictive performance of models developed with an imbalance correction to those developed without a correction for class imbalance across different data-generating scenarios (varying sample size, the number of predictors and event fraction). Our findings were illustrated in a case study using MIMIC-III data. In all simulation scenarios, prediction models developed without a correction for class imbalance consistently had equal or better calibration performance than prediction models developed with a correction for class imbalance. The miscalibration introduced by correcting for class imbalance was characterized by an over-estimation of risk and was not always able to be corrected with re-calibration. Correcting for class imbalance is not always necessary and may even be harmful for clinical prediction models which aim to produce reliable risk estimates on an individual basis.

**Keywords** Class Imbalance · Machine Learning · Calibration · Prediction Modeling

## 1 Introduction

Risk prediction models are increasingly used in healthcare to aid in clinical decision making; for example, to help decide if a patient is a good candidate for surgery or to communicate a patient's risk of disease [1, 2, 3]. As such, the purpose of a clinical prediction model is often to estimate a patient's risk of experiencing a particular event (e.g., successful surgery, disease) [4, 5]. Due to the rarity of many diseases, data available to train clinical prediction models often exhibit class imbalance i.e., observations from patients with vs. without the event of interest are not equally represented in the data. In machine learning literature, imbalance correction methods are commonly applied to correct class imbalance by artificially creating data that are more or perfectly balanced [6, 7, 8, 9], although the benefit of such corrections for model performance is not always clear.

An abundance of imbalance correction methods exist [7, 8, 9], yet, information regarding the effect of these imbalance corrections on model calibration is sparse. Model calibration captures the accuracy of risk estimates, relating to the agreement between the estimated (predicted) and observed number of events [3]. In clinical applications where a patient's predicted risk is the entity used to inform clinical decisions, it is essential to assess model calibration. If a model is poorly calibrated, it may produce risk estimates that do not approximate a patient's true risk well [3]. A poorly calibrated model may produce predicted risks that consistently over- or under-estimate true risk or that are too extreme (too close to 0 or 1) or too modest (too close to event prevalence) [3]. This can lead to poor treatment decisions or to clinicians communicating false assurances to patients [3, 10, 11]. If a clinician uses a poorly calibrated model to make a highly impactful decision (e.g., to determine if a patient should receive a bed in an intensive care unit), the costs of miscalibration to patients are real and can be far-reaching.

Some studies have evaluated the effect of class imbalance corrections on estimation of absolute risks/probabilities and thus, on model calibration [12, 13]. Research from van den Goorbergh and colleagues has demonstrated that class imbalance corrections may do more harm than good [13]; implementing imbalance corrections resulted in dramatically deteriorated model calibration, to the point that no corrections were recommended [13]. In the previous research, prediction models were developed using logistic regression and penalized logistic regression [12, 13]. In practice, prediction models developed for clinical applications increasingly use more flexible machine learning methods [14]. A recent systematic review of clinical prediction models indicates that machine learning algorithms like support vector machine and tree-based learning with random forest, are especially common [14]. The impact of imbalance corrections on model calibration is currently unknown for prediction models developed using these more flexible machine learning algorithms.

Building on previous research [12, 13], we assessed the impact of imbalance corrections on model calibration for prediction models trained with a wide variety of machine learning algorithms including: logistic regression, support vector machine, random forest, XGBoost, RUSBoost and EasyEnsemble. This paper is structured as follows. We present the design of our simulation study in section 2 and the results in section 3. A case study where we study the impact of imbalance corrections using empirical data is presented in section 4, followed by a discussion of our findings and their implications for researchers developing prediction models in the presence of class imbalance in section 5. Our conclusions are presented in section 6.

## 2 Methods

We implemented a simulation study to investigate the effects of imbalance correction methods across 18 unique data-generating scenarios. In our research, we focused on prediction models designed for dichotomous risk prediction. For each scenario, we compared the out-of-sample predictive performance (i.e., model performance on data not used to train the model) of models developed with an imbalance correction to those developed without a correction for class imbalance. In the next sections, details regarding the data-generating mechanism, model development procedure, simulation methods, performance measures, and software and error handling are presented. All code used for this project is publicly available on GitHub: [https://github.com/alexcarriero/class\\_imbalance\\_project](https://github.com/alexcarriero/class_imbalance_project).

### 2.1 Data Generating Scenarios

In our simulation study, 18 ( $3 \times 2 \times 3$ ) unique data-generating scenarios were studied (Table 1). This was achieved by varying the following three characteristics of the data: the event fraction (proportion of patients with an event), the number of predictors and sample size. Event fraction varied through the set {0.5, 0.2, 0.02} and number of predictors through the set {8, 16}. A class balanced scenario (event fraction = 0.5) was included to study the effects of imbalance corrections when they are tasked with correcting for chance imbalances in the simulated data. In all scenarios, data were generated to yield an expected concordance statistic of 0.85. Given the number of predictors, the event fraction and expected concordance statistic, we computed the minimum required sample size for a prediction model (N) developed under these conditions. Sample size calculations were carried out using the R package *pmsampsize* [15]. The sample size of data used to train the prediction models ( $n_{\text{train}}$ ) was then varied through the set  $\{\frac{1}{2}N, N, 2N\}$  implying half the required sample size, exactly the required sample size and double the required sample size, respectively.

### 2.2 Data Generating Mechanism

As we focused on dichotomous risk prediction, we generated data comprised of two classes. We refer to the non-events and events as class 0 and class 1, respectively. Data for each class were generated independently using distinct multivariate normal (*mvn*) distributions. As shown in equations (1) and (2), we specified a distinct mean and covariance structure for each class. The mean structures for the classes are represented as  $\mu_0$  and  $\mu_1$  for class 0 and 1, respectively. The covariance matrices are represented as  $\Sigma_0$  and  $\Sigma_1$  for class 0 and 1, respectively.

$$\text{Class 0 : } \mathbf{X} \sim mvn(\boldsymbol{\mu}_0, \boldsymbol{\Sigma}_0) = mvn(\mathbf{0}, \boldsymbol{\Sigma}_0), \quad (1)$$

$$\text{Class 1 : } \mathbf{X} \sim mvn(\boldsymbol{\mu}_1, \boldsymbol{\Sigma}_1) = mvn(\Delta_{\boldsymbol{\mu}}, \boldsymbol{\Sigma}_0 - \Delta_{\boldsymbol{\Sigma}}). \quad (2)$$

As shown in equation (2), the differences in parameter values between the two classes are represented by  $\Delta_{\boldsymbol{\mu}}$  and  $\Delta_{\boldsymbol{\Sigma}}$ ; a vector and matrix comprised of the differences in predictor means, and variances/ covariances, between the classes, respectively. We specified no variation in means among predictors within a class, making all elements in  $\Delta_{\boldsymbol{\mu}}$  equivalent; we denote these equivalent elements as  $\delta_{\boldsymbol{\mu}}$ . Similarly, we specified no variation in predictor variances within a class, making all diagonal elements in the matrix  $\Delta_{\boldsymbol{\Sigma}}$  equivalent, denoted by  $\delta_{\boldsymbol{\Sigma}}$ .

For class 0, all predictor means were fixed to zero and all variances to 1. Consequently for class 1, all predictor means were equal to  $\delta_{\boldsymbol{\mu}}$  and all variances equal to  $1 - \delta_{\boldsymbol{\Sigma}}$ . Finally, in both classes, we allowed 75% of the predictors to covary. All non-zero correlations among predictors in each class were set to 0.2. To ensure the correlation among predictors was not stronger in one class, we fixed the correlation matrices of the two classes to be equal. This was accomplished by computing the off-diagonal elements of  $\Sigma_1$  such that the correlation matrices of the two classes were equivalent (as shown below).

For instance, with 8 predictors, the mean and covariance structure for class 0 was,

$$\boldsymbol{\mu}_0 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \boldsymbol{\Sigma}_0 = \begin{bmatrix} 1 & 0.2 & 0.2 & 0.2 & 0.2 & 0.2 & 0 & 0 \\ 0.2 & 1 & 0.2 & 0.2 & 0.2 & 0.2 & 0 & 0 \\ 0.2 & 0.2 & 1 & 0.2 & 0.2 & 0.2 & 0 & 0 \\ 0.2 & 0.2 & 0.2 & 1 & 0.2 & 0.2 & 0 & 0 \\ 0.2 & 0.2 & 0.2 & 0.2 & 1 & 0.2 & 0 & 0 \\ 0.2 & 0.2 & 0.2 & 0.2 & 0.2 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix},$$

and mean and covariance structure for class 1 was,

$$\boldsymbol{\mu}_1 = \begin{bmatrix} \delta_\mu \\ \delta_\mu \end{bmatrix}, \boldsymbol{\Sigma}_1 = \begin{bmatrix} 1 - \delta_\Sigma & z & z & z & z & z & z & 0 & 0 \\ z & 1 - \delta_\Sigma & z & z & z & z & z & 0 & 0 \\ z & z & 1 - \delta_\Sigma & z & z & z & z & 0 & 0 \\ z & z & z & 1 - \delta_\Sigma & z & z & z & 0 & 0 \\ z & z & z & z & 1 - \delta_\Sigma & z & z & 0 & 0 \\ z & z & z & z & z & 1 - \delta_\Sigma & z & 0 & 0 \\ z & z & z & z & z & z & 1 - \delta_\Sigma & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 - \delta_\Sigma & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 - \delta_\Sigma \end{bmatrix}.$$

Here,  $z = (1 - \delta_\Sigma) * 0.2$ , to ensure equivalent correlation matrices between the two classes.

Parameter values for the data generating distributions ( $\delta_\mu$  and  $\delta_\Sigma$ ) of each scenario were selected to generate a concordance statistic ( $C$ ) of 0.85. Under the assumption of normality for all predictors (in each class), the concordance statistic of the data can be expressed as a function of  $\Delta_\mu$ ,  $\Sigma_0$  and  $\Sigma_1$  [16]. Optimal values of  $\delta_\mu$  and  $\delta_\Sigma$  for each scenario were computed analytically, based on the following formula [16]:

$$C = \Phi \left( \sqrt{\boldsymbol{\Delta}_\mu' (\boldsymbol{\Sigma}_0 + \boldsymbol{\Sigma}_1)^{-1} \boldsymbol{\Delta}_\mu} \right). \quad (3)$$

In equation (3),  $\Phi$  represents the cumulative density function of the standard normal distribution;  $\Delta_\mu$ ,  $\Sigma_0$  and  $\Sigma_1$  maintain their previous definitions. To ensure a unique solution,  $\delta_\Sigma$  was fixed at 0.3 for each scenario, while equation (3) was solved to yield the appropriate value of  $\delta_\mu$  in each scenario. The full analytical solution is provided in Appendix A. The parameter values for the data generating distributions in each simulation scenario are presented in Table 1.

Given that data for each class were generated independently, we had direct control over how many observations were generated under each class. The number of events ( $n_1$ ) was sampled from the binomial distribution with probability equal to the specified event fraction. The number of non-events ( $n_0$ ) was then computed as  $n - n_1$ , where  $n$  is the specified sample size for a given scenario.

### 2.3 Model Development

All prediction models were developed according to the following two-step procedure. First, data were pre-processed using a class imbalance correction technique. Then, the resulting artificially-balanced data were used to train a machine learning algorithm.

We implemented a 5 x 6 full-factorial design to compare the out-of-sample predictive performance of prediction models developed with 5 imbalance corrections (1 control and 4 corrections) and 6 machine learning algorithms. As a control, data were not corrected for imbalance and the uncorrected data went on to train the machine learning algorithms. In total, we compared the performance of 30 prediction models, each comprised of a unique combination of imbalance correction and machine learning algorithm.

### 2.3.1 Imbalance Corrections

The imbalance corrections studied in our simulation included four data pre-processing techniques: random under sampling (RUS), random over sampling (ROS), synthetic minority over sampling (SMOTE), synthetic minority over sampling with Wilson’s Edited Nearest Neighbor Rule (SENN), and a control in which no correction was implemented. As determined by a recent systematic review, RUS, ROS and SMOTE are the imbalance corrections that are commonly implemented when developing clinical prediction models, SMOTE being the most popular among them [14]. We included SENN as well, given literature indicating that it can outperform SMOTE under certain conditions [17, 18]. All imbalance corrections and the R packages used for their implementation in our simulation study are summarized in Table 2.

The functionality of these data pre-processing techniques is illustrated in Figure 1. In our simulation, imbalance corrections were implemented to achieve artificially class balanced data (event fraction  $\approx 0.5$ ). RUS achieves class balance by randomly disregarding observations from the majority class until a balance is achieved. This technique is similar to a case-control design without matching [19]. ROS achieves balance by randomly re-sampling from the minority class with replacement until a balance is achieved. SMOTE generates artificial observations for the minority class by interpolating from the existing minority class observations [20]. In our implementation, we specified the number of nearest neighbors for SMOTE ( $k$ ) to be 5 (package default) [21]. In SENN, class balance is achieved by using a combination of SMOTE and Wilson’s Edited Nearest Neighbor Rule (ENN) [22]. SMOTE is implemented first, to generate synthetic data for the minority class and then ENN is implemented to remove any observation which has a different outcome than the majority of its nearest neighbors [17]. This added step is implemented to make it easier for a classifier to distinguish between the classes, as when synthetic observations are generated for the minority class using SMOTE, it may cause an increase in noise near the class boundary. In our implementation, we specified the number of nearest neighbors in the SMOTE step ( $k_1$ ) to be 5, and the number of nearest neighbors in ENN step ( $k_2$ ) to be 3 (package defaults) [21]. Finally, in the control condition, data were not corrected for imbalance and moved directly to the second step of model development untouched (i.e., the imbalanced data were used to train the prediction models).

### 2.3.2 Machine Learning Algorithms

Machine learning algorithms were selected based on a recent systematic review identifying common algorithms used to develop prediction models in a medical context [14]. These algorithms include: logistic regression (LR), support vector machine (SVM), random forest (RF) and XGBoost (XG). Additionally, based on literature summarizing common strategies to handle class imbalance [7, 8, 23], we included two ensemble learning algorithms designed specifically to handle class imbalance: RUSBoost (RB) and EasyEnsemble (EE). While both of these algorithms use random undersampling innately, RUSBoost [24] is a boosting algorithm while EasyEnsemble [25] uses bagging. The hyperparameters selected for these machine learning algorithms, and the R packages used for algorithm implementation are summarized in Table 3.

Four machine learning algorithms (SVM, RF, XG and RB) required the specification of model hyperparameters. Hyperparameter tuning was conducted using the R package caret for SVM, RF and XG [26]. The methods of implementation were svmRadial, ranger and xgbTree for SVM, RF and XG, respectively. To select the hyperparameters, we implemented 5-fold cross-validation optimizing for model deviance. For SVM and XG, caret default tune grids and tune length were used. For RF, we specified a custom tuning grid: mtry (the number of candidate splitting variables allowed at each node in a tree) was allowed to vary from 1 to the total number of predictors, min.node.size (the minimum number of observations allowed in a leaf node) was allowed to vary from 1 to 10 and we specified ‘gini’ as the splitrule (the split which minimizes Gini impurity). Finally, in our implementation of RUSBoost we specified a support vector machine with a radial kernel as the weak classifier and an ensemble size of 10 (package defaults) [27].

Notably, since RB and EE innately correct for class imbalance, there are only 4/30 prediction models for which no attempt to correct for imbalance is made. Given our 5x6 full-factorial design, we are able to compare the performance of the models which make no attempt to correct for class imbalance (control models for LR, SVM, RF, XG) with those which correct for class imbalance via a data pre-processing technique (RUS, ROS, SMOTE, SENN), innately correct for class imbalance (RB, EE), or both.

## 2.4 Simulation Methods

Under each simulation scenario, 2000 data sets were generated. Each data set was comprised of training and validation data. The training and validation data were generated independently using identical data generating mechanisms. Validation data sets were generated to be ten times larger than the training data sets. The sample sizes of the training ( $n_{\text{train}}$ ) and validation ( $n_{\text{validation}}$ ) data for each simulation scenario can be found in Table 1.

For each generated data set, 30 (5 x 6) prediction models were developed (as described in section 2.3). All prediction models were trained using the training data. Predictive performance was then assessed using the validation data.

Since we expected many machine learning algorithms to exhibit miscalibration, especially in scenarios with considerable class imbalance, we also conducted logistic (re-)calibration for all prediction models, using the following procedure. For each observation in the validation set, the predicted risk and corresponding observed outcome (0 or 1) were stored. Then, the predicted risks were re-calibrated using the following logistic regression model:

$$\log \left( \frac{P(Y_i = 1)}{1 - P(Y_i = 1)} \right) = \beta_0 + \log \left( \frac{p_i}{1 - p_i} \right). \quad (4)$$

Here,  $Y_i$  represents the observed outcome for the  $i$ th observation in the validation set and  $p_i$  represents the predicted risk for the  $i$ th observation in the validation set, from a given prediction model. The logarithms in equation (4) represent the natural logarithm. This approach is similar to platt scaling [28], except, only an intercept term is estimated ( $\beta_0$ ), while platt scaling typically includes the estimation of both an intercept and slope (i.e., a slope coefficient is estimated, rather than included as an offset) [28]. After the re-calibration procedure was implemented, predictive performance was then re-assessed using the re-calibrated predictions.

In summary, predictive performance was assessed twice in our simulation: first using the raw predictions (no re-calibration) and subsequently using the re-calibrated predictions.

## 2.5 Performance Measures

Out-of-sample predictive performance was assessed using measures of calibration, discrimination and overall performance. All performance measures were computed using the raw predicted risks (resulting from the validation data) and subsequently, using the re-calibrated predictions, for each prediction model.

Model calibration measures the agreement between predicted risks and observed proportions of the event in the data [3]. Calibration was assessed using both visual and empirical metrics. We assessed calibration visually by means of flexible calibration curves; one flexible calibration curve was generated for each simulation iteration. Coordinates for the calibration curves were calculated using loess regression; implemented using the R package stats [29]. Calibration curves were then generated using ggplot2 [30]. Additionally, calibration intercept and slope were calculated according to their respective definitions in Steyerberg *et al.* (2010) [31]. In a flexible calibration curve, when predicted risks (x-axis) correspond well with the observed proportions in the data (y-axis), the curve follows a straight diagonal line ( $y = x$ ) [3]. With respect to calibration intercept and slope, ideal calibration is represented by values of 0 and 1, respectively [31].

The concordance statistic ( $C$ ) was used to measure model discrimination; computed using the R package pROC [32]. This metric captures a model's ability to yield higher risk estimates for patients with the event than for those without the event. For dichotomous outcomes, it is equivalent to the area under the Receiver Operator Characteristic curve [31]. A model which perfectly discriminates between the classes will have  $C = 1$ ; a model with no discriminative performance has  $C = 0.5$  [31].

Overall performance was measured by Brier score. This metric reflects both model discrimination and calibration and was calculated according to its definition in Steyerberg *et al.* (2010) [31]. In an ideal model, predicted risks approximate the observed outcome well for all individuals; perfect prediction models produce a Brier score of zero. As event fraction decreases, it is easier for a prediction model to achieve a low Brier score [31]. Comparisons for this performance measure should only be made among prediction models developed

with the same event fraction.

For empirical measures of model performance (concordance statistic, Brier score, calibration intercept and calibration slope), the median over the simulation iterations and corresponding Monte Carlo error were reported. The values of each performance measure across all 2000 simulation iterations were also visualized with violin plots, generated with ggplot2 [30].

## 2.6 Software and Error Handling

The simulation study was conducted using the University Medical Center Utrecht's high performance computing (HPC). This high performance computer uses two types of central processing units: Intel(R) Xeon (R) Silver and Intel(R) Xeon (R) Gold. The simulation study and processing of results were conducted using R versions 4.2.2 and 4.1.2, respectively [29]. For further details (e.g., R package versions, HPC specifications) please see Supplementary Materials (Section A).

Any warnings or errors which occurred during the simulation study were carefully monitored and saved. In case of an error with an imbalance correction or a machine learning algorithm, no new data were generated. If an error was produced by an imbalance correction, uncorrected data were allowed to proceed in the model development process (i.e., the uncorrected data were used to train the machine learning algorithms). In case of an error produced by a machine learning algorithm, predicted risks were saved as missing (NA). Consequently, empirical performance metrics were stored as missing and no flexible calibration curve was generated. Please see Supplementary Materials (Section B) for reporting of all warnings or errors generated.

## 3 Results

In the next sections, we focus on the results for simulation scenarios with 8 predictors, sample size equivalent to the minimum required sample size ( $N$ ) and balanced (event fraction = 0.5), moderately imbalanced (event fraction = 0.2) and strongly imbalanced (event fraction = 0.02) data, simulation scenarios 4-6, respectively. Results from all simulation scenarios are included in the Supplementary Materials (Section C) and are also presented in our Shiny App: [https://alex-carriero.shinyapps.io/class\\_imbalance/](https://alex-carriero.shinyapps.io/class_imbalance/).

We present the results from scenarios 4-6 because they are representative of the results across all 18 data-generating scenarios. Results did not vary greatly across the number of predictors or sample size settings considered (Appendix B). In particular, increasing the number of predictors or sample size slightly improved model discrimination for all prediction models, meanwhile, calibration intercept, calibration slope and brier score remained unchanged (Figures B1-B4, Appendix B).

### 3.1 Calibration

For balanced data (event fraction = 0.5) all machine learning algorithms, except EE, were well calibrated when training data were pre-processed with the control, RUS or SMOTE (Figure 2); this was reflected by calibration intercepts and slopes very near to 0 and 1, respectively (Figure 5). Interestingly, when training data were pre-processed with ROS, there was separation between the calibration curves (Figure 2) for models using tree-based algorithms (RF, XG, EE). This separation was reflected by separation in the calibration intercepts (Figure 5). The division among the flexible calibration curves and calibration intercepts occurred as a result of chance imbalance in the training data (approximately half the observed event fractions were  $> 0.5$  while the other half were  $< 0.5$ ). The top-curves (calibration intercepts  $> 0$ ) underestimated risk on average and were generated when chance imbalance favored events (i.e., more events than non-events). Bottom-curves (calibration intercepts  $< 0$ ) overestimated risk on average and were generated when chance imbalance favored non-events. When SENN was used to pre-process the training data, LR, SVM and XG exhibited worse calibration than their controls, meanwhile RF, RB and EE remained as well calibrated (RF and RB) or slightly better calibrated (EE) than their controls. In our reporting, for a given machine learning algorithm, the control refers to a model trained with data that were not corrected for imbalance. With respect to EE, regardless of the data pre-processing method, the predicted risks were too moderate (calibration slopes  $> 1$ , Figure 5).

When data exhibited moderate imbalance (event fraction = 0.2), control models for LR, SVM, RF and XG were well calibrated, while control models for RB and EE were not (Figure 3). In the RB and EE control models, predicted risks consistently over-estimated true risk (Figure 3); this miscalibration was characterized

by median calibration intercepts below 0 (RB: -1.27, EE: -1.3) and median calibration slopes above 1 (RB: 1.52, EE: 2.31), as shown in Figure 6. Similarly, when training data were pre-processed with any imbalance correction, prediction models produced risk estimates which consistently over-estimated true risk, regardless of the machine learning algorithm used (Figure 3). RF trained with ROS pre-processed data was protected against this general trend; for this one prediction model, model calibration was preserved (Figure 3).

When data were strongly imbalanced (event fraction = 0.02), all prediction models exhibited miscalibration (Figure 4). With respect to the control models, calibration curves for LR, SVM, RF and XG were unstable; there was large variation among the calibration curves produced over the simulation iterations. Meanwhile, the control models for RB and EE produced predicted risks which exhibited a specific pattern of miscalibration: all consistently over-estimated true risk, with very little variation among the calibration curves. Similarly, when training data were pre-processed with any imbalance correction, prediction models, again, produced risk estimates which largely over-estimated true risk. For oversampling corrections (ROS, SMOTE, SENN) calibration curves for SVM and XG models were extremely unstable. From Figure 7, it is clear that in this scenario, only the models which did not attempt to correct for class imbalance (the control models for LR, SVM, RF and XG) had calibration intercepts centered around 0. With respect to calibration slope, oversampling corrections (ROS, SMOTE, SENN) caused a decrease in calibration slope compared to controls (Figure 7); this resulted in worse calibration slopes for all algorithms except EE. Meanwhile, the undersampling correction (RUS) actually improved calibration slopes for SVM and RF compared to controls.

Overall, as imbalance between the classes was magnified, model calibration deteriorated for all prediction models. All imbalance corrections affected model calibration in a very similar fashion. Correcting for imbalance using pre-processing methods (RUS, ROS, SMOTE, SENN) and/or by using an imbalance correcting algorithm (RB, EE) resulted in prediction models which consistently over-estimated risk. On average, no model trained with imbalance corrected data outperformed the control models in which no imbalance correction was made, with respect to model calibration.

### 3.2 Discrimination

For class balanced data (event fraction = 0.5), when comparing models developed with the same machine learning algorithm, all models had equal or nearly equal discrimination; imbalance corrections had little or no effect on model discrimination (Figure 5). SVM models had the highest discrimination: all five models built with SVM (regardless of the data pre-processing method used) had higher median discrimination than any other prediction models in this class balanced scenario (Table 4). Median concordance statistics in this simulation scenario ranged from [0.82, 0.86].

For moderately imbalanced data (event fraction = 0.2), the effects of the imbalance corrections on model discrimination were highly dependent on the machine learning algorithm (Figure 6). On average, RUS and ROS decreased discrimination for LR, XG, RB and EE compared to controls, meanwhile, on average, they improved discrimination for SVM and RF compared to controls. SMOTE and SENN had, on average, no effect or worsened discrimination for LR, RF, XG, RB and EE, while they improved discrimination for SVM. These effects were small and are seen best by comparing the median concordance statistics (Table 4). Median concordance statistics in this simulation scenario ranged from [0.79, 0.85].

Finally, with strong class imbalance (event fraction = 0.02), the effects of the imbalance corrections on discrimination were again, highly dependent on the machine learning algorithm (Figure 7). For LR, imbalance corrections had no noticeable effect on discrimination, with the exception of RUS, which decreased discrimination (Figure 7). For SVM and RF, all imbalance corrections improved discrimination, meanwhile, for XG, RB, and EE, all imbalance corrections worsened discrimination (Figure 7). Median concordance statistics in this simulation scenario ranged from [0.71, 0.84].

Overall, as imbalance between the classes was magnified, discrimination worsened for most prediction models, on average. The effect of the (pre-processing) imbalance corrections on model discrimination was highly dependent on the machine learning algorithm. SVM benefited from all imbalance corrections, RF also benefited, but to a lesser extent. Meanwhile, XG, RB, EE and RUS-LR all suffered. Effects were most pronounced when class imbalance was strong (event fraction = 0.02). Notably, for any event fraction, discrimination for the machine learning algorithms which innately corrected for imbalance (RB, EE), was worse than the control-LR model.

### 3.3 Overall Performance

As Brier score depends on event fraction, we only compared Brier scores for scenarios with the same event fraction. For reference, we note that a trivial majority classifier (a model which produces the same predicted risk, 0, for all individuals) would achieve Brier scores of 0.50, 0.19 and 0.02 in scenarios 4, 5, and 6, respectfully.

For balanced data (event fraction = 0.5), median Brier scores ranged from [0.15, 0.19]. For models built with LR or RF, imbalance corrections had no noticeable effect on median Brier score (Figure 5; Table 4). For models built with SVM, XG, RB or EE, imbalance corrections had minimal effects; the largest difference in median Brier scores among prediction models built with the same machine learning algorithm was 0.1 (Table 4).

For moderately imbalanced data (event fraction = 0.2), median Brier scores ranged from [0.12, 0.20]. Notably, the models which did not attempt to correct for imbalance (control models for LR, SVM, RF and XG) outperformed all other prediction models, with respect to Brier score (Brier scores: 0.12). Again, with the exception of ROS-RF, which preformed equally as well as the aforementioned models (Brier Score: 0.12). In this scenario, models built with RUS had particularly poor performance relative to the others (Figure 6); all RUS models had median brier scores of 0.2, worse than a trivial majority classifier, with the exception of RUS-SVM which preformed slightly better (Brier Score: 0.16).

For data with strong imbalance (event fraction = 0.02), median Brier scores ranged from [0.02, 0.22]. Again, the models which did not attempt to correct for imbalance (control models for LR, SVM, RF and XG) outperformed all other prediction models (Brier scores: 0.02). In this scenario, ROS-RF and ROS-XG preformed just as well as the aforementioned models (Brier scores: 0.02). Models built with RUS had substantially worse Brier scores (ranging from [0.17, 0.22]) and with very large MCMC errors, compared to all other models (Figure 7). Finally, while imbalance corrections worsened median Brier score for all algorithms, the effect was most pronounced for LR (control: 0.02, RUS: 0.19, ROS: 0.16, SMOTE: 0.15, SENN: 0.16).

Overall, imbalance corrections worsened the overall performance for all machine learning algorithms, on average. Two models were robust against this effect: ROS-RF, ROS-XG. The effects of the imbalance corrections on overall performance were most pronounced when class imbalance was strong. Notably, the machine learning algorithms which innately corrected for class imbalance (RB, EE) conferred no noticeable benefit to overall performance compared to all other machine learning algorithms.

### 3.4 Re-calibration

The effect of re-calibration on model performance was constant across all simulation scenarios, and prediction models. Importantly, we observed that even after re-calibration, there were very few cases where, for a given machine learning algorithm, models trained with imbalance corrected data preformed better than when trained with uncorrected data, with respect to model calibration. These cases were restricted to RUS-(SVM, RF) and ROS-RF models, in scenarios with moderate (event fraction = 0.2) or strong class imbalance (event fraction = 0.02).

The re-calibration procedure adjusted calibration intercepts to be zero for all simulation iterations, while calibration slopes were unaffected. Consequently, after re-calibration, the flexible calibration plots improved: there was less variability visible among the calibration curves and less over-estimation of predicted risks. For the class balanced scenarios, the separation seen among the calibration curves disappeared. This can be viewed clearly using our Shiny App. With respect to discrimination, concordance statistics were relatively unaffected by re-calibration (Table 4). Finally, differences among the prediction models with respect to Brier score were minimized after re-calibration such that all prediction models yielded comparable Brier scores (Table 4).

In summary, in scenarios where control-RF or control-SVM under-estimated risk, RUS-(SVM, RF) and ROS-RF models slightly improved model calibration, after re-calibration. This was most commonly observed in simulation scenarios with 16 predictors (see Supplementary Materials Section C).

## 4 MIMIC-III Data Case Study

We conducted a case study to investigate how our simulation study results compare with prediction models developed using empirical rather than simulated data. Using the freely accessible MIMIC-III database [33, 34] we developed prediction models predicting ICU mortality using commonly assessed predictors. We developed and validated 30 (5 x 6) prediction models with the same methods applied in our simulation study to assess the impact of 5 imbalance corrections (1 control and 4 corrections) on out-of-sample predictive performance for 6 different machine learning algorithms.

The MIMIC-III database contains observations from 38,597 adult patients admitted to the ICU at Beth Israel Deaconess Medical Center in Boston, Massachusetts between 2008 and 2014 [33]. Many patients in the database had more than one admission to the ICU, in our analysis only data from the most recent admission was used. The outcome in our analysis was death within 90 days of ICU admission. All predictors were collected within the first 24 hrs of admission. For measurements taken more than once within the first 24hrs of admission, the maximum value was used, except for Glasgow coma score, where the minimum value was used. We selected 13 predictors including, age, Glasgow coma score, glucose, creatinine, hematocrit, hemoglobin, potassium, sodium, white blood cell count, heart rate, mean blood pressure, respiratory rate and temperature. We conducted a complete case analysis (as this study is only meant as an illustration), and removed records with suspected errors (two patients had a date of death recorded prior to their date of admission and 1,890 patients had a recorded age of over 300 years). This resulted in observations from 34,098 patients. We randomly split these data into two sets that resembled development and validation settings. All prediction models were developed using the same development data (sample size 976 with 166 events, the minimum required sample size) and the remainder of the data were used for validation (sample size 33,122 with 5567 events). The minimum required sample size calculation was based on the observed event fraction (0.17), number of predictors (13) and c-statistic (0.75), using the R package pmsampsize [15].

In Figure 8 the calibration plots for all 30 prediction models are presented, empirical performance metrics are included in Appendix C. From Figure 8 it is clear that in this case study, correcting for imbalance via a data pre-processing technique (RUS, ROS, SMOTE, SENN), an algorithm which innately corrects for class imbalance (RB, EE) or both, resulted in prediction models which overestimated risk. With respect to discrimination, all data pre-processing techniques used to correct for class imbalance (RUS, ROS, SMOTE, SENN) worsened discrimination for each machine learning algorithm considered except for support vector machine, for which a slight benefit was conferred (Appendix C). The model with the best discrimination was the control model for RF (Appendix C). Finally, all prediction models developed with a class imbalance correction had dramatically deteriorated overall performance as measured by the Brier score (Appendix C).

Overall, these results bear striking similarity to that of simulation scenario 5. In our simulation study, scenario 5 was characterized by data with similar characteristics to the MIMIC-III data (event fraction = 0.2, number of predictors = 8, sample size = minimum required sample size). One notable difference was observed: in this example the random forest model developed with oversampled data did exhibit miscalibration (Figure 8) whereas the random forest models developed with oversampled data in simulation scenario 5 did not exhibit miscalibration (Figure 6).

## 5 Discussion

In this paper, we studied the impact of class imbalance corrections on the out-of-sample predictive performance of clinical prediction models developed with a variety of machine learning algorithms. We found that when data exhibited class imbalance, implementing imbalance corrections often led to deteriorated model calibration and (consequently) deteriorated overall performance. For both moderate (event fraction = 0.2) and strong imbalance scenarios (event fraction = 0.02), we found that correcting for class imbalance with a data pre-processing technique (RUS, ROS, SMOTE, SENN) and/or an imbalance correcting algorithm (RB, EE) resulted in prediction models that consistently over-estimated risk. We noted one exception, ROS-RF models were often well calibrated in our simulation study. Furthermore, the effect of imbalance corrections on model discrimination was often small (or null) and highly dependent on the machine learning algorithm. Subsequent re-calibration of predicted risks improved model calibration and overall performance, yet, had no effect on discrimination. Even after re-calibration, there were few instances where models developed with an imbalance correction preformed better than models developed with no correction for class imbalance. Our findings were supported by the results of the case study. When prediction models were developed using the MIMIC-III

data, all prediction models which corrected for class imbalance (including ROS-RF) exhibited miscalibration characterized by an on average overestimation of risk.

Our findings are consistent with those of van den Goorbergh *et al.* (2022) [13]. In our simulation, pre-processing the data to correct for class imbalance had no noticeable benefit for model discrimination, and led to worse model calibration for all logistic regression models. For prediction models developed with logistic regression, we agree that imbalance corrections may do more harm than good. This finding does, however, not hold for every machine learning algorithm. In particular, for models developed with SVM or RF, the findings were more nuanced. While imbalance corrections did improve discrimination slightly, especially when data exhibited strong imbalance (event fraction = 0.02), this often came at the cost of model calibration. Using imbalanced corrected data to train SVM or RF models resulted in deteriorated model calibration that was often not able to be recovered even after re-calibration. After re-calibration, we noted three models where imbalance corrections conferred a slight benefit to both model discrimination and calibration in some simulation scenarios: RUS-(SVM, RF) and ROS-RF. Finally, while previous studies found that imbalance correcting algorithms improved model discrimination [23, 24, 25], we found these algorithms (RB, EE), on average conferred no benefit or worsened both model discrimination and calibration in the 8 predictor scenarios. With 16 predictors, RB and EE did show improved discrimination compared to the algorithms which did not innately correct for imbalance, often at the cost of model calibration.

Our study had two limitations which warrant discussion. Firstly, hyperparameter tuning for SVM and XG was not as extensive as it was for RF. More extensive tuning could perhaps improve model performance in general, but would be unlikely to alter the effects seen as a consequence of the imbalance corrections. Extensive tuning was implemented for RF based on guidance from Probst *et al.* (2019) [35], no such guidance was available for SVM and XG. Secondly, our work focused on low dimensional settings (8 or 16 predictors) which are typical for clinical prediction model development. Future research may assess the impact of imbalance corrections on machine learning models in higher dimensional settings. Additionally, the performance of the random forest algorithm in combination with random oversampling was an exception in our simulation study. Models developed with random oversampling and random forest were often well-calibrated in our simulation study, though not in our case study. Further research may focus on the performance of random forest in combination with random oversampling to better understand this finding.

Based on our findings we offer three considerations for researchers developing prediction models in the presence of class imbalance. (1) We found that correcting for class imbalance (with a data pre-processing technique and/or an imbalance correcting algorithm) compromised model calibration, resulting in prediction models which over-estimated risk, in low-dimensional settings. Notably, the miscalibration conferred by these corrections was often not restored by re-calibration and not accompanied by improved discrimination. (2) After re-calibration, we found that using random undersampling to pre-process training data for support vector machine and random forest models sometimes conferred slight benefit to predictive performance. In this case, we encourage researchers to consider the ethical implications of discarding a (potentially large) proportion of available data for what may be a small gain in predictive performance. (3) Finally, we wish to highlight that the machine learning algorithms which did not innately correct for class imbalance (logistic regression, support vector machine, random forest and XGBoost), were often well-calibrated when trained with imbalanced data in scenarios with moderate imbalance (event fraction = 0.2). These findings support the notion that it is not always necessary, and may indeed be harmful, to correct for class imbalance.

## 6 Conclusion

Data exhibiting class imbalance are common in medical settings when the modeled outcome is rare. Correcting for class imbalance is common, yet little attention is paid to the effect of correcting for imbalance on model calibration. If the goal of a clinical prediction model is to produce reliable risk estimates (i.e., to achieve good calibration), correcting for class imbalance with a data pre-processing technique and/or an imbalance correcting algorithm may do more harm than good.

Table 1: Summary of parameters for each of the 18 data-generating scenarios.

Scenario	No. Predictors	Sample Size	Event Fraction	n <sub>train</sub>	n <sub>validation</sub>	$\delta_\mu$	$\delta_\Sigma$	C
1	8	0.5N	0.50	193	1930	0.6043	0.3	0.85
2	8	0.5N	0.20	124	1240	0.6043	0.3	0.85
3	8	0.5N	0.02	899	8990	0.6043	0.3	0.85
4	8	N	0.50	385	3850	0.6043	0.3	0.85
5	8	N	0.20	247	2470	0.6043	0.3	0.85
6	8	N	0.02	1797	17970	0.6043	0.3	0.85
7	8	2N	0.50	770	7700	0.6043	0.3	0.85
8	8	2N	0.20	494	4940	0.6043	0.3	0.85
9	8	2N	0.02	3594	35940	0.6043	0.3	0.85
10	16	0.5N	0.50	193	1930	0.4854	0.3	0.85
11	16	0.5N	0.20	247	2470	0.4854	0.3	0.85
12	16	0.5N	0.02	1797	17970	0.4854	0.3	0.85
13	16	N	0.50	385	3850	0.4854	0.3	0.85
14	16	N	0.20	493	4930	0.4854	0.3	0.85
15	16	N	0.02	3593	35930	0.4854	0.3	0.85
16	16	2N	0.50	770	7700	0.4854	0.3	0.85
17	16	2N	0.20	986	9860	0.4854	0.3	0.85
18	16	2N	0.02	7186	71860	0.4854	0.3	0.85

\* N: the minimum required sample size for a prediction model.

\*  $\delta_\mu$ : the difference in predictor means between the classes, for all predictors.

\*  $\delta_\Sigma$ : the difference in predictor variances between the classes, for all predictors.

\* C: the data-generating concordance statistic.

Table 2: Summary of imbalance corrections included in the simulation study.

Method	Abbreviation	Hyperparameters	R Package
Random Undersampling	RUS		ROSE [36]
Random Oversampling	ROS		ROSE [36]
Synthetic Minority Over Sampling	SMOTE	$k = 5$	IRIC [21]
SMOTE - Edited Nearest Neighbours	SENN	$k1 = 5, k2 = 3$	IRIC [21]

\*  $k$ : the number of nearest neighbors in implementation of SMOTE.

\*  $k1$ : the number of nearest neighbors in the SMOTE step of SENN.

\*  $k2$ : the number of nearest neighbors in the ENN step of SENN.

Table 3: Summary of machine learning algorithms studied in the simulation study.

Method	Abbreviation	Hyperparameter Tuning Grid	R Package
Logistic Regression	LR		base R [29]
Support Vector Machine	SVM	default grid search	caret [26]
Random Forest	RF	mtry [1: all predictors], min.node.size [1:10], splitrule [gini]	caret [26]
XGBoost	XG	default grid search	caret [26]
RUSBoost	RB		ebmc [27]
EasyEnsemble	EE		IRIC [21]

\* mtry[1: all predictors]: indicates that the number of candidate splitting variables may take on any value from 1 to the total number of predictors.

\* min.node.size[1: 10]: indicates that the minimum number of observations allowed in a leaf node may take on any integer value from 1 to 10.

\* splitrule[gini]: indicates that all random forest models select the split which minimizes Gini impurity.

Table 4: Median performance measures and their Monte Carlo errors across 2000 simulation iterations for simulation scenarios 4-6.

	Control						RUS						ROS						SMOTE						SENN					
	LR	SVM	RF	XG	RB	EE	LR	SVM	RF	XG	RB	EE	LR	SVM	RF	XG	RB	EE	LR	SVM	RF	XG	RB	EE	LR	SVM	RF	XG	RB	EE
<b>Scenario 4</b>																														
Concordance Statistic	0.84	0.86	0.84	0.84	0.84	0.83	0.84	0.86	0.84	0.84	0.83	0.82	0.84	0.85	0.84	0.82	0.83	0.82	0.84	0.86	0.84	0.84	0.83	0.82	0.84	0.85	0.84	0.84	0.83	0.83
MCMC Error	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Brier Score	0.16	0.15	0.16	0.16	0.17	0.19	0.16	0.15	0.16	0.16	0.17	0.19	0.16	0.16	0.17	0.19	0.17	0.19	0.16	0.16	0.15	0.16	0.17	0.19	0.17	0.17	0.18	0.17	0.17	
MCMC Error	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	
Calibration Intercept	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	
MCMC Error	0.14	0.14	0.12	0.15	0.07	0.05	0.11	0.12	0.09	0.11	0.07	0.05	0.13	0.20	0.34	0.51	0.18	0.17	0.10	0.11	0.09	0.11	0.08	0.05	0.23	0.25	0.15	0.26	0.14	0.07
Calibration Slope	0.92	0.96	1.25	0.91	1.46	>10.0	0.92	0.96	1.25	0.90	1.46	>10.0	0.88	0.87	1.21	0.56	1.26	>10.0	0.90	0.94	1.21	0.89	1.43	>10.0	0.57	0.58	0.78	0.52	0.83	1.62
MCMC Error	0.10	0.11	0.18	0.12	0.17	0.17	0.11	0.11	0.18	0.12	0.17	0.17	0.12	0.11	0.19	0.10	0.15	0.16	0.10	0.11	0.18	0.12	0.10	0.20	0.27	0.21	0.33	0.34		
<b>Scenario 5</b>																														
Concordance Statistic	0.84	0.82	0.82	0.82	0.83	0.82	0.83	0.85	0.83	0.80	0.81	0.80	0.83	0.83	0.83	0.79	0.80	0.80	0.84	0.83	0.82	0.81	0.83	0.83	0.82	0.82	0.82	0.81	0.82	
MCMC Error	0.01	0.03	0.02	0.02	0.02	0.01	0.01	0.02	0.02	0.02	0.01	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	
Brier Score	0.12	0.12	0.12	0.12	0.17	0.20	0.18	0.16	0.18	0.19	0.20	0.20	0.17	0.15	0.12	0.15	0.15	0.15	0.14	0.13	0.15	0.14	0.15	0.19	0.16	0.15	0.17	0.16	0.15	
MCMC Error	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	
Calibration Intercept	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
MCMC Error	0.22	0.23	0.18	0.23	0.10	0.07	0.40	0.23	0.18	0.36	0.14	0.08	0.16	0.24	0.17	0.43	0.17	0.10	0.18	0.30	0.18	0.33	0.20	0.10	0.30	0.40	0.24	0.46	0.25	0.10
Calibration Slope	0.85	0.97	1.27	0.79	1.52	>10.0	0.67	0.96	1.26	0.62	1.30	>10.0	0.76	0.61	1.10	0.33	0.85	1.78	0.71	0.55	0.84	0.41	0.78	1.71	0.54	0.43	0.66	0.35	0.58	1.48
MCMC Error	0.14	0.55	0.20	0.13	0.24	0.27	0.17	0.26	0.31	0.14	0.24	0.27	0.14	0.11	0.20	0.05	0.13	0.18	0.10	0.15	0.07	0.13	0.17	0.12	0.08	0.15	0.10	0.05	0.16	
<b>Scenario 6</b>																														
Concordance Statistic	0.84	0.71	0.78	0.82	0.83	0.81	0.82	0.84	0.82	0.79	0.81	0.79	0.84	0.80	0.81	0.76	0.76	0.76	0.84	0.80	0.78	0.76	0.78	0.84	0.80	0.80	0.79	0.77	0.79	
MCMC Error	0.01	0.04	0.02	0.02	0.02	0.02	0.03	0.02	0.02	0.03	0.03	0.01	0.02	0.02	0.03	0.02	0.01	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	
Brier Score	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.05	0.03	0.04	0.04	0.05		
MCMC Error	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
Calibration Intercept	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
MCMC Error	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
Calibration Slope	0.90	0.90	0.46	>10.0	0.88	0.87	1.21	0.56	1.26	>10.0	0.90	0.96	0.94	1.21	0.89	1.43	>10.0	0.57	0.58	0.78	0.52	0.83	1.25	1.62	0.91	1.46	>10.0	0.92	0.96	1.25
MCMC Error	0.12	>10.0	0.20	0.13	0.28	0.30	0.18	0.66	0.32	0.12	0.26	0.28	0.13	0.04	0.18	0.16	0.19	0.20	0.27	0.21	0.33	0.18	0.34	0.12	0.17	0.17	0.11	0.11		
<b>Scenario 4 Recalibrated</b>																														
Concordance Statistic	0.84	0.84	0.83	0.82	0.84	0.85	0.84	0.82	0.83	0.84	0.86	0.84	0.84	0.83	0.82	0.84	0.84	0.85	0.84	0.84	0.83	0.84	0.84	0.84	0.84	0.84	0.84	0.84	0.84	
MCMC Error	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	
Brier Score	0.16	0.16	0.17	0.19	0.16	0.16	0.17	0.18	0.17	0.19	0.16	0.15	0.15	0.16	0.16	0.17	0.19	0.17	0.16	0.17	0.17	0.16	0.17	0.19	0.16	0.15	0.17	0.16	0.15	
MCMC Error	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
Calibration Intercept	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
MCMC Error	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01		
Calibration Slope	0.92	0.90	0.46	>10.0	0.88	0.87	1.21	0.56	1.26	>10.0	0.90	0.96	0.94	1.21	0.89	1.43	>10.0	0.57	0.58	0.78	0.52	0.83	1.25	1.62	0.91	1.46	>10.0	0.92	0.96	1.25
MCMC Error	0.10	0.12	0.17	0.17	0.12	0.11	0.19	0.10	0.15	0.16	0.10	0.11	0.18	0.05	0.13	0.18	0.05	0.15	0.07	0.13	0.17	0.12	0.05	0.11	0.17	0.11	0.11			
<b>Scenario 5 Recalibrated</b>																														
Concordance Statistic	0.84	0.80	0.81	0.80	0.83	0.83	0.79	0.80	0.80	0.84	0.82	0.83	0.82	0.80	0.81	0.83	0.82	0.82	0.82	0.82	0.83	0.82	0.83	0.82	0.83	0.82	0.83	0.83	0.83	
MCMC Error	0.01	0.02	0.02	0.02	0.01	0.02	0.02	0.02	0.02	0.02	0.01	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	
Brier Score	0.12	0.13	0.13	0.14	0.12	0.13	0.12	0.15	0.13	0.13	0.12	0.12	0.13	0.12	0.14	0.13	0.13	0.14	0.13	0.15	0.13	0.15	0.13	0.12	0.13	0.12	0			

<sup>1</sup> Imbalance Corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule)

<sup>2</sup> Machine Learning Algorithms: LR (logistic regression), SVM (support vector machine), RF (random forest), XG (XGBoost), RB (RUSBoost), EE (EasyEnsemble)

<sup>3</sup> Scenario 4: 8 predictors, minimum required sample size (N), class balanced data (event fraction = 0.5)

<sup>4</sup> Scenario 5: 8 predictors, minimum required sample size (N), moderately imbalanced data (event fraction = 0.2)

<sup>5</sup> Scenario 6: 8 predictors, minimum required sample size (N), strongly imbalanced data (event fraction = 0.02)



Figure 1: An illustration of the data pre-processing imbalance corrections studied in our simulation. The data shown have a sample size of 2000 and an event fraction of 0.02, imbalance corrections were applied to achieve a target event fraction of 0.5 (perfect balance).

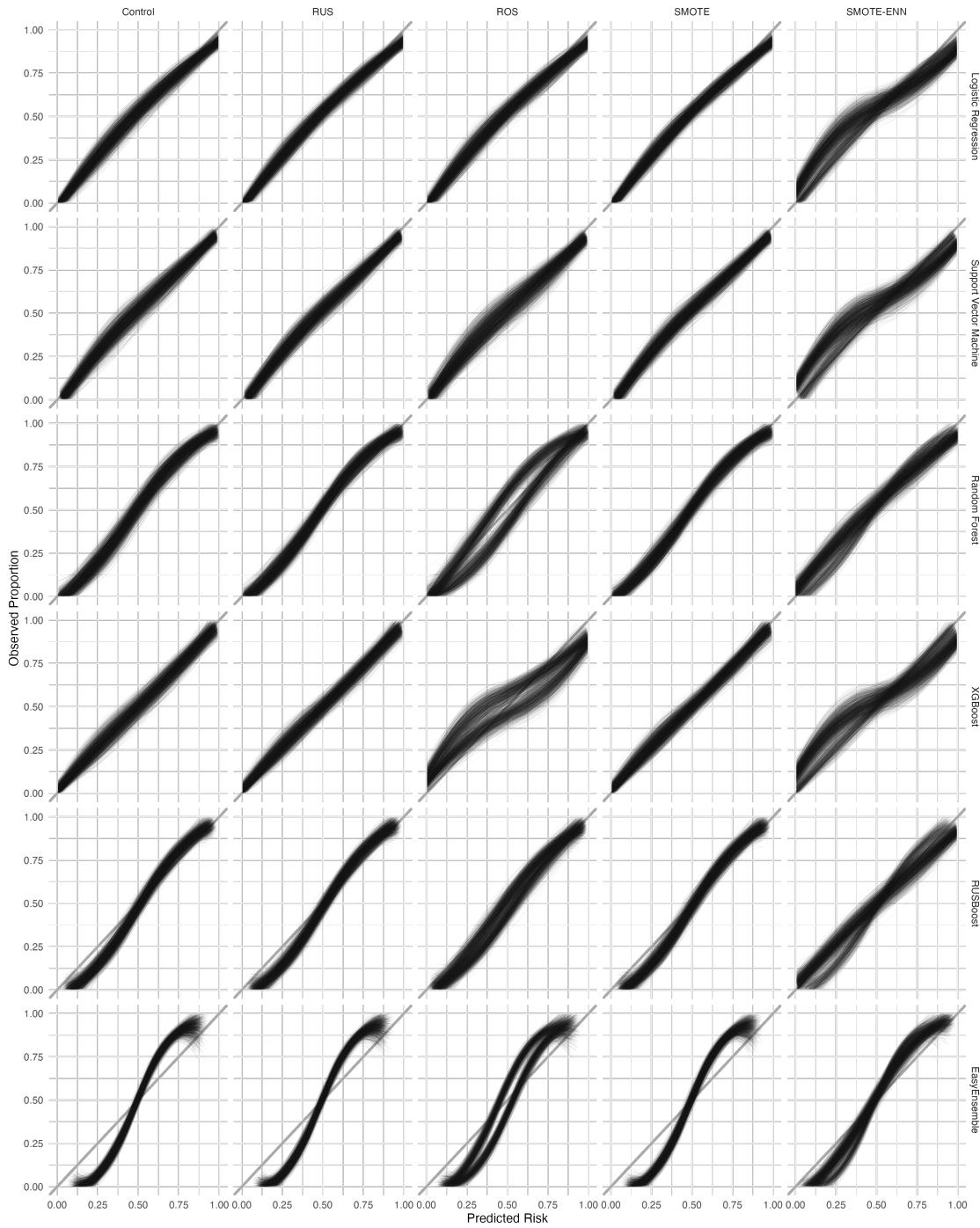


Figure 2: Flexible calibration curves for each of 2000 simulation iterations in simulation scenario 4. This simulation scenario is characterized by 8 predictors, exactly the minimum required sample size ( $N$ ) and class balanced data (event fraction = 0.5). Flexible curves were generated using raw predicted risks; no re-calibration. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SMOTE-ENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

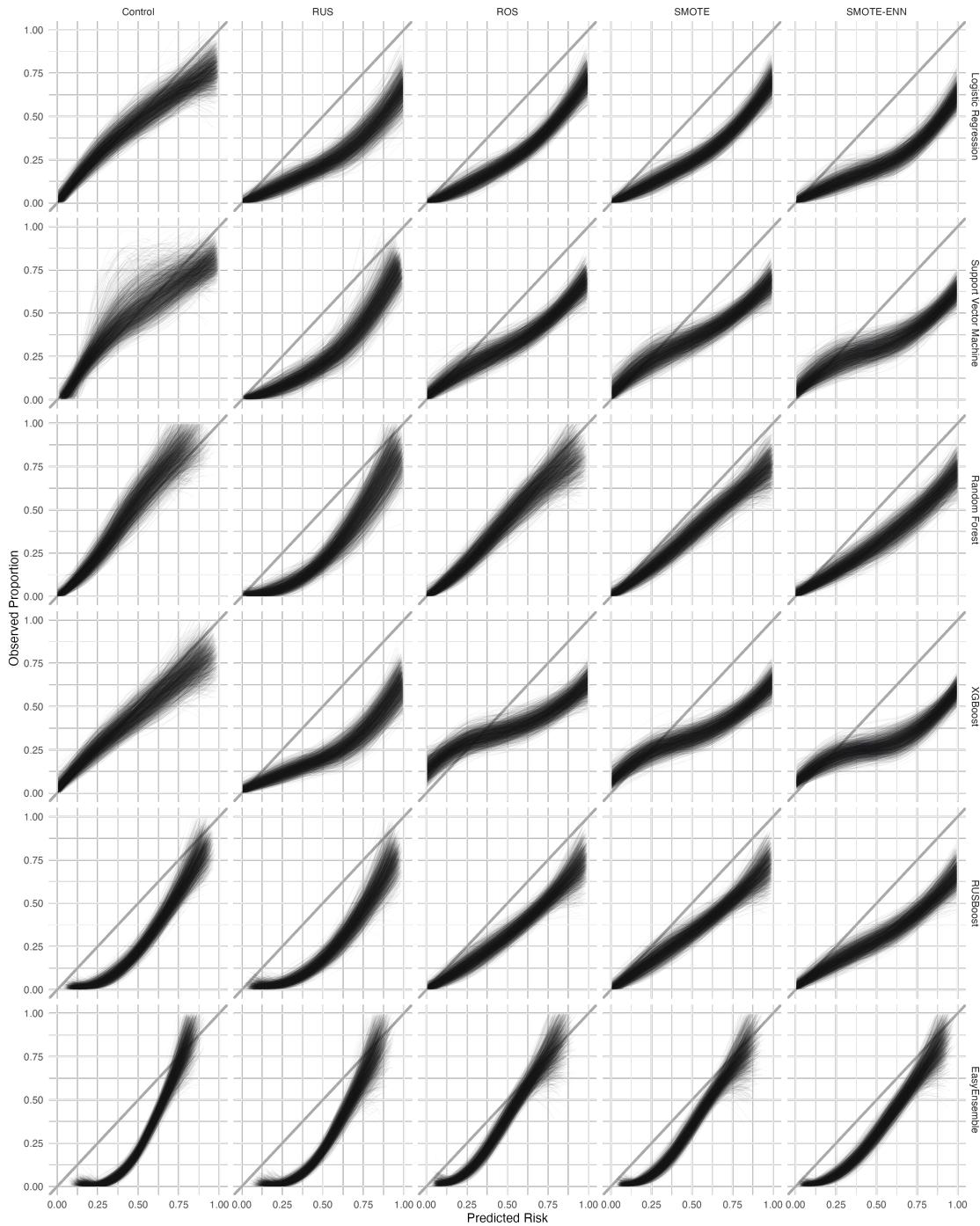


Figure 3: Flexible calibration curves for each of 2000 simulation iterations in simulation scenario 5. This simulation scenario is characterized by 8 predictors, exactly the minimum required sample size ( $N$ ) and moderately imbalanced data (event fraction = 0.2). Flexible curves were generated using raw predicted risks; no re-calibration. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SMOTE-ENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

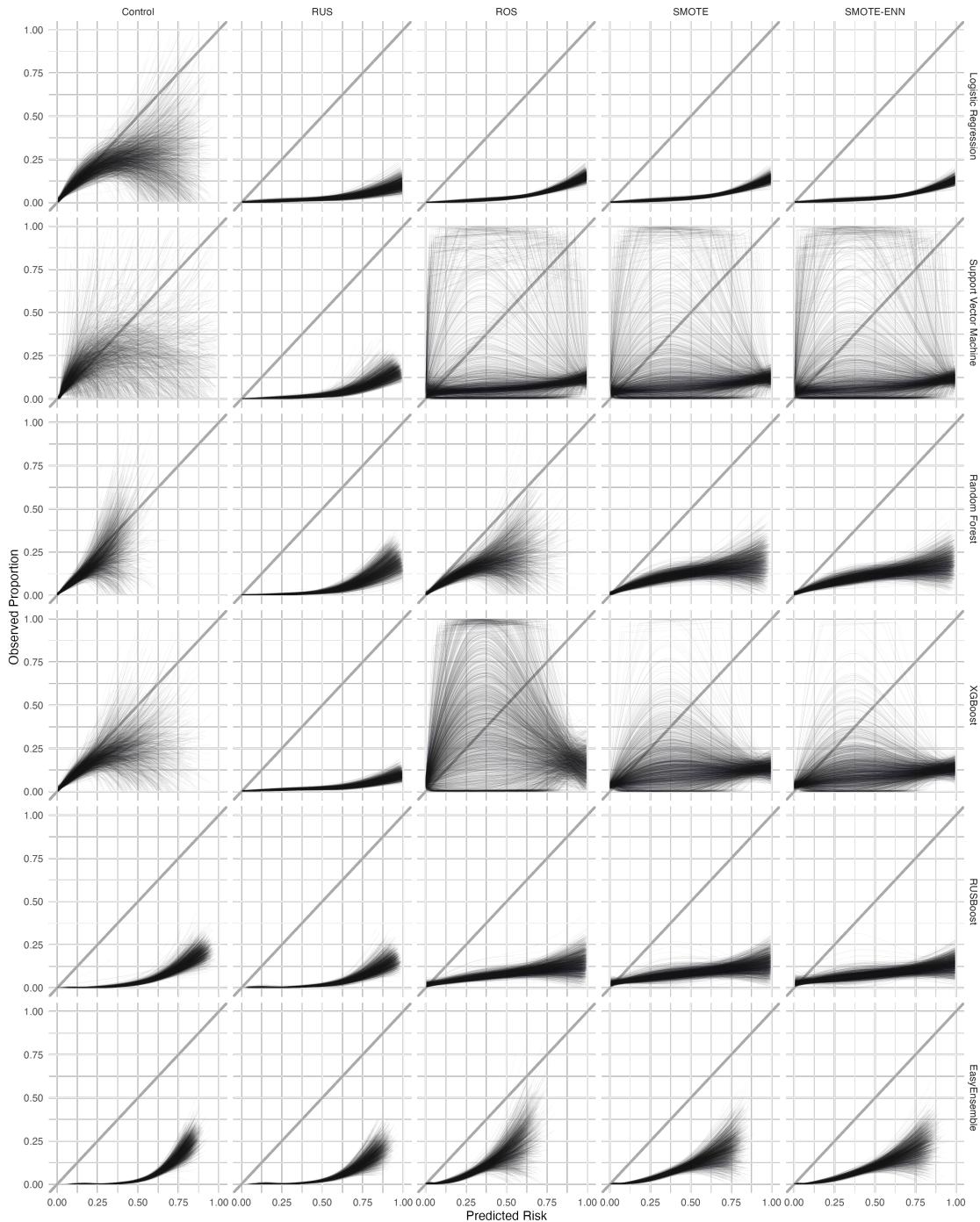


Figure 4: Flexible calibration curves for each of 2000 simulation iterations in simulation scenario 6. This simulation scenario is characterized by 8 predictors, exactly the minimum required sample size ( $N$ ) and strongly imbalanced data (event fraction = 0.02). Flexible curves were generated using raw predicted risks; no re-calibration. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SMOTE-ENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

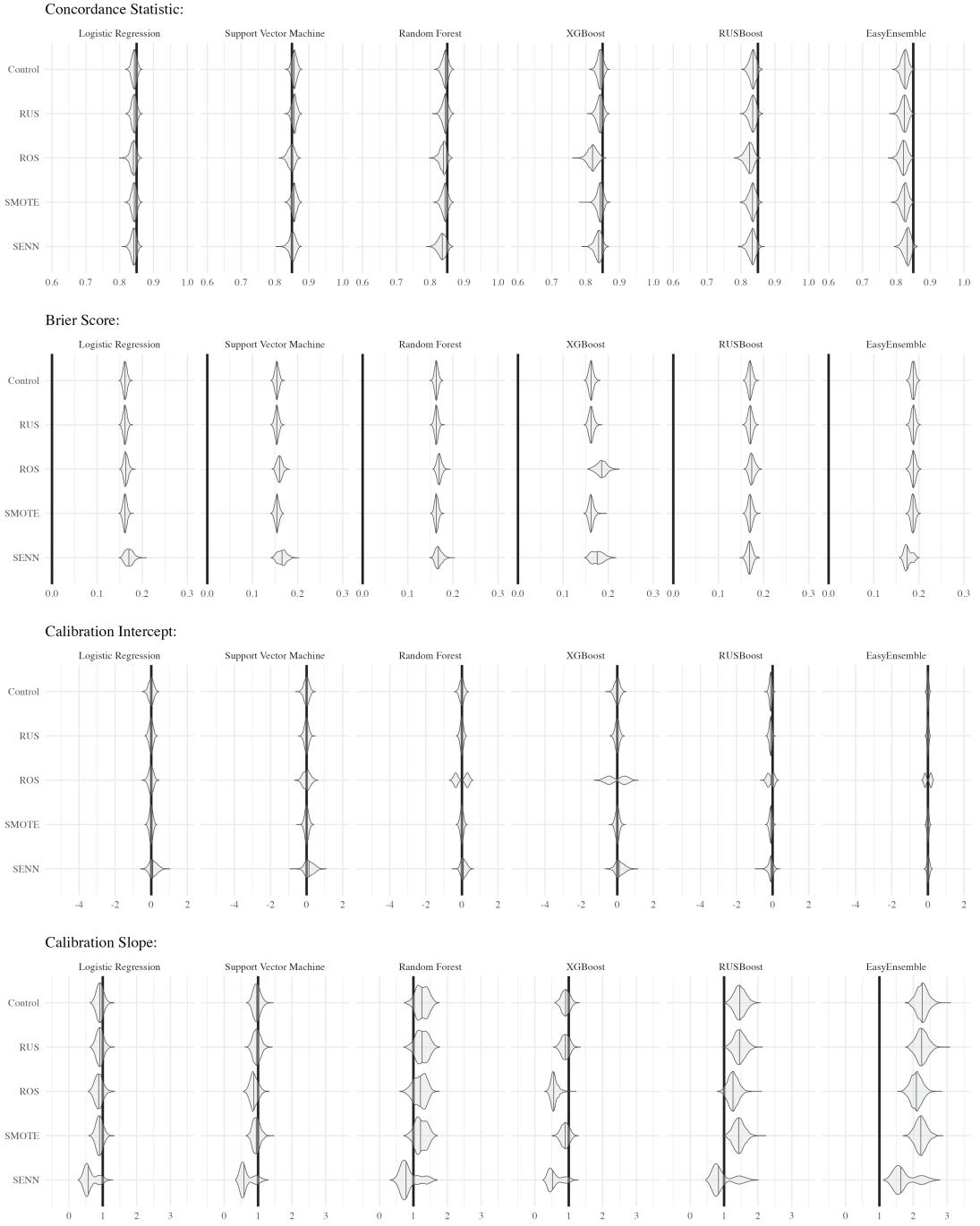


Figure 5: Empirical performance metrics for each of 2000 simulation iterations in simulation scenario 4. This simulation scenario is characterized by 8 predictors, exactly the minimum required sample size ( $N$ ) and class balanced data (event fraction = 0.5). Empirical performance metrics were computed with raw predicted risks; no re-calibration. The target value highlighted for the concordance statistic reflects the data-generating concordance statistic, 0.85. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

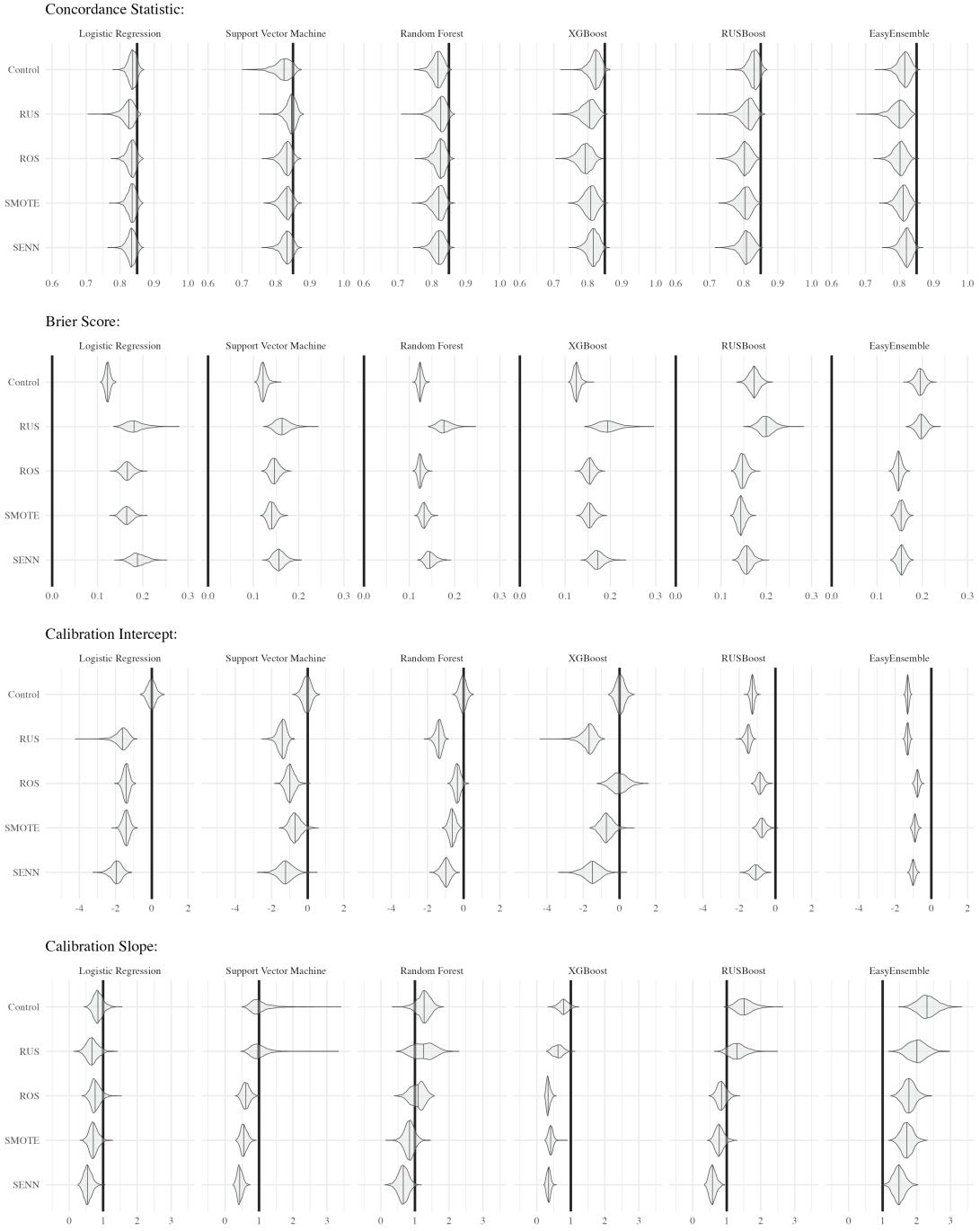


Figure 6: Empirical performance metrics for each of 2000 simulation iterations in simulation scenario 5. This simulation scenario is characterized by 8 predictors, exactly the minimum sample size ( $N$ ) and moderately imbalanced data (event fraction = 0.2). Empirical performance metrics were computed with raw predicted risks; no re-calibration. The target value highlighted for the concordance statistic reflects the data-generating concordance statistic, 0.85. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

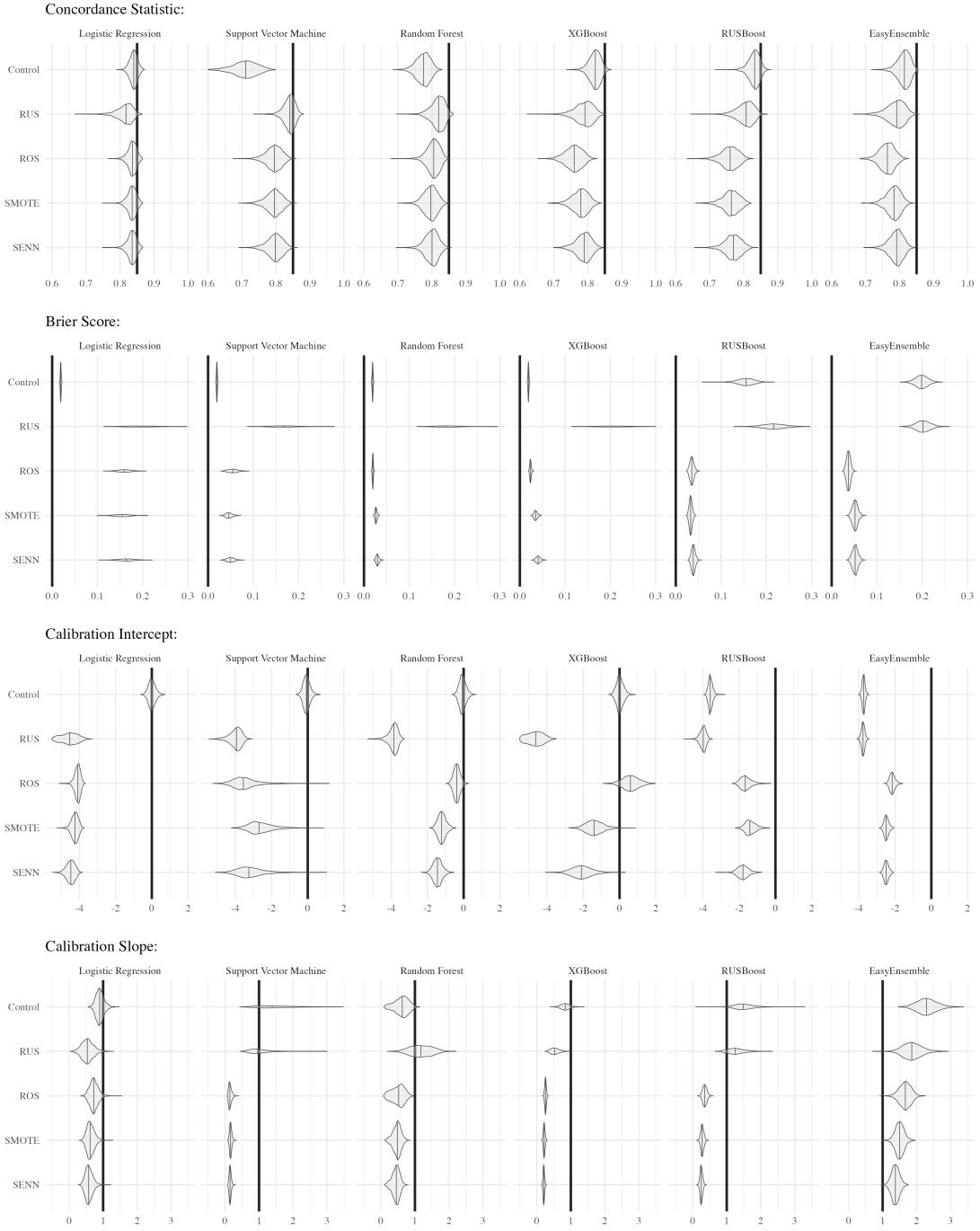


Figure 7: Empirical performance metrics for each of 2000 simulation iterations in simulation scenario 6. This simulation scenario is characterized by 8 predictors, exactly the minimum required sample size ( $N$ ) and strongly imbalanced data (event fraction = 0.02). Empirical performance metrics were computed with raw predicted risks; no re-calibration. The target value highlighted for the concordance statistic reflects the data-generating concordance statistic, 0.85. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

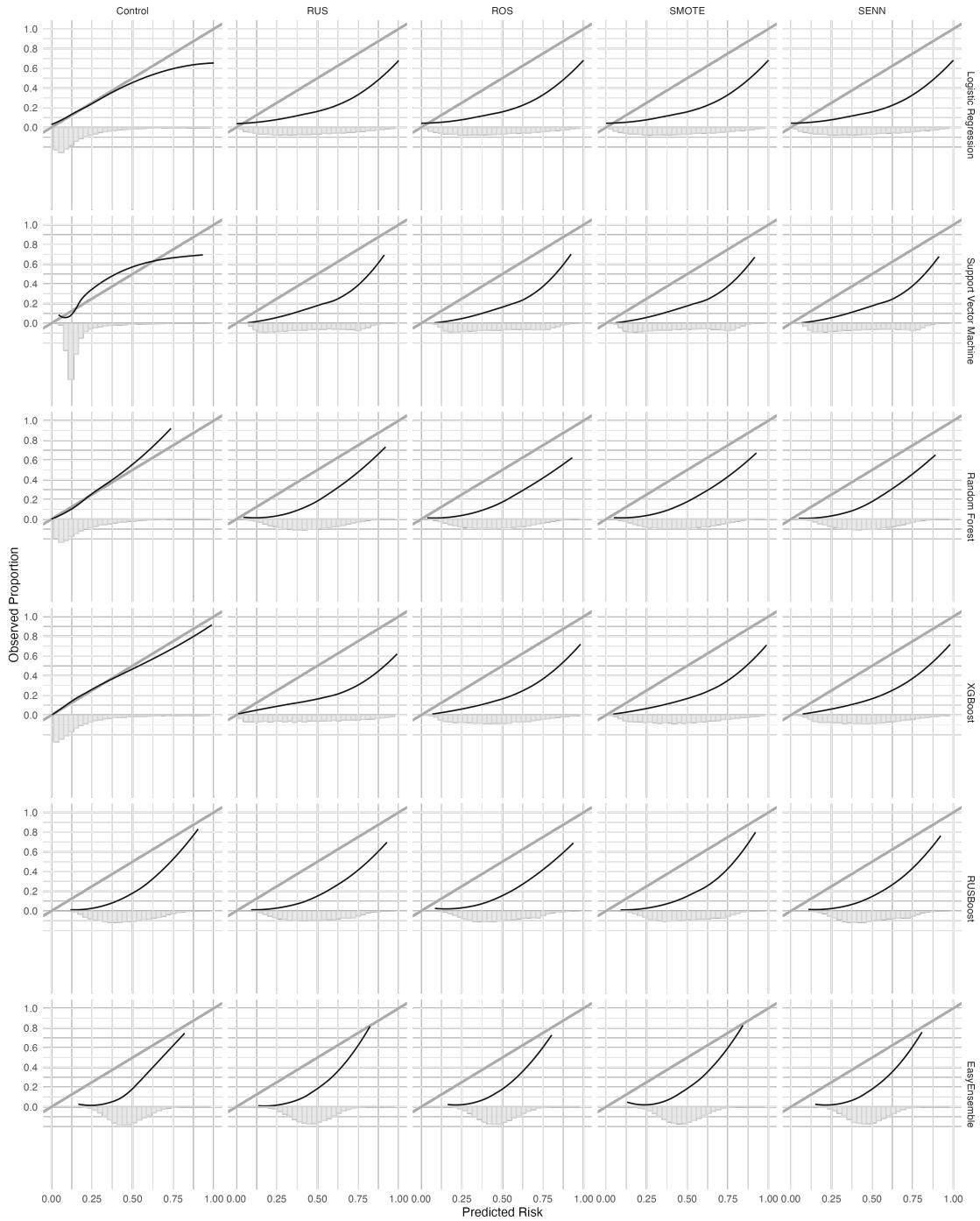


Figure 8: Flexible calibration curves for predictions models developed using the MIMIC-III database with histograms of the predicted risks. The development data are characterized by 13 predictors, exactly the minimum required sample size and an event fraction of 0.17. Imbalance corrections: RUS (random undersampling), ROS (random oversampling), SMOTE (synthetic minority oversampling), SENN (synthetic minority oversampling with Wilson's Edited Nearest Neighbor rule).

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