Prediction of Price Dynamics of Medicine in the Netherlands

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Introduction

- Within the HTA framework in the Netherlands, health economic models are used to determine the cost-effectiveness of new medicine.
- One of the core inputs in health economic evaluations is the price of medicine, both the new medicine and comparator.
- It is assumed that the prices of medicine are static, but this is rarely the case. Medicine prices are dynamic and therefore dynamic medicine prices should be used to estimate the real-life impact and effects.
- Previous research has shown that the price of medicine decreases over time, substantially impacting economic and health outcomes [1,2].
- The aim of this study is to develop a price life cycle (PLC) prediction model for medicine in the Netherlands to better inform HTA and reimbursement decision-making.

Methods

The PLC prediction model was built based on Dutch historic medicine price and volume data supplemented with other available sources to forecast future price dynamics of medicine, using an ensemble of machine learning models. Accuracy was assessed based on their performance in six measures of accuracy, primarily the root mean squared error (rmse). This resulted in the models' most accurate distribution and weight to determine the medicine price dynamics.

Primary regressors for price dynamics were determined based on previous research, internal discussions and based on data availability that was deemed relevant for medicine prices in the Netherlands. Data sources used were the Farminform database, European Medicine Agency data and Dutch Healthcare Authority data. This data was integrated and analyzed in a model to assess and test the primary regressors and prognostic factors. We identified six primary regressors used in the prediction of price dynamics. The used regressors to predict medicine price dynamics were: Main ATC group, Date of market entry, Initial price, Time-dependent regressors, Time on the market, Loss of exclusivity, and Time since loss of exclusivity.

As the aim is not to predict monthly fluctuations of prices, but the long-term trend, the prices were converted into moving annual averages. Using the average price per defined daily dose (DDD) in the first year, the prices were translated into relative prices, where a value of 100 indicates the starting price. For the analyses, these values were transformed using the box-cox transformation, so prices were shaped like a normal distribution.

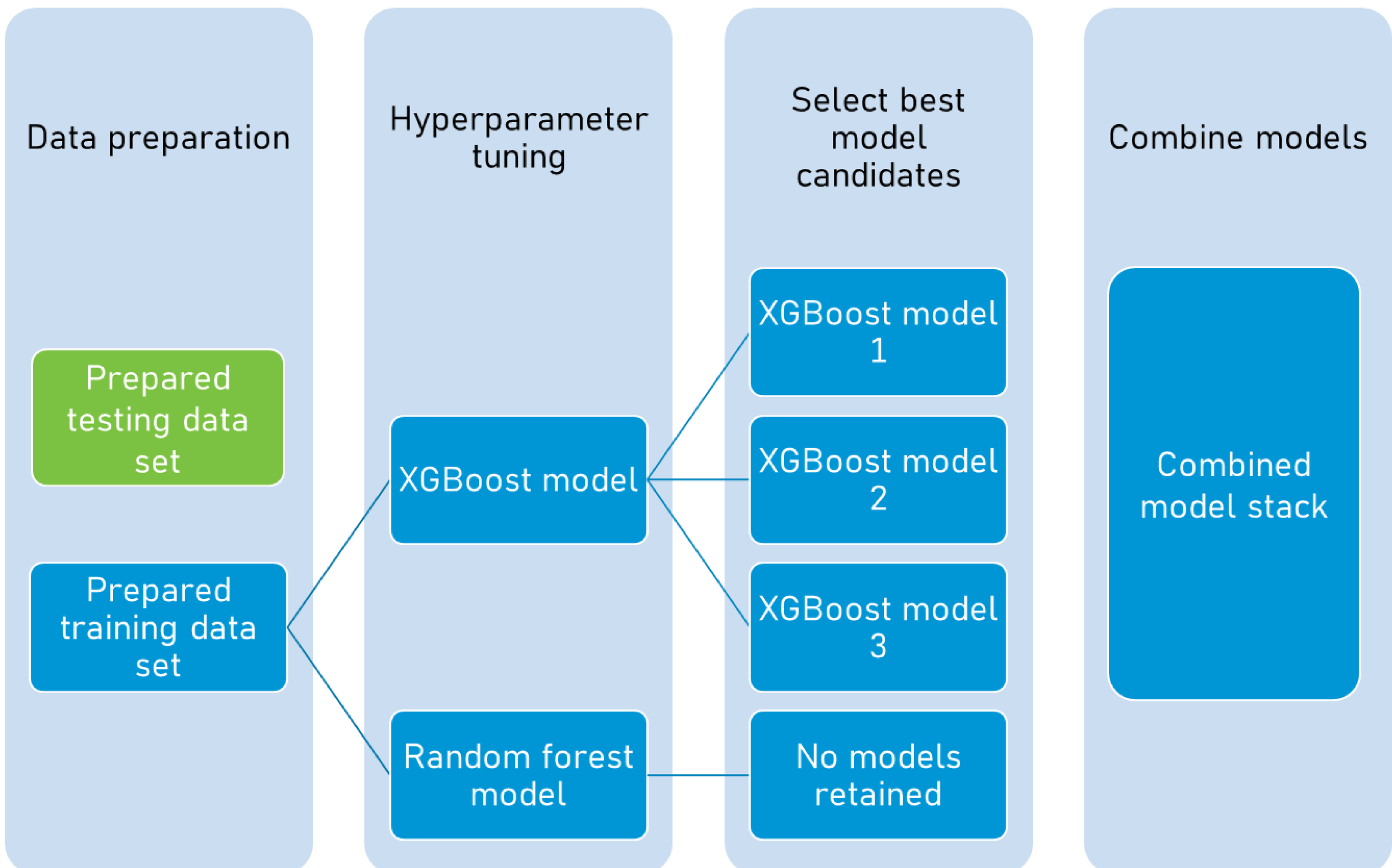

Figure 1. Schematic overview of the development of the ensemble model.

The dataset was separated into a testing and training data set. Two machine-learning models were used at the current stage: an XGBOOST model and a random forest model [3,4]. The training data set was used to tune the hyperparameters of the different machine-learning models according to the chart shown below. A Bayesian search algorithm was used to minimize the rmse by finding the optimal performing hyperparameters in the tuning set. Based on the training set, and tuning of the models, an ensemble of machine models with the highest performance was created. The ensemble model was created by weighing each candidate model using a linear regression model, again minimizing the rmse. The full process is displayed in Figure 1.

Results

We have assessed all 74 predicted time series of the testing set, using the ensemble model, compared to the observed price development. Based on the visual inspection of the results, the predictions are categorized into three categories: high accuracy, medium accuracy, and low accuracy.

Out of the 74 predictions made, 31 were deemed high-accuracy predictions. Two examples of high-accuracy predictions are shown in the figures 2a and 2b. Based on visual judgement these are close to the observed price development from the testing data set. 27 out of the 74 predictions made were deemed medium accurate. These predictions have in common that the overall trend is predicted accurately, but the y-axis coordinates were either too high or too low, making it less accurate. Another issue in some cases is that the scaling of the results is not accurate, for example, caused by a steep price decrease shortly after market introduction. Two examples of medium-accuracy predictions are shown in figures 3a and 3b. Out of the 74 predictions made, 18 are deemed to have low accuracy. We observed that in the low-accuracy predictions, the model seems less able to predict sudden increases or decreases in price. This is the basis of most low-accuracy predictions. These sudden price changes may be hard, if not impossible, to predict.

Figure 2a/b. Price predictions and price development of two case studies, examples of a high-accuracy prediction. The dashed line in the moment of loss of exclusivity.

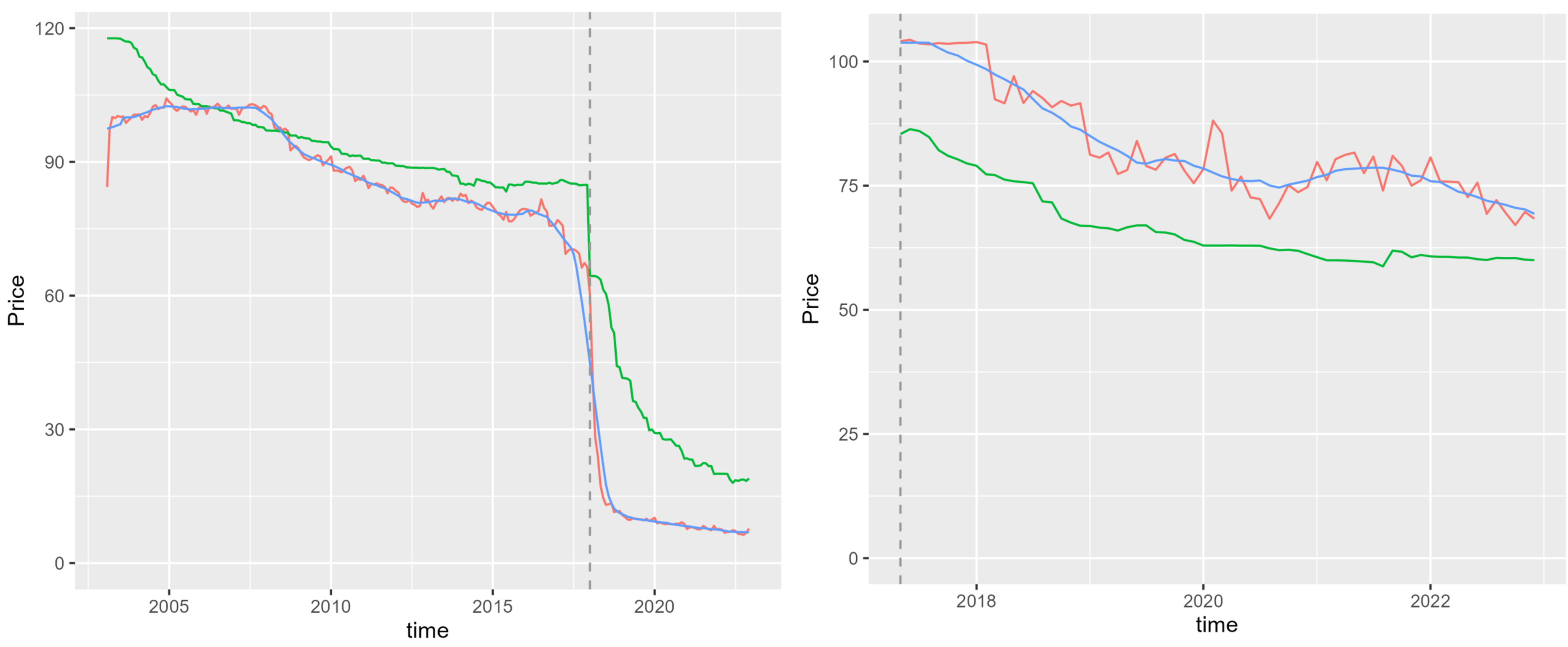

Figure 3a/b. Price predictions and price development of two case studies, examples of a medium-accuracy prediction. The dashed line in the moment of loss of exclusivity.

Conclusion

The PLC model demonstrated the capability to predict the price dynamics of medicine in the Netherlands. Currently, 42% of predictions were deemed high-accuracy, 36% were deemed medium-accuracy, and 22% were deemed low-accuracy predictions.

With the development of the model, we have shown the proof of concept that it is able to accurately predict the price dynamics of medicine. The next steps of the development of the price prediction model will focus on improving predictions by optimizing regressors and applying a larger set of machine learning algorithms.

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