Modeling Price Premiums of Oncology Drugs in Germany: A Cross-Validated Analysis Using XGBoost

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Background

- Oncology drug premiums carry significant economic and policy burden, thereby affecting patient access. The prices of these drugs are often not associated with added clinical benefit[1].
- The pricing of pharmaceutical products in Germany is linked to a benefit assessment score (1-6) determined by the G-BA, a body of healthcare and insurance providers, and is based on IQWiG evaluations[2].
- Prediction of the impact of benefit assessment on pricing would support evidence-based negotiation strategies.

Objective

To predict pharmaceutical premiums in Germany using machine learning approaches

Methods

- The XGBoost machine learning framework was utilized, which generates multiple gradient-boosted decision trees for improved prediction accuracy[3], with stratified cross-validation to reduce sampling bias (**Figure 1**).

Oncology drugs with completed assessments were used to evaluate the G-BA rating and the log price premium was predicted

Data: oncology drugs with completed assessments in AMNOG Monitor (N=258)

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Identify predictor features (8):
Mortality, morbidity, QOL, safety, mean price of active comparators at launch, orphan drug status, study design quality, G-BA probability of benefit

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Evaluate overall G-BA rating using the remaining of the 8 predictor features through XGBoost*

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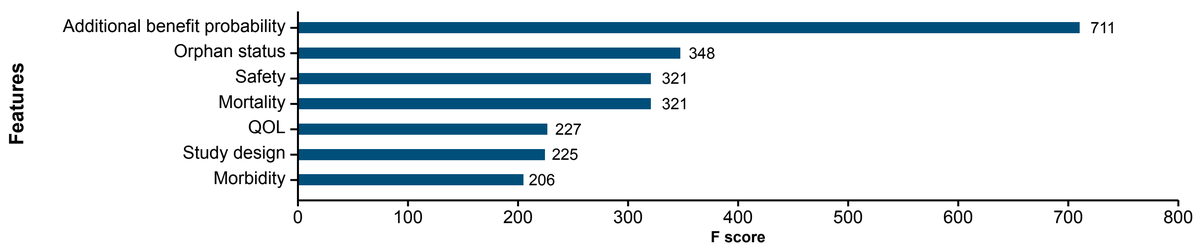
Predict log-transformed price premium using other predictors except orphan drug status using XGBRegressor
- Regularization**
- Cross-validation†

*Multi-objective softmax was applied as the G-BA rating is categorical.
**L1 (lasso) or L2 (ridge) regularization prevented overfitting by penalizing model complexity.
†Model performance was evaluated via a stratified 5-fold cross-validation with a 75-25 training-test split, preserving the distribution of premiums between folds.

Results

- The XGBoost classifier model achieved an overall accuracy of 78.5% when its ability to predict G-BA rating using a standard 80-20 training-test split was evaluated.
- Feature importance analysis revealed that additional benefit probability was the most dominant predictor, with an F score of 711 (**Figure 2**).

Figure 2: Feature importance analysis for predicting G-BA rating



Note: Safety, mortality, QOL, study design, and morbidity were as assessed by G-BA.

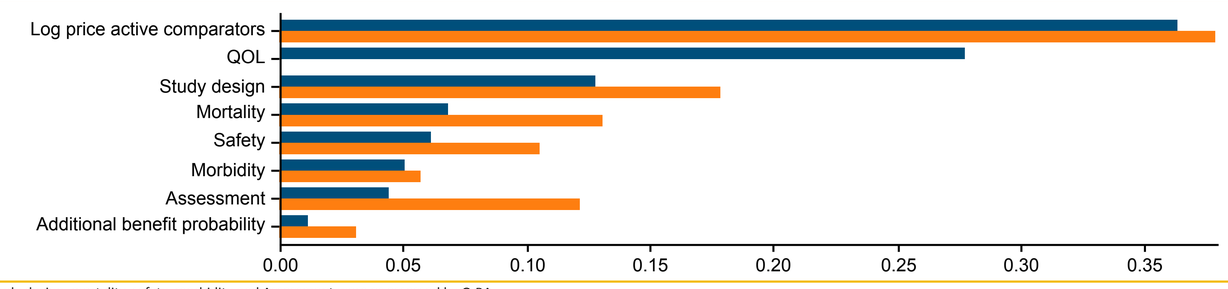
- To predict premiums, the full model had strong performance without cross-validation (**Table 1**) that decreased substantially with cross-validation, suggesting potential overfitting. L1-regularization with α=0.5 and constraining maximum tree depth to 3 improved model stability.

Table 1: Proportion of variance explained (R^2) by the premium prediction model according to regularization and cross-validation

Model configuration	Cross-validation	R^2
Full model (75-25 split)	None	0.834
Base model	5-fold	0.450
L1-regularized model (α=0.5, max depth=3)	None	0.798
L1-regularized model (α=0.5, max depth=3)	5-fold	0.547

- Feature importance analysis showed that the log price of active comparators was the strongest predictor, followed by QOL and study design quality (**Figure 3**). Regularization increased the relative contribution of G-BA assessment ratings and reduced safety and morbidity scores.

Figure 3: Feature importance analysis for predicting log price premiums, before (blue) and after (orange) regularization



Note: QOL, study design, mortality, safety, morbidity and Assessment were as assessed by G-BA.

- There is a strong correlation between actual log price and the price of active comparators, reflecting the feature importance analysis (**Figure 4**).
- There was a strong linear agreement between model predictions and observed values (**Figure 5**).

Figure 4: Correlation between actual log price premium and the log price of active comparators

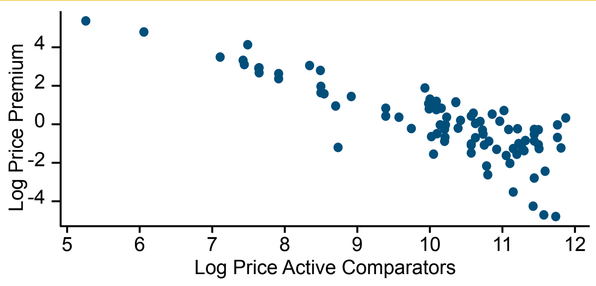
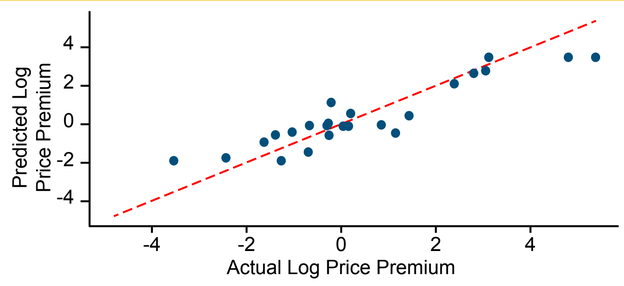


Figure 5: Correlation between model predictions and observed values in log price premium



Conclusions

- Comparator price emerged as the strongest predictor for drug price premiums (~37% importance), suggesting that market anchoring plays a crucial role.
- Mortality and study design quality also showed substantial predictive power, while QOL had a moderate impact.

Limitations

- The model achieved a cross-validated R^2 of 0.547 (**Table 1**), indicating moderate predictive performance after applying more rigorous validation.
- This suggests that clinical and regulatory features capture only part of the complexity.

Key Takeaways

Comparator prices, study design, and clinical features can be used to anticipate negotiated oncology drug prices in Germany.

The use of regularized gradient boosting combined with stratified cross-validation provides a more robust estimate of model performance.

This approach may support evidence-based pricing strategy and highlights opportunities for refining methodology in health assessment research.

Future Directions

- Incorporate **additional features**, e.g., budget impact, disease prevalence, unmet medical need indicators
- **Expand dataset** to improve generalization across indications
- Investigate **temporal trends** in post-launch pricing patterns
- Compare performance to **other therapeutic areas**
- Explore neural networks and ensemble methods to capture **non-linear interactions**

References

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Abbreviations

AMNOG: Act on the Reform of the Market for Medicinal Products; G-BA: Gemeinsamer Bundesausschuss (Federal Joint Committee); IQWiG: Institue for Quality and Efficiency in Health Care; QOL: quality of life

Acknowledgements

Medical writing, editorial, and graphics support were provided by Cactus Life Sciences.

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Disclaimer

The initial outline for this poster was generated with the help of AI. While this served as a starting point, the poster was then human-written, checked, and formatted.

Poster Presented at International Society for Pharmacoeconomics and Outcomes Research Europe 2025, 9-12 November 2025, Glasgow, Scotland, UK