

# Using machine learning to inform evidence development for optimising HTA outcomes in Europe

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## Objective

- This project applied Artificial Intelligence and Machine learning (AIML) techniques on relevant data with the goal of generating insights and predicting success for Health Technology Assessments (HTA) submissions in selected European markets (Germany, France, Italy, Spain)
- Support was explored in the areas of:
  - Evidence generation from clinical trials
  - Product positioning in oncology indications

## Conclusions

- This pilot project demonstrated the potential of AIML to supplement and enhance traditional approaches to HTA submission strategies by leveraging all previous submissions in a therapy area
- Models captured non-linear relationships among many features to produce quantitative outputs on the likelihood of favourable HTA outcomes
- Such approaches have the potential to radically change how companies prepare for HTA evaluation in the future

## Plain language summary



### Why did we perform this research?

To address inefficiencies and bias in traditional methods used to prepare a new pharmaceutical product for launch, and explore more quantitative supportive technique



### How did we perform this research?

A database of historical product assessments in oncology was utilized; this database included information on submitted clinical data and the design of clinical trials, and aspects relating to the need for new therapies in different tumour types. Several machine learning models were then built from this database and used to make predictions for future products



### What were the findings of this research and what are the implications?

AIML-based approaches to inform pharmaceutical product launch are both feasible and useful, opening the door for further innovation beyond traditional research-based methods

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## Disclosures

In relation to this poster, we declare that there are no conflicts of interest.

## Introduction

- Current methods to understand payer decision making and HTA appraisals include historical analogue-based analysis, and primary market research. These traditional methods rely on anecdotal evidence and consideration of a small number of features at a time, leaving opportunity for advanced analytical methods to generate more precise and relevant insights.
- AIML techniques have traditionally been used in other fields to find complex relationships between non-linear variables and make predictions based on historical behaviour.
- Applications of AIML techniques for HTA market access activities have previously been limited due to lack of relevant data and cross-functional expertise. This project is a first step to address these limitations by building an innovative tool to inform market access decision making.

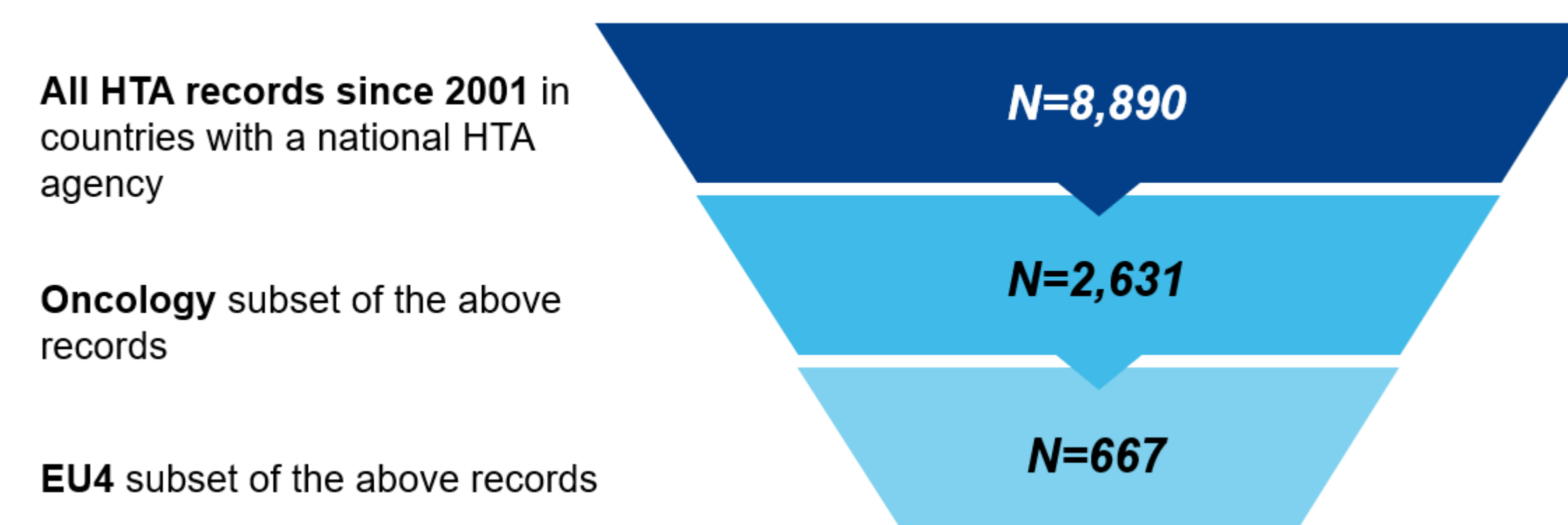
## Methods

- A database of previous oncology product launches and indication expansions in the last 10 years was built from a number of data sources. The database included data on historic HTA submissions (HTA Accelerator, IQVIA), clinical trails (AATC CTTI, Public) and disease information.
- Raw data was converted into a structured format and supplemented with a number of engineered features covering the disease indication, evidence generation and study design, and product information including competitor landscape.
- Using the database, various random forest binary classifiers were built at the individual country level for France and Germany, and cross-country for EU4 markets.
- Models were built in Python using the scikit learn package, with an iterative random grid search for hyperparameter optimisation and balanced class weights. The test/train data split remained constant at 20/80%, with average precision used as the model scoring criterion. Models were evaluated by area under the receiver operating characteristic curve, with the F1 threshold used to assign a binary score where necessary.

## Results and interpretation

- The database provided approximately 700 records across EU4 markets for analytics and AIML. These were split into individual and cross-country models to predict HTA outcomes (Figure 1)
- Two binary classifiers were used to predict HTA outcomes in EU4 markets, each with a different degree of 'strictness' based on local HTA frameworks (see Figure 2). In this way, predictive outputs of both models could be analysed in parallel to give a more detailed overall prediction (see Figure 3).
- For HTA models, AUC (area under the curve) scores were in the 0.82-0.86 range providing confidence in the model performance and qualitative validation using historical analogues demonstrated their application to real world examples (Figure 3). In this case, two binary classifiers were trained using two different partitions of positive or negative HTA rating providing more insights on the ASMR rating in France than possible with a single classifier.

Figure 1. Database creation



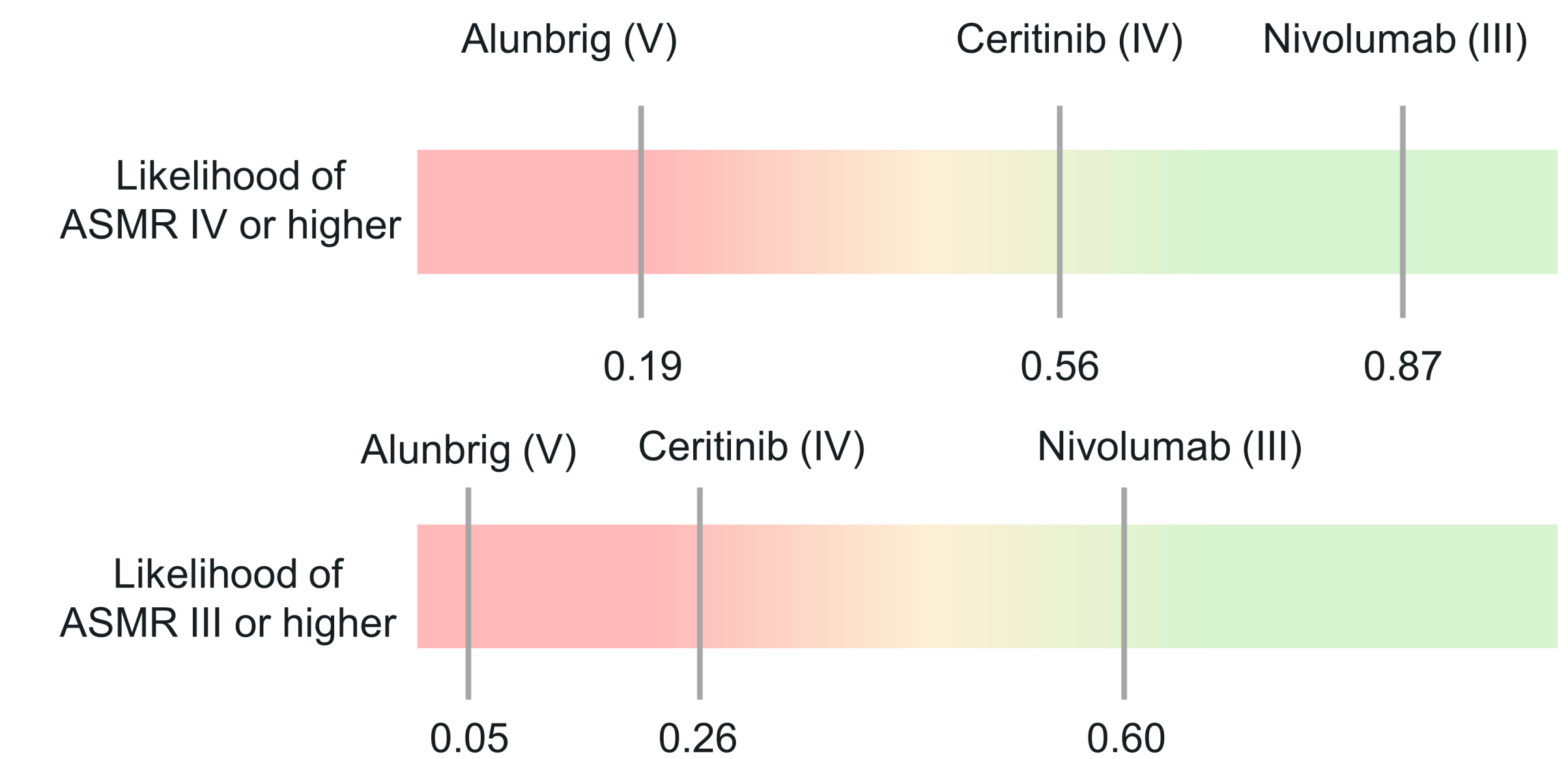
Scope	Number of Records
<b>EU4 (combined)</b>	<b>577</b>
<b>France (single country)</b>	<b>322</b>
<b>Germany (single country)</b>	<b>166</b>
<b>EU4 (combined country)</b>	<b>361</b>
<b>Germany (AMNOG rebate)</b>	<b>191</b>

Figure 2.

	Less Strict Classifier		More Strict Classifier*	
	Positive	Negative	Positive	Negative
	Major, Considerable, Non-Quantifiable, Minor	No added benefit, Less benefit	Major, Considerable, Non-Quantifiable, Minor	No added benefit, Less benefit
	ASMR I-IV	ASMR V	ASMR I-III	ASMR IV-V
	Positive & Restricted IPTs	Negative IPT	Positive IPT	Restricted and Negative IPT
	Innovative or Conditional status	No Innovation	Innovative status	No or Condition innovation

\*No change was made to the grouping of German HTA records due to loss of performance.

Figure 3. HTA model predictions of historical analogues in France



Double binary classifier system outlined in Figure 2, ground truth of HTA outcome shown in brackets. No F1 threshold selected. AUC ROC (Receiver Operating Characteristics curve) = 0.82-0.85

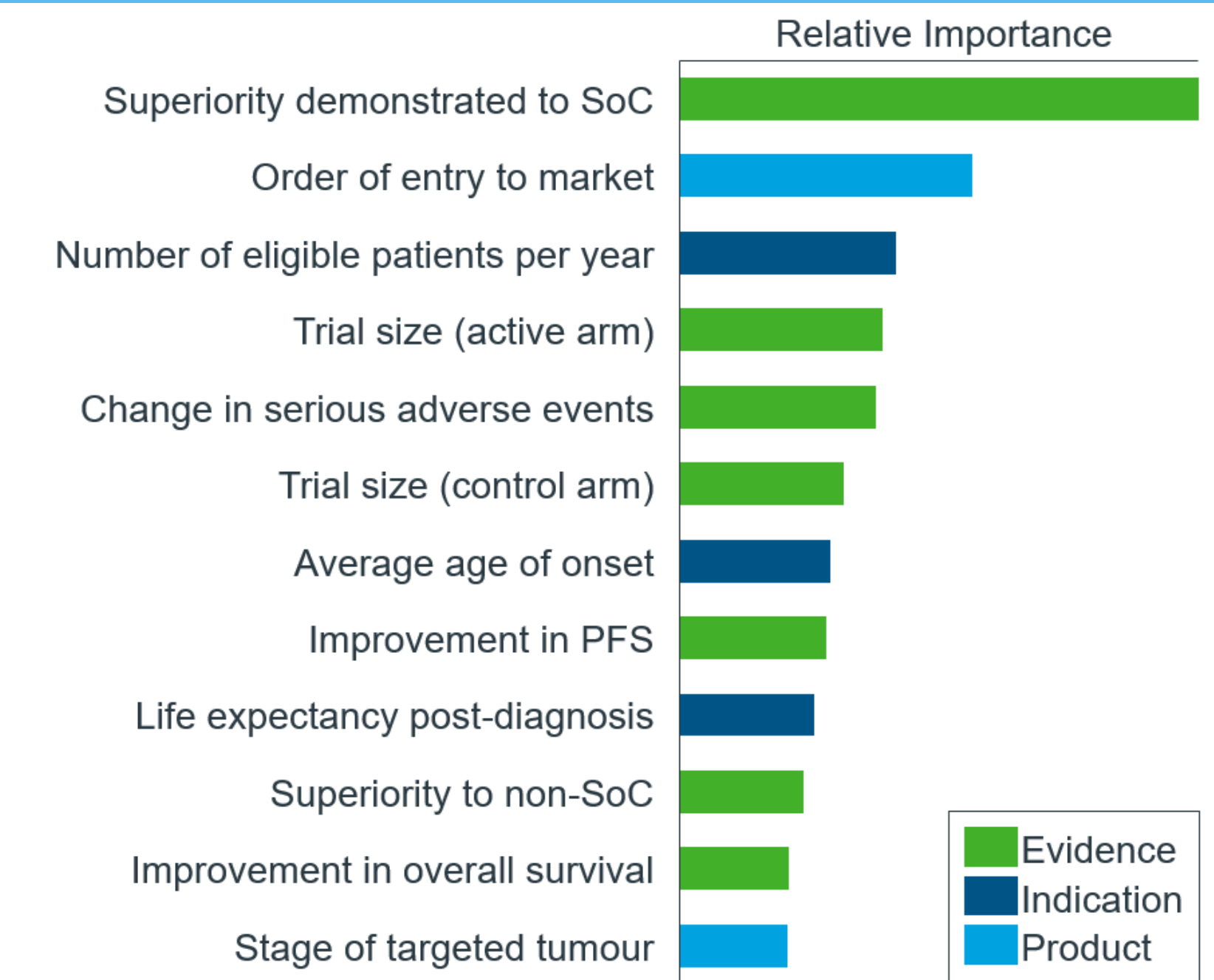
Figure 4. Feature importance

Figure 4: Feature importance was analysed for the HTA models, providing a view on key P&MA drivers (data shown for 'Less Strict Classifier' (see Figure 2), ranking based on Gini impurity measure)

As expected, demonstrating superiority to a standard of care (SoC) is an important feature, with evidence-related features generally the most important.

Some features, such as improvement in overall survival, are less important than expected, but this likely relates to the lower benchmark for success required in the 'less strict classifier'.

Note: Top twelve most important features shown.



## Discussion

- There are several challenges associated with AIML modelling in healthcare, including the relatively small set of historical records, large amounts of missing and/or unstructured data, and the constantly evolving P&MA landscape. We used imputation techniques and models specifically designed to handle smaller datasets to address these. In the future, data augmentation methods will be explored to create potentially larger datasets.
- While the models perform reasonably well, it is difficult to quantify the additional benefit over to traditional approaches, since these are not associated with similar measures of accuracy.
- In the future, we will improve the overall modelling with additional data, an expanded feature set, and the ability to consider wider records beyond oncology.

## Abbreviations

AIML: Artificial Intelligence & Machine Learning, AUC: Area Under Curve, HTA: Health Technology Assessment, IPT: Informes de Posicionamiento Terapeutico ROC: Receiver Operating Characteristic