Could Artificial Intelligence Support Prediction of Reimbursement Decisions in Scotland? A Pilot Project

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Background and objective

- An innovative medicine has been defined by the European Medicines Agency (EMA) as 'a medicine that contains an active substance or combination of active substances that has not been authorised before'. [1]
- Innovative medicines are promising with the potential for incurable diseases or diseases without satisfactory treatments.
- Due to technological advancement, more and more innovative drugs have been approved by EMA and the U.S. Food and Drug Administration in recent years.
- How to reimburse and price these drugs is a big challenge for decision-makers in health technology assessment (HTA) agencies as these drugs are usually associated with high prices and uncertainties in clinical and economic evidence.
- Few studies were conducted to investigate the important variables considered by decision-makers in HTA agencies for innovative drugs.
- This study aims to 1) investigate the critical factors and their relative importance for reimbursement recommendations of innovative medicines in Scotland, and 2) explore the feasibility of artificial intelligence algorithms to predict reimbursement decisions.

Method

- Data for this study were extracted from publicly available appraisals for innovative medicines made by the Scottish Medicines Consortium (SMC) between January 1, 2016 and December 31, 2020. [2]
- Only appraisals labelled as 'full submission' or 'resubmission' were included, and appraisals labelled as 'abbreviated submission', 'withdrawn' or 'independent review panel' were excluded.
- The SMC decisions as the dependent variables contained three classes: 'accepted', 'accepted with restricted use' and 'not recommended'.
- In total, 24 independent variables that may affect SMC decisions were selected and grouped into five categories:

Summary of independent variables	
Characteristics of disease	• Size of the eligible population • End of life • Disease burden
Characteristics of technology	• Type of assessment • Existence of comparators • Request of restriction on indication • Type of technology • Intended role in the therapeutic strategy • Medication routes of administration
Health outcomes	• Comparative efficacy • Study design • Type of comparators • Acceptance of comparators • Type of primary outcomes • Validated primary outcomes • Generalisability of clinical outcomes • Safety profile
Economic outcomes	• Type of economic analysis • Economic evaluation results • Uncertainty of economic evidence • Patient access scheme
Other aspects	• Patient and carer involvement • Guideline recommendation • Company size

- Univariable analysis was conducted to identify the statistically important variables based on the P-value ≤0.1.
- Six machine learning classifiers including decision tree, multivariable logistic regression model, random forest, support-vector machine, Xgboost and K-nearest neighbours were used to build prediction models with the identified important variables.
- Of the included appraisals, 80% were used as the training set to train the prediction models and 20% were used as the test set to evaluate the performance of the models, including accuracy, precision, recall and F1 score.

Result

- A total of 111 appraisals were identified, among which 47 were accepted, 48 were accepted for restricted use, and 16 were not recommended.

SMC decisions for innovative drugs from 2016 to 2020
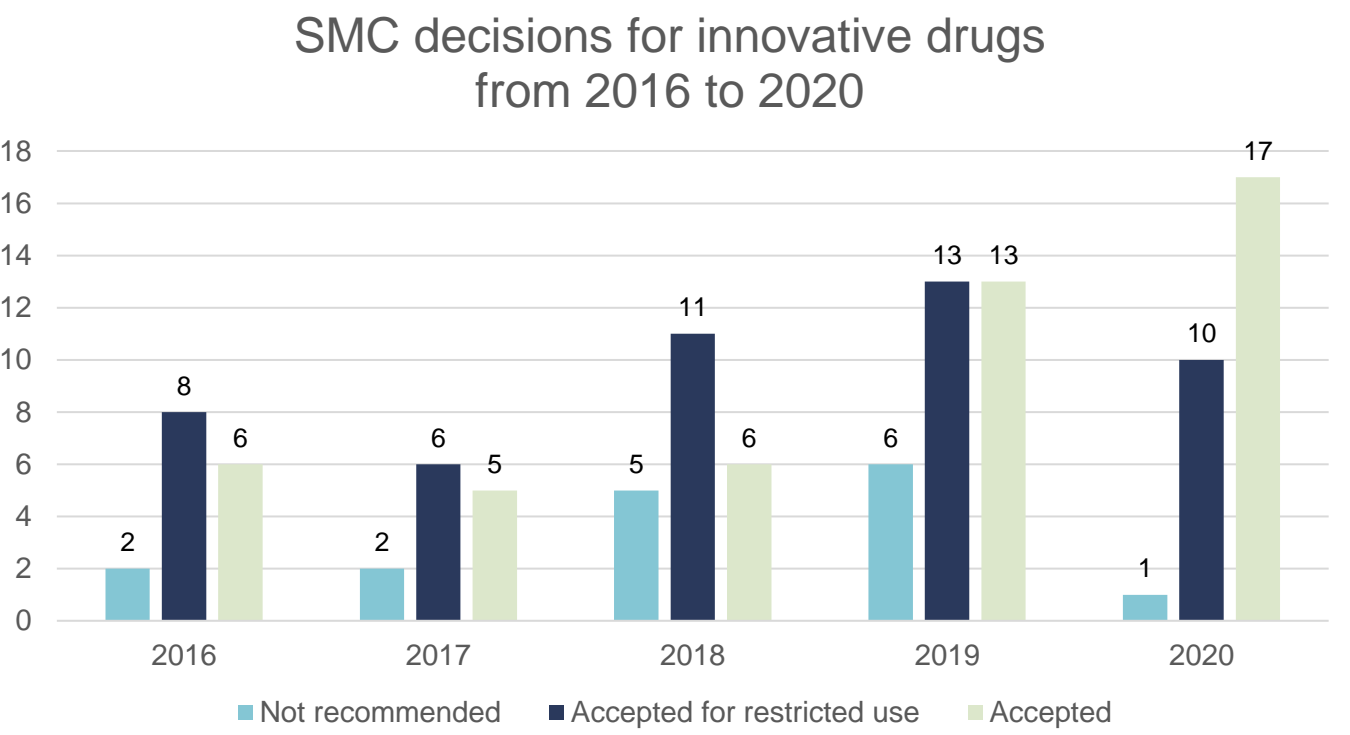
- Fourteen of 24 explanatory variables were selected through the univariable analysis and used in the prediction models.

Selected explanatory variables	
Characteristics of disease	Characteristics of technology
• Size of the eligible population	• Existence of comparators • Request of restriction on indication • Type of technology • Intended role in the therapeutic strategy • Medication routes of administration
Health outcomes	Economic outcomes
• Comparative efficacy • Type of comparators • Acceptance of a comparator • Validation of primary outcome • Safety profile	• Economic evaluation results • Type of economic analysis • Uncertainty of economic evidence

- The prediction models showed that indication restriction by manufacturer, uncertainty in economic evidence, validation of primary outcome and acceptance of a comparator were the most important drivers of SMC decision-makers.

- Four of six models, except the logistic regression model and K-nearest neighbours, had good prediction performance with an accuracy and F1-score over 0.9.

Performance of machine learning established prediction models				
	Accuracy	Precision	Recall	F1-score
Decision tree	0.96	0.96	0.96	0.96
Logistic regression model	0.88	0.88	0.87	0.87
Random forest	0.91	0.93	0.91	0.91
Xgboost	0.91	0.93	0.91	0.91
support-vector machine	0.91	0.93	0.91	0.91
K-nearest neighbours	0.83	0.84	0.83	0.83

- The model with the best prediction performance was a decision tree with an accuracy and F1-score of 0.96.

CONCLUSIONS

This pilot study showed that artificial intelligence algorithms may be used to predict reimbursement decisions and support portfolio management and evidence generation.

REFERENCES
1.EMA website. https://www.ema.europa.eu/en/glossary/innovative-medicine
2. SMC website. https://www.scottishmedicines.org.uk/