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## Opportunities and challenges of machine learning in transplant-related studies

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editorial; ethics; machine learning; statistics; artificial Intelligence

### 1. Introduction

Transplantation medicine is a complex field that is continually evolving, requiring multidisciplinary expertise and intricate decision-making. The increasing availability of electronic health records (EHRs) and other large data sets has created a fertile ground for employing machine learning algorithms to address a range of transplant-related research questions.<sup>1</sup> This paper will discuss how machine learning is gradually finding a place in transplant research and clinical practice, offering opportunities to improve patient outcomes, streamline donor-recipient matching, and optimize drug regimens. Concurrently, we will address the challenges and ethical considerations in implementing these technologies.

### 2. Machine learning and EHR: A powerful synergy

With the advent of EHRs, there is a tremendous amount of data that can be harnessed for research and clinical decision-making in transplantation. Machine learning models are particularly well-suited for mining these large data sets to identify patterns and risk factors.<sup>2</sup> These algorithms can analyze complex, multidimensional data that are often beyond human interpretability, providing insights into donor-recipient matching, graft survival, and other critical factors in transplantation.

#### 2.1. Risk factor identification

Machine learning is adept at analyzing a multitude of variables that impact transplant outcomes, including some that may not be obvious to clinicians. By delving into complex, multidimensional data sets, these algorithms identify correlations and patterns, thereby enhancing the predictive accuracy for metrics like graft survival and rejection rates. These algorithms evaluate various donor and recipient characteristics to offer a nuanced

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understanding of transplant risks, potentially revolutionizing risk stratification and enabling more personalized decision-making.

## 2.2. Predictive modeling

Recent studies have highlighted the effectiveness of machine learning in predicting key transplant-related outcomes with notable accuracy.<sup>3</sup> These algorithms, trained on extensive databases of donor and recipient data, have often surpassed traditional statistical methods in predictive power. For example, in the study of the primary graft dysfunction after lung transplantation,<sup>3</sup> it is shown that compared to logistic regression, the extreme gradient boosting can significantly improve the prediction accuracy. Another simple but commonly used method, K-nearest neighbors, also has promising improvements although it is not as good as extreme gradient boosting in this study. Other machine learning algorithms, such as decision tree, random forest, support vector machine, and deep neural network are powerful in predictive modeling in general. The good prediction performance of these methods requires fine-tuning and large sample sizes in the training data. The characteristics of major machine learning algorithms are summarized in the Table. Integrating these methods into clinical workflows could significantly improve patient outcomes and experiences, making machine learning a promising avenue for advancing transplant medicine.

## 2.3. Donor-recipient matching and drug dosage prediction

One of the most challenging aspects of transplantation is identifying the optimal match between a donor and recipient.<sup>4</sup> Machine learning algorithms have been employed to optimize this process by analyzing multiple variables such as genetic markers, blood type compatibility, and other health metrics. Similarly, machine learning can be used to predict the optimal dosage of immunosuppressive drugs for individual patients, reducing the risk of graft rejection and improving long-term outcomes.

## 3. Challenges and considerations

While the promise of machine learning in transplant medicine is unquestionably vast, it comes with its own set of challenges that need to be addressed for effective and ethical implementation. One of the foremost challenges is ensuring data quality and diversity right from the collection stage. This includes scrubbing data for inconsistencies, handling missing values, and importantly, anonymizing patient-specific information to align with data privacy standards like Health Insurance Portability and Accountability Act of 1996 (HIPAA). Feature engineering, often developed in consultation with medical experts, is crucial to create variables that are both meaningful and valuable in predicting or classifying medical conditions. One critical issue is that machine learning models can inadvertently perpetuate existing biases present in the training data. This is a concern because it could lead to inequitable outcomes or exacerbate existing health care disparities. Rigorous evaluation methods are thus essential to identify and correct any biased decision-making processes. Another challenge is the often opaque nature of complex machine learning models, such as neural networks. The lack of transparency can make it difficult for clinicians to fully trust or understand the reasoning behind the algorithmic predictions. This calls for additional research into creating more explainable AI models that clinicians can interpret and validate.

A common but often overlooked pitfall in machine learning applications is the issue of overfitting. This occurs when an algorithm is too tailored to the training data, resulting in poor generalizability to new or diverse patient populations. Overfitting is especially problematic in transplant medicine, where decision-making needs to be reliable across a wide range of cases.

Ethical considerations are paramount when applying machine learning to medical data. This involves testing for biases that may unfairly affect different population subgroups and ensuring that the model can be interpreted and explained, which is crucial for health care practitioners and patients alike. The model should also be clinically validated in consultation with health care experts to ensure its recommendations are medically sound. This is often carried out in a multidisciplinary setting, involving statisticians, data scientists, medical professionals, and ethicists.

#### 4. Conclusions

The integration of AI into transplant-related studies has shown significant promise in enhancing predictive accuracy, donor-recipient matching, and drug dosage optimization. However, the adoption of these technologies must be approached with caution, acknowledging the need for high-quality data, the potential for bias, and the difficulty in interpreting complex models. As the field continues to evolve, it will be crucial to balance the potential benefits with rigorous scientific evaluation and ethical considerations.<sup>5</sup>

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**Table**

Overview of characteristics for major machine learning algorithms.

Algorithm	Complexity and flexibility	Interpretability	Computational efficiency	Scalability for large data sets
Logistic regression	Low complexity; linear decision boundary.	High; model outputs are easy to understand.	High; generally fast to train and predict.	Good; efficient for moderate-sized data sets.
Decision tree	Medium complexity; can model nonlinear boundaries.	High; simple decision rules and tree structure.	Medium; fast to train but can be slow to predict if very deep.	Good; but can struggle with very large data sets due to overfitting.
KNN	Low complexity; flexibility depends on the "k" value.	Medium; rationale behind predictions isn't always clear.	Low; slow on large data sets due to distance computations.	Poor; performance degrades with data set size.
XGBoost	High complexity; highly flexible and tunable.	Low; difficult to interpret due to ensemble nature.	Medium; training is resource-intensive but predictions are fast.	Excellent; designed for performance on large data sets.
Random forest	High complexity; can model nonlinear boundaries well.	Medium; ensemble model makes interpretation harder.	Medium; requires more computational resources than a single tree.	Excellent; handles large data sets well and mitigates overfitting.
SVM	High complexity with kernels; linear otherwise.	Low to medium; kernel methods can be hard to interpret.	Low; training time increases rapidly with data set size.	Poor to medium; not ideal for very large data sets.
DNN	Very high complexity; highly flexible with deep structures.	Low; often considered a black box model.	Low; training is computationally intensive.	Excellent; can handle very large data sets and automatically extract features.

DNN, deep neural networks; KNN, K-nearest neighbors; SVM, support vector machine; XGBoost, extreme gradient boosting.