

# Drug-related fall risk in hospitals: a machine learning approach

Risco de queda relacionado a medicamentos em hospitais: abordagem de aprendizado de máquina

Riesgo de caída relacionado con medicamentos en hospitales: enfoque de aprendizaje de máquina

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## Abstract

**Objective:** To compare the performance of machine-learning models with the Medication Fall Risk Score (MFRS) in predicting fall risk related to prescription medications.

**Methods:** This is a retrospective case-control study of adult and older adult patients in a tertiary hospital in Porto Alegre, RS, Brazil. Prescription drugs and drug classes were investigated. Data were exported to the RStudio software for statistical analysis. The variables were analyzed using Logistic Regression, Naive Bayes, Random Forest, and Gradient Boosting algorithms. Algorithm validation was performed using 10-fold cross validation. The Youden index was the metric selected to evaluate the models. The project was approved by the Research Ethics Committee.

**Results:** The machine-learning model showing the best performance was the one developed by the Naive Bayes algorithm. The model built from a data set of a specific hospital showed better results for the studied population than did MFRS, a generalizable tool.

**Conclusion:** Risk-prediction tools that depend on proper application and registration by professionals require time and attention that could be allocated to patient care. Prediction models built through machine-learning algorithms can help identify risks to improve patient care.

## Resumo

**Objetivo:** Comparar o desempenho de modelos de aprendizado de máquina com o *Medication Fall Risk Score* (MFRS) na previsão de risco de queda relacionado a medicamentos prescritos.

**Métodos:** Trata-se de um estudo caso-controle retrospectivo de pacientes adultos e idosos de um hospital terciário de Porto Alegre, RS, Brasil. Medicamentos prescritos e classes de medicamentos foram investigados. Os dados foram exportados para o *software* RStudio para análise estatística. As variáveis foram analisadas por meio dos algoritmos de Regressão Logística, *Naive Bayes*, *Random Forest* e *Gradient Boosting*. A validação do algoritmo foi realizada usando validação cruzada de 10 vezes. O índice de Youden foi a métrica selecionada para avaliar os modelos. O projeto foi aprovado pelo Comitê de Ética em Pesquisa.

**Resultados:** O modelo de aprendizado de máquina que apresentou melhor desempenho foi o desenvolvido pelo algoritmo *Naive Bayes*. O modelo construído a partir de um conjunto de dados de um hospital específico apresentou melhores resultados para a população estudada do que o MFRS, uma ferramenta generalizável.

**Conclusão:** Ferramentas de previsão de risco que dependem de aplicação e registro adequados por parte dos profissionais demandam tempo e atenção que poderiam ser alocados ao cuidado do paciente. Modelos de previsão construídos por meio de algoritmos de aprendizado de máquina podem ajudar a identificar riscos para melhorar o atendimento ao paciente.

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**Conflicts to interest:** nothing to declare.

## Resumen

**Objetivo:** Comparar el desempeño de modelos de aprendizaje de máquina con *Medication Fall Risk Score* (MFRS) para la previsión del riesgo de caída relacionado con medicamentos prescritos.

**Métodos:** Se trata de un estudio caso-control retrospectivo de pacientes adultos y adultos mayores de un hospital terciario de Porto Alegre, estado de Rio Grande do Sul, Brasil. Se investigaron los medicamentos prescritos y las clases de medicamentos. Los datos fueron exportados al *software* RStudio para el análisis estadístico. Las variables se analizaron a través de los algoritmos de regresión logística *Naive Bayes*, *Random Forest* y *Gradient Boosting*. La validación del algoritmo se realizó usando validación cruzada de 10 veces. El índice de Youden fue la métrica seleccionada para evaluar los modelos. El proyecto fue aprobado por el Comité de Ética en Investigación.

**Resultados:** El modelo de aprendizaje de máquina que presentó el mejor desempeño fue el desarrollado por el algoritmo *Naive Bayes*. El modelo construido a partir de un conjunto de datos de un hospital específico presentó mejores resultados en la población estudiada que el MFRS, una herramienta generalizada.

**Conclusión:** Herramientas de previsión de riesgo que dependen de la aplicación y el registro adecuados por parte de los profesionales demandan tiempo y atención que podría ser destinado al cuidado del paciente. Modelos de previsión construidos mediante algoritmos de aprendizaje de máquina pueden ayudar a identificar riesgos para mejorar la atención al paciente.

## Introduction

Falls are the second leading cause of death from unintentional injury in the world, and each year approximately 684,000 fatal falls occur. Individuals aged 60 years and older experience the largest number of fatal falls.<sup>(1)</sup> There are more than 700 million elderly individuals (age  $\geq 65$  years) in the world, and this number is expected to double by 2050.<sup>(2)</sup>

Falls are defined as inadvertently coming to rest on the ground or at another lower level.<sup>(1)</sup> Falls are multifactorial, and aspects related to fall occurrence may be modifiable and non-modifiable.<sup>(3)</sup> Medications are highlighted as modifiable risk factors.

Falls can be one of the consequences of using risky drugs and/or drug interactions, and hospitalization considerably increases risk among the elderly. Drugs with central-nervous-system effects, such as opioids, hypnotics, anxiolytics, antidepressants, antipsychotics, and procedural sedatives, significantly increase the risk for falls.<sup>(4)</sup>

The only tool found in the literature that assesses medication-related fall risk was the Medication Fall Risk Score (MFRS). This score was developed as part of a pharmaceutical fall-prevention program and generates a score based on the degree of risk of medications under use. The recommendation is to consider patients who score six or higher at risk. The MFRS authors recommend the use of this tool together with other fall-risk assessment tools, considering other fall-related risk factors in addition to medication.<sup>(5)</sup> One study analyzed the predictive validity of using a fall risk scale together with the

Medication Fall Risk Score (MFRS). The results showed improvement in specificity, without compromising sensitivity in relation to the individual use of the fall risk scale.<sup>(6)</sup>

Electronic health records contain a range of information regarding patients' health conditions and enable new approaches to identify risk factors.<sup>(7)</sup> Supervised and unsupervised machine-learning algorithms have shown great potential in acquiring knowledge from large data sets.<sup>(8)</sup> Machine learning is a field of artificial intelligence in which systems obtain knowledge automatically, without explicit programming.<sup>(9)</sup> Supervised learning, the technique applied in this study, reflects the ability of an algorithm to generalize knowledge from available data about a target variable so that it can be used to predict new cases.<sup>(8)</sup>

The application of scores still requires time and interpretation from professionals, and it is one more among the many processes involving health care. The development of prediction models through machine learning can bring important information and even more qualified care, without depending on the correct application of scores. No medication-based fall-risk prediction models developed through machine-learning algorithms have been identified. This study was developed with the hypothesis that medication-related fall-risk prediction based on machine-learning models has better performance than the Medication Fall Risk Score. To this end, it aimed to compare the performance of machine-learning models with that of the Medication Fall Risk Score (MFRS) in predicting risk for falls related to prescription drugs.

## Methods

This study was reported according to recommendations by the Transparent Reporting of a Multivariable Prediction Model for individual prognosis or diagnosis (TRIPOD), since specific recommendations for models developed from machine learning are still under construction.<sup>(10,11)</sup>

This is a case-control study connected to an umbrella project, and it was conducted in a tertiary hospital in the southern region of Brazil. The population consisted of 9,037 adult ( $\geq 18$  years) and older adult ( $\geq 60$  years) patients who were hospitalized in 2016. Patients with notification of falls and medical prescription 48 hours before the fall were included in the fall group (case). All patients with no notification of falls comprised the non-fall group (control). Prescription drugs and drug classes were investigated. It was not possible to identify administered drugs because the institution of the study does not have electronic medication check. The medications were classified according to the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification System, a classification used in MFRS.<sup>(12)</sup>

All variables were extracted from a previously established database originating from the patients' electronic health records. Falls were extracted from the institution's computerized safety incident reporting system. Medications were extracted from electronic prescriptions. The medications prescribed 48 hours before the fall were identified for the fall group. As for the non-fall group, the mean number of days from hospital admission to the day when a fall occurred to the participants in the fall group was calculated, and the medications used 48 hours before that mean figure were then extracted. The mean number of days from hospital admission to the day when a fall occurred were 11. Medications prescribed 48 hours before the 11<sup>th</sup> day of hospitalization were extracted for the non-fall group.

The collected data were organized in Microsoft Excel 2010 spreadsheets and imported into the RStudio software, edition 1.3.1093, for statistical analysis.<sup>(13, 14)</sup> Descriptive data with absolute and relative frequencies were calculated. Model devel-

opment and validation were performed using the caret package, version 6.0-86, for hyperparameter fitting, and packages glmnet, version 4.1-1, Naive Bayes, version 0.9.7, Random Forest, version 4.6-24 and gbm, version 2.1.8, for model fitting. To define the best cutoff point, the Cutpoint package, version 1.1.0 was used.<sup>(15-20)</sup>

The features selected for the prediction model were medications belonging to the drug classes of analgesics, antipsychotics, anticonvulsants, benzodiazepines, antihypertensives, cardiac medications, antiarrhythmics, antidepressants, and diuretics, the same drug classes included in the Medication Fall Risk Score. In the MFRS analysis, each medication was scored according to MFRS, and a new variable was generated with the total score for each participant. Each high-risk medication receives three points and includes analgesics, antipsychotics, anticonvulsants, and benzodiazepines. Medium-risk medications receive two points each and encompass antihypertensives, cardiac medications, antiarrhythmics, and antidepressants. Diuretics are considered low risk and receive one point each.<sup>(5)</sup> The target outcome was fall-risk, and the possible values were zero (no) and one (yes).

The data were divided into training and testing data, 80% and 20% respectively, to avoid overestimating the models' performance. The training data were used for model creation, and the testing data were used for performance evaluation. The division occurred randomly, based on the outcome fall. The training sample was equal to 7,230 hospitalizations and the testing sample was equal to 1,807 hospitalizations.

The variables were analyzed in the following algorithms: Logistic Regression, Naive Bayes, Random Forest, and Gradient Boosting. The models output were fall and not fall.

The Logistic Regression algorithm is a likelihood-based statistical method used for classification problems. The goal is to create a straight line that best fits the data.<sup>(21)</sup>

The Naive Bayes algorithm is a probabilistic algorithm, based on Bayes' Theorem. This algorithm seeks to assign a set of data to a specific class.<sup>(7)</sup>

The Random Forest and Gradient Boosting algorithms are two ensemble methods. Ensemble

methods combine multiple machine-learning algorithms for decision-making. Combining multiple models allows the error of a single algorithm to be compensated for by the others, resulting in better performance over single models.<sup>(22)</sup>

The Random Forest algorithm builds multiple-decision tree models; each model votes for a decision and the choice of an outcome is a consensus among all the trees. Decision trees classify objects according to the value of variables. Each node in a decision tree represents a variable and the branches represent the values that the node can assume.<sup>(23)</sup>

The Gradient Boosting algorithm is also the result of multiple-decision trees; however, the construction of each tree depends on the previously constructed trees. Each new tree will learn from the mistakes of the previous tree.<sup>(23)</sup>

Algorithms like Naive Bayes and Logistic Regression are simpler and require less computational power.<sup>(23)</sup> Random Forest and Gradient Boosting improve the predictive performance of a single model by training multiple models and combining their predictions. However it requires more computational power.<sup>(22)</sup>

Algorithm validation was performed using 10-fold cross validation. Cross-validation is a data resampling method to evaluate the generalization ability of prediction models and avoid overfitting (when the model fits the training data very well, but performance reduces significantly when analyzing new data).<sup>(24)</sup>

In evaluating the models and the MFRS, the method of maximizing the metric function selected as a summary of the optimal cutoff points in each resampling was used for determining the best cutoff point in each model. The metric selected was the Youden index, as it was used in the paper that evaluated MFRS.<sup>(6)</sup> The MFRS was also evaluated at a cutoff score of 6, the cutoff specified by the MFRS developers.

The project was approved by the Medical School's Scientific Committee of Pontifical Catholic University of Rio Grande do Sul, and it is connected to the doctoral project entitled "Automatic detection of adverse events using natural language processing in the electronic medical records of a

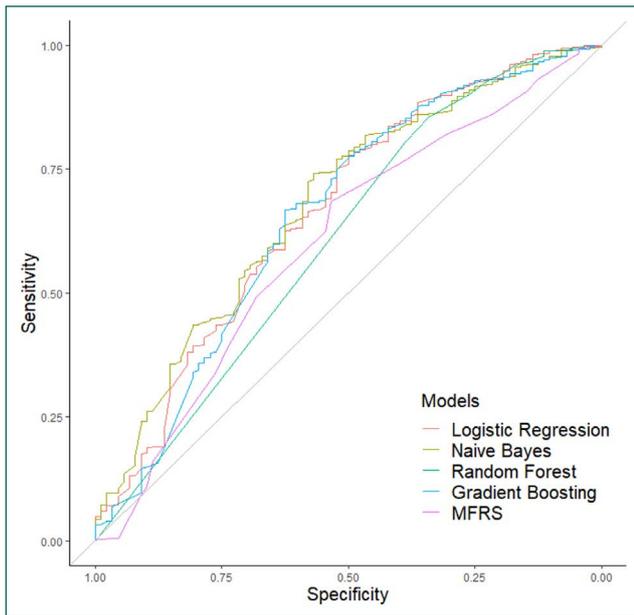
tertiary hospital", approved by the Research Ethics Committee (CAEE: 71571717.7.0000.5530). The researchers signed a term of commitment for data use, committing to and being responsible for handling and storing the information with the sole objective of the proposed analysis and absolute secrecy regarding the identification of the patients involved.

## Results

The population consisted of 9,037 patients. Of these, 4.9% (n = 442) were in the fall group and 95.1% (n = 8,595) were in the non-fall group. Regarding medication analysis, the least prescribed drug appeared in four prescriptions, and the most prescribed, in 7741 prescriptions. According to the Medication Fall Risk Score (MFRS), 24 belonged to the high-risk category, 19 belonged to the medium-risk category, and three belonged to the low-risk category. The median of the Medication Fall Risk Score was nine points (0-26). Most patients (83.9%) were classified as high risk for falls, according to the MFRS. In the fall group, the MFRS median was 10 points (2-25). The four algorithms were trained and, when tested, the model showing the best performance was the Naive Bayes model. The MFRS-based models were generated with cutoff point six, as recommended by the authors, and 11, the best cutoff point for maximizing the Youden index. The model-related results are shown in table 1 and figure 1. Table 1 shows the metrics for model performance analysis, according to the Youden index, AUC, sensitivity, and specificity, and figure 1 shows the ROC curves of the models generated from the algorithms and MFRS.

**Table 1.** Area under the curve (AUC), Youden index, sensitivity, and specificity of the machine-learning models and MFRS with the two cutoff points applied

Model	Youden	AUC	Sensitivity	Specificity
Logistic Regression	0.267	0.666	0.477	0.789
Naive Bayes	0.289	0.678	0.546	0.744
Random Forest	0.196	0.607	0.341	0.855
Gradient Boosting	0.260	0.656	0.534	0.726
Medication Fall Risk Score - MFRS (cutoff point = 11)	0.218	0.603	0.534	0.684
Medication Fall Risk Score - MFRS (cutoff point = 6)	0.045	0.603	0.886	0.159



**Figure 1.** ROC curves of the models generated from the algorithms and MFRS

Figure 2 presents the confusion matrix for the application of the Medication Fall Risk Score. Figure 3 presents the confusion matrix for the application of the Naive Bayes model, which performed better.

		Actual class	
		Fall	Not fall
Prediction class	Fall	78	1446
	Not fall	10	273

**Figure 2.** Confusion matrix for the application of the Medication Fall Risk Score

		Actual class	
		Fall	Not fall
Prediction class	Fall	48	441
	Not fall	40	1278

**Figure 3.** Confusion matrix for the application of the Naive Bayes model

## Discussion

The Medication Fall Risk Score, despite showing low discriminatory capacity, was developed to be a complement to other forms of fall-risk assessment.<sup>(6)</sup> When used together with the Morse Fall Scale (fall risk assessment scale), it showed better performance than when the latter was used individually. MFRS, however, is limited to some drug classes. Muscle re-

laxants, chemotherapy drugs, insulin, and ophthalmic medications, identified as risk factors in other studies, are not included.<sup>(25-28)</sup>

When the same drugs used to calculate MFRS were analyzed in the four machine-learning algorithms, the one showing the best performance was the model developed through the Naive Bayes algorithm. The area under the ROC curve was 0.678, and the Youden index achieved was 0.274, surpassing the respective scores of 0.603 and 0.218. The result of the Naive Bayes algorithm showing better performance compared to the two ensemble methods surprised the authors. Ensemble methods usually show better predictive performance.<sup>(22)</sup>

The Medication Fall Risk Score identified a greater number of positive true values. However, many patients were misclassified at risk. When many people are classified as at risk, there may be the possibility of a trivialization of risk. This can lead to a decrease in prevention strategies, which can lead to more fall events.

Different institutions may host populations with different characteristics. Generalizable risk-prediction tools may not work properly because they do not meet the individualities of each institution.<sup>(29)</sup> This study proved that, in the study population, a model built from a specific hospital's data set performs better than a generalizable tool. Two studies developed hospital-readmission risk-prediction models and performed a comparative analysis with a widely used method to calculate readmission risk. Both identified that the models developed performed better.<sup>(29,30)</sup> A systematic review identified 26 studies that compared machine learning models to existing risk scores. The majority (24 studies) reported that the models performed better.<sup>(31)</sup>

Tools such as the Medication Fall Risk Score are restricted to a few variables, considering that health care professionals themselves must evaluate and calculate the score.<sup>(32)</sup> The increase in the data volume present in electronic medical records allows the models to consider a larger number of predictor variables. Moreover, filling out these tools requires time and dedication from these professionals, which could be applied in care provision.

Fall risk prediction models were developed through machine learning, and data were extracted from the electronic health records.<sup>(7,33)</sup> However, these models depend on the quality of electronic records. A study analyzed the quality of the recording of falls at electronic health records compared to the notifications and identified a gap in the registration, as well as inconsistencies between the records at the notification system and electronic health records.<sup>(34)</sup>

This study developed and validated fall-risk prediction models based on medications prescribed, but not necessarily administered. This is the main limitation of the study. The authors did not include all prescribed medications, so that the comparison with the existing score was fair. Also, other fall risk factors, drug interactions, administered doses, the analysis of a series of prescriptions, feature importance were not included in this study. Furthermore, the analysis of the model built in combination with other fall-risk assessment scales was not performed.

Prediction models built by using machine-learning algorithms can help identify risks and improve patient care. The model developed in this study could be applied to prescription data and generate warnings. This approach could help professionals to identify and prevent risks. Healthcare professionals' work will not be replaced, and the time spent applying scales can be allocated to other important aspects of healthcare.

## Conclusion

This study proved the research hypothesis that the prediction model developed especially for the population attending the studied institution showed better performance as compared to the Medication Fall Risk Score. The algorithms used are well-established methods; however, their use in predicting the fall risk related to prescribed medications is a novelty. The need for further studies considering other medications in addition to those related to risk for falls by MFRS as well as new aspects, such as drug interactions, administered doses, the analysis of a series of prescriptions and feature importance, was identified. Features such as sex and age are easy to

get and have a relevant influence at fall risk. These features can be implemented in future studies, as well as feature selection techniques and model development through more advanced algorithms. Furthermore, it is suggested that the models built should be applied and analyzed as complementary to the fall prediction scales used in institutions.

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## Collaborations

Silva AP, Santos HDP, Rotta ALO, Baiocco GG, Vieira R and Urbanetto JS analyzed the data, drafted the article, critically reviewed relevant intellectual content. All authors approved the final version.

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