

Adaptative Clinical Decision Support System using Machine Learning and Authoring Tools

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Abstract: Clinical Decision Support Systems (CDSS) offer the potential to improve quality of clinical care and patients' outcomes while reducing medical errors and economic costs. The development of these systems results difficult since (i) generating the knowledge base that CDSS use to evaluate clinical data requires technical and clinical knowledge, and (ii) usually the reasoning process of CDSS is difficult to understand for clinicians leading to a low adherence to the recommendations provided by these systems. Hereafter, to address these issues, we propose a web-based platform, named Knowledge Generation Tool (KGT), which (i) enables clinicians to take an active role in the creation of the CDSSs in a simple way, and (ii) clinicians' involvement can turn in an improvement of the model predictor capabilities, while their comprehension of the reasoning process of the CDSS is increased. The KGT consist on three main modules: *DT building*, which implements machine learning methods to extract automatically decision trees (DTs) from clinical data frames; an *authoring tool (AT)*, which enables the clinicians to modify the DT with their expert knowledge, and the *DT testing*, which allows to test any DT, being able to test objectively any modification made by clinician's expert knowledge.

1 INTRODUCTION

A Clinical Decision Support System (CDSS) can be defined as “Software that is designed to be a direct aid to clinical decision-making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base and patient-specific assessments or recommendations are then presented to the clinician or the patient for a decision” (Sim et al., 2001). These systems provide personalized recommendations based on patient's data in order to help clinicians during the decision-making process. Its adoption by healthcare systems can improve patient's outcomes and wellbeing, provide best clinical practice to clinicians, while reducing medical errors and economic costs (Kaushal et al., 2003). However the development and deployment of these systems is not a simple task.

Among the factors that affect most the success of a CDSS there is the need of having an easy to maintain knowledge base (KB) (Isern and Moreno, 2008). The KB contains the clinical knowledge of the system used to provide personalised recommendations for each patient, thus an easy way to maintain its contents is necessary to keep the system updated with the latest available clinical knowledge. However, this demands both technical and clinical skills, limiting the role that clinicians can play into it (Douali and Jaulent, 2013). Furthermore, usually the reasoning process behind the provided recommendations is not easy to understand for clinicians, especially when complex predictor techniques such as as Machine Learning (ML) are used during the evaluation of clinical data (Ericsson et al., 2003). It has been shown that this non-comprehension is one of the main reasons why

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clinicians do not accept the recommendations made by CDSSs when deployed in real clinical settings.

Despite the general complexity of ML models and the difficulty to understand and edit its contents, its use in CDSSs has the potential to notoriously improve the predictive capabilities of already existent CDSSs (Larburu et al., 2018; Safdar et al., 2018; Tägil et al., 2008). Among ML classifiers, Decision Tree (DT) classifiers are particularly suitable for clinical classification tasks since they are easy to interpret by a non-statistician and are intuitive to follow. DTs support missing values and are able to combine heterogeneous data types into a single model, whilst making an automatic selection of the main characteristics (Shaikhina et al., 2019).

This scenario has led us to build a web-based Knowledge Generation Tool (KGT) for clinicians which allow handling and editing DT models to be used in CDSSs. Henceforth, clinicians are involved in the construction process of the KB (DT in our case) which has shown to be beneficial for deepening the understanding of the CDSSs' recommendations, and increasing the predictive capacity of the classifiers. Furthermore, it deals with the aforementioned trust issues of clinicians regarding the origin of the provided recommendations, as they can understand the reasoning process behind the provided recommendation due to their active involvement in the creation of the KB of the system.

Overall, this work presents a methodology to create, modify and test an adaptative Clinical Decision Support System that combines DT machine learning technique and expert's knowledge using authoring tools.

This paper is structured as follows: in Section 2 the state of the art regarding ML algorithms to generate DTs and frameworks that have been developed to generate DTs are presented; Section 3 presents the methods to build the adaptative DSS; Section 4 presents a use case of our application, and Section 5 concludes the paper and proposes future work lines.

2 STATE OF THE ART

In this section, it is shown how the use of ML methods improves the performance of CDSS in the literature, and, more precisely, the case of DTs. Following, several platforms developed to generate trees interactively with non-expert users are introduced.

2.1 Machine Learning Techniques in CDSS

Due to the capacity of Machine Learning (ML) methods to extract information from data, they are widely used to support CDSS. According to the review of Safdar et al. (Safdar et al., 2018), which works with ML-based CDSSs for heart disease diagnosis, the use of ML (i.e. logistic models, Bayesian neural networks and neural networks) in CDSS improves the diagnosis of Acute Myocardial Infarction from 84 to 95%. In the case of ischemia detection, the use of a CDSS based on a neural network improves its sensitivity from 81 to 86% (Tägil et al., 2008).

As mentioned before, tree-based ML methods are particularly used in CDSSs due to their easy comprehension for the clinicians and their suitable results. For example, taking a look at the survey of data mining algorithms and techniques in mental health (Alonso et al., 2018), we notice that the DT method is used between 27.27-57.14% among ML techniques in health illness (e.g. Alzheimer 33.33%, depression 27.27%, and schizophrenia and bipolar disorders 57.14%).

Vidhushavarshini et al. (Vidhushavarshini and Sathiyabhama, 2017) propose Naïve Bayes (NB) and J48 tree (J48 in Weka, also known as C4.5) ML methods to support a CDSS in order to detect thyroid disease. In this case, J48 tree outperforms the NB method (81.94 vs 51.77% of accuracy). Nijewemed'Hollosoy et al. (Lakshmi et al., 2018) also give support to CDSS using tree-based ML methods in lower back pain use cases. CDSSs assist clinicians by advising which would be the best option for the patient: consult a GP, consult a physiotherapist or perform self-care. They trained a decision tree, a random forest and a boosted tree in a database of 1,288 fictitious cases, and then tested those classifiers on a real-life database, reaching accuracies of 71%, 53%, and 71% respectively in the testing dataset. Kumar et al. (Kumar and Sarkar, 2018) made a classifier combining C4.5 and decision tables. They compared the performance of this hybrid classifier with the performance of C4.5 and decision table classifier in ten public datasets. In general, the hybrid classifier outperformed both the C4.5 and the decision table classifier. Finally, Kerexeta et al. (Kerexeta et al., 2018) presented two classifiers to predict readmission within 30-days when a Heart Failure patient is discharged. In the first classifier, they combined clustering methods with an NB classifier. In the second classifier, they combined DT

with NB. In this case, the first method is the one that showed better results.

2.2 Web-based Decision Tree Authoring tools

Different platforms have been developed to allow for the creation of DT models to analyse clinical data by non-expert users. Below, some of these platforms are introduced.

In the work of Kaminski et al. (Kamiński et al., 2018), a framework that allows the visual generation of decision trees was presented. The platform allows the user to build DTs from scratch: the user defines the nodes and the edges, and manually introduces model parameters. However, this platform does not generate DTs automatically using ML techniques.

Additional approaches that allow for user interaction are outlined in (Ankerst et al., 1999; Ware et al., 2001). Through different data visualization techniques, the user determines the splits on the data that will form the conditions of the nodes of the tree in a recursive manner until the user is satisfied with the tree's results. Trees generated using these platforms achieve similar results as automatically generated DTs. The main limitation is that the constructed DT cannot be pruned once it has been built.

In (S. J. Elzen and J. J. Wijk, 2011), the authors describe a platform that allows for the construction of trees from datasets combining manual modification and automatic methods. The user manually splits the data based on statistical parameters and visual representations of the data. In addition, the user can automatically grow sub-trees starting from a given node.

Lastly, there are many studies (Aoki et al., 2007; Poucke et al., 2016; Ramezankhani et al., 2014; Tenório et al., 2011) that used platforms that allow for the automatic generation of DTs as well as for their visualization. While the platforms used in those studies can be used by non-expert users to create DTs, test and visualize them, they are not able to cope with the lack of adaptability to changes in the tree. For this reason, the user's knowledge cannot be introduced into the models.

Overall, some interactive platforms (Ankerst et al., 1999; Kamiński et al., 2018; Ware et al., 2001) build DTs to support decision-making with the help of dataset visualization methods. These platforms are able to modify the DTs as the expert requires, but they do not use automatic ML methods to serve as a good starting point for the user. Doing so would allow for the conditioning of the entire tree. Other experts such

as (Aoki et al., 2007; Poucke et al., 2016; Ramezankhani et al., 2014; Tenório et al., 2011), provide the possibility of extracting the tree using ML methods, however, doing so does not allow for the editing of those DTs. Given this scenario, if any branch is non-compliant with the expert's knowledge, the expert is unable to fix the issue within the domain. A platform that successfully combines both approaches is the one presented in (S. J. Elzen and J. J. Wijk, 2011) ("BaobabView: Interactive construction and analysis of decision trees - IEEE Conference Publication," n.d.). This publication outlines a very good DT generator but cannot be used to evaluate single instances of data or generate trees without a dataset as our platform does (for formalization purposes). Aside from using a combined approach when generating the model, our platform allows the user to check the performance of the model in new frames as well as provide tools in order to easily analyze the DT (e.g. change the color of the tree depending on the outcome). In addition, the DT is immediately ready-to-use upon incorporating new patients' data as soon as it is built.

3 KNOWLEDGE GENERATION TOOL (KGT)

In this chapter, the modules of our adaptative web-based CDSS, named Knowledge Generation Tool (KGT) are described. KGT consists of three principal modules:

1. Automatic **DT building** module. Users are able to use five well-known ML methods to build DTs classifiers in a selected data frame (Section 3.2).
2. A web-based **Authoring Tool** (AT) that allows (i) building a DT right from the start and (ii) modifying the already built DT models using a visual representation of the model (Section 3.3).
3. A **DT testing** module to test any DT building method, being able to assess which one generalizes the best. It also allows the user to test any built DT, making possible to check if the changes made in the DT improve the quality of the model (Section 3.4).

This way, as users are involved in the construction of the model, their understanding of it is deeper, while the model's performance can be improved thanks to the clinicians' knowledge (Kwon et al., 2019). Out of the mentioned modules, firstly, Section 3.1 introduces the format that the other modules of the KGT follow in order to handle the DTs.

- **C5.0:** It is a C4.5 method's extension, adding new functions, such as boosting for improving the accuracy rate and the construction of cost-sensitive trees. (Pang and Gong, 2009). The package *C50* (Kuhn et al., 2018) is used in the KGT.

These five methods can be applied independently or can be combined to generate a forest of different DTs. This way, different DT methods knowledge can be combined to obtain a better model. Moreover, as the KGT allows to modify these models, the not desired part of the forest can be modified.

3.3 Authoring Tool

The AT facilitates (i) the modification of existing trees and (ii) allows for the construction of new trees from scratch. Below the most important features of the AT are listed. The AT interface of the KGT is shown in Figure 2.

1. **New Branches:** Starting in an already existing node, it is possible to create a new node (child) to which the next evaluation step should go if the specified conditions are met. In the same way that new nodes can be created, a chosen node or all its children can be deleted, keeping the selected node as a leaf node (end of branch).
2. **Edit Conditions:** The conditions of any node can be edited, i.e. the value of the checked variable or the variable itself can be changed.
3. **Edit Outcome:** The probability distribution of the outcome (e.g. alive or dead) is given in each node. These probabilities can be modified with the AT.
4. **DT Attributes:** When editing the conditions of the trees, their possible values are restricted (e.g. categorical variables have restricted values), which are automatically extracted when the tree is generated from a data frame. Non-contemplated attributes or possible values of an attribute can be added using the AT. When the DT is manually generated, the attributes must be defined by the user.

The AT provides a way of extending the DTs with clinical knowledge to cope with particular or complicated clinical cases not evaluated by the original model. After using the AT, it is possible that some patients fulfill more than one path or none. If more than one path is satisfied all fulfilled paths are highlighted in the tree. To test the model's efficiency, the average of all the outcomes is considered. If none of the branches are followed, the KGT would return that the CDSS is not suitable for that patient.

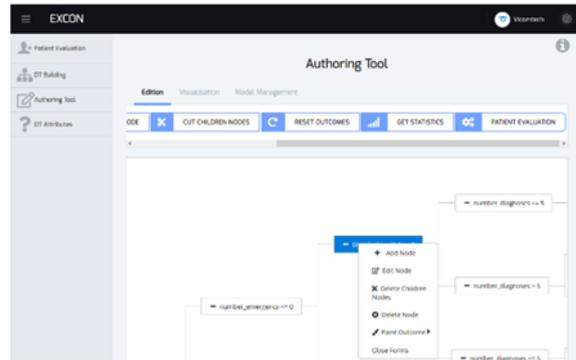


Figure 2: The dashboard of the AT of the KGT model.

Lastly, in order to facilitate the understanding of the reasoning process of the DT, the nodes of the tree can be colored according to the probability of each possible outcome in a node (green tones reflect higher probabilities, red tones indicate lower probabilities). This color scheme allows for the visualization of how the tree classifies the data, making it easier for the user to identify the most appropriate node to edit.

3.4 DT Testing

The KGT allows the user to analyse the performance of the DT building methods using 5-fold Cross-Validation (Arlot and Celisse, 2010). The KGT returns the precision, recall, f1-score and AUC values (Hand and Till, 2001) for each possible outcome (e.g. alive or dead). Therefore, this approach quickly identifies which DT has the best performance for any dataset of the KGT.

The tool also enables the possibility of testing a DT generated from knowledge or the modified DT by the AT. In order to carry out this testing, the user must select the dataset in which he/she wants to test the DT, preferably not with the same dataset that was used to build the tree in order to avoid overfitting.

The outcome of each branch (its leaves) is specified as a set of probabilities. As the precision, recall and f1-score testing values need an absolute answer (e.g. it lives or dies, not its probability), the outcome with the highest probability is selected when estimating these testing values.

In the case of the AUC values, originally it is used with 2-class outcomes. When there are more than two outcome classes (e.g. we want to differentiate Heart Failure, Atrial Fibrillation or Cardiomyopathy), the 1-vs-all (Hand and Till, 2001) method is used. For each possible value of the outcome, the other levels are joined which causes the issue to turn into a 2-class problem.

Statistic Analysis					
level	AUC	f1-score	precision	recall	support
Method: ctree					
Normal	0.6	0.13	0.25	0.09	11
Altered	0.6	0.93	0.89	0.97	86
Method: glmtree					
Normal	0.54	0.24	0.17	0.42	12
Altered	0.54	0.8	0.9	0.72	88
Method: CART					
Normal	0.6	0.27	0.18	0.58	12
Altered	0.6	0.68	0.89	0.55	71

Figure 3: Visualization of testing values.

In order to assist the user to understand the meaning of the measurements obtained, the table above highlights the cells with the best statistical measurements obtained for each possible outcome when testing the DTs. This way, if the best measurements are obtained by one specific algorithm, this will be seen clearly as its corresponding cells will be highlighted as seen in Figure 3.

4 USE CASE

The KGT has been tested in the public data frame of readmission of diabetic patients (Strack et al., 2014). The original data set consists of 47 attributes and 101,766 cases, each of which corresponds to a single patient diagnosed with diabetes. The variables describe encounters with diabetics such as diagnoses, medications, and the number of visits in the year prior to the encounter. Originally the classification task was divided into three classes: readmitted within 30 days, after 30 days or not readmitted. In this case, it has been decided to combine the last two groups in order to create a dichotomous classification system and hence, to test if the patients were readmitted within 30 days or not.

Before building the tree, the original dataset has been split into training (70%) and testing (30%) subsets, ensuring that each subset contained the same proportion of readmitted vs non-readmitted instances (approx. 1:9).

To demonstrate the functionality of the KGT, the addition of variables that improve the predictive capacity of a DT will be shown. For that, three variables (“admission type”, “number of inpatients” and “discharge id”) have been set aside before

constructing the initial DT. According to Bhuvan study (Bhuvan et al., 2016) who have worked on the same public dataset, these three variables are the most influent ones when predicting readmission. This way, it can be shown how clinicians can add new knowledge in the already developed DTs, taking advantage of the KGT.

4.1 First DT

The best DT-building method among the five options in the KGT is *ctree* (i.e. cross-validation shows that its performance is the best in the training set, judging by the obtained testing measurements). For this reason, it is the selected ML method to build the DT (shown in Figure 4).

The *First DT* consists of 30 nodes and uses 7 predictor variables. The benefit of using these predictor variables is that it provides a feature selection that reduces the necessity of the extraction from 44 variables to 7. This methodology achieves an AUC value of 0.57 in the testing set, which we will use as a benchmark to measure the loss/gain of predictivity when simplifying/editing the tree.

Despite obtaining a low predicting capacity shown by the AUC value, in literature, models that use this database with all the variables, with the same data pre-processing as in this study, obtain modest values (≈ 0.65), even for more complex classifiers such as Neural Networks or Random Forest (Bhuvan et al., 2016).

4.2 Pruned DT

The *First DT* obtained in the previous section is not very large, but it is large enough to prevent a correct interpretation by the user (e.g. clinician) when it can be simplified without losing much predictability. For this reason, this tool allows cutting and/or editing branches.

To seek which splits of the original DT can be omitted because of their low discriminative capacity, the nodes of the DT are colored according to the probability to readmit in each node. This way, poor splits can be found and deleted using the AT. The size of the resulting pruned DT is reduced to 10 nodes and uses only 4 predictor variables (see Figure 5). The performance of this edited DT has also been tested in the testing subset, with only a minor decrease from 0.57 to 0.56 in the AUC value (see Table 1). The new DT is much smaller, easier to follow, and moreover, it needs only 4 variables, avoiding the extraction of 3 features at the cost of a minor loss of predictability.



Figure 4: First DT built by the KGT using the *ctree* method to predict if some diabetic patient will readmit within 30 days. Node colors depend on the probability of not readmitting within 30 days (red, more probably to readmit, green more likely than not).



Figure 5: Pruned DT: the remainder DT after the pruning of First DT.

4.3 Extended DT

Before *First DT* construction we set aside three variables to simulate new discovery and to add them to the already developed DT.

The resulting DT from the combination of the previous knowledge and the new DT is shown in Figure 6 as *Extended DT*. It adds complexity to the previous DT since the new DT has 32 nodes. It can be seen by the coloring feature that the new variables discriminate much better than the old ones. Despite adding relatively little complexity to the model, the new DT performs better, with an AUC testing value of 0.64 in the testing set. This new AUC value of 0.64 demonstrates an improvement over the previous results (see Table 1) and nearly reaches the AUC values of 0.65 that are achieved in the literature, but using more complex and less interpretable ML

methods, such as Neural Networks or Random Forest (Bhuvan et al., 2016).

4.4 KGT's Contribution

In Table 1 the contribution of the KGT is presented for the elaboration of the DTs. The *First DT* has been built using the *ctree* method and has 44 variables in the training set. It achieves an AUC score of 0.57 with a rather complex tree to follow with 30 nodes and 7 different attributes. With the AT of the KGT, we have been able to get the *Pruned DT* simplifying the *First DT* to 10 nodes and 4 different attributes at the expense of only a 0.01 decrease in the AUC value. Finally, in the pruned DT with the additional variables, in which “new knowledge” has been added, the accuracy of the DT has been increased in terms of AUC to 0.64, at a cost of complexity of 32 nodes and 7 different attributes.



Figure 6: Extended DT: The produced DT after adding the new knowledge to the *Pruned DT*.

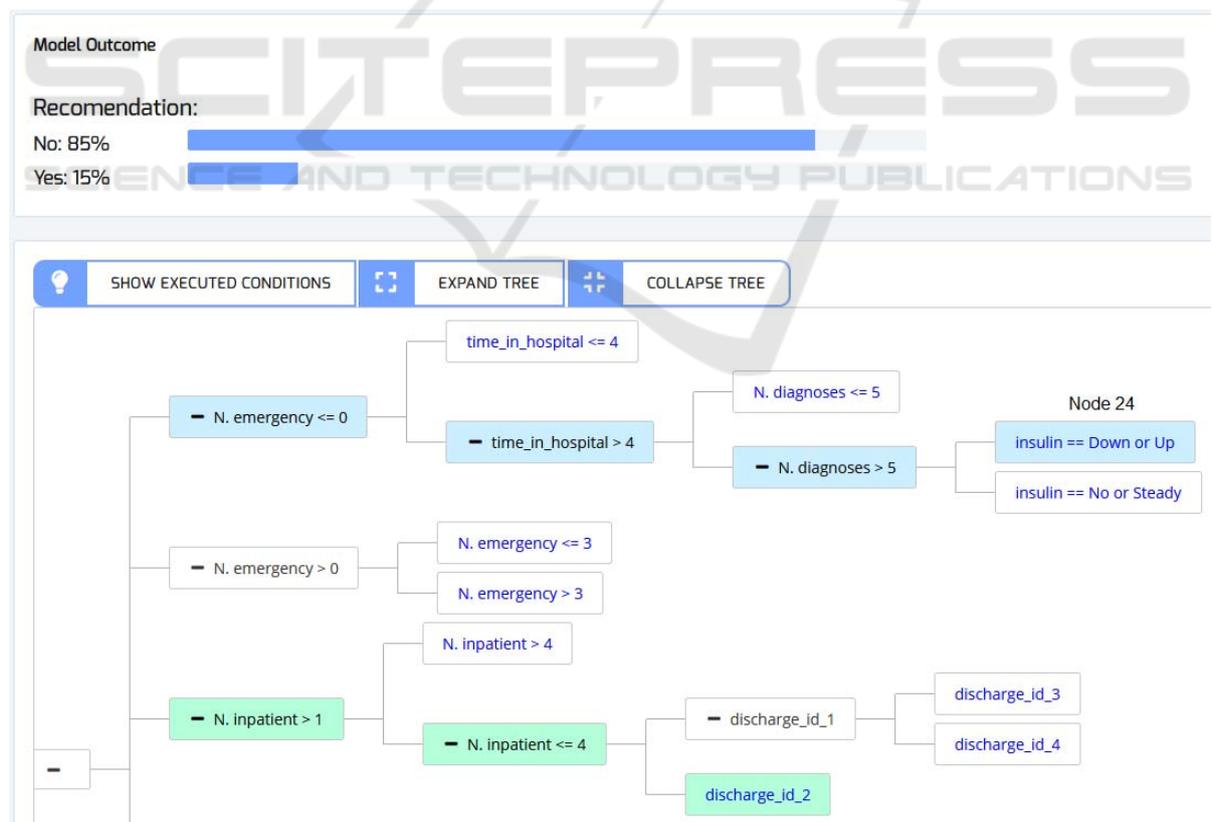


Figure 7: The evaluation of a simulated patient in the KGT, with its probability to readmit and the reasoning of the tree. It is the same DT that is in Figure 6, but cut in order to show the needed piece we are highlighting.

Table 1: The summary of the performance of each of the DT achieved in the KGT. The testing values of the DT in the testing datasets for each possible outcome (readmitted Yes/No), the number of nodes of the tree and the required number of attributes.

Outcome	AUC	Precision	Recall	F1-score	N. nodes	Variables
First DT						
No	0.57	0.92	0.21	0.35	30	7
Yes	0.57	0.12	0.85	0.2		
Pruned DT						
No	0.56	0.91	0.58	0.71	10	4
Yes	0.56	0.13	0.5	0.2		
Extended DT						
No	0.64	0.93	0.52	0.67	32	7
Yes	0.64	0.14	0.66	0.23		

4.5 Use Scenario

Once the DT is constructed, the KGT enables the user to apply it with new patients' data. In Figure 7, it is shown the probability to readmit the patient with the features shown in Table 2. Moreover, it can be appreciated how the KGT illustrates visually the reasoning process of the DT for this particular patient, highlighting the nodes of the fulfilled branches.

Table 2: Simulated data of patient evaluated in Figure 7.

Variables	Patient value
N. emergency	0
time in hospital	7
insulin	Down
N. inpatient	3
discharge_id_2	Urgency

5 CONCLUSIONS

This paper presents an adaptative CDSS based on an interactive framework, named Knowledge Generation Tool (KGT). This KGT has been created for Decision Tree (DT) building and modification, mainly for its usage in the medical domain. This tool can allow non-data-analysis experts to mine databases without the need to know about the insights of data-mining algorithms. Overall, our platform equips clinicians with an easy-to-use tool that makes data mining quick and accessible.

The KGT has two ways to build the DTs: the first one is from scratch, as the AT enables the user even to create a DT from the beginning (e.g. to formalize clinical practice guidelines). The second one is extracting the DT from a medical dataset, using Machine Learning (ML) methods. By using the ML methods, it is possible to discover non-contemplated patterns by clinicians. As the extracted patterns are

shown in a DT, a comprehensive manner for clinicians, they can choose whether or not to accept the extracted information.

In addition, we provide an Authoring Tool in the KGT that makes the user capable of editing the DT. This means that the clinical expert can add its clinical knowledge in the DT.

Moreover, the performance of the DT can be tested in the KGT. This feature not only allows the user to check the performance of the DT but to identify it also allows the user to analyze how positive the changes made in the DT are. This feature allows for easy assessment in a situation where the additional clinical knowledge that the user includes could potentially improve or worsen the DT's performance.

This platform is domain-independent, so it can be used to make predictions or create models in various domains (even if the domain is not clinical).

To summarize, our platform allows the end-user to automatically generate DT models using robust ML methods for its use in CDSS. These models can be tuned to the user's expert knowledge in a simple and understandable way.

Regarding future steps, clinical validation of our platform will be performed. This will consist firstly of a usability test and secondly of a clinical test with retrospective data in the context of emergency triaging for patients with chest pain. By exploiting retrospective data, a DT model will be used to help diagnose ischemic heart disease in the emergency room.

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