

Supporting decision-making in the clinical management of dengue using predictive and prescriptive modeling

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Abstract

Dengue is a vector-borne tropical disease that is widely distributed throughout the world. The clinical management of dengue consists of diagnosis and treatment of the disease. The development of approaches to aid decision-making in this disease is necessary to reduce morbidity and mortality rates. Despite the existence of guidelines for clinical management, the diagnosis and treatment of dengue remain a challenge. To address this problem, we aimed to develop methodologies, models, and approaches to support decision-making regarding the clinical management of this infection. We developed several studies to meet the proposed objectives. First, we reviewed the latest trends in dengue modeling using machine learning (ML) techniques. Then, we proposed several decision support systems to diagnose and detect complications of dengue using fuzzy cognitive maps (FCM). Subsequently, we developed an autonomous cycle of data analysis tasks (ACODAT) to support both diagnosis and treatment of the disease. Also, we presented a methodology based on FCM and optimization algorithms to generate prescriptive models in various science domains. Finally, we proposed three federated learning approaches to ensure the security and privacy of data related to the clinical management of dengue. These strategies were evaluated using diverse datasets with signs, symptoms, laboratory tests, and information related to disease treatment. The results showed the ability of the developed methodologies and models to predict the disease, classify patients according to severity, evaluate the behavior of severity-related variables, and recommend treatments based on World Health Organization (WHO) guidelines.

Keywords: Dengue, Predictive modeling, Prescriptive modeling, Artificial intelligence, Machine learning, Diagnosis, Treatment

1 Introducción

Dengue is one of the most important vector-borne tropical diseases worldwide [1]. This pathology has become a public health problem in tropical and subtropical regions, with a great epidemiological, social and economic impact [2–4]. The infection is transmitted to humans by the bite of mosquitoes of the genus *Aedes*, mainly *A. aegypti* and *A. albopictus*. [5]. According to WHO, more than 350 million dengue virus infections occur worldwide each year. In addition, 20,000 dengue-related deaths in the same time period [6]. The Pan American Health Organization’s annual arbovirus epidemiological bulletin reported 1,267,151 cases of dengue in the Americas region during 2021, with a cumulative incidence of 127.72 cases per 100,000 population. The countries in the Americas region with the highest number of cases during 2021 were Brazil, Colombia, and Peru with 975,474 cases (77.0%), 53,334 cases (4.2%), and 49,274 cases (3.9%), respectively [7].

In 1997, WHO classified the disease as dengue and dengue hemorrhagic fever [8]. In 2009, a new classification was proposed based on the level of severity of the disease: non-severe dengue (with or without alarm signs) and severe dengue [9]. Clinical management of dengue is the process by which health care professionals evaluate the patient to make a diagnosis based on severity and treat the patient palliatively to avoid life-threatening complications. The clinical management of dengue is a major challenge for medical professionals and health authorities worldwide [10]. The primary goal of early diagnosis and timely treatment activities is to decrease the morbidity and mortality rates associated with the disease [11]. Dengue mortality rates can be high when diagnosis and treatment are inadequate, reaching values of 20% [12]. In 2009, WHO published guidelines for the diagnosis, treatment, prevention and control of dengue [9]. These guidelines are currently used by medical personnel for the clinical management of dengue, from diagnosis to treatment of patients. However, difficulties remain in diagnosing and treating the disease.

The processes used to diagnose and treat dengue are complex due to the large amount of information that medical personnel must analyze in a short time to define the procedure to follow for each patient [13]. This information corresponds to demographic, clinical and laboratory variables such as age, signs and symptoms, among others, that a patient with dengue may present. In addition, the lack of experience of physicians could hinder the diagnosis because there are not always reasonable rules for analyzing a complex event such as dengue. According to experts, proper clinical management of patients with dengue depends on astute interpretation of clinical and laboratory findings to prevent or treat life-threatening complications [14].

One way to address this type of problem is with the development of clinical decision support systems (CDSS) based on predictive and prescriptive models to support decision-making by medical personnel caring for patients with dengue [15]. According to Sutton et al. [15], a CDSS is defined as a system that aims to improve healthcare delivery by supporting medical decisions with clinical knowledge and patient information. The main goal is for the physician to combine his or her clinical knowledge with suggestions from the CDSS to make the best possible decision. These systems use data to improve the processes performed by a human being [16].

Advances in artificial intelligence (AI) have driven the development of CDSS to support decision-making in clinical or hospital settings [17–19]. These systems are primarily based on predictive and prescriptive models using AI techniques. Predictive models can be used for disease detection or diagnosis through prediction or classification tasks [20]; while prescriptive models are models that can be used to prescribe appropriate treatment [21].

The literature widely reports the development of predictive models for the detection of dengue and to differentiate it from other diseases with similar clinical pictures, such as Zika, Chikungunya, Malaria and Leptospirosis [22]. These models are useful for the diagnosis of dengue, however, they have some disadvantages: 1) they only detect the disease, and 2) they do not evaluate the behavior of variables related to severity. Thus, the diagnosis of dengue is not only a problem of prediction or detection, but involves many factors related to severity that physicians must analyze to perform a correct classification of the clinical picture and an adequate management of the patient’s signs and symptoms. Thus, the development of CDSS that not only predict an outcome, but also evaluate the behavior of the variables involved in the process, are more useful to improve the diagnostic process of dengue [23].

Predictive models have focused on diagnosis, while prescriptive models have focused on treatment. Prescriptive models are a type of modeling to know what are the best actions to obtain a desired outcome [24]. In the case of dengue, no cure is available; its treatment is based on palliative care and continuous evaluation of signs to avoid complications leading to death.

Based on this context, this paper summarizes the objectives and contributions of the thesis entitled: **Predictive and prescriptive modeling for the clinical management of dengue** [25], which was carried out at Universidad EAFIT (Medellín, Colombia) and is structured as a compendium of articles. In this thesis, we set out to develop models, approaches and methodology to support decision-making in the clinical management of dengue. Specifically, the main contributions to the state of the art are: 1) A

systematic literature review about trends in dengue modeling using ML techniques; 2) Two CDSS for the diagnosis of dengue and evaluation of severity-related variables; 3) An ACODAT that integrates different tasks such as classification and prescription to support dengue diagnosis and treatment; 4) Two methodologies based on an extension of FCM combined with optimization algorithms to generate prescriptive models with generalization capabilities in different domains of science; 5) Federated learning approaches to support dengue diagnosis and treatment while ensuring data privacy and security.

The remainder of this paper is organized as follows: [Section 2](#) presents a literature review conducted to know about trends in dengue modeling using ML. [Section 3](#) shows the objectives and contributions of the thesis using the research questions. Finally, [Section 4](#) concludes the paper, describes the main limitations and future work.

2 Literature review

To gain insight into the latest trends in dengue modeling, we conducted a systematic literature review using three main approaches to dengue. First, diagnostic modeling to determine which ML models had been developed for disease diagnosis. Second, epidemic modeling to analyze dengue from the point of view of disease distribution and vector transmission. Finally, the modeling of interventions for disease control. [Figure 1](#) shows a schematic representation of the trends on dengue modeling using ML techniques where different aspects evaluated in the systematic review are visualized such as the preprocessing techniques used, the ML task implemented, the type of model developed and the aspect of dengue that was addressed. The width of the nodes and links is proportional to the frequency of papers reported in the literature that correspond to each of the aspects evaluated. Different colors have been used in the links to facilitate the visualization of the connections. The complete work product of this review can be accessed at [\[1\]](#).

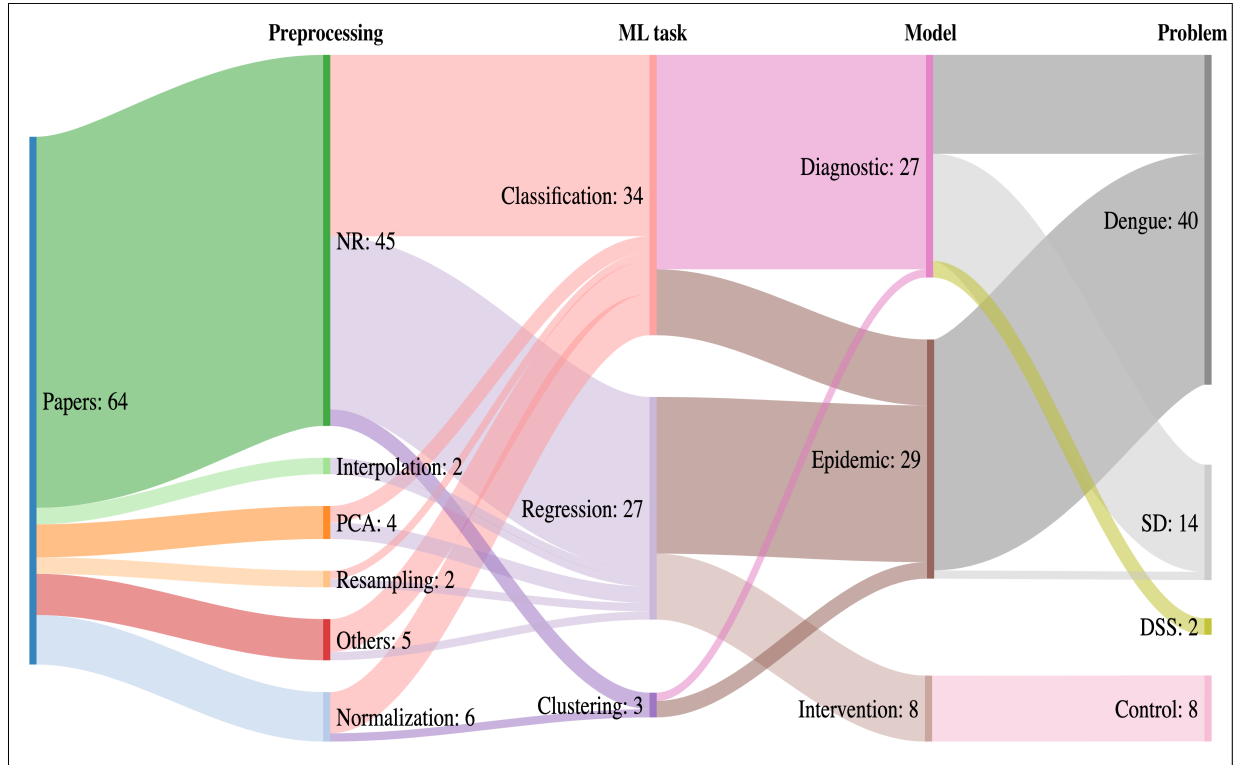


Figure 1: Trends in dengue modeling using ML techniques. NR = Not reported, PCA = Principal Component Analysis, SD: Severe Dengue, DSS = Dengue Shock Syndrome.

2.1 Modeling for dengue diagnosis

Most modeling approaches for dengue diagnosis using ML are based on logistic regression [\[22, 26–30\]](#). Logistic models are widely used in the healthcare field due to their simplicity in performing and interpreting the results. These models were developed primarily to assess factors associated with risk of dengue infection and to determine the association of predictors with disease severity. The categories of variables most commonly used to construct these models were demographic, clinical and laboratory parameters.

2.2 Predictive modeling for epidemic analysis

With respect to epidemic modeling, spatio-temporal analysis is the most studied field of dengue. There are many studies using ML techniques to assess vector and disease spread [31–41]. Compared to diagnostic models, in which logistic regression was used most frequently, in epidemic models there is variability in the frequency of modeling approaches used. Although linear regression was the most frequently used approach for prediction, other techniques, with a high frequency such as Random Forest, Support Vector Machines and Boosting Regression Trees. We found a relationship between the use of data types and modeling types. Models with linear regression used socioeconomic, demographic and environmental data. This type of data has been widely used for linear regression because it allows mapping of mosquito and disease distribution. These types of data were used in almost all epidemic modeling approaches, except for logistic regression, which did not use environmental data. Clinical and laboratory data were used primarily with logistic regression, a technique widely used by medical personnel and epidemiologists to predict the presence or absence of disease.

2.3 Dengue control intervention modeling

Dengue intervention models are developed to evaluate dengue control strategies. In our literature review, we found that few intervention models have been developed for the evaluation of dengue control strategies [42–44]. However, we found that generalized linear model (GLM) was the most applied technique for intervention modeling followed by Bayesian models and stochastic simulation. The GLM was applied with entomological, climatic and population data, with entomological being the most used. Stochastic simulation was only used in one paper, with entomological and population data. Finally, the Bayesian model was applied in one paper with entomological data. Entomological data are very frequent because dengue control is mainly based on the control of the mosquito, the vector of dengue transmission.

2.4 Limitations and challenges

We conducted a systematic literature review to identify challenges and research opportunities for dengue modeling using ML techniques. With respect to diagnostic modeling, models to detect the disease and differentiate it from other similar diseases are well implemented. However, it is essential to develop cause-effect models of dengue because they are necessary to understand the importance of the factors that may contribute to the disease. On the other hand, studies reported in the literature have used several types of features for the diagnosis of dengue. Adding new predictors for diagnosis could facilitate and improve detection time for treatment and avoid complications leading to death. Although the use of many predictors for diagnosis could be beneficial, it could also cause difficulties with respect to the dimension of the data. One opportunity is the creation or improvement of preprocessing techniques that allow the identification of key features most closely related to dengue.

The frequency of articles on modeling dengue interventions is low. Decision making for treatment and control of the disease depends on this modeling approach. Prescriptive analysis, in general, presents challenges that need to be taken into account. One is the limited number of automated prescriptive models for data-driven decision-making systems. The subjectivity of the domain expert could affect the quality of the decision made, and static models cannot handle the changes that occur. Data-driven and up-to-date prescriptions would be a valuable tool for dengue treatment and/or control.

Conventional ML approaches require centralization of training data in a device or data center. This could be a problem if the data are located in different locations. According to our review, all studies used centralized ML approaches where data were collected at a single location for model training which does not guarantee data privacy and security.

A common challenge identified in the three approaches reviewed in the literature, is the development of combined models (diagnosis and treatment), to automate the prescription. ACODAT that integrate the above models can help in making decisions as quickly as possible. In the case of dengue, this is crucial due to the high morbidity and mortality of the disease.

3 Goals and contributions

Considering the importance of the clinical management of dengue and the limitations found in the literature review, this thesis [25] proposed different methodologies and approaches to support decision-making regarding the diagnosis and treatment of dengue. In this context, the objectives of the thesis were achieved by answering the following research questions:

3.1 How could we predict dengue in an explanatory way using clinical and laboratory data?

Currently, the diagnosis of dengue is challenging because of its complexity. The process used to diagnose the disease is complex because the amount of information involved is high and the lack of experience of some clinicians could hinder the diagnosis [45]. According to clinical experts, the diagnosis of dengue depends on astute interpretation of clinical and laboratory findings, mainly in severe cases [13].

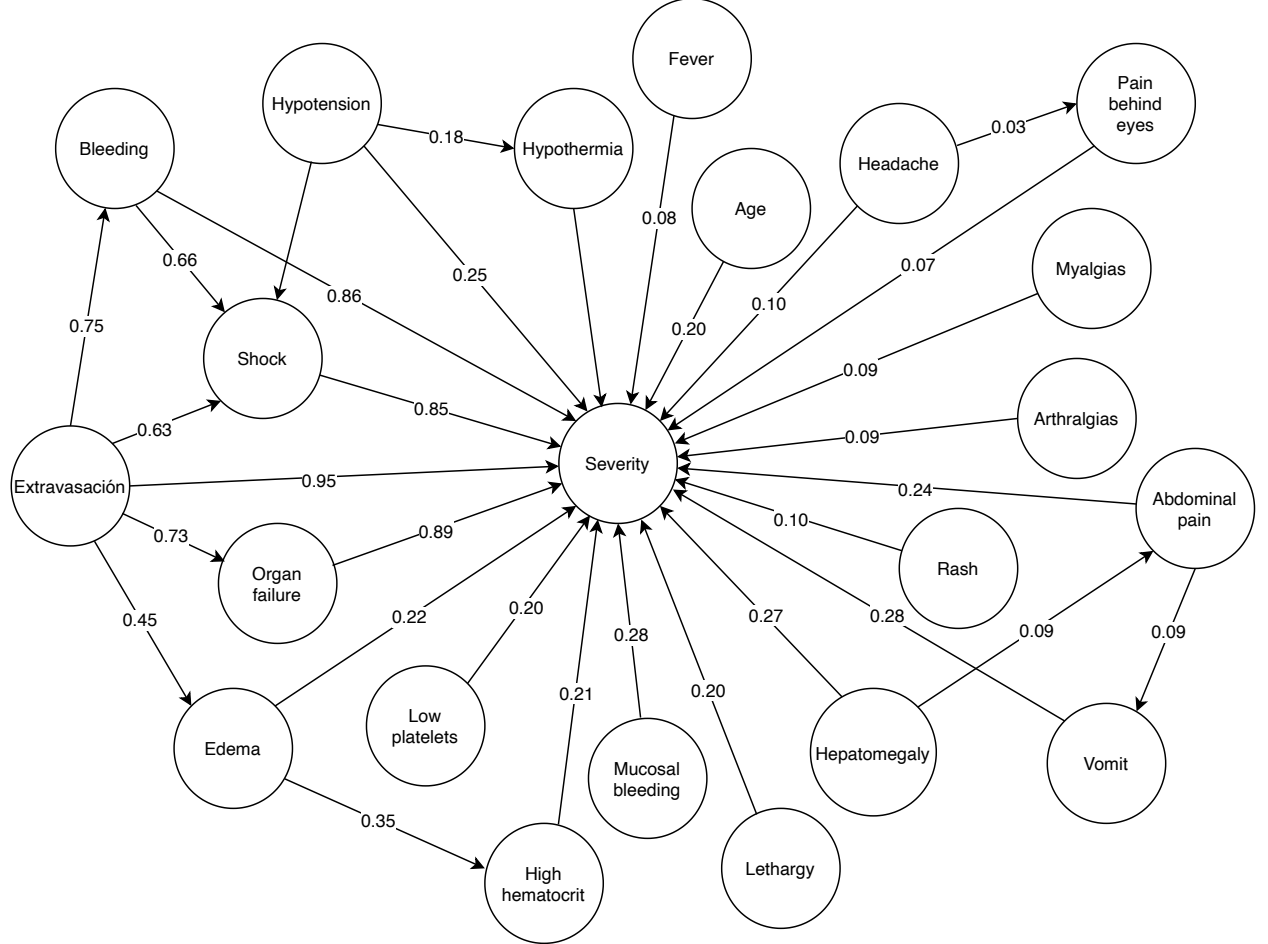


Figure 2: FCM model constructed for the diagnosis of dengue using sociodemographic, clinical and laboratory test variables.

Predictive models for detecting dengue have been widely reported in the literature [1]. However, approaches to know the dynamics of the variables used for diagnosis remain scarce [1]. Knowing in advance the behavior of variables related to dengue severity is crucial because complications leading to death can be avoided. For this reason, we developed an CDSS that uses FCMs both to predict dengue severity and to evaluate the behavior of these variables over time. This work can be accessed at [23]. Figure 2 shows the architecture of the final model built for this purpose. The results showed that the model can classify dengue patients with 89% accuracy. Our approach differs from those reported in the literature because it not only classifies the type of dengue, but also allows to analyze using scenario-based simulations the behavior of clinical and laboratory variables that physicians use for conventional dengue diagnosis. This capability can be seen in the Figure 3 where through simulated iterations we can analyze the behavior of the variables used for dengue diagnosis. In this way, we proposed an explainable method that maintains a competitive predictive accuracy of dengue severity. These capabilities make this system more robust and solve the problem of interpretability of results of ML systems, which is very important in sensitive and critical domains such as health. This crucial aspect is not taken into account in other works reported in the literature [1].

3.2 How could we detect complications in dengue using computational simulations?

Dengue is a disease of public health concern due to its rapid progression, which can lead to death. There is no specific cure for dengue, and treatment is based on alleviating symptoms and preventing complications. Early detection of complications is crucial to ensuring patient survival. In previous work, we showed how FCMs

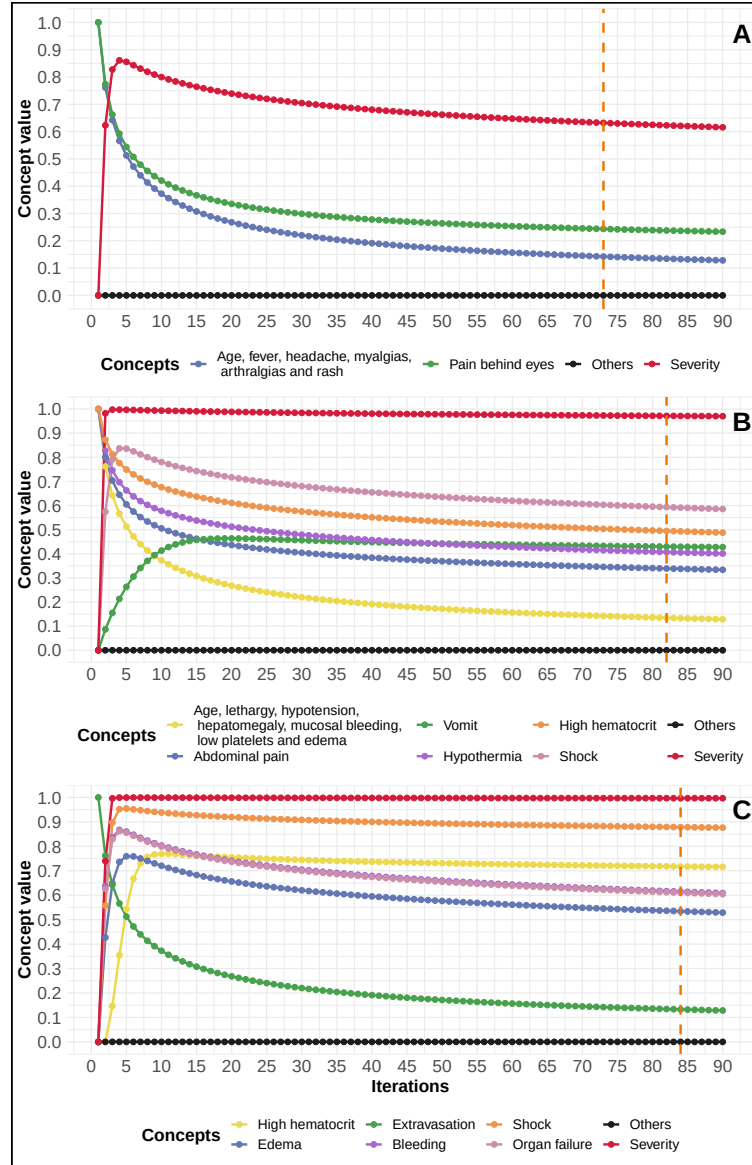


Figure 3: Scenario-based simulations for the analysis of variables related to dengue severity. **A** represents the behavior of the variables of a patient with dengue without alarm signs; **B** represents the behavior of the variables of a patient with dengue with alarm signs; **C** represents the behavior of the variables of a patient with severe dengue.

have the ability to predict, but also, the ability to analyze predictive variables to perform scenario-based analysis. Taking advantage of this ability and knowing the problem of dengue complications, we developed a system that detects dengue complications using computational simulations based on FCMs [46]. Figure 4 shows the workflow to achieve this system. To achieve our goal, we combined a computational approach with human reasoning to achieve a complete and comprehensive analysis of dengue complications [47]. Initially, a group of experts in the clinical management of the disease defined the variables of interest and established the relationships of influence between them. Then, the average of these influences was calculated to generate a global map that would allow the analysis of dengue through the detection of complications. The results showed that the model detects complications according to the type of dengue. The experts who contributed to the analysis of the results concluded that the tool designed could be helpful for implementation in low-resource clinical settings to reduce dengue mortality rates.

3.3 How could we integrate predictive and prescriptive models to support decision-making in the clinical management of dengue?

The clinical management of dengue primarily constitutes the diagnosis and treatment of the disease. The information obtained in the diagnostic process is vital to provide adequate and timely treatment to the patient with dengue. Currently, different CDSS for dengue exist [1]; however, the studies reported in the

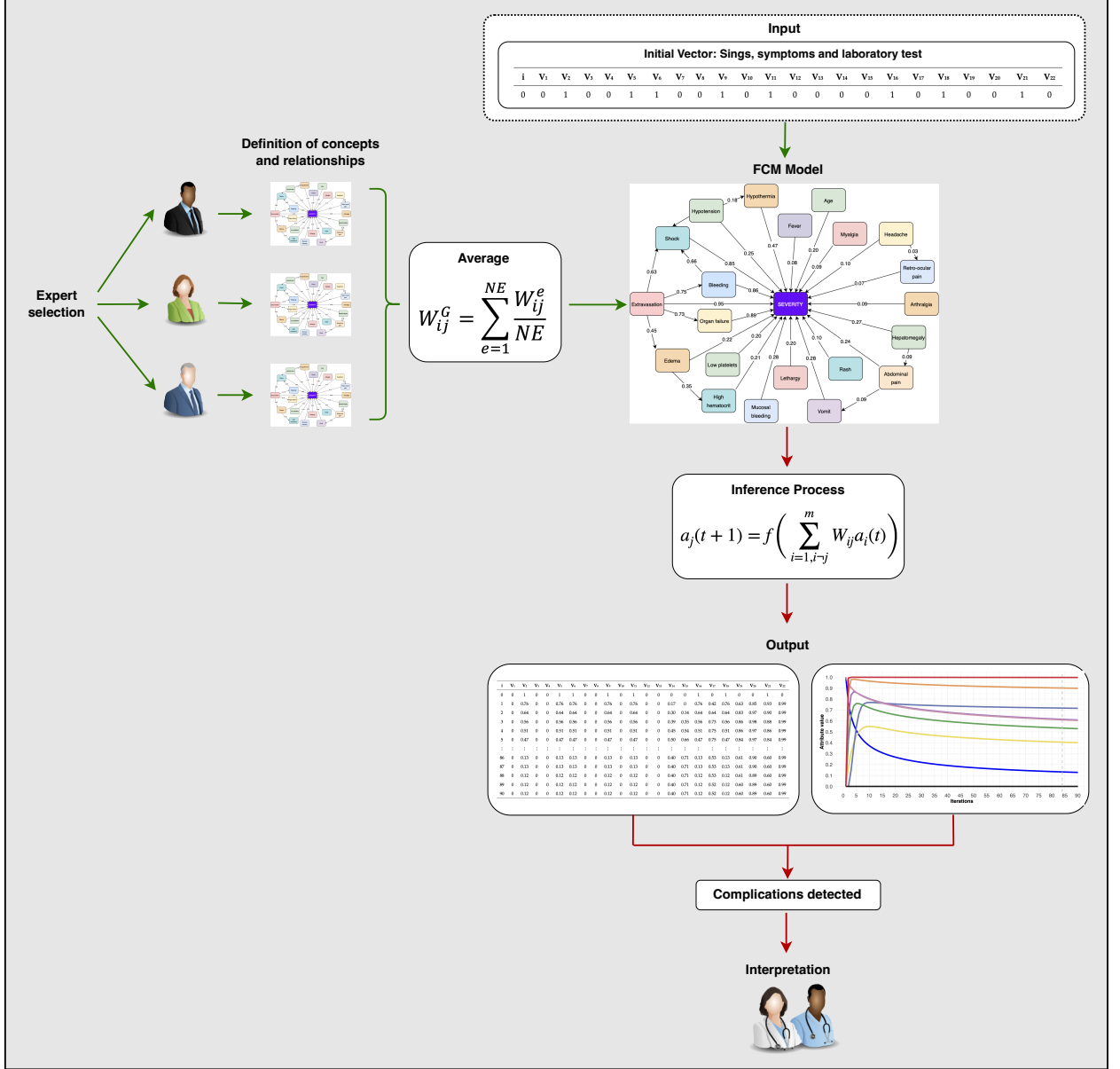


Figure 4: Flowchart to develop a system to detect dengue complications.

literature use separate predictive and prescriptive approaches, and to date, there are no models that integrate these two approaches, which are closely related to each other. Especially, prediction alone is not very useful when there is no prescriptive model to recommend the best options to solve the problem.

To overcome this problem, we proposed an ACODAT to support decision-making regarding the diagnosis and treatment of dengue. This work can be consulted in [48]. A schematic representation of ACODAT for the clinical management of dengue is shown in Figure 5. Specifically, ACODAT uses the interaction of different successive tasks with ML-based models to extract the knowledge needed to recommend improvements in a given process [49]. ACODAT uses monitoring tasks to detect possible anomalies in the data and correct them. Subsequently, it integrates a classification task to classify patients according to dengue type. Finally, the prescription task recommends an optimal treatment for a particular patient. The results of the first task demonstrate the ability to detect errors in the data and clean them for the next task. Dengue classification was performed with 98% accuracy using artificial neural networks and support vector machines, and a genetic algorithm recommends treatment options according to WHO guidelines. The approaches reported in the literature consider the diagnosis and treatment of dengue separately. Our approach is novel because it considers data preprocessing, classification, and prescription in a single architecture. Finally, our system is flexible and easily adaptable, which will allow the addition of new tasks for dengue analysis.

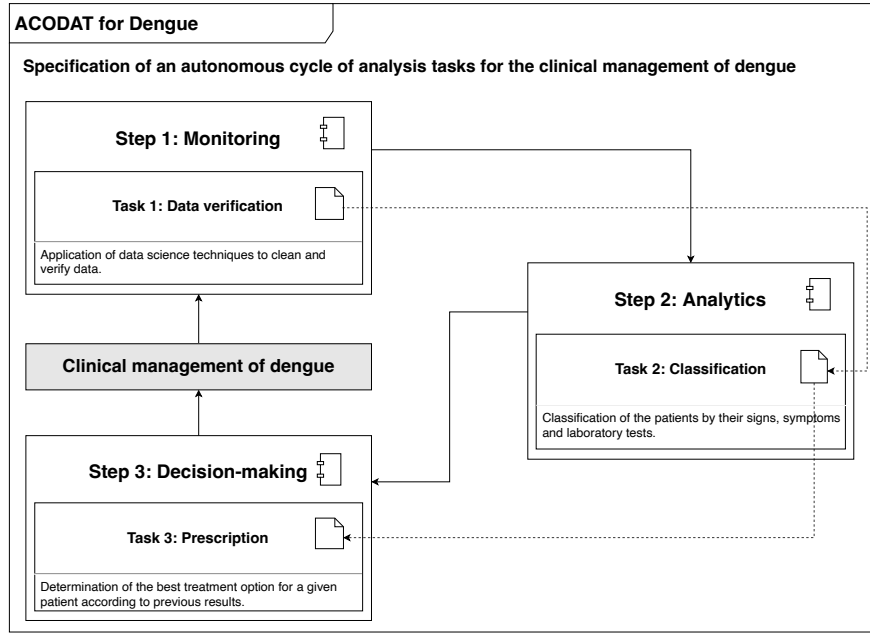


Figure 5: ACODAT for the clinical management of dengue.

3.4 How could we generate prescriptive models with excellent performance for both the clinical management of dengue and other diseases?

Prescriptive modeling is an area of data analytics that aims to recommend actions within a system to achieve a desired goal. [50]. It is one of the areas that has attracted the most interest in recent years, as it provides valuable support to decision-makers [24].

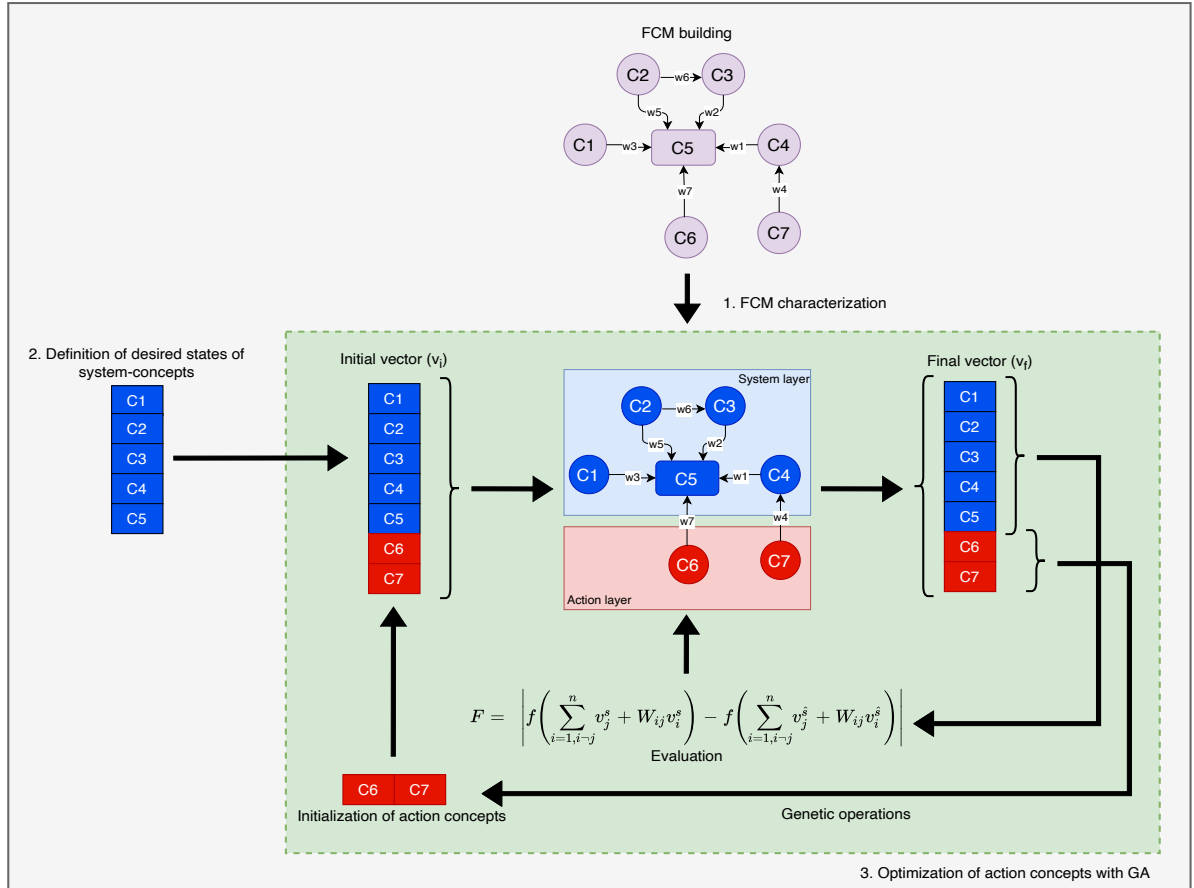


Figure 6: Architecture of the PRV-FCM methodology.

Based on this context and knowing the importance of developing prescriptive models to support decision-making in dengue, we proposed a methodology based on FCM and optimization algorithms to generate prescriptive models in clinical settings. This work can be accessed at [51]. Figure 6 shows a schematic representation of the methodology, which we call PrescRiptive-FCM (PRV-FCM) and consists of several stages. First, the characterization of the FCM is performed where a division of the map into two layers is established: system concepts and prescriptive concepts. The system concepts are the set of variables that describe/define the system to be modeled. Prescriptive concepts are action variables that the decision-maker executes to obtain a desired result in the system. The second stage consists of the initial desired instantiation of the system and the third stage consists of the optimization process using the inference of an FCM and a genetic algorithm to find the optimal values of the prescriptive variables or action variables. The algorithm 1 describes the steps of the optimization process, which are carried out to obtain the optimal values of the action concepts that generate the desired values of the system concepts. The algorithm must initially know the desired values of the system, a matrix of weights corresponding to the relationships that exist between all the concepts, a stopping condition of the algorithm to avoid an infinite loop, the dimensions of the vector of actions, and the fitness function to evaluate the individuals generated in the process. Steps 1 and 2 initialize the generation counter. Step 3 randomly generates individuals and step 4 combines system and action vectors to ensure correct matrix multiplication. Step 7 performs the inference process with the FCM and step 8 displays the equilibrium state of the FCM. The final equilibrium vector is divided into system vector and action vector to evaluate them with the fitness function in steps 10 and 11. Subsequently, the crossover and mutation genetic operators are applied to the action vector to generate new individuals (step 14) and create a new population with the best individuals (step 15). Finally, when the stop condition is reached, the optimal values for the action concepts are obtained (step 18), and thus constitute the optimal prescriptive variables leading to the desired state of the system.

Algorithm 1: Optimization algorithm to generate optimal values for action or prescriptive concepts.

Input : $\mathbf{v}^s(0)$ = desired system vector, $\mathbf{W}$ = weight matrix, F = fitness function, sc = stop condition
Output: Optimal $\mathbf{v}^a$

```

1 begin
2   Set the generations counter  $g = 0$ 
3   Generate randomly one population  $P(0)$  of individuals  $\mathbf{v}^a$ 
4   Generate initial vector  $\mathbf{v}(g)$  with the combination of  $\mathbf{v}^s(0)$  and  $\mathbf{v}^a$ 
5   while sc is not met do
6     for each initial vector  $\mathbf{v}(g)$  do
7       
$$\mathbf{v}_{final} = f\left(\sum_{i=1}^n \mathbf{W}\mathbf{v}(g)\right)$$

8       for each final vector  $\mathbf{v}_{final} \in P(g)$  do
9         Split final vector  $\mathbf{v}_{final}$  in  $\mathbf{v}^{\hat{a}}$  and  $\mathbf{v}^{\hat{s}}$ 
10        Evaluation of fitness:
11        
$$F = \left| f\left(\sum_{i=1, i \neq j}^n \mathbf{W}_{ij}\mathbf{v}_i^s\right) - f\left(\sum_{i=1, i \neq j}^n \mathbf{W}_{ij}\mathbf{v}_i^{\hat{s}}\right) \right|$$

12      end
13    end
14    Selection of best individuals  $\mathbf{v}^{\hat{a}}$  by genetic operators
15    Generation of a new population  $P(g+1)$ 
16     $g = g + 1$ 
17  end
18  return optimal  $\mathbf{v}^a$ 
19 end

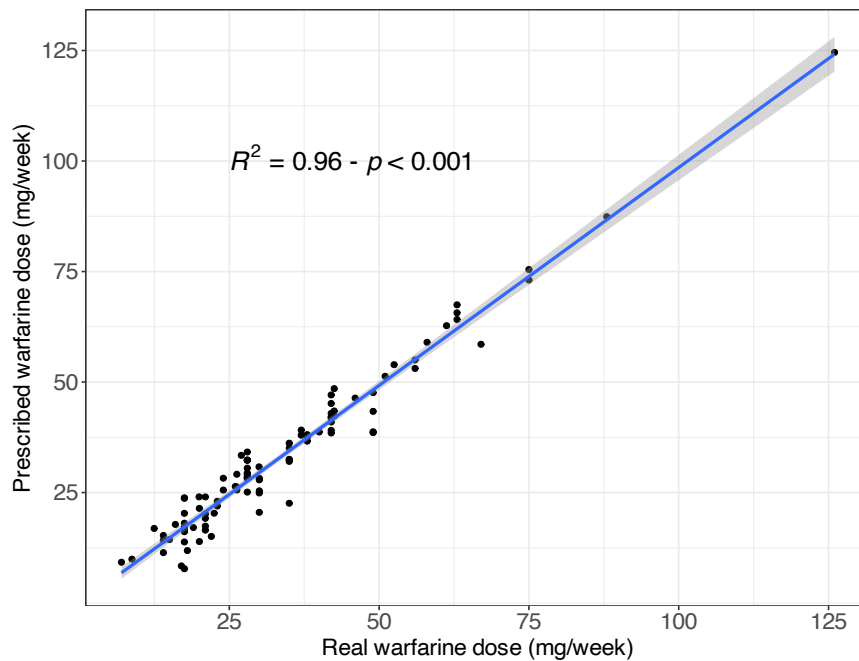
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We evaluated the proposed approach in three case studies related to treatment (severe dengue), monitoring (warfarin dose estimation) and prevention (geohelminthiasis) of diseases. The performance of the prescriptive models developed demonstrated the ability to prescribe treatment for severe dengue, estimate warfarin doses in coagulated patients, and generate actions aimed at the prevention of geohelminthiasis.

Table 1: Performance of prescriptive models for the treatment of severe dengue and prevention of geohelminthiasis..

Case study	Prescriptive concept	Variable name	Accuracy	Sensitivity	Specificity
Severe dengue treatment	C5	Red blood cell transfusions	0.81	0.64	1.00
	C6	Crystalloid solutions	0.87	0.80	0.93
	C7	Colloid solutions	1.00	1.00	1.00
	C8	Admission to ICU	0.84	0.87	0.83
Prevention of geohelminthiasis	C12	Child wears closed shoes	0.74	0.80	0.74
	C14	Child washes his hands before eating	0.67	0.78	0.55

Table 1 shows the prescription results for the treatment of severe dengue and prevention of geohelminthiasis, while Figure 7 shows the degree of agreement between the real warfarin values and those generated by our proposed approach. The developed models performed excellently in prescribing actions for disease monitoring, treatment, and prevention. First, the prescriptive model for estimating Warfarin doses was excellent, with low error values and a high degree of agreement between the prescribed values and the actual values. Similarly, for the treatment of dengue, the prescriptive models generated prescriptions with low error rates to prevent patient deaths from dengue. These recommendations followed WHO protocols and guidelines. Finally, the results of the prescriptive models for the prevention of geohelminthiasis were satisfactory, with average accuracies above 70%. This result is a significant achievement considering the size of the dataset for this last case study.

**Figure 7:** Relationship between real warfarin values and warfarin values prescribed by PRV-FCM.

3.5 How could we generate prescriptive models with excellent performance and generalizability to be applied to other domains of science?

The development of methodologies to generate prescriptive models should be usable in any domain of science. To demonstrate the generalizability of our methodology for generating prescriptive models, we tested it in fields such as education, business and medicine. Thus, we implemented the PRV-FCM methodology developed in the previous work to generate prescriptive models in different domains. This work can be found at [52]. Specifically, we applied a methodology based on FCMs and metaheuristic algorithms to generate prescriptive models. We proposed an extension of FCMs to develop prescriptive models to support decision-making in different domains. This adaptation characterizes FCMs, using system and prescriptive concepts. Then, it uses a metaheuristic algorithm (in this case, we use a genetic algorithm) to optimize the prescriptive concepts based on the system concepts and the stability of the FCM.

Our proposed prescriptive approach was tested in four scenarios in which it demonstrated its ability to find solutions that lead to the desired values for the variables of interest. Table 2 shows the test results in each of the case studies, where the error values are low. The Table 3 shows the mean comparisons between the real values and the values prescribed by PRV-FCM, showing that there are no significant differences between the

Table 2: Performance of prescriptive models developed with PRV-FCM. NA = not applicable, MAE = mean absolute error, MSE = mean squared error, RMSE = Root Mean Squared Error.

Case study	Prescriptive concept	Variable name	MAE	MSE	RMSE
Synthetic data	C2	NA	0.01146	0.00024	0.01559
	C9	NA	0.01341	0.00035	0.01872
Red wine	C6	Free sulfur dioxide	0.01761	0.00066	0.02583
	C8	Density	0.01991	0.00069	0.02644
Diabetes	C2	Plasma glucose concentration a 2 hours in an oral glucose tolerance test	0.01112	0.00020	0.01429
	C3	Diastolic blood pressure	0.00743	0.00010	0.01000
Student academic performance	C9	Raised hand	0.02674	0.00120	0.03466
	C10	Visited resources	0.03358	0.00188	0.04337
	C11	Viewing announcements	0.03560	0.00222	0.04717
	C12	Discussion groups	0.00999	0.00018	0.01349

real values and the prescribed values generated by PRV-FCM. The results of applying our methodology in education, business, and healthcare confirm its ability to create prescriptive models of excellent performance. These results also confirm its generalizability when applied in other contexts with similar results.

Table 3: Mean comparisons between the real values and the prescribed values using PRV-FCM. NA = not applicable, SD = standard deviation. † indicates that the Wilcoxon test was performed because the corresponding variable did not follow a normal distribution, ★ indicates that the Student’s t-test was performed because the corresponding variable follows a normal distribution.

Case study	Prescriptive concept	Variable name	Mean±SD		P
			Real	Prescribed	
Synthetic data	C2	NA	0.448±0.305	0.432±0.315	0.844†
	C9	NA	0.523±0.313	0.500±0.317	0.776†
Red wine	C6	Free sulfur dioxide	0.216±0.128	0.216±0.127	0.966★
	C8	Density	0.522±0.101	0.528±0.101	0.672†
Diabetes	C2	Plasma glucose concentration a 2 hours in an oral glucose tolerance test	0.547±0.130	0.547±0.129	0.973★
	C3	Diastolic blood pressure	0.557±0.172	0.558±0.169	0.970★
Student academic performance	C9	Raised hand	0.568±0.250	0.570±0.247	0.961★
	C10	Visited resources	0.697±0.263	0.694±0.257	0.934★
	C11	Viewing announcements	0.449±0.239	0.449±0.250	0.999★
	C12	Discussion groups	0.462 ± 0.256	0.462±0.257	0.987★

3.6 How could we improve the generation of prescriptive models using multilevel FCMs and metaheuristic algorithms?

In previous work, we proposed a methodology (PRV-FCM) for generating predictive and prescriptive models in different fields of science. The models generated performed well in terms of prediction and excellently in terms of prescription. The models were constructed in a single stage where the predictive level was trained together with the prescriptive level. However, each level expresses a different level of knowledge. Therefore, we proposed a methodology based on multilevel FCMs and metaheuristic algorithms (MFCM-MHA) [53]. Figure 8 shows the system architecture. The proposed system is initially based on an FCM composed of predictor variables, prescriptive variables, and the target. First, we trained the predictive level using the predictor variables and the target with a particle swarm optimization algorithm that adjusts the FCM weights to maximize accuracy. Then, we add the prescriptive level and perform a new training with a genetic algorithm to minimize the difference between the generated results and the desired results. The models generated with MFCM-MHA outperformed the models generated with PRV-FCM, demonstrating that level-based training helps to better detect patterns in the different case studies where they were tested.

3.7 How could we ensure the privacy and security of dengue patient data while supporting decision-making in the diagnosis and treatment of the disease?

The vast majority of work reported in the literature for dengue analysis uses the traditional ML approach, which collects dengue data in one place for training. This can raise issues with respect to the privacy and security of the data used. Transporting and shipping the data from one location to another can cause loss, damage, and violate laws related to personal data protection.

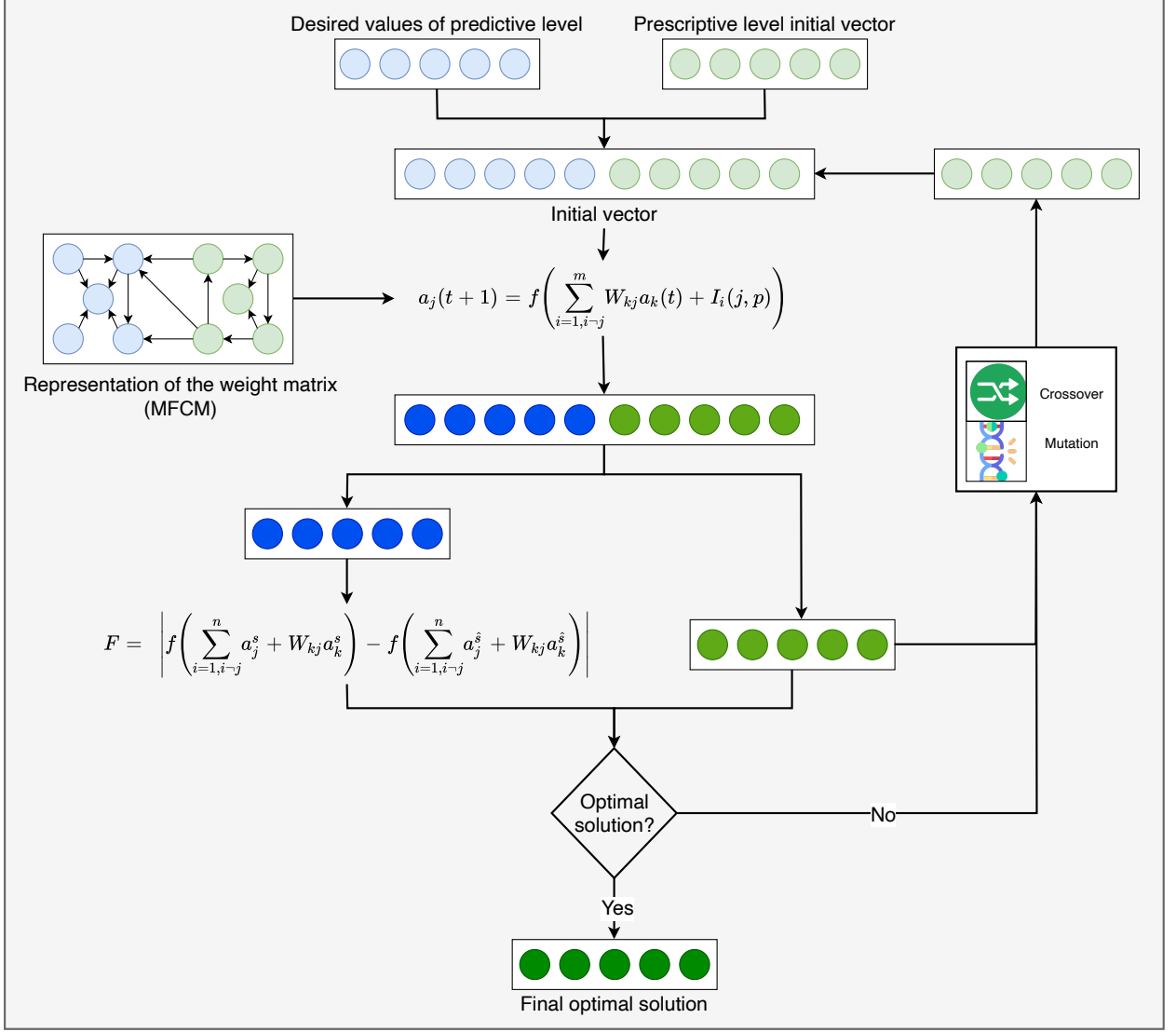


Figure 8: System architecture based on multilevel FCM and metaheuristic algorithms (MFCM-MHA) to generate prescriptive models.

To address this issue, we have proposed three approaches as medical support tools for the diagnosis and treatment of severe dengue. This full paper can be accessed at [54]. These approaches are characterized by using federated learning with FCM and optimization algorithms (particle swarm optimization and genetic algorithms) for the generation of predictive and prescriptive models. Figure 9 shows the schematic representation of each of the proposed approaches. The first approach called *total federated learning* is based on feature space similarity between participating clients or sites where the signs and treatment options of severe dengue are identical. The second called *target-based federated learning* is based on a target variable, where the only feature in common among all clients or parties is a decision variable (for our application domain, it was severe dengue mortality). Each client or party has different characteristics related to severe dengue mortality and treatment. Finally, the third approach called *federated transfer learning* uses parameter learning transfer to send information from one site/party to another. Specifically, the implemented approach transfers learned parameters from severe dengue treatment to mortality prediction.

The novelties proposed in the present study focus on several aspects: 1) the generation of federated learning approaches with a different architecture (*total federated learning* and *target-based federated learning*) from that reported in the literature; 2) the application domain, since to date there are no reports on the implementation of federated learning with FCMs for the diagnosis and treatment of dengue; 3) the combination of predictive and prescriptive models in a single architecture that enables integrated support for decision-making regarding the diagnosis and treatment of dengue. The results of the evaluation of each approach can be seen in the Table 4, Table 5 and Table 6. In all cases, we can observe that the use of federated learning improves the predictive and prescriptive capacity of the models, guaranteeing the privacy

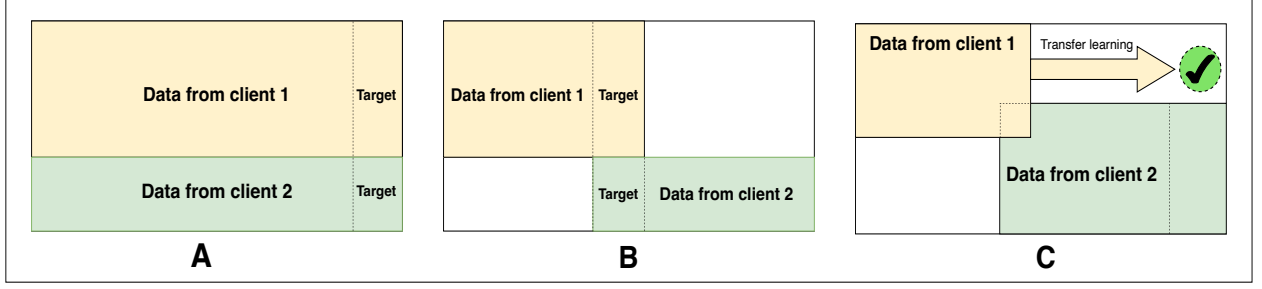


Figure 9: Schematic representation of our federated learning approaches. **A** represents total federated learning; **B** represents target-based federated learning; and **C** represents federated transfer learning

and security of dengue patient data. The proposed approaches will serve as a basis for the development of more robust methodologies that include the decentralization of the federation process across all nodes. Furthermore, an increase in the number of dengue-endemic regions could improve disease analysis by allowing for a greater number of data and variables of clinical interest.

Table 4: Performance of models developed with *total federated learning*. The * indicates the average of all prescriptive variables. NA = not applicable.

Type of data	Model	Data configuration	Task	Accuracy	Sensitivity	Specificity
Signs, treatment options and target	Local 1	Local from Medellín	Prediction	0.68	0.68	0.50
			Prescription	0.87*	0.75*	1.00*
	Local 2	Local from Córdoba	Prediction	0.74	0.77	0.51
			Prescription	0.86*	0.89*	0.81*
	Global federated	NA	Prediction	0.76	0.85	0.67
			Prescription	0.96*	0.92*	0.97*
	Global non-federated	All centralized data	Prediction	0.88*	0.83*	0.94*
			Prescription	0.88*	0.83*	0.94*

Table 5: Performance of models developed with *target-based federated learning*. The * indicates the average of all prescriptive variables. NA = not applicable.

Model	Data configuration	Type of data	Task	Accuracy	Sensitivity	Specificity
Local 1	Local from Medellín	Two signs, two treatment options and target	Prediction	0.71	0.76	0.48
			Prescription	0.75*	0.67*	0.80*
Local 2	Local from Córdoba	Two signs, two treatment options and target	Prediction	0.69	0.66	0.61
			Prescription	0.85*	0.78*	0.85*
Global federated	NA	All signs, treatment options and target	Prediction	0.76	0.90	0.66
			Prescription	0.95*	0.91*	0.96*
Global non-federated	All centralized data	All signs, treatment options and target	Prescription	0.88*	0.83*	0.94*

Table 6: Performance of models developed with *federated transfer learning*. The * indicates the average of all prescriptive variables. NA = not applicable.

Model	Data configuration	Type of data	Task	Accuracy	Sensitivity	Specificity
Local 1	Local from Medellín	Signs and treatment options	Prescription	0.95*	0.94*	0.93*
Local 2	Local from Córdoba	Signs and target	Prediction	0.69	0.71	0.50
Global federated	NA	Signs, treatment options and target	Prediction	0.73	0.86	0.61
			Prescription	0.98*	0.96*	0.99*
Global non-federated	All centralized data	Signs, treatment options and target	Prescription	0.88*	0.83*	0.94*

4 Conclusions

This paper summarizes the doctoral dissertation entitled: **Predictive and prescriptive modeling for the clinical management of dengue** [25], which addresses the problem of the clinical management of dengue from different aspects such as diagnosis, treatment and data privacy. The general objective was to develop and implement methodologies, approaches and models to support decision-making regarding the diagnosis and treatment of dengue.

Our first step was to identify future opportunities. To do this, we conducted a systematic review of the literature showing trends in dengue modeling using machine learning techniques. In this first study, we identified the main machine learning techniques that have been developed for dengue analysis from three

different problems: diagnosis, prediction, and intervention. The trends showed that explanatory models, the integration of different knowledge models, and federated learning were opportunities for future work.

For dengue diagnosis, we developed FCM-based models for disease classification, risk factor analysis, and complication detection. The systems developed performed competitively when compared to conventional techniques such as artificial neural networks and support vector machines. Finally, the systems developed anticipated the presence of complications, which is key to the clinical management of the disease.

Particularly, the clinical management of dengue involves the diagnosis and treatment of the disease. Diagnosis of the disease must be accompanied by timely treatment to avoid complications and death. We developed an ACODAT that integrates predictive models for diagnosis and prescriptive models for treatment. The system developed allowed the disease to be classified with high accuracy and generated treatment recommendations according to WHO guidelines.

Additionally, we proposed two methodologies for the development of predictive and prescriptive models that integrate different techniques such as FCMs and metaheuristic algorithms. The contributions of these techniques are the generation of high-performance predictive and prescriptive models in different fields of science, demonstrating their generalization capacity. Finally, to ensure data privacy, we proposed federated learning approaches with FCM to support decision-making in the clinical management of dengue. The models trained under federation performed better than conventional training, ensuring that the data did not leave the place of origin or collection.

This research has limitations. First, many variables related to dengue were not available and were not included in the predictive and prescriptive modeling. The use of related variables, such as cytokines and complete blood counts, could improve the performance of the models developed. Second, the number of regions used for modeling was low. We only developed models for two regions of Colombia, which could limit the scope of the results. It is advisable to develop models in more regions of Colombia with data from other sources. In this way, the representativeness of the models developed would be greater. Third, the proposed federated learning approaches were centralized. The results of the different local models was concentrated in a single node of the network. We recommend developing approaches with non-centralized federation. This would mean that if one node fails, the remaining nodes could take over the construction of the global model. Finally, another limitation of our research was the low availability of libraries or packages for training FCMs, either conventionally or in a federated manner. Future work should be directed toward the development of new computational tools to support research in the clinical management of dengue.

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